The Dictionary of Substances and their Effects

Second Edition

Editor
Sharat Gangolli

Volume 1
A–B

The Dictionary of Substances and their Effects

Second Edition

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RS•C
ROYAL SOCIETY OF CHEMISTRY

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Foreword

The lifestyle of the modern world can only be sustained by the effective utilisation of chemicals in the protection of our health, production of our food, manufacture and commerce. Yet these same chemicals in the wrong place can have potentially harmful effects. To understand the quantitative risks to human health and ecosystems, reliable information is required about the substances and their biological effects. *The Dictionary of Substances and their Effects* (DOSE) seeks to provide such information comprehensively yet in an easily accessible format.

As our understanding of the complexity of life and the intricate interactions which sustain ecosystems has grown, so has our requirement for information. The toxicologist, ecotoxicologist, and users and suppliers of chemicals need to know the properties, chemistry, biological effects and likely use of substances. Yet too often comprehensive data are difficult to obtain. The first edition of DOSE was hailed as an important breakthrough for those who needed a comprehensive and reliable compilation of data on chemicals with environmental impact. This second edition significantly updates the toxicological data and extends the number of chemicals to 4123.

While regulators might argue that the provision of toxicological data should be the responsibility of chemical suppliers, the reality is that often when such data are supplied they are overly brief or ridiculously over-cautious. I recently received a sample labelled "tap water" with the warning that it contained "hydrogen, which is a flammable substance". To have a single compilation of data, collected only from the peer-reviewed literature, and published under the authoritative imprimatur of the Royal Society of Chemistry, is surely the most effective answer to this problem.

The editorial team which has brought together this excellent second edition is to be congratulated on its achievement. DOSE will allow users to identify the hazards pertaining to given substances readily. Professor Lord Lewis in his introduction to the first edition emphasised the difference between hazard identification and risk assessment. Lord Lewis stressed the need for training to evaluate risks quantitatively and, in particular, the risks posed by combinations of chemicals. He quoted Paracelsus, the father of toxicology, and his famous dictum often translated as "the dose maketh the poison". In a world reliant on chemicals, but with an environment seriously threatened by anthropological damage, DOSE will enable scientists and regulators to ensure that the dose received by the organism will be far less than poison, indeed below that which has an effect.

Professor Les Ebdon
Deputy Vice-Chancellor (Academic)
University of Plymouth

Introduction

The risk evaluation of the potential adverse effects of a chemical on human health and the ecosystem, widely recognised by regulatory agencies as being of vital importance for the protection of man and his environment, requires the assessment of a broad range of information on the chemistry and biological properties of that chemical. Except for certain special human and veterinary medicine and some agrochemicals, relevant data for the vast majority of chemicals traded commercially are either not available or sparsely dispersed in the scientific literature. Thus, the assessment of the health and environmental risks of a chemical would be an onerous task without access to a single comprehensive compilation of relevant information.

In the publication of the first edition of *The Dictionary of Substances and their Effects* (DOSE), the Royal Society of Chemistry addressed the formidable logistical problems faced by scientists in obtaining the relevant data for the risk assessment of chemicals due to the paucity of publications containing compilations of appropriate data. The aim of this acclaimed publication was to collect and collate relevant chemical and biological data from peer-reviewed scientific literature to provide information for the quantitative risk evaluation of a chemical at its various levels of usage and conditions of exposure. The chemicals in the first edition were selected mainly from sources such as the Authorised and Approved List from the EC's Classification, Packaging and Labelling Regulations; the EC's "Black" and "Grey" lists of dangerous substances; the "Red" list prepared by the UK Department of the Environment; and the Priority Pollutant Lists from the USA and Canada, and the German Pollutant List. Data considered to be of relevance for each of the 4003 chemicals in the first edition included physico-chemical properties; toxic effects on various species in the ecosystem; persistence and degradability in the environment; and toxicity data, encompassing genotoxicity, reproductive effects and toxicokinetic studies in avian and mammalian species, including man. Relevant legislative information was also included.

The success of the first edition of DOSE as a unique reference source of essential information for the risk evaluation of chemicals was clearly reflected by sales, encouraging reviews and, most importantly, the favourable comments received from users. Since the publication of the first edition there has been a year on year increase in the numbers of research papers on topics relevant for the risk assessment of chemicals in the literature. These considerations, together with the burgeoning literature on the toxicology of chemicals subsequent to the publication of the first edition, were persuasive factors in influencing the Royal Society of Chemistry to embark on the preparation of the present second edition of DOSE. Relevant information is reported in DOSE if it has been published in the scientific literature, and it is interesting to note that toxicity data on many industrial chemicals are still not available. A recent US Environmental Protection Agency study[1] has shown that, of the estimated 3000 high production volume chemicals (i.e. in excess of 1 million pounds/annum) produced or imported in the USA, only 7% had a full set of basic toxicity data, and 43% had no toxicity data at all.

1. *Pesticide and Toxic Chemical News* 1998, **26** (28), 7-8.

A number of important additions have been incorporated in this second edition. Apart from updating the toxicological data for the original compounds in the first edition, the number of compounds has increased to 4123. Special classes of chemicals have been added, including several endocrine disrupting chemicals, a number of pesticides, a few of the high production volume chemicals for which data have recently been collected by the OECD, and compounds tested for carcinogenicity by IARC and/or NTP. Risk and safety phrases have been updated, and some headings have been changed to conform with current practice and convention. A new field, *Toxicity to other species*, has been included, occupational exposure data have been expanded to include values for France, Germany, Sweden and Japan as well as for the UK and USA. RTECS and EINECS numbers have also been included in the entries.
It is my fervent hope that the second edition of DOSE will constitute a scientifically sound foundation and a paradigm for future publications that will be required to satisfy the need for accurate and timely data in this important field.

I am grateful to members of the Editorial Advisory Board for their helpful suggestions and advice. I must also place on record my sincere thanks to the staff members of the Royal Society of Chemistry for their invaluable support and cooperation in the preparation of this edition of DOSE.

Sharat Gangolli
Editor

Guide to Content

The data for each chemical in DOSE are organised as follows:

DOSE No.
Chemical name
Structure/line formula
Molecular formula
Molecular weight
CAS Registry No.
Synonyms
EINECS No.
RTECS No.
Uses
Occurrence

Physical properties
Melting point
Boiling point
Flash point
Specific gravity
Partition coefficient
Volatility
Solubility

Occupational exposure
Limit values
UN number
HAZCHEM code
Conveyance classification
Supply classification
Risk phrases
Safety phrases

Ecotoxicity
Fish toxicity
Invertebrate toxicity
Toxicity to other species
Bioaccumulation

Environmental fate
Nitrification inhibition
Carbonaceous inhibition
Anaerobic effects
Degradation studies
Abiotic removal
Adsorption and retention

Mammalian and avian toxicity
Acute data
Sub-acute and sub-chronic data
Carcinogenicity and chronic effects
Teratogenicity and reproductive effects
Metabolism and toxicokinetics
Irritancy
Sensitisation

Genotoxicity

Other effects
Other adverse effects (human)
Any other adverse effects

Legislation

Other comments

References

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 xv.)

Ecotoxicity

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

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

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

Fish toxicity

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

Invertebrate toxicity

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

Toxicity to other species

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

Bioaccumulation

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

Environmental Fate

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

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

Nitrification inhibition

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

Carbonaceous inhibition

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

Anaerobic effects

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

Degradation studies

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

Abiotic removal

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

Adsorption and retention

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

Mammalian and avian toxicity

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

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

Acute data

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

Sub-acute and sub-chronic data

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

Carcinogenicity and chronic effects

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

Teratogenicity and reproductive effects

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

Metabolism and toxicokinetics

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

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

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

Genotoxicity

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

Other effects

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

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

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

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

References
Contains references to data from above sections.

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

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

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

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

Note

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

If you have any relevant information, please contact:

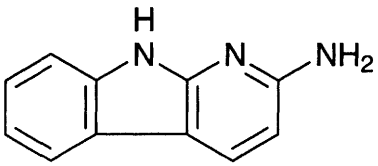
Chemical Databank Production
Royal Society of Chemistry
Thomas Graham House
Science Park
Cambridge CB4 0WF
UK
Telephone: +44 (0)1223 420066
Fax: +44 (0)1223 423429

Document Delivery

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

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

A1 A-α-C



$C_{11}H_9N_3$ **Mol. Wt.** 183.21 **CAS Registry No.** 26148-68-5

Synonyms 2-amino-α-carboline; 2-amino-9*H*-pyrido[2,3-*b*]indole; 1*H*-pyrido[2,3-*b*]indole-2-amine; 2-amino-1*H*-pyrido[2,3-*b*]indole

Uses Not used commercially.

Occurrence Not known to occur in nature.

Physical properties

M. Pt. 202°C

Solubility Organic solvents: dimethyl sulfoxide, methanol

Mammalian & avian toxicity

Carcinogenicity and chronic effects

No data for carcinogenicity to humans, sufficient evidence for carcinogenicity to animals, IARC classification Group 2B (1).

Oral mice (685 days) 800 mg kg^{-1} in diet. Tumours were observed in the livers and blood vessels of treated animals. No such tumours were seen in controls (2).

Metabolism and toxicokinetics

NADPH-dependent oxidation of A-α-C to form six products was catalysed by human, rat, and mouse hepatic microsomes. 3-Hydroxy-A-α-C and 6-hydroxy-A-α-C were the two major metabolites (*c.* 85% of total). *N*-Hydroxy-A-α-C and its oxidation products comprised the rest (3).

Genotoxicity

Salmonella typhimurium TA98 and TA98/1,8-DNP6 with metabolic activation positive (4).

Hepatocyte/DNA repair test (♂ rats, ♂ and ♀ mice, ♂ hamsters) positive (5).

Sister-chromatid exchanges in human lymphoblastoid cells with metabolic activation positive (6).

In transgenic mice fed A-α-C (800 ppm) in diet for 30, 60, or 90 days lacI mutations were induced in the colon (7).

Other effects

Any other adverse effects

Rats fed A-α-C suffered no atrophy of the salivary glands and pancreas whereas rats fed 3-Me-A-α-C suffered severely in most cases from one or the other, or both (8).

Other comments

Heterocyclic amine product formed by the cooking and pyrolysis of meat.

The most common heterocyclic amine found in all types of satay (chicken, mutton, pork) cooked according to Chinese and Malay styles (1.3-12 ppb) (9).

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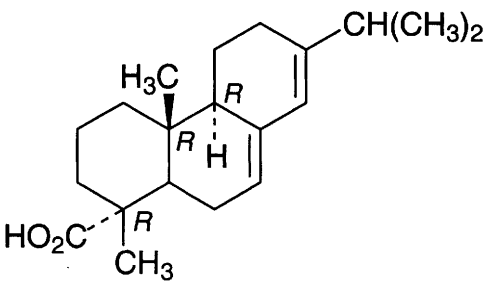
A2 abietic acid



$C_{20}H_{30}O_2$ **Mol. Wt.** 302.46 **CAS Registry No.** 514-10-3

Synonyms podocarpa-7,13-dien-15-oic acid, 13-isopropyl-; (–)-abietic acid; 7,13-abietadien-18-oic acid; sylvic acid

EINECS No. 208-178-3 (technical)

Uses In the manufacture of ester gums and of "metal resinates", soaps, plastics, and paper sizes.

Physical properties

M. Pt. 172-175°C (monoclinic plates from alcohol plus water), commercial abietic acid may be glassy or partly crystalline and may melt as low as 85°C

Solubility Water: insoluble. Organic solvents: acetone, alcohol, benzene, carbon disulfide, chloroform, ether

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) coho salmon 0.56 mg l^{-1} (1).

LC_{50} (96 hr) rainbow trout 0.7 mg l^{-1} (2).

An abietic acid mixture (37% abietic acid, 6% dehydroabietic acid, and a remainder of unknown compounds) showed slight oestrogenic activity in trout when administered in feed, but was completely inactive when given intraperitoneally in implant. The oestrogenic component of the mixture was not identified (3).

Invertebrate toxicity

LC_{50} (96 hr) shrimp 6.2 mg l^{-1} (4).

Mammalian & avian toxicity

Acute data

LD_{50} intravenous mouse 180 mg kg^{-1} (5).

Teratogenicity and reproductive effects

Ingestion of hexane extract of *Pinus ponderosa* needles causes reproductive failure in mice during the early stages of gestation. The active components of the hexane extract were identified as a mixture of diterpene resin acids, including abietic acid (6).

Metabolism and toxicokinetics

Abietic acid is metabolised in the rabbit to primary, secondary, and tertiary alcohols, with the primary alcohol predominating (7).

Other effects

Any other adverse effects

Abietic acid was oestrogenic in breast cancer cell lines MCF-7 and T-47D (3).

Abietic acid (≥25 μg ml^{-1} inhibited (Na,K)- and (H,K)-ATPases, both of which are typical membrane-bound enzymes. Abietic acid also inhibited gastric acid secretion caused by (H,K)-ATPase. Non-specific inhibition by abietic acid suggests that it acts primarily by inducing disorganisation of the cell membrane constitution (8).

Abietic acid (micromolar concentrations) depolarised mammalian synaptosomal membrane and caused acetylcholine release. These responses were not inhibited by tetradotoxin. Abietic acid caused weak inhibition of mammalian synaptosomal ATPase activity. Two actions of abietic acid which may contribute to neurotoxicity are membrane depolarisation and neurotransmitter release (9).

Other comments

Prepared by the isomerisation of rosin.

Abietic acid was detected only in the shell and not in the soft tissue of the gastropod mollusk *Austrocochlea constricta*. It is suggested that the shell may act as a "toxic waste sink" to facilitate the removal of potentially harmful compounds from the more metabolically active soft tissue (10).

Abietic acid was identified as a major toxicant to juvenile coho salmon in softwood debarking effluents and pulping waste streams (11).

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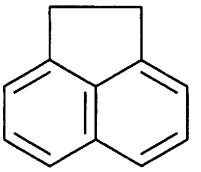
A3 acenaphthene



$C_{12}H_{10}$ **Mol. Wt.** 154.21 **CAS Registry No.** 83-32-9

Synonyms 1,2-dihydroacenaphthylene; 1,8-ethylenenaphthalene; periethylenenaphthalene

EINECS No. 201-469-6 **RTECS No.** AB 1000000

Uses A dyestuff intermediate, insecticide and fungicide. In the manufacture of plastics.

Occurrence A product of coal combustion, in coal tar and diesel fuel emissions. Volatile component of cassava and nectarines.

Physical properties

M. Pt. 93-95°C **B. Pt.** 279°C **Specific gravity** 1.0242 at 90°C with respect to water at 4°C

Partition coefficient log P_{ow} 3.92 **Volatility** v.p. 10 mmHg at 131°C

Solubility Organic solvents: benzene, ethanol

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) fathead minnow, channel catfish, rainbow trout, brown trout 600-1700 μg l^{-1} flow through bioassay, pH 7.5-7.6 (1).

LC_{50} (exposure unspecified) himedaka killifish 6.3 mg l^{-1} (2).

LC_{50} (96 hr) bluegill sunfish 1700 μg l^{-1} static bioassay (3).

Invertebrate toxicity

LC_{50} (96 hr) snail 2040 μg l^{-1} flow through bioassay (1).

LC_{50} (96 hr) mysid shrimp 970 μg l^{-1} static bioassay (3).

Bioaccumulation

Mussels, scallops and snails have no detectable aryl-hydrocarbon hydroxylase enzyme system and therefore accumulate acenaphthene (4).

Bluegill sunfish bioconcentration factor 387-389 (5,6).

Environmental fate

Nitrification inhibition

The microbial degradation of acenaphthene under denitrification conditions at soil-to-water ratios of 1.25 with soil containing 10^5 denitrifying organisms g^{-1} was investigated. Under excess nitrite conditions, acenaphthene was degraded to undetectable levels in <9 wk. Acclimation periods of 12-38 days were observed in tests with soil not previously exposed to polycyclic aromatic hydrocarbon (PAH) compounds. The acclimation period resulted from the time required for a small population of organisms capable of PAH degradation to attain sufficient densities to exhibit detectable PAH reduction. Under nitrite limiting conditions the PAH compounds were stable (7).

Anaerobic effects

Under anaerobic conditions no significant degradation was observed over a period of 70 days (7).

Degradation studies

Microbial degradation from initial aqueous phase concentration of 1 mg l^{-1} to non-detectable levels occurred within 10 days under aerobic conditions (7).

Concentrations of 25-150 μg l^{-1} were degraded at ambient temperatures within 3 days in groundwater (8).

In flooded soil contaminated with acenaphthene, biodegradation occurred under aerobic and denitrifying environments at rates of 0.39 and 0.30-0.32 ppm day^{-1}, respectively. No significant biodegradation was seen under sulfate-reducing or methanogenic environments (9).

Abiotic removal

Acenaphthene, in common with other polycyclic aromatic hydrocarbons and cyclic alkanes, resists environmental hydrolysis (10).

The photolytic $t_{1/2}$ of acenaphthene in water at 20°C exposed to 100 W Hg lamp is reported to be 3 hr (11).

Acenaphthene adsorbed on coal fly ash resists photo-oxidation (12).

Mammalian & avian toxicity

Carcinogenicity and chronic effects

Mammalian studies have yielded equivocal findings (13).

Metabolism and toxicokinetics

Acenaphthene, in common with other PAHs, accumulates in adipose tissue, but its transport into cells and between intracellular membranes is not well understood. Molecular volume is considered to be a rate-determining factor (14).

In mammals, PAHs are oxidised by aryl hydrocarbon hydroxylase activity and excreted as glucuronide conjugates (15).

Genotoxicity

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

Resistance to 8-azaguanine was induced in *Salmonella typhimurium* with metabolic activation (17).

Salmonella typhimurium TA1537, TA1538 with and without metabolic activation negative. Although non-mutagenic, all the 1,2-ring fused acenaphthenes were found to be indirect frameshift mutagens in strain TA1537 (18).

Escherichia coli PQ37 SOS chromotest with metabolic activation negative (19).

Other effects

Other adverse effects (human)

A case-control study was undertaken in Montreal to investigate the possible associations between occupational exposures and cancers of oesophagus, stomach, colorectum, liver, pancreas, lung, prostate, bladder, kidney, skin and lymphoid tissue. In total, 3726 cancer patients were interviewed between 1979-1985, to obtain detailed lifetime job histories, which were translated into a history of occupational exposures to PAHs (20).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Polycyclic aromatic hydrocarbons: maximum admissible concentration 0.2 μg l^{-1} (21).

Other comments

In a survey of UK drinking water treatment facilities acenaphthene was detected in treated samples at 2 of 14 facilities (22).

Detected in water bottom sediments and fish in Japan (23).

Experimental toxicology, human health effects and environmental effects reviewed (13,24).

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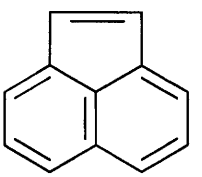
A4 acenaphthylene



$C_{12}H_8$ **Mol. Wt.** 152.20 **CAS Registry No.** 208-96-8

Synonyms cyclopenta[*de*]naphthalene

EINECS No. 205-917-1 **RTECS No.** AB 1254000

Occurrence In cigarette smoke and in soots generated by the combustion of aromatic hydrocarbon fuels containing pyridine (1).

Physical properties

M. Pt. 92-93°C **B. Pt.** 265-275°C **Specific gravity** 0.899 at 16°C with respect to water at 2°C
Volatility v.p. 9.12×10^{-4} mmHg at 25°C
Solubility Water: 16 mg l^{-1} at 25°C. Organic solvents: ethanol, diethyl ether, benzene

Occupational exposure

UN No. 2570

Ecotoxicity

Bioaccumulation

Bullhead catfish (Black River, Ohio) and striped bass (Potomac River, Maryland) contained 270 and 43 ppb acenaphthylene, respectively. Oysters and clams contained 36 and 130 ppb, respectively (2,3).

Environmental fate

Degradation studies

Concentrations of 25-150 $\mu g\ l^{-1}$ were almost totally degraded within 3 days at ambient temperatures in groundwater (4).

Microbial degradation of acenaphthylene in water samples was low (5).

In flooded soil contaminated with acenaphthylene, biodegradation occurred under aerobic and denitrifying environments at rates of 0.53 and 0.35-0.37 ppm day^{-1}. No significant biodegradation was seen under sulfate-reducing or methanogenic environments (6).

Abiotic removal

Acenaphthylene, in common with other polycyclic aromatic hydrocarbons (PAHs), is unlikely to undergo environmental hydrolysis (7).

Aqueous photolysis data for acenaphthylene indicate it is likely to undergo direct photolysis in the environment (8,9).

Acenaphthylene was completely degraded after 16 months incubation in the dark at 20°C, which suggests volatilisation is more important than biodegradation in the removal of this compound (10).

Mammalian & avian toxicity

Metabolism and toxicokinetics

In mammals, acenaphthylene and other PAHs are oxidised by aryl hydrocarbon hydroxylase activity and excreted as glucuronide conjugates (11).

Genotoxicity

Salmonella typhimurium TA1537, TA1538 with and without metabolic activation negative. Although non-mutagenic, all 1,2-ring fused acenaphthenes were found to be indirect frameshift mutagens in strain TA1537 (12).

Other effects

Other adverse effects (human)

A case-control study was undertaken in Montreal to investigate the possible associations between occupational exposures and cancers of oesophagus, stomach, colorectum, liver, pancreas, lung, prostate, bladder, kidney, skin and lymphoid tissue. In total, 3726 cancer patients were interviewed between 1979-1985 to obtain detailed lifetime job histories, which were translated into a history of occupational exposures to PAHs (13).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Polycyclic aromatic hydrocarbons: maximum admissible concentration 0.2 $\mu g\ l^{-1}$ (14).

Other comments

Found in Canadian drinking water 0.1-20 $ng\ l^{-1}$ (15).

Seafoods and agricultural produce can contain traces of acenaphthylene and other PAHs absorbed from the atmosphere and from contaminated water supplies (16).

Toxicity and hazards reviewed (17).

Reviews on human health effects, experimental toxicology, environmental effects and exposure levels listed (18).

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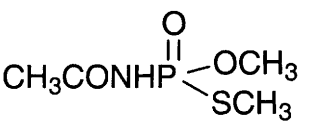
A5 acephate



$C_4H_{10}NO_3PS$ **Mol. Wt.** 183.17 **CAS Registry No.** 30560-19-1

Synonyms acetylphosphoramidothioic acid *O,S*-dimethyl ester; *O,S*-dimethyl acetylphosphoramidothioate; Orthene

EINECS No. 250-241-2 **RTECS No.** TB 4760000

Uses Contact and systemic insecticide.

Physical properties

M. Pt. 88-90°C; 82-93°C (technical grade) **Specific gravity** 1.35 (temperature unspecified)
Volatility v.p. 1.72×10^{-6} mmHg
Solubility Water: 790 g l^{-1} at 20°C. Organic solvents: acetone, benzene, ethanol, ethyl acetate, hexane

Occupational exposure

Supply classification harmful
Risk phrases Harmful if swallowed (R22)
Safety phrases Keep out of reach of children (if sold to general public) – Wear suitable protective clothing (S2, S36)

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) rainbow trout, largemouth black bass >1000, 1725 mg l^{-1}, respectively (1).
LC_{50} (96 hr) bluegill sunfish, channel cat fish 2050, 2230 mg l^{-1}, respectively (1).
Exposure (24 hr) to 400 mg l^{-1} depressed brain cholinesterase levels in rainbow trout for 15 days (2).

Invertebrate toxicity

LC_{50} (96 hr) pink shrimp, mysid shrimp 3.8-7.3 mg l^{-1} (3).
LD_{50} topically *Choristoneura occidentalis* and *Anagasta kuehniella* larvae 23-48 μg g^{-1} (4).
Administration of 0.25, 0.5, and 1 ppm acephate to bees for 14 days, caused a dose-dependent decrease in their numbers (5).
LD_{50} oral bee 1.2 μg adult bee^{-1}. Acephate classified as a poison without amorphogenic effects (6).

Environmental fate

Nitrification inhibition

Studies on the effect of acephate on growth and nitrogen fixation by *Westiellopsin prolifica* and *Anabaena* sp. showed that low concentrations of 1.0-50 μg ml^{-1} enhanced growth, while higher concentrations were lethal to organisms. Concentrations >5 μg ml^{-1} decreased total nitrogen content (7).

Degradation studies

$t_{1/2}$ in soil 7-10 days, methamidophos was identified as a metabolite. In plants residual activity lasted for 10-15 days (1).

Abiotic removal

50% hydrolysis occurred in 60 hr at pH 9 and 40°C and in 710 hr at pH 3 and 40°C (1).
Hydrolytic products formed at 37°C and varying pH, included methamidophos, *O,S*-dimethyl phosphorothiolate, and *O*-methyl acetylphosphoramidothiolate (8).

Mammalian & avian toxicity

Acute data

LD_{50} oral mallard duck, ringneck pheasant 140-350 mg kg^{-1} (1).
LD_{50} (24 hr) oral little brown bats 197-1500 mg kg^{-1}, prevented 9 of 30 surviving bats from righting themselves when placed on their backs 24 hr after dosing, initial sample size 50. From this information the calculated toxicity was ED_{50} 687 mg kg^{-1} (9).
LD_{50} oral dog >681 mg kg^{-1} (1).
LD_{50} oral rat 866-945 mg kg^{-1} (1).
LD_{50} oral mouse 361 mg kg^{-1} (1).
LD_{50} percutaneous rabbit >2000 mg kg^{-1} (1).

Sub-acute and sub-chronic data

Mouse and meadow voles were fed 0-400 ppm acephate for 5 days. Brain and plasma cholinesterase activities were reduced in a dose-dependent manner. Body, liver weight, plasma enzyme activities and cytochrome content were not affected (10).
The exposure of rats to 1 or 10 mg kg^{-1} of acephate for 15 wk, caused altered activity of the noncholinergic system without altering the cholinergic activity. The authors suggest that low level chronic exposure to organophosphones cannot be predicted by measuring cholinesterase or acetylcholinesterase enzyme activities (11).

Carcinogenicity and chronic effects

In a 2-yr feeding trial, rats receiving 30 mg kg^{-1} diet and dogs receiving 100 mg kg^{-1} diet showed depression of cholinesterase but no other significant side effects (1).

Teratogenicity and reproductive effects

50 and 100 mg kg^{-1} acephate administered orally to white-footed mice inhibited brain acetylcholinesterase activity 45% and 56% and reduced basal luteinising hormone concentration 29% and 25%, respectively, after 4 hr.

Dietary exposure to 25, 100 and 400 ppm inhibited brain acetyl cholinesterase activity but did not affect plasma basal luteinising hormone. Reproductive function effects could be possible (10).

Metabolism and toxicokinetics

Following an oral dose of acephate to mice, metabolic products detected in the liver up to 30 hr were methamidophos, *O,S*-dimethyl phosphoramidothiolate and *S*-methyl acetylphosphoramidothiolate. Acephate and methamidophos had inhibitory cholinesterase effects on mouse erythrocyte enzyme (8).

[^{14}C-acetyl]acephate (40 mg kg^{-1}) was administered orally to pregnant rats on day 18 of gestation. The rats were then killed after 10 min and at 0.5, 1, 3, 6, 12, 24 and 48 hr. At the end of 48 hr, 22.83% of the dose was exhaled as CO_2 with 1.25 and 0.6% being eliminated in the urine and faeces, respectively. Acephate was rapidly absorbed and distributed in the tissues with the highest concentration of radioactivity being found in the maternal stomach followed by the liver. A total of 0.72% of the dose was recovered from the foetus (12).

Genotoxicity

Acephate produced gene conversion and mitotic recombination in *Saccharomyces cerevisiae* and unscheduled DNA synthesis in human fibroblasts in culture (13).

In vivo tests in the mouse showed significant enhancement in chromosomal aberrations, differences in micronuclei and sperm abnormalities in acephate-treated animals. In a dominant lethal assay in mice, dead implants were significantly higher at wk 3 in treated animals (14).

The clastogenic potential of acephate was evaluated in a chick *in vivo* test system using the chromosome aberration assay in bone marrow cells and the micronucleus test in bone marrow cells and peripheral blood erythrocytes. 25, 50 and 100 mg kg^{-1} induced significant increases in micronuclei in both bone marrow and peripheral blood erythrocytes following intraperitoneal injection, but only 50 mg kg^{-1} induced significant bone marrow chromosome aberrations after a 24 hr exposure (15).

At dose levels limited by toxicity, negative results were observed for induction of sex-linked, recessive lethality in *Drosophila melanogaster* (16).

Acephate was positive in an assay for clastogenicity in *Vicia faba* (17).

Other effects

Other adverse effects (human)

Inhalation and skin exposure to acephate was evaluated in four workers engaged in the formulation of 97% pure technical product. Urine content, erythrocyte and plasma cholinesterase levels were monitored. High correlation was found between skin exposure level and urine elimination. One subject with urinary excretion levels between 3-8 mg l^{-1} had slightly decreased values of plasma and erythrocytes cholinesterase activities (18).

Any other adverse effects

Field application of acephate did not have any adverse effect on a population of meadow vole, although brain acetylcholinesterase and plasma cholinesterase activities were depressed (19,20).

Investigation of inhibition *in vitro* of human erythrocyte, rat brain and insect acetylcholinesterase levels indicated that acephate inhibits acetylcholinesterase *in vitro* in proportion to its toxicity *in vivo* (9,21).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides and related products: maximum admissible concentration 0.1 µg l^{-1} (22).

Included in Schedule 6 (Release into Land: Prescribed Substances) of Statutory Instrument No. 472, 1991 (23).

Other comments

Anticholinesterase properties of methamidophos and acephate in insects and mammals reviewed (14).

Acephate showed toxic effects on carbohydrate metabolism in rats and inhibited electron transfer in the respiration of isolated mitochondria. The activity of cytochrome c oxidase was severely inhibited at alkaline pH (24).

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A6 acetal

$$CH_3CH(OCH_2CH_3)_2$$

$C_6H_{14}O_2$ **Mol. Wt.** 118.18 **CAS Registry No.** 105-57-7

Synonyms acetaldehyde diethyl acetal; 1,1-diethoxyethane; diethyl acetal; ethylidene diethyl ether

EINECS No. 203-310-6 **RTECS No.** AB 2800000

Uses Solvent in synthetic perfumes such as jasmine. Used in organic synthesis, flavours. Formerly used as a hypnotic.

Physical properties

M. Pt. –100°C **B. Pt.** 102.7°C **Flash point** –20.5°C **Specific gravity** 0.8254 at 20°C with respect to water at 4°C **Volatility** v.p. 10 mmHg at 8°C ; v.den. 4.10

Solubility Water: 50 g l^{-1}. Organic solvents: diethyl ether, ethanol, ethyl acetate, heptane

Occupational exposure

UN No. 1088 **HAZCHEM Code** 3[illegible]E **Conveyance classification** flammable liquid

Supply classification highly flammable, irritant

Risk phrases Highly flammable – Irritating to eyes and skin (R11, R36/38)

Safety phrases Keep out of reach of children (if sold to general public) – Keep container in a well ventilated place – Keep away from sources of ignition – No smoking – Take precautionary measures against static discharges (S2, S9, S16, S33)

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, rabbit, mouse 3500-4600 mg kg^{-1} (1-3).
LC_{50} (4 hr) inhalation rat 4000 ppm (4).

Irritancy

Dermal rabbit (24 hr) 10 mg caused irritation and 500 mg instilled into rabbit eye caused irritation (4).

Other effects

Any other adverse effects

Central nervous system narcotic in high doses (3).

Other comments

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

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A7 acetaldehyde

$$CH_3CHO$$

C_2H_4O **Mol. Wt.** 44.05 **CAS Registry No.** 75-07-0

Synonyms acetic aldehyde; ethanal; ethylaldehyde

EINECS No. 200-836-8 **RTECS No.** AB 1925000

Uses In the manufacture of aniline dyestuffs, perfumes, flavours, plastics, synthetic rubbers and for silvering mirrors and hardening gelatin fibres.

Physical properties

M. Pt. –123.5°C **B. Pt.** 20.2°C **Flash point** –27°C **Specific gravity** 0.783 at 20°C
Partition coefficient log P_{ow} –0.40 (calc.) (1) **Volatility** v.p. 740 mmHg ; v.den. 1.52
Solubility Water: miscible. Organic solvents: diethyl ether, ethanol

Occupational exposure

DE-MAK 50 ppm (91 mg m^{-3})
FR-VME 100 ppm (180 mg m^{-3})
JP-OEL ceiling limit 50 ppm (90 mg m^{-3})
SE-LEVL 25 ppm (45 mg m^{-3}) **SE-STEL** 50 ppm (90 mg m^{-3})
UK-LTEL 20 ppm (37 mg m^{-1}) **UK-STEL** 50 ppm (92 mg m^{-1})
US-STEL ceiling limit 25 ppm (45 mg m^{-3})

UN No. 1089 **HAZCHEM Code** 2YE **Conveyance classification** flammable liquid

Supply classification extremely flammable, harmful
Risk phrases Extremely flammable – Irritating to eyes and respiratory system – Possible risk of irreversible effects (R12, R36/37, R40)
Safety phrases Keep out of reach of children (if sold to general public) – Keep away from sources of ignition – No smoking – Take precautionary measures against static discharges – Wear suitable protective clothing and gloves (S2, S16, S33, S36/37)

Ecotoxicity

Fish toxicity
LC_{50} (24 hr) pinperch 70 mg l^{-1} (2).
LC_{50} (96 hr) bluegill sunfish 53 mg l^{-1} (3).

Invertebrate toxicity
Cell multiplication inhibition test *Uronema parduczi* 57 mg l^{-1} (4).
EC_{50} (48 hr) *Daphnia magna* 9-14 g l^{-1} (5).
IC_{50} *Saccharomyces cerevisiae* 230 mg l^{-1} (6).

Environmental fate

Degradation studies
67-97% degradation occurred in an anaerobic system (7,8).
Biodegradable (9).
A number of studies confirm the degradability of acetaldehyde by acclimated sludge. Some loss may be attributed to volatilisation (10-14).

Abiotic removal
Photolytic $t_{1/2}$ 8-16 hr (calc.) (15).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 1930 mg kg^{-1} (6,16).
LD_{50} subcutaneous mouse 560 mg kg^{-1} (6).
LD_{50} intravenous mouse 212 mg kg^{-1} (17).

Carcinogenicity and chronic effects
Inadequate evidence for carcinogenicity to humans, sufficient evidence for carcinogenicity to animals, IARC classification group 2B (18).
Inhalation ♂, ♀ rat (≤28 month) 0, 1500 or 3000 ppm (6 hr day^{-1}, 5 day wk^{-1}) gradually reduced to 1000 ppm during the first 52 wk. Major compound-related effects include increased mortality, growth retardation, nasal tumours, and non-neoplastic nasal changes in each of the test groups. The treatment-related nasal changes comprised: degeneration, hyperplasia, metaplasia, and adenocarcinomas of the olfactory epithelium at all exposure levels; squamous metaplasia accompanied by slight to severe keratinisation and squamous cell carcinomas of the respiratory epithelium at the two highest exposure levels; and slight to severe rhinitis and sinusitis in the highest concentration group of rats (19,20).
Long-term inhalation and intratracheal instillation studies of acetaldehyde were carried out in Syrian hamsters. Exposure to acetaldehyde vapour at a concentration of 1500 ppm resulted in epithelial hyperplasia and metaplasia accompanied by inflammation in the nasal cavity and trachea. Extensive peribronchiolar adenomatoid lesions often accompanied by inflammatory changes occurred in the lungs after intratracheal instillation of acetaldhyde. There was no evidence of acetaldehyde possessing carcinogenic activity (21).

Teratogenicity and reproductive effects
In mice caused decreased weight and abnormal closure of neural tube (17).
Rat malformations included microcephaly, micromelia and digital anomalies (22).
Rat embryos were explanted on days 9.5 or 10 of gestation and cultured for 30-48 hours in rat serum containing 0, 10 or 20 μg ml^{-1} of acetaldehyde. Exposure of 9.5-day embryos to 20 μg ml^{-1} resulted in 100% embryolethality

whereas 10 μg ml^{-1} induced growth retardation and teratogenic effects. No effects were seen when 10-day embryos were exposed to 10 μg ml^{-1} (23).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537 with and without metabolic activation negative (24).
Escherichia coli PQ37 SOS chromotest with and without metabolic activation negative (25).
Escherichia coli K-12/343/113 DNA repair test without metabolic activation negative (26).
Acetaldehyde produced chromosomal aberrations including chromosomal fragments, achromatic lesions and chromatid breaks in metaphases at 12 hr and 24 hr in primary cultures of rat skin fibroblasts. Dose-related increases in aneuploidy were also observed (27).

Other effects

Other adverse effects (human)

Human foetal hepatic cell line (WRL-68) cells (which do not express alcohol dehydrogenase or cytochrome P450 activity) were exposed for 120 minutes to 10 mM acetaldehyde. No cell deaths or morphological alterations were observed by light microscopy. Lipid peroxidation values, measured as malondialdehyde production, were 60% compared to control values and studies on cell proliferation, cell adhesion capacity, neutral red incorporation into lysosomes, glutathione content, protein sulfhydryl compounds, lipid peroxidation, inner mitochondrial membrane integrity, lactate dehydrogenase activity and ultrastructural alterations indicated that acetaldehyde produced damage at the cellular level (28).
General narcotic. In humans large doses cause death by respiratory paralysis (29).
No health risks were found for workers exposed to acetaldehyde during the processing of heat shrinkable tubings on telephone cables (30).

Other comments

Toxicity and hazards reviewed (31,32).
Reviews on exposure data, experimental toxicology and human health effects listed (33).

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A8 acetaldehyde formylmethylhydrazone

$$H_3CCH{=}NNCH_3CHO$$

$C_4H_8N_2O$ **Mol. Wt.** 100.12 **CAS Registry No.** 16568-02-8

Synonyms acetaldehyde *N*-methyl-*N*-formylhydrazone; ethylidene gyromitrin; ethylidene methyl hydrazine carboxaldehyde; gyromitrin

RTECS No. LQ 8500000

Occurrence Fungal toxin from false morels, *Gyromitra* spp.

Physical properties

M. Pt. 5°C

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, mouse 320-340 mg kg^{-1} (1,2).
LD_{50} oral rabbit 50 mg kg^{-1} (3).
LD_{Lo} (unspecified route) human 10-20 mg kg^{-1} (4).

Sub-acute and sub-chronic data

TD_{Lo} (90 day) oral rabbit 5 mg kg^{-1} day^{-1} degeneration of liver observed (5).
TD_{Lo} (90 day) oral chicken 0.5 mg kg^{-1} day^{-1} degeneration of liver, kidneys and heart observed (5).

Carcinogenicity and chronic effects

No adequate evidence for carcinogenicity to humans, limited evidence for carcinogenicity to animals, IARC classification group 3 (6).
Acetaldehyde methylformylhydrazone administered 100 μg g^{-1} wk^{-1} by intragastric instillations for 52 wk in mice, induced tumours of the lungs, preputial glands, forestomach and clitoral glands (6,7).
Target organs of carcinogenicity: mouse clitoral gland and stomach (8).

Metabolism and toxicokinetics

After oral administration of acetaldehyde formylmethylhydrazone to rabbits, rats and chickens, some of the compound was excreted unchanged in the urine of rabbits (2).
At 37°C under acidic conditions (pH 1 to 3), acetaldehyde formylmethylhydrazone is converted into methylhydrazine a known tumour inducer in mice and hamsters via an intermediate, *N*-methyl-*N*-formylhydrazine (9).

Other effects

Other adverse effects (human)

Poisoning of a family of four at an unspecified exposure level has been reported, toxic effects included liver injury, seizures and haemolysis. Recovery occurred within 4-8 days (10).

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A9 acetaldoxime

$$CH_3CH{=}NOH$$

C_2H_5NO **Mol. Wt.** 59.07 **CAS Registry No.** 107-29-9

Synonyms acetaldehyde oxime; aldoxime; ethanal oxime; ethylidine hydroxylamine

EINECS No. 203-479-6 **RTECS No.** AB 2975000

Uses Chemical intermediate. Corrosion inhibitor.

Physical properties

M. Pt. 47°C **B. Pt.** 115°C **Volatility** v.p. 18.9 mmHg at 25°C

Solubility Water: 185 g l^{-1} at 25°C. Organic solvents: diethyl ether, ethanol

Occupational exposure

UN No. 2332 **HAZCHEM Code** 2Y **Conveyance classification** flammable liquid

Ecotoxicity

Bioaccumulation

The calculated bioconcentration factor of 0.5 indicates that environmental accumulation is unlikely (1).

Environmental fate

Carbonaceous inhibition

Acetaldoxime was utilised as a sole carbon source by one bacterium isolate and one fungus isolate obtained from a silty clay soil (2).

Degradation studies

Reduced to NO_2^- by *Pseudomonas aeruginosa* (3).

Soil mobility and leaching potential was predicted to be high (4,5).

Abiotic removal
The photolytic $t_{1/2}$ of acetaldoxime was calculated to be 7.3 days (5).

Mammalian & avian toxicity

Acute data
LD_{50} interperitoneal mouse 100 mg kg^{-1} (6).
LD_{50} unspecified route mouse 115 mg mg^{-1} (7).

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A10 acetamide

$$CH_3CONH_2$$

C_2H_5NO **Mol. Wt.** 59.07 **CAS Registry No.** 60-35-5

Synonyms acetic acid amide; amide C_2; ethanamide; methane carboxamide

EINECS No. 200-473-5 **RTECS No.** AB 4025000

Uses Solvent, plasticiser and stabiliser. Alcohol denaturant.

Physical properties

M. Pt. 79-81°C **B. Pt.** 222°C **Specific gravity** 1.159 at 20°C with respect to water at 4°C
Partition coefficient log P_{ow} –1.26
Solubility Water: 2 kg l^{-1}. Organic solvents: hot benzene, chloroform, ethanol, glycerol, pyridine

Occupational exposure

SE-LEVL 10 ppm (25 mg m^{-3}) **SE-STEL** 25 ppm (60 mg m^{-3})
Supply classification harmful
Risk phrases Possible risk of irreversible effects (R40)
Safety phrases Keep out of reach of children (if sold to general public) – Wear suitable protective clothing and gloves (S2, S36/37)

Ecotoxicity

Fish toxicity
LC_{50} (24-96 hr) mosquito fish 26-13 g l^{-1} (1).

Invertebrate toxicity
Cell multiplication inhibition test, *Microcystis aeruginosa* 6200 mg l^{-1}, *Entosiphon sulcatum* 99 mg l^{-1}, *Pseudomonas putida* >10,000 mg kg^{-1} (2).

Environmental fate

Nitrification inhibition

At 100 mg l^{-1} no inhibition of NH_3 oxidation by *Nitrosomonas* spp. (3).

Mammalian & avian toxicity

Acute data

LD_{50} intraperitoneal and subcutaneous rat 10 g kg^{-1} (4).

Carcinogenicity and chronic effects

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

Administration of 2.5% acetamide (1 yr) diet rats induced malignant liver tumours, hyperplastic nodules and precancerous lesions (6).

Oral administration of acetamide induced benign and malignant liver tumours in rats and an increased incidence of malignant lymphomas in ♂ mice (7-9).

Target organ of carcinogenicity: rat liver (10).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537 with metabolic activation negative (4).

Escherichia coli K-12/343/113 DNA repair test with and without metabolic activation negative (11).

Drosophila melanogaster white-ivory somatic mutation assay. Acetamide did not increase the frequency of mutant clones (12).

Drosophila melanogaster in vivo (white/white+) eye mosaic assay inactive (13).

Acetamide was inactive in morphological transformation assays in mouse embryo cells (14).

Other comments

Acetamide, a known animal carcinogen, is discussed in relation to humans receiving metronidazole therapy (15).

Human health effects, epidemiology, workplace experience, physico-chemical properties and experimental toxicity reviewed (16,17).

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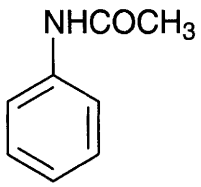
A11 acetanilide



C_8H_9NO **Mol. Wt.** 135.17 **CAS Registry No.** 103-84-4

Synonyms acetylaminobenzene; acetylaniline; *N*-phenylacetamide

EINECS No. 203-150-7 **RTECS No.** AD 7350000

Uses Manufacture of medicinals and dyestuffs. An antipyretic and analgesic. Used as a stabiliser for peroxide solutions and as an additive to cellulose ester varnishes.

Physical properties

M. Pt. 114-115°C **B. Pt.** 304-305°C **Flash point** 173°C (open cup) **Specific gravity** 1.2105 at 4°C with respect to water at 4°C **Partition coefficient** log P_{ow} 1.16 **Volatility** v.p. 1 mmHg at 114°C ; v.den. 4.65
Solubility Water: 5 g l^{-1}. Organic solvents: benzene, chloroform, diethyl ether, ethanol

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) bluegill sunfish 100 mg l^{-1} (40% survival in static bioassay at 23°C) (1).
LC_{50} (96 hr) inland silverside 115 mg l^{-1} (100-20% survival in static bioassy at 23°C) (1).

Invertebrate toxicity
IC_{50} *Saccharomyces cerevisiae* 109 mg l^{-1} (2).

Bioaccumulation
Bioconcentration factor in goldfish 1.2 (3).

Environmental fate

Degradation studies
Confirmed biodegradable (4).
BOD_{10} 1.20 mg l^{-1} oxygen using standard dilute sewage (5).
94% COD at 14.7 mg COD g dry inoculum^{-1} hr^{-1} at 20°C in an activated sludge system using the substance as sole carbon source. With influent of 50 mg l^{-1} and 365+ days acclimation 50% COD at 20°C was recorded in a observation period of 10 days, at a concentration of 600-1000 mg l^{-1} and under similar conditions inhibition was reported (6).
Aryl acylamine amidohydrolase (EC3.5.1), isolated from *Aspergillus nidulans* shows activity to acetanilide. Enzyme activity occurs over a range of pH values between 7.8 and 10.2 (7).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 800 mg kg^{-1} (2,8).
LD_{50} oral dog 500 mg kg^{-1} (9).
LD_{50} oral mouse 1210 mg kg^{-1} (2).
LD_{50} oral ♂, ♀ rat 594-4350 mg kg^{-1} (10).

LD_{50} intraperitoneal mouse 500 mg kg^{-1} (11).
Classified as harmful using the acute-toxic-class method, an alternative to the LD_{50} test (10).
LD_{Lo} (1 hr intermittently) oral human 56 mg kg^{-1} central nervous system and gastrointestinal effects (12).

Metabolism and toxicokinetics

Acetanilide is readily excreted in the urine as sulfate and glucuronide conjugates (13).
>99.9% of acetanilide remains un-ionised at body pH, facilitating absorption from blood to cerebrospinal fluid (14).
Readily absorbed from the gastrointestinal tract (15).
In healthy subjects given acetanilide orally at concentrations of 50 mg kg^{-1}, plasma clearance values varied from 12-25 ml hr^{-1} (16).

Other comments

Acetanilide has been replaced by safer analgesics (17).
Reviews on human health effects, experimental toxicology, environmental effects, ecotoxicology and exposure levels listed (18).

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A12 acetic acid

$$CH_3CO_2H$$

$C_2H_4O_2$ **Mol. Wt.** 60.05 **CAS Registry No.** 64-19-7

Synonyms ethanoic acid; ethylic acid; glacial acetic acid; methanecarboxylic acid; vinegar acid

EINECS No. 200-580-7 **RTECS No.** AF 1225000

Uses In the manufacture of various acetates and acetyl compounds. In plastics, rubber, tanning, printing and dyeing silks. An acidulant and preservative in foods and a solvent for gums, resins, volatile oils.

Physical properties

M. Pt. 17°C **B. Pt.** 118°C **Flash point** 39°C (closed cup) **Specific gravity** 1.049 at 25°C with respect to water at 25°C **Volatility** v.p. 11.4 mmHg at 20°C ; v.den. 2.07
Solubility Water: miscible. Organic solvents: acetone, benzene, diethyl ether, ethanol

Occupational exposure

DE-MAK 10 ppm (25 mg m^{-3})
FR-VLE 10 ppm (25 mg m^{-3})
JP-OEL 10 ppm (25 mg m^{-3})
SE-LEVL 5 ppm (13 mg m^{-3}) **SE-STEL** 10 ppm (25 mg m^{-3})
UK-LTEL 10 ppm (25 mg m^{-3}) **UK-STEL** 15 ppm (37 mg m^{-3})
US-TWA 10 ppm (25 mg m^{-3}) **US-STEL** 15 ppm (37 mg m^{-3})

UN No. 2789 (glacial or solutions >80%)
UN No. 2790 (solutions >10% ≤80%) **HAZCHEM Code** 2P (glacial or solutions >80%) **HAZCHEM Code** 2R (solutions >10% ≤80%) **Conveyance classification** corrosive substance
Supply classification corrosive
Risk phrases Flammable – Causes severe burns (R10, R35)
Safety phrases Keep locked up and out of the reach of children (if sold to general public) – Do not breathe vapour – In case of contact with eyes, rinse immediately with plenty of water and seek medical advice – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S23, S26, S45)

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) bluegill sunfish 75 mg l^{-1} (1).
LC_{50} (96 hr) fathead minnow 88 mg l^{-1} static bioassay 18-22°C (2).
LC_{50} (24 hr) goldfish 423 mg l^{-1}. Period of survival (48-96 hr) 100 mg l^{-1} at pH 6.8; period of survival (96 hr) 10 mg l^{-1} at pH 7.3 (3).

Invertebrate toxicity
EC_{50} (24-48 hr) *Daphnia magna*, brine shrimp 47-32 mg l^{-1} (1,4).
Cell multiplication inhibition test *Microcystis aeruginosa* 90 mg l^{-1}, *Scenedesmus quadricauda* 4000 mg l^{-1}, *Entosiphon sulcatum* 78 mg l^{-1}, *Uronema parduczi* 1350 mg l^{-1} (2,5).

Bioaccumulation
Acetic acid shows no potential for biological accumulation or food chain contamination (6).

Environmental fate

Nitrification inhibition
The effect of acetic acid on the nitrification activity of activated sludge was studied in laboratory batch experiments. The critical concentration at which activity ceased was 115 mM-acetic acid (7).

Carbonaceous inhibition
Cell multiplication inhibition test, *Pseudomonas putida* 2850 mg l^{-1} (8).

Degradation studies
Biodegradable (9).
BOD_{10} 82% reduction dissolved oxygen in fresh water and 88% reduction dissolved oxygen in seawater at 20°C (1).
$ThOD_5$ 40% 24 hr incubation activated sludge (4).
BOD values: 0.556 using a BOD biosensor; 0.34-0.88 using a conventional 5-day method (10).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 3310 mg kg^{-1} (11).

LC_{50} (1 hr) inhalation guinea pig 5000 ppm (12).

LD_{50} dermal rabbit 1060 mg kg^{-1} (13).

A single 50 µl intratesticular injection of 36% acetic acid produced sterility in male rats (14).

Sub-acute and sub-chronic data

Suckling rats were given 0.3 g l^{-1} acetic acid in drinking water from parturition until the pups were 18 days old. Offspring exposed to acetic acid were less active and showed significant weight gain compared to controls (15).

Carcinogenicity and chronic effects

Acetic acid applied repeatedly to the skin of papilloma-bearing mice resulted in an increased incidence of skin cancer (16).

Irritancy

Exposure can cause burns to skin and eye irritation (17).

The irritancy of acetic acid was evaluated using the chicken enucleated eye test. The compound had a moderate effect on corneal swelling and a severe effect on corneal opacity and fluorescein retention (18).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA1535, TA1537 with and without metabolic activation negative (19,20).

Escherichia coli PQ37 SOS chromotest with and without metabolic activation negative (21).

A single application of acetic acid to mouse epidermis induced a sustained stimulation of DNA, RNA and protein synthesis, indicating that acetic acid acted as a promoting agent (22).

Other effects

Any other adverse effects

Chronic exposure may cause erosion of dental enamel and bronchitis. Ingestion may cause severe corrosion of mouth and gastrointestinal tract with vomiting, haematemesis, diarrhoea, circulatory collapse, uremia and death (species unspecified) (17).

Other comments

The toxicity of acetic acid has been reviewed (23).

Reviews on human health effects, experimental toxicology, physico-chemical properties, epidemiology, workplace experience, ecotoxicology and environmental effects listed (24).

Incompatible with carbonates, hydroxides, oxides, phosphates. Corrosive.

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A13 acetic anhydride

$$(CH_3CO)_2O$$

$C_4H_6O_3$ **Mol. Wt.** 102.09 **CAS Registry No.** 108-24-7

Synonyms acetic acid, anhydride; acetic oxide; acetyl anhydride; acetyl ether; acetyl oxide; ethanoic anhydrate

EINECS No. 203-564-8 **RTECS No.** AK 1925000

Uses Manufacture of acetyl compounds and cellulose acetate fibres and plastics. An acetylating agent and solvent in examining wool, fat, glycerol, fatty and volatile oils, resins. Widely used in organic synthesis. A dehydrating agent and acetylating agent in the production of pharmaceuticals, dyestuffs, perfumes and explosives.

Physical properties

M. Pt. –73°C **B. Pt.** 139°C **Flash point** 49°C (closed cup) **Specific gravity** 1.082 at 20°C with respect to water at 4°C **Volatility** v.p. 3.5 mmHg at 20°C ; v.den. 3.52

Solubility Organic solvents: miscible with acetone, diethyl ether, ethanol; soluble in benzene, chloroform, dimethyl sulfoxide

Occupational exposure

DE-MAK 5 ppm (21 mg m^{-3}) **FR-VLE** 5 ppm (20 mg m^{-3})
JP-OEL ceiling limit 5 ppm (21 mg m^{-3}) **SE-CEIL** 5 ppm (20 mg m^{-3}) **UK-STEL** 5 ppm (21 mg m^{-3})
US-TWA 5 ppm (21 mg m^{-3})

UN No. 1715 **HAZCHEM Code** 2W **Conveyance classification** corrosive substance, danger of fire (flammable liquid)

Supply classification corrosive

Risk phrases Flammable – Causes burns (R10, R34)

Safety phrases Keep locked up and out of the reach of children (if sold to general public) – In case of contact with eyes, rinse immediately with plenty of water and seek medical advice – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S26, S45)

Ecotoxicity

Fish toxicity

Aquatic toxicity rating, designated non-toxic to trout, bluegill sunfish and goldfish (1).

Invertebrate toxicity

Cell multiplication inhibition test, *Pseudomonas putida* 1150 mg l^{-1}, *Scenedesmus quadricauda* 3400 mg l^{-1}, *Chlorella pyrenoidosa* 360 mg l^{-1}, *Entosiphon sulcatum* 30 mg l^{-1} (2,3).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 1780 mg kg^{-1} (4).

LD_{50} dermal rabbit 4000 mg kg^{-1} (5).

LC_{50} (4 hr) inhalation rat 1000 ppm (6).

Irritancy

10 mg applied to rabbit skin for 24 hr caused mild irritation, 250 μg instilled in rabbit eye caused severe irritation (4).

Skin, eye and upper respiratory tract irritant (7).

May cause dermatitis and occasional sensitisation (8).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537 with and without metabolic activation negative (9).

Other effects

Other adverse effects (human)

Workers exposed to (undetermined) high vapour concentrations reported burning sensations in nose and throat and dyspnoea (10).

Can cause bronchial and lung injury (11).

Lachrymator and may cause conjunctival oedema and corneal burns. Temporary or permanent interstitial keratitis with corneal opacity and loss of vision have been reported (12).

Other comments

Physical and chemical properties, hazards and current French legislation on acetic anhyride reviewed (13).

Reviews on experimental toxicology and human health effects listed (14).

Reacts with water to form acetic acid (*q.v.*). Explosion risk.

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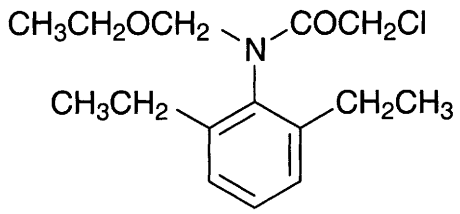
A14 acetochlor



$C_{14}H_{20}ClNO_2$ **Mol. Wt.** 269.77 **CAS Registry No.** 34256-82-1

Synonyms 2-chloro-*N*-(ethoxymethyl)-*N*-(2-ethyl-6-methylphenyl)acetamide; 2-chloro-*N*-ethoxymethyl-6'-ethylacet-*o*-toluidide

EINECS No. 251-899-3 **RTECS No.** AB 5457000

Uses Herbicide.

Physical properties

M. Pt. 0°C

Solubility Water: 223 mg l^{-1} at 25°C. Organic solvents: acetone, benzene, diethyl ether, ethanol, ethyl acetate, toluene

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) rainbow trout, bluegill sunfish 0.5, 1.3 mg l^{-1}, respectively (1).

Invertebrate toxicity

EC_{50} (48 hr) *Daphnia* 16 mg l^{-1} (1).

LD_{50}, 1.715 mg bee^{-1} (1).

Environmental fate

Degradation studies

Microbial degradation accounts for most loss from soil (2).

Abiotic removal

Strongly absorbed by soil (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral bobwhite quail 1590 mg kg^{-1} (1).

LD_{50} oral rat 1063-2183 mg kg^{-1} (2,3).

LD_{50} percutaneous rabbit 4166 mg kg^{-1} (2).

Sub-acute and sub-chronic data

Oral rat (42 day) 10-50 mg kg^{-1} administered 5 day wk^{-1} caused changes in enzyme activity, including cytochrome oxidase, lactate dehydrogenase and glucose-6-phosphate dehydrogenase, suggesting adverse effects on mitochondrial metabolic function (3).

Oral rabbit (12 month) 0.3-30 mg kg^{-1} induced atherosclerotic changes in aorta. Simultaneous administration of cholesterol and acetochlor induced more severe changes than single administration of either compound (4).

Teratogenicity and reproductive effects

Rats were given 2000 mg kg^{-1} of acetochlor (route unspecified). Severe body weight loss and some deaths occurred. In addition reduced implantation and pregnancy rates were observed at 18-25 days post-dosing. The ova of ♀ rats mated with ♂ rats exposed to acetochlor revealed a lack of fertilisation at 18-25 days (5).

Irritancy
Dermal guinea pig (10 day) 0.1 mg of 50% acetochlor caused irritation; the severity lessened with dilution (6).

Sensitisation
Intracutaneous guinea pig 50-200 μg l^{-1} followed by skin test showed no positive reaction in response to stimulation (6).
Intracutaneous guinea pig 250 μg with subsequent 7-fold application onto guinea pig skin caused hyperaemic reaction in a 24 hr spot test (6).
In a guinea pig epidermal sensitisation test, 0.5% acetochlor was negative (6).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides and related products: maximum admissible concentration 0.1 μg l^{-1} (7).
Included in Schedule 6 (Release into Land: Prescribed Substances) of Statutory Instrument No. 472, 1991 (8).

Other comments

Occupational health hazard from exposure to acetochlor discussed (4).
Metabolic pathways reviewed (9).

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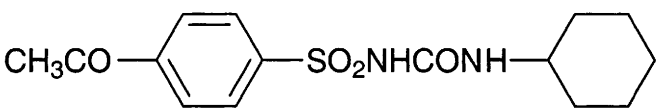
A15 acetohexamide



$C_{15}H_{20}N_2O_4S$ **Mol. Wt.** 324.40 **CAS Registry No.** 968-81-0

Synonyms benzenesulfonamide, 4-acetyl-*N*-[(cyclohexylamino)carbonyl]; 1-(*p*-acetylbenzenesulfonyl)-3-cyclohexylurea; 3-cyclohexyl-1-(*p*-acetylphenylsulfonyl)urea

EINECS No. 213-530-4 **RTECS No.** YR 7350000

Uses Antidiabetic.

Physical properties

M. Pt. 188-190°C (crystals from 90% aqueous ethanol)
Solubility Organic solvents: pyridine

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 5000 mg kg^{-1} (1).

Carcinogenicity and chronic effects

A Computer-Automated Structure Evaluation (CASE) prediction of the carcinogenicity of acetohexamide was negative; actual experimental evidence was also negative (2).

B6C3F mice, test routes feed, water, oral gavage and skin painting reported non-carcinogenic (3).

National Toxicology Program tested ♂ and ♀ rats and mice via dosed-feed. Negative evidence for carcinogenicity in all animals (4).

Metabolism and toxicokinetics

Acetohexamide was readily absorbed from the gastrointestinal tract and bound to plasma proteins. Maximum hypoglycaemic activity 3 hr after ingestion. Total duration of action was 12-24 hr. Major metabolite hydroxyhexamide had a plasma $t_{1/2}$ of 6 hr. Acetohexamide had plasma $t_{1/2}$ 1.3 hr (5).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA1535, TA1537 with metabolic activation negative (3).

Other comments

Metabolic reduction of acetohexamide reviewed (6).

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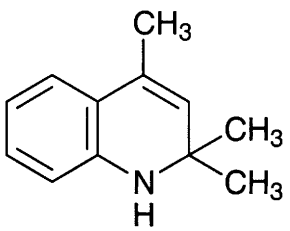
A16 acetonanil



$C_{12}H_{15}N$ **Mol. Wt.** 173.26 **CAS Registry No.** 26780-96-1

Synonyms 1,2-dihydro-2,2,4-trimethylquinoline homopolymer; quinoline, 1,2-dihydro-2,2,4-trimethyl-, homopolymer; Flectol H; Polnoks R; Antioxidant HS; Agerite Resin D; poly(1,2-dihydro-2,2,4-trimethylquinoline)

RTECS No. TQ 2625000

Uses Rubber antioxidant. Catalyst.

Physical properties

M. Pt. 355°C **B. Pt.** 132°C at 13 mmHg

Environmental fate

Abiotic removal

Treatment of wastewater by chlorination, alum coagulation and adsorption onto activated carbon was reported to be effective (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse, rat 1450-2000 mg kg^{-1} (2-4).

LD_{Lo} (4 hr) inhalation rat 7 mg m^{-3} (3).

Sub-acute and sub-chronic data

Oral rat 400 mg kg^{-1} day^{-1} (unspecified duration) caused a decrease in weight, anaemia, lowered hippuric acid urine excretion, increased amount of organic acids in urine, formation of emphysematous and atelecti foci in lungs and perivascular lymphocytic infiltration in liver (3).

Inhalation rat (5 month) 12.5 mg m^{-3} 4 hr day^{-1} caused a decrease in weight, hypodynamia, hypersalivation, decreased antitoxic function of liver, changes in blood, tracheobronchitis and lung haemorrhage, dystrophic changes in liver and brain (3).

Rats given 1.5% for 1 wk via diet developed bileduct hyperplasia after 4 wk (5).

Carcinogenicity and chronic effects

Dietary levels of 0.01, 0.1 and 1.5% fed to rats for 2 yr caused liver damage, including enlargement, nodule formation, tumours containing mucin eosinophilis, debris and leucocytes (5).

Dogs were given 0.008, 0.03 or 0.15% via diet for 1 yr, no tumours were observed (6).

Teratogenicity and reproductive effects

No foetal resorption observed (7).

Irritancy

Irritant to rabbit skin and conjuctival mucosa (concentration and duration unspecified) (3).

Sensitisation

Contact allergy observed from dust (8).

Genotoxicity

Salmonella typhimurium TA98, TA100 with and without metabolic activation negative (9-11).

Other comments

Partially polymerised.

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A17 acetone

CH_3COCH_3

C_3H_6O **Mol. Wt.** 58.08 **CAS Registry No.** 67-64-1

Synonyms 2-propanone; dimethyl ketone; dimethyl formaldehyde; dimethylketal; β-ketopropane; pyroacetic ether

EINECS No. 200-662-2 **RTECS No.** AL 3150000

Uses Solvent for fats, oils, waxes, resins, rubber, plastics, rubber cements and pharmaceuticals. Intermediate in chemical synthesis of rayon and photographic film. Used in paints and varnishes and in extraction processes to obtain various principles from animal and plant substances.

Occurrence Naturally occurring volatile metabolite in vegetation and insects (1).

Physical properties

M. Pt. –94°C **B. Pt.** 56.2°C **Flash point** –18°C (closed cup) **Specific gravity** 0.788 at 25°C with respect to water at 25°C **Partition coefficient** log P_{ow} –0.24 **Volatility** v.p. 231 mmHg at 25°C ; v.den. 2.00

Solubility Water: miscible. Organic solvents: miscible with chloroform, diethyl ether, dimethylformamide, ethanol

Occupational exposure

DE-MAK 500 ppm (1200 mg m^{-3})

FR-VME 750 ppm (1800 mg m^{-3})

JP-OEL 200 ppm (470 mg m^{-3})

SE-LEVL 250 ppm (600 mg m^{-3}) **SE-STEL** 500 ppm (1200 mg m^{-3})

UK-LTEL 750 ppm (1810 mg m^{-3}) **UK-STEL** 1500 ppm (3620 mg m^{-3})

US-TWA 500 ppm (1188 mg m^{-3}) **US-STEL** 750 ppm (1782 mg m^{-3})

UN No. 1090 **HAZCHEM Code** 2[redacted]E **Conveyance classification** flammable liquid

Supply classification highly flammable

Risk phrases Highly flammable (R11)

Safety phrases Keep out of reach of children (if sold to general public) – Keep container in a well ventilated place – Keep away from sources of ignition – No smoking – Do not breathe vapour – Take precautionary measures against static discharges (S2, S9, S16, S23, S33)

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) rainbow trout 5540 mg l^{-1} static bioassay (2).

LC_{50} (96 hr) bluegill sunfish 8300 mg l^{-1} (2).

LC_{50} (24 hr) goldfish 5000 mg l^{-1} (2).

TLm (24, 48, 96 hr) mosquito fish 13,000 mg l^{-1} (2).

LC_{50} (24 hr) harlequin fish 5700 ppm (3).

Oncorhychus mykiss sac-fry exposed to 0.1% acetone suffered changes to the hepatocyte membranes, including dilation of the interhepatocytic space and formation of intracellular myelinic figures, between the 1st and 7th days of exposure. Although these changes were minor and did not persist after 22 days of exposure, the authors suggest that since acetone causes changes in hepatocytes which could effect the toxicity of xenobiotics in test systems, the use of acetone as a solvent in toxicological experiments should be avoided (4).

Invertebrate toxicity

Asellus aquaticus (3 day) 3 ml l^{-1} caused 100% mortality (5).

LC_{50} (48 hr) juvenile *Anodonata ibecilis* 33.83 mg l^{-1} (22°C) (6).

LC_{50} (48 hr) *Daphnia magna* 3.9 µg l^{-1} (22°C) (7).
LC_{50} (24, 48 hr) brine shrimp 2100 mg l^{-1} at 24°C (8).
LC_{50} (4, 12 days) embryo grass shrimp *Palaemonetes pugio* 6.78, 6.94 g l^{-1}, respectively (9).
Cell multiplication inhibition test, *Entosiphon sulcatum* 28 mg l^{-1} (2).
EC_{50} (5, 25 min) *Photobacterium phosphoreum* 254 mM, 243 mM, respectively, Microtox test (10)

Bioaccumulation
Potential for acetone bioconcentration is negligible (1).

Environmental fate

Nitrification inhibition
EC_{50} 8100 mg l^{-1} caused nitrification inhibition (11).
0.1-0.4% (5 hr) cyanobacteria caused an unmeasured increase of nitrogen fixation at 22°C (12).

Anaerobic effects
The physiology of anaerobic acetone degradation was studied with a strain of Gram-negative denitrifying bacteria (not specified). The results provided evidence that acetone was channelled into the intermediary metabolism of the strain via carboxylation to acetoacetate (13).
100% degradation of acetone in 4 days, after a 5 day time lag, under anaerobic conditions was observed (14).

Degradation studies
In soil acetone can volatilise and leach into the ground where it is readily biodegradable (1).
Theoretical BOD_5 averaged 37-55% using results from a range of sewage inocula (15-18).
Activated sludge inocula, after 20 hr time lag, acetone degraded at a rate of 0.016 l hr^{-1}, theoretical BOD was 42% after 155 hr (19).
EC_{50} >1000 mg l^{-1} using Organisation for Economic Cooperation and Development (OECD) 209 Test closed system (20).

Abiotic removal
Volatilisation is likely in natural water (1).
Acetone reacts photochemically in atmosphere, annual average $t_{1/2}$ 22 day (21).
No photodegradation occurred when acetone was exposed to sunlight for 15 and 23 hr in stream and distilled water, respectively (22).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat, mouse, rabbit, dog 4-11 g kg^{-1} (23).

Sub-acute and sub-chronic data
LC_{50} (5 day diet) oral Japanese quail >40,000 ppm (24).

Teratogenicity and reproductive effects
No developmental toxic effects were seen in rats and mice exposed to atmospheric concentrations of acetone vapour up to 11,000 ppm and 6000 ppm, respectively, 6 hr day^{-1} for 7 days (25).

Metabolism and toxicokinetics
In perfused livers of rats, acetone was found to be metabolised to cholesterol and glycogen (23,26). Urinary elimination of acetone in workers occupationally exposed to the compound showed that there was a linear relationship between the amount of acetone absorbed and that excreted in the urine (27).

Irritancy
Rabbit eye 100% acetone caused severe irritation (28).
Rabbit eye 0.1 ml 99% acetone into conjunctival sac gave modified MAS value of 65.75 (29).

Genotoxicity

Salmonella typhimurium TA92, TA94, TA97, TA98, TA100, TA1535, TA1537 with metabolic activation negative (30,31).
Chinese hamster fibroblast (24 hr) without metabolic activation induced chromosomal aberrations (30).

Other effects

Other adverse effects (human)
Screen-printing workers exposed to acetone reported significantly greater frequencies of neurasthenic symptoms and other symptoms of peripheral neuropathy and autonomic dysfunction than a control group (32).
Women occupationally exposed to solvents, including acetone, in chemical plants showed deviations in haemoglobin and haematocrit values, erythrocyte, leukocyte, lymphocyte, monocyte and granulocyte counts, coagulation and bleeding times and in methanol absorption (33).
A group of 71 Romanian workers exposed to acetone in a coin printing factory and 86 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 acetone be reduced to <500 mg m^{-3} (34).
Prolonged or repeated topical use may cause erythema and dryness, while inhalation can cause headache, excitement, bronchial irritation and narcosis (35).

Any other adverse effects
In the hamster, 8% acetone administered in the drinking water, induced cytochrome P-450 in the liver, kidneys and lung, and produced differential changes in mixed function oxidase enzyme activities in these tissues (36).

Other comments

May be released into the environment as stack emissions, fugitive emissions and in wastewater (1).
Experimental toxicology, human health effects and metabolic fate reviewed (37-41).

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A18 acetone cyanohydrin

$$(CH_3)_2C(OH)CN$$

C_4H_7NO **Mol. Wt.** 85.11 **CAS Registry No.** 75-86-5

Synonyms 2-cyanopropan-2-ol; propanenitrile, 2-hydroxy-2-methyl-; lactonitrile, 2-methyl-; α-hydroxyisobutyronitrile; 2-hydroxyisobutyronitrile; methyl lactonitrile; 2-methyllactonitrile

EINECS No. 200-909-4 **RTECS No.** OD 9275000

Uses Used in the manufacture of insecticides, pharmaceuticals, foaming agents and polymerisation inhibitors. Intermediate for organic synthesis, especially methyl methacrylate.

Physical properties

M. Pt. –19°C **B. Pt.** 95°C **Flash point** 63°C (closed cup) **Specific gravity** 0.9267 at 25°C with respect to water at 4°C **Volatility** v.p. 0.8 mmHg at 20°C ; v.den. 2.93
Solubility Water: freely soluble. Organic solvents: diethyl ether, ethanol

Occupational exposure

US-STEL ceiling limit 4.7 ppm (5 mg m^{-3}) (as CN)

UN No. 1541 **HAZCHEM Code** 2XE **Conveyance classification** toxic substance
Supply classification very toxic, dangerous for the environment
Risk phrases Very toxic by inhalation, in contact with skin and if swallowed – Very toxic to aquatic organisms (R26/27/28, R50)
Safety phrases Keep locked up and out of the reach of children (if sold to general public) – Keep container tightly closed and in a well ventilated place – Take off immediately all contaminated clothing – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) – Avoid release to the environment. Refer to special instructions/safety data sheet (S1/2, S7/9, S27, S45, S61)

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) bluegill sunfish 0.57 ppm in fresh water at 23°C with mild aeration at 24 hr (1).
LC_{50} (96 hr) inland silverside 0.50 ppm in synthetic sea water at 23°C with mild aeration at 4 hr (1).

Environmental fate

Degradation studies

1 mg l^{-1} degraded completely to acetone and hydrogen cyanide in river water. Removal of the cyanide ion occurs by evaporation, therefore cyanide pollution is a danger in closed systems (2).

Abiotic removal

Adsorption on activated carbon: initial concentration 1000, 200 and 100 ppm, carbon dosage ×10. Residual concentrations 400, 110, 70 ppm, respectively, corresponding to removal of 60%, 45% and 30% acetone cyanohydrin (3).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, mouse, rabbit 13-17 mg kg^{-1} (4,5).
LC_{Lo} (4 hr) inhalation rat 63 ppm (6).

Sub-acute and sub-chronic data

Repeated oral administration of 5 mg twice weekly (duration unspecified) to rats caused kidney and liver damage (7).

Irritancy

In humans can cause burns and irritation to skin, mucous membranes and eye (8,9).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA1535, TA1537 with and without metabolic activation negative (10).

Other effects

Other adverse effects (human)

Very toxic by inhalation. Symptomatic effects include giddiness, headache, weakness, confusion, unconsciousness, convulsions, nausea and vomiting. Breathing may stop in severe cases due to hydrogen cyanide poisoning (9).

Other comments

A structure-activity relationship comparing the acute and sub-acute data, teratogenicity and biochemical mechanism of the toxicity of a series of structurally related aliphatic nitriles has been published (11).
Reviews on experimental toxicology, human health effects and environmental effects listed (12).

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A19 acetone thiosemicarbazide

$$(CH_3)_2C{=}NNHC(S)NH_2$$

$C_4H_9N_3S$ **Mol. Wt.** 131.20 **CAS Registry No.** 1752-30-3

Synonyms thiosemicarbazone acetone; 2-(1-methylethylidene)hydrazine carbothioamide

EINECS No. 217-137-9 **RTECS No.** AL 7350000

Uses Chemical intermediate. Fungicide.

Physical properties

M. Pt. 178-179°C
Solubility Organic solvents: acetone

Mammalian & avian toxicity

Acute data
LD_{Lo} oral rat 10 mg kg^{-1} (1).
LD_{50} intraperitoneal mouse 23 mg kg^{-1} (2).

Legislation

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

Other comments

Reviews on experimental toxicology, human health effects and environmental effects listed (5).

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A20 acetonitrile

CH_3CN

C_2H_3N **Mol. Wt.** 41.05 **CAS Registry No.** 75-05-8

Synonyms methyl cyanide; cyanomethane; ethanenitrile; ethylnitrile; methylcarbonitrile

EINECS No. 200-835-2 **RTECS No.** AL 7700000

Uses A solvent for organic and inorganic compounds, including polymers and gases. Used in plastics casting and moulding, and in dyeing textiles. Increasingly used in its highly purified form in electrochemistry and high-performance liquid chromatography. Used as a catalyst and stabiliser for chlorinated solvents.

Physical properties

M. Pt. –45°C **B. Pt.** 81.1°C **Flash point** 6°C (open cup) **Specific gravity** 0.7868 at 15°C with respect to water at 4°C **Partition coefficient** log P_{ow} 0.34 **Volatility** v.p. 74 mmHg at 20°C ; v.den. 1.42
Solubility Water: miscible. Organic solvents: miscible with acetone, diethyl ether, ethanol, ethyl acetate, methanol, methyl acetate

Occupational exposure

DE-MAK 40 ppm (68 mg m^{-3})
FR-VME 40 ppm (70 mg m^{-3})
SE-LEVL 30 ppm (50 mg m^{-3}) **SE-STEL** 60 ppm (100 mg m^{-3})
UK-LTEL 40 ppm (68 mg m^{-3}) **UK-STEL** 60 ppm (102 mg m^{-3})
US-TWA 40 ppm (67 mg m^{-3}) **US-STEL** 60 ppm (101 mg m^{-3})

UN No. 1648 **HAZCHEM Code** 2WE **Conveyance classification** flammable liquid
Supply classification highly flammable, toxic
Risk phrases Highly flammable – Toxic by inhalation, in contact with skin and if swallowed (R11, R23/24/25)
Safety phrases Keep locked up and out of the reach of children (if sold to general public) – Keep away from sources of ignition – No smoking – Take off immediately all contaminated clothing – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S16, S27, S45)

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) fathead minnow, guppy, bluegill sunfish 1000-1850 mg l^{-1} (1-3).

Invertebrate toxicity
Cell multiplication inhibition test, *Pseudomonas putida* 680 mg l^{-1}, *Entosiphon sulcatum* 1810 mg l^{-1}, *Scenedesmus quadricauda* 7300 mg l^{-1} (4).
LC_{50} (24 hr) *Artemia salina* (24, 72 hr-old larvae) 640, 400 mg l^{-1}, respectively (5).
Microcystis aeruginosa 520 mg l^{-1} (4,6).

Environmental fate

Nitrification inhibition
100 mg l^{-1} did not inhibit NH_3 oxidation by *Nitrosomonas* spp. (7).

Carbonaceous inhibition
Chromobacterium sp. and *Pseudomonas aeruginosa* both utilised high concentrations of acetonitrile as their sole carbon source. Maximum growth attained after 96 hr of incubation. Concentrations >25 g l^{-1} inhibited growth and oxygen uptake (8).

Degradation studies

Confirmed biodegradable (9).

Wastewater treatment, biodegradation by mutant microorganisms 500 mg l^{-1} at 20°C. 100% disruption in parent strain in 9 hr, 100% in mutant strain in 1.5 hr (10).

In soil *Pseudomonas putida* was capable of utilising high concentration of acetonitrile as the sole source of carbon and nitrogen. Metabolites included acetic acid and ammonia (11).

Nine yeast strains were examined for their ability to utilise a series of aliphatic mono- and dinitriles as sole source of nitrogen. The results indicate that while some species failed to utilise these nitriles, the property was nonetheless not uncommon among these microfungi. The hydrolysis probably involves a two-step reaction mediated by nitrile hydratase and amidose (12).

BOD_5 17% reduction in dissolved oxygen (13).

Acinetobacter sp. 51-2 degraded 25 g l^{-1} acetonitrile in 48 hr (14).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 3800 mg kg^{-1} (15).

LC_{50} (8 hr) inhalation rat 7500 ppm (16).

LD_{50} intraperitoneal mouse 500 mg kg^{-1}.

LD_{50} subcutaneous rabbit 130 mg kg^{-1} (15).

Teratogenicity and reproductive effects

Some toxicity in high-dose animal experiments (species unspecified), but no overt evidence of teratogenesis (17).

Inhalation rat (6 hr) 900-1800 ppm during days 6-20 of gestation. Embryolethality observed after exposure to 1800 ppm (18).

Metabolism and toxicokinetics

Acetonitrile was metabolised anaerobically by gastrointestinal microflora to produce cyanide and thiocyanate (19).

Elevated concentrations of cyanide and thiocyanate were detected in all tissues studied at 2.5 hr after an oral or intraperitoneal dose of acetonitrile (100-400 mg kg^{-1}) to Syrian golden hamsters (16).

Five minutes after intravenous injection of [2-^{14}C]acetonitrile into male ICR mice the highest levels of radioactivity occurred in the liver and kidneys; levels declined over time. At 24 and 48 hr acetonitrile-derived radioactivity was detected in the gastrointestinal tract, thymus, liver and male reproductive organs. Covalent binding studies showed that the irreversible association with tissues of radioactivity derived from [2-^{14}C]acetonitrile is due to the metabolic activation of acetonitrile and the covalent interaction of reactive metabolite(s) with lipid and macromolecular fractions of the cell (20).

Irritancy

In humans, may cause skin irritation (21).

Reported to cause dermatitis in rabbits at concentrations of 3900-7850 mg kg^{-1} (22).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537 with and without metabolic activation negative (23).

Saccharomyces cerevisiae D.61M positive mitotic chromosomal, malsegregation in diploid strain (24).

Chinese hamster ovary cells sister chromatid exchange without metabolic activation weakly positive, with metabolic activation negative (25).

Inhalation exposure adult ♀ *Drosophila melanogaster* induced aneuploidy, both chromosome loss and gain (26).

Other effects

Other adverse effects (human)

Symptomatic effects in humans include flushing of face, tightness of chest, increased salivation, eye and nose irritation. Exposure to high concentrations may cause headache, dizziness, rapid respiration and pulse rate,

nausea, vomiting, unconsciousness, convulsions and death. Onset of symptoms may be delayed for several hr, perhaps due to the low release of cyanide (27-29).

Any other adverse effects

Glutathione in brain and liver tissue and the activity of cytochrome oxidase in the brain of rats were studied. Acetonitrile reduced tissue glutathione content (30).

Other comments

IC_{50} (96 hr) duckweed *Lemna minor* L. growth inhibition 3685 mg l^{-1} (31).

Physical and chemical properties, experimental toxicology, epidemiology and human health effects reviewed (32-34).

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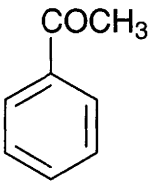
A21 acetophenone



C_8H_8O **Mol. Wt.** 120.15 **CAS Registry No.** 98-86-2

Synonyms methyl phenyl ketone; acetylbenzene; benzoyl methide; 1-phenylethanone; phenyl methyl ketone

EINECS No. 202-708-7 **RTECS No.** AM 5250000

Uses Used in the perfume industry. Catalyst for the polymerisation of olefins. Photosensitiser in organic synthesis. Hypnotic.

Occurrence In oils of castoreum and labdanum resin, and buds of balsam poplar. In heavy oil fractions of coal tar.

Physical properties

M. Pt. 19-20°C **B. Pt.** 202°C **Flash point** 82°C (closed cup) **Specific gravity** 1.03 at 20°C with respect to water at 4°C **Partition coefficient** log P_{ow} 1.58 **Volatility** v.p. 1 mmHg at 15°C ; v.den. 4.14

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

Occupational exposure

US-TWA 10 ppm (49 mg m^{-3})

Supply classification harmful

Risk phrases Harmful if swallowed – Irritating to the eyes (R22, R36)

Safety phrases Keep out of reach of children (if sold to general public) – In case of contact with eyes, rinse immediately with plenty of water and seek medical advice (S2, S26)

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) fathead minnow 155 mg l^{-1}, static bioassay at 18-22°C (1).

Invertebrate toxicity

EC_{50} (5, 25 min) *Photobacterium phosphoreum* 110, 133 μM Microtox test (2).

Environmental fate

Nitrification inhibition

Nitrosomonas europeae oxidation of ammonia to nitrite was 50% inhibited (10 min incubation) by 300 μM acetophenone. This was oxidised at the C-2 position of the substitutent to yield 2-hydroxyacetophenone, which was abiotically oxidised to phenylglyoxal (3).

Carbonaceous inhibition

Pseudomonas putida can oxidise acetophenone, the metabolite identified was a monohydroxy product 3-acetyl-2,4-cyclohexadien-1-ol (4).

Degradation studies

Confirmed biodegradable (5).

Water pollution factors, BOD_5 0.518 mg l^{-1} oxygen consumed, estimated ThOD 32 mg l^{-1} (6).

Acetophenone was reported to be 14% biodegradable (7).

Microbial metabolism of acetophenone was reported to occur via the formation of phenyl acetate with further metabolism occurring by hydrolysis (8).

Abiotic removal

Adsorbed by activated carbon 0.194 g g^{-1} carbon, 97% reduction, influent 1000 mg l^{-1}, effluent 28 mg l^{-1} (9,10).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 815 mg kg^{-1} (11).
LD_{50} intraperitoneal mouse 200 mg kg^{-1} (12).
LD_{Lo} subcutaneous mouse 330 mg kg^{-1} (13).

Irritancy

Dermal rabbit (24 hr) 515 mg caused mild irritation and 771 µg instilled into rabbit eye for 24 hr caused severe irritation (14,15).

Other effects

Other adverse effects (human)

Chinese hamster lung cells with metabolic activation induced chromosome aberrations (16).

Any other adverse effects

May be narcotic at high concentrations (17).

Other comments

Reviews on experimental toxicology and human health effects listed (18).

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A22 acetylacetone

$$CH_3COCH_2COCH_3$$

$C_5H_8O_2$ **Mol. Wt.** 100.12 **CAS Registry No.** 123-54-6

Synonyms 2,4-pentanedione; diacetylmethane

EINECS No. 204-634-0 **RTECS No.** SA 1925000

Uses Forms organometallic complexes which are used as gasoline additives, lubricant additives, driers for varnishes, printing inks, fungicides and insecticides.

Physical properties

M. Pt. -23°C **B. Pt.** 140°C **Flash point** 40°C **Specific gravity** 0.9727 at 25°C with respect to water at 4°C
Volatility v.p. 7 mmHg at 20°C ; v.den. 3.45
Solubility Water: 125 g l^{-1} (temperature unspecified). Organic solvents: acetone, benzene, chloroform, diethyl ether, ethanol, glacial acetic acid

Occupational exposure

UN No. 2310 **HAZCHEM Code** 2Y **Conveyance classification** flammable liquid
Supply classification flammable, harmful
Risk phrases Flammable – Harmful if swallowed (R10, R22)
Safety phrases Keep out of reach of children (if sold to general public) – When using do not smoke – Do not breathe vapour – Avoid contact with skin and eyes (S2, S21, S23, S24/25)

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) bluegill sunfish 29-201 mg l^{-1}. Ventilatory patterns and time to death suggested that acetylacetone was lethal by mechanisms other than narcosis (1).

Invertebrate toxicity
Cell multiplication inhibition test, *Pseudomonas putida* 67 mg l^{-1}, *Entosiphon sulcatum* 11 mg l^{-1}, *Scenedesmus quadricauda* 2.7 mg l^{-1}, *Microcystis aeruginosa* 8.5 mg l^{-1} (1-3).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 1000 mg kg^{-1} (4).
LC_{50} (4 hr) inhalation rat 1224 ppm (5).
LD_{50} intraperitoneal mouse 750 mg kg^{-1} (6).

Sub-acute and sub-chronic data
Fischer-344 rats were exposed to 0-650 ppm acetylacetone vapour 6 hr day^{-1}, 5 days wk^{-1} for 14 wk. Damage to thymus and brain was reported in animals exposed to 650 ppm (7).

Carcinogenicity and chronic effects
Subcutaneous rat (40 wk) 200 mg kg^{-1} 5 day wk^{-1} neurotoxic effects were reported (8).

Teratogenicity and reproductive effects
At concentrations of 398 ppm, acetylacetone showed maternal toxicity (reduced body weight) and foetotoxicity (reduced body weight and ossification), and at 202 ppm foetotoxicity (reduced body weight) was observed. Embryotoxicity or teratogenicity were not observed at any concentration. The no-observable-effect concentration was 53 ppm for both maternal and developmental toxicity (9).

Metabolism and toxicokinetics

Fischer 344 rats administered single intravenous doses of 4.3, 43, 148.5 or 430 mg kg^{-1} ^{14}C-acetylacetone exhibited biexponential decline in plasma concentration of ^{14}C-acetylacetone-derived radioactivity. Dose-linear kinetics occurred for the dose range 4.3-148.5 mg kg^{-1} but not with 430 mg kg^{-1}. Metabolism was rapid with the concentration of unmetabolised acetylacetone declining steadily to undectable level after 8 hr. ^{14}C-acetylacetone-derived radioactivity was eliminated mainly as $^{14}CO_2$ and in the urine. Excretion in expired volatiles and in faeces was small (10).

Irritancy

In rabbits, contact with 0.5 ml produced mild local erythema and oedema. Instilling 0.1 ml into the conjunctival sac caused mild conjunctivitis which lasted 24 hr. No corneal injury was reported (6).

Genotoxicity

Salmonella typhimurium TA104 without metabolic activation positive. Induced sister chromatid exchanges in Chinese hamster ovary cells without metabolic activation. Genotoxic activity can be related to the reactivity of acetyl acetone with DNA and its lipophilic character (11).
Bacillus subtilis direct or indirect DNA damaging potential in microsome recombination assay (12).

Other effects

Any other adverse effects

Inhalation ♂ Fischer 344 rats (5 day) 0-694 ppm 6 hr day^{-1}. No histopathological changes observed in brain, testes, or thymus from ♂ rats exposed to high concentrations, sacrificed after 8 wk of mating. Minor transient reproductive and gestational effects were present and the authors report, although not statistically significant, the results are dose related and compatible with a transient slight dominant lethal effect at the spermatid stage of spermatogenesis (13).

Other comments

Reviews on experimental toxicology and human health effects listed (14).

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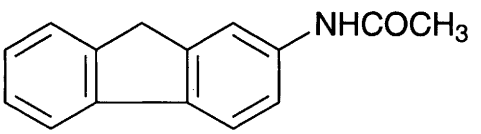
A23 2-acetylaminofluorene



$C_{15}H_{13}NO$ **Mol. Wt.** 223.27 **CAS Registry No.** 53-96-3

Synonyms *N*-2-fluorenylacetamide; *N*-9*H*-fluoren-2-ylacetamide; *N*-acetyl-2-aminofluorene; 2-acetamidofluorene; 2-acetaminofluorene; 2-fluorenylacetamide; AAF

EINECS No. 200-188-6 **RTECS No.** AB 9450000

Physical properties

M. Pt. 194°C **Partition coefficient** log P_{ow} 3.22 (1)
Solubility. Organic solvents: diethyl ether, ethanol, glycols

Ecotoxicity

Fish toxicity
Medaka exposed to 2-acetylaminofluorene exhibited an increase in total hepatocellular neoplastic lesions. The increase appeared related to exposure but not to concentration and was not statistically significant. Guppies exposed for 7 days exhibited statistically significant increases in total hepatocellular lesions (2).

Bioaccumulation
Calculated bioconcentration factor 165 (3).

Environmental fate

Degradation studies
Incubation of 500 ppm at 20°C in activated sludge for 6 days was toxic to microorganisms and some degradation occurred. ThOD 7-12% (4).

Abiotic removal
Chemical hydrolysis and oxidation are unlikely to be environmentally significant (5).
Vapour phase photolytic reaction in water and air with hydroxyl radicals $t_{1/2}$ 6 hr at 25°C (1).

Adsorption and retention
Estimated soil adsorption coefficient suggests low mobility in soil and strong adsorption to suspended solids and sediments in water (6).

Mammalian & avian toxicity

Acute data
LD_{50} oral mouse 1020 mg kg^{-1} (7).
LD_{50} intraperitoneal mouse 2200 mg kg^{-1} (8).

Sub-acute and sub-chronic data
Oral mouse (28 day) 30-150 mg kg^{-1} induced *N*-deoxyguanosin-8-yl-2-aminofluorene in liver and bladder DNA. In liver, correlating incidence of tumours was observed (9).

Carcinogenicity and chronic effects
Oral BALB/C mouse (6 month) 500 ppm. The mice were 1, 7 or 13 months old and were killed immediately, or 3 or 6 months after treatment terminated. Urinary bladder hyperplasia was less severe in young mice, mammary

tumourigenesis increased with age, old mice were sensitive to liver karyomegaly, and cytoplasmic and nuclear inclusions. Bladder tumourigenesis was not influenced by age (10).
Target organs of carcinogenicity: mouse and rat liver, rat mammary gland, rat skin, mouse bladder/urethra (11).

Metabolism and toxicokinetics

Repeated exposure can increase metabolic rate and increase excretion of *N*-hydroxy-*N*-2-fluorenylacetylacetylamine in urine as glucuronide conjugate in rabbits. The major enzyme involved in the bioactivation of 2-acetylaminofluorene in the human liver is P-450$_{PA}$ (phenacetin *O*-deethylase) (12). Deacetylation to 2-aminofluorene is catalysed by placental microsome carboxylesterase (13).

Genotoxicity

Salmonella typhimurium TA1535 with metabolic activation positive (14).
Salmonella typhimurium NM2009 with metabolic activation positive (15).
In vitro mouse bone marrow micronucleus cytochrome test positive (16).
In vivo/in vitro assay, ♂ rats were given single oral dose (concentration unspecified) of 2-acetylaminofluorene. Slight increase in the frequency of chromosomal aberrations and chromosome breaks. Sister chromatid exchange equivocal results (17).
In vitro human mammary epithelial cells, unscheduled DNA synthesis was induced (18).
Drosophila melanogaster DNA repair test positive, eye mosaic assay negative (19,20).

Other comments

Genotoxic and non-genotoxic effects reviewed (21-23).
The role of 2-acetylaminofluorene in carcinogenesis is reviewed (24,25).
The mutagenic properties of 2-acetylaminofluorene-derived DNA adducts reviewed (26).

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A24 acetyl bromide

CH_3COBr

C_2H_3BrO **Mol. Wt.** 122.95 **CAS Registry No.** 506-96-7

Synonyms acetic bromide; ethanoyl bromide; acetic acid bromide

EINECS No. 208-061-7 **RTECS No.** AO 5955000

Uses Paper manufacturing.

Physical properties

M. Pt. -96°C **B. Pt.** 74-77°C **Specific gravity** 1.6625 at 16°C with respect to water at 4°C
Solubility Organic solvents: miscible with benzene, diethyl ether, chloroform

Occupational exposure

UN No. 1716 **HAZCHEM Code** 4WE **Conveyance classification** corrosive substance

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) fathead minnow 40 mg l^{-1} (1).

Mammalian & avian toxicity

Acute data
LC_{50} inhalation rat, mouse 48 g m^{-3} (2).
LD_{50} intraperitoneal rat, mouse 250 mg kg^{-1} (2).

Irritancy
Reported to be irritating to eyes (species unspecified) (3).

Other comments

Decomposes violently in water and ethanol (3).

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A25 acetyl chloride

CH_3COCl

C_2H_3ClO **Mol. Wt.** 78.50 **CAS Registry No.** 75-36-5

Synonyms ethanoyl chloride; acetic acid chloride; acetic chloride

EINECS No. 200-865-6 **RTECS No.** AO 6390000

Uses Acetylating agent. Used in the synthesis of pharmaceuticals and dyestuffs, in the esterification of cellulose and in improving the wetfastness of yarns. Used as a rubber antiscorch agent.

Physical properties

M. Pt. –112°C **B. Pt.** 52°C **Flash point** 4°C **Specific gravity** 1.1051 at 20°C with respect to water at 4°C
Volatility v.p. 352.5 mmHg at 24°C
Solubility Organic solvents: miscible with acetone, benzene, carbon disulfide, chloroform, diethyl ether, glacial acetic acid, toluene

Occupational exposure

UN No. 1717 **HAZCHEM Code** 4WE **Conveyance classification** flammable liquid, corrosive
Supply classification highly flammable, corrosive
Risk phrases Highly flammable – Reacts violently with water – Causes burns (R11, R14, R34)
Safety phrases Keep locked up and out of the reach of children (if sold to general public) – Keep container in a well ventilated place – Keep away from sources of ignition – No smoking – In case of contact with eyes, rinse immediately with plenty of water and seek medical advice – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S9, S16, S26, S45)

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) fathead minnow 42 mg l^{-1} (1).

Environmental fate

Degradation studies
In view of the instability of the compound in aqueous media, it is unlikely to persist in an aquatic environment and soil (2).

Abiotic removal
Estimated $t_{1/2}$ for atmospheric photochemical reaction 3 months (3).

Mammalian & avian toxicity

Acute data
TC_{Lo} (1 min) inhalation human 2 ppm (4).

Irritancy
Extremely irritating to eyes. Corrosive, causes severe burns (species and concentration unspecified) (5).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA1535, TA1537 with and without metabolic activation negative (6).

Other comments

Reviews on physico-chemical properties, experimental toxicology, ecotoxicology and human health effects listed (7).
When heated to decomposition it emits highly toxic fumes of phosgene. Reacts violently with water and other hydrogen active compounds like amines, phenols and alcohols (2).

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A26 acetylene

$$HC{\equiv}CH$$

C_2H_2 **Mol. Wt.** 26.04 **CAS Registry No.** 74-86-2

Synonyms ethine; ethyne; acetylen; narcylen

EINECS No. 200-816-9 **RTECS No.** AO 9600000

Uses Used in soldering, in oxyacetylene welding and cutting.
Used in the chemical synthesis of acetaldehyde and acetic acid.
Occurrence Occurs in emission from vehicle exhausts.

Physical properties

M. Pt. –81°C (sublimes) **B. Pt.** –84°C **Flash point** –18°C **Specific gravity** 0.62 (liquefied)
Volatility v.p. 40 atm at 16.8°C ; v.den. 0.91
Solubility Organic solvents: acetone, benzene, chloroform

Occupational exposure

UN No. 1001 **Conveyance classification** flammable gas
Supply classification extremely flammable
Risk phrases Heating may cause an explosion – Explosive with or without contact with air – Extremely flammable (R5, R6, 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

Fish toxicity
LC_{50} (33 hr) river trout 200 mg l^{-1} (1).

Environmental fate

Nitrification inhibition
Effective in inhibiting the reduction of N_2O in denitrification, even for prolonged incubation periods of up to 96 hr under moist or saturated soil/water conditions (2).
Inhibits biodegradation processes in *Nitrosomonas europaea* and *Nitrosococcus oceanus* by inhibiting ammonia monooxygenase enzyme activity (3).

Carbonaceous inhibition
Acetylene vapour 1.5-6.5% completely inhibited carbon dioxide fixation by nitrifying and methanotrophic microorganisms, while 24-45% acetylene inhibited carbon dioxide fixation by thiomic and heterotrophic bacteria (4).

Other effects

Other adverse effects (human)

Concentrations of 20-40% acetylene reported to cause dyspnoea, headache in humans, higher concentrations can cause asphyxiation and narcosis (5).

Any other adverse effects

Inhibits cytochrome P-450 catalysed reactions by suicide inactivation (6).

Legislation

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

Other comments

Mixtures with air between 3% and 65% gas are explosive (5).

Reviews on physico-chemical properties, exposure, ecotoxicology, experimental toxicology and human health effects listed (8).

The effectiveness of acetylenic structures for the inactivation of enzymes in cancer cell metabolism reviewed (9).

Not explosive at atmospheric pressure but at ≥2 atmospheres is explosive by spark or decomposition.

Forms insoluble explosive compounds with copper and silver, therefore copper and brass containers must not be used.

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A27 acetyl iodide

CH_3COI

C_2H_3IO **Mol. Wt.** 169.95 **CAS Registry No.** 507-02-8

Synonyms ethanoyl iodide; acetic acid iodide; acetic iodide

EINECS No. 208-062-2 **RTECS No.** AP 4670000

Physical properties

B. Pt. 108°C **Specific gravity** 2.0674 at 20°C with respect to water at 4°C **Partition coefficient** log P_{ow} 1.5491

Solubility Organic solvents: benzene, diethyl ether

Occupational exposure

UN No. 1898 **HAZCHEM Code** 2X **Conveyance classification** corrosive substance

Mammalian & avian toxicity

Irritancy

Reported to be a strong irritant (species and concentrations unspecified) (1).

Other effects

Any other adverse effects

Acetyl iodide vapours reported to cause pulmonary oedema (species and concentrations unspecified) (1).

Other comments

Decomposes in water and ethanol.

References

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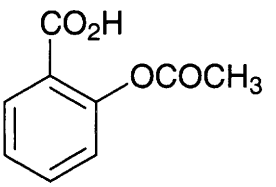
A28 acetylsalicylic acid



$C_9H_8O_4$ **Mol. Wt.** 180.16 **CAS Registry No.** 50-78-2

Synonyms *o*-acetyloxybenzoic acid; 2-acetoxybenzoic acid; 2-acetyloxybenzoic acid; salicylic acid acetate; Aspirin

EINECS No. 200-064-1 **RTECS No.** VO 0700000

Uses Analgesic, antipyretic, anti-inflammatory agent.

Physical properties

M. Pt. 135°C (rapid heating) **B. Pt.** 140°C

Solubility Water: 3.3 g l^{-1} at 25°C. Organic solvents: chloroform, diethyl ether, ethanol

Occupational exposure

UK-LTEL 5 mg m^{-3}

US-TWA 5 mg m^{-3}

Ecotoxicity

Fish toxicity

No effect on stickleback, steelhead trout or sockeye salmon at 30 mg l^{-1} (1).

Invertebrate toxicity

EC_{50} (24 hr) *Daphnia magna* 8.15 mM (2).

EC_{50} (24 hr) *Daphnia pulex* 2.00 mM (2).

IC_{50} *Saccharomyces cerevisiae* 1744 mg l^{-1} (3).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, mouse, rabbit 1010-1800 mg kg^{-1} (4-7).
LD_{50} intraperitoneal mouse, rabbit 280-500 mg kg^{-1} (6,8).

Sub-acute and sub-chronic data

TD_{Lo} (16 hr) oral child 81 mg kg^{-1} pulmonary, central nervous system and systemic effects (9).
TD_{Lo} (8 wk) oral human 2880 mg kg^{-1} ear and gastrointestinal tract effects (10).

Teratogenicity and reproductive effects

Salicylates readily cross the placenta and have been shown to be teratogenic in animals. Although some studies and anecdotal reports have implicated acetylsalicylic acid in the formation of congenital abnormalities, most large studies have failed to find any significant risk or evidence of teratogenicity (11-13).

Metabolism and toxicokinetics

Absorption of non-ionised acetylsalicylic acid occurs in the stomach. Acetylsalicylates and salicylates are also readily absorbed from the intestine. Hydrolysis to salicyclic acid occurs rapidly in the intestine and in the circulation. Salicylates are extensively bound to plasma proteins, acetylsalicylic acid to a lesser degree. Acetylsalicylic acid and salicylates are rapidly distributed to all body tissues; they appear in milk and cross the placenta. Major excretory products in the urine are free salicylic acid and glucuronide conjugates of salicylic and gensitic acids; the rate of urinary excretion increasing with pH, and is greatest at pH 7.5 and above (species not specified) (14,15).

Sensitisation

Some adults exhibit hypersensitivity to acetylsalicylic acid; symptoms include rhinitus, sinusitis, asthma and urticaria (14,16,17).
In a retrospective study in 86 patients with urticaria, confirmed by a positive challenge test in 84, acetylsalicylic acid was the responsible agent in one case (18).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537, TA1538 with and without metabolic activation negative (19).
Escherichia coli PQ37 with and without metabolic activation negative (20).
In vitro Chinese hamster V79 6TG metabolic co-operation assay negative (21).
In vitro mouse C3H/10T1/2 0.5-2 mg ml^{-1} cytotoxic effects demonstrated by decreased plating efficiency (22).

Other effects

Other adverse effects (human)

In humans symptomatic effects include nausea, dyspepsia, vomiting, dizziness, tinnitus, deafness, sweating and headache. Symptoms of severe intoxication, including overdosing, include hyperventilation, fever, restlessness, ketosis, respiratory alkalosis and metabolic acidosis. Depression of the central nervous system may lead to coma, cardiovascular collapse and respiratory failure. In children drowsiness and metabolic acidosis commonly occur. Has been implicated in Reye's syndrome in children (14).
Transient myopia occurred in a patient following the ingestion of 2.7 g acetylsalicylic acid (23).
The Boston Collaborative Drug Surveillence Program monitored consecutively 32,812 medical inpatients. Drug-induced deafness occurred in a dose-related manner in 32 of 2974 patients given acetylsalicylic acid (24).
Of 15,438 patients hospitalised between 1975 and 1982 none of the allergic skin reactions detected were attributed to acetylsalicylic acid among 984 recipients of the drug (25).
Thirteen cases of toxic epidermal necrolysis have been reported with the use of acetylsalicylic acid or methyl salicylate (26).

Any other adverse effects

Oral administration of 600 mg acetylsalicylic acid to five adult Sprague-Dawley rats, followed by fasting for 16 hr

caused urinary excretion of γ-glutamyl transpeptidase, *N*-acetyl-β-δ-glucosaminidase proteins, glucose and blood urea nitrogen after 24 hr, indicative of nephrotoxic effect (27).

Aspirin has been demonstrated to be an inhibitor of lung tumourigenesis in A/J mice. Lung tumours were induced by 4-(methylnitrosoamino)-1-(3-pyridyl)-1-butanone (NNK) administered in drinking water between week 0 and week 7. Groups of mice were fed acetylsalicyclic acid (ASA; 294 mg kg^{-1}), non-buffered Aspirin (294 mg kg^{-1}) or buffered Aspirin (294 mg $^{-1}$) in the diet from week –2 to the end of the bioassay (week 23). These doses are comparable to the maximal doses recommended for humans. ASA and non-buffered Aspirin reduced lung multiplicities by 60 and 62%, respectively. Inhibition by buffered Aspirin was not statistically significant (28).

Other comments

Caution required in administration to patients with renal or hepatic problems. Should not be given to patients suffering from haemophilia or other haemorrhagic disorders. Stable in dry air, but gradually hydrolyses in contact with moisture to acetic and salicylic acids (14).

The properties of acetylsalicylic acid including workplace experience, experimental toxicology, and human health effects have been reviewed (29-35).

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A29 1-acetyl-2-thiourea

$CH_3CONHCSNH_2$

$C_3H_6N_2OS$ **Mol. Wt.** 118.16 **CAS Registry No.** 591-08-2

Synonyms *N*-acetylthiourea; acetamide, *N*-(aminothiooxomethyl)

EINECS No. 209-699-9 **RTECS No.** YR 7700000

Uses Reagent for the synthesis of thiols.

Physical properties

M. Pt. 165-169°C

Solubility Organic solvents: ethanol, diethyl ether

Ecotoxicity

Bioaccumulation

The calculated bioconcentration factor of 0.9 indicates that environmental accumulation is unlikely (1).

Environmental fate

Abiotic removal

The hydrolytic $t_{1/2}$ is 2.7 hr at pH 9.6. Hydrolysis products include acetic acid and thiourea. Acetylthiourea may undergo direct photolysis in the environment (2,3).

Mammalian & avian toxicity

Acute data

LD_{Lo} oral rat and mouse 50-94 mg kg^{-1} (4,5).

LD_{50} intraperitoneal mouse 100 mg kg^{-1} (6).

References

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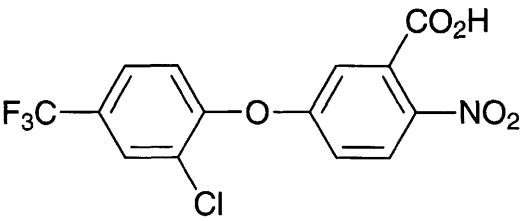
A30 acifluorfen



$C_{14}H_7ClF_3NO_5$ **Mol. Wt.** 361.66 **CAS Registry No.** 50594-66-6

Synonyms 5-(2-chloro-α,α,α-trifluoro-*p*-tolyloxy)-2-nitrobenzoic acid; 5-[2-chloro-4-(trifluoromethyl)phenoxy]-2-nitrobenzoic acid; Blazer

EINECS No. 256-634-5 **RTECS No.** DG 5643070

Uses Post-emergence herbicide.

Physical properties

M. Pt. 151-157°C **Partition coefficient** log P_{ow} –4.85 (calc.) (1) **Volatility** v.p. 7.52×10^{-8} mmHg at 20°C
Solubility Water: >120 mg l^{-1} at 25°C. Organic solvents: acetone, dichloromethane, ethanol, xylene

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) rainbow trout, bluegill sunfish 17, 62 mg l^{-1}, respectively (2).

Invertebrate toxicity
Non-toxic to bees (2).

Environmental fate

Degradation studies
Under anaerobic conditions in soil the acetamide, amino and denitro derivatives were formed, $t_{1/2}$ 1 month (1). In an aerobically incubated soil, $t_{1/2}$ 170 days. Dominant residue compounds after 6 months were unchanged acifluorfen and bound materials (1).

Abiotic removal
In soil, photodecomposes to non-herbicidal products, $t_{1/2}$ 30-60 days (2).
Stable to hydrolysis. No degradation observed in solutions at pH 3, pH 6 or pH 9 within a 28 day interval, temperature range 18-40°C. Under laboratory conditions with continuous exposure to light approximating natural sunlight, $t_{1/2}$ 92 hr. Primary degradation product detected in solution was the decarboxy derivative. In a 179 day study of silt loam soil, removal by leaching was negligible (1).

Adsorption and retention
During a 7-month incubation of organic soil dosed with 220 mg kg^{-1} of acifluorfen, 22% of the applied dose remained in the soil of which only 0.8% was found to be in the bound form. 75% of the dose was converted into aminoacifluorfen of which 60% was extractable and 15% remained bound to the soil. Most of the bound aminoacifluorfen was associated with the humin fraction of the soil (3).

Mammalian & avian toxicity

Acute data
LD_{50} oral mallard duck 2821 mg kg^{-1} (2).
LD_{50} oral bobwhite quail 325 mg kg^{-1} (2).

LD_{50} oral rat, mice 1370-2050 mg kg^{-1} (2).
LD_{50} (4 hr) inhalation rat >6.9 mg l^{-1} (2).
LD_{50} percutaneous rabbit >2000 mg kg^{-1} (2).

Sub-acute and sub-chronic data
LC_{50} (8 day) oral bobwhite quail, mallard duck >10 g kg^{-1} in diet (2).

Carcinogenicity and chronic effects
Oral ♂, ♀ B6C3F1 mice (18 month) 0, 625, 1250, 2500 ppm in diet induced benign and malignant liver tumours in both sexes and stomach papillomas in ♀ mice (4).
Oral ♂, ♀ CR-CD1 mice (2 yr) 0, 7.5, 45, 270 ppm induced benign and malignant liver tumours in both sexes (5).
Oral F344 rats (2 yr) 0, 25, 150, 500, 2500, 5000 ppm in diet. High-dose animals suffered increased mortality and reduced body weight gain, increases in liver weight and liver and renal enzyme activities (alkaline phosphatase, blood urea nitrogen and creatine), renal changes (nephritis, pyelonephritis and glomerulonephritis), a reduction in testes size and stomach ulcers. Lowest no-effect-dose 500 ppm (5).

Metabolism and toxicokinetics
Oral rat acifluorfen was rapidly and completely absorbed from the gastrointestinal tract (70-90%) within 96 hr. No unusual organ or tissue accumulation of acifluorfen or its metabolites occurred. 46-82% excreted via the urine as unchanged acifluorfen (minor amounts of amine and glucuronide moieties detected) and 5-41% via the faeces, majority as amine metabolite with minor amounts of unchanged acifluorfen and acetamide (4).

Irritancy
Severe eye irritant and moderate skin irritant in rabbits (2).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537, TA1538 with and without metabolic activation negative (1).
Saccharomyces cerevisiae D5 DNA damage (mitotic recombination) positive (5).
Saccharomyces cerevisiae D4 with and without metabolic activation negative (1).
In vitro rodent hepatocytes unscheduled DNA synthesis negative (5).
Drosophila melanogaster chromosomal aberrations positive (5).
In vivo rat bone marrow and mouse lymphoma chromosome aberrations and gene mutation negative (5).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides and related products: maximum admissible concentration 0.1 $\mu g\ l^{-1}$ (6).
Included in Schedule 6 (Release Into Land: Prescribed Substances) of Statutory Instrument No. 472, 1991 (7).

Other comments

Extensive animal toxicity studies have been carried out using acifluorfen sodium (CAS no. 62476-59-9) (1).
Metabolic pathways reviewed (8).

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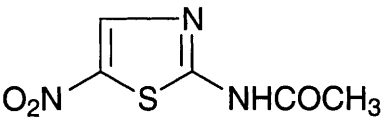
A31 acinitrazole



$C_5H_5N_3O_3S$ **Mol. Wt.** 187.18 **CAS Registry No.** 140-40-9

Synonyms aminitrozole; *N*-(5-nitro-2-thiazolyl)acetamide; 2-acetamido-5-nitrothiazole; 2-acetylamino-5-nitrothiazole; acetyl enheptin

EINECS No. 205-414-7 **RTECS No.** XJ 1570000

Uses Used as an antibacterial agent and in veterinary medicine.

Physical properties

M. Pt. 264-265°C

Mammalian & avian toxicity

Acute data

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

LD_{50} oral dog 125 mg kg^{-1} (2).

Genotoxicity

Salmonella typhimurium TA100 and *Klebsiella pneumoniae* with and without metabolic activation positive (3).

In vivo oral administration for mouse bone marrow micronucleus test, bone marrow depression observed.

Acinitrazole was reported to be extremely toxic (4).

Other effects

Any other adverse effects

At toxic concentration in unspecified species caused blood cell count changes and weight loss (1,2).

References

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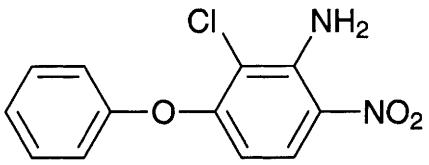
A32 aclonifen



$C_{12}H_9ClN_2O_3$ **Mol. Wt.** 264.67 **CAS Registry No.** 74070-46-5

Synonyms 2-chloro-6-nitro-3-phenoxyaniline; 2-chloro-6-nitro-3-phenoxybenzenamine

EINECS No. 277-704-1 **RTECS No.** CX 9858650

Uses Pre-emergence herbicide.

Physical properties

M. Pt. 81-82°C **Volatility** v.p. 6.8×10^{-6} mmHg at 20°C

Solubility Water: 2.5 mg l^{-1} at 20°C. Organic solvents: hexane, methanol, toluene

Occupational exposure

Supply classification dangerous for the environment

Risk phrases Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment (R50/53)

Safety phrases This material and/or its container must be disposed of as hazardous waste – Avoid release to the environment. Refer to special instructions/safety data sheet (S60, S61)

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) rainbow trout, carp 0.67, 1.7 mg l^{-1}, respectively (1).

Invertebrate toxicity

EC_{50} (48 hr) *Daphnia* 2.5 mg l^{-1} (1).

LD_{50} oral >100 mg bee^{-1} (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral canary >15,000 mg kg^{-1} (1).

LD_{50} oral Japanese quail >15,000 mg kg^{-1} (1).

LD_{50} oral rat, mouse >5000 mg kg^{-1} (1).

LC_{50} (4 hr) inhalation rat >5.06 mg l^{-1} (1).

LD_{50} percutaneous rat >5000 mg kg^{-1} (1).

Sub-acute and sub-chronic data

In a 90-day feeding study in rats and a 180-day study in dogs, the no-observed-effect levels were 28 and 3 mg kg^{-1} day^{-1}, respectively (1).

Teratogenicity and reproductive effects

Not embryotoxic or teratogenic in rats (1).

Did not affect reproduction in rats at 2000 ppm over two generations (1).

Metabolism and toxicokinetics

In rats, following oral administration, 62-65% was excreted in urine within 24 hr, principally as polar compounds (1).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides and related products: maximum admissible concentration 0.1 μg l^{-1} (2).
Included in Schedule 6 (Release Into Land: Prescribed Substances) of Statutory Instrument No. 472, 1991 (3).

References

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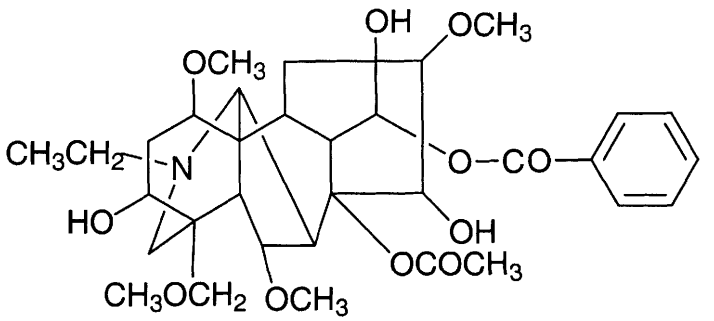
A33 aconitine



$C_{34}H_{47}NO_{11}$ **Mol. Wt.** 645.75 **CAS Registry No.** 302-27-2

Synonyms 16-ethyl-1,16,19-trimethoxy-4-(methoxymethyl)aconitane-3,8,10,11,18-pentol 8-acetate 10-benzoate; acetyl benzoyl aconine

EINECS No. 206-121-7 **RTECS No.** AR 5960000

Uses An antipyretic drug.
Occurrence Several isomers from *Aconitum napellus* L., Ranunculaceae and other aconites.

Physical properties

M. Pt. 204°C
Solubility Water: 300 mg l^{-1}. Organic solvents: absolute ethanol, benzene, chloroform

Occupational exposure

Supply classification very toxic
Risk phrases Very toxic by inhalation and if swallowed (R26/28)
Safety phrases Keep locked up and out of the reach of children (if sold to general public) – Avoid contact with the skin – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S24, S45)

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse 1 mg kg^{-1} (1).
LD_{50} intravenous rat 80 μg kg^{-1} (2).
LD_{Lo} intraperitoneal rat 125 μg kg^{-1} (3).
LD_{Lo} subcutaneous rabbit 131 μg kg^{-1} (4).

Sub-acute and sub-chronic data

LD_{Lo} (duration unspecified) oral human 28 mg kg^{-1} central nervous system and gastrointestinal tract effects (5).

Other effects

Other adverse effects (human)

Moderately toxic doses produce a tingling of the tongue, mouth, stomach and skin followed by numbness and anaesthesia. Aconitine has variable effects on the heart leading to heart failure. It also affects the central nervous system. Symptoms of aconitine poisoning may appear almost immediately and are rarely delayed beyond 1 hr. In fatal poisoning death usually occurs within 6 hr, although with large doses it may be instantaneous. Symptomatic effects include gastrointestinal disturbances, irregular pulse, difficult respiration, cold, clammy and livid skin, muscular weakness, incoordination and vertigo (6).

Other comments

Toxicology and arrhythmogenic properties reviewed (7).

References

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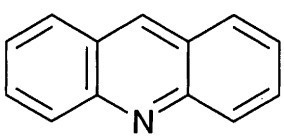
A34 acridine



$C_{13}H_9N$ **Mol. Wt.** 179.22 **CAS Registry No.** 260-94-6

Synonyms 10-azaanthracene; 2,3,5,6-dibenzopyridine; 2,3-benzoquinoline; benzo[*b*]quinoline; dibenzo[*b,e*]pyridine

EINECS No. 205-971-6 **RTECS No.** AR 7175000

Uses Intermediate in manufacture of dyestuffs, alkaloids and antibacterials.
Occurrence In coal tar, wood preservative sludge and coke oven emissions.

Physical properties

M. Pt. 110.5°C **B. Pt.** 346°C **Specific gravity** 1.005 at 19.7°C **Partition coefficient** log P_{ow} 3.40
Volatility v.p. 1 mmHg at 129.4°C
Solubility Organic solvents: benzene, carbon disulfide, diethyl ether, ethanol, hydrocarbons

Occupational exposure

UN No. 2713 **HAZCHEM Code** 1X **Conveyance classification** toxic substance

Ecotoxicity

Fish toxicity
Trout, bluegill sunfish, goldfish 5 ppm death occurred in 4-6 hr (1).

Invertebrate toxicity
LC_{50} (24 hr) *Daphnia pulex* 2.9 mg l^{-1} (2).
EC_{50} (5-30 min) *Photobacterium phosphoreum* 7.47 mg l^{-1} Microtox test (3).
LC_{100} (16 hr, dark) *Tetrahymena pyriformis* 0.2 mM, no-observed-effect concentration (16 hr, dark) 0.059 mM (4).

Bioaccumulation
Daphnia pulex bioconcentration factor 29.6 (2).
Fathead minnow bioconcentration factors 125-874. Depuration was rapid, possible pathways for uptake include interaction, ingestion of contaminated zooplankton and invertebrates and direct uptake (5).
Guppy bioconcentration factor 1300 (6).

Environmental fate

Degradation studies
Using three different inocula, degradation was investigated under methanogenic, denitrifying and sulfate-reducing conditions at 1-6 μg ml^{-1} in 1-3 wk (7).

Mammalian & avian toxicity

Acute data
LD_{50} subcutaneous mouse 400 mg kg^{-1} (8).
LD_{50} intravenous rabbit 100 mg kg^{-1} (8).

Sub-acute and sub-chronic data
The sub-chronic toxicity of acridine was investigated in rats following dietary exposure at 0, 1, 10, 100, and 500 ppm for 13 wk. The growth rate and food consumption were not affected by treatment and no clinical signs of toxicity were observed. There was a slight but significant decrease in spleen weight, both in absolute terms and as a percentage of body weight, in the 500 ppm ♂ and a slight increase in absolute thymus weight in the ♀ of the same dose group. Both hepatic ethoxyresorufin O-deethylase and pentoxyresorufin O-dealkylase activities were slightly, but significantly, elevated in ♀ in the 500 ppm dose group. No haematological or other biochemical changes were observed. Females also displayed dose-related increases in inorganic phosphate and uric acid levels. Treatment-related histopathological changes were seen in the thyroid, liver and kidney and included hepatic anisokaryosis and vesiculation of nuclei and glomerular adhesions, reticulin sclerosis, and nuclear pyknosis in the kidney. Residue data showed a dose-dependent accumulation of acridine in the liver, kidney and adipose with the highest concentration being found in the fat of the 500 ppm dose group. Based on these data, the no-observable-adverse-effect level of acridine was judged to be 100 ppm or 12 mg kg^{-1} day^{-1} (9).

Irritancy
Severe irritant to eyes, skin and respiratory tract (10,11).

Sensitisation
It is a skin photosensitiser (11).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537, TA1538 with and without metabolic activation positive (12). *Saccharomyces cerevisiae* forward mutation studies non-definite (12).

Other comments

US EPA suggested ambient air limit of 162 μg m^{-3} and an ambient level in water of 800 μg l^{-1} (11). Toxicology and genotoxicity reviewed (12,13).

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A35 acrolein

$$CH_2{=}CHCHO$$

C_3H_4O **Mol. Wt.** 56.06 **CAS Registry No.** 107-02-8

Synonyms acrylaldehyde; allyl aldehyde; 2-propenal; prop-2-enal; ethylene aldehyde; acrylic aldehyde

EINECS No. 203-453-4 **RTECS No.** AS 1050000

Uses In the manufacture of glycerol and glutaraldehyde. Aquatic herbicide and fungicide used in water and wastewater treatment. Used in military poison gas mixtures, manufacture of plastics perfumes and warning agent in methyl chloride refrigerant.

Physical properties

M. Pt. –87°C **B. Pt.** 52°C **Flash point** –26°C **Specific gravity** 0.843 at 20°C
Partition coefficient log P_{ow} 0.101 (1) **Volatility** v.p. 210 mmHg at 20°C ; v.den. 1.9
Solubility Water: 20.6% at 20°C. Organic solvents: acetone, diethyl ether, ethanol

Occupational exposure

FR-VLE 0.1 ppm (0.25 mg m^{-3})
JP-OEL 0.1 ppm (0.23 mg m^{-3})
SE-LEVL 0.1 ppm (0.2 mg m^{-3}) **SE-STEL** 0.3 ppm (0.7 mg m^{-3})
UK-LTEL 0.1 ppm (0.23 mg m^{-3}) **UK-STEL** 0.3 ppm (0.7 mg m^{-3}) **US-STEL** ceiling limit 0.1 ppm

UN No. 1092 **HAZCHEM Code** 2WE **Conveyance classification** toxic substance, danger of fire (flammable liquid)

Supply classification highly flammable, toxic
Risk phrases Highly flammable – Toxic if swallowed – Very toxic by inhalation – Causes burns (R11, R25, R26, R34)
Safety phrases Keep locked up and out of the reach of children (if sold to general public) – Keep in a cool well ventilated place away from oxidising agents, acids and bases – 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 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, S3/9/14, S26, S36/37/39, S38, S45)

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) bluegill sunfish, goldfish 0.04-0.31 mg l^{-1} (2-4).
Death occurred at 30 mg l^{-1} for stickleback and steelhead trout in 1-2 hr and 0-1 hr, respectively (5).
5 ppm of acrolein administered to trout, bluegill sunfish, perch and goldfish caused death in 2-6 hr (6).
LC_{50} (4 day) fathead minnow 20 µg l^{-1} (7).
LC_{50} (24, 48 hr) harlequin fish 0.14-0.06 mg l^{-1}. Estimated lethal threshold 0.03 mg l^{-1} (8).
Bluegill sunfish (*Lepomis machrochirus*) and channel catfish (*Ictalurus punctatus*) exposed under static conditions to two applications 0.02 ppm, with 7 days between the two dosings. Glycidol and 1,3-propanediol were the major metabolites found in the edible tissue of catfish and bluegill, respectively, 24 hr after the second dosing. Acrolein and its oxidative and reductive metabolites, acrylic acid and allyl alcohol, were not detected as metabolism is very rapid in the edible tissues (9).

Invertebrate toxicity
EC_{50} (24-48 hr) *Daphnia magna* 0.23-0.083 mg l^{-1} (conditions unspecified) (10).
Cell multiplication inhibition test, *Pseudomonas putida* 0.21 mg l^{-1}, *Microcystis aeruginosa* 0.04 mg l^{-1}, *Uronema parduczi* 0.44 mg l^{-1} (11).
After a 24 hr exposure to 10 mg l^{-1}, 98% of adult snails and 100% of snail embryos died (12).
EC_{50} (5 min) *Photobacterium phosphoreum* 0.674 mg l^{-1} Microtox test (13).
Northern crayfish (*Orconectes virilis*) and unionacean clam (*Elliptio complanata*) were exposed under static conditions to two applications of 0.1 ppm, with 7 days between the two dosings. Glycerol and glyceric acid were the major metabolites found in the edible tissue of crayfish and clam, respectively, 24 hr after the second dosing. Acrolein and its oxidative and reductive metabolites, acrylic acid and allyl alcohol, were not detected as metabolism is very rapid in the edible tissues (9).

Bioaccumulation
Bioconcentration factor has been measured as 344 in bluegill sunfish (14).
The calculated bioconcentration factor 0.6 suggests that bioaccumulation in aquatic organisms is not significant (15).

Environmental fate

Degradation studies
Non-biodegradable (16).
Under aerobic conditions, acrolein undergoes reversible hydration to β-hydroxypropionaldehyde $t_{1/2}$ 21 days (17).
BOD_5 no oxygen removal (18).
No evidence of degradation was observed for 50 mg l^{-1} of acrolein as organic carbon when incubated for 8 wk in a 10% anaerobic sludge inoculum (19).

Abiotic removal
Evaporates rapidly from dry soil surfaces. In the atmosphere, acrolein reacts photochemically with hydroxyl radicals ($t_{1/2}$ 10-13 hr) to produce carbon dioxide, formaldehyde and glycoaldehyde. When nitrogen oxides are present, products include peroxynitrate and nitric acid (2).
Estimated $t_{1/2}$ 18 days with ozone (20).

Adsorption and retention

The low soil adsorption coefficient of 24 suggests that acrolein will be unlikely to adsorb to suspended solids and sediments in water and will be highly mobile in soil (3,21).

Mammalian & avian toxicity

Acute data

LD_{50} oral rabbit, mouse 7-40 mg kg^{-1} (22,23).
LC_{Lo} (6 hr) inhalation rabbit 24 mg m^{-3} (24).
LC_{Lo} (10 min) inhalation human 153 ppm (25).
LD_{50} dermal rabbit 562 mg kg^{-1} (26).
LD_{50} intraperitoneal rat, mouse 4-9 mg kg^{-1} (27,28).

Sub-acute and sub-chronic data

Inhalation rat (3 wk) 0-3 ppm 6 hr day^{-1} 5 day wk^{-1} induced exfoliation, erosion and necrosis of the respiratory epithelium and squamous metaplasia. Body and spleen weights decreased for rats exposed to 3 ppm (29).
Dogs were administered gelatin capsules containing a 0.1% aqueous solution of acrolein equivalent to 0.1, 0.5 or 1.5 mg kg^{-1} day^{-1}, 7 days wk^{-1} for 53 wk; after 4 wk the highest dose was increased to 2 mg kg^{-1} day^{-1}. The major effect observed was vomiting after dosing. This was dose-dependent and the frequency decreased with time, suggesting an adaptive effect. One mid-dose ♀ died during the test of vomitus aspiration. Serum albumin, calcium and total protein value were depressed in high-dose animals (30).

Carcinogenicity and chronic effects

No adequate evidence for carcinogenicity to humans, limited evidence for carcinogenicity to animals, IARC classification group 3 (31).
Oral rats, hamsters (2 yr) (unspecified dose) in drinking water. The authors report a non-significant increase in the incidence of neoplasms, target tissues included liver, uterus and thyroid gland (32).
Oral CD-1 mice (18 months) 0-2 or 4.5 mg kg^{-1} day^{-1}. A decreased body weight gain was seen in all treated mice and ♂ mice showed increased mortality, particularly at the highest dose level. Gross and microscopic lesions were not obviously dose-dependent and acrolein was not considered oncogenic (33).
Gavage rat (18 months) 0.0, 0.05, 0.5 or 2.5 mg kg^{-1} in water. The only effects noted in treated rats that were statistically different from controls were consistent depression of creatinine phosphokinase levels, and consistent increases in early cumulative mortalities in both ♂ and ♀ (34).

Teratogenicity and reproductive effects

Acrolein is a toxic and reactive metabolite of the widely used anticancer drug and known teratogen cyclophosphamide. To determine if acrolein was responsible for the production of limb malformations, excised limbs were exposed to 10 or 50 μg ml^{-1} acrolein for the first 20 hr of a 6-day culture period. Exposure to acrolein produced malformed limbs, had little effect on growth parameters, and did not effect alkaline phosphatase and creatine phosphatase activity in excised limbs (35).
In vitro rat embryo caused 25% and 48% deaths at 50 and 100 μg, respectively and 46% incidence of malformations and growth retardation at 100 μg (36).
Pregnant New Zealand white rabbits were administered 0.0, 0.1, 0.75 or 2 mg kg^{-1} day^{-1} via a stomach tube on days 7-19 of gestation then subjected to Caesarean sectioning on day 29. Three does died during the study. In the high-dose group transient effects on body weight gain and feed consumption were noted with knock-on effects in both foetal and maternal weights. Foetal malformations were distributed evenly among all groups and were consistent with controls. Resorptions were elevated in the high-dose group but the effect was not statistically significant. At higher doses (4 and 6 mg kg^{-1} day^{-1}) high incidences of maternal mortality, spontaneous abortion, resorptions, gastric ulceration and/or sloughing of the gastric mucosa were noted (37).
♂ and ♀ rats were intubated with 0, 1, 3 or 6 mg kg^{-1} day^{-1} for 70 days. The rats (F_0 generation) were then assigned to a 21-day period of cohabitation and ♀ were dosed through cohabitation, gesation and lactation. F_1 generation rats were chosen from the pups and subjected to a similar regime resulting in F_2 generation pups. Reproductive parameters were unaffected by the treatment with the exception of reduced pup weights in the F_1 generation at the high-dose level (6 mg kg^{-1}). Gastric lesions were observed in high-dose animals and some rats treated with 3 mg kg^{-1}. Effects on body weight gain were frequently seen in high-dose animals and were

statistically significant in mid-dose animals. An increase in mortality was seen with all high-dose animals compared to controls (38).

Metabolism and toxicokinetics

Exposure of pulmonary artery endothelial cells in culture to acrolein caused alterations in plasma membrane-dependent transport leading to reduced availability of precursor amino acids for protein synthesis (39).

Irritancy

Dermal rabbit (24 hr) 500 mg caused severe irritation, while 50 μg instilled into rabbit eye for 24 hr caused severe irritation (40).

Sensitisation

The alleged dermal sensitisation properties of acrolein were evaluated by its ability to induce allergic contact dermatitis. Challenge treatment with acrolein (species unspecified) failed to produce positive skin reactions (41).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537 with and without metabolic activation positive (42).
In vitro Chinese hamster V79 cells with and without metabolic activation positive (43).
Chinese hamster ovary HGPRT assay with and without metabolic activation, results showed acrolein was very cytotoxic but no significant mutagenic response observed (44).
Drosophila melanogaster sex-linked recessive level test positive. Studies using several metabolic modifiers also showed that acrolein is not only a direct mutagen but is also transformed, by oxidative activities of cytochrome P-450 after glutathione conjugation, into an active metabolite, possibly glycidaldehyde (45).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides and related products: maximum admissible concentration 0.1 μg l^{-1} (46).
Included in Schedule 6 (Release Into Land: Prescribed Substances) of Statutory Instrument No. 472, 1991 (47).

Other comments

Occurs in exhaust gas emissions, tobacco smoke, wastewater effluents and as a photooxidation product of hydrocarbon pollutants (2).
Volatile component of essential oil extracted from the wood of oak trees. Has been detected in emissions from plants manufacturing acrylic acid and coffee roasting (3).
Acrolein residues have been detected in some foodstuffs (3).
Human health effects, experimental toxicology, ecotoxicology, physico-chemical properties, environmental effects, exposure levels, epidemiology and workplace experience reviewed (48-52).
Health and toxicological information reviewed (53).
Acrolein is produced in the pyrolysis of animal fats.

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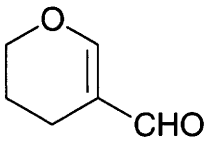
A36 acrolein dimer



$C_6H_8O_2$ **Mol. Wt.** 112.13 **CAS Registry No.** 100-73-2

Synonyms 2*H*-pyrancarboxaldehyde, 3,4-dihydro-; pyranaldehyde; 5-hexanal, 2,6-epoxy; 2-formyl-3,4-dihydro-2*H*-pyran; 3,4-dihydro-2*H*-pyran-2-carboxaldehyde

EINECS No. 202-884-5 **RTECS No.** UP 6825000

Uses Intermediate for pharmaceuticals and dyestuffs.

Physical properties

B. Pt. 153°C **Flash point** 48°C (open cup) **Specific gravity** 1.0775 at 20°C with respect to water at 4°C **Partition coefficient** log P_{ow} 1.0775 at 20°C

Occupational exposure

UN No. 2607 **HAZCHEM Code** 2Y **Conveyance classification** flammable liquid

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 4920 mg kg^{-1} (1).

Irritancy

Dermal rabbit 500 mg caused mild irritation, while 750 µg instilled into rabbit eye caused severe irritation (1,2).

References

1. *Arch. Ind. Hyg. Occ. Med.* 1954, **10**, 61.
2. *Union Carbide Data Sheet* 1965, Union Carbide Corp., New York, NY, USA

A37 acrolein diacetate

$$(CH_3CO_2)_2CHCH{=}CH_2$$

$C_7H_{10}O_4$ **Mol. Wt.** 158.15 **CAS Registry No.** 869-29-4

Synonyms 2-propene-1,1-diylbis(acetate); 2-propene-1,1-diol, diacetate; allylidene acetate; allylidene diacetate

EINECS No. 212-789-0 **RTECS No.** UC 9625000

Physical properties

M. Pt. –36.6°C **B. Pt.** 107°C at 50 mmHg **Specific gravity** 1.0749 at 20°C **Volatility** v.den. 5.46

Mammalian & avian toxicity

Acute data

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

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

Irritancy

Dermal rabbit 500 mg caused severe irritation (duration of exposure unspecified) (2).

10 mg instilled into the eye of a rabbit caused severe irritation (duration unspecified) (2).

References

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2. *Union Carbide Data Sheet* 27 December 1971

A38 acrolein dibromide

$CH_2BrCHBrCHO$

$C_3H_4Br_2O$ **Mol. Wt.** 215.87 **CAS Registry No.** 5221-17-0

Synonyms 2,3-dibromopropionaldehyde; 2,3-dibromopropanal

EINECS No. 226-017-5 **RTECS No.** UE 0800000

Physical properties

B. Pt. 73-75°C at 10 mmHg **Specific gravity** 2.198 at 15°C

Solubility Organic solvents: diethyl ether, dimethyl sulfoxide

Mammalian & avian toxicity

Acute data

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

LD_{50} intravenous mouse 56 mg kg^{-1} (2).

Genotoxicity

Salmonella typhimurium TA100 with and without metabolic activation positive (3).

References

1. *J. Agric. Food Chem.* 1982, **30**, 627.
2. US Army Armament Research and Development Command, Chemical Systems Laboratory, Report No 02408, NIOSH Exchange Chemicals, Aberdeen Proving Ground.
3. Rosen, J. D. et al *Mutat. Res.* 1980, **78**(2), 113-119

A39 acrolein diethyl acetal

$$(CH_3CH_2O)_2CHCH{=}CH_2$$

$C_7H_{14}O_2$ **Mol. Wt.** 130.19 **CAS Registry No.** 3054-95-3

Synonyms 3,3-diethoxypropene; 3,3-diethoxy-1-propene; acrolein acetal; acrylaldehyde diethyl acetal; propenal diethyl acetal

EINECS No. 221-276-0 **RTECS No.** AS 1370000

Physical properties

B. Pt. 125°C **Flash point** 4°C **Specific gravity** 0.8543 at 15°C
Solubility Water: miscible. Organic solvents: diethyl ether, ethanol

Occupational exposure

UN No. 2374 **HAZCHEM Code** 3YE **Conveyance classification** flammable liquid

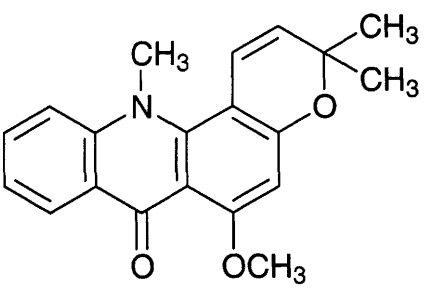
Genotoxicity

Salmonella typhimurium TA1535 with metabolic activation positive (1).

References

1. Lijinsky, W. et al *Teratog., Carcinog., Mutagen.* 1980, **1**(3), 259-267

A40 acronycine



$C_{20}H_{19}NO_3$ **Mol. Wt.** 321.38 **CAS Registry No.** 7008-42-6

Synonyms 3,12-dihydro-6-methoxy-3,3,12-trimethyl-7*H*-pyrano[2,3-*c*]acridin-7-one; acronine; acromycine

RTECS No. UQ 0330000

Uses Antineoplastic agent with broad-spectrum antitumour activity.
Occurrence Alkaloid from *Acroynchia baueri* and *Melicope leptococca*.

Physical properties

M. Pt. 175-176°C

Ecotoxicity

Fish toxicity

LC_{Lo} (24-96 hr) harlequin fish 850-200 mg l^{-1} (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral, intraperitoneal mouse 522-613 mg kg^{-1} (2).

Metabolism and toxicokinetics

Acronycine is metabolised by humans and excreted in urine mainly as the 9-hydroxy- and 11-hydroxyacronycine compounds (3).

References

1. Svoboda, G. H. et al *J. Pharm. Sci.* 1966, **55**, 758-768.
2. *National Cancer Inst. Screening Program Data Summary* 1978, NCI-CG-TR, 49.
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A41 acrylamide

$$H_2C{=}CHCONH_2$$

C_3H_5NO **Mol. Wt.** 71.08 **CAS Registry No.** 79-06-1

Synonyms acrylic amide; ethylene carboxamide; propenamide; 2-propenamide

EINECS No. 201-173-7 **RTECS No.** AS 3325000

Uses Intermediate in polymer manufacture, especially polyacrylamides which are used in the treatment of municipal drinking water and wastewater. Flocculant. In the pulp and paper, textile, and paints and coatings industries. Has been used as thickening agent in cosmetics and toiletries.

Occurrence Occurs in discharges from water treatment plants which use polyacrylamides and flocculants.

Physical properties

M. Pt. 84.5°C **B. Pt.** 125°C at 25 mmHg **Flash point** 138°C **Specific gravity** 1.122 at 30°C with respect to water at 4°C **Volatility** v.p. 1.6 mmHg at 84.5°C ; v.den. 2.45

Solubility Water: 2155 g l^{-1} at 30°C. Organic solvents: acetone, benzene, chloroform, ethanol, ethyl acetate, methanol

Occupational exposure

FR-VME 0.1 ppm (0.3 mg m^{-3})
JP-OEL 0.3 mg m^{-3}
SE-LEVL 0.03 mg m^{-3} **SE-STEL** 0.1 mg m^{-3}
UK-LTEL MEL 0.3 mg m^{-3}
US-TWA 0.03 mg m^{-3}

UN No. 2074 **HAZCHEM Code** 2WE **Conveyance classification** toxic substance
Supply classification toxic
Risk phrases May cause cancer – May cause heritable genetic damage – Toxic in contact with skin and if swallowed – Toxic: danger of serious damage to health by prolonged exposure through inhalation, in contact with skin and if swallowed (R45, R46, R24/25, R48/23/24/25)

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

Ecotoxicity

Fish toxicity

LC_{50} (24-96 hr) brown trout, harlequin fish 130-460 mg l^{-1} (1,2).

Rainbow trout exposed to waterborne acrylamide monomer 0-50 mg l^{-1} for 14 days, reversible dose-related histological lesions detected in the liver, characterised by necrosis around the central vein (3).

Bioaccumulation

Fingerling trout bioconcentration factor in carcass and viscera were 0.86 and 1.12, respectively, at 12°C for 72 hr under static conditions, indicating that no appreciable bioaccumulation occurred. In freshwater, acrylamide levels declined to 75% after 96 hr (4).

Environmental fate

Degradation studies

In 14 days under waterlogged conditions 64-89% degradation occurred (5).

In 56 days, no degradation occurred when acrylamide was incubated with digester sludge (6).

Complete degradation occurred in filtered river water in 10-12 days. In soil, 100% degradation occurred in 6 days with 60% converted into carbon dioxide (7).

BOD_5 standard dilution technique, acclimated sludge oxygen 0.97 mg l^{-1} consumed at 20°C (1).

BOD_5 69-75% theoretical BOD obtained using acclimated sewage seed (8,9).

In river and estuary water with and without added sediment, 0.5 and 10 ppm acrylamide was completely degraded within 8 days (10).

Batch cultures of *Pseudomonas* spp. and *Xanthomonas multiphilia* (isolated from herbicide-contaminated soil samples) capable of utilising acrylamide as the sole source of C and N completely degraded 62.8 mM acrylamide to acrylic acid and NH_3 in 24 and 48 hr, respectively. Cells of the isolates immobilised in Ca alginate degraded acrylamide to acrylic acid and NH_3 in <6 hr (11).

Abiotic removal

Acrylamide does not absorb light at >250 nm, therefore direct photolysis is not expected (12).

Vapour phase acrylamide reacts with photochemically produced hydroxyl radicals $t_{1/2}$ 6.6 hr (13).

Adsorption and retention

Activated carbon 8 mg l^{-1}, pH 5.0, 0.5 hr 13% removed (1).

No significant adsorption occurred in short-term experiments on natural sediments, industrial and sewage sludges, clays, peat or synthetic resins (14).

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse, rat 107, 170 mg kg^{-1}, respectively (15,16).

LD_{50} intraperitoneal mouse 170 mg kg^{-1} (17).

Sub-acute and sub-chronic data

In vitro rats, acrylamide inhibited creatine kinase activity from brain and sciatic nerve. *In vivo* rats (8 day) 50 mg kg^{-1} day^{-1} caused paralysis of hind limbs and suppressed creatine kinase activity in the cerebrum, cerebellum, spinal cord and muscle (18).

Carcinogenicity and chronic effects

No adequate evidence for carcinogenicity to humans, sufficient evidence for carcinogenicity to animals, IARC classification group 2B (19).

Fischer 344 rats (2 yr) 0, 0.01, 0.1, 0.5 or 2 mg kg^{-1} in drinking water. Increased incidence of adrenal pheochromocytomas, mesotheliomas of the tunica of the testes and follicular adenomas of the thyroid were observed in ♂. In ♀, increased incidences of pituitary adenomas, thyroid follicular tumours, mammary adenomas

and adenocarcinomas, oral cavity papillomas, uterine adenocarcinomas and clitoral gland adenomas were reported. In ♀ rats tumour of the central nervous system of glial origin or glial proliferation suggestive of early tumour were also increased (20).

Teratogenicity and reproductive effects

Gavage mice (6-17 day gestation) 0, 3, 15 or 45 mg kg^{-1} day^{-1}, gavage rats (6-20 day gestation) 0, 2.5, 7.5, 15 mg kg^{-1} day^{-1}. Maternal toxicity effects, including reduced body weight gain, were observed in both species, while hindlimb splaying occurred in mice only. Embryo/foetal toxicity was not observed in rats but foetal weight was reduced in mice given 45 mg kg^{-1} day^{-1}. No increase in incidence of malformations was observed but the incidence of variations, predominantly extra rib, increased with the dose (21).

Swiss CD-1 mice were tested in a modified Reproductive Assessment by Continuous Breeding Protocol. Exposure to dose levels in water of 30 ppm (9.2 mg kg^{-1}) resulted in slight reproductive toxicity (decreased number of pups in litter and decreased spermatid head counts) and increased post-implantation loss (dominant lethal effect) in the absence of demonstrable neurotoxicity for theF0 animals. F1 animals were more severely affected than the F0 animals, exhibiting a more profound effect on fertility in the presence of slight neurotoxicity (decreased grip) strength in ♂ mice (22).

Acute oral mouse 100 or 150 mg kg^{-1}, effects to testis were studied for 10 days after treatment. Severe initial testicular damage was repaired 7-10 days after treatment. Vulnerable stage identified as Golgi phase I-III (23).

The developmental consequences of paternal exposure to acrylamide (50 mg kg^{-1} intraperitoneally for 5 days) was assessed in pre-implantation mouse embryos. A significant increase in morphological abnormalities was observed. More than 80% of abnormal embryos had at least one fragmented nucleus. Morphologically normal and abnormal embryos showed a 10- and 20- fold increase in micronuclei, respectively (24).

Metabolism and toxicokinetics

Intravenous rat 10 mg kg^{-1} distributed rapidly to tissues. Initial absorption in liver, kidney, testes, plasma and fat cells. Concentration in blood remained constant at 12% of the initial dose for 7 days, while plasma concentrations were eliminated readily. Less than 2% of initial dose was excreted unchanged in urine and bile (25).

Whole-body autoradiographs of mice administered radiolabelled compound at 120 mg kg^{-1} orally revealed accumulated radioactivity in the gastrointestinal tract, liver, pancreas, testis, gall bladder, brain, epithelia of oral cavity, oesophagus and bronchi (26).

Pregnant intravenous rat, rabbit, dog, pig 5 or 10 mg kg^{-1} crossed the placenta in all four species within 1-2 hr (27).

Irritancy

Dermal rabbit (3 day) 50 mg caused mild irritation and 10 mg instilled in rabbit eye for 30 sec caused mild irritation (16).

100 mg instilled into rabbit eye for 24 hr caused moderate irritation (28).

Genotoxicity

Salmonella typhimurium TA98, TA100 with metabolic activation weakly positive (29).

Bacillus subtilis spore-rec assay 10-40 mg $disk^{-1}$ strongly positive (21).

In vitro mouse lymphoma L51178Y tk+/tk– without metabolic activation positive (30).

Mouse embryo spot test (18 day foetus) examined. Single treatment of 50-75 mg kg^{-1} to mice induced increased number of offspring with colour spots, indicating positive mutagen, and three treatments with 75 mg kg^{-1} caused tail kink, demonstrating teratogenic potential (31).

In vivo mouse bone marrow cells chromosomal aberrations and micronucleus assay positive (32).

Extensive *in vitro* investigations using Chinese hamster V79H3 and mouse BALB/c3T3 cells show that acrylamide seems to be a typical clastogenic rodent carcinogen without any gene mutation potential (33).

Cultured human HT1080 fibrosarcoma cells were exposed to 2.5, 5 and 10 mmol acrylamide for 4 hr. A concentration-dependant increase in the number of cells arrested in mitosis was observed (34).

Other effects

Other adverse effects (human)

In industry main route of contamination occurs via skin, though poisoning via inhalation and ingestion is possible (17,35).

Risk of irreversible nervous system damage, time delay of up to 8 yr before onset (16).

A study was undertaken of 71 acrylamide workers and 51 unexposed controls. Early symptoms of poisoning included weak legs, numb hands and feet, skin peeling from hands, impairment of vibration sensation in toes and loss of ankle reflexes. Three cases had cerebellar involvement followed by polyneuropathy due to heavy exposure. Total prevalence of acrylamide poisoning was 73.2% (36,37).

The mortality of 371 employees in acrylamide monomer and polymer production was studied for deaths from cancers of central nervous system, thyroid gland, other endocrine glands and mesotheliomas. Until 1982 a total of 29 deaths observed versus 38 expected. No statistically significant excesses were noted in the total cohort and no deaths were found for hypothesised sites of cancer. Total observed deaths from all cancers was 11 versus 7.9 expected; however, this was due entirely to cancers of respiratory system and digestive tract in workers with previous exposure to organic dyestuffs. The study does not support a relationship between exposure to acrylamide and overall mortality, total malignant neoplasms or any specific cancers (37).

Any other adverse effects

Can be absorbed through intact skin, mucous membranes, lung and gastrointestinal tract. Can cause central nervous system paralysis (species unspecified) (38,39).

Exposure of 4 monkeys, *Macaca fascicularis*, to prolonged intoxication with low levels of acrylamide caused a slow response across the spinal-medullary function. Associated morphological changes were preterminal accumulation of axonal neurofilaments without synaptic disruption in the nucleus. Short latency somatosensory response and axon morphology were reversible after 7 months of recovery. However, the extreme delay in onset of neurological dysfunction 940 days after administration of a presumed safe level of acrylamide exposure prompts the authors to conclude that permissible levels of human exposure should be reassessed (40).

Other comments

A single dose of 1 mg caused changes in the elements of the toad *Bufo regularis* Golgi complex, endoplasmic reticulum, ribosome granules, and glycogen particles and increased the number of mitochondria and their cristae. Profound alteration of protein synthesis in liver cells was observed (41).

Production, uses, environmental fate, and neurotoxicity reviewed (42).

Neurotoxicity, metabolism, developmental and reproductive effects, genotoxicity and carcinogenicity reviewed (43,44).

Rapid and exothermic polymerisation occurs at melting point.

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A42 acrylic acid

$$H_2C{=}CHCO_2H$$

$C_3H_4O_2$ **Mol. Wt.** 72.06 **CAS Registry No.** 79-10-7

Synonyms acroleic acid; ethylenecarboxylic acid; propene acid; 2-propenoic acid; vinylformic acid

EINECS No. 201-177-9 **RTECS No.** AS 4375000

Uses Intermediate in polymer manufacture. Also used as a tackifier and flocculant.

Occurrence Occurs in wastewater effluents as a by-product of propylene oxidation (1).

Physical properties

M. Pt. 13°C **B. Pt.** 141°C (polymerises) **Flash point** 68°C (open cup) **Specific gravity** 1.062 at 16°C

Partition coefficient log P_{ow} 0.31/0.43 (calc.) (1) **Volatility** v.p. 10 mmHg at 39.9°C ; v.den. 2.45

Solubility Water: miscible. Organic solvents: acetone, benzene, diethyl ether, ethanol

Occupational exposure

FR-VME 2 ppm (6 mg m^{-3})
FR-VLE 10 ppm (30 mg m^{-3})
SE-LEVL 10 ppm (30 mg m^{-3})
SE-STEL 15 ppm (45 mg m^{-3})
UK-LTEL 10 ppm (30 mg m^{-3})
UK-STEL 20 ppm (60 mg m^{-3})

US-TWA 2 ppm (5.9 mg m^{-3})
UN No. 2218 **HAZCHEM Code** 2WE **Conveyance classification** corrosive substance, danger of fire (flammable liquid)
Supply classification corrosive
Risk phrases Flammable – Causes burns (R10, 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)

Ecotoxicity

Fish toxicity
LC_{50} (24-96 hr) harlequin fish, brown trout 130-460 mg l^{-1} (2-4).

Invertebrate toxicity
Cell multiplication inhibition test, *Pseudomonas putida* 41 mg l^{-1}, *Microcystis aeruginosa* 0.15 mg l^{-1}, *Scenedesmus quadricauda* 18 mg l^{-1}, *Entosiphon quadricauda* 20 mg l^{-1}, *Uronema parduczi Chatton-Lwoff* 11 mg l^{-1} (2,3).

Bioaccumulation
Calculated bioconcentration factor 0.78 indicates environmental accumulation will be unlikely (4).

Environmental fate

Nitrification inhibition
No inhibition of nitrifying bacteria at 10 mg l^{-1} (4).

Anaerobic effects
8-wk incubation using 10% activated sludge caused >75% theoretical methane production while another study showed acrylic acid was toxic and poorly utilised by unacclimated anaerobic acetate-enriched cultures. A possible explanation suggested is that acetate cultures have to exhaust acetic acid as a carbon and energy source before using alternative compounds (5).

Degradation studies
Arthrobacter sp. strain NO-18 degrades acrylic acid (6).
Rhodococcus spp. converted acrylic acid into ammonia and carbon dioxide (7).
In a 42-day screening study using a sewage sludge inoculum, 71% of acrylic acid was mineralised (8).

Abiotic removal
Vapour phase photochemical reaction with atmospheric hydroxyl radicals $t_{1/2}$ 6.5 day (9).
Activated carbon adsorbability 0.129 g g^{-1} carbon 64.5% reduction: influent 1000 mg l^{-1} (2).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 250 mg kg^{-1} (10).
LD_{50} oral mouse 2400 mg kg^{-1} (11).
LD_{50} dermal rabbit 280 mg kg^{-1} (12).

Carcinogenicity and chronic effects
No adequate data for carcinogenicity to humans and animals, IARC classification group 3 (13).
Oral Wistar rats (♂ 26 months; ♀ 28 months) 0-1200 ppm in drinking water. No indications of carcinogenic potential or toxic changes revealed (14).

Teratogenicity and reproductive effects
Inhalation pregnant New Zealand White rabbits 30, 60, 125, or 250 ppm acrylic acid vapour on gestation days 10-22 (range finding study) and 25, 75, or 225 ppm acrylic acid vapour on gestation days 6-18 (the major period of organogenesis – definitive study). Animals from the range-finding groups were killed on gestation days 23 or 29,

those from the definitive study on gestation day 29. Consistent concentration-related reductions in food consumption and body weight gains occurred in both studies throughout the exposure periods for concentrations of acrylic acid vapour of 60 ppm and above. Perinasal and perioral wetness and severe nasal congestion occurred in both studies at or above vapour concentrations of 75 ppm. Nasal turbinates from does killed on gestation day 29 showed nasal lesions in the the 60, 125 and 250 ppm groups. Despite the severe effects on nasal mucosa in does of both studies, no evidence of developmental toxicity, including teratogenicity, was seen in any of the does from the definitive study (15).

In a two-generation reproduction toxicity study on ♂ and ♀ Wistar rats receiving acrylic acid in the drinking water (0-5000 ppm) for at least 70 days prior to mating, through mating, gestation, lactation, to weaning the no-observed-advers-effect level was 5000 ppm for fertility and reproductive performance of the parents, 2500 ppm (F0 parents), or 500 ppm (F1 parents) for general systemic toxicity and 500 ppm for developmental toxicity (16).

Metabolism and toxicokinetics

Sprague-Dawley ♂ rats [1,2,3-^{13}C]acrylic acid (400 mg kg^{-1} in water, orally), respiratory emission and excreta collected 72 hr. Expiration of $^{14}CO_2$ was the major rate (~80%) of radiolabel elimination; approximately 6% was excreted in the urine. At the dose level studied the urinary metabolites could not be attributed to the primary vitamin B_{12}-dependent pathway of propionate metabolism, but were consistent with an accumulation of an intermediate from the secondary β-oxidation pathway of propionic acid metabolism (17).

Rapidly metabolised in mice to CO_2 and acetyl-CoA via a secondary pathway of propionic acid catabolism. Kidneys and liver are major sites of detoxification of acrylic acid (18).

Irritancy

Acutely irritating at sites of initial contact in mice but causes little systemic toxicity, probably due to its rapid metabolism (18).

Dermal rabbit 500 mg and 1 mg instilled in rabbit eye caused severe irritation (duration unspecified) (19).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537 with and without metabolic activation negative (20).

In vitro mouse lymphoma L5178Y tk+/tk– without metabolic activation positive (21).

Syrian hamster embryo fibroblast cells with and without metabolic activation negative (22).

CHO/HGPRT gene mutation assay, chromosome aberrations in CHO cells in culture, and unscheduled DNA synthesis in rat hepatocytes in culture all negative. *Drosophila* sex-linked recessive lethal assay by both the feeding and injection routes, the *in vivo* cytogenetic assay in rat bone marrow cells after a 1-day and a 5-day oral dosing regimen, and a dominant lethal assay in mice by both an acute and a 5-day dosing regimen all negative. The clearance of acrylic acid in animals and the evidence of genetic testing indicate a lack of genetic toxicity *in vivo* (23).

Other comments

Acrylic acid is rapidly oxidised in water therefore wastewater containing the compound can deplete reserviors of oxygen (24).

Reviews on human health effects, experimental toxicology and environmental effects listed (25).

Environmental health criteria reviewed (26).

Fire hazard when exposed to heat or flame.

Corrosive, exothermic polymerisation at room temperature may become explosive if confined.

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A43 acrylonitrile

$CH_2=CHCN$

C_3H_3N **Mol. Wt.** 53.06 **CAS Registry No.** 107-13-1

Synonyms 2-propenenitrile; vinyl cyanide; cyanoethylene

EINECS No. 203-466-5 **RTECS No.** AT 5250000

Uses In the production of acrylic and modacrylic fibres, nitrile rubbers and various plastics. Also used in fumigants.

Physical properties

M. Pt. –83.5°C **B. Pt.** 77-79°C **Flash point** –5°C **Specific gravity** 0.806 at 20°C with respect to water at 4°C
Partition coefficient log P_{ow} –0.92 **Volatility** v.p. 100 mmHg at 22.8°C ; v.den. 1.83
Solubility Water: 73 g l^{-1} at 20°C. Organic solvents: acetone, benzene, diethyl ether, ethanol

Occupational exposure

FR-VME 2 ppm (4.5 mg m^{-3}) **FR-VLE** 15 ppm (32.5 mg m^{-3})
JP-OEL 2 ppm (4.3 mg m^{-3})
SE-LEVL 2 ppm (4.5 mg m^{-3}) **SE-STEL** 6 ppm (13 mg m^{-3})
UK-LTEL MEL 2 ppm (4.4 mg m^{-3})
US-TWA 2 ppm (4.3 mg m^{-3})

UN No. 1093 **HAZCHEM Code** 3WE **Conveyance classification** flammable liquid, toxic
Supply classification highly flammable, toxic
Risk phrases May cause cancer – Highly flammable – Toxic by inhalation, in contact with skin and if swallowed – Irritating to the skin (R45, R11, R23/24/25, R38)
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, fathead minnow, pinfish, guppy 10-33 mg l^{-1} flow-through and static bioassays (1,2).

Invertebrate toxicity

LC_{50} (24 hr) *Asellus aquaticus* 50 mg l^{-1}.
LC_{50} (50 hr) *Gammarus gassorium* 32 mg l^{-1} (3).
LC_{50} (24 hr) brown shrimp 10-33 mg l^{-1} (4).
EC_{50} (24, 48 hr) *Daphnia magna* 13-7.6 mg l^{-1} (5).
EC_{50} (30 min) *Photobacterium phosphoreum* 254 mg l^{-1} Microtox test (6).

Bioaccumulation

The bioconcentration factor for bluegill sunfish exposed to unspecified concentrations of acrylonitrile for 28 days or until equilibrium was obtained in a flowing water system was 48 (7).
Bioaccumulation in aquatic organisms is unlikely, but cyanoethylation of proteins in the aquatic environment is probable (8).

Environmental fate

Nitrification inhibition

NH_3 oxidation, not inhibitory to *Nitrosomonas* spp. (9).
Saprophytic microorganisms can utilise 150 mg l^{-1} acrylonitrile. Concentrations of >50 ppm may inhibit bacterial nitrification, adversely affecting activated sludge processes (10).
Inhibition cell multiplication *Pseudomonas putida* commences at 53 mg l^{-1} (11).

Degradation studies

Concentrations of <20 mg l^{-1} were readily biodegraded during anaerobic digestion processes operating in municipal sewage treatment facilities. *Pseudomonas putida* in sludge degraded up to 35% acrylonitrile at concentrations of 500 mg l^{-1}. BOD_5 70% reduction in dissolved oxygen (8).
Numerous studies indicate that acrylonitrile was degraded in aerobic systems after acclimation. Using activated sludge inocula >95% degradation and 100% degradation occurred within 7 days in screening studies with sewage seed (12,13).

Abiotic removal

Acrylonitrile does not absorb light >290 nm, therefore does not undergo direct photolysis (14).
Can react photochemically with hydroxyl radicals in the atmosphere, $t_{1/2}$ 3.5 day (15).
Hydrolysis is negligible, 10 ppm acrylonitrile was stable in aqueous solution pH 4-10 for 23 day (16).

Adsorption and retention

Acrylonitrile does not adsorb strongly to soil and is very volatile (17).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 78 mg kg^{-1} (18).
LC_{50} (4 hr) inhalation guinea pig 0.99 mg kg^{-1} (19).
LD_{50} intraperitoneal mouse 44 mg kg^{-1} (20).
LD_{50} intravenous rabbit 69 mg kg^{-1} (21).

Carcinogenicity and chronic effects

Limited evidence for carcinogenicity to humans, sufficient evidence for carcinogenicity to animals, IARC classification group 2A (22).
Inhalation rat (≤104 wk) 5-60 ppm increased the incidence of encephalic glioma in both sexes, mammary gland neoplasm in ♀ and Zymbal gland neoplasm in ♂ (23).
♂ Sprague-Dawley rats (2 yr) 0, 20, 500 ppm in drinking water. High-dose animals exhibited early mortality,

retarded weight gain and tumours of Zymbal gland. No increases in tumours of organ systems detected but a trend toward the development of forestomach papillomas was noted (24).

Teratogenicity and reproductive effects

Administration of 63 mg kg^{-1} (repeat doses) on days 8-15 gestation were toxic to ♀ Sprague-Dawley rats, produced malformations and embryotoxicity (25,26).

Day-10 rat embryos cultured in rat serum for 26 hr in the presence of acrylonitrile (76-760 μM). Survival was not affected at the concentrations tested. Normal development observed at 76 μM; statistically significant concentration-related decreases in growth parameters at concentrations ≥304 μM. Malformations, mainly reduction of the brain and a shortened caudal extremity, occurred at ≥152 μM (27).

In rats treated with 5 mg kg^{-1} from day 5-21 gestation (route unspecified), pups showed no adverse effects on functional or postnatal morphological development. However, altered brain levels of 5-hydroxytryptamine, norepinephrine and monoamine oxidase were detected (28).

Decrease in sperm count and degeneration of seminferous tubules detected. The authors conclude that acrylonitrile may affect the ♂ reproductive function by causing testicular injury (29).

Inhalation (6 hr day^{-1}) Sprague-Dawley rats (days 6-20 of gestation) 12-100 ppm. Foetotoxicity observed after exposure to 25 ppm; overt signs of maternal toxicity present (30).

Metabolism and toxicokinetics

Metabolised to cyanide and then to thiocyanate which in turn is eliminated in urine (31).

Inhalation rat (8 hr) 1, 5, 10, 50 or 100 ppm, urine samples were collected up to 32 hr after initial exposure, metabolites included hydroxyethyl mercapuric acid, S-carboxymethyl cysteine, cyanoethyl mercapuric acid and at higher concentrations unmetabolised acrylonitrile (32).

Rat extrahepatic tissues such as intestinal mucosa are capable of metabolising acrylonitrile to CN^-; intestinal cytochrome P450, particularly cytochrome P450 2E1, plays a major role (33).

Oral and intravenous (unspecified concentrations) of distribution of ^{14}C-acrylonitrile in rat and monkey was studied by whole body autoradiography. Radioactivity was observed in blood, liver, kidney, lung, adrenal cortex and stomach mucosa (34).

Genotoxicity

Salmonella typhimurium TA1535, pSK1002 with and without metabolic activation negative (35).

In vitro human KB cells (72 hr incubation) 5.7 μg ml^{-1} showed cytoplasmic projections and altered morphology on cell surface. After 72 hr, 30 μg ml^{-1} completely inhibited cell growth (36).

In vitro human bronchial epithelial cells induced of sister chromatid exchange and DNA single-strand breaks at concentrations of 150-500 μg ml^{-1} (37).

Histological and biochemical results provided evidence for the acute genetic toxicity of acrylonitrile (and/or its metabolites) in lung tissue following a single oral dose (46.5 mg kg^{-1}) to Sprague-Dawley ♂ rats (38).

Other effects

Other adverse effects (human)

Effects in humans included significant excess of prostate cancers observed in workers exposed to acrylonitrile (39).

There were no statistically significant excesses in overall cancer incidence or mortality among ♂ employees occupationally exposed to acrylonitrile at a textile fibre plant from 1944-1970 and followed through 1981 for mortality and through 1983 for cancer incidence. However, a statistically significant excess of prostate cancer was found (5 cases versus 1.9 expected). Mortality from all causes was significantly lower than expected based on US rates (40).

In humans, symptoms of over-exposure include headache, sleeplessness, nausea, vomiting, diarrhoea, fatigue, mild jaundice, irritation and inflammation of the eyes and respiratory tract, including nose and throat. In severe cases unconsciousness and convulsions can occur (4).

Fatalities have been reported following the use of fumigant mixtures containing acrylonitrile, carbon tetrachloride and methylene chloride. Exact exposure conditions not known (4).

Any other adverse effects

Acrylonitrile can be readily absorbed by mouth, through intact skin or by inhalation (species unspecified) (41). Oral mice (60 day) 10 mg kg^{-1} day^{-1} caused a decrease in testicular sorbitol dehydrogenase and acid phosphatase and increases in lactate dehydrogenase and β-glucuronidase activities. Acrylonitrile interacts with rat blood by binding to cytoplasmic and membrane proteins and may cause damage in red cells by mechanisms other than the release of cyanide (42).

Other comments

In auto exhaust and cigarette smoke emissions and in wastewater discharges associated with its production.
IC_{50} (96 hr) duckweed *Lemna minor* L. growth inhibition 27.08 mg l^{-1} (43).
Physico-chemical properties, acute and chronic toxicity, metabolic fate, teratogenicity, genotoxicity and carcinogenicity extensively reviewed (44-52).

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A44 acryloyl chloride

$H_2C{=}CHCOCl$

C_3H_3ClO **Mol. Wt.** 90.51 **CAS Registry No.** 814-68-6

Synonyms acrylic chloride; acrylic acid chloride; acrylyl chloride; 2-propenoyl chloride

EINECS No. 212-399-0 **RTECS No.** AT 7350000

Uses Chemical intermediate.

Physical properties

B. Pt. 72-76°C **Flash point** 16°C **Specific gravity** 1.114
Solubility Organic solvents: chloroform

Mammalian & avian toxicity

Acute data

LC_{Lo} (4 hr) inhalation rat 25 ppm (1).
LC_{50} (2 hr) inhalation mouse 92 mg m^{-3} (2).
LD_{50} intravenous mouse 180 mg kg^{-1} (3).

Sub-acute and sub-chronic data

Inhalation rat (3 wk) <25 ppm in air caused respiratory damage (1).

Other comments

Decomposes on contact with water.

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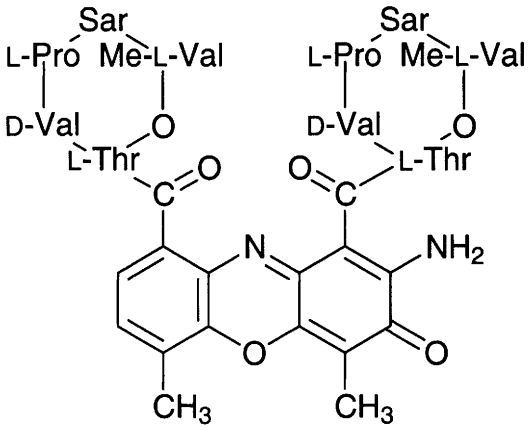
A45 actinomycin C



$C_{62}H_{86}N_{12}O_{16}$ **Mol. Wt.** 1255.44 **CAS Registry No.** 8052-16-2

Synonyms 1*H*-pyrrolo[2,1-*i*][1,4,7,10,13]oxatetraazacyclohexadecine, cyclic peptide deriv.; 3*H*-phenoxazine, actinomycin C deriv.; Cactinomycin; Sanamycin; HBF 386; NSC 8722

EINECS No. 232-485-1 **RTECS No.** AU 1400000

Uses Antineoplastic antibiotic.

Occurrence Obtained from cultures of *Streptomyces chrysomallus*, *S. antibioticus* and *S. parvulus*.

Physical properties

M. Pt. 246-247°C (trihydrate)

Solubility Organic solvents: ethanol, propylene glycol (trihydrate)

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, mouse 7-13 mg kg^{-1} (1,2).

LD_{50} intraperitoneal rat 100 μg kg^{-1} (1).

Sub-acute and sub-chronic data

Rats treated with 7% of the LD_{50} dose for 14 wk (unspecified route) caused immunosuppressive effects (3).

Carcinogenicity and chronic effects

Inadequate evidence for carcinogenicity to humans, limited evidence for carcinogenicity to animals, IARC classification group 3 (4).

Irritancy

Systemic skin irritant by intravenous route (5).

Genotoxicity

Drosophila melanogaster wing mosaic assay displayed low level of genotoxicity (6).

Other effects

Other adverse effects (human)

In humans can cause bone marrow depression, oral and gastrointestinal effects and tissue damage (2,7). Symptoms include nausea, vomiting and alopecia (7).

Other comments

Actinomycin C is a mixture of actinomycin D, C_2 and C_3 (7).

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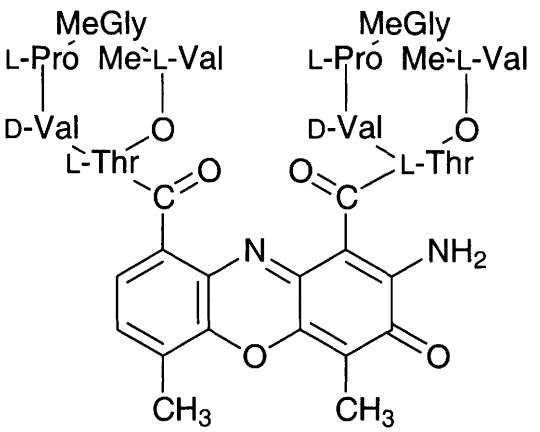
A46 actinomycin D



$C_{62}H_{86}N_{12}O_{16}$ **Mol. Wt.** 1255.44 **CAS Registry No.** 50-76-0

Synonyms 1*H*-pyrrolo[2,1-*i*][1,4,7,10,13]oxatetraazacyclohexadecine, cyclic peptide deriv.; 3*H*-phenoxazine, actinomycin D deriv.; 3*H*-phenoxazine-1,9-dicarboxamide, 2-amino-*N*,*N*'-bis(hexadecahydro-6,13-dissopropyl-2,5,9-trimethyl-1,4,7,11,14-pentaoxo-1*H*-pyrrolo[2,1-*i*][1,4,7,10,13]oxatetraazacyclohexadecin-10-yl)-4,6-dimethyl-2-oxo-Actinomycin C1; Dactinomycin; Meractinomycin; Oncostatin K

EINECS No. 200-063-6 **RTECS No.** AU 1575000

Uses Antineoplastic antibiotic.

Occurrence Antibiotic substance belonging to the actinomycin complex, produced by several *Streptomyces* spp.

Physical properties

M. Pt. 241.5-243°C (decomp.)

Solubility Organic solvents: ethanol, propylene glycol

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse, rat 7.2-13 mg kg^{-1} (1).

Carcinogenicity and chronic effects

Inadequate evidence for carcinogenicity to humans, limited evidence for carcinogenicity to animals, IARC classification group 3 (2).

Mice and rats given 3 intraperitoneal injections wk^{-1} of the maximum tolerated dose (duration unspecified) induced cancer in the peritoneal cavity (3).

Teratogenicity and reproductive effects

Intraperitoneal albino rats (day 8 of gestation) 0.2 $\mu g\ g^{-1}$ inhibited collagen formation by chondrocytes and the formation of matrix in the epiphyseal phase of newborn rats (4).

Gavage (days 8-12 of gestation) ICR/SIM mice, Chernoff/Kavlock development toxicity screen positive teratogen, significant reduction in live-born litter size (5).

Day-9.5 Wistar rat embryos cultured in rat serum for 72 hr in the presence of 0-0.001 $\mu g\ l^{-1}$. Embryonic death and malformations (mainly neural tube and pericardium defects) were both concentration related (6).

Metabolism and toxicokinetics

A 1 mg kg^{-1} dose of actinomycin D administered intravenously to rabbits resulted in <10% of initial concentration detected in blood after 2 hr, rising slightly after 10 hr. Actinomycin D was found in kidney, heart, spleen, liver, bile and urine (7).

Genotoxicity

Salmonella typhimurium TA1535, TA1538, TA1537, with and without metabolic activation positive (8).

Saccharomyces cerevisiae induction of diploidy and aneuploidy negative (9).

Mouse lymphoma tk+/tk– forward mutation assay positive (10).

In vitro human lymphocyte sister chromatid exchange positive (11).

Vicia faba sister chromatid exchange positive (11).

Other effects

Other adverse effects (human)

Studies with human neutrophils indicated that actinomycin D impaired intracellular killing by human neutrophils through an effect on respiratory activity and directed cell migration of human neutrophils (12).

Any other adverse effects

Direct injection of 8 $\mu g\ ml^{-1}$ into encephalon of 42 hr-old chick embryos and incubation for 6-8 hr induced lesions of the ocular structures within 8 hr. Damage to nerve cell layers was observed (13).

Other comments

Historical background of actinomycin D and chemistry, carcinogenicity, toxicology, pharmacology reviewed (1,7).

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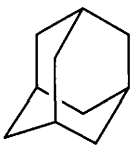
A47 adamantane



$C_{10}H_{16}$ **Mol. Wt.** 136.24 **CAS Registry No.** 281-23-2

Synonyms tricyclo[3.3.1.1^{3,7}]decane

EINECS No. 206-001-4

Uses A chemical intermediate used in polymers, lubricating oils, pharmaceuticals and sublimation carriers.

Physical properties

M. Pt. 268°C (sealed tube), 205-210°C (sublimes) **Specific gravity** 1.07
Solubility Organic solvents: acetone

Other comments

Found in petrochemical fractions.
Review of adamantane in medicinal chemistry (1).

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A48 adipic acid

$$HO_2C(CH_2)_4CO_2H$$

$C_6H_{10}O_4$ **Mol. Wt.** 146.14 **CAS Registry No.** 124-04-9

Synonyms hexanedioic acid; 1,4-butanedicarboxylic acid

EINECS No. 204-673-3 **RTECS No.** AU 8400000

Uses Artificial resins, nylon, urethane foams, intermediate in oil additive lubricants, sometimes substituted for tartaric acid in baking powder (due to lower hygroscopicity). pH control in food and drugs.
Occurrence Found in beetroot juice.

Physical properties

M. Pt. 152°C **B. Pt.** 337.5°C **Flash point** 196°C **Specific gravity** 1.36 at 25°C with respect to water at 4°C
Partition coefficient log P_{ow} 0.08 (1)
Solubility Water: 14.4 g l^{-1}. Organic solvents: chloroform, diethyl ether, ethanol

Occupational exposure

US-TWA 5 mg m^{-3}
Supply classification irritant
Risk phrases Irritating to the eyes (R36)
Safety phrases Keep out of reach of children (if sold to general public) (S2)

Ecotoxicity

Fish toxicity

LC_{50} (24-96 hr) bluegill sunfish, fathead minnow 330-97 mg l^{-1} static bioassay at 18-22°C (2).

Bioaccumulation

The low partition coefficient indicates that bioconcentration in fish will be negligible (3).

Environmental fate

Degradation studies

After 10 days acclimation 82% adipic acid was degraded under anaerobic conditions (4).

BOD_5 0.598 mg l^{-1} oxygen consumed at 20°C, 36% ThOD (2).

In river water 50-90% degradation occurred in 3.5 and 7 days, respectively; initial concentrations 700 mg l^{-1} (5).

Abiotic removal

Photochemical reactions occur with hydroxyl radicals in the atmosphere, $t_{1/2}$ 4.4 days (6).

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse 1900 mg kg^{-1} (7).

LD_{50} intravenous, intraperitoneal mouse 275, 680 mg kg^{-1}, respectively (7,8).

Sub-acute and sub-chronic data

Fifteen repeat exposures inhalation rat (6 hr), total exposure 126 g l^{-1}; no adverse effects reported (9).

Metabolism and toxicokinetics

Only partially metabolised by humans, remainder eliminated unchanged in urine (10).

Irritancy

20 mg instilled in rabbit eye for 24 hr caused severe irritant effects (11).

Other comments

Adipic acid exists mainly in its dissociated form in the environment, forming salts with cations (12).

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A49 adiponitrile

$$NC(CH_2)_4CN$$

$C_6H_8N_2$ **Mol. Wt.** 108.14 **CAS Registry No.** 111-69-3

Synonyms 1,4-dicyanobutane; hexanedinitrile; adipic acid dinitrile; hexanedioic acid dinitrile; tetramethylene cyanide

EINECS No. 203-896-3 **RTECS No.** AV 2625000

Uses Organic syntheses. Intermediate in the manufacture of nylon.

Physical properties

M. Pt. 1-3°C **B. Pt.** 295°C **Flash point** >110°C **Specific gravity** 0.951 (temperature unspecified)
Volatility v.den. 3.73
Solubility Organic solvents: acetone, chloroform, ethanol

Occupational exposure

US-TWA 2 ppm (8.8 mg m^{-3})

UN No. 2205 **HAZCHEM Code** 3X **Conveyance classification** toxic substance

Ecotoxicity

Bioaccumulation
Calculated bioconcentration factor <1 indicates environmental accumulation is unlikely (1).

Environmental fate

Degradation studies
Confirmed biodegradable (2).
Unacclimated river water treated with initial concentration 0.5-10 mg l^{-1} stored sewage seed, negligible degradation in 2 days, 40% theoretical BOD in 5 days and 100% theoretical BOD in 12 days (3).
Activated sludge exposed to initial substrate concentration 500 mg l^{-1} theoretical BOD 2.2-2.8% in 72 hr (4).
Bench scale activated sludge unit, influent concentration equivalent to 275-350 mg l^{-1}, mean aeration retention time 7-13 hr, 93-98% BOD removal achieved (5).
Aeromonas spp. BN 7013 isolated from soil used adiponitrile as its sole carbon source (6).
Brevibacterium spp. can utilise adiponitrile as a carbon and nitrogen source, suggesting these strains could be used to degrade nitriles in waste water (7).

Abiotic removal
Adiponitrile vapour reacts photochemically with hydroxyl radicals $t_{1/2}$ 11 days (8).

Adsorption and retention
Calculated soil adsorption coefficients 9-16 were estimated for adiponitrile using a linear regression equation based on a measured log K_{ow} of –0.32. These results suggest adiponitrile will be highly mobile in soil with no significant adsorptions to suspended solids and sediments in water (9).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat, mouse, rabbit 172-300 mg kg^{-1} (1,10).
LC_{50} (4 hr) inhalation rat 1710 mg m^{-3} (11).
LD_{50} subcutaneous guinea pig 50 mg kg^{-1} (12).
LD_{50} intraperitoneal mouse 40 mg kg^{-1} (13).

Sub-acute and sub-chronic data

Inhalation rat (4 or 13 wk) 493 or 99 mg m^{-3}, respectively, 6 hr day^{-1}, 5 day wk^{-1}; increased mortality, reduced weight gain and slight anaemia for high-dose animals. No histopathological evidence of organ toxicity or abnormal reproductive effects in animals exposed to 99 mg m^{-3} (14).

Teratogenicity and reproductive effects

Gavage Sprague-Dawley rats (day 6-19 gestation) 0, 20, 40 and 80 mg kg^{-1} induced maternal toxicity in high doses, maternal effects at middle dosages, slight foetotoxicity at the highest dose and no teratogenic effects (15).

Metabolism and toxicokinetics

Toxicity due in part to its action as a cyanide when absorbed or ingested (1).

Of a single 50 mg kg^{-1} dose administered to guinea pigs 79% was excreted as thiocyanate in the urine (16).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA1535, TA1537 with and without metabolic activation negative (13).

Other effects

Any other adverse effects

Causes disturbances of respiration and circulation, irritation of stomach and intestines, and weight loss (17).

Other comments

Toxicological properties including acute and sub-chronic toxicity, teratogenicity and biochemical mechanism studies discussed (18,19).

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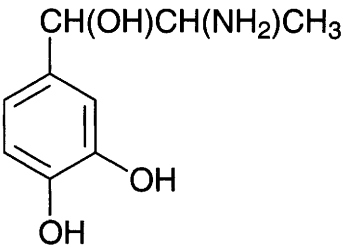
A50 D-adrenaline



$C_9H_{13}NO_3$ **Mol. Wt.** 183.21 **CAS Registry No.** 150-05-0

Synonyms 1-(+)-adrenaline; D-epinephrine

EINECS No. 205-752-5

Uses Cardiac stimulant, vasoconstrictor and bronchodilator.

Occurrence The principal sympathomimetic hormone produced by the adrenal medulla in most species. Occurs as the *l*-form in animals and humans.

Physical properties

M. Pt. 211-212°C

Solubility Organic solvents: acetic acid, ethanol

Ecotoxicity

Toxicity to other species

LD_{Lo} subcutaneous frog 5000 mg kg^{-1} (1).

Mammalian & avian toxicity

Acute data

LD_{Lo} subcutaneous mouse, rabbit, rat 4, 10, 80 mg kg^{-1}, respectively (1-3).

LD_{50} intravenous rabbit, rat 50, 800 µg kg^{-1}, respectively (1,3).

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

Metabolism and toxicokinetics

In man adrenaline is methylated to metanephrine by catechol-*O*-methyltransferase (COMT) followed by oxidative deamination by the mixed function oxidase system to 4-amino-3-methoxymandelic acid, or first oxidatively deaminated by the mixed function oxidase system to 3,4-dihydroxymandelic acid which is then methylated by COMT, and finally converted into 4-hydroxy-3-methoxymandelic acid. The metabolites are excreted in the urine mainly as their glucuronide and ether sulfate conjugates (4).

Other comments

It is important to note that endogenous adrenaline is the laevo-isomer (4).

Adrenaline crosses the placenta to enter foetal circulation (4).

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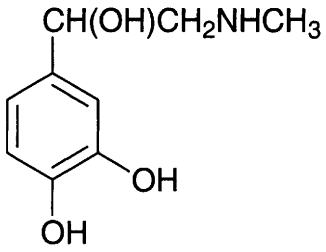
A51 L-adrenaline



$C_9H_{13}NO_3$ **Mol. Wt.** 183.21 **CAS Registry No.** 51-43-4

Synonyms epinephrine; 1-(3,4-dihydroxyphenyl)-2-(methylamino)ethanol; 3,4-dihydroxy-1-[1-hydroxy-2-(methylamino)ethyl]benzene; methylaminoethanolcatechol; Epifrin; Glaucon; Simplene

EINECS No. 200-098-7 **RTECS No.** DO 2625000

Uses Cardiac stimulant, vasoconstrictor and bronchodilator.

Occurrence The principal sympathomimetic hormone produced by the adrenal medulla in most species. Occurs as the *l*-form in animals and humans.

Physical properties

M. Pt. 211-212°C

Solubility Organic solvents: acetic acid

Mammalian & avian toxicity

Teratogenicity and reproductive effects

Oral administration of 500 μg kg^{-1} on day 7-10 of pregnancy caused pre-implantation wastage in hamsters (1).

Metabolism and toxicokinetics

In the rat major metabolites included 3,4-dihydroxyphenylacetic acid, homovanillic acid, 3-methoxy, 4-hydroxyphenylethylene glycol and 5-hydroxyindoleacetic acid (2).

♀ Wistar rat intraperitoneal (unspecified dose) reduced cytochrome P450 and inhibited hexobarbital biotransformation. Glycogen and cytochrome P450 loss and functional impairment of the mixed function monooxygenase system were dose related (3).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA102, TA104 without metabolic activation positive (4).

In vitro mouse lymphoma L5178V tk+/tk– without metabolic activation positive (4).

Other effects

Other adverse effects (human)

Adrenaline was infused for 8.5 hr into normal, healthy adult males on four separate occasions at concentrations of 0, 0.5, 1 and 2 μg min^{-1} to elevate circulating adrenaline into the high physiological range seen in stress and trauma. Adrenaline produced long-term elevation of the metabolic rate with minimal effect on protein metabolism beyond acute changes affecting amino acid levels (5).

In trabecular meshwork explants from human eyes, adrenaline at 1.8 mg l^{-1} caused abnormal cytokinesis and cell retraction, inhibited mitosis and phagocytosis and induced a 4- to 5-fold increase in cAMP. After 7-10 days degenerative changes observed (6).

Any other adverse effects

Neck implant rat 15-30 mg adrenaline (slow release) caused damage to kidneys and impaired their function (7).

Other comments

Effects of adrenaline on fish uterus function are discussed (8).

Effects on central nervous system and neurological disorders reviewed (9,10).

Physical properties, biosynthetic pathways and human health effects reviewed (11-13).

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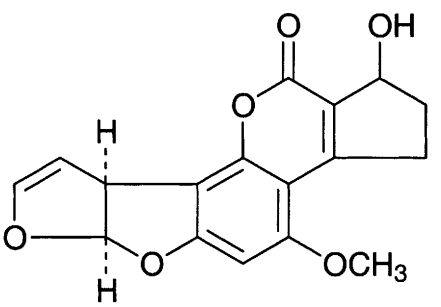
A52 aflatoxicol



$C_{17}H_{14}O_6$ **Mol. Wt.** 314.29 **CAS Registry No.** 29611-03-8

Synonyms aflatoxin R_0; [(1*S*-(1α,6aβ,9a,β)]-2,3,6a,9a-tetrahydro-1-hydroxy-4-methoxycyclopenta[*c*]furo-[3′, 2′:4,5]furo[2,3-*h*][1]benzopyran-11(1*H*)-one

EINECS No. 249-727-7 **RTECS No.** GY 1934000

Occurrence Metabolic product of aflatoxin B_1.

Physical properties

M. Pt. 224-226°C

Solubility Organic solvents: ethanol, methanol

Ecotoxicity

Fish toxicity

Rainbow trout (1 yr) in feed induced hepatocellular carcinoma (1-3).

Mammalian & avian toxicity

Sub-acute and sub-chronic data

TD_{Lo} (1 yr) oral rat 1092 mg kg^{-1} (4).

Carcinogenicity and chronic effects

Sufficient evidence for carcinogenicity to humans and animals, IARC classification group 1 (5).
Weanling rat (1 yr) 50 and 200 ppb in feed induced 20% and 70% hepatocellular carcinoma, respectively (4).

Metabolism and toxicokinetics

Oral pig 0.1 mg kg^{-1} distributed to kidney, liver and muscle (6).
Liver postmitochondrial and microsomal fractions from humans and eight other species were compared. Major metabolic pathway was the dehydrogenation of aflatoxicol yielding aflatoxin B1. The aflatoxicol dehydrogenase activity was associated with the microsomal fraction and required a hydrogen ion acceptor but was not inhibited by carbon monoxide, indicating that it was not dependent on the haem-containing microsomal drug metabolising system. Postmitochondrial liver fractions oxidised aflatoxicol to at least five other metabolites, including aflatoxin Q1, P1, H1, M1 and B2, none of which were formed in the presence of carbon monoxide (7).

Genotoxicity

Salmonella typhimurium TA98, TA100 without metabolic activation positive. Direct mutagenesis occurred with stereo-specificity shown to be important with unnatural aflatoxicol having greater mutagenicity potential than its natural epimer (8).
Escherichia coli sfiA:lacZ SOS spot test, some inhibition of bacterial growth (9).
Escherichia coli K12 PQ37 SOS chromotest with metabolic activation positive (10).

Other effects

Any other adverse effects

Intraperitoneal rat (2 hr) inhibition of total liver nuclear RNA synthesis 68.2% and activity of total RNA polymerase I, II and III reduced 51.7% (11).

Other comments

Toxicity and hazards reviewed (12).

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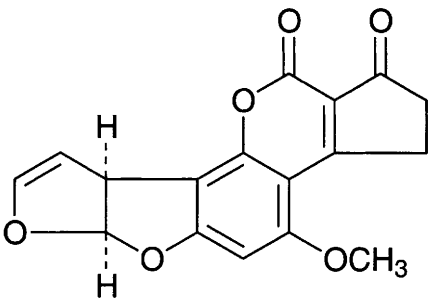
A53 aflatoxin B_1



$C_{17}H_{12}O_6$ **Mol. Wt.** 312.28 **CAS Registry No.** 1162-65-8

Synonyms AFBI; aflatoxin B; (6a*Rcis*)2,3,6a,9a-tetrahydro-4-methoxycyclopenta[*c*]furo[3′,2′:4,5]furo[2,3-*h*][1]benzopyran-1,11-dione

EINECS No. 214-603-3 **RTECS No.** GY 1925000

Occurrence Mycotoxin isolated from *Aspergillus flavus* and *Aspergillus parasiticus*.

Physical properties

M. Pt. 268-269°C (decomp.)

Solubility Water: <1 mg ml^{-1}. Organic solvents: acetone, ethanol

Ecotoxicity

Fish toxicity

Exposure to aflatoxin B1 caused inhibition of larval development in zebra fish and hepatocarcinogenicity in rainbow trout, concentration and duration unspecified (1).

Oral walleye fish (30 day) 50-100 ppb via feed. Pale livers and significant degenerative changes observed. Aflatoxin B_1 detected in the musculature. After two weeks of aflatoxin withdrawal, no aflotoxin was detectable in the fish muscle, but marked histopathological lesions were still observed (2).

Toxicokinetics, tissue distribution and excretion of ^{14}C-labelled aflatoxin B_1 examined after oral administration (250 μg kg^{-1}) in channel catfish. Toxicokinetic modelling and tissue data demonstrate a very low potential for the accumulation of aflatoxin B_1 and its metabolites in the edible flesh of channel catfish through the consumption of contaminated feed (3).

Rainbow trout (number and age not specified) fed aflatoxin B_1 at 0 or 8 μg kg^{-1} for up to 12 months suffered liver lesions, ranging from small neoplastic foci to hepatocellular cholangiocellular and mixed neoplasms (4).

Invertebrate toxicity

EC_{50} (5-15 min) *Photobacterium phosphoreum* 19.3-23.2 mg l^{-1} Microtox text (5).

Mammalian & avian toxicity

Acute data

LD_{50} oral duckling 730 μg kg^{-1} (6).

LD_{50} oral hamster, rat, monkey 2-10 mg kg^{-1} (7,8).

Sub-acute and sub-chronic data

Chickens fed dietary 1.5 mg kg^{-1} (duration unspecified) developed liver lesions (9).

Macaca fascicularis dietary level of 1.8 mg kg^{-1} (duration unspecified) produced liver damage characterised by centrilobular necrosis, bile ducts proliferation and fibrosis (10).

Carcinogenicity and chronic effects

Sufficient evidence for carcinogenicity to humans and animals, IARC classification group 1 (11).

♂ Fischer rats (7 wk – 19 month) 50 μg kg^{-1} in diet induced hepatocellular carcinomas (12).

Fed rainbow trout (8 month) 56% incidence of carcinoma (13).

Teratogenicity and reproductive effects

Aflatoxin B_1 is unable to pass the blood-brain barrier of pregnant rats but it passed the uteroplacental junction to foetuses and subsequently reached liver, brain and other organs. No significant change observed in plasma consitutents of offspring of ♀ rats treated with a 2 mg kg^{-1} intraperitoneal dose during days 8-10 or 15-17 of gestation. The only significant increase detected was liver triglyceride content in the offspring of rats exposed to aflatoxin B_1 during days 8-10 of gestation (14). Low-level dietary exposure does not have a direct effect on the reproductive performance of female mink (*Mustela vison*) but can impair early kit growth and survival (15).

Metabolism and toxicokinetics

Mammalian (including human) metabolism involves the conversion of aflatoxin B_1 into hydroxylated metabolites prior to excretion in (mainly) bile and urine (16).

In the milk of farm animals fed a diet containing aflatoxin B_1, a significant amount of the toxic metabolite M_1 has been found (17).

This metabolite has also been seen in the urine of human subjects who have ingested aflatoxin contaminated foods (16).

Intraperitoneal monkey 5.6% of initial unspecified dose was retained by the liver principally bound to liver proteins after 4 days (17).

Oral monkey (unspecified dose) during day 1-4 excreted in urine and faeces as unchanged parent compound, aflatoxin M_1, aflatoxin B_1 β-glucuronide and sulfate conjugate (17).

Acid hydrolysis of aflatoxin B_1 adducts yielded 2,3-dihydro-2,3-dihydroxyaflatoxin B_1 (18).

Oral pig 0.1 mg kg^{-1} distributed to kidney, liver and muscle (19).

Biotransformation potential investigated using hepatic microsomes from rat, mouse, monkey and human. At low substrate concentrations representative of environmental exposure striking differences were observed in ratios of metabolites between species. Exposure to 38 mg l^{-1} primate liver formed large amounts of aflatoxin Q_1 but failed to produce detectable P_1 levels, and the proportion of B_1 converted into B_1 8,9-expoxide increased in rat and human microsomes but not in mouse or monkey (20).

The metabolism of aflatoxin B_1 was investigated in tracheal cultures and purified tracheal microsomes from rabbit, hamster and rat. Metabolic pathways involved cytochrome P450 enzymes and cytosolic GSH transferase activities but differed between the species. In the upper airway epithelium in rabbit metabolic activity involved aflatoxin B_1 activation whereas detoxification pathways predominated in the hamster (21). Aflatoxin B_1 penetrated isolated human epidermis *in vitro*. Rate of penetration was low under non-occluded conditions but was approximately 40-times greater under conditions of occlusion (22).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1538 with metabolic activation positive (23).

Salmonella typhimurium, Streptococcus sanguis, Mycobacterium tuberculosis all tests positive (1).

Escherichia coli PQ37 with and without metabolic activation positive (24).

Early cultures of LNRL (untransformed rat liver cell line) were co-cultivated with Chinese hamster ovary cells, sister chromatid exchange positive (25).

Chinese hamster V79 cells with metabolic activation induced ouabain-resistant mutants of V79 cells (26).

Other effects

Other adverse effects (human)

Numerous studies have been carried out on the possible impact of aflatoxin contamination on human groups. A study has also implicated aflatoxins in the development of colonic cancer in two research workers (27).

Aflatoxins have been implicated in a variety of liver diseases and in the deaths of patients who were suffering from Reye's syndrome (27).

In a study of primary liver cancer patients, aflatoxin B_1 was found in 51.3% of urine samples compared with 38.4% for controls (28).

Any other adverse effects

Intraperitoneal rat (2 hr) 3 mg kg^{-1} inhibited RNA polymerase II activity only in the target tissue, liver, and not in the non-target tissues, e.g. lung and brain (29).

Oral chicken (21 day) 3 μg g^{-1} day^{-1}. Vacuolation of liver cells during the initial days of administration and cellular depletion in the follicle medulla of the bursa of Fabricius were the first lesions to appear and these persisted during a 10-day recovery phase. A significant-reduction in the body weight and absolute weights of liver, bursa of Fabricius, spleen and thymus gland also observed (30).

Rabbits were administered a daily oral dose of aflatoxin B_1 of 0.05 or 0.10 mg kg^{-1} for 5 days. Neither liver cytochrome b5 content nor NADPH-cytochrome were affected. A dose-dependent decrease in cytochrome P450 content and increases in both haem oxygenase and bilirubin reductase activities were observed. An exponential dose-dependent increase in plasma bilirubin concentration combined with reduced bilirubin UDP-glucuronyl-transferase activity suggest that the hyperbilirubinaemia associated with aflatoxin B_1 is related to increased haem catabolism (31).

Other comments

Carcinogenicity, genotoxicity and adduct formations with DNA and oncogene mutation reviewed (32-34).

Interactions between nutrition, toxicology and pharmacology reviewed (35).

Toxicity and hazards reviewed (36).

Carcinogenic risk to humans reviewed (37).

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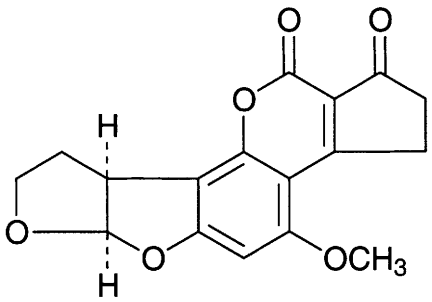
A54 aflatoxin B_2



$C_{17}H_{14}O_6$ **Mol. Wt.** 314.29 **CAS Registry No.** 7220-81-7

Synonyms dihydroaflatoxin B_1; 2,3,6aα,8,9,9aα-hexahydro-4-methoxycyclopenta[*c*]furo[3′,2′:4,5]furo-[2,3-*h*][1]benzopyran-1,11-dione

EINECS No. 230-618-8 **RTECS No.** GY 1722000

Occurrence Fungal toxin from *Aspergillus flavus* and *Aspergillus parasiticus*.

Physical properties

M. Pt. 286-289°C (decomp.)
Solubility Organic solvents: chloroform, ethanol

Ecotoxicity

Invertebrate toxicity
EC_{50} (5-30 min) *Photobacterium phosphoreum* 62.7 mg l^{-1} Microtox test (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral mallard duck 1700 μg kg^{-1} (2).
LD_{50} oral mouse 570 mg kg^{-1} (3).
Oral rat 116 mg kg^{-1} (duration of exposure unspecified) non-toxic (4).
LD_{50} intravenous rat 10.5 mg kg^{-1} (5).

Carcinogenicity and chronic effects
Sufficient evidence for carcinogenicity to humans and animals, IARC classification group 1 (6).

Teratogenicity and reproductive effects
Pregnant ♀ rats administered 25% aflatoxin B_2 0.7-7.0 mg kg^{-1} on day 8 or 16 of gestation no foetal malformation observed (7).

Metabolism and toxicokinetics

After administration of aflatoxin B_2 to rats, adducts were found in hepatic DNA and ribosomal RNA. Levels of hepatic protein aflatoxin adducts were 35-70% as great for aflatoxin B_2-treated rats as for aflatoxin B_1-treated rats (8).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1538 with and without metabolic activation negative (9).
Escherichia coli PQ37 with and without metabolic activation positive (10).

Other effects

Any other adverse effects

Intraperitoneal rat (2 hr) 3 mg kg^{-1} inhibited RNA polymerase II activity only in the target tissue, liver, and not in the non-target tissues, e.g. lung and brain (11).

Other comments

Investigations in the Sudan, Ghana, Kenya and Nigeria confirmed aflatoxins cross the human placental membrane (12).
Toxicity and hazards reviewed (13).

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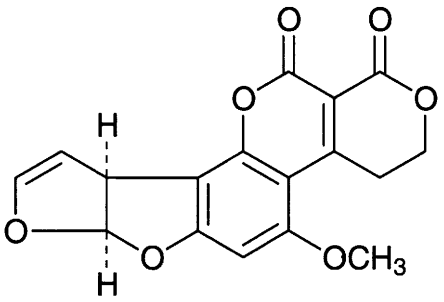
A55 aflatoxin G_1



$C_{17}H_{12}O_7$ **Mol. Wt.** 328.28 **CAS Registry No.** 1165-39-5

Synonyms 3,4,7aα,10aα-tetrahydro-5-methoxy-1*H*,12*H*-furo[3',2':4,5]furo[2,3-*h*]pyrano[3,4-*c*][1]benzopyran-1,12-dione

EINECS No. 214-615-9 **RTECS No.** LV 1720000

Occurrence Fungal toxin from *Aspergillus flavus* and *A. parasiticus*.

Physical properties

M. Pt. 244-246°C

Solubility Organic solvents: ethanol, chloroform

Ecotoxicity

Fish toxicity

TD_{Lo} (12 min) rainbow trout 20 ppb (1).

LC_{50} (24 hr) zebra fish 0.75 μg ml^{-1} (2).

LC_{50} (96 hr) rainbow trout 1.9 mg kg^{-1} (3).

Invertebrate toxicity

EC_{50} (5-30 min) *Photobacterium phosphoreum* 36 mg l^{-1} Microtox test (4).

Streptomyces sp. exposed to 5 μg aflatoxin G_1 showed a decrease in proteolytic, amylolytic, denitrification and/or antibiotic activity (5).

Mammalian & avian toxicity

Acute data

LD_{50} oral mallard duck 784 μg kg^{-1} (6).

LD_{50} oral rat 2-4 mg kg^{-1} (7).

LD_{50} intraperitoneal rat 14.9 mg kg^{-1} (8).

Carcinogenicity and chronic effects

Sufficient evidence for carcinogenicity to humans and animals, IARC classification group 1 (9).

Intramuscular injection and oral intubation ♀ rhesus monkey (5 yr) dose unspecified developed a metastasising intrahepatic bile-duct carcinoma which was detected at autopsy at death, 25 yr after toxin administration was discontinued (10).

Gavage rat (8 wk) 40 equal doses 1.4-2.0 mg induced hepatocellular carcinoma and adenocarcinomas of the kidney (7).

Metabolism and toxicokinetics

Bioactivation occurs via the mixed function oxidase system (11).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1538 with metabolic activation positive (12-14).
Escherichia coli PQ37 with metabolic activation positive (15).
Saccharomyces cerevisiae gene conversion and reverse mutation with and without metabolic activation negative (16).
In vitro Chinese hamster cells sister chromatid exchange and chromosomal aberrations with metabolic activation positive (17).
Drosophila melanogaster white/white^{+} eye mosaic test interchromosomal mitotic recombination positive (18).

Other effects

Other adverse effects (human)

A study of 35 women from Songkhla, Thailand, had samples of human cord sera and sera immediately after birth analysed for aflatoxin contamination. Aflatoxin at concentrations 0.064-13.6 nmol ml^{-1} were obtained from 48% of participants. Results confirmed that transplacental transfer occurs (19).

Any other adverse effects

Intraperitoneal rat (2 hr) 3 mg kg^{-1} RNA polymerase II activity only in the target tissue, liver, and not in non-target tissues, e.g. lung and brain (20).

Other comments

Toxicity and hazards reviewed (21,22).

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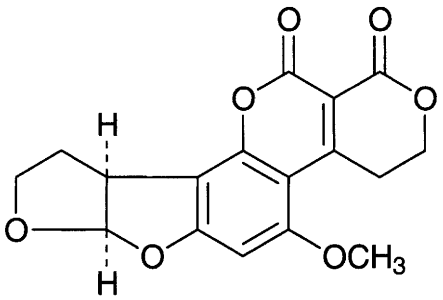
A56 aflatoxin G_2



$C_{17}H_{14}O_7$ **Mol. Wt.** 330.29 **CAS Registry No.** 7241-98-7

Synonyms 3,4,7aα,9,10,10aα-hexahydro-5-methoxy-1*H*,12*H*-furo[3′,2′:4,5]furo[2,3-*h*]pyrano[3,4-*c*][1]benzopyran-1,12-dione

EINECS No. 230-643-4 **RTECS No.** LV 1700000

Occurrence Fungal toxin from *Aspergillus flavus* and *Aspergillus parasiticus*.

Physical properties

M. Pt. 237-240°C

Solubility Organic solvents: ethanol, chloroform

Ecotoxicity

Fish toxicity

LC_{50} (24 hr) zebra fish larvae 4.2 μg ml^{-1} (1).

Invertebrate toxicity

EC_{50} (30 min) *Photobacterium phosphoreum* 69 mg l^{-1} Microtox test (2).

Mammalian & avian toxicity

Acute data

LD_{50} oral duckling 3450 μg kg^{-1} (1 day old) (3).

Oral rat 232 mg kg^{-1} non-toxic (4).

Carcinogenicity and chronic effects

Sufficient evidence for carcinogenicity to humans and animals, IARC classification group 1 (5).

Genotoxicity

Salmonella typhimurium TA100, TA98, TA1538 with metabolic activation negative (6).

Salmonella typhimurium strain unspecified with metabolic activation weakly positive (7).

Escherichia coli PQ37, PQ35 with and without metabolic activation negative (8).

Drosophila melanogaster white/white+ eye mosaic test interchromosomal mitotic recombination positive (9).

Early cultures of LNRL (untransformed rat liver cell line) were co-cultivated with Chinese hamster ovary cells, sister chromatid exchange positive (10).

Chinese hamster V79 cells with and without metabolic activation negative (11).

In vitro Chinese hamster cells with metabolic activation sister chromatid exchanges positive (12).

Other effects

Any other adverse effects

Intraperitoneal rat (2 hr) 3 mg kg^{-1} inhibited RNA polymerase II activity only in the target tissue, liver, and not in the non-target tissues, e.g. lung and brain (13).

Other comments

Toxicity and hazards reviewed (14,15).

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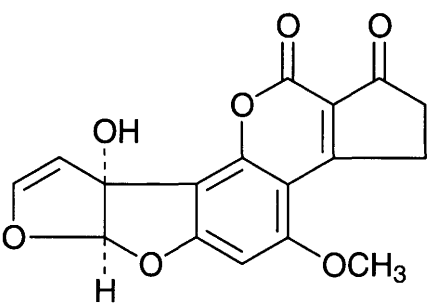
A57 aflatoxin M_1



$C_{17}H_{12}O_7$ **Mol. Wt.** 328.28 **CAS Registry No.** 6795-23-9

Synonyms 4-hydroxyaflatoxin B_1; 2,3,6a,9a-tetrahydro-9a-hydroxy-4-methoxycyclopenta[*c*]furo-[3′,2′:4,5]furo[2,3-*h*]benzopyran-1,11-dione

EINECS No. 229-865-4 **RTECS No.** GY 1880000

Occurrence Metabolic product of aflatoxin B_1. A common source is animal milk, e.g. cattle fed plant material containing aflatoxin B_1.

Physical properties

M. Pt. 299°C (decomp.)
Solubility Organic solvents: ethanol, dimethylformamide, methanol

Ecotoxicity

Fish toxicity
Hepatocarcinogenic to rainbow trout (1,2).
Rainbow trout (1 yr) in food (concentrations unspecified) induced hepatocellular carcinoma (3).
Rainbow trout were fed diets containing 0, 5.9 or 27.3 μg kg^{-1} aflatoxin M_1 (and some aflatoxin M_2) or 5.9 μg kg^{-1} aflatoxin B_1 for up to 16 months. The hepatocarcinogenic effect of aflatoxins M_1 and M_2 was much weaker than that of aflatoxin B_1 with the incidence of hepatocellular carcinomas at 16 months being 0/49 in low-dose aflatoxin M_1 and M_2-treated fish, 1/48 high-dose aflatoxin M_1 and M_2-treated fish and 6/48 aflatoxin B_1-treated fish (4).

Mammalian & avian toxicity

Acute data
LD_{50} oral duckling 16 μg kg^{-1} (5).
LD_{Lo} oral rat 1500 μg kg^{-1} (6).

Sub-acute and sub-chronic data
TD_{Lo} (8 wk) oral rat 8 mg kg^{-1} (7).

Carcinogenicity and chronic effects
Possibly carcinogenic to humans, IARC classification group 2B (8).
♂ Fischer rats (7 wk-21 month) 0-50 μg kg^{-1} in diet induces hepatocellular carcinomas and neoplastic nodules (9).
♂ weanling Fischer rats were given 0 or 25 μg in 0.5 ml distilled water by gastric intubation 5 days wk^{-1} for 8 wk. Only 1/29 animals had developed a hepatocellular carcinoma by 96 wk. The remaining animals were killed after 100 wk and 8 had preneoplastic liver lesions (7).

Metabolism and toxicokinetics
Aflatoxin M_1 is the main unconjugated metabolite of aflatoxin B_1 in the urine of rats, sheep, pigs and cows and is excreted in the milk of many mammals. Aflatoxins also cross the placental barrier (8).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535 with metabolic activation positive (10,11).
In vitro rat primary hepatocytes without metabolic activation unscheduled DNA synthesis positive (12).
Drosophila melanogaster DNA repair test. Aflatoxin M_1 registered as a DNA-damaging agent with an activity ~3-fold lower than that of aflatoxin B_1 (13).
Drosophila melanogaster wing spot test. Aflatoxin M_1 exerted a genotoxic effect compatible to that of aflatoxin B_1 (13).

Other effects

Other adverse effects (human)
In a study of primary cancer liver patients aflatoxin M_1 was found in 51.3% of urine samples compared to 38.4% for controls (14).

Other comments

Contamination of dairy produce reviewed (15).
Toxicity and hazards reviewed (8,16).

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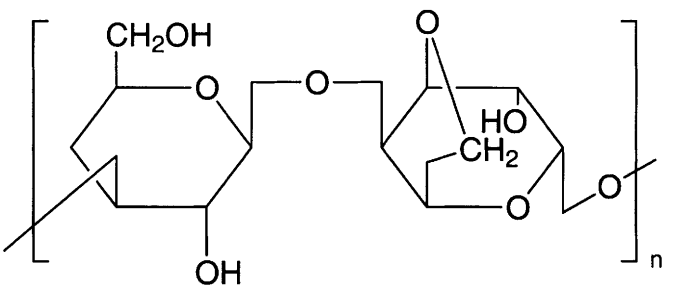
A58 agar



CAS Registry No. 9002-18-0

Synonyms agar-agar; Bengal isinglass; Ceylon isinglass; Chinese isinglass; Japan isinglass; Japan agar

EINECS No. 232-658-1 **RTECS No.** AW 7950000

Uses Suspending or thickening agent in pharmaceutical and food products used as a substitute for gelatin. Corrosion inhibitor. Sizing agent for paper and textiles. In nutrient media for bacterial cultures. In human and veterinary medicine used as a laxative.

Occurrence Polysaccharide complex obtained from various species of Rhodophyceae algae (British Pharmacopoeia specifies the genus *Gelidum*) (1,2).

Environmental fate

Degradation studies

Cytophaga HK-5, a marine bacterial strain was capable of degrading a number of marine plant polysaccharides, including agar (3).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, mouse, rabbit, hamster 6-16 g kg^{-1} (1).

Carcinogenicity and chronic effects

The National Toxicology Program tested ♂ and ♀ rats and mice via dosed-feed. No evidence of carcinogenicity was seen in any animals (4).

Oral rat (103 wk) 25,000 to 50,000 ppm increased adrenal cortex adenoma for higher dose in ♀ and increased liver adenoma for both doses in ♂ (5).

Other comments

The use of agar in food is limited only by good manufacturing practice. Toxicological information, properties and applications of agar in food products reviewed (6,7).

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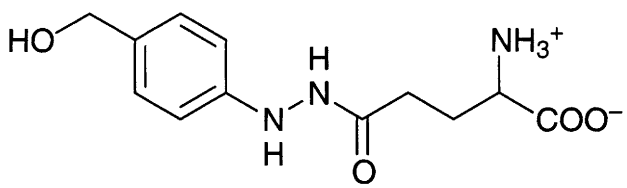
A59 agaritine



$C_{12}H_{17}N_3O_4$ **Mol. Wt.** 267.28 **CAS Registry No.** 2757-90-6

Synonyms L-glutamic acid, 5-[2-[4-(hydroxymethyl)phenyl]hydrazide]; β-*N*-[γ-L(+)-glutamyl]-4-hydroxymethylphenylhydrazine

RTECS No. MA 1284000

Occurrence Found in the edible mushroom *Agaricus bisporus* (Lange) (~0.4g kg^{-1} fresh weight).

Physical properties

M. Pt. 205-209°C (decomp.)

Solubility Water: freely soluble. Organic solvents: practically insoluble in most anhydrous organic solvents

Mammalian & avian toxicity

Acute data

Mice were administered single injections of 25, 50, 100, 200 or 400 mg kg^{-1}. High doses caused excitation, uncoordinated running, convulsions and paralysed lower backs. Oedema and desquamation of bladder epithelium, hyperaemia and haemorrhages of the lung, and vacuolated cells in the liver and kidney tubules were also observed (1).

Carcinogenicity and chronic effects

No adequate data for carcinogenicity to animals, inadequate evidence of carcinogenicity to humans, IARC classification group 3(2).

Mice administered agaritine in drinking water (625 mg l^{-1}) daily for life showed no increase in the incidence of tumours over controls (3).

Swiss mice injected subcutaneously with 100 μg g^{-1} 5 × at wkly intervals or with a single dose of 100 μg for ♀, 50 μg for ♂ showed no detectable carcinogenic effects (4).

Oral ♀ A/J mouse (26 week) the equivalent of agaritine 92 or 166 mg kg^{-1} body weight day^{-1} as a semisynthetic diet containing 11% or 22% freeze dried *Agaricus bisporus*. No statistically significant increase in the numbers of lung adenomas were observed (5).

Metabolism and toxicokinetics

Agaritine may be converted into L-glutamate and 4-(hydroxymethyl)phenylhydrazine by enzymes found in mammalian gut (6).

In mice given 3 mg agaritine by gavage, agaritine was detected in all parts of the gastrointestinal tract 15 min after dosing, but none was detectable in the gut after 3 hr (7).

Experiments using precision-cut rat, mouse and human liver slices demonstrated that agaritine can be metabolised by enzymes present in mammalian liver and lung (8).

γ-Glutamyltranspeptidase from pig's kidney decomposed agaritine to glutamic acid and 4-(hydroxymethyl)-phenylhydrazine (7).

Salmonella typhimurium TA104 was used to determine the level of activation of agaritine by rat and mouse liver and kidney enzyme systems. Rat and mouse kidney homogenates, which have high levels of γ-glutamyl transpeptidase enhanced the mutagenic response. Hepatic microsomes did not influence mutagenicity and have low levels of γ-glutamyl transpeptidase. Agaritine is a good substrate for purified γ-glutamyl transpeptidase and is converted into 4-(hydroxymethyl)-phenylhydrazine by the loss of the glutamyl moiety (9).

Genotoxicity

Salmonella typhimurium TA100 microsome mutagenicity assay weakly positive (10).

Salmonella typhimurium TA98 with and without metabolic activation negative (10).

Salmonella typhimurium TA98, TA100, TA2637 microsome mutagenicity assay, significant mutagenic activity (11).

Salmonella typhimurium TA97, TA1537 Ames test without metabolic activation positive (12).

Other comments

N'-Acetyl-4-(hydroxymethyl)phenylhydrazine (an hydrolysis product of agaritine) produced increased incidences of lung tumours and tumours of the blood vessels when administered to mice in drinking water (625 mg l^{-1}) for life (13).

4-(Hydroxymethyl)benzenediazonium ion tetrafluoroborate (a stabilised hydrolysis product of agaritine) increased the incidence of fibrosarcomas and of skin papillomas and carcinomas at the injection site of mice administered 50 mg kg^{-1} once wkly for 26 wk subcutaneously (14).

The convulsive, toxic and lethal effects of single injections of agaritine to Swiss mice were prevented by administering pyridoxone hydrochloride before and(or) after injection (15).

Canned mushroom soup and canned mushrooms did not contain detectable agaritine (7).

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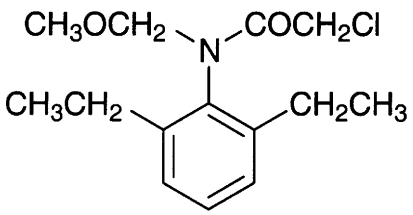
A60 alachlor



$C_{14}H_{20}ClNO_2$ **Mol. Wt.** 269.77 **CAS Registry No.** 15972-60-8

Synonyms 2-chloro-2′,6′-diethyl-*N*-methoxymethylacetanilide; 2-chloro-*N*-(2,6-diethylphenyl)-*N*-(methoxymethyl)acetamide; *N*-(methoxymethyl)-2,6-diethyl-2-chloroacetanilide; 2-chloro-2′,6′-diethyl-*N*-(methoxymethyl)acetanilide; α-chloro-2′,6′-diethyl-*N*-(methoxymethyl)acetanilide

EINECS No. 240-110-8 **RTECS No.** AE 1225000

Uses Pre- or early post-emergence herbicide.

Physical properties

M. Pt. 39.5-41.5°C **B. Pt.** 100°C at 0.02 mmHg **Specific gravity** 1.133 at 25°C
Volatility v.p. 2.1×10^{-5} mmHg at 25°C
Solubility Water: 242 mg l^{-1} at 25°C. Organic solvents: acetone, benzene, ethanol, diethyl ether, ethyl acetate

Occupational exposure

Supply classification harmful
Risk phrases Harmful if swallowed – Possible risk of irreversible effects – May cause sensitisation by skin contact (R22, R40, R43)
Safety phrases Keep out of reach of children (if sold to general public) – Wear suitable protective clothing, gloves and eye/face protection (S2, S36/37/39)

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) guppy, rainbow trout, bluegill sunfish 0.75-2.8 mg l^{-1} (1,2).

Invertebrate toxicity
EC_{50} (48 hr) *Daphnia magna* 10 mg l^{-1} (1).
EC_{50} (96 hr) *Daphnia magna* 0.05 mg l^{-1} (2).
LC_{50} (96 hr) crayfish 19.5 ppm (3).
LC_{50} (24-96 hr) mud crab larvae 27-10 mg l^{-1} (4).
Mud crab at salinity >24 ppt were hypo-osmotic while at lower salinities they were hyper-osmotic. Salinity

decreases from 10-0 ppt elevated the oxygen consumption rate and critical oxygen temperature but this response was unaffected by alachlor concentrations as high as 25 ppm (5).

Toxicity to other species

LC_{50} (route unspecified) *Bufo americanus* larvae 3.3 mg l^{-1} (6).

Environmental fate

Nitrification inhibition

Nitrogen fixation was adversely affected by concentrations of 20-80 μg l^{-1} in *Nostoc muscorum* (7).

Degradation studies

In moist sandy loam soil half-lives varied from 17 days at 25°C to 110 days at 5°C, and at 15°C varied from 46 days at 12% soil moisture to 238 days at 3.8% (8).

Anaerobic degradation was less rapid in surface soils $t_{1/2}$ 100 day, in subsurface soil (0.5-2.4 m) $t_{1/2}$ 144 day and in aquifer samples $t_{1/2}$ 337-553 days (9).

Loss from soil primarily by microbial degradation. Persists in soil for 6-10 wk depending on conditions (1).

Under aerobic conditions, $t_{1/2}$ 23 day in surface soil, $t_{1/2}$ 73-284 day in the vadose zone and $t_{1/2}$ 320-324 day in aquifers. Addition of organic nutrients enhanced aerobic degradation in subsurface soils and one aquifer sample (9).

Rapidly biodegraded by soil fungi to release the chloride ion. Other metabolites detected include 2-chloro-2′,6′-diethylacetanilide, 2,6-diethyl-*N*-(methoxymethyl)aniline, 2,6-diethylaniline and 1-chloroacetyl- 2,3-dihydro-7-ethylindole. Soil incubation studies using alkaline hydrolysis suggest that metabolites were bound to soil organic matter (10).

Alachlor incubated under upland soil conditions for 80 days yielded four major degradation products 8-ethyl-2-hydroxy-*N*-(methoxymethyl)-1,2,3, 4-tetrahydroquinoline, *N*-hydroxyacetyl- 2,3-dihydro-7-ethylindole, 2-hydroxy-2′,6′-diethyl-*N*-(methoxymethyl)acetanilide and 9-ethyl-1,5-dihydro-1-(methoxymethyl)-5-methyl-4,1-benzoxazeprin-2(3*H*)-one (11).

Mammalian & avian toxicity

Acute data

LD_{50} oral mallard duck >2000 mg kg^{-1} (12).

LD_{50} oral mouse, rat 462-1200 mg kg^{-1} (13,14).

LD_{50} oral rat 930-1200 mg kg^{-1} (1).

LD_{50} oral mouse 1100 mg kg^{-1} (1).

LC_{50} (4 hr) inhalation rat 1.04 mg l^{-1} (1).

LD_{50} dermal rabbit 3500 mg kg^{-1} (15).

Sub-acute and sub-chronic data

LC_{50} (8 day feeding trial) oral pheasant, bobwhite quail >5000-10,000 ppm (3).

Ninety-day feeding trials, no effect observed in rats or dogs ≤200 mg kg^{-1} diet (1).

Carcinogenicity and chronic effects

No-observable-effect level (2 yr) for rats ≤2.5 mg kg^{-1} body weight day^{-1} (1).

Metabolism and toxicokinetics

In vitro incubation with microsomal fractions prepared from liver and nasal turbinates of rats and mice. Biotransformation to 3,5-diethylbenzoquinone-4-imine occurred via oxidation of 2,6-diethylaniline and 4-amino-3,5-diethylphenol intermediates (16).

Intraperitoneal ♂ rat (7 day) 1 or 100 mg kg^{-1} metabolised via the monooxygenase system (17).

Incubation of alachlor in the presence of GSH with the cytosolic fraction from rat, mouse and monkey livers produced the GSH conjugate of alachlor as the initial metabolite; further degradation occurred via the mercapturic acid pathway to yield cysteinylglycine, cysteine and *N*-acetylcysteine conjugates of alachlor. Species and gender differences were observed (18).

Following intravenous administration to rhesus monkeys, an average of 88% and 10% of radiolabelled alachlor was recovered in the urine and faeces, respectively, within 48 hr (19).

Irritancy
Reported to be a mild irritant to rabbit skin and non-irritating to rabbit eyes (1).

Sensitisation
Contact sensitisation reactions observed in guinea pigs (1).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537, TA1538 with and without metabolic activation negative (20).
Saccharomyces cerevisiae D4 with metabolic activation positive for technical grade alachlor (20).
Tradescantia paludosa (18-24 hr) 0.8% alachlor increased the incidence of chromosomal aberrations (21).
In vitro human lymphocytes and *in vivo* rat bone marrow cells dose-dependent increase in chromosomal aberrations and clastogenic effects (22).
Induced a dose-dependent increase in sister chromatid exchanges in human lymphocytes *in vitro*. Alachlor also increased DNA single strand breaks and alkali labile lesions of DNA (23).
Drosophila melanogaster wing spot test. Alachlor induced significant increases in both small and total spots at all four concentrations assayed, and in the frequency of twin spots at the highest concentration tested (10 mM) (24).
Mouse bone marrow micronucleus test negative (25).

Other effects

Other adverse effects (human)
Passive exposure studies carried out by the US EPA to predict the dosage range received by US farmers during use established a range of 0.0054-0.54 μg kg^{-1} lb^{-1} of active ingredient during open pour mixing and loading and a range of 0.0034-0.34 μg kg^{-1} lb^{-1} of active ingredients during mechanical mixing and loading (26).
Cancer incidence among chemical workers with occupational and environmental exposure to alachlor was investigated in an historical cohort study among 943 workers with at least one year cumulative employment at a Monsanto plant from start up in 1968 to 1990. Approximately 96% of workers were traced and their cancer status determined; 18 workers were diagnosed with cancer during the follow-up period. The standardised incidence ratio for all cancers, particularly colorectal cancers and chronic myeloid leukaemia, was slightly elevated for workers exposed to alachlor compared to Iowa residents (27).

Legislation

WHO Toxicity Class III (28).
EPA Toxicity Class III (1).
Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides and related products: maximum admissible concentration 0.1 μg l^{-1} (29).
Included in Schedule 6 (Release into Land: Prescribed Substances) of Statutory Instrument No. 472, 1991 (30).

Other comments

Tolerable daily intake for humans 0.1 mg kg^{-1} day^{-1} (31).
The properties, toxicology, pharmacokinetics, environmental fate and health effects in humans and animals reviewed (32-34).
Metabolic pathways reviewed (35).

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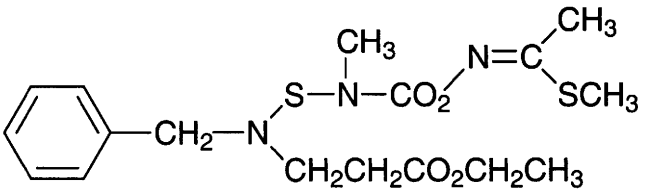
A61 alanycarb



$C_{17}H_{25}N_3O_4S_2$ **Mol. Wt.** 399.54 **CAS Registry No.** 83130-01-2

Synonyms ethyl(*Z*)-*N*-benzyl-*N*-[[methyl(1-methylthioethylideneamino-oxycarbonyl)amino]thio]-β-alaninate; (*Z*)-ethyl 3,7-dimethyl-6-oxo-9-(phenylmethyl)-5-oxa-2,8-dithia-4,7,9-triazadodec-3-en-12-oate

Uses Insecticide and nematicide.

Physical properties

M. Pt. 46.8-47.2°C **Flash point** 134°C (closed cup) **Specific gravity** 1.207 at 20°C
Partition coefficient log P_{ow} 3.43 (19-21°C, pH 7) **Volatility** v.p. 3.5×10^{-8} mmHg (20°C)
Solubility Water: 20 mg l^{-1} (20°C). Organic solvents: acetone, benzene, dichloromethane, ethyl acetate, methanol, xylene

Ecotoxicity

Fish toxicity
LC_{50} (48 hr) carp 1.0 mg l^{-1} (1).

Invertebrate toxicity
LC_{50} *Daphnia magna* (3 hr) > 9.4 mg l^{-1} (1). LD_{50} (topical) 0.8 μg bee^{-1} (1).

Environmental fate

Degradation studies
DT_{50} in soil 1-2 days. Alanycarb is rapidly degraded to methomyl by chemical or microbial action. Methomyl formed is further degraded to methomyl oxime, which is eventually degraded to carbon dioxide (1).

Abiotic removal
Degraded on glass plate under sunlight, DT_{50} 6hr (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 440 mg kg^{-1} (1).
LC_{50} (4 hr) rat >205 mg m^{-3} air (1).
LD_{50} dermal ♂ rat > 2000 mg kg^{-1} (1).
LC_{50} (8 days) bobwhite quail, mallard ducks 3553, >5000 ppm in diet, respectively (1).

Teratogenicity and reproductive effects
Non-teratogenic in rats and rabbits (1).

Metabolism and toxicokinetics
Alanycarb is rapidly metabolishd in rats. This occurs either directly or via methomyl, to methomyl oxime, which is subsequently metabolised to unstable intermediates. These are converted into acetonitrile and carbon dioxide, which are eliminated mainly via respiration and in the urine (1).

Irritancy
Slightly irritating to eyes but not to skin of rabbits (1).

Sensitisation
Non-sensitising to the skin of guinea pigs (1).

Genotoxicity

Ames test negative (1).

Legislation

WHO Toxicity Class II (2).
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) of Statutory Instrument No. 472, 1991 (4).

Other comments

The initial metabolic step in plants is N-S bond cleavage to give methomyl, which is further metabolised through methomyl oxime to acetic acid or acetonitrile. The final metabolic product is carbon dioxide (5).

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A62 aldicarb

$$CH_3SC(CH_3)_2CH{=}NOCONHCH_3$$

$C_7H_{14}N_2O_2S$ **Mol. Wt.** 190.27 **CAS Registry No.** 116-06-3

Synonyms carbanalate; 2-methyl-2-(methylthio)propionaldehyde; *O*-(methylcarbamoyl)oxime; 2-methyl-2-(methylthio)propanol; *O*-[(methylamino)carbonyl]oxime; Temik; UC21149

EINECS No. 204-123-2 **RTECS No.** UE 2275000

Uses An insecticide, acaricide and nematocide.

Physical properties

M. Pt. 99-100°C **Specific gravity** 1.1950 at 20°C with respect to water at 25°C
Partition coefficient log P_{ow} 1.359 (1) **Volatility** v.p. 9.8×10^{-6} mmHg at 20°C
Solubility Water: 6 g l^{-1} at 25°C. Organic solvents: acetone, benzene, xylene, dichloromethane

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) – 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) zebrafish, guppy 52.9 μM, 3.5 μM, respectively (2).
LC_{50} (96 hr) rainbow trout, bluegill sunfish, fathead minnow 0.88-13.4 mg l^{-1} (3-5).
Puntius conchonius chronic exposure to sublethal concentrations 0.8 ppm caused hepatic lesions, including hypertrophy, vacuolisation, nuclear pycnosis and karyolysis (6).
Exposure of *Barbus conchonius* (15 and 30 day) 48 μg l^{-1} caused hypercholesterolaemia, moderate polycythemia, a rise in haemoglobin content and decrease in blood glucose levels. Main target organ liver (7).
LC_{50} value varies at different temperatures and water hardness (1).

Invertebrate toxicity
LC_{50} (24 hr) *Paramecium multimicronucleatum* static bioassay 93 ppm (8).
LC_{50} (14 day) *Lumbricus terrestris* 530 mg kg^{-1} dry soil substrate (9).
LC_{50} (14 day) *Eisenia foetida* 65 mg kg^{-1} dry soil substrate (9).
Two 1 hr exposures of aldicarb caused significantly fewer symptoms of intoxication than a 2 hr continuous exposure in the midge *Chironomus riparius* if at least 2 to 6 hr in clean water was provided between doses (10).
Toxic to bees (3).

Environmental fate

Nitrification inhibition

Aldicarb at concentrations of 5 ppm caused 100% inhibition of *Nitrosomonas europaea* (11).

Severe damage was observed to a soil nitrifying population for the first 16 wk after application of 2.5 g m^{-2} aldicarb. Incubations in the field and under laboratory conditions without substrate addition showed negligible effects whereas incubation with ammonium sulfate led to an reduction in nitrification (12).

Degradation studies

Surface soils up to 75 cm deep $t_{1/2}$ 20-361 days and in subsurface soils up to 183 cm $t_{1/2}$ 131-233 days. Metabolites detected included aldicarb sulfoxide and sulfone and their oximes and sulfoxide nitrile (13).

Under aerobic conditions, aldicarb was metabolised rapidly to aldicarb sulfoxide which was slowly oxidised to aldicarb sulfone. These reactions were more rapid in surface and shallow subsurface soils than in deeper subsurface soils. Additional metabolites detected were oxime, nitrile and acid derivatives of aldicarb sulfoxide; $t_{1/2}$ 29-78 days for total toxic residues (14).

Acclimated *Pseudomonas* sp. degraded 50% of an unspecified initial concentration of aldicarb in 24-32 hr (15).

In a model ecosystem aldicarb demonstrates a high degree of persistence and a low biodegradability potential (16).

Degraded rapidly in soils depending on soil type; loamy, sandy and clay soils were 5, 6, 10 days, respectively. Main degradation products were sulfoxide and sulfone derivatives which were further degraded by soil microorganisms, including *Bacillus* sp. (17).

In loamy sand soil reported $t_{1/2}$ 9 days with no residues present 4 months after application (18).

Biotransformation rate in surface waters 0.004-0.01 day^{-1} ($t_{1/2}$ 70-173 days). In small hydrological systems such as field ditches and channels it appears to be transformed rapidly, but persists for longer in large water bodies such as main discharge channels and lakes (19).

Abiotic removal

No degradation was observed in sterile or unsterile groundwater in 60-65 day at pH 5.2 and 6.0. Its metabolite sulfone or its hydrolysis products were not detected (13,20).

Hydrolytic $t_{1/2}$ at 20°C in water were 6 and 131 days at pH 8.85 and 3.95, respectively, while hydrolytic $t_{1/2}$ at 15°C in soil were 10 and 990 days at pH 7 and 5.4, respectively (21-23).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 0.93 mg kg^{-1} (24).

LC_{50} (5 min) inhalation rat, mouse, guinea pig 200 mg m^{-3} (1).

LD_{50} dermal rabbit 5 mg kg^{-1} (24).

LD_{50} dermal rat 850 mg kg^{-1} (1).

Classified as very toxic using the acute-toxic-class method, an alternative to the LD_{50} test (25).

Sub-acute and sub-chronic data

LC_{50} (8 day) dietary bobwhite quail 71 mg kg^{-1} (3).

Adult ♀ mice (34 day) 1, 10, 100 ppb day^{-1} in water. Effects to T-cells, T-suppressor, T-helper and B-cells were evaluated and the authors concluded that aldicarb does not result in adverse effects to the immune system in mice (26).

Carcinogenicity and chronic effects

No adequate data for carcinogenicity to humans, inadequate data for carcinogenicity to animals, IARC classification group 3 (27).

The National Toxicology Program tested ♂ and ♀ rats and mice via dosed-feed. Negative evidence of carcinogenicity in all animals (28).

In a 2-yr feeding trial, rats given 0.3 mg kg^{-1} day^{-1} were unaffected (3).

Teratogenicity and reproductive effects

Chick embryo brain and limb bud cultures were treated with aldicarb with or without activation for 5 days.

Without activation 40-200 ppm of aldicarb has no effect on limb cell cytotoxicity but at >160 ppm and with activation cellular cytotoxicity was reduced. In both instances aldicarb caused a significant increase in the spread of the brain but not limb colonies (29).
Pregnant ♀ rats (18th day gestation) were given a single 0.1 mg kg^{-1} dose aldicarb by gastric intubation. Rats were sacrificed at 1, 6, 12 and 24 hr after administration. Significant reduction of acetylcholinesterase activity detected in blood, brain and liver tissues of both dams and foetuses (30).
Pregnant rats were fed 0-1.0 mg kg^{-1} aldicarb throughout pregnancy until pups were weaned. No significant effects on fertility, viability of offspring, lactation or other parameters observed (1).
Aldicarb was injected into chicks *in ovo* on day 15 of incubation at 0.2, 0.4 and 3.5 mg kg^{-1} egg weight. At lower doses a trend was seen towards decreases in cerebral dopamine and homovanillic acid. At higher doses significant decreases were seen in homovanillic acid and 5-hydroxyindolacetic acid. Persistent locomotion alterations were observed only at the highest dose (31).
In a study of 1500 subjects who had consumed water from wells contaminated with 8-66 µg l^{-1} aldicarb during 1981, the rate of spontaneous abortions was high in women consuming water contaminated with >66 µg l^{-1} (1).

Metabolism and toxicokinetics

In numerous animal studies the principal excretion route for aldicarb and its metabolites, which include aldicarb sulfoxide, aldicarb sulfone, oxime sulfoxide, oxime sulfone, nitrile sulfoxide and nitrile sulfone, is via the urine (>90%). Small amounts are also excreted via the faeces and exhaled as carbon dioxide (32).
In rat *in vitro* hepatic, renal and pulmonary microsomal metabolic studies the only metabolite produced was aldicarb sulfoxide. Further conversion into aldicarb sulfone was negligible. The average maximal velocities for the sulfoxidation of aldicarb in liver, kidney and lung microsomes were 5.41, 39.51 and 2.45 µmol min^{-1} mg^{-1} protein, respectively. Corresponding Michaelis constant values were 184, 1050, and 188 µmol, respectively (33).

Irritancy

Four cases of contact dermatitis and one case of eye irritation (chemical conjunctivitis) have been reported after contact with temik (34).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA1535, TA1537 with and without metabolic activation negative (35).
In vitro mouse lymphoma L5178Y tk+/tk– with metabolic activation positive (36).
In vitro Chinese hamster ovary cells induction of micronuclei dose and sample-time dependent (37).
In vivo mouse bone marrow erythrocytes induction of micronuclei dose and sample-time dependent (37).

Other effects

Other adverse effects (human)

In 1985, a study linked ingestion of aldicarb-contaminated drinking water with altered T-cell distribution in humans. In a follow-up study in 1987, 45 of the 50 initial participants and a further 27 women took part. From this group only 5 were found to be exposed currently. This group of 5 women compared to 39 unexposed controls had an increased percentage of lymphocytes and an increased number of CD2 and T-cells. No identified water contaminant apart from aldicarb could explain these findings (38).
Symptomatic effects include headache, dizziness, anxiety, excessive sweating, salivation, lachrymation, increased bronchial secretions, vomiting, diarrhoea, abdominal cramps, muscle fasciculations and pinpoint pupils (1).

Any other adverse effects

The toxicity of aldicarb is based on its transient inhibition of acetylcholinesterase. Carbamates form unstable complexes with cholinesterase by carbamolyation of the active site of the enzymes. The process is quickly reversible (39,40).

Legislation

In 1982 the FAO/WHO set the acceptable daily intake in food of 5 mg kg^{-1} body weight (41).
Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides and related products: maximum admissible concentration 0.1 µg l^{-1} (42).
Included in Schedule 6 (Release into Land: Prescribed Substances) of Statutory Instrument No. 472, 1991 (43).

Other comments

Aldicarb residues have been found in potable water sources from wells in the US and some fruit and vegetables (44,45).

Mint can absorb aldicarb in sufficient concentrations rendering the plant toxic to pests and highly dangerous when consumed by humans in small amounts (46).

Biochemical properties, toxicology, mutagenicity, teratogenicity, carcinogenicity and environmental effects reviewed (27,47-51).

Reviews on human health effects, experimental toxicology, physico-chemical properties and exposure levels are listed (52).

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A63 aldol

$$CH_3CH(OH)CH_2CHO$$

$C_4H_8O_2$ **Mol. Wt.** 88.11 **CAS Registry No.** 107-89-1

Synonyms 3-hydroxybutanal; 3-hydroxybutyraldehyde; acetaldol; β-hydroxybutyraldehyde; oxybutyric aldehyde

EINECS No. 203-530-2 **RTECS No.** ES 3150000

Uses In the manufacturing of rubber vulcanisers, accelerators and age resisters. Ore flotation. An hypnotic and sedative.

Physical properties

M. Pt. 0°C **B. Pt.** 83°C at 20 mmHg **Flash point** 65.5°C (open cup) **Specific gravity** 1.109 at 16°C with respect to water at 4°C **Volatility** v.p. 21 mmHg at 20°C
Solubility Water: miscible. Organic solvents: miscible with diethyl ether, methanol

Occupational exposure

UN No. 2839 **HAZCHEM Code** 2X **Conveyance classification** toxic substance

Environmental fate

Degradation studies
BOD_{10} 0.9 using standard dilute sewage (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 2180 mg kg^{-1} (2).
LD_{50} dermal rabbit 140 mg kg^{-1} (3).

Carcinogenicity and chronic effects
The length of exposure prior to the appearance of cancer was 26 ± 4 yr for 4 patients 55-59 yr old and 4 patients >65 yr; all smoked 5-10 cigarettes day^{-1}. One patient developed cancer at 58 yr after 13 yr exposure and smoking >30 cigarettes day^{-1}. Of the cancers, 5 affected the bronchi, 2 the mouth, 1 the stomach and 1 the caecum. Syncarcinogenic effects of the aliphatic aldehyde mixture and the possible carcinogenicity of acetaldehydes are discussed (4)

Irritancy
100 mg instilled in rabbit eye (duration unspecified) caused mild irritant effects (2).

Other comments

Decomposes to crotonaldehyde and water when heated.

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A64 aldoxycarb

$$CH_3SO_2C(CH_3)_2CH{=}NOCONHCH_3$$

$C_7H_{14}N_2O_4S$ **Mol. Wt.** 222.27 **CAS Registry No.** 1646-88-4

Synonyms 2-methyl-2-methylsulfonylpropionaldehyde *O*-methylcarbamoyloxime; 2-methyl-2-methylsulfonylpropionaldehyde *O*-methylcarbamoyloxime; 2-methyl-2-methyl sulfonyl propionaldehyde *O*-methylcarbamoyloxime; 2-methyl-2-(methlsulfonyl)propanal *O*-(methylcarbamoyl)oxime

EINECS No. 216-710-0 **RTECS No.** UE 2080000

Uses Systemic insecticide, acaricide and nematicide.

Physical properties

M. Pt. 140-142°C **Volatility** v.p. 9.0×10^{-5} mmHg at 25°C
Solubility Water: 10 g l^{-1} at 25°C. Organic solvents: acetone, acetonitrile, chloroform, methanol

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) trout, bluegill sunfish 40, 55 mg l^{-1}, respectively (1).

Invertebrate toxicity
Low toxicity to bees (1).

Environmental fate

Degradation studies
In anaerobic reduced subsoil yielded corresponding nitriles and aldehydes as degradation products (2).
Residual activity in soil for 4-8 wk (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral mallard duck 33.5 mg kg^{-1} (1).
LD_{50} oral rat 26.8 mg kg^{-1} (technical material in corn oil) (1,3).
LC_{50} (4 hr) inhalation rat 0.14 mg l^{-1} air (1).
LD_{50} dermal rabbit 1000 mg kg^{-1} (4).
LD_{50} percutaneous rabbit 200 mg kg^{-1} (1).

Sub-acute and sub-chronic data

LC_{50} (8-day dietary) bobwhite quail, mallard duck 5706, >10,000 mg kg^{-1}, respectively (1).

Carcinogenicity and chronic effects

Life-span feeding trials (2 yr) no-effect levels were mouse 9.6 mg kg^{-1} day^{-1} and rat 2.4 mg kg^{-1} day^{-1} (1).

Metabolism and toxicokinetics

Aldoxycarb is degraded (species unspecified) through the hydrolysis of the carbamate ester to aldoxycarb oxime, and elimination of the methylcarbamate group to give aldoxycarb nitrile (1).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides and related products: maximum admissible concentration 0.1 $\mu g\ l^{-1}$ (5).
Included in Schedule 6 (Release Into Land: Prescribed Substances) of Statutory Instrument No. 472, 1991 (6).

Other comments

Major metabolite of aldicarb (7).

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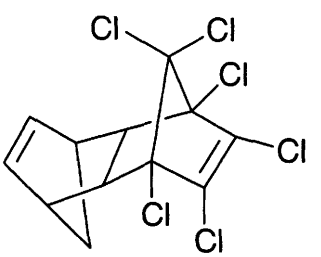
A65 aldrin



$C_{12}H_8Cl_6$ **Mol. Wt.** 364.91 **CAS Registry No.** 309-00-2

Synonyms (1*R*,4*S*,4a*S*,5*S*,8*R*,8a*R*)-1,2,3,4,10,10-hexachloro-1,4,4a,5,8,8a-hexahydro-1 ,4:5,8-dimethanonaphthalene; 1,2,3,4,10,10-hexachloro-1,4,4a,5,8,8a-hexahydro-*exo*-1,4-*endo*-5,8-dimethanonaphthalene; HHDN; 1,2,3,4,10,10-hexachloro-1α,4α,4aβ,5α,8α,8aβ-hexahydro-1,4:5,8-dimethanonaphthalene

EINECS No. 206-215-8 **RTECS No.** IO 2100000

Uses Insecticide.

Physical properties

M. Pt. 104-104.5°C **B. Pt.** 145°C at 2 mmHg **Specific gravity** 1.70 at 20°C **Volatility** v.p. 6.45×10^{-5} mmHg at 20°C

Solubility Water: <0.05 mg l^{-1}. Organic solvents: acetone, benzene, xylene

Occupational exposure

DE-MAK 0.25 mg m^{-3} (inhalable dust fraction) **FR-VLE** 0.25 mg m^{-3}

UK-LTEL 0.25 mg m^{-3} **UK-STEL** 0.75 mg m^{-3}

US-TWA 0.25 mg m^{-3}

Supply classification toxic, dangerous for the environment

Risk phrases Toxic in contact with skin and if swallowed – Possible risk of irreversible effects – Toxic: danger of serious damage to health by prolonged exposure in contact with skin and if swallowed – Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment (R24/25, R40, R48/24/25, R50/53)

Safety phrases Keep locked up and out of the reach of children (if sold to general public) – Do not breathe dust – Wear suitable protective clothing and gloves – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) – This material and/or its container must be disposed of as hazardous waste – Avoid release to the environment. Refer to special instructions/safety data sheet (S1/2, S22, S36/37, S45, S60, S61)

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) chinook salmon, rainbow trout, fathead minnow, black bullhead, channel catfish, bluegill sunfish, largemouth bass 2.6-53 μg l^{-1} in a static bioassay at 13-24°C (1).

LC_{50} (96 hr) threespine stickleback 27.4 ppb in a static bioassay (2).

Sub-acute dose 0.14 ppm aldrin induced hyperchloraemia in catfish within 4 days, while sublethal doses 0.035 ppm caused hypochloraemia at 15, 25, 35, 50 and 70 days after exposure. The decrease in chlorine concentration was not significant in treated fish at 25 and 35 days (3).

In long-term static bioassays ≤4 months *Puntius conchonius* 0.0466 μg l^{-1} only stage III oocytes were totally resistant to damage (4).

Invertebrate toxicity

Mercenaria mercenaria 10-day eggs treated with 1000 ppb 0% survival (2).

LC_{50} (96 hr) *Pteronarcys californica, Acroneuria pacifica* 180-200 μg l^{-1} (5).

LC_{50} (96 hr) scud, glass shrimp, stonefly 1.3-4300 μg l^{-1} in a static bioassay at 15-21°C (1).

EC_{50} (48 hr) daphnid, seed shrimp 18-32 μg l^{-1} in a static bioassay at 15-21°C (1).

In vitro administration of aldrin (concentration and duration unspecified) *Panaeid* prawn caused inhibition of acid and alkali phosphatase activity in stomach, muscle, gill and brain in a dose-dependent manner (6).

Sublethal concentrations induced persistent hyperplasia and proliferation of mucosal epithelium to the midgut of the freshwater crab *Paratelphusa masoniana* (7).

Bioaccumulation

Confirmed to be accumulated at a high level (8).

Bioconcentration factors in molluscs 4571, golden orfe 3890 and *Chlorella fusca* 12,260 (9-11).

Anabaena sp. and *Aulosira fertilissima* bioconcentration ranges were 3.9-247.5 μg g^{-1} and 6.3-302.3 μg g^{-1}, respectively. Maximum concentration of aldrin was reached in 8.16 hr and metabolism to dieldrin occurred (12).

Environmental fate

Degradation studies

Biodegradable (8).

75%-100% disappearance from soil in 1-6 yr (2).

No biodegradation of aldrin at 5 and 10 mg l^{-1} was observed using a mixed culture inoculum from sewage (13).

Dunaliella sp. degraded 23.3% initial aldrin (concentration unspecified) to dieldrin and 5.2% to the diol (14).

Abiotic removal

Degradation products of 5 mg saturated aldrin vapour treated with a sunlamp for 45 hr were dieldrin (50-60 μg) and photoaldrin (20-30 μg) (15).

Adsorption and retention

Calculated soil sorption coefficient suggest minimal leaching to groundwater (16).

Mammalian & avian toxicity

Acute data

LD_{50} oral bobwhite quail 7 mg kg^{-1} (1).
LD_{Lo} oral child 1250 μg kg^{-1} (17).
LD_{50} oral rat, rabbit, hamster, guinea pig 33-100 mg kg^{-1} (18).
LD_{50} dermal rat, rabbit 15-98 mg kg^{-1} (18).
Classified as toxic using the acute-toxic-class method, an alternative to the LD_{50} test (19).

Carcinogenicity and chronic effects

Inadequate evidence for carcinogenicity to humans, IARC classification group 3 (20).
Feed F344 rats, B6C3F1 mice (74-80 wk) 0.0008-0.006% caused liver carcinomas only in mice, US National Toxicology Program classification D, single sex of a single species with a single tissue affected (21).
Target organ of carcinogenicity: mouse liver (22).
The National Toxicology Program tested mice and rats via dosed-feed. Equivocal evidence of carcinogenicity in ♂ and ♀ rats, negative evidence in ♀ mice and positive evidence in ♂ mice (23).

Teratogenicity and reproductive effects

Oral rat (13 or 26 day) unspecified concentration of aldrin caused extensive degeneration of all varieties of germ cells at stage VII, reduction in sperm count, luteinising hormone and testosterone. It was concluded that aldrin may have a direct inhibitory influence on gonadotropin release, and the possibility of direct action on the testes was discussed (24).

Metabolism and toxicokinetics

Intravenous rat (concentration unspecified) detected in liver, duodenum, intestine and faeces (25).
In rats, topically applied aldrin is metabolised to dieldrin in the skin during absorption, but the overall proportion of metabolism that takes place in the skin is small compared with the contribution of the liver (26).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA102 with and without metabolic activation negative (27).
Escherichia coli PQ37 SOS-Chromotest with or without metabolic activation negative (27,28).
Oral mouse 13, 19.5 and 39 mg kg^{-1} caused dose-dependent increases in the frequency of autosomal univalents and sex univalents. Aneuploidy and translocations were reported only for highest dose while polyploidy was significantly increased at 19.5 and 39 mg kg^{-1} (29).
Sister chromatid exchanges frequencies were not elevated in workers handling aldrin (30).

Other effects

Other adverse effects (human)

In a study of 100 women, aldrin was detected in maternal blood, placenta and umbilical cord blood, indicating placental transfer (31).
Central nervous system disturbances including nausea, vomiting, tremors, ataxia, muscular incoordination, epileptic convulsions, renal damage, albuminuria, haematuria and respiratory failure (23).

Any other adverse effects

Following aldrin administration to goats blood, lactate, pyruvate and glucose levels increased significantly and the activity of the serum enzymes aldolase and lactate dehydrogenase increased. The levels of the gluconegenic enzymes (glucose-6-phosphatase and fructose-1,6-biphosphatase) and glycolytic enzymes (aldolase, hexokinase and lactate dehydrogenase) did not change significantly (32).

Legislation

Included in Schedules 5 and 6 (Release into Water/Land: Prescribed Substances) of Statutory Instrument No. 472, 1991 (33).

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides and related products: maximum admissible concentration 0.1 $\mu g\ l^{-1}$ (34).

Other comments

Has been detected but not quantified in drinking water in the Netherlands, Canada and the US (35-37).

Toxicology, human exposure and health effects reviewed (38-41).

The environmental fate and occurrence of aldrin in human food and human tissue have been extensively reviewed (41,42).

The response of fish to toxicants of this type is heavily dependent upon the manner in which they are formulated, because this effects the distribution of the compound in the water.

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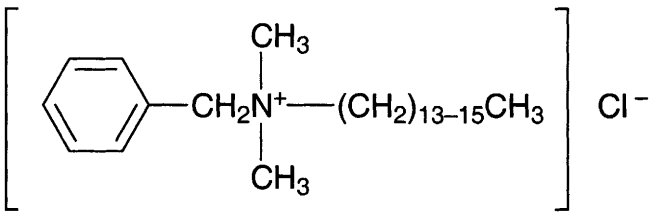
A66 alkyl(C_{14}-C_{16})dimethylbenzylammonium chloride



CAS Registry No. 63449-41-2

Synonyms benzyldimethylalkyl(C_{14}-C_{16})ammonium chloride; Roccal; Tret-o-lite XC511

EINECS No. 264-151-6 **RTECS No.** BO 3151000

Uses Bactericide. Fungicide.

Occupational exposure

Supply classification corrosive, dangerous for the environment

Risk phrases Harmful in contact with skin and if swallowed – Causes burns – Very toxic to aquatic organisms (R21/22, R34, R50)

Safety phrases Keep out of reach of children (if sold to the 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 (S2, S36/37/39, S45, S61)

Ecotoxicity

Fish toxicity

LC_{50} (24-96 hr) harlequin fish 2.45-0.62 mg l^{-1} (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, mouse 150-300 mg kg^{-1} (2,3).

LD_{50} dermal rat 1420 mg kg^{-1} (2).

Irritancy

2 mg instilled into eye of rat, mouse, dog, guinea pig and hamster caused severe irritation (4,5).

Other effects

Other adverse effects (human)

Human fatalities have been reported for alkyldimethylbenzylammonium chloride. where the alkyl group ranges from C_8-C_{18} and C_{15}-C_{18}, after intramuscular or intravenous administration as well as intra-uterine instillation (6).

References

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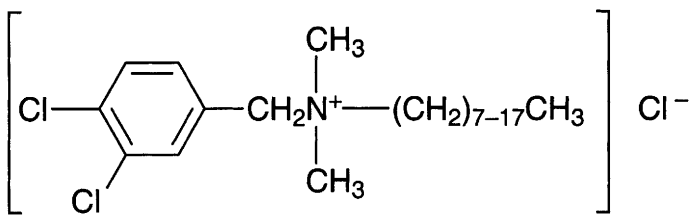
A67 *N*-alkyl(C_8-C_{18})dimethyl-3,4-dichlorobenzylammonium chloride



CAS Registry No. 8023-53-8

Synonyms Tetrosan 3,4D; 3,4-dichlorobenzylammonium chloride, *N*-alkyldimethyl-

RTECS No. BO 3200000

Uses Antiseptic, germicide, algicide, sanitiser and deodorant.

Mammalian & avian toxicity

Acute data

LD_{50} oral guinea pig, rat, mouse 316-2000 mg kg^{-1} (1).

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

Irritancy

1% instilled in rabbit eye (unspecified duration) caused severe irritant effects (2).

Other comments

Toxicity reviewed (3).

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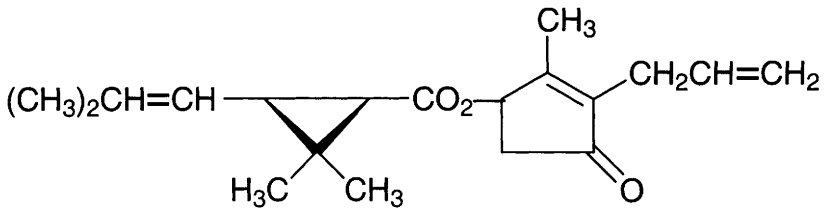
A68 allethrin



$C_{19}H_{26}O_3$ **Mol. Wt.** 302.41 **CAS Registry No.** 584-79-2

Synonyms cyclopropanecarboxylic acid, 2,2-dimethyl-3-(2-methyl-1-propenyl)-, 2-methyl-4-oxo-3-(2-propenyl)-2-cyclopenten-1-yl ester; 2-cyclopenten-1-one, 2-allyl-4-hydroxy-3-methyl-2,2-dimethyl-3-(2-methylpropenyl)cyclopropanecarboxylate; chrysanthemummonocarboxylic acid, 3-allyl-2-methyl-4-oxo-2-cyclopenten-1-one

EINECS No. 209-542-4 **RTECS No.** GZ 1925000

Uses Synthetic pyrethroid, non-systemic with contact and respiratory action, used against household pests.

Physical properties

M. Pt. ≈4°C (*dl-trans*-allethrin 51°C) **B. Pt.** 140°C at 0.1 mmHg **Flash point** 87°C
Specific gravity 1.005 at 25°C with respect to water at 4°C **Volatility** v.p. 1.2×10^{-4} mmHg at 30°C
Solubility Water: practically insoluble in water. Organic solvents: miscible with carbon tetrachloride, 1,2-dichloroethane, ethanol, hexane, light petroleum, 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) – Wear suitable protective clothing (S2, S36)

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) channel catfish, bluegill sunfish, rainbow trout, steelhead, salmon 10-56 μg l^{-1} (1,2).

Invertebrate toxicity
LC_{50} (96 hr) freshwater shrimp 8-11 μg l^{-1} (1).
EC_{50} (48 hr) Daphniidae 21-56 μg l^{-1} (1).
LC_{50} (96 hr) *Pteronarcys californica* 2.1 μg l^{-1} (1). LD_{50} oral honey bee 3.4 μg bee^{-1} at 26-27°C (3).
LD_{50} contact honey bee 9.1 μg bee^{-1} at 26-27°C (3).

Environmental fate

Abiotic removal
Photochemical changes occurring in the acid moiety involve stepwise oxidation of the *trans*-methyl group to the alcohol, aldehyde, carboxyl derivatives and oxidation of the double bond to a keto-group with subsequent formation of *trans*-carbonic acid esters (4).

Mammalian & avian toxicity

Acute data

LD_{50} oral bobwhite quail 2030 mg kg^{-1} (5).
LD_{50} oral ♂, ♀ rat 1100, 585 mg kg^{-1} respectively (5).
LD_{50} percutaneous rat >2500 mg kg^{-1} (5).
LD_{Lo} intravenous rat, intracerebral mouse 4 mg kg^{-1} (6,7).

Sub-acute and sub-chronic data

Wistar rats in diet (12 wk) 5000-15,000 mg kg^{-1} caused decrease in body-weight gain and an increase in liver-to-kidney weight ratio (8).
♂ ICR mice were exposed to mosquito-coil smoke with or without *d*-allethrin at airborne particle concentrations 0 or 1.27 mg m^{-3} for 7 hr day^{-1}, 7 days wk^{-1} for 1, 3, 6 or 12 months. After 1 month exposure alterations were seen in the alveolar pattern in the treated and sham mice, and histopathological lesions included the loss of cilia. After exposure for 3 and 6 months the lesions in the trachea persisted. The intercellular fibrosis in the lung was increased in both the treated and sham groups at 6 months and became more severe at later stages. After 12 months, an increase in vascularity of the alveolar wall was seen and fine granular debris was present in the alveolar space (9).

Metabolism and toxicokinetics

In mammals, following oral administration one of the two terminal methyl groups of the chrysanthemic acid moiety is oxidised in the liver to an alcohol group, and further to a carboxyl group (5).
Allethrin administered orally to mammals is absorbed from the intestinal tract and distributed to tissues. A 500 mg kg^{-1} dose of the *trans*-isomer was excreted via the urine and faeces within 20 days (8).
Oral rat 1-5 mg kg^{-1} 60% eliminated in urine and faeces within 48 hr. Major metabolic reactions include ester hydrolysis, oxidation at *trans*-methyl of the isobutenyl group, *gem*-dimethyl of cyclopropane ring, and the methylene of the allyl group and 2,3-diol formation at the allylic group. Major urinary metabolites were chrysanthemum dicarboxylic acid, and allethrolone (10).

Irritancy

Application of 10% olive oil solution to rabbit eye, slight hyperaemia of the conjunctiva and eye discharge observed 10 min and 2 hr after application, respectively. A 5% olive oil solution applied to guinea pig skin on alternate days for 20 days, animals were challenged with an intradermal injection 2 wk later, no sensitisation observed but slight lymphocytic and monocytic infiltration of the dermis was noted (10).

Genotoxicity

In vitro Chinese hamster ovary cells sister chromatid induction negative (11).

Other effects

Any other adverse effects

Symptomatic effects in a range of species include hyperactivity, tremors, convulsion and paralysis (10).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides and related products: maximum admissible concentration 0.1 μg l^{-1} (12).
Included in Schedule 6 (Release Into Land: Prescribed Substances) of Statutory Instrument No. 472, 1991 (13).

Other comments

Comprehensive review of toxicology and environmental fate (10).
The toxicology of pyrethroids, including epidemiology studies and neurotoxicological potential, have been reviewed (14,15).
Allethrin refers to a mixture of *cis*- and *trans*-allethrins.

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A69 allidochlor

$$ClCH_2CON(CH_2CH{=}CH_2)_2$$

$C_8H_{12}ClNO$ **Mol. Wt.** 173.64 **CAS Registry No.** 93-71-0

Synonyms *N,N*-diallylchloroacetamide; 2-chloro-*N,N*-di-2-propenylacetamide; CDAA; Randox; α-chloro-*N,N*-diallylacetamide

EINECS No. 202-270-7 **RTECS No.** AB 5250000

Uses Herbicide.

Physical properties

B. Pt. 125°C (decomp.) **Specific gravity** 1.09 at 25°C **Volatility** v.p. 0.0094 mmHg at 20°C
Solubility Water: 2 g l^{-1}. Organic solvents: ethanol, hexane

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) – 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 (S2, S26, S28, S36/37/39)

Ecotoxicity

Fish toxicity
LC_{50} (24 hr) carp, rainbow trout 2-8 mg l^{-1} at 15°C (1-3).

Invertebrate toxicity
Toxic to bees (4).

Toxicity to other species

LC_{50} (duration unspecified) tadpole 3.3 ppm at pH 7-9 (5).

Environmental fate

Degradation studies

Major route of decomposition is via microbial degradation (6).

Abiotic removal

Hydrolysis is secondary to microbial breakdown when considering degradation (6).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 700 mg kg^{-1} (7).

LD_{50} percutaneous rabbit 1350 mg kg^{-1} (4).

Metabolism and toxicokinetics

Allidochlor is readily absorbed through skin, rapid hydrolytic action leads to the removal of the chlorine atom. Metabolite detected was glycol acid (7).

Irritancy

Skin irritant in humans. Can be absorbed directly via the skin (4,8).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides and related products: maximum admissible concentration 0.1 $\mu g\ l^{-1}$ (9).

Included in Schedule 6 (Release Into Land: Prescribed Substances) of Statutory Instrument No. 472, 1991 (10).

Other comments

Reviews on experimental toxicology and human health effects listed (11).

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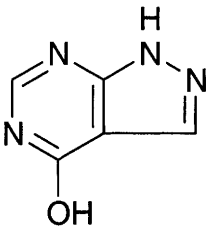
A70 allopurinol



$C_5H_4N_4O$ **Mol. Wt.** 136.11 **CAS Registry No.** 315-30-0

Synonyms 1,5-dihydro-4*H*-pyrazolo[3,4-*d*]pyrimidin-4-one; 1*H*-pyrazolo[3,4-*d*]pyrimidin-4-ol; 4-hydroxypyrazolo[3,4-*d*]pyrimidine; Zyloric; Zyloprim

EINECS No. 206-250-9 **RTECS No.** UR 0785000

Uses Treatment of hyperuricaemia and gout; inhibitor of xanthine oxidase.

Physical properties

M. Pt. >350°C

Solubility Water: 0.5 g l^{-1} at 25°C. Organic solvents: dimethyl formamide

Mammalian & avian toxicity

Acute data

LD_{50} intraperitoneal rat 900 mg kg^{-1} (1).

Sub-acute and sub-chronic data

LD_{Lo} (22 day) oral woman 88 mg kg^{-1} intermittent blood effects (2).

LD_{Lo} (5 day) oral man 22.4 mg kg^{-1} intermittent central nervous system, blood and liver effects (2).

Teratogenicity and reproductive effects

The effect of allopurinol on the fertilisation and early development of sea urchin embryos was studied. Pre-hatching exposure to 10 μM to 10 mM did not affect cleavage but did induce developmental defects. Post-hatching exposure failed to affect the embryogenesis (3).

The effect of 0.33-1.83 mM allopurinol was studied using the rat whole-embryo culture system. Embryos were explanted at day 10 of gestation and cultured for 48 hr in the absence or presence of rat or human S9. The compound proved to be potentially embryolethal and teratogenic in the absence of S9, embryolethal in the presence of rat S9 and dysmorphogenic in the presence of human S9 (4).

Metabolism and toxicokinetics

Converted in the liver into oxypurinol, an inhibitor of xanthine oxidase activity, clearance $t_{1/2}$ 18-30 days (1,5). Following oral administration, 20% of an initial unspecified dose was excreted in faeces in 48-72 hr. Peak plasma concentration was reached in 2-6 hr. Allopurinol and its metabolite alloxanthine are distributed in total tissue water (except the brain) without binding to plasma proteins (6).

Genotoxicity

Subcutaneous rat 10-100 mg kg^{-1} (duration unspecified) negative results for mitotic index and chromosomal aberrations (7).

Other effects

Other adverse effects (human)

Can cause cataracts if given as a treatment for gout in human diabetic patients (8).

Symptoms of allergy include fever chills, leucopenia, leucocytosis, eosinophilia, arthralgia and vasculitis leading to renal and hepatic damage. These reactions can be severe or fatal. Other side-effects include peripheral neuritis, nausea, vomiting, diarrhoea, headache, drowsiness and vertigo (5).
Used for treating heart or stroke victims to increase blood flow and reduce tissue damage to the injured ischaemic tissue (9).

Other comments

A 15-yr-old girl who swallowed 22.5 g of allopurinol did not suffer any ill effects (10).
Use of allopurinol in providing organ protection following hepatic transplantation reviewed (11).
Pharmacokinetics in humans reviewed (12).

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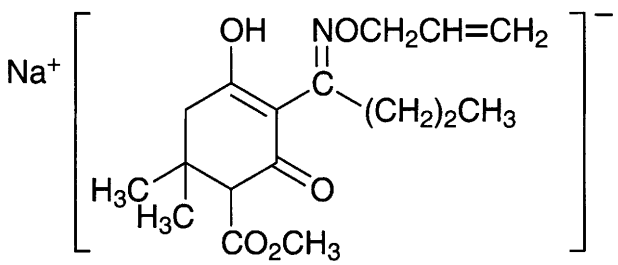
A71 alloxydim-sodium



$C_{17}H_{24}NNaO_5$ **Mol. Wt.** 345.37 **CAS Registry No.** 66003-55-2

Synonyms cyclohexanecarboxylic acid, 2,2-dimethyl-4,6-dioxo-5-[1-[(2-propenyloxy)imino]butyl]-, methyl ester, ion(1–), sodium; alloxydimedon sodium; BAS 9021; Fervin; Kusgard; NP 48; Tritex

EINECS No. 259-733-1 **RTECS No.** GU 8390000

Uses Post-emergence herbicide.

Physical properties

M. Pt. 185.5°C (decomp.) **Partition coefficient** log P_{ow} –0.20 **Volatility** v.p. $<1.0 \times 10^{-6}$ mmHg at 25°C
Solubility Water: 2 kg l^{-1} at 30°C. Organic solvents: dimethylformamide, ethanol, methanol

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) carp, trout 2600, 2000 mg l^{-1}, respectively (1).

Invertebrate toxicity

Non-toxic to bees (1).

Environmental fate

Degradation studies

$t_{1/2}$ in soil 2-10 days, variable with time of year (1,2).

Mammalian & avian toxicity

Acute data

LD_{50} oral Japanese quail 2970 mg kg^{-1} (1).
LD_{50} oral ♀, ♂ rat 2260, 2322 mg kg^{-1}, respectively (1).
LD_{50} oral mice 3000-4600 mg kg^{-1} (1).
LD_{50} percutaneous rabbit, rat >2000, >5000 mg kg^{-1}, respectively (1).
LD_{50} intraperitoneal rat 1700 mg kg^{-1} (1).

Carcinogenicity and chronic effects

In 2-yr feeding studies mice and rats given 100 mg kg^{-1} in diet showed no adverse effects (1).

Metabolism and toxicokinetics

Oral rat (7-day-old) 1,5-^{14}C-labelled compound was excreted within 48 hr in the urine (3).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides and related products: maximum admissible concentration 0.1 μg l^{-1} (4).
Included in Schedule 6 (Release into Land: Prescribed Substances) of Statutory Instrument No. 472, 1991 (5).

Other comments

Metabolic pathways reviewed (6).

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A72 allyl acetate

$$CH_3CO_2CH_2CH{=}CH_2$$

$C_5H_8O_2$ **Mol. Wt.** 100.12 **CAS Registry No.** 591-87-7

Synonyms acetic acid, allyl ester; acetic acid, 2-propenyl ester; 3-acetoxypropene

EINECS No. 209-734-8 **RTECS No.** AF 1750000

Uses Intermediate in polymer manufacture.

Physical properties

B. Pt. 104°C **Flash point** 6°C **Specific gravity** 0.928 **Volatility** v.den. 3.45
Solubility Organic solvents: acetone, diethyl ether, ethanol

Occupational exposure

UN No. 2333 **HAZCHEM Code** 3WE **Conveyance classification** flammable liquid, toxic

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, mouse 130-170 mg kg^{-1} (1,2).
LC_{50} (1 hr) inhalation rat 1000 ppm (1).
LD_{50} dermal rabbit 1021 mg kg^{-1} (1).

Metabolism and toxicokinetics

Allyl acetate is absorbed through intact skin and rapidly hydrolysed in the body to allyl alcohol and acetic acid (3).

Irritancy

Dermal rabbit (24 hr) 10 mg and 100 mg instilled in rabbit eye caused mild irritation (1,3).

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A73 allyl alcohol

$$CH_2{=}CHCH_2OH$$

C_3H_6O **Mol. Wt.** 58.08 **CAS Registry No.** 107-18-6

Synonyms 2-propen-1-ol; 3-hydroxypropene; vinyl carbinol

EINECS No. 203-470-7 **RTECS No.** BA 5075000

Uses Used in the manufacture of resins and plasticisers. As an intermediate in the manufacture of pharmaceuticals, flavourings and other organic chemicals. In the manufacture of glycerol, acrolein, military poisons.

Physical properties

M. Pt. –50°C **B. Pt.** 96-97°C **Flash point** 21°C **Specific gravity** 0.8573 at 15°C
Partition coefficient log P_{ow} –0.25 **Volatility** v.p. 10 mmHg at 10.5°C ; v.den. 2.0
Solubility Water: miscible. Organic solvents: miscible with chloroform, diethyl ether, ethanol, light petroleum

Occupational exposure

FR-VME 2 ppm (5 mg m^{-3})
FR-VLE 4 ppm (10 mg m^{-3})
JP-OEL 1 ppm (2.4 mg m^{-3})
SE-LEVL 2 ppm (5 mg m^{-3})
SE-STEL 6 ppm (14 mg m^{-3})
UK-LTEL 2 ppm (4.8 mg m^{-3})
UK-STEL 4 ppm (9.7 mg m^{-3})
US-TWA 0.5 ppm (4.8 mg m^{-3})

UN No. 1098 **HAZCHEM Code** 2WE **Conveyance classification** toxic substance, danger of fire (flammable liquid)
Supply classification toxic, dangerous for the environment
Risk phrases Flammable – Toxic by inhalation, in contact with skin and if swallowed – Irritating to eyes, respiratory system and skin – Very toxic to aquatic organisms (R10, R23/24/25, R36/37/38, R50)
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 insufficient ventilation, wear suitable respiratory equipment – 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, S38, S45, S61)

Ecotoxicity

Fish toxicity
LC_{50} (24 hr) goldfish 1 mg l^{-1} (1).

Invertebrate toxicity
IC_{50} *Saccharomyces cerevisiae* 108 mg l^{-1} (2).

Environmental fate

Nitrification inhibition
Ammonia oxidation inhibition in activated sludge was 75% at concentrations of 19.5 mg l^{-1} (3).

Degradation studies
Confirmed biodegradable (4).
BOD_5 9.1% reduction of dissolved oxygen concentration using settled sewage seed at 20°C increasing to 81.8% in 20 days (5).

Abiotic removal
13.9% degradation to carbon dioxide after 24 hr following photo-oxidation in aqueous medium at 50°C (6).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat, mouse 64, 139 mg kg^{-1}, respectively (2).
LD_{50} oral rat, mouse, rabbit 71-105 mg kg^{-1} (7).
LC_{50} (1-4 hr) inhalation rat 76-165 ppm (8).
LD_{50} percutaneous rabbit 89 mg kg^{-1} (9).
LD_{50} intraperitoneal mouse 60 mg kg^{-1} (10).
Classified as toxic using the acute-toxic-class method, an alternative to the LD_{50} test (11).

Carcinogenicity and chronic effects
Gavage ♂ Syrian hamsters (lifetime study) 2 mg wk^{-1} induced tumours of the pancreatic ducts and forestomach. The authors reported that the incidence was insignificant (10).

Teratogenicity and reproductive effects

Chronic treatment with allyl alcohol (dose and duration unspecified) to ♂ rats caused no adverse reproductive effects (12).

Metabolism and toxicokinetics

Converted by alcohol dehydrogenase in the liver into acrolein resulting in liver toxicity (13).

Allyl alcohol was readily oxidised in minutes following an intravenous injection of 30 mg kg^{-1} to rats and within 1 hr the alcohol had almost disappeared from blood (14).

Oral rat 42 mg kg^{-1} was oxidised to acrolein within 10-15 min. Allyl alcohol elevated alanine aminotransferase, α-glutamyl transpeptidase and glutamate dehydrogenase activity in the plasma and induced lesions in the periportal regions of the liver (15).

Irritancy

Vapour and liquid are intensely irritating to skin and mucous membrane. Produces lachrymation and corneal burns (16).

Shows severe *in vitro* activity in the bovine corneal opacity and permeability test for ocular irritancy (17).

Genotoxicity

In vitro Chinese hamster V79 cells with and without metabolic activation positive (18).

Other effects

Any other adverse effects

Inhalation mice 3.9 ppm depressed the respiratory rate by 50% due to sensory irritation (19).

Can be absorbed through intact skin in both toxic and lethal concentrations. Exposure to toxic concentrations can lead to deep muscle pain, presumably due to spasm (20,21).

Other comments

Experimental toxicology, epidemiology, physico-chemical properties, workplace experience, exposure levels and human health effects reviewed (22-24).

Allyl alcohol-induced liver injury has been reviewed (25).

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A74 allylamine

$$CH_2{=}CHCH_2NH_2$$

C_3H_7N **Mol. Wt.** 57.10 **CAS Registry No.** 107-11-9

Synonyms 2-propen-1-amine; 3-aminopropene; 3-aminopropylene; 2-propenamine; monoallylamine; 2-propenylamine

EINECS No. 203-463-9 **RTECS No.** BA 5425000

Uses Used in the manufacture of pharmaceuticals especially mercurial diuretics. Used to improve dyeability of acrylic fibres.

Physical properties

M. Pt. –88.2°C **B. Pt.** 56.5°C **Flash point** –29°C (open cup) **Specific gravity** 0.762 at 20°C **Volatility** v.p. not available ; v.den. 2.0

Solubility Water: miscible. Organic solvents: miscible with diethyl ether, ethanol

Occupational exposure

SE-LEVL 2 ppm (5 mg m^{-3}) **SE-STEL** 6 ppm (14 mg m^{-3})

UN No. 2334 **HAZCHEM Code** 2WE **Conveyance classification** toxic substance, danger of fire (flammable liquid)

Supply classification highly flammable

Supply classification toxic

Supply classification dangerous for the environment

Risk phrases Highly flammable – Toxic by inhalation, in contact with skin and if swallowed – Toxic to aquatic organisms (R11, R23/24/25, R51)

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 – Avoid contact with skin and eyes – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) – Avoid release to the environment. Refer to special instructions/safety data sheet (S1/2, S9, S16, S24/25, S45, S61)

Ecotoxicity

Invertebrate toxicity

Cell multiplication inhibition test, *Microcystis aeruginosa* 0.35 mg l^{-1}, *Scenedesmus quadricauda* 2.2 mg l^{-1}, *Pseudomonas putida* 700 mg l^{-1}, *Entosiphon sulcatum* 23 mg l^{-1} (1,2).

Toxicity to other species

LC_{50} (48 hr) clawed toad 5.0 mg l^{-1} (3).

Environmental fate

Degradation studies

Non-biodegradable (4).

Degradation by *Aerobacter* sp. 200 mg l^{-1} at 30°C (5).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, mouse 57-106 mg kg^{-1} (6).

LC_{50} (4 hr) inhalation rat 286 ppm (6).

LD_{50} percutaneous rabbit 35 mg kg^{-1} (6).

TC_{Lo} inhalation man 5 ppm min^{-1} adverse pulmonary effects (7).

Sub-acute and sub-chronic data

Gavage Sprague-Dawley rat 100 mg kg^{-1} day^{-1}, 10 doses in 11 days caused myocardial necrosis (8).

Oral rat 100 mg kg^{-1} two doses on successive days and sacrificed 24 hr after final dose, endothelial cell proliferation and interstitial cell activation reported (9).

Metabolism and toxicokinetics

Allylamine was metabolised to acrolein which caused generalised tissue destruction (10).

Irritancy

Dermal rabbit (24 hr) 500 mg and 50 mg instilled in rabbit eye for 20 sec caused severe irritation (6).

Other effects

Other adverse effects (human)

Mucous membrane irritation and chest discomfort in some humans at 2.5 ppm, intolerable to most at 14 ppm (6).

Any other adverse effects

Chick myocardial myocyte aggregates treated with 0.5 or 5 mg l^{-1} allylamine showed myocyte necrosis and reduction in tissue compactness (10).

Other comments

Experimental and chemical use and general toxicity and human health effects reviewed (11,12).

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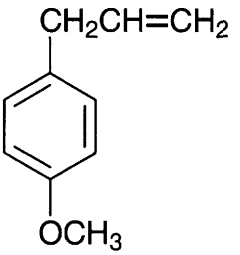
A75 4-allylanisole



$C_{10}H_{12}O$ **Mol. Wt.** 148.20 **CAS Registry No.** 140-67-0

Synonyms 1-methoxy-4-(2-propenyl)benzene; *p*-propenylanisole; *p*-allylanisole; *p*-propenylphenyl methyl ether; chavicol methyl ether; methylchavicol; estragole; estragol

EINECS No. 205-427-8 **RTECS No.** BZ 8225000

Uses Used in the manufacture of anisaldehyde. Used in the perfume and flavouring industries. A sensitiser in bleaching colours in colour photography. An imbedding material in microscopy.
Occurrence Oil from *Artemisia dracunculus* (tarragon).

Physical properties

M. Pt. 22.5°C **B. Pt.** 235.3°C **Specific gravity** 0.9882 at 20°C with respect to water at 4°C
Solubility Organic solvents: miscible with chloroform, diethyl ether, ethanol

Mammalian & avian toxicity

Acute data
LD_{50} oral redwing blackbird 316 mg kg^{-1} (1).
LD_{50} oral rat, mouse, guinea pig 2090-3050 mg kg^{-1} (2).

Metabolism and toxicokinetics
In rabbit and rat studies, the *trans*-isomer was found concentrated in liver, lungs and brain after intravenous administration whereas after oral dosage, it remained in the stomach (3).
Absorbed from the digestive tract by passive diffusion (4).

Other comments

Forms azeotropic mixtures in water.

References

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2. Opdyke, D. L. J. *Food Cosmet. Toxicol.* 1964, **2**, 327.
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A76 allyl bromide

$$H_2C{=}CHCH_2Br$$

C_3H_5Br **Mol. Wt.** 120.98 **CAS Registry No.** 106-95-6

Synonyms 3-bromo-1-propene; 3-bromopropylene; bromallylene; 1-bromo-2-propene

EINECS No. 203-446-6 **RTECS No.** UC 7090000

Uses Used in the manufacture of synthetic perfumes and the synthesis of other allyl compounds.

Physical properties

M. Pt. –119°C **B. Pt.** 71°C **Flash point** –1°C **Specific gravity** 1.398 at 20°C with respect to water at 4°C
Volatility v.den. 4.17
Solubility Organic solvents: miscible with carbon disulfide, carbon tetrachloride, diethyl ether, ethanol

Occupational exposure

UN No. 1099 **HAZCHEM Code** 2WE **Conveyance classification** flammable liquid, toxic

Mammalian & avian toxicity

Acute data
LD_{50} oral guinea pig 30 mg kg^{-1} (1).
LD_{50} intraperitoneal mouse 108 mg kg^{-1} (2).

Metabolism and toxicokinetics
Gavage rat 120 mg kg^{-1} in water, 3-hydroxypropylmercapturic acid (an intermediate in the formation of acrolein) was detected at levels of 3% in the urine (3).

Genotoxicity

Salmonella typhimurium TA100 without metabolic activation positive (4).

Other effects

Other adverse effects (human)
May injure liver and kidneys and can lead to fatalities (5).
Toxic amounts may be absorbed through the skin (6).

References

1. Hann, W. et al *Water Quality Characteristics of Hazardous Materials*, 1974, **4**, A & M Univ., Texas, USA.
2. Fischer, G. W. et al *J. Prakt. Chem.* 1978, **320**, 133.
3. Sanduja, R. et al *J. Appl. Toxicol.* 1989, **9**(4), 235-238.
4. Eder, E. et al *Biochem. Pharmacol.* 1980, **29**, 993.
5. *Handling Chemicals Safely* 1980, Dutch Chemical Industry Association and Dutch Safety Institute, Amsterdam, Netherlands.
6. *National Fire Protection Association. Fire Protection Guide on Hazardous Materials* 7th ed., 1978, 49, National Fire Protection Association, Boston, MA, USA

A77 allyl butyrate

$$CH_3(CH_2)_2CO_2CH_2CH{=}CH_2$$

$C_7H_{12}O_2$ **Mol. Wt.** 128.17 **CAS Registry No.** 2051-78-7

Synonyms allyl butanoate; vinyl carbinyl butyrate

EINECS No. 218-129-8 **RTECS No.** ES 5775000

Uses Used in perfumery.

Physical properties

B. Pt. 142°C

Solubility Organic solvents: miscible with ethanol

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 250 mg kg^{-1} (1).

LD_{50} dermal rabbit 530 mg kg^{-1} (2).

Irritancy

Human skin irritant (1,2).

Other comments

Experimental toxicology and human health effects reviewed (3,4).

References

1. Taylor, J. M. et al *Toxicol. Appl. Pharmacol.* 1964, **6**, 378.
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3. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium.
4. *BIBRA Toxicity Profile* 1987, British Industrial Biological Research Association, Carshalton, Surrey, UK

A78 allyl chloride

$$CH_2{=}CHCH_2Cl$$

C_3H_5Cl **Mol. Wt.** 76.53 **CAS Registry No.** 107-05-1

Synonyms 1-propene, 3-chloro-; 3-chloropropene; 3-chloropropylene; 2-propenyl chloride; chlorallylene; chloroallylene; 1-chloroprop-2-ene; 1-chloro-2-propene; α-chloropropylene; 3-chloro-1-propylene; NCI-CO4615

EINECS No. 203-457-6 **RTECS No.** UC 7350000

Uses Used as a chemical intermediate in epichlorohydrin manufacture. A polymerisation monomer in the manufacture of resins, polymers, varnishes and adhesives. In the synthesis of medicinal derivatives, such as barbiturates, diuretics and cyclopropane.

Physical properties

M. Pt. –134.5°C **B. Pt.** 44.6°C **Flash point** –31.7°C (closed cup) **Specific gravity** 0.9376 at 20°C with respect to water at 4°C **Partition coefficient** log P_{ow} 1.450 **Volatility** v.p. 368 mmHg at 25°C ; v.den. 2.64
Solubility Organic solvents: miscible with chloroform, diethyl ether, ethanol, light petroleum

Occupational exposure

FR-VME 1 ppm (3 mg m^{-3})
SE-LEVL 1 ppm (3 mg m^{-3}) **SE-STEL** 3 ppm (9 mg m^{-3})
US-TWA 1 ppm (3 mg m^{-3}) **US-STEL** 2 ppm (6 mg m^{-3})

UN No. 1100 **HAZCHEM Code** 3WE **Conveyance classification** flammable liquid, toxic
Supply classification highly flammable, very toxic, dangerous for the environment
Risk phrases Highly flammable – Very toxic by inhalation – Very toxic to aquatic organisms (R11, R26, R50)
Safety phrases Keep locked up and out of the reach of children (if sold to general public) – Keep away from sources of ignition – No smoking – Do not empty into drains – Take precautionary measures against static discharges – 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, S16, S29, S33, S45, S61)

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) fathead minnow 10 mg l^{-1} (1).
LC_{50} (24 hr) goldfish 19.8 mg l^{-1} (2).
LC_{50} (2 wk) guppy 1.2 mg l^{-1} (3).

Invertebrate toxicity
Cell multiplication inhibition test, *Scenedesmus quadricauda* 6.3 mg l^{-1}, *Entosiphon sulcatum* 8.4 mg l^{-1}, *Uronema parduczi* >240 mg l^{-1}, *Pseudomonas putida* 115 mg l^{-1} (4).

Environmental fate

Nitrification inhibition
75% inhibition of NH_3 oxidation by activated sludge 180 mg l^{-1} (5).

Degradation studies
BOD_5 14% and 25% reduction of dissolved oxygen concentration using nonacclimated and acclimated seed, respectively (2).
Using activated sludge, allyl chloride was readily degradable (6).

Abiotic removal
Photochemical degradation occurs via reaction with hydroxyl radicals in the atmosphere, calculated daily loss of 91.1% in 12 hr (7).
Ozonolytic $t_{1/2}$ 9 hr (6).
Hydrolytic $t_{1/2}$ 7.2 days in water at 25°C produces allyl alcohol and hydrochloric acid (8).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 700 mg kg^{-1} (9).
LD_{50} oral mouse 425 mg kg^{-1} (10).
LC_{50} (2 hr) inhalation rat, mouse 11, 11.5 g kg^{-1}, respectively (10).
LD_{50} dermal rabbit 2066 mg kg^{-1} (9).
Twenty-five ♂ ICR mice were subcutaneously injected with a single dose of 496, 600, 720, 864 or 1037 mg kg^{-1} of allyl chloride. 16 mice died by the 7th day after injection and showed liver and kidney damage and marked congestion with severe haemorrhage and oedema in the lung. All of the 9 mice surviving after the 7th day showed various degrees of damage to the testes (11).

Sub-acute and sub-chronic data

Inhalation rat, guinea pig, rabbit (1 month) 8 ppm 7 hr day^{-1}, 5 day wk^{-1} induced liver injury (12).
Inhalation rat (34 wk) 10, 50 and 100 ppm 8 hr day^{-1} 5 day wk^{-1} reduction of motor and sensory nerve conduction velocities and nerve action potentials after 28 wk for higher concentration and retarded motor distal latency for the last period of exposure. Depressed amplitude of nerve action potentials was evident in rats exposed to 50 ppm (13).

Carcinogenicity and chronic effects

No adequate evidence for carcinogenicity to humans, limited evidence for carcinogenicity to animals, IARC classification group 3 (14).
The National Toxicology Program have tested rats and mice via gavage. Negative evidence for carcinogenicity in ♂ and ♀ rats, equivocal evidence for carcinogenicity in ♂ and ♀ mice (15).
TD_{Lo} oral mouse (78 wk intermittent) 50 g kg^{-1} equivocal tumourigenic effects (16).
TD_{Lo} intraperitoneal mouse (8 wk intermittent) 5880 mg kg^{-1} equivocal tumorigenic effects (17).

Teratogenicity and reproductive effects

Inhalation rat (7 hr day^{-1} during major organogenesis) 30 or 300 ppm. Caused maternal toxicity at 300 ppm. Slight delay in foetal development at 300 ppm may have been associated with observed effects in maternal animals (18).
Subcutaneous mouse 124 mg kg^{-1} by single injection. Histopathological changes within testis investigated for a period of 39 days. Complete or partial lack of specific spermatogenic cells frequently occurred following treatment. Severe atrophy of the seminiferous tubules was frequently noted (19).

Irritancy

Upper respiratory tract irritant and concentrations of 50-100 ppm very irritating to eyes in humans (12).

Genotoxicity

Salmonella typhimurium TA100, TA1535 without metabolic activation positive (20).
Salmonella typhimurium TA98, TA100, TA1535, TA1538 with and without metabolic activation negative (21).
Escherichia coli WP_2, WP_2uvrA with and without metabolic activation positive (21).
Saccharomyces cerevisiae JD1 with and without metabolic activation positive (21).

Other effects

Other adverse effects (human)

A study of 1064 ♂ workers involved in the production or use of allyl chloride and epichlorohydrin for at least 1 month from 1957-1986 showed no significantly elevated standardised mortality ratios for all malignant neoplasms, lung cancer, circulatory system disease or arteriosclerotic heart disease when compared to US populations (22).

Any other adverse effects

Acute exposure can cause unconsciousness while chronic exposure can cause injury to liver and kidneys (species unspecified) (23).

Other comments

Hardness of water decreases toxicity (1).
Hazardous potential reviewed (24).
Experimental toxicology, human health effects, epidemiology and workplace experience reviewed (25,26).
A dangerous fire hazard when exposed to heat, flame or oxidisers, and releases hydrogen chloride on combustion. It is incompatible with nitric acid, ethyleneimine, ethylenediamine, chlorosulfonic acid, oleum and sodium hydroxide. Violent exothermic polymerisation may occur on contact with aluminium chloride, boron trifluoride or sulfuric acid.

References

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2. Bridie, A. L. et al *Water Res.* 1979, **13**, 627-630.
3. Hermens, J. et al *Ecotox. Environ. Saf.* 1985, **9**, 321-326.
4. Bringmann, G. et al *Water Res.* 1980, **14**, 231-241.
5. Tomlinson, T. G. et al *J. Appl. Bacteriol.* 1966, **29**(2), 266-291.
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7. Singh, H. B. et al *Environ. Sci. Technol.* 1982, **16**, 872-880.
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15. *National Toxicology Program Research and Testing Division* 1995, Report No. TR-073, NIEHS, Research Triangle Park, NC 27709, USA.
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20. Eder, E. et al *Biochem. Pharmacol.* 1980, **29**, 993.
21. Dean, B. J. et al *Mutat. Res.* 1985, **153**, 57-77.
22. Olsen, G. W. et al *Am. J. Ind. Med.* 1994, **25**(2), 205-218.
23. *The Merck Index* 11th ed., 1989, Merck & Co. Inc, Rahway, NJ, USA.
24. *Dang. Prop. Ind. Mater. Rep.* 1988, **8**(1), 20-28.
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26. *IARC Monograph* 1985, **36**, 39-54

A79 allyl chloroformate

$$CH_2{=}CHCH_2CO_2Cl$$

$C_4H_5ClO_2$ **Mol. Wt.** 120.54 **CAS Registry No.** 2937-50-0

Synonyms allyl chlorocarbonate; formic acid, chloro-, allyl ester; chloroformic acid, allyl ester

EINECS No. 220-916-6 **RTECS No.** LQ 5775000

Physical properties

M. Pt. –80°C **B. Pt.** 106-114°C **Flash point** 31°C (closed cup) **Specific gravity** 1.1 at 25°C
Volatility v.den. 4.2

Occupational exposure

UN No. 1722 **HAZCHEM Code** 2WE **Conveyance classification** toxic substance, danger of fire (flammable liquid), corrosive

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse, rat 210-244 mg kg^{-1} (1).

LC_{Lo} (duration unspecified) inhalation mouse 2000 mg m^{-3} (2).

Other effects

Any other adverse effects

Affects the respiratory system and causes dyspnoea (1,3).

References

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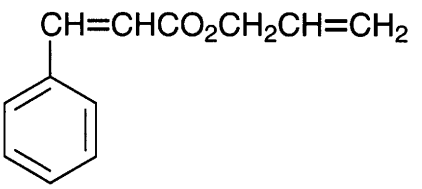
2. *Nat. Defence Res. Commun. Prog. Rep.* 1943.
3. Lenga, R. E. *The Sigma-Aldrich Library of Chemical Safety Data* 2nd ed., 1988, **2**

A80 allyl cinnamate



$C_{12}H_{12}O_2$ **Mol. Wt.** 188.23 **CAS Registry No.** 1866-31-5

Synonyms allyl-3-phenylpropenoate; allyl-β-phenylacrylate; propenyl cinnamate; vinyl carbinylcinnamate

EINECS No. 217-477-8 **RTECS No.** GD 8050000

Uses Flavouring ingredient in foods and cosmetics.

Physical properties

B. Pt. 150-152°C at 15 mmHg **Specific gravity** 1.048 at 23°C

Solubility Organic solvents: diethyl ether, ethanol

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 1520 mg kg^{-1} (1).

LD_{50} dermal rabbit <5 g kg^{-1} (2).

Irritancy

Human skin irritant (2).

Sensitisation

Non-sensitiser in humans (2).

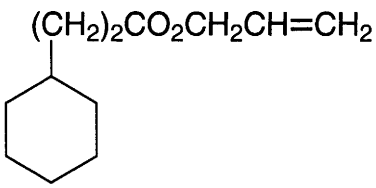
Other comments

Experimental toxicology and health effects reviewed (3,4).

References

1. Jenner, P. M. et al *Food Cosmet. Toxicol.* 1964, **2**, 327-343.
2. Opdyke, D. C. J. *Food Cosmet. Toxicol.* 1977, **15**(6), 615-616.
3. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium.
4. *BIBRA Toxicity Profile* 1987, British Industrial Biological Research Association, Carshalton, Surrey, UK

A81 allyl cyclohexylpropionate



$C_{12}H_{20}O_2$ **Mol. Wt.** 196.29 **CAS Registry No.** 2705-87-5

Synonyms allyl cyclohexane propionate; 3-allylcyclohexyl propionate; allyl hexahydrophenyl propionate; allyl-3-cyclohexyl propionate; allyl-β-cyclohexyl propionate

EINECS No. 220-292-5 **RTECS No.** GV 6735000

Uses Food flavouring material.

Physical properties

M. Pt. 196.3°C **B. Pt.** 91°C at 1 mmHg **Specific gravity** 0.95 at 25°C with respect to water at 25°C
Solubility Organic solvents: ethanol

Mammalian & avian toxicity

Acute data
LD_{50} oral rat, guinea pig 380-585 mg kg^{-1} (1).

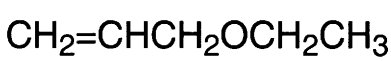
Other comments

Experimental toxicology and human health effects reviewed (2,3).

References

1. Jenner, P. M. et al *Food Cosmet. Toxicol.* 1964, **2**, 327-343.
2. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium.
3. *BIBRA Toxicity Profile* 1993, British Industrial Biological Research Association, Carshalton, Surrey, UK

A82 allyl ethyl ether



$C_5H_{10}O$ **Mol. Wt.** 86.13 **CAS Registry No.** 557-31-3

Synonyms 3-ethoxy-1-propene; ethyl allyl ether

EINECS No. 209-169-7

Physical properties

M. Pt. 66-67°C **B. Pt.** <21°C **Flash point** –20°C **Specific gravity** 0.765 at 20°C with respect to water at 4°C
Partition coefficient log P_{ow} 1.388
Solubility Organic solvents: miscible with diethyl ether, ethanol

Occupational exposure

UN No. 2335 **HAZCHEM Code** 3WE **Conveyance classification** flammable liquid, toxic

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 320 mg kg^{-1} (1).

References

1. Smyth, H. F. et al *J. Ind. Hyg. Toxicol.* 1949, **31**, 60

A83 allyl formate

$$HCO_2CH_2CH{=}CH_2$$

$C_4H_6O_2$ **Mol. Wt.** 86.09 **CAS Registry No.** 1838-59-1

Synonyms formic acid, 2-propenyl ester; formic acid, allyl ester; 3-propenyl methanoate

EINECS No. 217-413-9 **RTECS No.** LQ 9800000

Physical properties

B. Pt. 83°C **Flash point** <22°C (closed cup) **Specific gravity** 0.948 at 18°C with respect to water at 4°C

Solubility Organic solvents: ethanol

Occupational exposure

UN No. 2336 **HAZCHEM Code** 3WE **Conveyance classification** flammable liquid, toxic

Ecotoxicity

Fish toxicity

Oral trout (24 hr) 100 µl kg^{-1} induced liver necrosis (1).

Bioaccumulation

Biodegrades to allyl alcohol and formic acid which are also ultimately biodegradable (2).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, mouse 124, 136 mg kg^{-1}, respectively (2).

LC_{50} (3 hr) inhalation mouse 14 g m^{-3} (3).

References

1. Droy, B. F. et al *Mar. Environ. Res.* 1988, **24**(1-4), 259-264.
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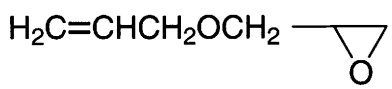
A84 allyl glycidyl ether



$C_6H_{10}O_2$ **Mol. Wt.** 114.14 **CAS Registry No.** 106-92-3

Synonyms allyl-2,3-epoxypropyl ether; 1-(allyloxy)-2,3-epoxpropane; [(2-propenyloxy)methyl]oxirane; 1,2-epoxy-3-allyloxypropane

EINECS No. 203-442-4 **RTECS No.** RR 0875000

Uses Used as an additive for epoxy resins and as a co-monomer in polyglycols and polyolefins synthesis. Stabiliser for chlorinated compounds.

Physical properties

M. Pt. –100°C **B. Pt.** 153.9°C **Flash point** 56°C (open cup) **Specific gravity** 0.9698 at 20°C with respect to water at 4°C **Volatility** v.p. 4.7 mmHg at 25°C ; v.den. 3.94

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

Occupational exposure

FR-VME 5 ppm (22 mg m^{-3})

UK-LTEL 5 ppm (24 mg m^{-3}) **UK-STEL** 10 ppm (47 mg m^{-3})

US-TWA 1 ppm

UN No. 2219 **HAZCHEM Code** 2Y **Conveyance classification** flammable liquid

Supply classification harmful

Risk phrases Harmful by inhalation – May cause sensitisation by skin contact (R20, R43)

Safety phrases Keep out of reach of children (if sold to general public) – Avoid contact with skin and eyes (S2, S24/25)

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) goldfish 30 mg l^{-1} (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse, rat 390, 922 mg kg^{-1}, respectively (2,3).

LC_{Lo} (4 hr) inhalation mouse, rat 270, 860 ppm, respectively (2).

LD_{50} dermal rabbit 2550 mg kg^{-1} (3).

Sub-acute and sub-chronic data

Inhalation mouse (4-14 day) 7.1-2.5 ppm 6 hr day^{-1} induced lesions in nasal cavity, necrosis of respiratory epithelium and erosion of olfactory epithelium (4).

Carcinogenicity and chronic effects

The National Toxicology Program tested mice and rats via inhalation. Equivocal evidence of carcinogenicity in ♂ rats and ♀ mice, no evidence in ♀ rats but some evidence in ♂ mice (5).

Inhalation (2 yr) rat, mouse 0, 5 or 10 ppm for 6 hr day^{-1}, 5 day wk^{-1} induced papillary adenoma, squamous cell carcinoma and adenocarcinomas of the nasal passage (6).

Teratogenicity and reproductive effects

Exposure to allyl glycidyl ether (concentration and duration unspecified) has been reported to cause testicular atrophy in rats, rabbits and dogs (7).

Irritancy

Dermal rabbit (24 hr) 500 mg and 250 µg instilled in rabbit eyes for 24 hr caused severe irritation (2).
In rats exposed to 260 ppm slight eye irritation was reported, while concentrations of 600 and 900 ppm caused severe irritation and corneal opacities. Severe but reversible conjunctivitis, iritis and corneal opacity were reported in rabbits (8).

Sensitisation

Dermatitis, with itching, swelling and blistering, and sensitisation have been reported in humans. Contact allergies and reaction to allyl glycidyl ether subsequent to patch tests have been reported in resin workers (9,10).

Genotoxicity

Salmonella typhimurium TA100, TA1535 with and without metabolic activation positive (11).
Escherichia coli PQ37 SOS chromotest with and without metabolic activation positive (12).

Other effects

Any other adverse effects

Rats exposed to >260 ppm (route and duration unspecified) were found to have bronchopneumonia, emphysema, bronchiectasis, pneumonitis, haemorrhage, discoloured liver and adrenals at autopsy (13).

Other comments

Reviews on exposure data, human health effects, physico-chemical properties, workplace experience, epidemiology and experimental toxicology listed (14).

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2. Sax, N. I. et al *Dangerous Properties of Industrial Materials* 7th ed., 1989, Van Nostrand Reinhold, New York, NY, USA.
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A85 allyl iodide

$$CH_2=CHCH_2I$$

C_3H_5I **Mol. Wt.** 167.98 **CAS Registry No.** 556-56-9

Synonyms 3-iodo-1-propene; 3-iodopropylene

EINECS No. 209-130-4 **RTECS No.** UD 0450000

Uses In the synthesis of allyl compounds.

Physical properties

M. Pt. –99°C **B. Pt.** 101-103°C **Flash point** <21°C **Specific gravity** 1.848 at 12°C
Solubility Organic solvents: miscible with chloroform, diethyl ether, ethanol

Occupational exposure

UN No. 1723 **HAZCHEM Code** 2WE **Conveyance classification** flammable liquid, corrosive
Supply classification corrosive
Risk phrases Flammable – Causes burns (R10, R34)
Safety phrases Keep locked up and out of the reach of children (if sold to general public) – Keep container tightly closed – In case of contact with eyes, rinse immediately with plenty of water and seek medical advice – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S7, S26, S45)

Mammalian & avian toxicity

Irritancy
Produces irritation of eyes and respiratory passages. Readily absorbed through skin (1).

Other effects

Other adverse effects (human)
Acute exposure can cause unconsciousness while chronic exposure can cause injury to liver and kidney (1).

Other comments

Health effects and safety precautions are similar to those for allyl bromide and allyl chloride (1).
Reviews on experimental toxicology and human health effects listed (2).

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A86 allylisopropylacetamide

$$CH_2=CHCH_2CH(CONH_2)CH(CH_3)_2$$

$C_8H_{15}NO$ **Mol. Wt.** 141.21 **CAS Registry No.** 299-78-5

Synonyms 2-(1-methylethyl)-4-pentenamide; 2-isopropyl-4-pentenamide

Physical properties

M. Pt. 107°C

Mammalian & avian toxicity

Sub-acute and sub-chronic data

A single dose of 225 mg kg^{-1} to rabbits or doses of 35 mg kg^{-1} day^{-1} for 7 days caused an increase in liver microsomal enzymes (1).

Oral administration of 2 g to rabbits caused a short-term rise in liver and bile porphyrin levels (2).

Other effects

Any other adverse effects

Subcutaneous administration of 600 mg kg^{-1} over 24 hr induced porphyrin in rats (3).

Allyl isopropylacetamide was found to stimulate an overproduction of porphyrins, causing porphyria in rabbits, fowls and rats. These were found to excrete relatively high levels of porphobilinogen and porphyrins (4).

In vivo administration (dose and duration unspecified) to phenobarbital-pretreated rats results in a marked loss of hepatic cytochrome P450 content in liver and kidney (5).

A dose of 3 mg increased the level of δ-aminolevulinic acid synthetase in a culture of liver parenchyma cells from a chick embryo (6).

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A87 allyl isothiocyanate

$$H_2C=CHCH_2NCS$$

C_4H_5NS **Mol. Wt.** 99.16 **CAS Registry No.** 57-06-7

Synonyms 2-propenyl isothiocyanate; 3-isothiocyanato-1-propene; allyl thiocarbonimide; allyl isosulfocyanate; allyl isorhodanide; synthetic mustard oil

EINECS No. 200-309-2 **RTECS No.** NX 8225000

Uses Used in the manufacture of ointments and counter-irritants. Fumigant. Manufacture of military poison gas.

Occurrence Isolated from black mustard seed *Brassica nigra*.

Physical properties

M. Pt. –80°C **B. Pt.** 151°C **Flash point** 46°C **Specific gravity** 1.015 at 15°C with respect to water at 4°C
Partition coefficient log P_{ow} 2.11 (calc.) (1) **Volatility** v.p. 10 mmHg at 38.3°C ; v.den. 3.41
Solubility Organic solvents: acetone, benzene, diethyl ether, ethanol

Occupational exposure

UN No. 1545 **HAZCHEM Code** 3WE **Conveyance classification** toxic substance

Environmental fate

Nitrification inhibition
75% inhibition of nitrification process in activated sludge at 1.9 mg l^{-1} (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat, mouse 108, 339 mg kg^{-1}, respectively (2-4).
LD_{50} subcutaneous mouse, rat 80, 92 mg kg^{-1}, respectively (5).
LD_{50} dermal rabbit 88 mg kg^{-1} (3).

Sub-acute and sub-chronic data
Oral rat (6 wk) 0-40 mg kg^{-1}, 5 day wk^{-1}; high doses caused histopathological changes in liver and kidneys (6).

Carcinogenicity and chronic effects
Inadequate evidence for carcinogenicity to humans, limited evidence for carcinogenicity to animals, IARC classification group 3 (7).
The National Toxicology Program tested mice and rats via gavage. No evidence of carcinogenicity in ♂ and ♀ mice, equivocal evidence in ♀ rats and positive evidence in ♂ rats (8).
Target organ of carcinogenicity: rat urinary bladder/urethra (9).
Gavage rat (2 yr) 25 mg kg^{-1}, 5 day wk^{-1} induced urinary bladder transitional cell papilloma and subcutaneous tissue fibrosarcoma (10).
Gavage F344 rats, B6C3F1 mice (2 yr) 25 mg kg^{-1}, US National Toxicology Program classification D, single sex of a single species with single tissue affected, genotoxic carcinogen (11).

Teratogenicity and reproductive effects
Oral Wistar rats 0, 60 or 120 mg kg^{-1} body weight in corn oil on days 12 or 13 of gestation. Maternal toxicity occurred at the highest dose but no adverse effects on the foetuses were found (12).
Subcutaneous Holtzman rats 50 or 100 mg kg^{-1} body weight in water or propylene glycol on days 8 and 9 of gestation. Maternal toxicity occurred at the highest dose. Foetuses were examined on day 20; an increased incidence of resorptions was seen in the high-dose group and foetuses in the low-dose group weighed significantly less than controls (5).

Metabolism and toxicokinetics
Fifteen minutes after intravenous injection of 25 mg kg^{-1} to mice and rats, the highest concentration of allyl isothiocyanate-derived radioactivity was found in the urinary bladder of ♂ rats and mice and in the kidneys of ♂ mice. The bladders of ♂ animals contained 5-10 × more radioactivity than the bladders of ♀. Most of the radioactivity was cleared through urine (70-80%) with exhaled air and faeces containing less (13-15% and 3-5%, respectively) (13).
Oral Fischer 344 rats and B6C3F1 mice administered 2.5 and 25 mg kg^{-1} allyl[14C]isothiocyanate excreted 50-80% of radioactivity in the urine, 6-12% in faeces, and 3-7% in expired air. Retention of radioactive label after 4 days was greater within rats (18-24% of dose) than mice (2-5% of dose). Hydrolysis was the major metabolic pathway in the mouse, whereas in the rat glutathione conjugation was the major route. More labelled allyl[14C]isothiocyanate or its metabolites were found in the bladder of ♂ than ♀ rats (14).

Irritancy

Contact dermatitis was reported in a waitress who handled salad plants; patch testing with radishes and allyl isothiocyanate produced positive results (15).

Has produced irritation of mucous membranes and eczematous or vesicular skin reaction (16).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537, TA1538 with and without metabolic activation. Both positive and negative results reported (17).

Escherichia coli WP67 with metabolic activation positive (18).

Bacillus subtilis rec^+/rec^- DNA-repair assay negative (19).

Drosophila melanogaster both positive and negative results reported for induction of sex-linked recessive lethal mutations (17).

In vitro Chinese hamster ovary cells with metabolic activation induced sister chromatid exchange, with and without metabolic activation chromosome aberration weakly positive (20).

Mouse lymphoma L5178Y tk+/tk– cells without metabolic activation positive (21).

Allyl isothiocyanate was unable to induce either sister chromatid exchanges or chromosome aberrations in Chinese hamster ovary cells, even at highly cytotoxic doses (22).

Mouse bone marrow micronucleus test negative to 150 mg kg^{-1} administered 3 × day^{-1} by intraperitoneal injection (23).

Other effects

Any other adverse effects

Shown to exert a slight goitrogenic effect in rats (17).

Other comments

Experimental toxicology and human health effects reviewed (17,24,25).

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A88 allyl isovalerate

$$(CH_3)_2CHCH_2CO_2CH_2CH{=}CH_2$$

$C_8H_{14}O_2$ **Mol. Wt.** 142.20 **CAS Registry No.** 2835-39-4

Synonyms 3-methylbutanoic acid, 2-propenyl ester; allyl isovalerianate; 3-methylbutanoic acid, allyl ester; 2-propenyl isovalerate; isovaleric acid, allyl ester

EINECS No. 220-609-7 **RTECS No.** NY 1412000

Uses Flavouring material for foods and cosmetics.

Physical properties

B. Pt. 89-90°C
Solubility Organic solvents: acetone, ethanol

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 230 mg kg^{-1} (1).
LD_{50} dermal rabbit 560 mg kg^{-1} (1).

Carcinogenicity and chronic effects
Limited evidence for carcinogenicity to animals, inadequate evidence for carcinogenicity to humans, IARC classification group 3 (2).
Gavage rat, mouse (2 yr) 62 mg kg^{-1}, 5 day wk^{-1} induced haematopoietic system leukaemia and malignant lymphoma (3).
Target organ of carcinogenicity: rat haematopoietic system (4).
The National Toxicology program tested mice and rats via gavage. No evidence of carcinogenicity in ♀ rats and ♂ mice but positive evidence in ♀ mice and ♂ rats (5).
Rats fed at 31-62 mg kg^{-1}, 5 × wk^{-1} over 103 wk, showed cholangiofibrosis, nodular degeneration, cirrhosis, focal necrosis, fatty metamorphosis and cytoplasmic vacuolation of the liver (6).

Metabolism and toxicokinetics
Allyl isovalerate is hydrolysed *in vivo* in rats to allyl alcohol and isovaleric acid; allyl alcohol is then oxidised to acrolein (7).

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

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537 with and without metabolic activation negative (8).
In vitro Chinese hamster ovary cells with and without metabolic activation sister chromatid exchanges positive, with metabolic activation chromosomal aberrations positive, without negative (9).

Other comments

Experimental toxicology and human health effects reviewed (7,10).

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A89 allyl octanoate

$$CH_3(CH_2)_6CO_2CH_2CH{=}CH_2$$

$C_{11}H_{20}O_2$ **Mol. Wt.** 184.28 **CAS Registry No.** 4230-97-1

Synonyms allyl caprylate; allyl octylate; octanoic acid, 2-propenyl ester

EINECS No. 224-184-9

Uses Food flavouring material (synthetic pineapple flavour).

Physical properties

B. Pt. 87-88°C at 5.5 mmHg **Specific gravity** 0.8729 at 30°C
Solubility Organic solvents: diethyl ether, ethanol

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 570 mg kg^{-1} (1).

Irritancy
Dermal rabbit (24 hr) 310 mg caused moderate irritancy (1).

Other comments

Experimental toxicology and human health effects reviewed (2,3).

References

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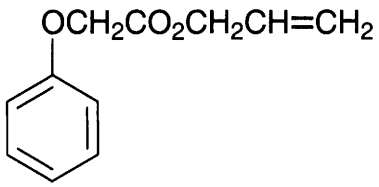
A90 allyl phenoxyacetate



$C_{11}H_{12}O_3$ **Mol. Wt.** 192.21 **CAS Registry No.** 7493-74-5

Synonyms acetate PA

EINECS No. 231-335-2 **RTECS No.** AJ 2240000

Uses Flavouring in foods and cosmetics.

Physical properties

B. Pt. 100-102°C

Solubility Organic solvents: diethyl ether, ethanol

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 475 mg kg^{-1} (1).

LD_{50} dermal rabbit 820 mg kg^{-1} (1).

Irritancy

Non-irritant in humans (1).

Sensitisation

Non-sensitiser in humans (1).

Other comments

Experimental toxicology and human health effects reviewed (2,3).

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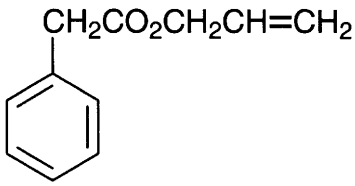
A91 allyl phenylacetate



$C_{11}H_{12}O_2$ **Mol. Wt.** 176.22 **CAS Registry No.** 1797-74-6

Synonyms allyl α-toluate; 2-propenyl phenylacetate; benzeneacetic acid, 2-propenyl ester; phenylacetic acid, allyl ester

EINECS No. 217-281-2 **RTECS No.** AJ 2450000

Uses Flavouring in food and cosmetics.

Physical properties

B. Pt. 89-93°C at 3 mmHg
Solubility Organic solvents: diethyl ether, ethanol

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 650 mg kg^{-1} (1).

Irritancy
Dermal human (48 hr) 30 mg caused irritation, while dermal rabbit (24 hr) 310 mg caused moderate irritation (1).

Sensitisation
Sensitisation reported in humans but thought to be due to free allyl alcohol (1).

Other comments

Experimental toxicology and human health effects reviewed (2,3).

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A92 allyl propyl disulfide

$C_6H_{12}S_2$ **Mol. Wt.** 148.29 **CAS Registry No.** 2179-59-1

Synonyms onion oil; 2-propenyl propyl disulfide

EINECS No. 218-550-7 **RTECS No.** JO 0350000

Occurrence Chief volatile constituent of onion oil.

Physical properties

M. Pt. –15°C **B. Pt.** 56.5°C
Solubility Organic solvents: aceone, benzene, diethyl ether, ethanol

Occupational exposure

DE-MAK 2 ppm (12 mg m^{-3})
FR-VME 2 ppm (12 mg m^{-3})
US-TWA 2 ppm (12 mg m^{-3}) **US-STEL** 3 ppm (18 mg m^{-3})

Mammalian & avian toxicity

Sub-acute and sub-chronic data
Oral administration of 100 mg kg^{-1} day^{-1} for 15 days improved glucose tolerance of alloxan diabetic rabbits (1).

Sensitisation
In garlic-sensitive humans, allyl propyl disulfide provokes allergic reactions including dermatitis (2).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA1535, TA1537 with and without metabolic activation negative (3).

Other effects

Other adverse effects (human)
Oral administration to healthy, fasted humans caused a significant drop in blood glucose levels and a rise in serum insulin (4).

Any other adverse effects
Rats fed with allyl propyl disulfide (dose and duration unspecified) exhibited lower blood sugar, lipid and albumin levels, compared to controls, together with increased levels of adipose tissue lipase (5).

Other comments

Reviews on experimental toxicology, epidemiology, workplace experience and human health effects listed (6).

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A93 allylthiourea

$$H_2C{=}CHCH_2NHCSNH_2$$

$C_4H_8N_2S$ **Mol. Wt.** 116.19 **CAS Registry No.** 109-57-9

Synonyms allyl thiocarbamide; thiosinamine; allyl sulfocarbamide; 2-propenylthiourea; 1-allyl-2-thiourea; Aminosin

EINECS No. 203-683-5 **RTECS No.** YR 8050000

Uses Corrosion inhibitor. In veterinary medicine has been used to minimise scar tissue. As a laboratory reagent for BOD testing.

Physical properties

M. Pt. 70-72°C **Specific gravity** 1.11
Solubility Organic solvents: diethyl ether, ethanol

Environmental fate

Nitrification inhibition
No inhibition occurred at 0.58 mg l^{-1}, 16% inhibition at 1.1 mg l^{-1} (oxidised N production), 38% inhibition at 1.1 mg l^{-1} (inhibition of ammonia loss) using activated sludge inocula (1).
Approximately 50% inhibition of ammonia oxidation by *Nitrosomonas* sp. at 1.2 mg l^{-1} (2).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 200 mg kg^{-1} (3).
LD_{50} intraperitoneal rat 500 mg kg^{-1} (4).
LD_{Lo} intravenous dog 110 mg kg^{-1} (5).

Sensitisation
Causes eczema in sensitised humans (6).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA1535, TA1537 with and without metabolic activation negative (7).

Other effects

Any other adverse effects
Neuroteratogenic to cultured brain cells (3).

Other comments

Neurotoxic potential reviewed (6).

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A94 allyltrichlorosilane

$$CH_2{=}CHCH_2SiCl_3$$

$C_3H_5Cl_3Si$ **Mol. Wt.** 175.52 **CAS Registry No.** 107-37-9

Synonyms trichloro-2-propenylsilane; silane, trichloro-2-propenyl-

EINECS No. 203-485-9 **RTECS No.** VV 1530000

Uses Chemical synthesis in cycloaddition reactions. In heat-resisting adhesives.

Physical properties

B. Pt. 117.5°C **Flash point** 35°C (open cup) **Specific gravity** 1.217 at 27°C **Volatility** v.den. 6.0

Occupational exposure

UN No. 1724 **HAZCHEM Code** 4WE **Conveyance classification** corrosive substance, danger of fire (flammable liquid)

Mammalian & avian toxicity

Acute data

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

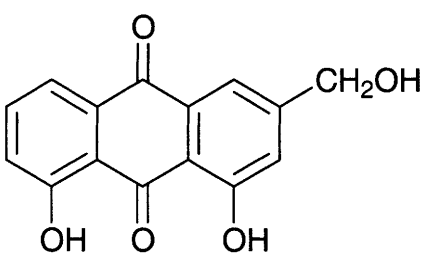
Other comments

Only minimal toxicity information is reported to be available on chlorosilanes (1).
Corrosive.

References

1. *U.S. Army Armament R&D Command* NX 04219

A95 aloe emodin



$C_{15}H_{10}O_5$ **Mol. Wt.** 270.24 **CAS Registry No.** 481-72-1

Synonyms 9,10-anthracenedione, 1,8-dihydroxy-3-(hydroxymethyl)-; 3-hydroxymethylchrysazin; rhabarberone

EINECS No. 207-571-7 **RTECS No.** CB 6712200

Uses Cathartic.

Occurrence Occurs in the free state and as a glycoside in *Rheum*, in senna leaves and in various species of *Aloe* (Liliaceae).

Physical properties

M. Pt. 223-224°C

Genotoxicity

Salmonella typhimurium TA98, TA1537, TA1538 without metabolic activation positive (1).
Salmonella typhimurium TA98 with and without metabolic activation negative, TA100 with metabolic activation positive, without negative (2).
In vivo primary rat hepatocytes caused a 2- to 3-fold increase in DNA synthesis (3).

Other effects

Any other adverse effects
Intraperitoneal mice with P388 leukaemia (7 day) 40 mg kg^{-1} increased the survival time of the mice by 36%, also reduced the ascites volume and tumour cell number. Results indicated inhibition of biosynthesis of DNA, RNA and P388 leukaemia cell protein (4).
Intraperitoneal mice (7 day) 44 mg kg^{-1} day^{-1} decreased cytochrome P450 in hepatic microsomes by 66.3% (5).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Polycyclic aromatic hydrocarbons: maximum admissible concentration 0.2 μg l^{-1} (6).

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A96 aluminium

Al

Al **Mol. Wt.** 26.98 **CAS Registry No.** 7429-90-5

Synonyms aluminum; aluminium fibre; C.I. 77000; aluminium flake; aluminium powder

EINECS No. 231-072-3 **RTECS No.** BD 0330000

Uses Used as the pure metal or as alloys for aircraft, utensils, apparatus and electrical conductors. Explosives, fireworks and in paints.
Occurrence One of the most abundant metals in the earth's crust; 8.8% by weight. Does not occur in free state in nature, but is found combined with oxygen, fluorine and silicon. Bauxite is the principal ore, and the richest source of aluminium.

Physical properties

M. Pt. 660°C **B. Pt.** 2327°C **Specific gravity** 2.70 **Volatility** v.p. 1 mmHg at 1284°C
Solubility Water: insoluble in water

Occupational exposure

DE-MAK 1.5 mg m^{-3} (respirable fraction of the aerosol)
FR-VME 10 mg m^{-3} (metal), 5 mg m^{-3} (powder and soldering fumes)
SE-LEVL 5 mg m^{-3} (total dust); 2 mg m^{-3} (respirable dust)
UK-LTEL 10 mg m^{-3} (total inhalable dust), 4 mg m^{-3} (respirable dust)
US-TWA 10 mg m^{-3} (metal dust); 5 mg m^{-3} (pyro powders and welding fumes) (as Al)

UN No. 1309 (powder, coated)

UN No. 1396 (powder, uncoated) **HAZCHEM Code** 4Y (powder uncoated) **HAZCHEM Code** 4Z (powder coated) **Conveyance classification** flammable solid (powder, coated) **Conveyance classification** substance which on contact with water emits flammable gas **Conveyance classification** (powder, uncoated)
Supply classification highly flammable
Risk phrases Contact with water liberates extremely flammable gases – Spontaneously flammable in air (R15, R17)
Safety phrases Keep out of reach of children (if sold to general public) – Keep container tightly closed and dry – In case of fire, use dry chemical powder extinguisher (S2, S7/8, S43)

Ecotoxicity

Fish toxicity
LC_{50} (4 wk) rainbow trout 0.56 mg l^{-1} (1).
Lowest observed effective concentration (3 wk) longnose sucker, brook trout 0.1 and 0.2 mg l^{-1}, respectively (2).
Yolk fry of Atlantic salmon exposed to 135 µg l^{-1} at pH 5 and 1°C for ≈30day caused ≈6% mortality. Acidification increased aluminium accumulation but ≈60% of aluminium was absorbed by the fish body surface and was lost early during depuration (3).
The effect on brown trout of lime being administered to an acid stream rich in aluminium was studied 0-100 metres from the mixing zone. Within 15 metres of dosing, filterable aluminium content fell from 580 to 230 µg l^{-1} and to 120 µg l^{-1} within 30 metres although total aluminium was unchanged. After 24 hr, fish mortality was 100% at untreated acidic sites, 80% at <30 metres downstream of loading and 0% at 100 metres. Mortalities correlated with aluminium concentration in gill tissues and filterable aluminium in the water (4).
The relative sensitivity of seven freshwater fish species to acid aluminium-rich water was determined. The results showed decreasing sensitivity in the order: Atlantic salmon, roach, minnow, perch, grayling, brown trout and Arctic char. Substantial mortality was observed in all species (5).

Invertebrate toxicity
LC_{50} (48-96 hr) *Asellus aquaticus* 6.57-4.37 mg l^{-1} specific toxicological reaction to mobility (6).
EC_{50} (48 hr) *Daphnia magna* 1.4 mg l^{-1} (7).
EC_{50} (3 wk) *Daphnia magna* 0.68 mg l^{-1} reproductive effects (7).
EC_{Lo} (3 wk) *Daphnia magna* 0.32 mg l^{-1} reproductive effects (7).
Freshwater clams *Anodonta anatina* and *Unio pictorium* (3 wk continuous or 24 day fluctuating) 300 and 900 µg l^{-1} caused accumulation in kidney, midgut gland, restgill and mantle in decreasing order of concentration. During the 3-wk exposure, aluminium in the gills and kidney increased linearly and saturation was not reached. Ambient pH had a significant effect on accumulation in the gills whereas water hardness did not (8).
EC_{50} Sydney Rock oyster *Saccostrea commercialis*, embryo development to the D-veliger stage, 150 µg l^{-1} aluminium added to sea water; no-observed-effect level 100 µg l^{-1}. All embryos showed developmental abnormalities at concentrations of ≥400 µg l^{-1} (9).

Toxicity to other species
Elevated aluminium levels in common frog and moor frog larvae increased the rate of defects, including spinal curvature and vesicles on the head and thorax, and altered the feeding behaviour (10).

Arnica montana, *Cirsium dissectum* and *Calluna vulgaris* were cultured at high aluminium concentrations (200-500 μmol l^{-1}). In both *A. montana* and *C. dissectum* indications of aluminium toxicity were observed, including poor root development, yellowed leaves and reduced magnesium and phosphorus content. *C. vulgaris* showed no signs of aluminium toxicity (11).

Bioaccumulation

Accumulation of aluminium by the freshwater snail *Lymnaea stagnalis* at neutral pH, where most aluminium would be predicted to be in an insoluble form [$Al(OH)_3$], was studied. Snails were exposed to 38-285 mg l^{-1} aluminium for 30 days, followed by 20 days in clean water. Concentration factors ranged from 4.5×10^{-3} in the whole soft tissues to 6.3×10^4 in the kidney (800 to 7500 μg g^{-1}, respectively). Following transfer to clean water, rapid loss of aluminium from the whole soft tissues and gut was seen over the first 10 days. Aluminium is clearly available to the snail at neutral pH, the most likely route of entry being the gut (12).

Mammalian & avian toxicity

Sub-acute and sub-chronic data

Intravenous Japanese quail (18 hr) accumulation of 51% of aluminium ion in liver in ♂. Cumulative maximum in egg components (10 day) 38% in yolks and 0.54% in shells (13).

Intravenous rabbit (1 month) 100 μ mol kg^{-1}. Frontal cortical glial fibrillary acidic protein expression increased twofold suggesting CNS injury (14).

Metabolism and toxicokinetics

Poorly absorbed through the gastrointestinal tract, the absorption which does occur has been suggested to be mediated, at least in part, by an active-transport process controlled by parathyroid hormone (15).

70-90% of total aluminium was bound to plasma proteins (60-70% to a high molecular weight protein and 10-20% to albumin while only 10-30% was unbound). This high affinity of aluminium for plasma proteins strongly suggests high levels of binding of aluminium to a variety of tissue proteins (16).

Other effects

Other adverse effects (human)

Workers exposed to aluminium had urinary concentrations 80-90 times higher than those occupationally non-exposed workers, $t_{1/2}$ 5-6 wk. Among retired workers $t_{1/2}$ <1-8 yr and was related to the number of years since retirement, suggesting aluminium is retained and stored in several compartments of the body and eliminated at different rates (17).

Exposure of 65 welders to aluminium for a long period revealed neuropsychiatric symptoms (18).

Aluminium affects the central nervous system (19).

Aluminium content in blood serum, aqueous humour and lenses of humans with senile cataracts gradually increased and was optimum during the period of the mature cataract (20).

Chronic inhalation of fumes and dusts containing high concentrations of aluminium may cause dyspnoea, cough, weakness, emphysema, and non-nodular pulmonary fibrosis (aluminosis). Shavers disease is the only industrial disease attributable to aluminium exposure, and is characterised by pulmonary fibrosis and emphysema (21).

Any other adverse effects

Inhibits both the cytosolic and mitochondrial hexokinase activities in the rat brain. IC_{50} 4-9 mg kg^{-1} (22).

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} (23).

Other comments

Nutritional aspects of aluminium toxicity reviewed in relation to its possible role in Alzheimer's disease and other neurodegenerative diseases (24).

Absorption, plasma $t_{1/2}$ and excretion reviewed (25).

Mutagenic and carcinogenic potential reviewed (26,27).
Reviews on physico-chemical properties, human health effects, experimental toxicology, environmental effects and workplace experience are listed (28).
Reproductive and developmental toxicity reviewed (29,30).
Haematopoietic effects of aluminium toxicity reviewed (31).
Metabolism and toxicity reviewed (32).
Toxicological and environmental aspects reviewed (33).
Effects on bone and role in the pathogenesis of renal osteodystrophy reviewed (34).
A comprehensive review is presented on aluminium and its compounds in the environment (35).
Chemical and biological behaviour of aluminium products and aluminium compounds following exposure to environmental media reviewed (36).
Environmental health criteria reviewed (37).
The toxicity of aluminium is dependent on the ability of the organism to absorb it. Therefore toxicity data refer to bioavailable forms, such as the ion in solution or particulate matter.
The solution chemistry of aluminium is complex, and the response of the biota to the metal is dependent upon the chemical form of the toxicant. pH values and water hardness are highly influential.

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A97 aluminium bromide

$AlBr_3$

$AlBr_3$ **Mol. Wt.** 266.69 **CAS Registry No.** 7727-15-3

Synonyms aluminium tribromide; tribromoaluminium

EINECS No. 231-779-7 **RTECS No.** BD 0350000

Uses Catalyst in organic synthesis.

Physical properties

M. Pt. 94-98°C **B. Pt.** 250-270°C **Specific gravity** 3.205 at 18°C with respect to water at 4°C
Volatility v.p. 1 mmHg at 81°C
Solubility Organic solvents: acetone, benzene, carbon disulfide, ethanol, nitrobenzene, simple hydrocarbons, toluene, xylene

Occupational exposure

US-TWA 2 mg m^{-3}

UN No. 1725 (anhydrous)

UN No. 2580 (solution) **HAZCHEM Code** 4X (anhydrous) **HAZCHEM Code** 2X (solution) **Conveyance classification** corrosive substance

Mammalian & avian toxicity

Irritancy
Inhalation of powders and vapours can cause severe irritation. Aluminium bromide has a high affinity for water which can cause severe tissue burns on contact with skin (1).

Other effects

Other adverse effects (human)
In humans, symptoms of mild poisoning include shortness of breath, coughing, wheezing, nausea, aching muscles and slight fever, while severe poisoning can cause convulsions, liver and kidney damage. Inhalation may prove fatal as a result of spasm, inflammation and oedema of the larynx and bronchi, chemical pneumonitis and pulmonary oedema. Prolonged exposure may lead to inorganic bromide poisoning, the symptoms of which include depression, emaciation and, in severe cases, psychoses and mental deterioration (1).

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} (2).

Other comments

Aluminium and its compounds have been implicated in Alzheimer's disease (3-6).

Highly corrosive to metals. Reacts violently with water, alcohols and acids. Incompatible with strong oxidising agents and mixtures with sodium or potassium.

References

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A98 aluminium carbide

$$Al_4C_3$$

Al_4C_3 **Mol. Wt.** 143.96 **CAS Registry No.** 1299-86-1

Synonyms tetraaluminium tricarbide

EINECS No. 215-076-2

Uses Reduction of metal oxides. Manufacture of aluminium nitride. Ceramic manufacture. Generation of methane.

Physical properties

M. Pt. 2100°C **B. Pt.** 2200°C (decomp.) **Specific gravity** 2.360

Occupational exposure

UN No. 1394 **HAZCHEM Code** 4Y **Conveyance classification** substance which in contact with water emits flammable gas.

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} (1).

Other comments

Aluminium has been implicated in Alzheimer's disease (2-5).
Reacts violently with acids and is incompatible with strong oxidisers.

References

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A99 aluminium chloride

$AlCl_3$

$AlCl_3$ **Mol. Wt.** 133.34 **CAS Registry No.** 7446-70-0

Synonyms trichloroaluminium; aluminium trichloride

EINECS No. 231-208-1 **RTECS No.** BD 0525000

Uses Acid catalyst especially in Friedel-Crafts type reactions. In cracking of petroleum and in the manufacture of rubbers, lubricants and antiperspirants, and treatment of wastewaters.

Physical properties

M. Pt. 194°C (5.2 atm) **B. Pt.** 181°C (sublimes), 262°C (decomp.) **Specific gravity** 2.44 at 25°C **Volatility** v.p. 1 mmHg at 100°C

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

Occupational exposure

US-TWA 2 mg m^{-3}

UN No. 1726 (anhydrous)

UN No. 2581 (solution) **HAZCHEM Code** 4X (anhydrous) **HAZCHEM Code** 2X (solution) **Conveyance classification** corrosive substance

Supply classification corrosive

Risk phrases Causes burns (R34)

Safety phrases Keep locked up and out of the reach of children (if sold to general public) – Keep container tightly closed and dry – 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, S7/8, S28, S45)

Ecotoxicity

Fish toxicity

LC_{50} (12-96 hr) goldfish 100 mg l^{-1} (1).

Invertebrate toxicity

EC_{50} (48 hr) *Daphnia magna* 3.9 mg l^{-1} (2).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, mouse 3730, 3805 mg kg^{-1}, respectively (3,4).

Teratogenicity and reproductive effects

LD_{50} 1.1 μg l^{-1} injected egg^{-1} chick embryo air sac of egg on day-3 of incubation. Minimal lethal dose was 0.3 μg l^{-1} egg^{-1}. Development of the embryos was retarded and teratogenic effects were apparent (5).

Rats administered 0.025-5 mg l^{-1} in drinking water for 6 months before and during pregnancy showed signs of embryotoxicity and neurotoxicity (6).

Metabolism and toxicokinetics

Aluminium chloride (concentration unspecified) added to the drinking water of mice resulted in the accumulation of aluminium in organs, especially the brain and bones, which interfered with calcium and phosphorus metabolism, increased brain acetylcholinesterase activity and damaged kidney, bone and brain and reduced growth and development (7).

Irritancy

Acute biological hazards of aluminium chloride are mostly due to the extremely acid products of its reaction with

water, which it takes from the tissues. Aluminium chloride dust and vapours are irritants and can cause severe burns or allergic skin reactions. In its hydrated form, inhibits sweating and causes clinical irritation after prolonged exposure (8).

Genotoxicity

Bacillus subtilis H17 (rec^+), M45 (rec^-) negative DNA damage (9).
Escherichia coli SOS chromotest negative (10).
Intraperitoneal mouse 1.3-13 g l^{-1} induced chromosomal aberrations in bone marrow cells (11).

Other effects

Any other adverse effects
Inhalation can be fatal as a result of spasm, inflammation of the larynx and bronchi, chemical pneumonitis and pulmonary oedema. Symptoms of exposure may take several hr to appear and include a burning sensation, coughing and wheezing, headache, nausea and vomiting. Prolonged exposure may result in lung damage. Increased lung:body weight ratio, bronchiolitis and secondary effects on liver and kidney weights have been reported in chronic inhalation studies (12).
Can cause irritation, especially if applied to damp skin, attributed to the formation of hydrochloric acid (13).

Legislation

Limit 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} (14).

Other comments

Reviews on physico-chemical properties, experimental toxicology, human health effects and environmental effects listed (15).
Aluminium and its compounds have been implicated in Alzheimer's disease (16-19).
Reacts violently with water to release heat and toxic fumes of hydrogen chloride, aluminium oxide and aluminium chlorate.

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A100 aluminium hydride

AlH_3

AlH_3 **Mol. Wt.** 30.01 **CAS Registry No.** 7784-21-6

Synonyms aluminium trihydride; α-aluminium trihydride

EINECS No. 232-053-2 **RTECS No.** BD 0930000

Uses Catalyst for polymerisation. Reducing agent. In photoimaging. Former interest as a high energy additive to solid rocket propellants.

Occupational exposure

UN No. 2463 **Conveyance classification** substance which in contact with water emits flammable gas

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} (1).

Other comments

Reviews on environmental effects, human health effects, ecotoxicology and experimental toxicology listed (2). Aluminium and its compounds have been implicated in Alzheimer's disease (3-6).

The solution chemistry of aluminium is complex, and the response of the biota to the metal is dependent upon the chemical form of the toxicant. pH values and water hardness are highly influential. The aquatic toxicity of aluminium is dependent upon the chemical state of the metal, and/or the associated hydroxide complexes.

References

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A101 aluminium isopropoxide

$Al[OCH(CH_3)_2]_3$

$C_9H_{21}AlO_3$ **Mol. Wt.** 204.25 **CAS Registry No.** 555-31-7

Synonyms aluminium triisopropoxide; aluminium isopropylate

EINECS No. 209-090-8 **RTECS No.** BD 0975000

Uses Formulation of paints, waterproofing textiles, formation of aluminium soaps. Chemical synthesis of alkoxides, chelates, acylates. In ester exchange and Meerwein-Ponndorf reaction.

Physical properties

M. Pt. 134-138°C **B. Pt.** 135°C at 10 mmHg
Solubility Organic solvents: benzene, chloroform, ethanol, isopropanol, toluene

Occupational exposure

Supply classification highly flammable
Risk phrases Highly flammable (R11)
Safety phrases Keep out of reach of children (if sold to general public) – Keep container dry – Keep away from sources of ignition – No smoking (S2, S8, S16)

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 11.3 g kg^{-1} (1).

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} (2).

Other comments

Reviews on physico-chemical properties, experimental toxicology, human health effects and environmental effects listed (3).
Aluminium and its compounds have been implicated in Alzheimer's disease (4-7).

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A102 aluminium nitrate nonahydrate

$$Al(NO_3)_3.9H_2O$$

$AlN_3O_{18}H_{18}$ **Mol. Wt.** 375.13 **CAS Registry No.** 7784-27-2

RTECS No. BD 1050000

Uses Tanning leather, anti-perspirant, corrosion inhibitor, salting-out agent in extraction of actinides.
Occurrence Occurs in several states of hydration of which the nonahydrate is the most stable.

Physical properties

M. Pt. 73°C **B. Pt.** 135°C (decomp.)
Solubility Water: very soluble. Organic solvents: acetone, ethanol

Occupational exposure

SE-LEVL 1 mg m^{-3}
UK-LTEL 2 mg m^{-3}
US-TWA 2 mg m^{-3}

UN No. 1438 **HAZCHEM Code** 1Y **Conveyance classification** oxidising substance

Ecotoxicity

Fish toxicity

LC_{50} (10 day) stickleback 0.07 mg l^{-1} as aluminium metal (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 4.28 g kg^{-1} (2).

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} (3).
Included in Schedule 6 (Release Into Land: Prescribed Substances) of Statutory Instrument No. 472, 1991 (4).

Other comments

Reviews on human health effects, experimental toxicology and workplace experience listed (5).
Aluminium and its compounds have been implicated in Alzheimer's disease (6-9).
The solution chemistry of aluminium is complex, and the response of the biota to the metal is dependent upon the chemical form of the toxicant. pH values and water hardness are highly influential. The aquatic toxicity of aluminium is dependent upon the chemical state of the metal, and/or the associated hydroxide complexes.

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A103 aluminium oxide

Al_2O_3

Al_2O_3 **Mol. Wt.** 101.96 **CAS Registry No.** 1344-28-1

Synonyms alumina; activated aluminium oxide; aluminium sesquioxide; α-alumina; β-alumina; γ-alumina

EINECS No. 215-691-6 **RTECS No.** BD 1200000

Uses Used as an adsorbent, desiccant and a filler for paints and varnishes. In the manufacture of alloys, ceramics, electrical insulators and resistors. Catalyst for organic reactions.
Occurrence As the minerals bauxite, bayerite, boehmite, corundum, disapore, gibbsite.

Physical properties

M. Pt. 2072°C **B. Pt.** 2977°C **Specific gravity** 4.0 at 20°C with respect to water at 4°C
Volatility v.p. 1 mmHg at 2158°C

Occupational exposure

DE-MAK 1.5 mg m^{-3} (respirable dust fraction)
FR-VME 10 mg m^{-3}
SE-LEVL 5 mg m^{-3} (total dust); 2 mg m^{-3} (respirable dust)
UK-LTEL 10 mg m^{-3} (total inhalable dust); 4 mg m^{-3} (respirable dust)
US-TWA 10 mg m^{-3}

Mammalian & avian toxicity

Acute data
Intratracheal rat 5 mg caused a mild increase in the number of polymorphonuclear leukocytes in the lung 7 days after administration (1).

Carcinogenicity and chronic effects
Cancer morbidity and total morbidity pattern were studied among workers manufacturing abrasive materials who had been exposed to aluminium oxide (total dust levels 0.1-1 mg mg^{-3}) from 1958 to 1983. No significant increase was found in mortality cases or incidence of non-malignant respiratory diseases (2).
Occasional mesotheliomata reported in rats after intrapleural injection of 0.5-20 mg aluminium oxide (3).
Solid rods of aluminium oxide containing yttrium oxide, used for orthopaedic implants, were implanted in the thigh muscle of C57BL/6N mice for 24 months. No evidence of carcinogenicity or chronic toxicity was seen (4).

Irritancy
Skin irritation and a congestive, anaesthetic condition can result from prolonged exposure (5).

Genotoxicity

Bacillus subtilis H17(rec^+), M45(rec^-) negative DNA damage (6).

Other effects

Other adverse effects (human)
Thirty-three foundry workers were exposed to inhalation of aluminium oxide dust at <1 mg m^{-3}. Aluminium in serum was significantly raised but not in urine, suggesting incomplete excretion of aluminium (7).
Exposure to inhaled aluminium oxide in 38 pot-room workers with no airway symptoms and 20 healthy office workers (all non-smokers) was low, 15-20% of the Swedish exposure limits (8).
Inhalation of particles of aluminium oxide has been implicated in Shavers disease, an often fatal and rapidly progressive interstitial fibrosis of the lung, although it is believed that silica fume may be partially responsible (9).

Any other adverse effects

Intratracheal hamster induced dose-related increase in the incidence and severity of alveolar septal fibrosis (duration of exposure unspecified) (10).

The fibrogenicity of seven aluminium oxide samples was tested in rats by intratracheal instillation and in mice by intraperitoneal injection. None of the five samples used for primary aluminium production showed any fibrogenic potential, while the other two, a chemical grade and a laboratory produced sample, induced fibrotic lesions (11).

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} (12).

Other comments

Toxicity to lungs reviewed (13).

Aluminium and its compounds have been implicated in Alzheimer's disease (14-17).

Reviews on human health effects, experimental toxicology, epidemiology and environmental effects listed (18).

The aquatic toxicity of aluminium is dependent upon the chemical state of the metal, and/or the associated hydroxide complexes.

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A104 aluminium phosphide

AlP

AlP **Mol. Wt.** 57.96 **CAS Registry No.** 20859-73-8

Synonyms Phostoxin; Celphos

EINECS No. 244-088-0 **RTECS No.** BD 1400000

Uses Fumigant for killing insects in stored feed, grain, seeds, nuts. Source of phosphine in semiconductor research. Acute rodenticide.

Physical properties

M. Pt. >1000°C **Specific gravity** 2.85 at 25°C with respect to water at 4°C

Occupational exposure

UN No. 1397 **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 – Contact with acids liberates very toxic gas (R15/29, R28, R32)
Safety phrases Keep locked up and out of the reach of children (if sold to general public) – Keep in a cool well ventilated place away from water, oxidising agents, mineral acids – Never add water to this product – 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, S3/9/14, S30, S36/37, S45)

Mammalian & avian toxicity

Acute data
LD_{50} oral ♂ rat 13.9-14.8 mg kg^{-1} (1).
LC_{Lo} inhalation rat 1 ppm (2).

Other effects

Other adverse effects (human)
Phosphine detected post-mortem in stomach and contents, blood and liver specimens of a man who had ingested tablets containing aluminium phosphide (3).
Two incidents were reported of children exposed to fumigated grain on ship. Symptoms included headache, nausea, vomiting, dyspnoea, fatigue and jaundice. Fatalities reported, myocardial infiltration with necrosis and pulmonary oedema were found on autopsy (4,5).

Any other adverse effects
Aluminium phosphide releases phosphine on contact with moisture. Symptomatic effects of phosphine exposure include weakness, vertigo, pains around the diaphragm, dyspnoea, bronchitis, oedema and other lung damage, convulsions and coma (6).

Legislation

Included in Schedule 6 (Release into Land: Prescribed Substances) of Statutory Instrument No. 472, 1991 (7). 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} (8).

Other comments

Reacts with water to produce phosphine. Hazardous potential reviewed (9).

Reviews on physico-chemical properties, human health and environmental effects, experimental toxicology, ecotoxicology and exposure levels listed (10).
Aluminium and its compounds have been implicated in Alzheimer's disease (11-14).

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A105 aluminium potassium sulfate

$$KAl(SO_4)_2$$

$AlKO_8S_2$ **Mol. Wt.** 258.21 **CAS Registry No.** 10043-67-1

Synonyms *Anhydrous:* sulfuric acid, aluminium potassium salt; burnt alum; exsiccated alum; *Dodecahydrate:*alum; potassium alum; kalinite; alum flour

EINECS No. 233-141-3 **RTECS No.** WS 5690000

Uses Used in dyeing/printing fabrics. In the manufacture of dyestuffs, paper, vegetable glue, cement and explosives. Used in the tanning, hardening and electrolytic copperplating industries.

Physical properties

M. Pt. 92.5°C
Solubility Water: 138.99 g l^{-1}

Occupational exposure

SE-LEVL 1 mg m^{-3}
UK-LTEL 2 mg m^{-3}
US-TWA 2 mg m^{-3}

Environmental fate

Anaerobic effects
Alum-, iron- and lime-treated fluid and air-dried anaerobically digested sewage sludges were added to soil. The sludge supplied twice the total nitrogen than for common fertilisers (1).

Degradation studies

Nitrification took place in the reactors treating both primary and mixed primary (alum added) chemical sludge. The high content of aluminum did not inhibit the nitrifiers (2).

Mammalian & avian toxicity

Carcinogenicity and chronic effects

Oral B6C3F1 mice (20 months) 1, 2.5, 5.0 and 10.0% in diet. Body-weight gain increased in mice given 1.0 and 2.5% but decreased in the group given 10%. The survival rate of all treated animals was higher than the control group and increased with dosage. The incidence of hepatocellular carcinoma was significantly decreased in ♀ in all groups and in ♂ in the group given 10%. The authors conclude that the long-term administration of aluminium potassium sulfate does not exert tumorigenic or any other toxic actions in B6C3F1 mice (3).

Genotoxicity

Escherichia coli SOS/umu test negative (4).

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} (5).

Other comments

Reviews on human health effects, experimental toxicology, environmental effects and ecotoxicology listed (6).
Aluminium and its compounds have been implicated in Alzheimer's disease (7-10).
The aquatic toxicity of aluminium is dependent upon the chemical state of the metal, and/or the associated hydroxide complexes.

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A106 aluminium resinate

$$Al(C_{44}H_{63}O_5)_3$$

$C_{132}H_{189}AlO_{15}$ **Mol. Wt.** 2042.93 **CAS Registry No.** 61789-65-9

Synonyms resin acids and rosin acids, aluminium salts; size precipitate

EINECS No. 263-075-0

Uses In paper size.

Occupational exposure

UN No. 2715 **HAZCHEM Code** 1Z **Conveyance classification** flammable solid

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} (1).

Other comments

Reviews on human health effects, experimental toxicology, environmental effects and ecotoxicology listed (2). Aluminium and its compounds have been implicated in Alzheimer's disease (3-6).

The solution chemistry of aluminium is complex, and the response of the biota to the metal is dependent upon the chemical form of the toxicant. pH values and water hardness are highly influential. The aquatic toxicity of aluminium is dependent upon the chemical state of the metal, and/or the associated hydroxide complexes.

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A107 aluminium sulfate

$$Al_2(SO_4)_3$$

$Al_2O_{12}S_3$ **Mol. Wt.** 342.15 **CAS Registry No.** 10043-01-3

Synonyms anhydrous aluminium sulfate

EINECS No. 233-135-0 **RTECS No.** BD 1700000

Uses Tanning leather, sizing paper, mordant. Water purification. Fireproofing and waterproofing cloth. Antiperspirant.

Occurrence Occurs in nature as the mineral alunogenite.

Physical properties

M. Pt. 770°C (decomp.) **Specific gravity** 1.61

Solubility Water: 313 g l^{-1} at 0°C, 891 g l^{-1} at 100°C

Occupational exposure

FR-VME 2 mg m^{-3}

SE-LEVL 1 mg m^{-3}

UK-LTEL 2 mg m^{-3}

US-TWA 2 mg m^{-3}

Ecotoxicity

Fish toxicity

LC_{50} (12-96 hr) goldfish 100 mg l^{-1} (1).

Invertebrate toxicity

EC_{50} (48-72 hr) *Asellus aquaticus* 6.57-4.37 mg l^{-1} (2).

EC_{50} (48-96 hr) *Crangonyx pseudogracilis* 12.80-9.19 mg l^{-1} (2).

Bioaccumulation

Bioconcentration of aluminium in rainbow trout tissue and plankton was studied from aluminium sulfate-contaminated water. Statistical comparison of experimental and control tissues revealed no significant differences between exposed and non-exposed organisms (3).

Environmental fate

Nitrification inhibition

Threshold for sulfate is 500 mg l^{-1} (4).

Degradation studies

Rapid biodegradation occurred in three sludges which contained aluminium sulfate. Degradation rates of the sludge increased as pH increased (5).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, mouse 1930, 6207 mg kg^{-1}, respectively (6,7).

Sub-acute and sub-chronic data

Oral rat 0.25-2 g kg^{-1} (duration unspecified) caused significant reduction of relative liver weight but no lethal effect (8).

Teratogenicity and reproductive effects

TD_{Lo} (30 day) subcutaneous mouse 27.4 mg kg^{-1} reproductive effects (9).

Metabolism and toxicokinetics

Gastrointestinal absorption of ingested aluminium is poor due to transformation of salts into insoluble aluminium phosphate in the digestive tract, brought about by pH changes and presence of phosphate in the diet. In rats only 10% of 200 mg kg^{-1} aluminium administered orally as the sulfate was absorbed. Distributed to all tissues, including bone, liver, testes and brain. Main route of excretion was via faeces (7).

Genotoxicity

Bacillus subtilis H17(rec+), M45(rec-) negative DNA damage (10).

In vitro human lymphocyte cells (72 hr) 20 μg ml^{-1} induced chromosomal aberrations in cells from ♂ and ♀ subjects, while the frequency of translocations and dicentrics was low (11).

Oral rat (prolonged exposure) induced dose-dependent inhibition of dividing cells and increased chromosomal aberrations, uninfluenced by duration of exposure (12).

Other effects

Other adverse effects (human)

In 1988 a substantial quantity of aluminium sulfate was accidentally released into the drinking water supply of 20,000 people in the vicinity of Camelford, UK. Exposures were very variable but it is likely that for up to 3 days consumers were supplied with water of pH 3.9-5.0. The maximum aluminium concentration recorded in this water was 620 mg l^{-1}, but it is estimated that most consumers received concentrations of 10-50 mg l^{-1}. A wide range of short-term symptoms were reported immediately following the incident including gastrointestinal disturbances, rashes and mouth ulcers. The existence of longer term effects is still under study (13).

A study was undertaken to determine blood and urine levels of workers employed in the production of

aluminium sulfate. All workers had significantly higher blood and urine concentrations than unexposed control group (14).

Any other adverse effects

Ingestion may result in ulceration and necrosis of the mucosa of the mouth, throat and oesophagus. Systemic effects include epigastric pain, nausea, vomiting, diarrhoea, thirst, haemorrhagic gastroenteritis and circulatory collapse (15).

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} (16).

Other comments

Reviews on human health effects, experimental toxicology, workplace experience and environmental effects listed (17).

Aluminium and its compounds have been implicated in Alzheimer's disease (18-21).

The solution chemistry of aluminium is complex, and the response of the biota to the metal is dependent upon the chemical form of the toxicant. pH values and water hardness are highly influential. The aquatic toxicity of aluminium is dependent upon the chemical state of the metal, and/or the associated hydroxide complexes.

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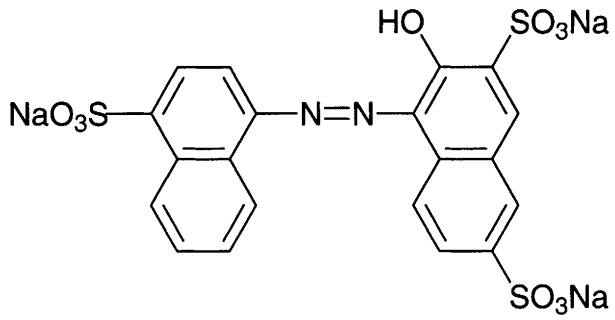
A108 Amaranth



$C_{20}H_{11}N_2Na_3O_{10}S_3$ **Mol. Wt.** 604.48 **CAS Registry No.** 915-67-3

Synonyms C.I. Acid Red 27; 3-hydroxy-4-[(4-sulfo-1-naphthalenyl)azo]-2,7-naphthalenedisulfonic acid trisodium salt; 1-(4-sulfo-1-naphthylazo)-2-naphthol-3,6-disulfonic acid, trisodium salt; FD&C Red No. 2; C.I. Food Red 9; E123

EINECS No. 213-022-2 **RTECS No.** QJ 6550000

Uses As a colouring agent in medicine, food and cosmetics. Also used for dyeing wool and silk bright bluish-red, as an indicator in hydrazine titrations and in colour photography.

Physical properties

Solubility Water: ~70 g l^{-1}. Organic solvents: cellosolve, ethanol (slightly soluble)

Mammalian & avian toxicity

Acute data

LD_{50} intraperitoneal, intravenous rat >1000 mg kg^{-1} (1).

Carcinogenicity and chronic effects

No adequate data for carcinogenicity to humans, inadequate evidence for carcinogenicity to animals, IARC classification group 3 (2).

Oral 100 Osborne-mendel and 100 Sprague-Dawley rats 10 and 20 g kg^{-1} of diet for 2 yr. No statistically significant increase in tumour incidence was observed (compared to a group of 100 controls) (3).

Target organ of carcinogenicity in rats: haematopoietic system (4).

Teratogenicity and reproductive effects

Tested in Charles River and Osborne-Mendel rats at 200 mg kg^{-1} by gavage or via water bottle during days 0-19, 6-15 or 7-9 of gestation. No significant skeletal or visceral effects were seen. In the Osborne-Mendel strain, no increase in resorptions occurred, but in Charles River rats treated on days 0-19 of gestation, a significant increase in the number of litters with >2 resorptions was observed (5).

In hamsters, 100 mg kg^{-1} administered on day-8 of gestation was not embryotoxic (6). Oral mice 0, 0.03, 0.09 and 0.27% in diet from 5 wk of age in F0 generation mice to 9 wk of age in the F1 generation. No effect on litter size or pup weight was seen. During the lactation period, treated mice showed less increase in body weight, and the survival index of the 0.27% group on postnatal day-21 was reduced. Significant effects on developmental parameters such as direction of swimming on postnatal day-4 in ♂ pups and olfactory orientation in ♂ and ♀ pups were observed (7).

Oral cats 92, 187 or 264 mg kg^{-1} day^{-1} from 0-22 days before gestation to days 61-62 of gestation. No evidence of maternal toxicity or embryotoxicity was found (8).

Metabolism and toxicokinetics

Amaranth is reduced by intestinal microflora to 1-amino-4-naphthalenesulfonic acid (naphthionic acid) as the major metabolite and 1-amino-2-hydroxy-3,6-naphthalenedisulfonic acid, which are both absorbed from the

intestine. After a single oral dose to rats, the serum naphthionic acid concentration reached a peak at ~2 hr post-dosing, and remained constant for 6 hr; 69% of the dose was excreted as naphthionic acid in the urine and faeces within 72 hr. Following three oral dose levels, the urinary naphthionic acid levels showed a dose-response relationship. Repeated daily oral doses of the dye led to a cyclic pattern of serum naphthionic acid concentration but no evidence of accumulation of naphthionic acid was seen. Consumption of the dye in food resulted in constant serum naphthionic acid concentration over time (9).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537, TA1538, with and without metabolic activation negative (10).
Salmonella typhimurium TA92, TA94, TA98, TA100, TA1535, TA1537 with metabolic activation negative (11).
In vitro Chinese hamster fibroblasts chromosomal aberrations test without metabolic activation positive (11).
Drosophila melanogaster somatic and germ line cell tests negative (12).
Escherichia coli PQ37 SOS-chromotest negative (13).
In vivo albino mice dominant lethal mutations assay negative at 250 or 500 mg kg^{-1} (14).

Other effects

Any other adverse effects
In rats, 5% in the diet depresses growth (15).
The effects of a 1% solution on intestinal sucrase were investigated *in vitro* and in rats in a jejunum perfusion *in vivo*. No inhibitory effect on sucrase activity was detected *in vitro*; *in vivo*, a release of intestinal sucrase from the intestine was observed. The toxicity of Amaranth may be due to its exfoliating or solubilising effects on the brush border membrane of the small intestine (16).

Other comments

Addition of the holocellulose fraction of dietary fibres to the diet of treated rats ameliorates the toxic effects of Amaranth (15).
Relationship between the structure of phenylazoanilines and their mutagenicity investigated (17).
Acceptable daily intake up to 0.5 mg kg^{-1}. Human health effects and experimental toxicology reviewed (18).

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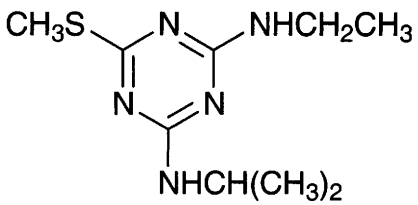
A109 ametryn



$C_9H_{17}N_5S$ **Mol. Wt.** 227.33 **CAS Registry No.** 834-12-8

Synonyms 1,3,5-triazine-2,4-diamine, *N*-ethyl-*N'*-(1-methylethyl)-6-(methylthio)-; *N*-ethyl-*N'*-(1-methylethyl)-6-(methylthio)-1,3,5-triazine-2,4-diamine; 2-(ethylamino)-4-(isopropylamino)-6-(methylthio)-*s*-triazine; 2-ethylamino-4-isopropylamino-6-methylmercapto-*s*-triazine; Ametrex; Gesapax

EINECS No. 212-634-7 **RTECS No.** XY 9100000

Uses Herbicide.

Physical properties

M. Pt. 84-85°C **Specific gravity** 1.19 at 20°C with respect to water at 4°C **Partition coefficient** log P_{ow} –1.72 (calc.) (1) **Volatility** v.p. 8.4×10^{-7} mmHg at 20°C

Solubility Water: 185 ppm at 20°C. Organic solvents: acetone, hexane, 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) – Wear suitable protective clothing (S2, S36)

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) bluegill sunfish, rainbow trout, channel catfish 19, 5, 25 mg l^{-1}, respectively (2).

No acute mortality to mosquito fish within 48 hr at ≤10 ppm in laboratory experiments, or within 5 days at 5 lb $acre^{-1}$ active ingredient in field ponds. At larvicidal rates (1-5 ppm), most formulations were highly toxic in the laboratory, but no acute toxicity was observed at the larvicidal rate (0.25-1.0 lb $acre^{-1}$) in the field (3).

Invertebrate toxicity

EC_{50} (96 hr) *Selenastrum capricornutum, Dunaliella tertiolecta* 6.2, 16 μg l^{-1}, respectively (4).

EC_{50} (24 hr) *Artemia salina* larvae 33 mg l^{-1} (4).

EC_{50} (15 min) *Photobacterium phosphoreum* 9 mg l^{-1} Microtox test (4).

EC_{50} (96 hr) *Daphnia* 28 mg l^{-1} (2).

LC_{50} (14 days) earthworms 166 mg kg^{-1} soil (2).

Chlorococcum sp. (technical solution) 20 ppb 50% decrease in oxygen evolution. *Chlorococcum* sp. 10 ppb 50% decrease in growth after 10 days. *Phaeodactylum tricornutum* 20 ppb 50% decrease in growth after 10 days (5).

LC_{50} (96 hr) oyster >1.0 ppm (conditions of bioassay unspecified) (6).

Scenedesmus sp. growth rate, chlorophyll a content, and ratio of chlorophylls decreased as the concentration increased. Microscopical examination in all tested cultures showed marked morphological changes (7).

Ametryn was a strong photosynthesis poison to *Ankistrodesmus falcatus* (8).

Ametryn exerted a depressive effect on the total count of cellulose decomposing fungi after 1 and 3 wk of treatment with a high dose (54 mg active ingredient kg^{-1} dry soil), and 5 wk after treatment with medium (27 mg)

and low doses. This inhibitory effect was alleviated after 8 wk, whereas after 12 wk ametryn had a promoting effect on decomposing fungi at the low dose (5.4 mg) (9).
When incorporated in the agar medium, this herbicide was toxic to the total count and to the counts of almost all fungal genera and species at the three doses (25, 125, 250 ppm). The growth and sporulation of test fungal species were partially or completely inhibited by the three doses, except, *Aspergillus niger*, *Chaetomium globosum* and *Gliocladium roseum* which were not affected by the low dose (9).
Low toxicity to bees (2).

Bioaccumulation
Estimated bioconcentration factor is 33 using water solubility of 185 mg l^{-1} which suggests that bioaccumulation in aquatic organisms will be insignificant (10).

Environmental fate

Nitrification inhibition
Toxic to *Nitrosomonas* spp. in soil. No inhibition at 5 ppm; inhibitory concentration 100 ppm (11).

Anaerobic effects
A concentration of 5 and 10 mg l^{-1} of ametryn in feed reduced methane gas production by 12.5%. The removal value was 37% at the lower concentration investigated (12).

Degradation studies
Under aerobic conditions $t_{1/2}$ 2-3 wk in soil. Metabolites included 2-amino-4-isopropylamino-6-methylthio-*s*-triazine; 2-amino-4-ethylamino-6-methylthio-*s*-triazine and 2,4-diamino-6-methylthiotriazine (1).
Rate of metabolism decreases under anaerobic conditions; $t_{1/2}$ 122 days (1).

Abiotic removal
Under aqueous conditions, ametryn is stable in natural sunlight $t_{1/2}$ >1 wk. When exposed to artificial sunlight for 6 hr, 75% remained, with 2-ethylamino-4-hydroxy-6-isopropylamino-*s*-triazine as photolysis product (1).
Direct photolysis can occur when exposed to sunlight. On the surface of three sandy loam soils <10-30% photolytic loss was observed in 7 days, thought to be a result of light-induced free radical oxidation (13,14).
Volatilisation from soil is an important route of removal from the environment despite its very low vapour pressure (15).
At 20°C hydrolysis occurs to the herbicidally inactive 6-hydroxy analogue (2).

Adsorption and retention
Ametryn has a pKa of 3.12, indicating that it is almost entirely undissociated at environmental pHs. Ametryn and humic acid form stable complexes and ionic, hydrogen bonding, donor-acceptor and covalent forces contribute to the binding (16,17).

Mammalian & avian toxicity

Acute data
LD_{50} oral mg kg^{-1} mouse, rat 965, 1110 mg kg^{-1}, respectively (2).
LC_{50} (4 h) inhalation rat >5170 mg m^{-3} (2).
LD_{50} percutaneous rabbit, rat >8160, >3100 mg kg^{-1}, respectively (2).
Sub-acute and sub-chronic data
LC_{50} (8 day) oral bobwhite quail 30 g kg^{-1} (2).
LC_{50} (8 day) oral mallard duck 23 g kg^{-1} (2).
Oral (90 days) rats at 100 mg kg^{-1} day^{-1} in feed, animals were comparable to controls except for slight histological changes in the liver (18).

Carcinogenicity and chronic effects
Oral (2 yr) rats, dogs no observable effect level 1000 mg kg^{-1} diet (67 and 33 mg kg^{-1} day^{-1}, respectively) (2).

Teratogenicity and reproductive effects
Pregnant ♀ Wistar albino rats were treated with 1/50 of the LD_{50} of ametryn and niclosamide, either individually or in combination, on days 5-15 of gestation then killed on day-20. Maternal and foetal body weight gain were

significantly reduced in rats administered ametryn. Gravid uterine weight and litter size were statistically reduced, and post-implantation deaths were significantly raised in dams treated with either ametryn alone or the combined dose. An increase in the incidence of malformations was seen in foetuses from all treated dams (19).

Metabolism and toxicokinetics

In 24 hr, following oral administration to rat (dose unspecified) 52% of ametryn was excreted in urine and 18% in faeces. Within 72 hr, elimination was almost complete, a further 6% had been excreted in urine, 14% in faeces leaving <2% in carcass. After 6 hr, ametryn levels were maximal in stomach, liver, kidneys, spleen and lung, decreasing with time, although blood levels remained constant for 72 hr (20).

[^{14}C]ametryn was administered to rats, lactating goats and laying hens. In all three species the majority of the administered dose was eliminated in excreta. Residues were observed in milk, eggs, tissues and organs with the liver and kidneys showing the highest total radioactive residue levels. Ametryn undergoes extensive metabolic transformation by *N*-dealkylation oxidation/hydroxylation and conjugation with sulfate, glutathione derivatives and glucuronic acid (21).

Irritancy

76 mg instilled into rabbit eye caused mild irritation (22).

Moderate skin irritant and mild eye irritant in rabbits (2).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537, TA1538 with and without metabolic activation negative (1).

Bacillus subtilis (strains unspecified) rec-assay negative (23).

Escherichia coli WP2 utilising auxotrophic strains in reversion assays negative (23).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides and related products: maximum admissible concentration 0.1 $\mu g\ l^{-1}$ (24).

Included in Schedule 6 (Release into Land: Prescribed Substances) of Statutory Instrument No. 472, 1991 (25).

Other comments

Ametryn was severely phytotoxic when foliage (windbreak trees) was sprayed (26).

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A110 amidithion

$$(CH_3O)_2PS_2CH_2CONHCH_2CH_2OCH_3$$

$C_7H_{16}NO_4PS_2$ **Mol. Wt.** 273.31 **CAS Registry No.** 919-76-6

Synonyms *S*-(*N*-2-methoxyethylcarbamoylmethyl)-*O*,*O*-dimethyl dithiophosphate; *O*,*O*-dimethyl-*S*-(2-methoxyethylcarbamoylmethyl)dithiophosphate; *S*-[2-[(2-methoxyethyl)amino]-2-oxoethyl] *O*,*O*-dimethyl phosphorodithioic acid ester

RTECS No. TE 1575000

Uses Acaricide and insecticide.

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 – Wear suitable protective clothing (S2, S24, S36)

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 600 mg kg^{-1} (1).
LD_{50} dermal rat 1600 mg kg^{-1} (2).

Sub-acute and sub-chronic data
Oral rat (3-4 month) 8 mg kg^{-1} day^{-1} decreased activity of cholinesterase in the blood, brain, liver and kidneys and that of alkaline phosphatase in the serum (3).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides and related products: maximum admissible concentration 0.1 μg l^{-1} (4).
Included in Schedule 6 (Release Into Land: Prescribed Substances) of Statutory Instrument No. 472, 1991 (5).

Other comments

Use as an insecticide discontinued.

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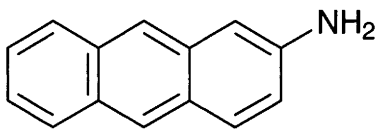
A111 2-aminoanthracene



$C_{14}H_{11}N$ **Mol. Wt.** 193.25 **CAS Registry No.** 613-13-8

Synonyms β-aminoanthracene; 2-anthracylamine; 2-anthrylamine; 2-anthramine

EINECS No. 210-330-9 **RTECS No.** CA 9275000

Uses Dyestuffs intermediate.

Physical properties

M. Pt. 238°C **B. Pt.** sublimes at 293°C **Partition coefficient** log P_{ow} 3.4
Solubility Organic solvents: diethyl ether, ethanol

Ecotoxicity

Fish toxicity

Exposure of rainbow trout to 122 mg l^{-1} for six days initiated biochemical effects including glycogen uptake, changes to cholesterol levels and lipids (1).

Bioaccumulation

Using the calculated bioconcentration factor of 3140, based on a measured water solubility, it is concluded that accumulation in aquatic organisms is likely (2).

Environmental fate

Abiotic removal

2-Aminoanthracene contains no hydrolysable functional groups and therefore is not expected to undergo environmental hydrolysis (2).

Photochemical reaction with atmospheric hydroxyl radicals estimated $t_{1/2}$ 1.8 hr (3).

Adsorption and retention

Extremely strong adsorption to soil and suspended solids and sediments in water is reported (4).

Genotoxicity

Salmonella typhimurium TA1535 with and without metabolic activation positive (5).
Salmonella typhimurium TA98, TA100 with metabolic activation positive (6,7).
Salmonella typhimurium YG1012, YG1024 with metabolic activation positive (8).
Salmonella typhimurium NM2009 gene expression *umuC* with metabolic activation positive (9).
Escherichia coli PQ37 SOS chromotest positive (7).
Escherichia coli K-12 *uvrb/recA* DNA repair rest positive (10).
Drosophila melanogaster white/white$^+$ eye mosaic assay interchromosomal mitotic recombination marginally positive (11).
Drosophila melanogaster DNA repair test positive (12).
2 μM was found to inhibit DNA synthesis by 50% in a DNA-synthesis inhibition test (13).
Vibrio fischeri M169 Mutatox assay positive (7).
Human peripheral blood lymphocytes were exposed at 37°C for 18 hr and showed 2 or 3 adducts from 8-1500 mol μg^{-1} DNA (14).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Polycyclic aromatic hydrocarbons: maximum admissible concentration 0.2 μg l^{-1} (15).

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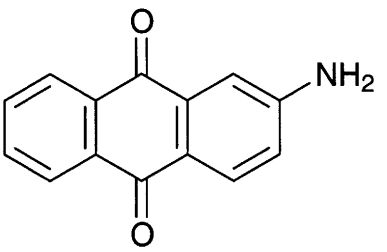
A112 2-aminoanthraquinone



$C_{14}H_9NO_2$ **Mol. Wt.** 223.23 **CAS Registry No.** 117-79-3

Synonyms 9,10-anthracenedione, 2-amino-; 2-amino-9,10-anthracenedione; β-aminoanthraquinone; NCI-CO1876

EINECS No. 204-208-4 **RTECS No.** CB 5120000

Uses Important intermediate in the preparation of indanthrene colorants. Used in the manufacture of pharmaceuticals.

Physical properties

M. Pt. 292-295°C (decomp.) **B. Pt.** sublimes

Solubility Organic solvents: acetone, benzene, chloroform, ethanol

Mammalian & avian toxicity

Acute data

LD_{50} intraperitoneal rat 1500 mg kg^{-1} (1).

Sub-acute and sub-chronic data

Oral Fischer 344 rat (1 wk) 2% in feed led to nephrotoxicity in ♀ caused by deposits of crystalline materials in the kidney tubules (2).

Carcinogenicity and chronic effects

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

F344 rats and B6C3F1 mice (78 wk) 0.69 and 1% (daily) in feed, respectively, induced haematopoietic system tumours, liver carcinomas and adenomas in ♂ rats, ♀ and ♂ mice (5).

Target organ of carcinogenicity: mouse haematopoietic system (6).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA1535, TA1537 with and without metabolic activation positive (7).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Polycyclic aromatic hydrocarbons: maximum admissible concentration 0.2 $\mu g\ l^{-1}$ (8).

Other comments

Reviews on experimental toxicology, human health effects and environmental effects listed (9).

It is known that some quinonoid compounds cause blindness in fish by retinal detachment.

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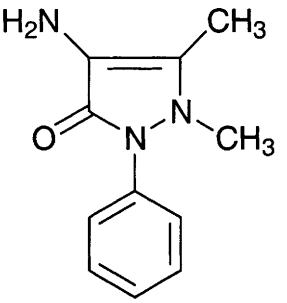
A113 4-aminoantipyrene



$C_{11}H_{13}N_3O$ **Mol. Wt.** 203.24 **CAS Registry No.** 83-07-8

Synonyms 4-amino-2,3-dimethyl-1-phenyl-3-pyrazolin-5-one; 4-aminophenazone; ampyrone; 3*H*-pyrazol-3-one, 4-amino-1,2-dihydro-1,5-dimethyl-2-phenyl-

EINECS No. 201-452-3 **RTECS No.** CD 2480000

Uses Used as an analgesic and antipyretic stabiliser. Production of azo dyestuffs. Reagent for glucose and for detection of alkylphenols.

Physical properties

M. Pt. 107-109°C

Solubility Organic solvents: benzene, diethyl ether, ethanol

Mammalian & avian toxicity

Acute data

LD_{50} intraperitoneal mouse, rat 270-1700 mg kg^{-1} (1-3).

Metabolism and toxicokinetics

Observed dose-dependent disposition of 4-aminoantipyrine in rabbits is a result of reduced renal and hepatic blood flow caused by the drug itself (4).

Vitamin B deficiency increased urinary excretion of total and acetylated 4-aminoantipyrine following intraperitoneal administration of 30 mg kg^{-1} aminopyrine (5).

1 g single oral dose of 4-aminoantipyrine to healthy human volunteers showed peak plasma concentrations 2.7 μg ml^{-1} and 1.6 μg ml^{-1} $t_{1/2}$ 5.5 hr and 3.8 hr in slow and rapid acetylations, respectively (6).

Genotoxicity

Salmonella typhimurium TA97 with metabolic activation positive. Possible long-term hazards are discussed in view of their pluripotent direct genotoxicity (7).

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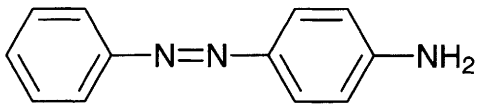
A114 4-aminoazobenzene



$C_{12}H_{11}N_3$ **Mol. Wt.** 197.24 **CAS Registry No.** 60-09-3

Synonyms benzeneamine, 4-(phenylazo)-; Aniline Yellow; *p*-aminodiphenylimide; C.I. Solvent Yellow 1; *p*-(phenylazo)aniline; 4-phenylazoaniline; C.I. 11000

EINECS No. 200-453-6 **RTECS No.** BY 8225000

Uses Used in the manufacture of dyestuffs. Insecticide.

Physical properties

M. Pt. 123-126°C **B. Pt.** >360°C **Partition coefficient** log P_{ow} 2.98 (calc.) (1)
Solubility Organic solvents: benzene, chloroform, 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)

Ecotoxicity

Invertebrate toxicity
EC_{50} (5-30 min) *Photobacterium phosphoreum* 2.66 mg l^{-1} Microtox test (2).

Toxicity to other species
Frogs (*Rana pipiens*) administered 0.3-0.5 mg in olive oil directly below the kidney capsule developed kidney nodules, which induced adenocarcinomas (3).

Bioaccumulation
Using the calculated bioconcentration factor of 58 based on the estimated log P_{ow} it is concluded that accumulation in aquatic organisms will be minimal (4).

Environmental fate

Nitrification inhibition
Ammonia oxidation by *Nitrosomonas* sp. at 100 mg l^{-1} 54% inhibition, at 50 mg l^{-1} 47% inhibition, at 10 mg l^{-1} 0% inhibition (5).

Degradation studies
Aeromonas hydrophila 24B is able to degrade 4-aminoazobenzene to aniline and can be applied to wastewater treatment (6).
Pseudomonas cepacia 13NA degraded 4-aminoazobenzene to yield metabolites, including aniline, *p*-phenylenediamine, acetanilide, *p*-aminoacetanilide and *p*-phenylenediacetamide (7).
Readily degradable using an activated sludge inoculum with 89% degradation occurring in 13 days, including a 7-day lag (8).
No BOD consumption with sewage and activated sludge inocula after 5 and 6 day incubations, respectively (9,10).
For static cultures, the lag period increased with concentration and with 100 ppm of 4-aminoazobenzene, 46% degradation occurred after 24 hr and 59% degradation after 48 hr in shaking and static cultures, respectively, at 37°C (11).

Strongly inhibited the growth of activated sludge microorganisms. The partition coefficients of azobenzenes between octanol and water correlated inversely with growth inhibition (12).

Abiotic removal

The photochemical $t_{1/2}$ produced from hydroxyl radicals was estimated at 5.8 hr (13).

Mammalian & avian toxicity

Acute data

LD_{Lo} intraperitoneal mouse 3.3 mg kg^{-1} (14).

Carcinogenicity and chronic effects

No adequate evidence for carcinogenicity to humans, sufficient evidence for carcinogenicity to animals, IARC classification group 2B (14).

TD_{Lo} (2-yr intermittent) dermal rat 1965 mg kg^{-1} neoplastic liver tumours (15).

Single intraperitoneal injection to mice (dose unspecified) induced hepatomas in 46-93% of animals tested (16).

Subcutaneous injection to pregnant ♀ and newborn ♂ mice (dose unspecified) increased the incidence of liver tumour and tumours of haematopoietic and lymphoid tissues (17).

Genotoxicity

Salmonella typhimurium TA98, TA100 without metabolic activation positive (18).

Escherichia coli 700 μg $well^{-1}$ gene conversion and mitotic recombination (19).

Intravenous rat 0.00098 mg l^{-1} caused unscheduled DNA synthesis (20).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides and related products: maximum admissible concentration 0.1 μg l^{-1} (21).

Included in Schedule 6 (Release Into Land: Prescribed Substances) of Statutory Instrument No. 472, 1991 (22).

Other comments

Reviews on physico-chemical properties, human health effects and experimental toxicology listed (23).

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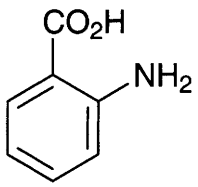
A115 2-aminobenzoic acid



$C_7H_7NO_2$ **Mol. Wt.** 137.14 **CAS Registry No.** 118-92-3

Synonyms *o*-anthranilic acid; vitamin L; *o*-aminobenzoic acid

EINECS No. 204-287-5 **RTECS No.** CB 2450000

Uses Acaricide. Dyestuffs, pharmaceuticals, perfume.

Physical properties

M. Pt. 144-146°C **Specific gravity** 1.412 at 20°C **Partition coefficient** log P_{ow} 1.21
Solubility Organic solvents: diethyl ether, ethanol

Ecotoxicity

Fish toxicity
Designated non-toxic to trout, bluegill sunfish, yellow perch and goldfish (1).

Environmental fate

Nitrification inhibition
At 100 mg l^{-1} no inhibition of NH_3 oxidation by *Nitrosomonas* sp. (2).

Degradation studies
Biodegradable (3).
97.5% COD, activated sludge at 20°C (4).
Decomposition by soil microflora 2 days (5).
Under anaerobic conditions in the presence of nitrate, 2-aminobenzoic acid oxidised to carbon dioxide by *Pseudomonas sp.* which involved 2-aminobenzoyl-CoA reductase. Aerobic degradation was via gentisic acid (6).
Four strains of the two actinomycete species *Streptomyces violaceoruber* and *Amycolata autotrophica* degraded 2-aminobenzoic acid, *A. autotrophica* 43093 being the most active strain (7).
2-aminobenzoic acid was degraded as sole source of carbon and energy in methanogenic enrichment cultures obtained from anoxic sediments and sewage sludge, to acetate, carbon monoxide, methane and ammonia (8).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 4550 mg kg^{-1} (9).
LD_{50} intraperitoneal mouse 2500 mg kg^{-1} (10).

Carcinogenicity and chronic effects

No adequate data for carcinogenicity to humans, inadequate evidence for carcinogenicity to animals, IARC classification group 3 (11).

National Toxicology Program tested ♂ and ♀ dosed rats and mice via feed. Negative evidence of carcinogenicity in all animals (12).

Metabolism and toxicokinetics

Intraperitoneal administration to rat resulted in <10% of dose (18 or 101 mg kg^{-1} body weight) excreted in bile (13).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537 with and without metabolic activation negative (14).

Escherichia coli K-12 *uvrB/recA* DNA repair host-mediated assay with and without metabolic activation negative (15).

In vitro rat hepatocytes replicative DNA synthesis test negative (16).

In vitro L5178Y tk+/tk– mouse lymphoma cells without metabolic activation weakly positive (17).

In vivo B6C3FI mice carcinogenic/non-carcinogenic pair was *o*-toluidine hydrochloride/2-aminobenzoic acid, respectively. Intraperitoneal administration of the pair up to the maximum tolerated dose to mice bone marrow , Geneva.cells did not increase the frequency of chromosomal aberrations or micronuclei. 2-aminobenzoic acid had a positive effect on sister chromatid exchange (18).

Other comments

Human health effects, experimental toxicology and ecotoxicology reviewed (13,19).

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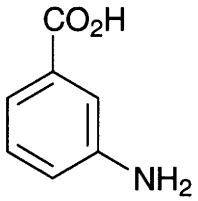
A116 3-aminobenzoic acid



$C_7H_7NO_2$ **Mol. Wt.** 137.14 **CAS Registry No.** 99-05-8

Synonyms *m*-aminobenzoic acid

EINECS No. 202-724-4 **RTECS No.** DG 1225000

Physical properties

M. Pt. 174°C **Specific gravity** 1.51 at 20°C with respect to water at 4°C **Partition coefficient** log P_{ow} 0.14
Solubility Organic solvents: diethyl ether, ethanol

Ecotoxicity

Fish toxicity
Designated non-toxic to trout, bluegill sunfish, yellow perch and goldfish (1).

Environmental fate

Degradation studies
Biodegradable (2).
97% removal in adapted activated sludge at 20°C (3).
Decomposition by soil microflora in >64 days (4).

Mammalian & avian toxicity

Acute data
LD_{50} intraperitoneal mouse 500 mg kg^{-1} (5).

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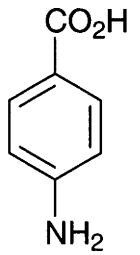
A117 4-aminobenzoic acid



$C_7H_7NO_2$ **Mol. Wt.** 137.14 **CAS Registry No.** 150-13-0

Synonyms *p*-aminobenzoic acid; PABA; AMBEN; paraminol; vitamin B_x; Chromotrichia factor

EINECS No. 205-753-0 **RTECS No.** DG 1400000

Uses Veterinary products. Manufacture of esters for local anaesthetics. Production of azo dyestuffs. Sunburn prevention treatments.

Physical properties

M. Pt. 187°C **Specific gravity** 1.474 at 20°C with respect to water at 4°C **Partition coefficient** log P_{ow} 0.68
Solubility Organic solvents: ethanol, ethyl acetate

Ecotoxicity

Invertebrate toxicity
EC_{50} (30 min) *Photobacterium phosphoreum* 27.4 mg l^{-1} Microtox test (1).

Environmental fate

Nitrification inhibition
At 100 mg l^{-1} no inhibition of NH_3 oxidation by *Nitrosomonas* sp. (2).

Anaerobic effects
Complete degradation was achieved at a concentration of 50 mg carbon l^{-1} of 4-aminobenzoic acid using anaerobic digesting sludge under methanogenic conditions (3).

Degradation studies
Biodegradable (4).
Decomposition by soil microflora in >8 days (2).
Adapted activated sludge removal 96% at 20°C (5).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 6000 mg kg^{-1} (6).
LD_{50} oral rabbit 1830 mg kg^{-1} (7).
LD_{50} oral mouse 2850 mg kg^{-1} (7).
LD_{50} intravenous rabbit 2000 mg kg^{-1} (7).

Sub-acute and sub-chronic data
Intramuscular rabbits (2 wk) 500 mg kg^{-1} day^{-1} showed 1-2 large nucleoli/oocyte nucleus with sizes 3-4-fold greater than those in controls. Increases corresponded to periods of accelerated oogenesis (8).

Carcinogenicity and chronic effects

No adequate evidence for carcinogenicity to humans, limited evidence of carcinogenicity in animals, IARC classification group 3 (9,10).

Exposure of 4-aminobenzoic acid to UV radiation and application to the backs of hairless light-pigmented mice prior to daily UV irradiation for 30 wk retarded the induction time of tumours and reduced the number of squamous cell carcinomas (11).

Metabolism and toxicokinetics

Percutaneous absorption and metabolism through hairless guinea pig skin was greater through nonviable skin. 4-Aminobenzoic acid was extensively *N*-acetylated during dermal absorption (12).

4-Aminobenzoic acid, a metabolite of procaine, appeared in the intestinal mucosa of rat ileum, duodenum and jejunum and increased with parent compound concentration (13).

When administered to humans orally, 4-aminobenzoic acid is absorbed from the gastrointestinal tract, metabolised in the liver and excreted in the urine as the unchanged drug and metabolites (14).

N-acetyl-4-aminobenzoic acid is found in human placental tissue perfused with 4-aminobenzoic acid (15).

Sensitisation

Contact and photocontact allergic dermatitis reported following the topical administration of aminobenzoate sunscreen agents (14). Subcutaneous, intraperitoneal, intravenous application to mice caused no toxicity with single or repeated doses. It did not stimulate immediate or delayed allergic responses after repeated administration of antigens in sensitised animals (16).

Aminobenzoate sunscreen agents should not be used by patients with previous experience of photosensitive or allergic reactions to chemically related drugs, such as sulfonamides, thiazide diuretics and certain local anaesthetics, particularly benzocaine (14).

Other comments

Human health effects and experimental toxicology reviewed (10,17).

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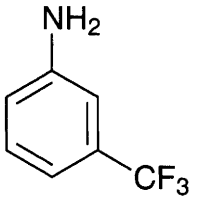
A118 3-aminobenzotrifluoride



$C_7H_6F_3N$ **Mol. Wt.** 161.13 **CAS Registry No.** 98-16-8

Synonyms benzenamine, 3-(trifluoromethyl)-; *m*-toluidine, α,α,α-trifluoro-; *m*-aminobenzal fluoride; 3-(trifluoromethyl)aniline

EINECS No. 202-643-4 **RTECS No.** XU 9180000

Physical properties

M. Pt. 5-6°C **B. Pt.** 187°C **Flash point** 85°C **Specific gravity** 1.290 **Volatility** v.den. 5.56

Occupational exposure

UN No. 2948 **HAZCHEM Code** 2X **Conveyance classification** toxic substance

Ecotoxicity

Invertebrate toxicity

EC_{50} (24 hr) *Daphnia magna* 6.6 mg l^{-1} (1).

EC_{50} (48 hr) *Daphnia magna* 2.7 mg l^{-1} (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse 220 mg kg^{-1} (2).

LC_{50} (4 hr) inhalation rat 440 mg m^{-3} (2).

LC_{50} (2 hr) inhalation mouse 690 mg m^{-3} (2).

Other comments

Reviews on human health effects, experimental toxicology, environmental effects, ecotoxicology, exposure levels listed (3).

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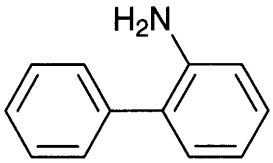
A119 2-aminobiphenyl



$C_{12}H_{11}N$ **Mol. Wt.** 169.23 **CAS Registry No.** 90-41-5

Synonyms 2-biphenylamine; *o*-aminobiphenyl; *o*-biphenylamine; *o*-phenylaniline; 2-phenylaniline; (1,1'-biphenyl)-2-amine

EINECS No. 201-990-9 **RTECS No.** DU 8850000

Uses Intermediate in organic synthesis of carbazoles, resins and synthetic rubbers.

Physical properties

M. Pt. 51-53°C **B. Pt.** 299°C **Flash point** >110°C **Partition coefficient** log P_{ow} 2.84 **Volatility** v.den. 5.8
Solubility Organic solvents: diethyl ether, ethanol

Ecotoxicity

Fish toxicity
Lethal concentration (4 hr) trout, bluegill sunfish and goldfish 5 ppm (1).

Invertebrate toxicity
EC_{50} (5-30 min) *Photobacterium phosphoreum* 6.74 mg l^{-1} Microtox test (2).

Mammalian & avian toxicity

Acute data
LD_{50} oral rabbit, rat 1020, 2340 mg kg^{-1}, respectively (3).

Carcinogenicity and chronic effects
♂ mouse 3000 ppm in feed day^{-1} equivocal evidence of carcinogenicity (4).
♀ mouse 3000 ppm feed day^{-1} positive carcinogenic effects, circulatory system haemangiosarcoma (4).

Metabolism and toxicokinetics
2-Aminobiphenyl is metabolised at *o*- and *p*-positions with respect to the amino group but does not form *N*-oxidation products *in vitro* (5).
Predominantly metabolised *in vivo* to 3- and 5-hydroxy-conjugated derivatives in mice, rats, hamsters and guinea pigs. In some species, 2-aminobiphenyl is also excreted as *N*-conjugated derivatives. During 24 hr, renal excretion accounts for ~30-40% of the administered dose. The 5-*o*-sulfate and 5-*o*-glucuronide of 2-amino-5-hydroxybiphenyl are major metabolites in all species, and 2-amino-3-hydroxybiphenyl-*o*-sulfate is formed to a lesser extent (6).

Genotoxicity

Salmonella typhimurium TA98, TA100 with metabolic activation negative (7).
Escherichia coli with metabolic activation phage inhibition capacity (7).

In vitro Chinese hamster ovary cells without metabolic activation chromosomal aberrations positive (8).
Drosophila melanogaster wing spot test negative (9).
Drosophila melanogaster eye mosaic test negative (10).

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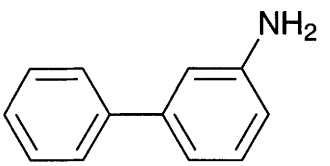
A120 3-aminobiphenyl



$C_{12}H_{11}N$ **Mol. Wt.** 169.23 **CAS Registry No.** 2243-47-2

Synonyms (1,1'-biphenyl)-3-amine; *m*-aminobiphenyl; *m*-phenylaniline; 3-phenylaniline; 3-biphenylamine

RTECS No. DU 8900000

Physical properties

M. Pt. 36°C **B. Pt.** 254°C
Solubility Organic solvents: acetone, benzene, diethyl ether, ethanol

Mammalian & avian toxicity

Metabolism and toxicokinetics
Metabolised by rat liver microsomal preparations to hydroxylamines and the nitro compounds of 3-nitrosobiphenyl and 3-nitrobiphenyl (1).

Genotoxicity

Salmonella typhimurium TA100 without metabolic activation weakly positive (2).
Salmonella typhimurium TA98 with and without metabolic activation positive (2).
In vitro F344 rat hepatocytes unscheduled DNA synthesis negative (3).

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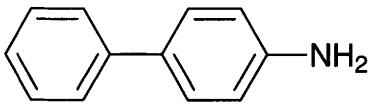
A121 4-aminobiphenyl



$C_{12}H_{11}N$ **Mol. Wt.** 169.23 **CAS Registry No.** 92-67-1

Synonyms 4-biphenylamine; *p*-biphenylamine; *p*-aminobiphenyl; *p*-aminodiphenyl; 4-aminodiphenyl; *p*-phenylaniline; (1,1'-biphenyl)-2-amine; biphenyl-4-amine; xenylamine

EINECS No. 202-177-1 **RTECS No.** DU 8925000

Uses In chemical analysis to detect sulfate ion. As a carcinogen in research. Formerly used as a rubber antioxidant.

Physical properties

M. Pt. 53°C **B. Pt.** 302°C **Flash point** > 110°C **Specific gravity** 1.16 at 20°C
Partition coefficient log P_{ow} 2.80
Solubility Organic solvents: chloroform, ethanol

Occupational exposure

FR-VME 0.001 ppm (0.007 mg m^{-3})
Supply classification toxic
Risk phrases May cause cancer – Harmful if swallowed (R45, R22)
Safety phrases Restricted to professional users – Avoid exposure – obtain special instruction before use – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S53, S45)

Ecotoxicity

Invertebrate toxicity
EC_{50} (5-30 min) *Photobacterium phosphoreum* 6.74 mg l^{-1} Microtox test (1).

Bioaccumulation
Using the estimated log P_{ow} of 2.80, bioconcentration factor is 79 (2).

Environmental fate

Degradation studies
In a static biodegradability test in which 2 mg l^{-1} of 4-aminobiphenyl was seeded with sludge, 50% degradation occurred after 7 days (3).

Abiotic removal
Sensitive to oxidation in air and darkens on standing (4).
Photochemical reaction with hydroxy radicals in the atmosphere, estimated $t_{1/2}$ 6.9 hr which suggests that hydrolysis will not be significant (5).

Adsorption and retention
Estimated soil adsorption coefficient of 417 indicates moderate adsorption to soil (2).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat, rabbit, mouse 205-690 mg kg^{-1} (6,7).
LD_{Lo} intraperitoneal mouse 250 mg kg^{-1} (8).

Carcinogenicity and chronic effects

Sufficient evidence for carcinogenicity in humans and animals, IARC classification group 1 (7).

Dose-related neoplasms angiosarcomas, bladder urothelial carcinomas and heptocellular neoplasms were found in ♂ and ♀ BALB/cStCr1fC3Hf/Nctr mice given up to 300 ppm in their drinking water (duration unspecified). Non neoplastic dose-related lesions were left atrical thrombosis, bladder urothelial hyperplasia, splenic haemosiderosis and spleneic erythropoeisis. The incidences of bladder carcinomas and atrial thrombosis were higher in the ♂s and the incidences of hepatocellular neoplasms and angiosarcomas were higher in the ♀ (8).

Intraperitoneal B6C3FI mouse administered maximum tolerated dose on days 1, 8, 15 and 22 after birth, killed after 9 or 12 months revealed multiple hepatocellular adenomas and carcinomas (9).

Teratogenicity and reproductive effects

Oral pregnant ICR mice (day-18 of gestation) killed 24 hr after treatment with 135 mg kg^{-1} 4-aminobiphenyl dissolved in trioactamin revealed binding of 4-aminobiphenyl to the DNA of maternal and foetal liver, lung, kidney, heart, brain, intestine, skin, maternal uterus and placenta. 4-Aminobiphenyl bound preferentially to DNA of maternal liver and kidney but showed no preference among foetal tissues (10).

Metabolism and toxicokinetics

A single intraperitoneal dose of 5 mg to rat, had a $t_{1/2}$ 15.6, 17 and 17 hr, respectively, for urinary, faecal and total elimination (11).

Catalysed in humans by cytochrome $P\text{-}450_{PA}$ and in rats by cytochrome $P\text{-}450_{ISF\text{-}G}$ (12).

Thin-layer chromatography of the 24-48 hr urine of rats dosed with 4-aminobiphenyl (route and concentration unspecified), metabolites included 4-acetylaminobiphenyl; 4'-hydroxy-4-aminobiphenyl; 2'-hydroxy-4-acetylaminobiphenyl; 4'-hydroxy-4-acetylaminobiphenyl; 3'-hydroxy-4'-methoxy-4-acetylaminobiphenyl; 4'-hydroxy-3'-methoxy-4-acetylaminobiphenyl; and 3',4'-dihydroxy-4-acetylaminophenyl (13).

The metabolic pathway appears to be via *N*-hydroxylation and *N*-glucuronide in the liver, *N*-glucuronides are transported to the bladder where hydrolysis to highly reactive electrophilic amyl nitrenium ions occurs (14).

Genotoxicity

Salmonella typhimurium TA98, TA100 with metabolic activation positive (15-17).

Escherichia coli PQ37 SOS chromotest with metabolic activation negative (18).

Escherichia coli K-12 *uvrB/recA* DNA repair host mediated assay negative (19).

In vitro Chinese hamster bone marrow positive induction of sister chromatid exchange (20).

In vitro ♂ B6C3FI mice bone marrow and peripheral blood micronuclei test positive (21,22).

In vitro primary rat hepatocytes weakly induced unscheduled DNA synthesis (23).

In vitro mouse lymphocytes induced chromosome aberrations (24). No significant heterogenicity in the survival of human epithelial cells from five donors after exposure to 4-aminobiphenyl. Cultures of normal fibroblasts from 41 donors showed an unexpected heterogenous response to the cytotoxic effects of 4-aminobiphenyl (25).

Drosophila melanogaster eye mosaic test negative (26).

Other effects

Other adverse effects (human)

Human peripheral lung tissue samples obtained from 17 workers of known occupational and smoking histories revealed 4-aminobiphenyl-DNA adducts detected by ELISA (27).

The potent tobacco carcinogen 4-aminobiphenyl can cross the human placenta and bind to foetal haemoglobin in concentrations that are significantly higher in smokers than in non-smokers (28).

Human pancreatic tissues were examined for their ability to metabolise 4-aminobiphenyl and other aromatic amines and carcinogens. The results were consistent with the hypothesis that aromatic amines and nitroaromatic hydrocarbons may be involved in the aetiology of human pancreatic cancer (29).

Any other adverse effects

In experimental animals convulsions, ataxia, dyspnoea, methaemoglobinemia, carbohaemoglobinemia have been reported (9,30).

Other comments

Found in tobacco smoke.
Reviews on human health effects, epidemiology, workplace experience, experimental toxicology, ecotoxicology, and physico-chemical properties listed (31).
Carcinogenic risk evaluated (14).

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A122 (4-aminobutyl)diethoxymethylsilane

$$H_3CSi(OCH_2CH_3)_2CH_2CH_2CH_2CH_2NH_2$$

$C_9H_{23}NO_2Si$ **Mol. Wt.** 205.37 **CAS Registry No.** 3037-72-7

Synonyms silane, (4-aminobutyl)diethoxymethyl-

EINECS No. 221-236-2 **RTECS No.** EO 4200000

Physical properties

B. Pt. 26°C at 113 mmHg **Specific gravity** 0.91 at 25°C (liquid)

Mammalian & avian toxicity

Acute data

LD_{Lo} oral rat 6500 mg kg^{-1} (1).

LD_{50} dermal rat, mouse, rabbit 45 mg kg^{-1} (2).

Irritancy

Dermal rabbit (24 hr) 10 mg caused mild irritation (1).

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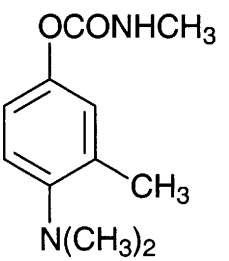
A123 aminocarb



$C_{11}H_{16}N_2O_2$ **Mol. Wt.** 208.26 **CAS Registry No.** 2032-59-9

Synonyms 4-dimethylamino-3-methylphenyl methylcarbamate; methylcarbamic acid, 4-dimethylamino-*m*-tolyl ester; 4-dimethylamino-3-cresyl methylcarbamate; Metacil

EINECS No. 217-990-7 **RTECS No.** FC 0175000

Uses Insecticide and molluscicide.

Physical properties

M. Pt. 93-94°C **Volatility** v.p. 1.3×10^{-5} mmHg at 20°C

Occupational exposure

Supply classification toxic

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

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

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) walleye 880 µg l^{-1} at 18°C (1).

LC_{50} (96 hr) bluegill sunfish, largemouth bass, yellow perch 3.1-6.4 mg l^{-1} in hard water 12-20°C (1).

LC_{50} (96 hr) Atlantic salmon, fathead minnow, channel catfish, rainbow trout, brown trout, brook trout 7.6-16 mg l^{-1} (1).

LC_{50} (96 hr) cutthroat trout 31 mg l^{-1} in hard water at 10°C (1).

Invertebrate toxicity

LC_{50} (96 hr) *Gammarus pseudolimnaeus* >50 μg l^{-1} (1).

EC_{50} (48 hr) *Daphnia magna*, *Chironomus* 10-270 μg l^{-1} (1).

LC_{50} (96 hr) *Gammarus lacustris* 12 μg l^{-1} (2).

Toxic to bees (3).

LD_{50} topical application to thorax *Apis mellifera* 0.121 μg bee^{-1}, *Andrena erythronii* 0.06 μg bee^{-1}, *Megachile rotundata* 0.068 μg bee^{-1}, *Bombus terricola* 3.07 μg bee^{-1} (4).

Bioaccumulation

Bioconcentration factor *Mytilus edulis* 3.8-4.9 (5).

Aminocarb and its metabolite, 4-methylamino-*m*-tolyl *N*-methylcarbamate were detected in the tissue of fingerling rainbow trout 96 hr after exposure to 21.3, 29.1 or 0.36 mg l^{-1} aminocarb, and >50% of the total residue was the parent compound. Bioaccumulation factor was 1.70-3.32. Both compounds were eliminated rapidly after transfer of the fish to clean water (6).

Environmental fate

Degradation studies

Chlamydomonas variabilis and *Selenastrum capricornutum* degraded 50% and 100% aminocarb, within 6 and 14 days of incubation, respectively (7).

Abiotic removal

An initial concentration of 0.01 mg l^{-1} in river water was completely degraded in sunlight and artificial fluorescent light in 4 wk (8).

Mammalian & avian toxicity

Acute data

LD_{50} oral redwing blackbird, starling 50 mg kg^{-1} (9).

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

LD_{50} dermal rat 275 mg kg^{-1} (10).

LD_{50} intraperitoneal rat, mouse 7, 21 mg kg^{-1}, respectively (11,12).

Sub-acute and sub-chronic data

Gavage mice (exposure unspecified) sublethal doses and bone marrow was assessed by marrow transplantation to normal mice. Exposure of 0.08-5.0 mg kg^{-1} to donor animals did not affect regenerating bone marrow in the recipient mice. At 0.08 and 0.32 mg kg^{-1} a marked shift in surface IgM density on marrow B cells was noted (3).

Carcinogenicity and chronic effects

Rat 2-yr feeding study 200 mg kg^{-1} in the diet suffered no ill-effects (13).

Metabolism and toxicokinetics

Metabolised in liver to 4-amino-3-cresyl methylcarbamate, 4-methylamino-3-cresyl methylcarbamate, and 4-dimethylamino-3-cresyl *N*-hydroxymethylcarbamate (14).

Aminocarb was hydrolysed to 4-(dimethylamino)-3-methylphenol which in turn was converted into 2-methyl-1,4-benzoquinone by a direct means or via 2-methyl-1,4-dihydroquinone (species unspecified) (15).

In rhesus monkeys, 74% of aminocarb ($t_{1/2}$ 25 hr) was absorbed from the forehead whereas 37% ($t_{1/2}$ 31 hr) was absorbed from ventral forearm. In rats, 88% of aminocarb ($t_{1/2}$ 17 hr) was absorbed from the mid-dorsal region (16).

Genotoxicity

Topical administration to mouse of aminocarb over 24 hr induced a dose-dependent increase in the frequency of hair follicle nuclear aberrations (17).

Other effects

Other adverse effects (human)

Carbamate insecticide which acts as a cholinesterase inhibitor. Symptomatic effects may include respiratory discomfort, nausea, vomiting, diarrhoea, headache, blurred vision, salivation, sweating and confusion. Central nervous system effects include ataxia, slurred speech and paralysis. Severe exposure may result in hypotension, pulmonary oedema, convulsions, coma and death from respiratory failure or cardiac arrest (18,19).

Legislation

Included in Schedule 6 (Release into Land: Prescribed Substances) of Statutory Instrument No. 472, 1991 (20). Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides and related products: maximum admissible concentration 0.1 $\mu g\ l^{-1}$ (21).

Other comments

Probable human lethal dose is 5-50 $mg\ kg^{-1}$ (18).

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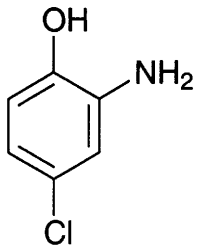
A124 2-amino-4-chlorophenol



C_6H_6ClNO **Mol. Wt.** 143.57 **CAS Registry No.** 95-85-2

Synonyms *p*-chloro-*o*-aminophenol; C.I. Oxidation base 18; C.I. 76525

EINECS No. 202-458-9 **RTECS No.** SJ 5700000

Uses Dyestuff intermediate.

Physical properties

M. Pt. 139°C

Occupational exposure

UN No. 2673 **HAZCHEM Code** 2X **Conveyance classification** toxic substance

Environmental fate

Degradation studies

Degraded aerobically by *Alcaligenes* TK-2 (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, mouse 690, 1030 mg kg^{-1} respectively (2).

Genotoxicity

Salmonella typhimurium TA1535 with metabolic activation, weakly positive, negative results reported in other strains (3).

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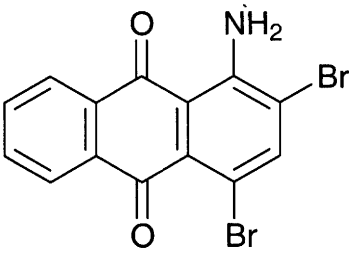
A125 1-amino-2,4-dibromoanthraquinone



$C_{14}H_7Br_2NO_2$ **Mol. Wt.** 381.02 **CAS Registry No.** 81-49-2

Synonyms 2,4-dibromo-1-anthraquinololylamine; 1-amino-2,4-dibromo-9,10-anthracenedione

EINECS No. 201-354-0

Uses Dyestuff synthesis.

Physical properties

M. Pt. 226-227°C

Mammalian & avian toxicity

Carcinogenicity and chronic effects

Retrospective characterisation of morphological and stereological features of altered hepatocellular foci in haematoxylin and eosin stained sections was performed in 2-yr carcinogenicity studies in Fischer 344 rats. There was clear evidence of hepatocarcinogenicity (1).

National Toxicology Program tested mice and rats via dosed-feed. Clear evidence for carcinogenicity in ♂ and ♀ rats and mice (2).

Irritancy

500 mg instilled into rabbit eye (24 hr) caused mild irritation (3).

Genotoxicity

Salmonella typhimurium TA1537 with and without metabolic activation positive (4).

In vitro Chinese hamster ovary cells with and without metabolic activation sister chromatid exchange positive, with metabolic activation chromosomal aberrations negative (5).

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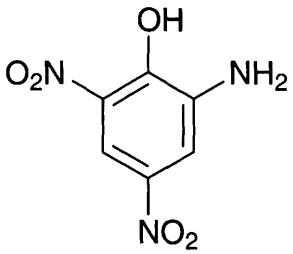
A126 2-amino-4,6-dinitrophenol



$C_6H_5N_3O_5$ **Mol. Wt.** 199.12 **CAS Registry No.** 96-91-3

Synonyms picramic acid; dinitroaminophenol; 4,6-dinitro-2-aminophenol

EINECS No. 202-544-6 **RTECS No.** SJ 5800000

Uses Manufacture of azo dyestuffs. Reagent for albumin. Rarely used as indicator.

Physical properties

M. Pt. 168°C **Flash point** 210°C

Solubility Water: 0.65 g l^{-1} at 22-25°C. Organic solvents: acetic acid, aniline, benzene, ethanol

Occupational exposure

Supply classification explosive, harmful

Risk phrases Explosive when dry – Harmful by inhalation, in contact with skin and if swallowed – Harmful to aquatic organisms, may cause long-term adverse effects in the aquatic environment (R1, R20/21/22, R52/53)

Safety phrases Keep out of reach of children (if sold to general public) – This material and its container must be disposed of in a safe way (S2, S35)

Ecotoxicity

Fish toxicity

No inhibition in growth of rainbow trout exposed to 0.02 mg l^{-1} but petechial haemorrhages along abdomen wall developed with over 80% having lesions in 42 days (1).

LC_{50} (96 hr) rainbow trout 46.2 mg l^{-1} (2).

Invertebrate toxicity

American oysters exposed to 0.02 mg l^{-1} for 42 days showed significant inhibition of shell deposit. Also discoloration of nacre layers and body mass (1).

LC_{50} (14 hr) American oyster 70 mg l^{-1} (2).

Bioaccumulation

Rainbow trout exposed for 42 days to 2-amino-4,6-dinitrophenol showed no bioconcentration in epaxial muscle tissues. American oyster bioconcentration factor after 42-day exposure to 0.02 mg l^{-1} was 49.3 (3).

$t_{1/2}$ for elimination in trout, measured, 9-9.5 days (4).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA1535 with and without metabolic activation positive (5).

Other comments

Toxicity is reported similar to 2,4-dinitrophenol, for which LD_{50} oral rat is 30 mg kg^{-1}, and which is readily

absorbed through the intact skin causing rise in metabolic rate and temperature, even collapse and death. It may cause dermatitis, cataracts and weight loss (3).
Comments on drinking water guidelines have been published (6).
Reviews on physico-chemical properties, human health effects and experimental toxicology listed (7).

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A127 2-(2-aminoethoxy)ethanol

$$NH_2CH_2CH_2OCH_2CH_2OH$$

$C_4H_{11}NO_2$ **Mol. Wt.** 105.14 **CAS Registry No.** 929-06-6

Synonyms diethyleneglycolamine; diethylene glycol; diglycol

EINECS No. 213-195-4 **RTECS No.** KJ 6125000

Uses Rust-proofing steels. Gas sweetening. Gas purification (especially removal of COS). In zeolite preparation.

Physical properties

B. Pt. 218-224°C **Specific gravity** 1.048 at 25°C with respect to water at 4°C

Occupational exposure

UN No. 3055 **HAZCHEM Code** 2X **Conveyance classification** corrosive substance

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 5660 mg kg^{-1} (1).
LD_{50} dermal rabbit 1190 mg kg^{-1} (1).

Irritancy

Dermal rabbit (24 hr) 10 mg caused severe irritation, and 250 µg instilled into rabbit eye caused severe irritation (1).

Other comments

N-nitrosodiethanolamine and *N*-nitrosomorpholine have been found in cutting oils containing 2-(2-aminoethoxy)ethanol after the fluid has been heated to 100°C for 48 hr (2).

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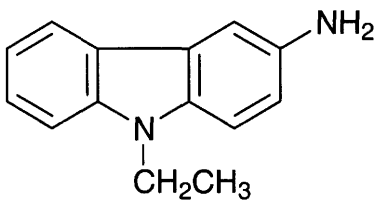
A128 3-amino-9-ethylcarbazole



$C_{14}H_{14}N_2$ **Mol. Wt.** 210.28 **CAS Registry No.** 132-32-1

Synonyms 3-amino-*N*-ethylcarbazole; 9-ethyl-9*H*-carbazol-3-amine

EINECS No. 205-057-7 **RTECS No.** FE 3590000

Uses Pigment synthesis. Colorimetric enzyme assay, peroxidase enzyme activity assay.

Physical properties

M. Pt. 98-100°C

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 144 mg kg^{-1} (1).

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

Carcinogenicity and chronic effects

Target organs of carcinogenicity: rat ear/Zymbal gland, mouse and rat liver, rat skin (3).

Other comments

Reviews on human health and environmental effects, epidemiology, workplace experience and experimental toxicology listed (4).

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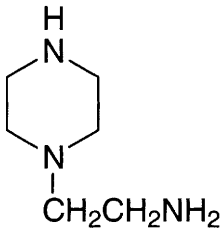
A129 *N*-aminoethylpiperazine



$C_6H_{15}N_3$ **Mol. Wt.** 129.21 **CAS Registry No.** 140-31-8

Synonyms *N*-(β-aminoethyl)piperazine

EINECS No. 205-411-0 **RTECS No.** TK 8050000

Uses Epoxy curing agent.

Physical properties

M. Pt. –19°C **B. Pt.** 220°C **Flash point** 93°C (open cup) **Specific gravity** 0.98 at 20°C with respect to water at 20°C **Volatility** v.den. 4.4

Occupational exposure

UN No. 2815 **HAZCHEM Code** 2X **Conveyance classification** corrosive substance

Supply classification corrosive

Risk phrases Harmful in contact with skin and if swallowed – Causes burns – May cause sensitisation by skin contact – Harmful to aquatic organisms, may cause long-term adverse effects in the aquatic environment (R21/22, R34, R43, R52/53)

Safety phrases Keep locked up and out of the reach of children (if sold to general public) – In case of contact with eyes, rinse immediately with plenty of water and seek medical advice – Wear suitable protective clothing, gloves and eye/face protection – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) – Avoid release to the environment. Refer to special instructions/safety data sheet (S1/2, S26, S36/37/39, S45, S61)

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 2140 mg kg^{-1} (1).

LD_{50} dermal rabbit 880 mg kg^{-1} (2).

LD_{50} intraperitoneal mouse 250 mg kg^{-1} (3).

Irritancy

100 mg instilled into rabbit eye caused moderate irritation (duration unspecified) (4).

Genotoxicity

Salmonella typhimurium TA98, TA100 with and without metabolic activation negative (5).

Other comments

Evaluation of morpholine piperazine and analogues in the mouse lymphoma L-5178Y and BALB-3T3 transformation assays have been carried out. Results available as conference proceedings (6).

References

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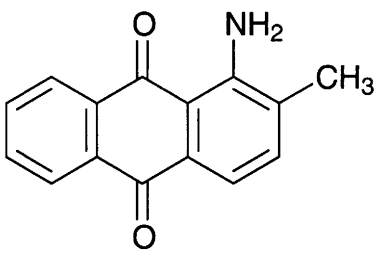
A130 1-amino-2-methylanthraquinone



$C_{15}H_{11}NO_2$ **Mol. Wt.** 237.26 **CAS Registry No.** 82-28-0

Synonyms Acetate Fast Orange R; Acetoquinone Light Orange JL; 1-amino-2-methyl-9,10-anthracenedione; Artisil Orange 3RP; Celliton Orange R; Disperse Orange II; C.I. 60700; 2-methyl-1-anthraquinonylamine

EINECS No. 201-408-3 **RTECS No.** CB 5740000

Uses Synthetic dye and dye intermediate.

Physical properties

M. Pt. 204-206°C

Solubility Water: <1 mg ml^{-1} at 20°C. Organic solvents: acetone, benzene, DMSO, ethanol, ethylene glycol monoethyl ether, linseed oil

Mammalian & avian toxicity

Acute data

LD_{50} oral redwinged blackbird 40 mg kg^{-1} (1).

Sub-acute and sub-chronic data

In a 7-week feeding study with up to 4% 1-amino-2-methylanthraquinone in the diet, all rats fed 1.5% or more, all ♀ fed 0.5% or more and all ♂ mice fed 0.24% or more in the diet died. Reductions in weight gain of 5-25% were recorded in rats and mice receiving 0.24% and 0.12% in the diet, respectively. Lesions observed in rats fed 0.24% in the diet and mice fed 0.06% included enlarged kidneys and lymph nodes as well as discoloration of kidneys and adrenals (2).

In a chronic feeding study in rats with 0.24% (time-weighted average concentration) 1-amino-2-methylanthraquinone in the diet, lesions observed included inflammatory changes in the lungs, spleen, myocardium, bile duct, pancreas and kidneys. Similar lesions were reported in mice fed 0.06% (time-weighted average concentration), although to a lesser extent (2).

Carcinogenicity and chronic effects

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

National Toxicology Program tested rats and mice via dosed-feed. Positive evidence for carcinogenicity in ♂ and ♀ rats and ♀ mice. Negative evidence for carcinogenicity in ♂ mice (4).
Target organs of carcinogenicity: rat kidney/ureter, mouse and rat livers (5).
TD_{Lo} oral rat (78 weeks continuous administration) 30 g kg^{-1}. Evidence of carcinogenicity (6).
TD_{Lo} oral mouse (73 weeks continuous administration) 37 g kg^{-1}. Evidence of carcinogenicity (6).
TD oral rat (77 weeks continuous administration) 39 g kg^{-1}. Neoplastic effects (7).
TD oral mouse (73 weeks continuous administration) 307 g kg^{-1}. Equivocal tumorigenic agent (8).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535 and TA97/TA1537 with and without metabolic activation positive (9).
L5178Y/tk$^{+/-}$–3.72C mouse lymphoma cell assay positive (10).

Other comments

A review on 1-amino-2-methylanthraquinone appears in the IARC Monograph Volume 27, 1982, (8).

References

1. Schafer, E. W. et al *Arch. Environ. Contam. Toxicol.* 1983, **12**, 355-382.
2. *National Cancer Institute, Tech. Rep. Ser. No. 111, DHEW Publ. No. (NIH) 78-1366*, Washington DC, US Government Printing Office, 1978.
3. *IARC Monograph* 1987, **Suppl. 7**, 57.
4. *National Toxicology Program Research and Testing Division* 1995, Report No. TR-111 NIEHS, Research Triangle Park, NC 27709, USA.
5. Gold, L. S. et al *Mutat. Res.* 1993, **286**, 75-100.
6. *National Cancer Institute Carcinogenesis Technical Report Series* NCI-CG-TR-III, 78.
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8. *IARC Monograph* 1982, **27**, 199-204.
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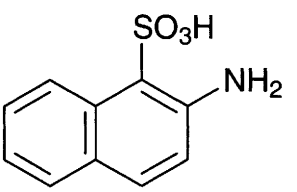
10. Harrington-Brock, K. et al *Mutagenesis* 1991, **6**(1), 35-46

A131 2-aminonaphthalene-1-sulfonic acid



$C_{10}H_9NO_3S$ **Mol. Wt.** 223.25 **CAS Registry No.** 81-16-3

Synonyms 2-amino-1-naphthalenesulfonic acid; 2-naphthylamine-1-sulfonic acid

EINECS No. 201-331-5 **RTECS No.** QK 1250000

Uses Dyestuff intermediate.

Physical properties

M. Pt. 180°C (diethylammonium salt)
Solubility Organic solvents: diethyl ether, ethanol

Environmental fate

Degradation studies

Pseudomonas sp. TA-2 degraded 2-aminonaphthalene-1-sulfonic acid to produce intermediate metabolites 1-naphthalenesulfonate and 2-naphthol-1-sulfonate, and the release of ammonia, sulfate and sulfite. It is suggested that degradation occurs as a result of 1,2-dioxygenation in the initial process (1).
In an aqueous screening test, 95-97% loss was observed in 108-118 days at a concentration of 1 mg l^{-1} (2).

Abiotic removal

Reported as generally resistant to hydrolysis (3).
Atmospheric $t_{1/2}$ 2 hr based on photochemically produced hydroxyl radicals (4).

Adsorption and retention

High mobility of 2-aminonaphthalene-1-sulfonic acid in soil is suggested (5).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 19.4 g kg^{-1} (6).

Carcinogenicity and chronic effects

Oral BALB/c mice (66 wk) 2500, 5000 and 10,000 ppm in diet. The animals were kept under observation until 140 wk of age when the experiment was terminated. No tumour type at any site was related to treatment (7).

Metabolism and toxicokinetics

Intravenous and oral administration of 1 mg kg^{-1} to rats resulted in almost exclusive urine elimination and equal elimination in urine and faeces, respectively. There was significant absorption from the gastrointestinal tract (8).

Irritancy

500 mg instilled into rabbit eye for 24 hr caused mild irritation (6).

Genotoxicity

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

Other effects

Other adverse effects (human)

The lymphocytotoxicity of workers exposed to 2-aminonaphthalene-1-sulfonic acid was investigated. Workers using this acid have lymphocytes with a normal range of reactivity towards bladder cancer cells, which is in keeping with the suggestion that the compound is non-carcinogenic (10).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Polycyclic aromatic hydrocarbons: maximum admissible concentration 0.2 µg l^{-1} (11).

Other comments

Reviews on human health effects, experimental toxicology, environmental effects, ecotoxicology and exposure levels listed (12).

References

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2. Bosch, F. M. et al *Doc. Eur. Sewage Refuse Symp. Eas. 4th* 1978, 272-286.
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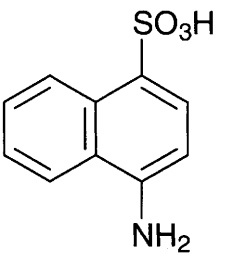
11. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
12. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

A132 4-aminonaphthalene-1-sulfonic acid



$C_{10}H_9NO_3S$ **Mol. Wt.** 223.25 **CAS Registry No.** 84-86-6

Synonyms 1-aminonaphthalene-4-sulfonic acid; 1-naphthylamine-4-sulfonic acid; Piria's acid; 1-amino-4-sulfonaphthalene; 1,4-naphthionic acid; USAF M-5

EINECS No. 201-567-9 **RTECS No.** QK 1270000

Uses The sodium salt is an important dyestuff intermediate in the manufacture of Congo red, Fast Red A, azo rubine and similar azo dyestuffs.

Physical properties

M. Pt. Decomposes on heating without melting **Specific gravity** 1.673 at 25°C with respect to water at 4°C
Solubility Water: 0.31 g l^{-1} at 20°C

Environmental fate

Degradation studies
Non-biodegradable (1).

Mammalian & avian toxicity

Acute data
LD_{50} intraperitoneal mouse 300 mg kg^{-1} (2).

Carcinogenicity and chronic effects
Tested in inbred A/St ♂ and ♀ mice by the pulmonary adenoma bioassay. No tumorigenic activity observed (3).

Metabolism and toxicokinetics
Identified as a metabolite in the faeces of rat, mouse and guinea pig following administration of carmoisine, amaranth and Brown HT (4).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Polycyclic aromatic hydrocarbons: maximum admissible concentration 0.2 μg l^{-1} (5).

Other comments

The sodium salt is an haemostatic agent (6).

References

1. *MITI Report* 1984, Ministry of International Trade and Industry, Tokyo, Japan.
2. *NTIS Report* AD 277-689, National Technical Information Service, Springfield, VA, USA.
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4. Phillips, J. C. et al *Food Chem. Toxicol.* 1987, **25**(12), 927-925, 947-954, 1013-1019.
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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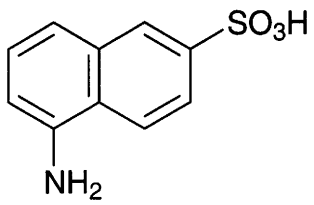
A133 5-aminonaphthalene-2-sulfonic acid



$C_{10}H_9NO_3S$ **Mol. Wt.** 223.25 **CAS Registry No.** 119-79-9

Synonyms 5-amino-2-naphthalenesulfonic acid; 1-naphthylamine-6-sulfonic acid; 1,6-Cleve's acid

EINECS No. 204-351-2 **RTECS No.** QK 1285000

Uses Dyestuff intermediate.

Physical properties

M. Pt. 180-190°C

Solubility Water: 1 g l^{-1}

Environmental fate

Degradation studies

Pseudomonas sp. BN6 degraded 5-amino-2-naphthalenesulfonic acid (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 14.2 g kg^{-1} (2).

Irritancy

500 mg instilled in rabbit eye for 24 hr caused mild irritant effects (2).

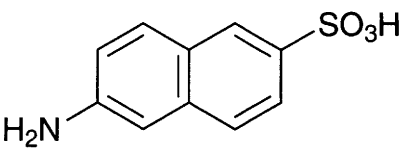
Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Polycyclic aromatic hydrocarbons: maximum admissible concentration 0.2 μg l^{-1} (3).

References

1. Noertemann, B. et al *Appl. Environ. Microbiol.* 1986, **52**(5), 1195-1202.
2. Le, J. et al *Food. Chem. Toxicol.* 1985, **23**, 695.
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

A134 6-aminonaphthalene-2-sulfonic acid



$C_{10}H_9NO_3S$ **Mol. Wt.** 223.25 **CAS Registry No.** 93-00-5

Synonyms 6-amino-2-naphthalenesulfonic acid; 2-naphthylamine-6-sulfonic acid; Broenners acid

EINECS No. 202-208-9

Uses Manufacture of azo dyestuffs, e.g. CI Direct Red 4.

Environmental fate

Degradation studies

The degradation of 6-aminonaphthalene-2-sulfonic acid is inhibited by simultaneous oxidation of α-aminonaphthalene-2-sulfonic acid which in submerged cultures leads to accumulation of inhibiting fermentation products (1).

Degradation by a mixed bacterial community in river water induced the action by *Pseudomonas* BN6 converting 6-aminonaphthalene-2-sulfonic acid into 5-aminosalicylate (2).

A mixed bacterial culture consisting of 11 different strains belonging to three genera, *Flavobacterium, Bacillus* and *Pseudomonas*, was able to degrade 6-aminonaphthalene-2-sulfonic acid although none of the single strains could degrade the compound (3).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Polycyclic aromatic hydrocarbons: maximum admissible concentration 0.2 μg l^{-1} (4).

References

1. Hattendorf, C. et al *DECHEMA Biotechnol. Conf. 7 1990*, **4**(4), 581-584.
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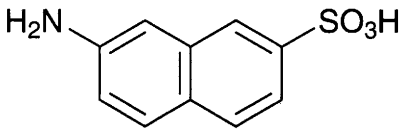
A135 7-aminonaphthalene-2-sulfonic acid



$C_{10}H_9NO_3S$ **Mol. Wt.** 223.25 **CAS Registry No.** 494-44-0

Synonyms 7-amino-2-naphthalenesulfonic acid; 2-naphthylamine-7-sulfonic acid; β-naphthylamine-8-sulfonic acid; Cassella's acid F; Bayer's acid; Amido-F acid

EINECS No. 207-789-2

Uses Manufacture of azo dyestuffs.

Physical properties

Solubility Water: 0.3 g in 100 g at 100°C

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Polycyclic aromatic hydrocarbons: maximum admissible concentration 0.2 μg l^{-1} (1).

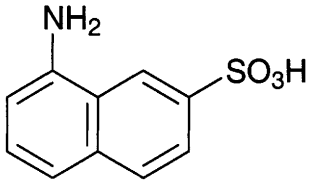
Other comments

There is evidence of low chronic toxicity and low carcinogenic potential in these sulfonated derivatives (2).

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. Anliker, R. in *Toxic Hazard Assessment of Chemicals*, M. L. Richardson (Ed.), 1986, The Royal Society of Chemistry, London, UK

A136 8-aminonaphthalene-2-sulfonic acid



$C_{10}H_9NO_3S$ **Mol. Wt.** 223.25 **CAS Registry No.** 119-28-8

Synonyms 8-amino-2-naphthalenesulfonic acid; 1-naphthylamine-7-sulfonic acid; 1,7-Cleve's acid

EINECS No. 204-311-4

Uses Manufacture of azo dyestuffs, e.g. CI Direct Green 51.

Physical properties

M. Pt. >300°C
Solubility Water: 0.45 g in 100 g. Organic solvents: ethanol

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Polycyclic aromatic hydrocarbons: maximum admissible concentration 0.2 μg l^{-1} (1).

Other comments

The sulfonated aromatic amines of this family appear to have low chronic toxicity and low carcinogenic potential (2).

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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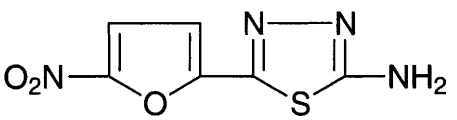
A137 2-amino-5-(5-nitro-2-furyl)-1,3,4-thiadiazole



$C_6H_4N_4O_3S$ **Mol. Wt.** 212.19 **CAS Registry No.** 712-68-5

Synonyms 2-(5-nitro-2-furyl)-5-amino-1,3,4-thiadiazole; 5-amino-2-(5-nitro-2-furyl)-1,3,4-thiadiazole; 5-(5-nitro-2-furanyl)-1,3,4-thiadiazol-2-amine; 5-(5-nitro-2-furyl)-2-amino-1,3,4-thiadiazole; furidiazine; Triafur

EINECS No. 211-925-6 **RTECS No.** XI 3600000

Uses Used as antimicrobial agent in human and veterinary medicine, as a conservation chemical, and as an ingredient in cosmetic preparations and synthetic textile materials.

Physical properties

M. Pt. 280°C
Solubility Organic solvents: acetic acid, dimethylformamide

Mammalian & avian toxicity

Sub-acute and sub-chronic data

TD_{Lo} (46 wk intermittent) oral rat 6 g kg^{-1} (1).
TD_{Lo} (32 wk continuously) oral rat 2240 mg kg^{-1} (2).

Carcinogenicity and chronic effects

No adequate evidence for carcinogenicity to humans, sufficient evidence for carcinogenicity to animals, IARC classification 2B (3).
Sprague-Dawley ♀ rats administered 4 g over 75 wk via feed showed tumours of mammary glands, fibroadenomas and adenocarcinomas; tumours of forestomach, lung and kidney were also observed. Initial dose levels were reduced due to growth retardation (4).

Genotoxicity

Salmonella typhimurium TA100 with and without metabolic activation positive (5).
Escherichia coli WP2, WP2*uvrA* with and without metabolic activation negative (5).
DNA repair test positive (5).

Other comments

Toxic to *Salmonella* and *Shigella* spp., *Escherichia coli* and *Staphylococcus aureus* (6).
Human health effects and experimental toxicology reviewed (7,8).

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1. Cohen, S. M. et al *J. Natl. Cancer Inst.* 1975, **54**(4), 841-850.
2. Erturk, E. et al *Fed. Proc.* 1970, **29**, 817.
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6. Skagius, K. *Antibiot. Chemotherapy* 1961, **10**, 37-45.
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.
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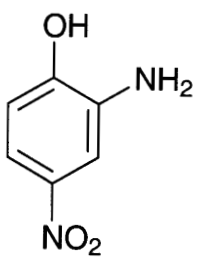
A138 2-amino-4-nitrophenol



$C_6H_6N_2O_3$ **Mol. Wt.** 154.13 **CAS Registry No.** 99-57-0

Synonyms 3-amino-4-hydroxynitrobenzene; *p*-nitro-*o*-aminophenol; 2-hydroxy-5-nitroaniline

EINECS No. 202-767-9 **RTECS No.** SJ 6300000

Uses In dyestuff synthesis. Organic synthesis intermediate.

Physical properties

M. Pt. 143-145°C (anhydrous); 80-90°C (hydrated) **Partition coefficient** log P_{ow} 1.13 (1)
Solubility Organic solvents: acetic acid, hot benzene, diethyl ether, ethanol, methanol

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 1030 mg kg^{-1} (2).
LD_{50} oral rat 2400 mg kg^{-1} (1).
LD_{50} intraperitoneal mouse, rat 143, 246 mg kg^{-1}, respectively (1,3).

Sub-acute and sub-chronic data

Gavage (15 days) rats, mice 0, 313, 625, 1250, 2500 or 5000 mg kg^{-1} in corn oil. Reduced survival was seen in animals receiving the two highest doses, and all animals except those receiving 313 mg kg^{-1} suffered from diarrhoea (1).

Carcinogenicity and chronic effects

Inadequate evidence for carcinogenicity to humans, limited evidence for carcinogenicity to animals, IARC classification group 3 (1).

The National Toxicology Program tested mice and rats via gavage. Some evidence of carcinogenicity in ♂ rats, no evidence of carcinogenicity in ♀ rats and ♂ and ♀ mice (4).

Target organ of carcinogenicity: rat kidney/ureter (5).

Metabolism and toxicokinetics

Within 3 hr of oral administration of 2 ml ^{14}C-2-amino-4-nitrophenol (0.2% in saline) 4% of the radioactivity was excreted in the bile. Five days later ~68.3% of the radioactivity had been excreted in the urine and ~25.4% in the faeces. Following subcutaneous administration, 89% of the dose was eliminated after one day (1).

Irritancy

100 mg instilled into rabbit eye caused moderate irritation in 24 hr (2).

Genotoxicity

Salmonella typhimurium TA98, TA100 with metabolic activation positive (6).

Bacteriophage T4D 22.7 μg ml^{-1} induced rapid lysis mutants (7).

In vitro Chinese hamster ovary cells with and without metabolic activation chromosomal aberrations and sister chromatid exchange positive (8).

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

Legislation

Human health effects and experimental toxicology reviewed (1).

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1. *IARC Monograph* 1993, **57**, 167-176.
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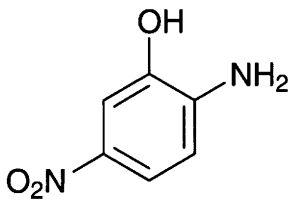
A139 2-amino-5-nitrophenol



$C_6H_6N_2O_3$ **Mol. Wt.** 154.13 **CAS Registry No.** 121-88-0

Synonyms 2-hydroxy-4-nitroaniline; 4-amino-3-hydroxynitrobenzene; 5-nitro-2-aminophenol

EINECS No. 204-503-8 **RTECS No.** SJ 6302500

Uses Organic synthesis intermediate. Ingredient in hair dyes.

Physical properties

M. Pt. 207-208°C

Solubility Organic solvents: benzene, diethyl ether, ethanol

Mammalian & avian toxicity

Acute data

LD_{50} oral rat >4000 mg kg^{-1} (1).

LD_{50} intraperitoneal rat >800 mg kg^{-1} (1).

Sub-acute and sub-chronic data

Gavage (16 days) mice 0, 156, 313, 625, 1250, 2500, 5000 mg kg^{-1} in corn oil. A dose-related reduction in survival was seen in ♀ mice (1).

Carcinogenicity and chronic effects

Inadequate evidence for carcinogenicity to humans, limited evidence for carcinogenicity to animals, IARC classification group 3 (1).

The National Toxicology Program tested rats and mice via gavage. Some evidence of carcinogenicity was seen in ♂ rats, no evidence of carcinogenicity was seen in ♀ rats and ♂ and ♀ mice (2).

Target organ of carcinogenicity: rat pancreas (3).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1537 with and without metabolic activation positive (4).

In vitro L5178Y mouse lymphoma cells without metabolic activation positive (5).

Other comments

Non-toxic to rabbits by percutaneous administration of hair dyes containing 2-amino-5-nitrophenol (6).

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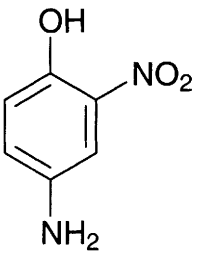
A140 4-amino-2-nitrophenol



$C_6H_6N_2O_3$ **Mol. Wt.** 154.13 **CAS Registry No.** 119-34-6

Synonyms 4-hydroxy-3-nitroaniline; *o*-nitro-*p*-aminophenol; 2-nitro-4-aminophenol; Oxidation base 25

EINECS No. 204-316-1 **RTECS No.** SJ 6303000

Physical properties

M. Pt. 131°C

Solubility Organic solvents: acetone, diethyl ether, ethanol

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) fathead minnow 34 mg l^{-1} (1).

Invertebrate toxicity

ED_{50} (5-30 min) *Photobacterium phosphoreum* 38.7 mg l^{-1} Microtox test (2).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, mouse 1470 mg kg^{-1} (3).

LD_{50} intraperitoneal rat 302 mg kg^{-1} (4).

Carcinogenicity and chronic effects

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

The National Toxicology Program tested rats and mice via dosed-feed. Positive evidence of carcinogenicity in ♂ rats, equivocal evidence in ♀ rats and negative evidence in ♂ and ♀ mice (6).

Target organ of carcinogenicity: rat urinary bladder/urethra (7).

Irritancy

100 mg instilled into rabbit eye caused severe irritation in 24 hr (8).

Genotoxicity

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

Salmonella typhimurium TA98, TA100, TA1535, TA1537, TA1538 with or without metabolic activation negative (10).

Other comments

Human health effects, epidemiology, workplace experience and experimental toxicology reviewed (11,12).

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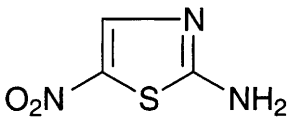
A141 2-amino-5-nitrothiazole



$C_3H_3N_3O_2S$ **Mol. Wt.** 145.15 **CAS Registry No.** 121-66-4

Synonyms aminonitrothiazole; aminonitrothiazolium; 5-nitro-2-aminothiazole; 5-nitro-2-thiazolylamine; Enheptin

EINECS No. 204-490-9 **RTECS No.** XJ 2800000

Uses Antiprotozoal agent.

Physical properties

M. Pt. 202°C (decomp.)
Solubility Organic solvents: diethyl ether, ethanol

Mammalian & avian toxicity

Acute data

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

Carcinogenicity and chronic effects

No adequate evidence for carcinogenicity to humans, limited evidence for carcinogenicity to animals, IARC classification group 3 (2).

The National Toxicology Program tested rats and mice via dosed-feed. Positive evidence of carcinogenicity in ♂ rats, negative evidence in ♀ rats and ♂ and ♀ mice (3).

Target organs of carcinogenicity: rat kidney/ureter, rat lung and rat mammary gland (4).

Teratogenicity and reproductive effects

TD_{Lo} (10 day) oral ♂ rat 600 mg kg^{-1} caused temporary sterility and decreased prostate weight (5).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537, TA1538 with and without metabolic activation positive (6).
Escherichia coli PQ37 SOS chromotest without metabolic activation positive (7).
Mouse lymphoma L5178Y tk+/tk– without metabolic activation positive (8).

Other comments

Experimental toxicology and human health effects reviewed (9).

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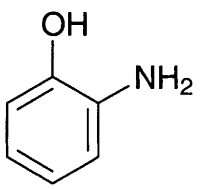
A142 2-aminophenol



C_6H_7NO **Mol. Wt.** 109.13 **CAS Registry No.** 95-55-6

Synonyms 2-amino-1-hydroxybenzene; 2-hydroxyaniline; *o*-aminophenol

EINECS No. 202-431-1 **RTECS No.** SJ 4950000

Uses Manufacture of azo- and sulfur-dyestuffs. Used in the dyeing of fur and hair.

Physical properties

M. Pt. 170-174°C **B. Pt.** sublimes at 153°C at 11 mmHg **Partition coefficient** log P_{ow} 0.52-0.62
Solubility Water: 17 g l^{-1} at 0°C. Organic solvents: diethyl ether, ethanol

Occupational exposure

UN No. 2512 **HAZCHEM Code** 2X **Conveyance classification** toxic substance
Supply classification harmful
Risk phrases Harmful by inhalation and if swallowed – Possible risk of irreversible effects (R20/22, R40)
Safety phrases Keep out of reach of children (if sold to general public) – After contact with skin, wash immediately with plenty of water – Wear suitable protective clothing and gloves (S2, S28, S36/37)

Ecotoxicity

Fish toxicity

LD_{100} (48 hr) goldfish 20 mg l^{-1} (1).

Invertebrate toxicity

Cell multiplication inhibition test *Chlorella pyrenoidosa* 47 mg l^{-1} (2).

EC_{50} (5 and 30 min) *Photobacterium phosphoreum* 134 mg l^{-1} Microtox test (3).

Environmental fate

Degradation studies

Concentrations of 50 mg l^{-1} >80% degradation occurred using anaerobic digesting sludge (4).

Adapted activated sludge at 20°C used product as sole carbon source 21.1 mg COD g^{-1} dry inoculum hr^{-1} (5).

Biodegradable (6).

95% COD at 21 mg COD g^{-1} dry inoculum l^{-1} (7).

Reported decomposition period by soil microflora was 4 days (8).

Mammalian & avian toxicity

Acute data

LD_{50} oral quail 320 mg kg^{-1} (9).

LD_{50} oral mouse 1250 mg kg^{-1} (10).

LD_{50} intraperitoneal mouse 200 mg kg^{-1} (10).

LD_{50} subcutaneous cat 37 mg kg^{-1} (11).

Teratogenicity and reproductive effects

TD_{Lo} (8-day pregnant) intraperitoneal hamster 150 mg kg^{-1} caused body wall and musculoskeletal system abnormalities (12).

Irritancy

100 mg instilled in rabbit eye caused mild irritant effects (13).

The position of the substituted amino or hydroxyl group influences the potency of primary skin irritation, sensitivity and cytotoxicity. The *o*-isomer was marginally less potent than the *p*-isomer (14).

Genotoxicity

Salmonella typhimurium TA98 without metabolic activation positive (15,16).

Did not inhibit the direct-acting mutagenicity of 4-nitroquinoline 1-oxide in *Salmonella typhimurium* TA100 (17).

Vicia faba chromosome aberrations and sister chromatid exchanges positive (18).

Other effects

Other adverse effects (human)

May produce dermatitis, methaemoglobinia, bronchial asthma and restlessness (19).

Other comments

Reviews on experimental toxicology, human health effects, exposure conditions and environmental effects listed (20).

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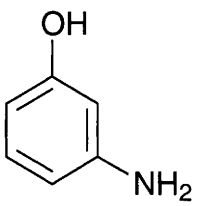
A143 3-aminophenol



C_6H_7NO **Mol. Wt.** 109.13 **CAS Registry No.** 591-27-5

Synonyms 3-amino-1-hydroxybenzene; 3-hydroxyaniline; *m*-aminophenol

EINECS No. 209-711-2 **RTECS No.** SJ 4900000

Uses Dyestuff intermediate.

Physical properties

M. Pt. 122-123°C **Partition coefficient** log P_{ow} 0.15-0.17

Solubility Water: 26 g l^{-1}. Organic solvents: amyl alcohol, diethyl ether, ethanol

Occupational exposure

UN No. 2512 **HAZCHEM Code** 2X **Conveyance classification** toxic substance

Supply classification harmful

Supply classification dangerous for the environment

Risk phrases Harmful by inhalation, in contact with skin and if swallowed – Toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment (R20/21/22, R51/53)

Safety phrases Keep out of reach of children (if sold to general public) – After contact with skin, wash immediately with plenty of water – Avoid release to the environment. Refer to special instructions/safety data sheet (S2, S28, S61)

Ecotoxicity

Invertebrate toxicity

Cell multiplication inhibition test *Chlorella pyrenoidosa* 100 mg l^{-1} (1).

Bioaccumulation

Non-accumulative or low accumulative (2).

Environmental fate

Carbonaceous inhibition

Inhibition of glucose degradation *Pseudomonas fluorescens* 0.6 mg l^{-1} (3).

Degradation studies

Biodegradable (2).

Arthrobacter sp. mA3 was capable of utilising 3-aminophenol as sole source of carbon and nitrogen (4).

Adapted activated sludge 20°C as sole carbon source 90% COD removal (5).

Reported decomposition by soil microflora >64 days (6).

Mammalian & avian toxicity

Acute data

LD_{50} oral redwing blackbird, starling 240 mg kg^{-1} (7).

LD_{50} dermal rat 1000 mg kg^{-1} (8).

LD_{50} intraperitoneal mouse 150 mg kg^{-1} (9).

Irritancy

Dermal rabbit (24 hr) 12.5 mg caused mild irritant effects (8).

Sensitisation

Guinea pig maximisation test (GPMT) positive sensitiser (10).

A 5% solution was applied to the dorsum of both ears of CBA/Ca mice for 3 consecutive days. 3-6 days after initial topical application, mice were challenged, results confirm positive sensitisation potential (11).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA1535, TA1537 with and without metabolic activation positive (12).

In vivo mouse bone marrow (4-month study) increased the rate of chromosomal aberrations at toxic concentrations (13).

Vicia faba sister chromatid exchange and chromosomal aberrations negative (14).

Neurospora crassa 220 mg l^{-1} induced sex chromosome loss and non-disjunction (15).

Other effects

Any other adverse effects

ICR mice (concentration and duration unspecified) blood GSH levels decreased but no difference in tissue GSH observed. Slight nephrotic effect observed (16).

Other comments

Reviews on experimental toxicology, physico-chemical properties and human health effects listed (17).

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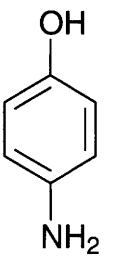
A144 4-aminophenol



C_6H_7NO **Mol. Wt.** 109.13 **CAS Registry No.** 123-30-8

Synonyms 4-amino-1-hydroxybenzene; *p*-hydroxyaniline; azol; paranol; Unal

EINECS No. 204-616-2 **RTECS No.** SJ 5075000

Uses Photography. Intermediate in azo- and sulfur-dyestuff manufacture.

Physical properties

M. Pt. 189-190°C **B. Pt.** 284°C (decomp.) **Partition coefficient** log P_{ow} 0.04
Solubility Water: 11 g l^{-1} at 0°C. Organic solvents: methyl ethyl ketone

Occupational exposure

UN No. 2512 **HAZCHEM Code** 2X **Conveyance classification** toxic substance
Supply classification harmful
Supply classification dangerous for the environment
Risk phrases Harmful by inhalation and if swallowed – Possible risk of irreversible effects – Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment (R20/22, R40, R50/53)
Safety phrases Keep out of reach of children (if sold to general public) – After contact with skin, wash immediately with plenty of water – Wear suitable protective clothing and gloves – 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, S28, S36/37, S60, S61)

Ecotoxicity

Fish toxicity

LC_{50} (48 hr) goldfish 2 mg l^{-1} (1).

Exposure of trout, bluegill sunfish and goldfish to 5 ppm caused death in 22 hr (2).

LC_{50} (96 hr) fathead minnow 24 mg l^{-1} static bioassay at 18-22°C (3).

Invertebrate toxicity

Cell multiplication inhibition test *Chlorella pyrenoidosa* 140 mg l^{-1}, *Scenedesmus quadricauda* 6 mg l^{-1} (4).

EC_{50} (5 and 30 min) *Photobacterium phosphoreum* 3.3 mg l^{-1} Microtox test (5).

Environmental fate

Degradation studies

Adapted activated sludge 87% COD (6).

Nostoc linckia and *Nostoc muscorum* >2 μg ml^{-1} decreased cell numbers, chlorophyll and total carbohydrate and inhibited carbon dioxide uptake, and nitrate reductase and nitrogenase (7).

Mammalian & avian toxicity

Acute data

LD_{50} oral redwing blackbird, starling 56 mg kg^{-1} (8).

LD_{50} oral rat, mouse 375, 420 mg kg^{-1}, respectively (9,10).

Teratogenicity and reproductive effects

Intraperitoneal mice (5 day) 500 mg kg^{-1} caused sperm morphology effects (11).

Metabolism and toxicokinetics

In the presence of oxyhaemoglobin 4-aminophenol forms numerous adducts with GSH and is converted into thioethers within the erythrocytes (12).

Irritancy

100 mg instilled in rabbit eye caused mild effects (duration unspecified) (9).

The position of the substituted amino or hydroxyl groups in aminophenol influences the potency of primary skin irritation, delayed contact sensitivity and cell toxicity. The *p*-isomer exhibited the greatest irritation, sensitivity and cytotoxicity in guinea pigs (13).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA1535, TA1537 with and without metabolic activation negative (14).

Escherichia coli K-12/343/113 DNA repair host-mediated assay without metabolic activation positive, with metabolic activation negative (15).

Mouse lymphoma assay positive with the compound inducing a large number of small colonies (16).

Showed no mutagenic activity in a modified Chinese hamster ovary cell bioassay (16).

In vitro mouse lymphoma with metabolic activation positive (17).

Chinese hamster ovary hypoxanthine-guanosine phosphoribosyl transferase assay with and without metabolic activation negative (18).

In vivo mouse hepatocytes increased the incidence of micronuclei (19).

Drosophila melanogaster wing somatic mutation and recombination test positive (20).

Vicia faba chromosome aberrations and sister chromatid exchange positive (21).

Did not inhibit the direct-acting mutagenicity of 4-nitroquinoline 1-oxide in *Salmonella typhimurium* TA100 (22).

Other effects

Any other adverse effects

Known to cause nephrotoxicity in rats where it produces selective necrosis to renal proximal tubules (23).

In a study of mutagenicity, teratology, haemotology and histopathological changes in rats dosed with 0.07, 0.2 or

0.7% in diet for 6 months, no significant haemotological changes observed. Nephrosis was observed in high-dose animals. The compound was considered non-teratogenic although an increase in developmental variations associated with maternal toxicity was noted at the mid- and high-dose levels. Mutagenic activity was not detected in the urine (24).

Intraperitoneal rat (concentration and duration unspecified) caused necrosis of renal tubular epithelial cells and elevated urinary *N*-acetyl-β-D-glucosaminidase and γ-glutamyltranspeptidase activities (25).

Other comments

Reviews on experimental toxicology, human health effects, exposure conditions and environmental effects listed (26).

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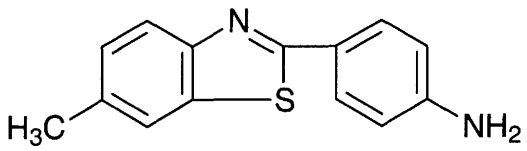
A145 2-(4-aminophenyl)-6-methylbenzothiazole



$C_{14}H_{12}N_2S$ **Mol. Wt.** 240.33 **CAS Registry No.** 92-36-4

Synonyms dehydrothio-*p*-toluidine; DHPT; *p*-(6-methylbenzothiazol-2-yl)aniline; 4-(6-methyl-2-benzothiazolyl)benzenamine

EINECS No. 202-150-4 **RTECS No.** DL 2820000

Uses Manufacture of dyestuffs.

Physical properties

M. Pt. 191°C **B. Pt.** 434°C

Solubility Water: <1 g l^{-1} at 20°C. Organic solvents: acetone, dimethyl sulfoxide, ethanol

Mammalian & avian toxicity

Acute data

LC_{Lo} (4 hr) inhalation rat 3000 mg m^{-3} (1).

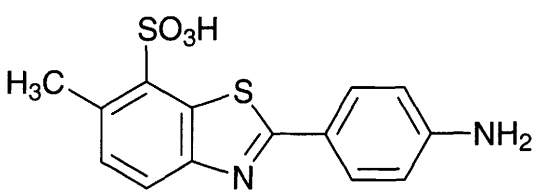
Irritancy

Irritating to the eyes, skin, mucous membranes and upper respiratory tract (species unspecified) (2).

References

1. *Food Chem. Toxicol.* 1984, **22**, 289.
2. Lenga, R. E. (Ed.) *Sigma-Aldrich Library of Chemical Safety Data* 2nd ed., 1988, **1**, 210, Sigma-Aldrich, Milwaukee, WI, USA

A146 2-(4-aminophenyl)-6-methyl-7-benzothiazolesulfonic acid



$C_{14}H_{12}N_2O_3S_2$ **Mol. Wt.** 320.39 **CAS Registry No.** 130-17-6

Synonyms 2-(4-aminophenyl)-6-methyl-7-benzothiazolylsulfonic acid; 6-methyl-2-(*p*-aminophenyl)-7-benzothiazole sulfonic acid

EINECS No. 204-979-7 **RTECS No.** DL 6420000

Uses Manufacture of dyestuffs.

Mammalian & avian toxicity

Acute data

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

Other comments

Based on data for benzothiazole, significant toxicity may be expected.

References

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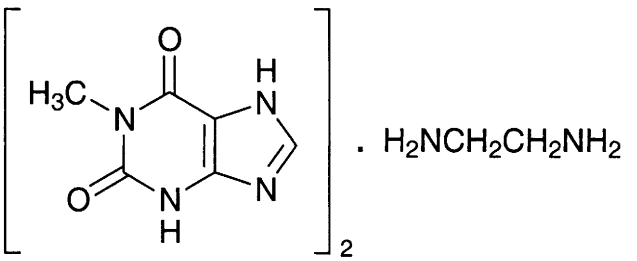
A147 aminophylline



CAS Registry No. 317-34-0

Synonyms 3,7-dihydro-1,3-dimethyl-1*H*-purine-2,6-dione with 1,2-ethanediamine (2:1); ethylenediamine, compound with theophylline; Euphyllin

EINECS No. 206-264-5 **RTECS No.** XH 5600000

Uses Pharmaceutical applications as a smooth muscle relaxant and a bronchodilator.

Physical properties

Solubility Water: 200 g l^{-1} at 25°C

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse 540 mg l^{-1} (1).

LD_{50} intraperitoneal rat, guinea pig 200-250 mg kg^{-1} (2,3).

Intravenous single dose Wistar rat 5, 10, 20, 40 or 80 mg kg^{-1} hypoventilation with corresponding hypoxemia and hypercapnia observed in phrenicotomised rats (4).

Sub-acute and sub-chronic data

Oral NJH mice (8-10 day) 25, 50 or 100 mg kg^{-1} day^{-1} immune system effects included increased haemolytic ability of plaque-forming cells and antibody concentration and decreased delayed-type hypersensitivity reaction and peripheral white blood cell phagocytosis (5).

Intravenous newborn New Zealand rabbits 0.6 mg kg^{-1} (duration unspecified) increased diuresis, renal vascular resistance and filtration fraction (6).

Metabolism and toxicokinetics

Pulmonary absorption of aminophylline 500 μg rat^{-1} was 96% within 1 min (7).

At least 7 hr are required to clear blood completely in normal adult subjects after intravenous administration of 300-500 mg; >10 hr are required before an oral dose disappears entirely from the blood (8).

Other effects

Other adverse effects (human)

In human poisoning symptomatic effects include restlessness, anorexia, nausea, fever, vomiting and dehydration. Can result in cardiovascular and respiratory collapse, shock, cyanosis and death (8).

Other comments

Incompatible with a range of materials, including acids, bleomycin sulfate, chlorpromazine hydrochloride, corticotrophin, doxorubicin and erythromycin. Commonly administered as the hydrate (9).
Mixture of theophylline and ethylenediamine.

References

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6. Gouyon, J. B. et al *Life Sci.* 1988, **42**(13), 1271-1278.
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8. Gosselin, R. E. et al *Clinical Toxicology of Commercial Products* 4th ed., 1976, 16-20, William & Wilkins, Baltimore, MD, USA.
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A148 1-amino-2-propanol

$$CH_3CHOHCH_2NH_2$$

C_3H_9NO **Mol. Wt.** 75.11 **CAS Registry No.** 78-96-6

Synonyms 1-aminopropan-2-ol; 2-hydroxypropylamine; MIPA; α-aminoisopropyl alcohol; isopropanolamine; monoisopropanolamine

EINECS No. 201-162-7 **RTECS No.** UA 5775000

Uses Emulsifying agent, dry cleaning, soaps, soluble textile oils, wax removers, metal cutting oils, cosmetics, emulsion paints, plasticisers, insecticides.

Physical properties

M. Pt. –2°C **B. Pt.** 160°C **Flash point** 77.2°C **Specific gravity** 0.9619 **Partition coefficient** log P_{ow} –0.96
Volatility v.p. <1 mmHg at 20°C ; v.den. 2.6

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)

Ecotoxicity

Fish toxicity

LC_{50} (24 hr) goldfish >5000 mg l^{-1} (1).

Invertebrate toxicity

EC_{50} (30 min) *Photobacterium phosphoreum* 27.3 mg l^{-1} Microtox test (2).

Environmental fate

Degradation studies

BOD_{10} 34% ThOD 2.5 mg l^{-1} in mineralised dilution water with settled sewage seed at 20°C (3).

Abiotic removal

Activated carbon: adsorbability 40 mg g^{-1}; 20% reduction, influent 1 g l^{-1}, effluent 800 mg l^{-1} (4).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 2100 mg kg^{-1} (3).

LD_{50} dermal rabbit 1640 mg kg^{-1} (5).

Irritancy

Dermal rabbit (duration unspecified) 485 mg caused moderate irritation and 970 μg instilled into rabbit eye caused severe irritation (5).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537 with and without metabolic activation equivocal results (6).
Drosophila melanogaster sex-linked recessive lethal assay negative (7).

Other effects

Any other adverse effects

At test toxic concentrations causes somnolence and gastro-intestinal hypermotility and diarrhoea (5).

Other comments

Corrosive and moderately flammable. Incompatible with oxidising materials (5).
Based on available data from a study of the chemical, metabolic and toxicological properties, it was concluded that 1-amino-2-propanol is safe as a cosmetic ingredient in the present practices of use and concentration (8).

References

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2. Kaiser, K. L. E. et al *Water Poll. Res. J. Canada* 1991, **26**(3), 361-431.
3. Ettinger, M. B. *Ind. Eng. Chem.* 1956, **48**, 256.
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6. Zeiger, E. et al *Environ. Mutagen.* 1987, **9**(Suppl. 9), 1-109.
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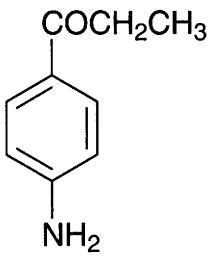
A149 4′-aminopropiophenone



$C_9H_{11}NO$ **Mol. Wt.** 149.19 **CAS Registry No.** 70-69-9

Synonyms 1-(4-aminophenyl)-1-propanone; ethyl *p*-aminophenyl ketone; *p*-aminopropiophenone; paraminopropiophenone; *p*-aminophenylpropanone

EINECS No. 200-742-7 **RTECS No.** UG 7350000

Uses Chemical intermediate. Cyanide antidote.

Physical properties

M. Pt. 140°C

Solubility Organic solvents: chloroform, ethanol

Environmental fate

Nitrification inhibition

Nitrosomonas sp. 75-100% inhibition of ammonia oxidation at 100 mg l^{-1} (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral starling 133 mg kg^{-1} (2).

LD_{50} oral mouse, rat 168, 177 mg kg^{-1}, respectively (3,4).

LD_{50} oral guinea pig 1020 mg kg^{-1} (5).

LD_{Lo} intraperitoneal rat 525 mg kg^{-1} (6).

LD_{50} intraperitoneal mouse 80 mg kg^{-1} (7).

Other effects

Any other adverse effects

Oral rat (unspecified concentration) brought about peak methaemoglobin levels at 15-40 min while intravenous administration caused peak methaemoglobin levels 15-25 min after dosing (8).

Other comments

Oral dog 0.5 mg kg^{-1} protected against cyanide poisoning induced by intravenous HCN dose of 0.67 or 1.34 mg kg^{-1}. Protection caused sequestration of cyanide inside red cells (9).

References

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2. Schafer, E. W. et al *Arch. Environ. Contam. Toxicol.* 1983, **12**(3), 355-382.
3. Savaric, P. J. et al *Bull. Environ. Contam. Toxicol.* 1983, **30**(1), 122-126.
4. Pan, H. P. et al *Gen. Pharmacol.* 1983, **14**(4), 465-467.
5. Scawin, J. W. et al *Toxicol. Lett.* 1984, **23**(3), 359-365.

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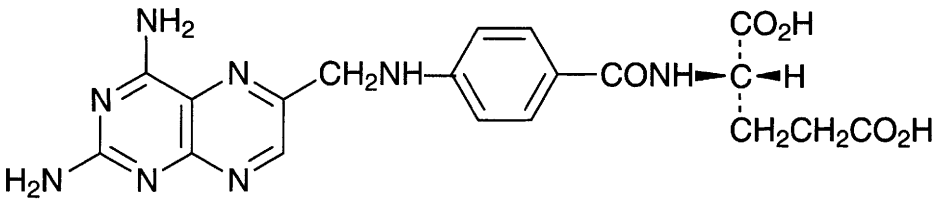
A150 aminopterin



$C_{19}H_{20}N_8O_5$ **Mol. Wt.** 440.42 **CAS Registry No.** 54-62-6

Synonyms aminopteridine; *N*-(*p*-[(2,4-diamino-6-pteridylmethyl)amino]benzoyl)glutamic acid; (((diaminopteridinyl)methyl)amino)benzoylglutamic acid

EINECS No. 200-209-9 **RTECS No.** MA 1050000

Uses Antineoplastic and antileukaemic. Antagonist of folic acid.

Physical properties

M. Pt. 260-265°C (decomp.) [L-form]

Mammalian & avian toxicity

Acute data

LD_{Lo} oral rat 2500 μg kg^{-1} (1).

LD_{50} intraperitoneal mouse, rat 1900-3400 μg kg^{-1} (1,2).

Teratogenicity and reproductive effects

Intraperitoneal mice (5 day) 2 mg kg^{-1} caused sperm morphology changes (2).

TD_{Lo} (40 day pregnant) oral woman 200 μg kg^{-1} caused spontaneous abortion (3).

Injection mouse (meiosis I, or 3 hr prior to meiosis I) 2-4 mg kg^{-1} no effect on ovulation, rate of fertilisation, cleavage or implantation (4).

In vitro microassay of human embryonic palatal mesenchymal cells with metabolic activation to determine teratogenic potential. IC_{50} 38.7 μg l^{-1} positive teratogenic potential (5).

Genotoxicity

Drosophila melanogaster mutant *vg* strains yielded more offspring on a medium containing aminopterin than on normal medium (6).

Other comments

Physiology, metabolism and pharmacology reviewed (7,8).

References

1. Philips, F. S. et al *J. Pharmacol. Exptl. Therap.* 1949, **95**(3), 303-311.

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3. Thiersch, J. B. *Am. J. Obstet. Gynecol.* 1952, **63**, 1298-1304.
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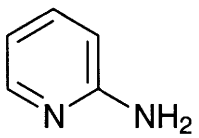
A151 2-aminopyridine



$C_5H_6N_2$ **Mol. Wt.** 94.12 **CAS Registry No.** 504-29-0

Synonyms α-aminopyridine; *o*-aminopyridine; amino-2-pyridine; α-pyridylamine; α-pyridinamine; 2-pyridinamine

EINECS No. 207-988-4 **RTECS No.** US 1575000

Uses Organic synthetic intermediate. Used in pharmaceutical manufacture, particularly antihistamines.

Physical properties

M. Pt. 57-58°C **B. Pt.** 204-210°C **Flash point** 92°C **Partition coefficient** log P_{ow} –0.22 (1)
Volatility v.den. 3.25
Solubility Organic solvents: acetone, diethyl ether, ethanol

Occupational exposure

DE-MAK 0.5 ppm (2 mg m^{-3})
FR-VME 0.5 ppm (2 mg m^{-3})
UK-LTEL 0.5 ppm (2.0 mg m^{-3}) **UK-STEL** 2 ppm (7.8 mg m^{-3})
US-TWA 0.5 ppm (1.9 mg m^{-3})

UN No. 2671 **HAZCHEM Code** 2X **Conveyance classification** toxic substance

Ecotoxicity

Invertebrate toxicity
EC_{50} (5-30 min) *Photobacterium phosphoreum* 284 mg l^{-1} Microtox test (2).
EC_{50} (60 hr) *Tetrahymena pyriformis* 390 mg l^{-1} (3).

Bioaccumulation
Non-accumulative or low accumulative (4).
Calculated bioconcentration factor 0.14 (5).

Environmental fate

Degradation studies
Adapted activated sludge at 20°C used product as sole carbon source, 97.3% COD at 41.0 mg COD g^{-1} dry inoculum hr^{-1} (6).

Of 17 ppm incubated in soil at pH 7 and 28°C <1% degraded within 30 days, as evidenced via the release of inorganic nitrogen (7).

Mammalian & avian toxicity

Acute data

LD_{50} oral redwing blackbird, starling 32 mg kg^{-1} (8).
LD_{50} oral quail 130 mg kg^{-1} (8).
LD_{50} intraperitoneal mouse 35 mg kg^{-1} (9).
LD_{50} intravenous mouse 23 mg kg^{-1} (10).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537 with and without metabolic activation negative (11).

Other comments

Reviews on experimental toxicology, epidemiology, workplace experience and human health effects listed (12).

References

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11. Zeiger, E. et al *Environ. Mutagen.* 1987, **9**(Suppl. 9), 1-109.
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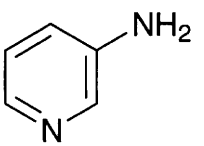
A152 3-aminopyridine



$C_5H_6N_2$ **Mol. Wt.** 94.12 **CAS Registry No.** 462-08-8

Synonyms amino-3-pyridine; *m*-aminopyridine; 3-pyridinamine; 3-pyridylamine

EINECS No. 207-322-2 **RTECS No.** US 1650000

Uses Organic synthetic intermediate. In drug and dyestuff manufacture.

Physical properties

M. Pt. 64°C **B. Pt.** 251°C

Solubility Organic solvents: benzene, diethyl ether, ethanol

Occupational exposure

UN No. 2671 **HAZCHEM Code** 2X **Conveyance classification** toxic substance

Ecotoxicity

Invertebrate toxicity

EC_{50} (5-30 min) *Photobacterium phosphoreum* 682 mg l^{-1} Microtox test (1).

EC_{50} (60 hr) *Tetrahymena pyriformis* 283 mg l^{-1} (2).

Bioaccumulation

Non-accumulative or low accumulative (3).

Mammalian & avian toxicity

Acute data

LD_{50} oral redwing blackbird, starling 13.3 mg kg^{-1} (4).

LD_{50} oral quail 178 mg kg^{-1} (4).

LD_{50} intraperitoneal mouse 28 mg kg^{-1} (5).

LD_{50} intravenous mouse 24 mg kg^{-1} (6).

References

1. Kaiser, K. L. E. et al *Water Pollut. Res. J. Canada* 1991, **26**(3), 361-431.
2. Shultz, T. W. et al *Ecotoxicol. Environ. Safety* 1987, **13**, 76.
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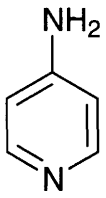
A153 4-aminopyridine



$C_5H_6N_2$ **Mol. Wt.** 94.12 **CAS Registry No.** 504-24-5

Synonyms amino-4-pyridine; γ-aminopyridine; 4-pyridinamine; 4-pyridylamine; *p*-aminopyridine

EINECS No. 207-987-9 **RTECS No.** US 1750000

Uses Organic synthetic intermediate. Bird repellent.

Physical properties

M. Pt. 155-158°C **B. Pt.** 273°C **Partition coefficient** log P_{ow} 0.28

Solubility Organic solvents: benzene, diethyl ether

Occupational exposure

UN No. 2671 **HAZCHEM Code** 2X **Conveyance classification** toxic substance

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) bluegill sunfish 2.8-7.5 mg l^{-1} static bioassay at 12-22°C (1). LC_{50} (96 hr) channel catfish 2.4-5.8 mg l^{-1} static bioassay at 12-22°C (1).

Invertebrate toxicity

EC_{50} (5-30 min) *Photobacterium phosphoreum* 284 mg l^{-1} Microtox test (2).
EC_{50} (60 hr) *Tetrahymena pyriformis* 260 mg l^{-1} (3).

Bioaccumulation

Non-accumulative or low accumulative (4).

Environmental fate

Anaerobic effects

Soil degradation under anaerobic conditions was negligible for up to 2 months (5).

Degradation studies

Under aerobic conditions, using ^{14}C-labelled 4-aminopyridine, at 30°C and 50% moisture, $^{14}CO_2$ was evolved at 0.4% to >50% depending upon the soil type (5).
In a 90-day period, 54.6, 10.74 and 4.88% of original radio-labelled concentration of 10 ppm were mineralised to CO_2 from a loamy sand and sandy clay loam at 30°C and pHs of 7.8, 7.7 and 7.6, respectively, which correspond to $t_{1/2}$ of 90, 330 and 960 days. For a loam with pHs of 5.8, 5.6 and 4.1 losses of 5.95, 16.52 and 0.35% corresponding to $t_{1/2}$ 600, 240 and >660 days (5).

Abiotic removal

Oxidation with ozone in aqueous solution increases with increasing pH, complete oxidation occurs at pH 9.3 in 50 min (6).
<1% of 14.6 ppm was mineralised in >30 days as evidenced via the release of inorganic nitrogen (7).
Photochemical reaction with hydroxyl radicals in the atmosphere $t_{1/2}$ 8 hr (8).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, mouse 20, 42 mg kg^{-1}, respectively (4,9).
LD_{50} intraperitoneal rat, mouse 6.5, 11.5 mg kg^{-1}, respectively (9-12).
LD_{50} subcutaneous mouse, rat 5, 18.5 mg kg^{-1}, respectively (11,12).

Metabolism and toxicokinetics

Nine healthy subjects (7 ♂ and 2 ♀) received a single intravenous injection of 20 mg 4-aminopyridine. Five of the subjects received the same dose in the form of enteric-coated tablets and four the same dose in uncoated tablets, treatments were 2 wk apart. Saliva concentrations were higher than those in serum after 5 min. The $t_{1/2}$ and volume distribution calculated from serum and saliva concentrations were of the same order. The total urinary excretion of unchanged drug was 90.6% after intravenous doses and 88.5% after oral doses of enteric-coated tablets (13).

Genotoxicity

Salmonella typhimurium TA1537, TA2637 without metabolic activation negative (14).

Other effects

Any other adverse effects

The effect of 4-aminopyridine on [^{3}H]acetylcholine release was studied in rat cerebral cortical synaptosomes. Results suggested that 4-aminopyridine blocks potassium channels involved in regulating membrane potential in isolated cholinergic terminals but that changes in these channels are not important in the nerve terminal's response to depolarisation (15).

Birds that consume grain treated with 4-aminopyridine exhibit erratic behaviour and emit vocalisation to scare away the rest of the flock (16).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides and related products: maximum admissible concentration 0.1 $\mu g\ l^{-1}$ (17).

Included in Schedule 6 (Release Into Land: Prescribed Substances) of Statutory Instrument No. 472, 1991 (18).

Other comments

4-Aminopyridine is the only repellent that can be legally used in the US to reduce bird damage in ripening grain fields (16).

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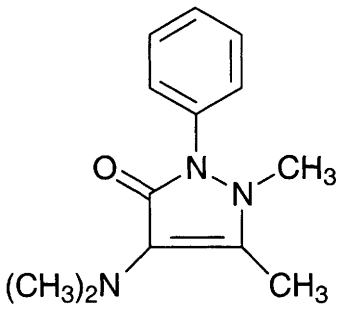
A154 aminopyrine



$C_{13}H_{17}N_3O$ **Mol. Wt.** 231.30 **CAS Registry No.** 58-15-1

Synonyms amidopyrine; 4-aminophenazone; 4-dimethylamino-2,3-dimethyl-1-phenyl-3-pyrazolin-5-one; dimethylaminophenyldimethylpyrazolone; 4-dimethylaminoantipyrine

EINECS No. 200-365-8 **RTECS No.** CD 2625000

Uses Antipyretic, analgesic.

Physical properties

M. Pt. 107-109°C

Solubility Water: 55.6 g l^{-1}. Organic solvents: benzene, chloroform, diethyl ether, ethanol

Ecotoxicity

Invertebrate toxicity

IC_{50} *Saccharomyces cerevisiae* 244 mg l^{-1} (1).

Toxicity to other species

LD_{Lo} parenteral frog 900 mg kg^{-1} (2).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 1.7 g kg^{-1} (3).

LD_{50} oral rabbit 600 mg kg^{-1} (4).

LD_{50} oral rat, mouse 1000, 1850 mg kg^{-1}, respectively (1).

Carcinogenicity and chronic effects

Syrian golden hamsters (8-10 wk) combined administration of 0.1% nitrite and 0.1% aminopyrine in drinking water resulted in subsequent development of hepatocellular nodules and cholangiofibrotic lesions and cholangiocellular carcinomas (5).

B6C3F1 mice (104 wk) 0, 0.04, 0.08% in drinking water, no significant incidence in tumour frequency between treated and control groups (6).

Teratogenicity and reproductive effects

Subcutaneous mice (days 7, 8 and 9 of gestation) 200 mg kg^{-1} induced malformations, including omphalocele, club foot and kinky tail (7).

Metabolism and toxicokinetics

Injection rats (concentration unspecified), after 30 min uniform distribution was detected throughout the body. Preferential localisation was found in the nasal mucosa and liver (8).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA102, TA104 with and without metabolic activation negative (9).
Did not inhibit the direct-acting mutagenicity of 4-nitroquinoline 1-oxide in *Salmonella typhimurium* TA100 (10).

Other effects

Other adverse effects (human)

A life-threatening asthmatic attack has been reported due to administration of amidopyrine (11).
Agranulocytosis has been reported in humans after administration of amidopyrine (12,13).
The Boston Collaborative Drug Surveillance Program monitored consecutively 32,812 medical in-patients.
Drug-induced anaphylaxis occurred in 1 out of 1992 patients given amidopyrine (14).
Implicated as a causative agent in immune haemolytic anaemia (15).

Other comments

Metabolism, pharmacokinetics and human health effects reviewed (16-18).

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A155 11-aminoundecanoic acid

$$NH_2(CH_2)_{10}CO_2H$$

$C_{11}H_{23}NO_2$ **Mol. Wt.** 201.31 **CAS Registry No.** 2432-99-7

EINECS No. 219-417-6 **RTECS No.** YQ 2293000

Uses Polymer intermediate.

Physical properties

M. Pt. 190-192°C

Mammalian & avian toxicity

Sub-acute and sub-chronic data

Intravenous cat (duration unspecified) 2 mg kg^{-1} caused transient lowering of blood pressure (1).

Carcinogenicity and chronic effects

No adequate evidence for carcinogenicity in humans, limited evidence for carcinogenicity in experimental animals, IARC classification group 3 (2,3).

The National Toxicology Program tested rats and mice via dosed-feed. Positive evidence for carcinogenicity in ♂ rats, equivocal evidence in ♂ mice and negative evidence in ♀ rats and mice (4).

Gavage Fischer 344 rats, B6C3F1 mice (2 yr) in corn oil benign liver tumours observed (5).

Target organ of carcinogenicity: rat liver (6).

Metabolism and toxicokinetics

Oral rat (concentration unspecified) minor incorporation in DNA nucleosides of the liver within 24 hr. No DNA alkylation observed (7).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537 with and without metabolic activation negative (2,8).

Chinese hamster ovary cells without metabolic activation sister chromatid exchange positive, with metabolic activation negative (8,9).

Chinese hamster ovary cells with and without metabolic activation chromosomal aberrations negative (8).

Mouse bone marrow micronucleus test negative (10).

Mouse lymphoma L-5178Y tk+/tk– with and without metabolic activation negative (8,11).

Other comments

Experimental toxicology, environmental effects and human health effects reviewed (3,12).

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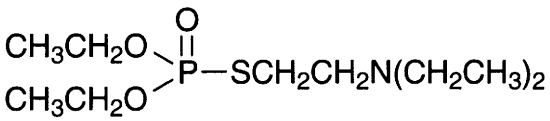
A156 amiton



$C_{10}H_{24}NO_3PS$ **Mol. Wt.** 269.35 **CAS Registry No.** 78-53-5

Synonyms *S*-[2-(diethylamino)ethyl]phosphorothioic acid *O,O*-diethyl ester; *O,O*-diethyl *S*-(β-diethylamino)-ethyl phosphorothiolate

RTECS No. TF 0525000

Uses Superseded insecticide, acaricide.

Physical properties

B. Pt. 88°C

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 5.4 mg kg^{-1} (1).

LD_{50} subcutaneous rat, mouse, hamster, guinea pig 80-120 μg kg^{-1} (2).

Other effects

Any other adverse effects

Organophosphate pesticide. Symptomatic effects of this type of compound include respiratory discomfort, nausea, vomiting, diarrhoea, headache and blurred vision. Can cause central nervous system disorders. Death is primarily due to respiratory failure although cardiac arrest can be implicated (3).

Legislation

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

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

Other comments

Insecticidal and acaricidal properties reported (6,7).

Contact insecticide, acaricide, no longer in widespread use.

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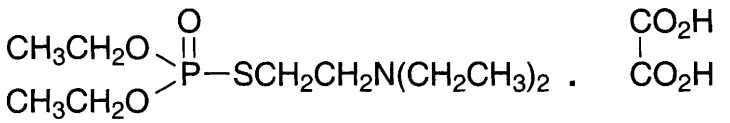
A157 amiton oxalate



$C_{12}H_{28}NO_7PS$ **Mol. Wt.** 361.40 **CAS Registry No.** 3734-97-2

Synonyms phosphorothioic acid, *S*-[2-(diethylamino)ethyl]-, *O,O*-diethyl ester, oxalate; amiton hydrogen oxalate

EINECS No. 223-100-8 **RTECS No.** TF 1400000

Uses Superseded contact insecticide and acaricide.

Physical properties

M. Pt. 98-99°C

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 3-9 mg kg^{-1} (1,2).

LD_{50} intraperitoneal mouse 500 μg kg^{-1} (3).

Other effects

Any other adverse effects

Irreversible anticholinesterase agent (4).

Organophosphate pesticide. Symptomatic effects of this type of compound include respiratory discomfort, nausea, vomiting, diarrhoea, headache and blurred vision. Can cause central nervous system disorders. Death is primarily due to respiratory failure, although cardiac arrest can be implicated (5).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides and related products: maximum admissible concentration 0.1 μg l^{-1} (6).

Included in Schedule 6 (Release Into Land: Prescribed Substances) of Statutory Instrument No. 472, 1991 (7).

Other comments

Insecticidal and acaricidal properties reported (8,9).

No longer in widespread use.

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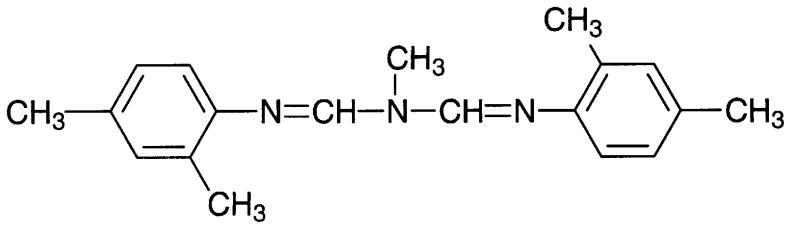
A158 amitraz



$C_{19}H_{23}N_3$ **Mol. Wt.** 293.41 **CAS Registry No.** 33089-61-1

Synonyms ATA; Mitac; Triatox; *N'*-(2,4-dimethylphenyl)-*N*-[[(2,4-dimethylphenyl)imino]methyl]-*N*-ethylmethanimidamide; *N*-methyl-*N'*-2,4-xylyl-*N*-(*N*-2,4-xylylformimidoyl)formamidine; *N,N'*-[(methylimino)dimethylidyne]di-2,4-xylidine; 2-methyl-1,3-di(2,4-xylylimino)-2-azapropane

EINECS No. 251-375-4 **RTECS No.** ZF 0480000

Uses Veterinary acaricide used in the treatment of demodecosis in dogs. Insecticide.

Physical properties

M. Pt. 86-88°C **Specific gravity** 1.128 at 25°C **Volatility** v.p. 3.8×10^{-5} mmHg
Solubility Water: 1 mg l^{-1} at 25°C. Organic solvents: acetone, toluene, xylene

Occupational Exposure

Supply classification harmful
Risk phrases Harmful if swallowed (R22)
Safety phrases Keep out of reach of children (if sold to general public) – Do not breathe dust (S2, S22)

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) rainbow trout, bluegill sunfish, sheepshead minnow 0.74, 0.45, >2.4 mg l^{-1}, respectively (1).

Invertebrate toxicity
EC_{50} (48 hr) *Daphnia* 0.035 μg l^{-1} (1).
EC_{50} (duration unspecified) *Selenastrum capricornutum* >12 mg l^{-1} (1).
LC_{50} (14 days) earthworm >1000 mg kg^{-1} (1).
LD_{50} 4.42 μg bee^{-1} in feed (2).

Environmental fate

Degradation studies
Amitraz has been investigated in laboratory microcosms using three different sediments (acidic, loamy sand and clay) and their associated water. Amitraz was applied to the water surface and the microcosms incubated at 25°C in a stream of moist air. Rapidly dissipated from the water column via hydrolysis and adsorption to sediment. Times for 90% decline of amitraz in the microcosms ranged from 1.3-8 days. Degradation was slower in acidic compared to alkaline medium (3).

Abiotic removal
Amitraz was rapidly dissipated from water via hydrolysis and adsorption to sediment (3).

Mammalian & avian toxicity

Acute data

LD_{50} oral mallard duck, Japanese quail, bobwhite quail 7000, 1800, 788 mg kg^{-1}, respectively (1).
LD_{50} oral mouse 800->1600 mg kg^{-1} (1).
LD_{50} oral rat 600-800 mg kg^{-1} (1).
LC_{50} (6 hr) inhalation rat 65 mg l^{-1} air (1).
LD_{50} percutaneous rabbit, rat 200, >1600 mg kg^{-1}, respectively (1,4).
A single oral, intraperitoneal dose rat 20, 60 and 100 mg kg^{-1} caused a depressant effect on the central nervous system (5).
555 ppm was administered to fasting dogs 4 hr prior to a single intravenous injection of 0.6 g kg^{-1} glucose. Plasma glucose concentrations increased but the increase in plasma insulin concentration which usually follows intravenous administration of glucose was suppressed. It was concluded that amitraz induces hyperglycaemia (6).

Sub-acute and sub-chronic data

No-adverse-effect level in rats 50 mg kg^{-1} in diet. ≥100 mg kg^{-1} inhibited monoamine oxidase in rats, negligible inhibition of acetylcholine esterase (7).
Intravenous dog repeat doses of 1, 2 and 5 mg kg^{-1} caused transient increase in blood pressure, decrease in heart rate and depressed respiratory rate. High dosage caused hyperventilation (8).

Carcinogenicity and chronic effects

In 2-yr feeding trials no-adverse-effect levels were seen in rats receiving 50-200 ppm in diet or in dogs given 0.25 mg kg^{-1} day^{-1} (1).

Teratogenicity and reproductive effects

Pregnant rats were orally gavaged with 20 mg kg^{-1} or with distilled water on days 1, 4, 7, 10, 13, 16 or 19 of gestation. After birth, cross-fostering was performed generating the following groups: control pups nursed by control dams (CC); control pups nursed by treated dams (CT); treated pups nursed by control dams (TC); and treated pups nursed by treated dams (TT). Compared to pups of group CC, pups from groups TC and TT showed a decreased age of vaginal opening and pups from groups CT and TT showed earlier fur development. Rats and offspring from group TT also showed a delay in incisor eruption, a higher locomotor activity and rearing frequency, and a shorter immobility time compared to those of group CC. The exposure did not affect the ages of pinna detachment, eye and ear opening, testes descent and reflex development (9).

Metabolism and toxicokinetics

In rats, the principal metabolites included 2,4-dimethylformanilide, 2,4-dimethylaniline, 4-formamido-3-methylbenzoic acid and 4-amino-3-methylbenzoic acid (10).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA102 with and without metabolic activation negative (11).
Escherichia coli PQ243 SOS chromotest negative (11).

Other effects

Any other adverse effects

In Sprague-Dawley, Long-Evans and Fischer 344 rats symptoms of amitraz exposure included excitability, hyperreactivity and physiological and autonomic changes. All effects increased with repeated dosing (12).
Intraperitoneal Long-Evans rat (1-4 hr, 1-8 day) 10, 25, 50, 100 or 200 mg kg^{-1}, symptoms included depressed arousal and rearing activity, hypothermia, body weight loss, ptosis, chromodacryorrhoea resulting in facial crustiness, loss of pupil reflex and decreased defecation. Altered gait and decreased foot splay landing ability were also observed (13).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides and related products: maximum admissible concentration 0.1 μg l^{-1} (14).

Included in Schedule 6 (Release Into Land: Prescribed Substances) of Statutory Instrument No. 472, 1991 (15).
WHO Toxicity Class III (16).
EPA Toxicity Class III (1).

Other comments

Unstable at pH >7. Slow deterioration of moist compound on prolonged standing.

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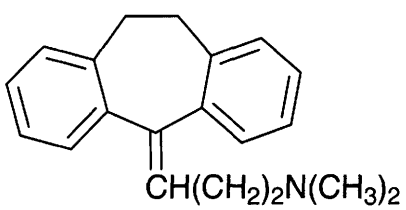
A159 amitriptyline



$C_{20}H_{23}N$ **Mol. Wt.** 277.41 **CAS Registry No.** 50-48-6

Synonyms 1-propanamine, 3,10-dihydro-5*H*-dibenzo(a,d)cyclohepten-5-ylidene, *N*,*N*-dimethyl-

EINECS No. 200-041-6 **RTECS No.** HO 9275000

Uses Antidepressant.

Physical properties

M. Pt. 196-197°C **Partition coefficient** log P_{ow} 4.92 (1)
Solubility Organic solvents: acetone, chloroform, ethanol, methanol

Ecotoxicity

Invertebrate toxicity
EC_{50} (24 hr) *Daphnia magna*, *Daphnia pulex* 4.15, 3.73 μM, respectively (2).

EC_{50} (5 min) *Photobacterium phosphoreum* 77.6 μmol l^{-1} Microtox test (1).
EC_{50} (24 hr) *Artemia salina, Streptocephalus proboscideus, Daphnia magna, Brachionus calyciflorus* 131.8, 2.75, 17.8, 2.9 μmol l^{-1}, respectively (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral mouse, rat 140, 320 mg kg^{-1}, respectively (3,4).
LD_{50} intraperitoneal rat 72 mg kg^{-1} (5).
LD_{50} intravenous mouse 16 mg kg^{-1} (6).

Sub-acute and sub-chronic data
Oral rat (21 day) 10 mg kg^{-1}, 2 × day^{-1} reduced the concentration of 5-α-dihydrotestosterone in serum, cerebral cortex and hypothalamus, a decrease in testosterone level was also observed in the hypothalamus (7).

Metabolism and toxicokinetics
Mostly hydroxylated at position 10, *N*-demethylation and glucuronide conjugation. About 1% is converted into the *N*-oxide. It is excreted in the urine, mainly in the form of its metabolites, either free or in a conjugated form (8,9).
Intraperitoneal rat (6-9 hr) 20 mg kg^{-1} major metabolites included E-10-hydroxyamitriptyline, 10,11-dihydroxyamitriptyline, and the phenol E-2-hydroxyamitriptyline. Minor metabolites included 2,10- and 2,11-dihydroxyamitriptyline, 2,10,11-trihydroxyamitriptyline and 2-hydroxy-3-methoxyamitriptyline and the dehydration product 3-hydroxy-10,11-dehydroxyamitriptyline (10).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535 with and without metabolic activation negative (11).
In vitro human lymphocytes exposed to plasma levels showed no evidence of chromosome aberrations, mitotic index and sister chromatid exchange. High doses 1 and 10 μg ml^{-1} slightly increased frequencies of chromosome aberrations and sister chromatid exchange (12).
Drosophila melanogaster wing spot somatic mutation and recombination test negative (13).

Other effects

Other adverse effects (human)
Six drug-free, healthy elderly subjects received a single oral dose 50 mg of amitriptyline. Observed effects included reduced salivary volume, drowsiness and impaired psychomotor performance (14).
In a 13-day study of 12 healthy men given 150 mg day^{-1} symptomatic effects included delay in intracardiac conduction, increased heart rate, decreased salivation, constipation and sedation (15).

Any other adverse effects
In perfused rat heart amitriptyline caused protein degradation and structural damage (16).

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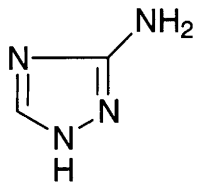
A160 amitrole



$C_2H_4N_4$ **Mol. Wt.** 84.08 **CAS Registry No.** 61-82-5

Synonyms aminotriazole; 1*H*-1,2,4-triazol-3-ylamine; 3-amino-1*H*-1,2,4-triazole; 3-amino-*s*-triazole; amizol; cytrol; Weedazol

EINECS No. 200-521-5 **RTECS No.** XZ 3850000

Uses Non-selective herbicide. Cotton defoliant. Photographic reagent. Use restricted to non-food crops.

Physical properties

M. Pt. 157-159°C; 150-153°C (technical grade) **Specific gravity** 1.138 at 20°C
Volatility v.p. 7.5×10^{-6} mmHg at 20°C
Solubility Water: 280 g l^{-1} at 25°C. Organic solvents: acetonitrile, chloroform, dichloromethane, ethanol, methanol

Occupational Exposure

DE-MAK 0.2 mg m^{-3} (inhalable dust fraction)
FR-VME 0.06 ppm (0.2 mg m^{-3})
US-TWA 0.2 mg m^{-3}
Supply classification harmful, dangerous for the environment
Risk phrases Possible risk of irreversible effects – Harmful: danger of serious damage to health by prolonged exposure if swallowed – Toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment (R40, R48/22, R51/53)
Safety phrases Keep out of reach of children (if sold to general public) – Wear suitable protective clothing – Wear suitable gloves – Avoid release to the environment. Refer to special instructions/safety data sheet (S2, S36, S37, S61)

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) mosquito fish 2100 mg l^{-1} (1).
LC_{50} (48 hr) silver salmon 325 mg l^{-1} (2).
LC_{50} (48 hr) bluegill sunfish >180 mg l^{-1} (3).
LC_{50} (2 hr) whitebait 0.45% corresponding to active ingredient concentration of 26 mg l^{-1} (4).

Invertebrate toxicity
Mud crab (4-hr exposure) direct spray full strength mixture no mortality (4).
EC_{50} (5-30 min) *Photobacterium phosphoreum* 180-582 mg l^{-1} Microtox test (5).

No-effect level (48 hr) for *Gammarus fasciatus, Asellus brevicaudus, Palaemonetes kadiakensis, Orconectes nais* all 100 mg l^{-1} (6).
Non toxic to bees (7).

Bioaccumulation
Calculated bioconcentration factor 0.5 (8).
Reported as having no or low bioaccumulation (9).

Environmental fate

Nitrification inhibition
50% inhibition of ammonia oxidation in *Nitrosomonas* sp. at 70 mg l^{-1} (10).

Degradation studies
Persists in soil for 2-4 wk, breakdown principally by microbial action (7).

Mammalian & avian toxicity

Acute data
LC_{50} oral Japanese quail, ring-necked pheasant >5000 ppm in diet, no mortality in 10- or 12-day old birds (11).
LD_{50} oral rat, mouse 1.1, 2.5 g kg^{-1}, respectively (8,12).
LD_{50} intraperitoneal mouse 200 mg kg^{-1} (13).
LD_{50} percutaneous rat >10,000 mg kg^{-1} (7).

Sub-acute and sub-chronic data
Prolonged feeding study (68 wk) 50 mg kg^{-1} in diet caused enlarged thyroids in ♂ rats after 13 wk (7,14).
Intraperitoneal rat (8-10 wk) 1 g kg^{-1} 3 × wk^{-1} liver effects included reduced activity of catalase and superoxide dismutase and increased GSH level. Heart catalase activity was also decreased (15).
Oral rabbits (43 day) 0.2% in drinking water produced cataractous changes and 50% reduction in iris and ciliary process catalase activity (16).

Carcinogenicity and chronic effects
Inadequate evidence for carcinogenicity to humans, sufficient evidence for carcinogenicity to animals, IARC classification 2B (17).
Oral, subcutaneous rat, mouse (dose unspecified) induced thyroid and liver tumours (18).
Target organs of carcinogenicity: mouse liver, rat thyroid gland (19).

Teratogenicity and reproductive effects
Gavage (8-12 day gestation) ICR/SIM mouse 10 g kg^{-1} total dose Chernoff/Kavlock development toxicity screen non-teratogenic, non-embryotoxic (20).

Genotoxicity

Salmonella typhimurium TA98 negative using prostaglandin H synthase as the activating system and at various pH levels (21).
Salmonella typhimurium TA97, TA98, TA100, TA1535, TA1537 with and without metabolic activation negative (22).
Escherichia coli PQ37 SOS chromotest negative (23).
Mouse C3H/10T1/2 embryonic fibroblasts without metabolic activation negative (24).
L5178Y mouse lymphoma cell forward mutation assay tk+/tk– negative (25).
Drosophila melanogaster wing spot test (48 and 72 hr) positive (26).
Drosophila melanogaster sex-linked recessive lethal assay negative (27).
Aspergillus nidulans mutagenic effects negative (28).

Other effects

Other adverse effects (human)
Studies on Swedish railway workers (1957-78) showed increased incidence of tumours but not corroborated (14).

In a study of 348 railroad workers exposed to amitrole, 5 reported deaths resulted from cancer, including 2 lung cancers, 1 pancreatic cancer, 1 reticulum-cell sarcoma and 1 maxillary sinus cancer, versus 3.3 expected (29).

Any other adverse effects

Following administration of amitrole, rats showed enlarged thyroids with decreasing colloid content and a proliferation of the follicular epithelia (30).

1 g kg^{-1} fed to ♂ rats produced moderate liver necrosis and increased serum glutamic-pyruvic transaminase activity (31).

Antithyroid agent, inhibits liver and kidney catalase (32).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides and related products: maximum admissible concentration 0.1 μg l^{-1} (33).

Included in Schedule 6 (Release Into Land: Prescribed Substances) of Statutory Instrument No. 472, 1991 (34).

Other comments

Reviews on environmental fate, experimental toxicology and human health effects listed (35).

Metabolic pathways reviewed (36).

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A161 ammonia

NH_3

NH_3 **Mol. Wt.** 17.03 **CAS Registry No.** 7664-41-7

EINECS No. 231-635-3 **RTECS No.** BO 0875000

Uses In the manufacture of nitric acid, explosives, synthetic fibres and fertilisers. In refrigeration and as a chemical intermediate in the production of cyanides, amides, nitrates and dyestuffs.

Physical properties

M. Pt. –77.7°C **B. Pt.** –33.4°C (decomp.) **Specific gravity** 0.771 g l^{-1} at 760 mmHg (temperature unspecified)
Volatility v.p. 7600 mmHg at 25.7°C ; v.den. 0.6
Solubility Water: 531 g l^{-1} at 20°C. Organic solvents: chloroform, diethyl ether, ethanol, methanol

Occupational Exposure

DE-MAK 20 ppm (14 mg m^{-3})
FR-VME 25 ppm (18 mg m^{-3}) **FR-VLE** 50 ppm (36 mg m^{-3})
JP-OEL 25 ppm (17 mg m^{-3})
SE-LEVL 25 ppm (18 mg m^{-3}) **SE-CEIL** 50 ppm (35 mg m^{-3})
UK-LTEL 25 ppm (18 mg m^{-3}) **UK-STEL** 35 ppm (25 mg m^{-3})
US-TWA 25 ppm (17 mg m^{-3}) **US-STEL** 35 ppm (24 mg m^{-3})

UN No. 1005 **HAZCHEM Code** 2RE **Conveyance classification** toxic gas, corrosive
Supply classification toxic
Supply classification dangerous for the environment
Risk phrases Flammable – Toxic by inhalation – Causes burns – Very toxic to aquatic organisms (R10, R23, R34, R50)
Safety phrases Keep locked up and out of the reach of children (if sold to general public) – Keep container in a well ventilated place – Keep away from sources of ignition – No smoking – In case of contact with eyes, rinse immediately with plenty of water and seek medical advice – Wear suitable protective clothing, gloves and eye/face protection – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) – Avoid release to the environment. Refer to special instructions/safety data sheet (S1/2, S9, S16, S26, S36/37/39, S45, S61)

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) fathead minnow, goldfish 2.5-8.2 mg l^{-1} (1,2).
LC_{50} (96 hr) rainbow trout 0.53 mg l^{-1} (3).
Goldfish were exposed to 213 mg l^{-1} and 0.91 mg l^{-1}. Fish exposed to 213 mg l^{-1} died within 96 hr. Exposure caused hyperexcitability, hyperventilation, post-mortem investigation showed gill congestion and haemorrhage (4).

LC_{50} (96 hr) 1 and 4 months old spotted seatrout 0.98 and 1.72 mg l^{-1}, respectively (5).
Juvenile rainbow trout (4 wk) exposure to 0.25 mg l^{-1} ammonia. Initial effects recorded were increased ventilation frequency, reduced food intake and decreased weight gain. Rapid adaption took place and no change from exposure to the pollutant could be detected in the number of mucous cells in the epidermis at the end of the experiment (6).
LC_{50} (96 hr) juvenile chinook salmon 0.45 mg l^{-1} in water at 7°C. Ammonia concentration in aquatic sediment was 31 g l^{-1} (7).
A depressed growth-rate was seen in the larvae of red seabream exposed to 0.002 and 0.02 mg l^{-1} un-ionised ammonia for 72 hr. When 3-day-old larvae were exposed to 0.05, 0.08 and 0.15 mg l^{-1} for 24 hr they developed cytoplasmic vacuoles in the chondrocytes (8).
Juvenile gilthead seabream were exposed to ammonia for 20 days. Suppressed growth and reduced survival were observed at 8.2 and 13 mg l^{-1} total ammonia-N. Fish exposed to 13 mg l^{-1} also showed signs of liver pathology (9).
LC_{50} (96 hr) Atlantic salmon 0.031 mg l^{-1} un-ionised ammonia at 2.1°C and pH 6, 0.111 mg l^{-1} at 17.1°C and pH 6, 0.030 mg l^{-1} at 1.8°C and pH 6.4 and 0.146 mg l^{-1} at 12.5°C and pH 6.4 (10).
LC_{50} (96 hr) juvenile inanga 1.60 mg l^{-1} at 15°C and pH ≥8 (11).

Invertebrate toxicity
Ammonia toxicity to *Gammarus lacustris* and *Asellus aquaticus* at room temperature increased with decreasing pH. Synergism of ammonium ion and hydrogen ion toxicity to sodium transport in gills of crustaceans is discussed in relation to water pollution with acids (12).
LC_{50} (96 hr) *Musculium transversum* 1.10 mg l^{-1} (3).
LC_{50} (24, 48, 96, 120 hr) juvenile *Penaeus chinensis* 3.29, 2.10, 1.53 and 1.44 mg l^{-1}, respectively, for un-ionised ammonia as nitrogen by a static renewal method in 33% seawater at pH 7.94 and 26°C. The threshold was found at 120 and 192 hr for ammonia and nitrate, respectively (13).
LC_{50} (48 hr) juvenile grass shrimp 1.2 mg l^{-1} (14).
LC_{50} (48 hr) juvenile killifish 1.6 mg l^{-1} (14).
EC_{50} (5 min) *Photobacterium phosphoreum* 2 mg l^{-1} Microtox test (15).
LC_{50} (24-26 hr) nauplii, zoeae, myses, post-larvae *Penaeus paulensis* 5.49-102.30 mg l^{-1} total ammonia-N (16).
LC_{50} (24-96 hr) juvenile, adult *Penaeus paulensis* 38.72-61.63 mg l^{-1} total ammonia-N (16).
LC_{50} (96 hr) *Rhepoxynius abronius, Eohaustorius estuarius, Ampelisca abdita, Grandidierella japonica* 78.7, 125.5, 49.8, 148.3 mg l^{-1} total ammonia, respectively (17).

Bioaccumulation
32 μg l^{-1} accumulation in channel catfish (18).

Environmental fate

Nitrification inhibition
Synechococcus sp. SF1 isolated from *Sargassum fruitans* was capable of autotrophic growth using ammonia as the sole source of nitrogen; carbonate supplied the carbon source (19).
Nitrobacter sp. ammonia tolerance limit 0.1-1.0 mg l^{-1} dependent on concentration, pH, time of exposure and biomass concentration (20).
Arthrobacter P1 ammonia assimilation involved NADP-dependent glutamate dehydrogenase, NAD-dependent alanine dehydrogenase and glutamine synthetase as key enzymes (21).
At >0.1 mg l^{-1} ammonia significantly inhibited the oxidative activity of the *Nitrobacter* population in a nitrifying biofilm; at <0.1 mg l^{-1} the *Nitrobacter* population rapidly recovered its lost metabolic activity (22).

Abiotic removal
In the atmosphere ammonium ions are oxidised to nitrous oxides and the nitrate ion which represent a significant contribution to acid rain (23).

Adsorption and retention
Ammonia strongly adsorbs to soil and sediment particles and colloids in water (23).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 350 mg kg^{-1} (24).

LC_{50} (1 hr) inhalation rat, mouse, rabbit 3360-7050 mg m^{-3} (23,25,26).

Sub-acute and sub-chronic data

Inhalation rat (3-42 day) 30-150 ppm decreased ability to clear bacteria from lungs and caused encephalopathy (27,28).

Inhalation rat (5-15 day) 25 or 300 ppm 6 hr day^{-1} showed dose-dependent increases of blood ammonia, blood and brain glutamine levels and hepatic citrulline synthesis. High-dose animals exhibited slight acidosis (29).

Carcinogenicity and chronic effects

Rats were treated with 83 mg l^{-1} MNNG for 24 wk then given 0.01% ammonia or tap water as drinking water for another 24 wk. The ammonia-treated animals showed a significantly higher incidence of gastric cancer. The authors conclude that ammonia may be a promoter in *Helicobacter pylori*-related gastric carcinogenesis (30).

Metabolism and toxicokinetics

Foetal uptakes of amino acids and ammonia via umbilical circulation were measured in single pregnant ewes at mid-gestation 66-81 days. Significant net fluxes from placenta to foetus of ammonia and 12 amino acids and net fluxes from foetus to placenta of glutamate and serine took place (31).

Intravenous rat (6 hr) exposure to ammonia increased brain glutamine, decreased brain serotonin (32).

Inhalation rat (5-15 day) 25 ppm increased brain glutamine (33).

Ammonia is normally present in all tissues constituting a metabolic pool. Its distribution is pH-dependent, since NH_3 diffuses more easily that NH_4^+. Ammonia is taken up by glutamic acid in many tissues, and this will take part in a variety of transaminations and other reactions, the nitrogen being incorporated in non-essential amino acids. In the liver, ammonia is used in the synthesis of urea by the Krebs-Henseleit cycle. Mammals excrete urea and secrete ammonium salts in the kidney tubules as a means of hydrogen ion abstraction. Faecal and respiratory excretion are insignificant (34).

Irritancy

Inhalation human (5 min) 134 ppm caused irritation to eyes nose and throat (35).

Caused intradermal irritation in rats, mice and guinea pigs at 0.05%. Produced primary skin irritation in rats and mice at 25% (36).

In humans is an eye irritant and causes lachrymation. Can cause conjunctival oedema, corneal damage and acute glaucoma. Late complications include closed-angle glaucoma, opaque corneal scars, atrophy of the iris and formation of cataracts (37).

Genotoxicity

Escherichia coli without metabolic activation positive (38).

Other effects

Other adverse effects (human)

In two plants in the USSR, workers engaged in the manufacture of carbon fibres by pyrolysis of polyacrylonitrile were exposed to carbon dust and low concentrations of ammonia, hydrogen cyanide, acrylonitrile and carbon monoxide. Occupational diseases of the respiratory tract, skin and eyes reported (39).

Increased rates of skin, laryngeal, gastrointestinal and bronchopulmonary diseases were observed among workers engaged in the manufacture of enzyme preparations by microbial fermentation. The workers were exposed to airborne enzymes protease and pectinase in excess of permissible limits in addition to airborne ammonia and formaldehyde (40).

Eight human subjects were exposed to 2 mg m^{-3} ammonia for 42 days in a closed chamber. Exposure-time related changes were observed in urinary concentrations of adrenaline, noradrenaline, DOPA, dopamine and urea, blood concentrations of histamine, serotonin, urea and activities of acetylcholinesterase, non-specific cholinesterase and ammonia concentration in expired air (41).

Healthy, mature, non-starved brain incorporated 7.22 μg ammonia 100 g^{-1} min^{-1}. In patient suffering from incipient early onset dementia of the Alzheimer type, the brain released 25 μg ammonia 100 g^{-1} min^{-1}. Ammonia may be involved in the morphological changes in astrocytes and in the gliosis observed in early degeneration related to Alzheimer (42).

Any other adverse effects

Exposure of gilts to 35 ppm depressed daily gain for 2 wk, but did not alter the onset of puberty or litter size at day-30 of gestation (43).

Symptoms of exposure include a burning sensation in the eyes, nose and throat, respiratory distress, lachrymation, coughing and increased respiratory rate. Severe exposure can result in laryngeal and pulmonary pneumonia and bronchopneumonia. Symptoms of exposure are usually reversible but chronic bronchitis and bronchiectasis have been reported (species unspecified) (44).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Ammonium: guide level 0.05 mg l^{-1}, maximum admissible concentration 0.5 mg l^{-1} (45).

In the UK the use of ammonia in cosmetics is prohibited by law (37).

Other comments

Produced as a result of farming practices, crude sewage, breakdown of animal and vegetable waste. In fuel emissions-coal, oil, natural gas, wood (18,46-48).

Physical properties, neurotoxicology, metabolism, toxicology, fish toxicity, human health effects, environmental fate and storage reviewed (49-67).

Dilute solutions of ammonia have been used as reflex stimulants either as smelling salts, solutions or oral administration (37).

The impact of ammonia on the environment discussed (68).

Ammonia does not present a direct threat to humans except as a result of accidental exposure, particularly in industry.

Decomposes to hydrogen and nitrogen at high temperatures. Explosion risk.

At neutral pH ammonia exists as its ionic form which is less toxic than ammonia.

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A162 ammonium acetate

$CH_3CO_2NH_4$

$C_2H_7NO_2$ **Mol. Wt.** 77.08 **CAS Registry No.** 631-61-8

Synonyms acetic acid, monoammonium salt; ethanoic acid, ammonium salt

EINECS No. 211-162-9 **RTECS No.** AF 3675000

Uses A diaphoretic and diuretic in pharmaceutical applications. A mordant in dyeing wool. A reagent in analytical chemistry. In preserving meats. In the manufacture of foam rubbers and vinyl plastics.

Physical properties

M. Pt. 114°C **B. Pt.** decomp. **Specific gravity** 1.17 at 20°C with respect to water at 4°C
Solubility Water: 148 g in 100 g at 4°C. Organic solvents: acetone, ethanol

Ecotoxicity

Fish toxicity
LC_{50} (24 hr) mosquito fish 238 mg l^{-1} in fresh water, conditions of bioassay not specified (1).
LC_{50} (48 hr) carp for un-ionised ammonia 1.15-1.06 mg l^{-1} (2).
In a study of cichlids it was concluded that ammonium acetate harmed fish because of its neurotoxic effect. Target organ: muscle (3).

Environmental fate

Nitrification inhibition
NH_3 inhibition of nitrification 436 and 1000 mg l^{-1} (4).

Degradation studies
Treatment of wastewater by activated sludge was facilitated by the presence of 1-50 mg l^{-1} ammonium acetate which prevented sludge bulking when the carbon:nitrogen ratio was low (5).

Mammalian & avian toxicity

Acute data
LD_{50} intravenous mouse 100 mg kg^{-1} (6).
LD_{50} intraperitoneal rat 632 mg kg^{-1} (7).

Other effects

Any other adverse effects
Fifteen minutes after intraperitoneal injection of 7 mmol kg^{-1} of ammonium acetate to rats, the activity of acetylcholinesterase in the brain was reduced. The inhibitory effect varied widely, with a maximum decrease of 60%, and was proportional to the amount of ammonia reaching the brain (8).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Ammonium: guide level 0.05 mg l^{-1}, maximum admissible concentration 0.5 mg l^{-1} (9).

Other comments

Short-term regulation of the urea cycle, the mechanism of ammonia toxicity and clinical implications are discussed (10).

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A163 ammonium arsenate

$$(NH_4)_2HAsO_4$$

$AsH_9N_2O_4$ **Mol. Wt.** 176.00 **CAS Registry No.** 7784-44-3

Synonyms diammonium monohydrogen arsenate; ammonium acid arsenate

EINECS No. 232-067-9 **RTECS No.** CG 0850000

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. 1546 **HAZCHEM Code** 2X **Conveyance classification** toxic substance
Supply classification toxic
Risk phrases May cause cancer – Toxic by inhalation and if swallowed (R45, R23/25)
Safety phrases Restricted to professional users – Avoid exposure – obtain special instruction before use – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S53, S45)

Ecotoxicity

Fish toxicity
Designated non-toxic to trout, bluegill sunfish and goldfish (1).

Mammalian & avian toxicity

Carcinogenicity and chronic effects
Sufficient evidence for carcinogenicity to humans, limited evidence for carcinogenicity to animals, IARC classification group 1 for arsenic and its compounds (2).

Legislation

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

References

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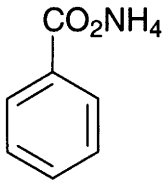
A164 ammonium benzoate



$C_7H_9NO_2$ **Mol. Wt.** 139.15 **CAS Registry No.** 1863-63-4

Synonyms benzoic acid, ammonium salt

EINECS No. 217-468-9 **RTECS No.** DG 3378000

Uses Component in certain rubber formulations. Used to preserve glue and latex. Urinary anti-infective.

Physical properties

M. Pt. 198°C (decomp.) **Specific gravity** 1.26 at 25°C

Solubility Water: 19.6 g in 100 ml at 14°C. Organic solvents: diethyl ether, ethanol, glycerol

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Ammonium: guide level 0.05 mg l^{-1}, maximum admissible concentration 0.5 mg l^{-1} (1).

Other comments

Gradually loses ammonia on exposure to air. Incompatible with ferric salts, acids, alkali hydroxides or carbonates.

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

A165 ammonium bicarbonate

NH_4HCO_3

CH_5NO_3 **Mol. Wt.** 79.06 **CAS Registry No.** 1066-33-7

Synonyms acid ammonium carbonate; ammonium hydrogen carbonate

EINECS No. 213-911-5 **RTECS No.** BO 8600000

Physical properties

M. Pt. 60°C (decomp.) **Specific gravity** 1.586
Solubility Water: 174 g l^{-1} at 20°C. Organic solvents: glycerol

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Ammonium: guide level 0.05 mg l^{-1}, maximum admissible concentration 0.5 mg l^{-1} (1).

Other comments

Anti-fungal activity attributed to ammonium bicarbonate results from concentrations of disassociated free ammonia (2).
Pharmaceutical incompatibility with acids and caustic alkalis (3).

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A166 ammonium bisulfite

$$NH_4HSO_3$$

H_5NO_3S **Mol. Wt.** 99.11 **CAS Registry No.** 10192-30-0
Synonyms ammonium hydrogen sulfite
EINECS No. 233-469-7 **RTECS No.** WT 3595000
Uses Preservative.

Physical properties

Solubility Water: 2670 g l^{-1} at 10°C

Occupational Exposure

UN No. 2693 (aqueous solution) **HAZCHEM Code** 2X **Conveyance classification** corrosive substance (aqueous solution)

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Ammonium: guide level 0.05 mg l^{-1}, maximum admissible concentration 0.5 mg l^{-1} (1).

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

A167 ammonium carbamate

$$NH_2CO_2NH_4$$

$CH_6N_2O_2$ **Mol. Wt.** 78.07 **CAS Registry No.** 1111-78-0

Synonyms ammonium carbaminate; ammonium aminoformate

EINECS No. 214-185-2 **RTECS No.** EY 8575000

Uses Ammoniating agent.

Physical properties

M. Pt. 60°C volatilises

Solubility Water: miscible. Organic solvents: ethanol

Mammalian & avian toxicity

Acute data

LD_{50} intravenous rat, mouse 39, 77 mg kg^{-1}, respectively (1).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Ammonium: guide level 0.05 mg l^{-1}, maximum admissible concentration 0.5 mg l^{-1} (2).

References

1. *Am. J. Vet. Res.* 1968, **29**, 897.
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

A168 ammonium carbonate

$$(NH_4)_2CO_3$$

$CH_8N_2O_3$ **Mol. Wt.** 96.09 **CAS Registry No.** 506-87-6

Synonyms sal volatile; carbonic acid ammonium salt; carbonic acid diammonium salt

EINECS No. 208-058-0 **RTECS No.** BP 1925000

Uses Baking powders, washing and defatting woollens, dyeing, manufacture of rubber articles.

Physical properties

M. Pt. 58°C (decomp.)

Solubility Water: 250 g l^{-1}. Organic solvents: aqueous methanol

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) fathead minnow 37 mg l^{-1} (1).

Invertebrate toxicity
Ammonium carbonate at 5, 10, 25 or 50 mg NH_4^+ l^{-1}. Decreased the fertility of *Daphnia magna* at 50 mg NH_4^+ l^{-1}, disrupted embryonic development at 10, 25 or 50 mg NH_4^+ l^{-1} and impaired post-embryonic growth of the crustacea. Industrial sewage entering fishing waters should contain ≤1 mg NH_4^+ l^{-1} (2).

Mammalian & avian toxicity

Acute data
LD_{50} intravenous mouse 96 mg kg^{-1} (3).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Ammonium: guide level 0.05 mg l^{-1}, maximum admissible concentration 0.5 mg l^{-1} (4).

References

1. Curtis, M. W. et al *J. Hydrol.* 1981, **51**, 359.
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A169 ammonium chloride

NH_4Cl

ClH_4N **Mol. Wt.** 53.49 **CAS Registry No.** 12125-02-9

Synonyms ammonium muriate

EINECS No. 235-186-4 **RTECS No.** BP 4550000

Uses Flux for galvanising and tinning. In dry and Leclanche batteries. Used in the dyeing, tanning and electroplating industries. Detergents. Veterinary expectorant, diaphoretic and acidifying diuretic.

Physical properties

M. Pt. 340°C (sublimes) **B. Pt.** 520°C **Specific gravity** 1.5275 at 25°C **Volatility** v.p. 3.6×10^{-2} mmHg
Solubility Water: 28.3% at 26°C. Organic solvents: ethanol, methanol

Occupational Exposure

FR-VME 10 mg m^{-3} (fume)
UK-LTEL 10 mg m^{-3} (fume) **UK-STEL** 20 mg m^{-3} (fume)
US-TWA 10 mg m^{-3} (fume) **US-STEL** 20 mg m^{-3} (fume)
Supply classification harmful
Risk phrases Harmful if swallowed – Irritating to the eyes (R22, R36)
Safety phrases Keep out of reach of children (if sold to general public) – Do not breathe dust (S2, S22)

Ecotoxicity

Fish toxicity
LC_{50} (48 hr) carp 109 mg l^{-1} (total ammonia), 1.6 mg l^{-1} (un-ionised ammonia) static bioassay (1).

Freshwater fish *Oreochromis mossambicus* exposed to 600 mg l^{-1} for 24 hr showed 100% mortality. No mortality occurred at 400 mg l^{-1} for 96 hr. The LC_{50} was 450 mg l^{-1} for 96 hr exposure (2).

Invertebrate toxicity

Ammonium chloride at 5, 10, 25 or 50 mg NH_4^+ l^{-1}. Decreased the fertility of *Daphnia magna* at 50 mg NH_4^+ l^{-1}, disrupted embryonic development at 10, 25 or 50 mg NH_4^+ l^{-1} and impaired post-embryonic growth of the crustacea. Industrial sewage entering fishing waters should contain ≤1 mg NH_4^+ l^{-1} (3).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 1650 mg kg^{-1} (4).
LD_{Lo} oral rabbit 1000 mg kg^{-1} (5).
LD_{Lo} intravenous guinea pig 240 mg kg^{-1} (6).

Metabolism and toxicokinetics

Following oral administration to ewes, ammonium chloride is rapidly absorbed from the gastrointestinal tract, complete absorption occurring within 3-6 hr (7).
In humans ammonium chloride is absorbed from the gastrointestinal tract. The ammonium ion is converted into urea in the liver; the anion thus liberated into the blood stream and extracellular fluid causes a metabolic acidosis and decreases the pH of the urine, and this is followed by transient diuresis (8).

Other effects

Any other adverse effects

Ewes fed ammonium chloride (dose unspecified) once a day with a mineral-trace element supplement (50 g) for 7-40 days around the time of fertilisation were 100% fertile, as compared with 18% barren for controls, and had on average 17.2% more lambs. Blood calcium, phosphorus and total protein levels were increased by the supplements and blood haemoglobin levels were decreased (9).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Ammonium: guide level 0.05 mg l^{-1}, maximum admissible concentration 0.5 mg l^{-1} (10).

Other comments

Reviews on human health effects, physico-chemical properties and experimental toxicology are listed (11).
Sublimes without melting. Strongly endothermic in water. Incompatible with alkalis and their carbonates, lead and silver salts.

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

A170 ammonium chloroplatinate(IV)

$$(NH_4)_2PtCl_6$$

$Cl_6H_8N_2Pt$ **Mol. Wt.** 443.87 **CAS Registry No.** 16919-58-7

Synonyms ammonium hexachloroplatinate(IV); ammonium platinic chloride; platinic ammonium chloride; ammonium chloroplatinate

EINECS No. 240-973-0 **RTECS No.** BP 5425000

Uses Platinum plating. Manufacture of spongy platinum.

Physical properties

M. Pt. decomp. **Specific gravity** 3.07
Solubility Water: slightly soluble. Organic solvents: insoluble

Occupational Exposure

UK-LTEL MEL 0.002 mg m^{-3} (as Pt)
US-TWA 0.002 mg m^{-3} (as Pt)

Mammalian & avian toxicity

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

Other effects

Other adverse effects (human)
Acute rhinitis, conjunctivitis and bronchial asthma in platinum refinery workers (2,3).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Ammonium: guide level 0.05 mg l^{-1}, maximum admissible concentration 0.5 mg l^{-1} (4).

References

1. Veselov, V. G. *Gig. Tr. Prof. Zabol.*, 1977, (7), 55 (Russ.) (*Chem. Abstr.* **87**, 112601).
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3. Pepys, J. et al *Clin. Allergy* 1972, **2**(4), 39.
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

A171 ammonium chromate

$$(NH_4)_2CrO_4$$

$CrH_8N_2O_4$ **Mol. Wt.** 152.07 **CAS Registry No.** 7788-98-9

Synonyms ammonium chromate(VI)

EINECS No. 232-138-4 **RTECS No.** GB 2880000

Uses Used in textile printing pastes. Sensitising gelatin in photography. Fixer for chromate dyes on wool. Reagent in analytical chemistry.

Physical properties

M. Pt. 185°C (decomp.) **Specific gravity** 1.8
Solubility Water: 198 g l^{-1} at 0°C. Organic solvents: methanol, acetone

Occupational Exposure

FR-VME 0.05 mg m^{-3} (as Cr)
SE-LEVL 0.02 mg m^{-3} (as Cr)
UK-LTEL MEL 0.05 mg m^{-3} (as Cr)
US-TWA 0.05 mg m^{-3} (as Cr)
Supply classification toxic
Supply classification dangerous for the environment
Risk phrases May cause cancer by inhalation – May cause sensitisation by skin contact – Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment (R49, R43, R50/53)
Safety phrases Avoid exposure – obtain special instruction before use – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) – This material and/or its container must be disposed of as hazardous waste – Avoid release to the environment. Refer to special instructions/safety data sheet (S53, S45, S60, S61)

Ecotoxicity

Fish toxicity
LC_{50} (48, 96 hr) mosquito fish 212, 136 ppm, respectively (1).

Invertebrate toxicity
LC_{50} silkworm larva <10 ppm (2).

Bioaccumulation
Trout can accumulate Cr(VI) even at levels of 0.001 ppm. Bioconcentration factor for chromium in marine plants 2000, freshwater and brown algae 100-500, marine invertebrates 2000, marine fish 400 and freshwater fish 200 (1). Bioconcentration factors for Cr(VI) range from 125 to 236 for bivalve molluscs and polychaetes (3).

Environmental fate

Abiotic removal
Up to 300 ppm were removed by all types of soil in column studies; soil pH is a major factor for uptake. Crop damage may result from levels above 0.5 ppm free chromate in soil (1).
Chromium is usually present as Cr(III) in the soil and is characterised by its lack of mobility, except in cases where Cr(VI) is involved. Chromium(VI) of natural origin is rarely found (4).

Mammalian & avian toxicity

Carcinogenicity and chronic effects
Sufficient evidence for carcinogenicity to humans and animals for chromium(VI) compounds, IARC classification group 1 (5).
Chromium salts are human and experimental carcinogens of the lungs, nasal cavity and paranasal sinus and are also experimental carcinogens of the stomach and larynx (6).
Cancer-causing chromium exposure has been attributed to industrial processes involving ammonium chromate (7).

Metabolism and toxicokinetics
In the airways and in the gastrointestinal tract, soluble Cr(VI) compounds are apparently taken up by epithelial cells, by simple diffusion, through the plasma membrane. After entry, Cr(VI) reduction occurs by enzymatically

mobilised electrons, available from GSH, NADPH and NADH. The reducing capacity inside the cell is limited, so that Cr(VI) and Cr(III) exist simultaneously inside the cytoplasm; Cr(VI) is then released from the cell by simple diffusion into the bloodstream and taken up into blood cells. Unlike the trivalent compounds, those of Cr(VI) tend to cross biological membranes fairly easily and are somewhat more readily absorbed through the gut or the skin (3).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Chromium: maximum admissible concentration 50 $\mu g\ l^{-1}$ (8).
Included in Schedule 6 (Release into Land: Prescribed Substances) of Statutory Instrument No. 472, 1991 (9).

Other comments

Chromium(VI) detected in industrial effluent from chromate manufacturing processes and landfill sites (3).
Background ambient air concentrations of total chromium have ranged from as low as 0.005 ng m^{-3} (at the South Pole) to 1.1 ng m^{-3} in other remote areas of the world. Because Cr(III) is highly stable and Cr(VI) reacts over time to form Cr(III), it is assumed that most chromium in ambient air occurs in the trivalent state (3).
Detected in drinking water, ground water in US and Canada (4).

References

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

A172 ammonium dichromate

$$(NH_4)_2Cr_2O_7$$

$Cr_2H_8N_2O_7$ **Mol. Wt.** 252.07 **CAS Registry No.** 7789-09-5

Synonyms ammonium bichromate(VI)

EINECS No. 232-143-1 **RTECS No.** HX 7650000

Uses Used in pyrotechnics, lithography and photoengraving. Mordant. Catalyst. Used in porcelain finishes. Intermediate in the manufacture of pigments. Magnetic recording materials. Source of pure nitrogen.

Physical properties

M. Pt. 180°C (decomp.) **Specific gravity** 2.15 **Volatility** v.den. 8.7
Solubility Water: 27% at 20°C. Organic solvents: ethanol

Occupational Exposure

FR-VME 0.05 mg m^{-3} (as Cr)
SE-LEVL 0.02 mg m^{-3} (as Cr)

UK-LTEL MEL 0.05 mg m^{-3} (as Cr)
US-TWA 0.05 mg m^{-3} (as Cr)

UN No. 1439 **HAZCHEM Code** 2X **Conveyance classification** oxidising substance
Supply classification explosive
Supply classification very toxic
Supply classification dangerous for the environment
Risk phrases May cause cancer by inhalation – May cause heritable genetic damage – Explosive when dry – Contact with combustible material may cause fire – Harmful in contact with skin – Toxic if swallowed – Very toxic by inhalation – Irritating to respiratory system and skin – Risk of serious damage to eyes – May cause sensitisation by skin contact (R49, R46, R1, R8, R21, R25, R26, R37/38, R41, R43)
Safety phrases Avoid exposure – obtain special instruction before use – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) – This material and/or its container must be disposed of as hazardous waste – Avoid release to the environment. Refer to special instructions/safety data sheet (S53, S45, S60, S61)

Ecotoxicity

Fish toxicity
LC_{50} (48, 96 hr) mosquito fish 212-136 ppm, respectively (1).

Bioaccumulation
Trout can accumulate Cr(VI) even at levels of 0.001 ppm. Bioconcentration factors for chromium in marine plants 2000, freshwater and brown algae 100-500, marine invertebrates 2000, marine fish 400, freshwater fish 200 (1). Bioconcentration factors for Cr(VI) range from 125 to 236 for bivalve molluscs and polychaetes (2).

Environmental fate

Abiotic removal
Up to 300 ppm were removed by all types of soil in column studies, soil pH is a major factor for uptake. Crop damage may result from levels above 0.5 ppm free chromate in soil (1).
Chromium is present usually as Cr(III) in the soil and is characterised by its lack of mobility, except in cases where Cr(VI) is involved. Chromium(VI) of natural origin is rarely found (3).

Mammalian & avian toxicity

Acute data
LD_{50} intravenous rat 30 mg kg^{-1} (4,5).
LD_{Lo} subcutaneous guinea pig 25 mg kg^{-1} (4).

Sub-acute and sub-chronic data
Inhalation rat (1-6 month) dust at 1 mg m^{-3} for 2 hr 3 × wk^{-1} caused disturbances in the blood circulation in lungs and emphysema in the perivascular and peribronchial tissues (6).
Inhalation rat (6 month) 0.05 mg m^{-3} 2 hr every other day caused papillary growths in the bronchi, and in some cases pneumonia (7).

Carcinogenicity and chronic effects
Pre-cancerous changes were reported in rats pre-treated with a non-carcinogenic dose of benzo[*a*]pyrene, following intrapleural administration of 0.5-1.0 μg m^{-3} ammonium dichromate, 2 hr day^{-1}, 3 × wk^{-1} for 18 months (8).

Metabolism and toxicokinetics
In the airways and in the gastrointestinal tract, soluble Cr(VI) compounds are apparently taken up by epithelial cells, by simple diffusion, through the plasma membrane. After entry, Cr(VI) reduction occurs from the action of enzymatically mobilised electrons, available from GSH, NADPH and NADH. The reducing capacity inside the cell is limited, so that Cr(VI) and Cr(III) exist simultaneously inside the cytoplasm; Cr(VI) is then released from the cell by simple diffusion into the bloodstream and taken up into blood cells (4).

Irritancy

Causes skin irritation, ulceration ("chrome sores"), perforation of nasal septum, and pulmonary irritation (4).

Other effects

Other adverse effects (human)

If swallowed prompts vomiting, but if retained leads to kidney injury and stomach ulceration. Unlike the trivalent compounds, those of Cr(VI) tend to cross biological membranes fairly easily and are more readily absorbed through the gut or the skin (4).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Chromium: maximum admissible concentration 50 $\mu g\ l^{-1}$ (9).

Included in Schedule 6 (Release into Land: Prescribed Substances) of Statutory Instrument No. 472, 1991 (10).

Other comments

Detected in drinking water, ground water in US and Canada (4-11).

Chromium(VI) detected in industrial effluent from chromate manufacturing processes and landfill sites (4).

Background ambient air concentrations of total chromium have ranged from as low as 0.005 ng m^{-3} (at the South Pole) to 1.1 ng m^{-3} in other remote areas of the world. Because Cr(III) is highly stable and Cr(VI) reacts over time to form Cr(III), it is assumed that most chromium in ambient air occurs in the trivalent state (4).

Flammable self-sustaining decomposition at 225°C with swelling and evolution of heat and nitrogen, leaving chromic(III) oxide (12).

Reviews on human health effects, physico-chemical properties, ecotoxicology, environmental effects and experimental toxicology listed (13).

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A173 ammonium fluoride

NH_4F

FH_4N **Mol. Wt.** 37.04 **CAS Registry No.** 12125-01-8

Synonyms neutral ammonium fluoride

EINECS No. 235-185-9 **RTECS No.** BQ 6300000

Uses Laboratory reagent. Etching and frosting glass. Preserving wood. Printing and dyeing.

Physical properties

M. Pt. 125.6°C **Specific gravity** 1.009 at 25°C
Solubility Water: 453 g l^{-1} at 25°C. Organic solvents: ethanol

Occupational exposure

DE-MAK 2.5 mg m^{-3} (as F) (inhalable dust fraction)
FR-VME 2.5 mg m^{-3} (as F)
SE-LEVL 2 mg m^{-3} (as F)
UK-LTEL 2.5 mg m^{-3} (as F)
US-TWA 2.5 mg m^{-3} (as F)

UN No. 2505 **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) – In case of contact with eyes, rinse immediately with plenty of water and seek medical advice – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S26, S45)

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) silver carp 1.6 ppm. 100 ppm caused 70% inhibition of cholinesterase activity. Teratogenicity reported in white amur grass carp exposed to 15 ppm fluoride (1).

LC_{50} (96 hr) silver carp, white amur grass carp, carp 1.6, 9.3 and 11.8 ppm, respectively. 70 ppm induced the formation of micronuclei erythrocytes in carp and amitosis in the cell. Inhibitory effects on the activity of cholinesterase in fish. 100 ppm caused a 70% inhibition, and at 10 ppm caused a 20% inhibition of the enzyme activity. Teratogenicity was found when eggs were hatched and young fish were kept in water containing 15 ppm fluoride. In teratomatous fish, maximum bone fluoride contents were found to be 9608 ppm, which was 100-300-fold higher than the values found in the bones of normal fish (1).

LC_{50} (96 hr) fathead minnow 364 mg l^{-1} (2).

Invertebrate toxicity

LC_{50} (96 hr) grass shrimp 75 mg l^{-1} (2).

LC_{50} silkworm larva <15 ppm (3).

Mammalian & avian toxicity

Acute data

LD_{50} intraperitoneal rat 32 mg kg^{-1} (4).

Metabolism and toxicokinetics

Fluorides are absorbed from the gastro-intestinal tract, lungs and skin with the gastro-intestinal tract being the major site of absorption. Fluoride is preponderantly deposited in the skeleton and teeth and the degree of skeletal storage is related to intake and age. Major route of excretion is via kidneys. Also excreted in small amounts by

sweat glands, breast milk and the gastrointestinal tract. About 90% of fluoride ion filtered by glomerulus is re-absorbed by renal tubules (5,6).
Following ingestion, soluble fluorides are rapidly absorbed from the gastrointestinal tract at least to the extent of 97%. Absorbed fluoride is distributed throughout the tissues of the body by the blood. Fluoride concentrations in soft tissues fall to pre-exposure levels within a few hours of exposure. Fluoride exchange with hydroxyl groups of hydoxyapatite (the inorganic constituent of bone) to form fluorohydroxyapatite. Fluoride that is not retained is excreted rapidly in urine (6).

Other effects

Other adverse effects (human)
Ingestion causes nausea, vomiting, diarrhoea and abdominal pains. Chronic effects include shortness of breath, cough, elevated temperature and cyanosis (4).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Ammonium: guide level 0.05 mg l^{-1}, maximum admissible concentration 0.5 mg l^{-1} (7).

Other comments

Reviews on human health effects, physico-chemical properties and experimental toxicology listed (8).
Corrodes glass. On heating decomposes to ammonia and hydrogen fluoride.

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A174 ammonium fluorosilicate

$$(NH_4)_2SiF_6$$

$F_6H_8N_2Si$ **Mol. Wt.** 178.15 **CAS Registry No.** 16919-19-0

Synonyms ammonium silicofluoride; ammonium hexafluorosilicate; silicate(2–), hexafluoro-, diammonium; diammonium hexafluorosilicate; cryptohalite; ammonium fluosilicate; diammonium fluosilicate

EINECS No. 240-968-3 **RTECS No.** VV 7800000

Uses Used in the manufacture of pesticides. Soldering flux. Etching glass.
Occurrence In nature as the mineral cryptohalite.

Physical properties

M. Pt. 120°C (decomp.) **Specific gravity** 2.01
Solubility Water: 181 g l^{-1} at 17°C

Occupational exposure

SE-LEVL 2 mg m^{-3} (as F)
UK-LTEL 2.5 mg m^{-3} (as F)

UN No. 2854 **HAZCHEM Code** 2Z **Conveyance classification** toxic substance
Supply classification toxic
Risk phrases Toxic by inhalation, in contact with skin and if swallowed (R23/24/25)
Safety phrases Keep locked up and out of the reach of children (if sold to general public) – In case of contact with eyes, rinse immediately with plenty of water and seek medical advice – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S26, S45)

Ecotoxicity

Fish toxicity
Exposure of steelhead trout and bridgelip sucker to 10 mg l^{-1} in a static 24 hr bioassay resulted in neither death nor loss of equilibrium in either species (1).
Exposure of threespine stickleback to 10 mg l^{-1} in a 24 hr bioassay resulted in loss of equilibrium within 1-2 hr and death in 6-24 hr (2).

Invertebrate toxicity
LD_{50} oral silkworm larvae >10 ppm (3).

Toxicity to other species
LD_{Lo} subcutaneous frog 224 mg kg^{-1} (4).

Mammalian & avian toxicity

Acute data
LD_{Lo} oral rat 100 mg kg^{-1} (5).
LD_{50} intragastric rat, mouse 45-64 mg kg^{-1} (6).

Metabolism and toxicokinetics
Following ingestion, soluble fluorides are rapidly absorbed from the gastrointestinal tract at least to the extent of 97%. Absorbed fluoride is distributed throughout the tissues of the body by the blood. Fluoride concentrations in soft tissues fall to pre-exposure levels within a few hours of exposure. Fluoride exchange with hydroxyl groups of hydroxyapatite (the inorganic constituent of bone) to form fluorohydroxyapatite. Fluoride that is not retained is excreted rapidly in urine (7).

Irritancy
50 mg instilled into rabbit eye caused severe corneal damage after 3 hr, while weak hyperaemia was observed after skin contact in rabbits (6).

Other effects

Other adverse effects (human)
In the manufacture of ammonium fluorosilicate, workers are exposed to air pollution by hydrogen fluoride, fluorosilicate and aerosols containing ammonium fluorosilicate. The urine of exposed workers showed the presence of fluoride. Exposure to ammonium fluorosilicate was associated with disorders of the nervous system and liver function (8).
The dust is irritating to the respiratory tract and inhalation may be fatal due to spasm. Symptoms of acute exposure include inflammation and oedema of the larynx and bronchi, chemical pneumonitis and pulmonary oedema. Chronic effects include coughing, sore throat, dyspnoea, headache, nausea and vomiting (9).

Any other adverse effects
Minimum toxic concentration inhalation (4 hr) rat 7.4-9.6 mg m^{-3}, non-toxic concentration 0.8 mg m^{-3}. Main toxic effects were decreases in the number of blood cells and decreased activities of cholinesterase and lactate dehydrogenase in blood serum (6).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Ammonium: guide level 0.05 mg l^{-1}, maximum admissible concentration 0.5 mg l^{-1} (10).

Other comments

Reviews on human health effects, experimental toxicology and physico-chemical properties listed (11). Serves as preservative in impregnation of prefabricants used for house building (12).

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A175 ammonium hydrogen difluoride

$$NH_4HF_2$$

F_2H_5N **Mol. Wt.** 57.04 **CAS Registry No.** 1341-49-7

Synonyms ammonium bifluoride; ammonium acid difluoride; ammonium hydrogen fluoride

EINECS No. 215-676-4 **RTECS No.** BQ 9200000

Uses Aluminium anodising. Corrosion resisting treatment of magnesium and its alloys. Sterilising dairy and other food equipment. Solubilising silica. Textiles. Wood preservative.
Occurrence Manufactured by gas-phase reaction of anhydrous ammonia and anhydrous hydrogen fluoride.

Physical properties

M. Pt. 125°C **B. Pt.** 239.5°C **Specific gravity** 1.51
Solubility Water: 415 g l^{-1} at 25°C. Organic solvents: ethanol

Occupational exposure

DE-MAK 2.5 mg m^{-3} (as F) (total dust)
FR-VME 2.5 mg m^{-3} (as F)

SE-LEVL 2 mg m^{-3} (as F)
UK-LTEL 2.5 mg m^{-3} (as F)
US-TWA 2.5 mg m^{-3} (as F)

UN No. 1727 (solid); 2817 (solution) **HAZCHEM Code** 2X **Conveyance classification** corrosive substance (solid); corrosive substance, toxic substance (solution)
Supply classification toxic, corrosive
Risk phrases Toxic if swallowed – Causes burns (R25, R34)
Safety phrases Keep locked up and out of the reach of children (if sold to general public) – Do not breathe dust – In case of contact with eyes, rinse immediately with plenty of water and seek medical advice – Wear suitable gloves – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S22, S26, S37, S45)

Environmental fate

Nitrification inhibition
Fluoride ions caused 10% inhibition of nitrification on biological film reactor at 135 mg F l^{-1} (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral guinea pig 150 mg kg^{-1} (2).

Metabolism and toxicokinetics
Fluorides are absorbed from the gastrointestinal tract, lungs and skin with the gastrointestinal tract being the major site of absorption. Fluoride is preponderantly deposited in the skeleton and teeth and the degree of skeletal storage is related to intake and age. Major route of excretion is via kidneys. Also excreted in small amounts by sweat glands, breast milk and the gastrointestinal tract. About 90% of fluoride ion filtered by glomerulus is re-absorbed by renal tubules (3).
Following ingestion, soluble fluorides are rapidly absorbed from the gastrointestinal tract at least to the extent of 97%. Absorbed fluoride is distributed throughout the tissues of the body by the blood. Fluoride concentrations in soft tissues fall to pre-exposure levels within a few hours of exposure. Fluoride exchanges with hydroxyl groups of hydroxyapatite (the inorganic constituent of bone) to form fluorohydroxyapatite (4).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Ammonium: guide level 0.05 mg l^{-1}, maximum admissible concentration 0.5 mg l^{-1} (5).

Other comments

Reviews on human health effects, experimental toxicology and physico-chemical properties listed (6).

References

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A176 ammonium hydroxide

NH_4OH

H_5NO **Mol. Wt.** 35.05 **CAS Registry No.** 1336-21-6

Synonyms ammonia water; aqua ammonia

EINECS No. 215-647-6 **RTECS No.** BQ 9625000

Uses Detergent. Stain remover. Bleaching agent in calico printing. Manufacture of ammonium salt and aniline dyestuffs.

Physical properties

M. Pt. –77°C **Specific gravity** 0.947 (aqueous ammonia) at 15°C

Occupational exposure

UN No. 2073 (35-50% NH_3)

UN No. 2672 (10-35% NH_3)

UN No. 1006 (≥50% NH_3) **HAZCHEM Code** 2RE (35-50% NH_3) **HAZCHEM Code** 2P (10-35% NH_3) **HAZCHEM Code** 2RE (≥50% NH_3) **Conveyance classification** non-flammable non-toxic gas (35-50% NH_3) **Conveyance classification** corrosive substance (10-35% NH_3) **Conveyance classification** toxic gas, corrosive (≥50% NH_3)

Supply classification corrosive

Supply classification harmful for the environment

Risk phrases Causes burns – Very toxic to aquatic organisms (R34, R50)

Safety phrases Keep locked up and out of the reach of children (if sold to general public) – In case of contact with eyes, rinse immediately with plenty of water and seek medical advice – Wear suitable protective clothing, gloves and eye/face protection – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) – Avoid release to the environment. Refer to special instructions/safety data sheet (S1/2, S26, S36/37/39, S45, S61)

Ecotoxicity

Fish toxicity

LC_{50} (48 hr) bluegill sunfish 0.024-0.093 mg l^{-1} (1).

LC_{50} (7 day) channel catfish 0.974-1.97 mg l^{-1}. Temperature range 21.1-22.8°C, pH range 7.7-8.0 (2).

LC_{50} (96 hr) fathead minnow 8.2 mg l^{-1} (3).

LC_{50} (24 hr) Atlantic salmon smolt 5-8 mg l^{-1} (4).

LC_{50} (24 hr) chinook salmon 2.2 mg NH_3 l^{-1} (9.6% salinity) (5).

Invertebrate toxicity

EC_{50} (48 hr) *Daphnia magna* 0.66 mg l^{-1} at 22°C (6).

EC_{50} (120 hr) diatom 420 mg l^{-1} 50% growth reduction hard and soft water at 22°C (6).

LC_{50} (96 hr) snail 90 mg l^{-1} in soft water at 20°C (6).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 350 mg kg^{-1} (7).

LC_{50} (1 hr) inhalation rat 7338 ppm (8).

Irritancy

A 10% solution of ammonium hydroxide was tested by applying 100 µl into the lower conjunctival sac of rabbits.

The mean surface of corneal damage was 98 (maximum 100) after 4 hr and 70 after 96 hr. The mean score of corneal opacity was 2 (maximum 4) after 4 hr and 4 after 96 hr (9).

Other effects

Other adverse effects (human)

Ingestion causes severe pain in the mouth, throat and gastrointestinal tract, severe local oedema and salivation with coughing, vomiting and shock. Burns to the oesophagus and stomach may result in perforation (10).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Ammonia: guide level 0.05 mg l^{-1}, maximum admissible concentration 0.5 mg l^{-1} (11).

Other comments

Reviews on human health effects and experimental toxicology listed (12).

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A177 ammonium metavanadate

$$NH_4VO_3$$

H_4NO_3V **Mol. Wt.** 116.98 **CAS Registry No.** 7803-55-6

Synonyms ammonium vanadate; vanadic acid, ammonium salt

EINECS No. 232-261-3 **RTECS No.** YW 0875000

Uses Catalyst. Dyeing and printing. Photographic developer. Producing vanadium lustre on pottery. Reagent in analytical chemistry.

Physical properties

M. Pt. 200°C (decomp.) **Specific gravity** 2.33

Solubility Water: 6 g l^{-1}

Occupational exposure

UN No. 2859 **HAZCHEM Code** 1Z **Conveyance classification** toxic substance

Ecotoxicity

Fish toxicity

LC_{50} (144 hr) goldfish, guppy 1.5-3.8 ppm (1).

Bioaccumulation

Studies of vanadium transfer and accumulation to molluscs revealed that the type of absorption of vanadium was dependent on species; work on marine bacteria, phytoplankton, invertebrates, crustaceans and fish showed that direct absorption of vanadium from water was more important than by feeding. Vanadium uptake rates in a mussel varied inversely with both salinity and vanadium concentration in water (2).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 160 mg kg^{-1} (3).

LD_{100} subcutaneous guinea pig 3 mg kg^{-1} (4).

LD_{100} intravenous rabbit 3 mg kg^{-1} (4).

Sub-acute and sub-chronic data

♂ and ♀ Wistar rats were given an aqueous solution of ammonium metavanadate containing 0.01, 0.05, 0.15 or 0.30 mg of V ml^{-1} as their sole drinking liquid for 4 wk. All animals given the two higher doses showed a significant decrease in their uptake of food and liquid compared to controls, and a distinct decrease of L-ascorbic acid in the liver, kidneys, spleen and adrenals. The latter was also noted in single cases of animals receiving the two lower doses (5).

♂ Wistar rats were given an aqueous solution of ammonium metavanadate equivalent to 0.15 mg V ml^{-1} instead of water for 14 days. The haematocrit index was slightly increased but the erythrocyte count and Hb level in the blood remained the same. Spontaneous lipid peroxidation in kidney and liver homogenates was increased; no change was seen in lipid peroxidation in erythrocytes. The treatment also resulted in a decrease in the activity of catalase and glutathione peroxidase in the kidney and liver. The activity of blood enzymes was unchanged (6).

In rats exposed to 2 mg m^{-3} of vanadium as ammonium metavanadate (AMV) (0.32 μm diameter) for 8 hr day^{-1} for 4 days in a nose-only exposure system, lung vanadium-burdens increased in a time-dependent manner and lung immune responses were modulated. A major target was the pulmonary alveolar macrophages (PAM) with a <15 μm diameter and significant immunotoxicity occurred at the level of PAM cytokine related function (7).

Teratogenicity and reproductive effects

The exposure of pregnant Syrian golden hamsters to ammonium metavanadate from days 5-10 of gestation resulted in a significant increase in skeletal anomalies and a decrease in the male:female foetal sex ratio. Skeletal anomalies included micrognathia, supernumerary ribs, and alterations in sternebral ossification. Although not significant, external anomalies included meningocoele, one foetus with multiple anomalies, and the presence of a molar pregnancy. Soft tissue anomalies did not differ significantly among groups but included hydronephrosis/hydroureter and kidney dysplasia. The numbers of malformed offspring were small, and there was no dose-response relationship (8).

Metabolism and toxicokinetics

Absorbed vanadium is widely distributed in the body. In animals the highest values are found in bone, kidney, liver, spleen and, after intratracheal instillation, in lung. Bone maintains essentially unchanged levels for several weeks. The lowest values are found in the brain (9).

Genotoxicity

Bacillus subtilis gene conversion and mitotic recombination positive (10,11).

Saccharomyces cerevisiae D61M induced aneuploidy (12).

In vitro Chinese hamster V79 cells with and without metabolic activation negative. Potent cytotoxic agent (12).

In vitro Chinese hamster ovary cells with and without metabolic activation sister chromatid exchange positive (13).

Other effects

Other adverse effects (human)

An increased incidence of bronchopulmonary diseases such as infections and lung cancer are observed in workers exposed to atmospheres that contain vanadium compounds (7).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Ammonium: guide level 0.05 mg l^{-1}, maximum admissible concentration 0.5 mg l^{-1} (14).

Other comments

Vanadium compounds, when absorbed, are rapidly excreted and exhibit low degrees of toxicity, as indicated by minor irritation and lack of systemic effects (15).

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A178 ammonium nitrate

$$NH_4NO_3$$

$H_4N_2O_3$ **Mol. Wt.** 80.04 **CAS Registry No.** 6484-52-2

Synonyms ammonium saltpeter

EINECS No. 229-347-8 **RTECS No.** BR 9050000

Uses Oxidising agent. Used in the manufacture of nitrous oxide. Explosive. Fertiliser. Anaesthetic.

Physical properties

M. Pt. 210°C (decomp.) **B. Pt.** decomposes at about 210°C **Specific gravity** 1.725 at 20°C with respect to water at 4°C

Solubility Water: 2000 g l^{-1}. Organic solvents: acetone, ethanol, methanol

Occupational exposure

UN No. 1942 (<0.2% combustible substances) **HAZCHEM Code** 1Y **Conveyance classification** oxidising substance

Ecotoxicity

Invertebrate toxicity

Ammonium nitrate at 5, 10, 25 or 50 mg NH_4^+ l^{-1} decreased the fertility of *Daphnia magna* at 50 mg NH_4^+ l^{-1}. Disrupted embryonic development, and at 10, 25 or 50 mg NH_4^+ l^{-1} impaired post-embryonic growth of the crustacea. Industrial sewage entering fishing waters should contain ≤1 mg NH_4^+ l^{-1} (1).

The nematodes *Aphelenchus avenae, Meloidogyne incognita* and *Ditylenchus dipsaci* isolated from mushroom *Fusarium graminearum* mycelia, cucumber roots and onions, respectively, had decreased body dimensions when the plants were fertilised with ammonium nitrate. Egg laying was also decreased in *Aphelenchus avenae*. Various morphophysiological changes in these nematodes under the above fertiliser conditions are discussed (2).

LC_{50} (40 hr) *Aspergillus niger* 15 mg l^{-1} 36°C (3).

Environmental fate

Degradation studies

Ammonium nitrate will be taken up by bacteria. Nitrate is more persistent in water than the ammonium ion. Nitrate degradation is fastest in anaerobic conditions (4).

Abiotic removal

The immediate loss of fertiliser nitrogen as nitrous oxide (by biochemical and microbiological action) into the atmosphere was determined by *in situ* measurements of the nitrous oxide evolution rates from uncultivated Eolian sand. The net loss was equivalent to 0.05% for ammonium nitrate. The total immediate loss of nitrous oxide-nitrogen after application of mineral fertiliser is estimated to be 0.004-1.2 teragram yr^{-1} (5).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 4820 mg kg^{-1} (6).

Metabolism and toxicokinetics

12 healthy volunteers ingested orally 7-10.5 g ammonium nitrate in a single dose. Samples of blood, saliva and urine were collected just before a 24 hr period. Saliva and urine were analysed for volatile *N*-nitrosamines (NA), nitrate and nitrite. Blood was analysed for nitrate. Neither in urine nor in saliva were NA other than *N*-nitrosodiethylamine (NDMA) detected. Of the 188 urine samples, 13% contained >0.1 mg NDMA kg^{-1}, the highest level being 0.5 μg kg^{-1}. In 92% of the 179 saliva samples, <0.5 μg NDMA l^{-1} was found. Nitrite was detected in 26% of the urine samples. An average of 75% of administered nitrate was excreted in urine in 24 hr. Nitrate contents in blood, urine and saliva after 24 hr were still higher than before the nitrate intake (7).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Ammonia: guide level 0.05 mg l^{-1}, maximum admissible concentration 0.5 mg l^{-1} (8).

Included in Schedule 6 (Release Into Land: Prescribed Substances) of Statutory Instrument No. 472, 1991 (9).

Other comments

Reviews on human health effects, experimental toxicology and environmental effects listed (10).

References

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2. Zinoveva, S. V. et al *Tr. Gel'mintol. Lab. Akad. Nauk SSSR* 1980, **30**, 5-19.
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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.
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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

A179 ammonium oxalate

$$HO_2CCO_2NH_4$$

$C_2H_5NO_4$ **Mol. Wt.** 107.07 **CAS Registry No.** 5972-73-6

EINECS No. 238-135-4

Physical properties

M. Pt. decomposes **B. Pt.** 240-273°C **Flash point** 118°C **Specific gravity** 1.5
Solubility Water: 25.4 g l^{-1} at 0°C

Environmental fate

Degradation studies

Using ammonium oxalate as the sole carbon source 92.5% was degraded at 9.3 mg COD g^{-1} dry inoculum hr^{-1} by adapted activated sludge (1).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Ammonium: guide level 0.05 mg l^{-1}, maximum admissible concentration 0.5 mg l^{-1} (2).

References

1. Pitter, P. *Water Res.* 1976, **10**, 231-235.
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

A180 ammonium perfluorooctanoate

$$F_3C(CF_2)_6CO_2NH_4$$

$C_8H_4F_{15}O_2N$ **Mol. Wt.** 431.10 **CAS Registry No.** 3825-26-1

Synonyms pentadecafluorooctanoic acid, ammonium salt

EINECS No. 223-320-4 **RTECS No.** RH 0782000

Uses Surfactant. Dispersant for manufacture of powdered poly(tetrafluoroethylene).

Occupational exposure

US-TWA 0.01 mg m^{-3}

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 430 mg kg^{-1} (1).

LC_{50} inhalation (4 hr) rat 980 mg m^{-3}. This concentration produced both an increase in liver size and corneal opacity (2).

LD_{50} dermal rabbit 4300 mg kg^{-1} (3).

Sub-acute and sub-chronic data

Inhalation (2 wk) rat 0, 1, 8 or 84 mg m^{-3} exposure for 6 hr day^{-1}, 5 days wk^{-1}. Suppressed body weight gain observed at 84 mg m^{-3}. Reversible liver weight increases, reversible increases in serum enzyme activities and microscopic liver pathology including necrosis occurred at exposures of 8 and 84 mg m^{-3}. No ocular changes were produced. Concentrations of organofluoride in the blood showed a dose relation with initial levels of 108 ppm in rats treated with 84 mg m^{-3} falling to 0.84 ppm after 84 days with a blood $t_{1/2}$ of 5-7 days. The no-observed-effect level was 1 mg m^{-3} and a mean organofluoride blood level of 13 ppm was detected in rats immediately after 10th exposure to an atmospheric level of 1 mg m^{-3} (2).

Mouse (14 or 21 days) ≥3 ppm in diet increased the weight of mouse liver in a dose-dependent manner (4).

Teratogenicity and reproductive effects

Inhalation rat (6-15 days gestation) 0, 0.1, 1, 10 and 25 mg m^{-3} 6 hr day^{-1} or by gavage 100 mg kg^{-1} day^{-1} in corn oil. Maternal deaths occurred in the groups given highest levels by each route and overt toxicity was evident among the surviving dams and among those of the 10 mg m^{-3} group. No teratogenic responses were demonstrated (5).

Irritancy

0.5 g applied to rabbit skin for 24 hr caused mild irritation (3).

Other effects

Any other adverse effects

Total hepatic DNA content was similar in control and ammonium perfluorooctanoate treated rats, therefore hepatomegaly represented a hypertrophic rather than a hyperplastic response. Cytochrome P450 content and activity of benzphetamine *N*-demethylase increased in the livers of treated rats, indicating the proliferation of the smooth endoplasmic reticulum. Glutathione *S*-transferase and UDP-glucuronyltransferase were unaffected. Morphological studies confirmed the proliferation of the endoplasmic reticulum, mitochondria and peroxisomes in the livers of treated animals. Ammonium perfluorooctanoate does not possess hypolipidaemic activity (6).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Ammonium: guide level 0.05 mg l^{-1}, maximum admissible concentration 0.5 mg l^{-1} (7).

Other comments

Reviews on experimental toxicology, workplace experience and human health effects listed (8).

References

1. *Am. Ind. Hyg. Assoc. J.* 1980, **41**, 576.
2. Kennedy, G. L. et al *Food Chem. Toxicol.* 1986, **24**(12), 1325-1329.
3. Kennedy, G. L. *Toxicol. Appl. Pharmacol.* 1985, **81**(2), 348-355.
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7. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
8. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

A181 ammonium peroxydisulfate

$$(NH_4)_2S_2O_8$$

$H_8N_2O_8S_2$ **Mol. Wt.** 228.20 **CAS Registry No.** 7727-54-0

Synonyms ammonium persulfate; diammonium peroxodisulfate

EINECS No. 231-786-5 **RTECS No.** SE 0350000

Uses Agent for bleaching foodstuffs. Water purification treatment. Reducer and retarder in photography. In the manufacture of aniline dyestuffs. In etching and metal cleaning. Maturing agent for wheat flour. For the detection and determination of manganese.

Physical properties

M. Pt. 120°C (decomp.) **Specific gravity** 1.982
Solubility Water: 794 g l^{-1} at 20°C

Occupational exposure

UK-LTEL 1 mg m^{-3} (as $[S_2O_8]$)
US-TWA 0.1 mg m^{-3}

UN No. 1444 **HAZCHEM Code** 2W **Conveyance classification** oxidising substance
Supply classification oxidising, harmful
Risk phrases Contact with combustible material may cause fire – Harmful if swallowed – Irritating to eyes, respiratory system and skin – May cause sensitisation by inhalation and skin contact (R8, R22, R36/7/38, R42/43)
Safety phrases Keep out of reach of children (if sold to the general public) – Do not breathe dust – Avoid contact with the skin – In case of contact with eyes, rinse immediately with plenty of water and seek medical advice – Wear suitable gloves (S2, S22, S24, S26, S37)

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 820 mg kg^{-1} (1).

Carcinogenicity and chronic effects

Dermal ♀ Sencar mice (1 yr) 5 μg diluted in 0.2 ml acetone, administered 2 × wk^{-1} 2/20 mice developed skin tumours. The authors conclude ammonium persulfate was inactive as a promoter or complete carcinogen (2).

Other effects

Any other adverse effects

Ammonium persulfate inhibited intracellular uptake of calcium and accelerated calcium release, thus raising the cytosolic calcium concentration and causing cell contraction in isolated rat heart cells in a concentration- and time-dependent manner (3).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Ammonium: guide level 0.05 mg l^{-1}, maximum admissible concentration 0.5 mg l^{-1} (4).

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

Other comments

Reviews on experimental toxicology, workplace experience and human health effects listed (6).

Decomposes in the presence of moisture (7).

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5. *S.I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
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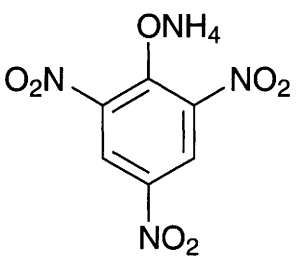
7. *The Merck Index* 12th ed., 1996, Merck & Co., Inc., Whitehouse Station, NJ, USA

A182 ammonium picrate



$C_6H_6N_4O_7$ **Mol. Wt.** 246.14 **CAS Registry No.** 131-74-8

Synonyms 2,4,6-trinitrophenol, ammonium salt; ammonium picronitrate; ammonium carbazoate; Obeline picrate; Explosive D; picrate of ammonia

EINECS No. 205-038-3 **RTECS No.** BS 3855000

Uses In explosives, fireworks and rocket propellants.

Physical properties

M. Pt. decomposes **B. Pt.** 423°C (explodes) **Specific gravity** 1.72
Solubility Water: 11 g l^{-1} at 20°C. Organic solvents: ethanol

Occupational exposure

UN No. 1310 (wetted with ≥10% water by mass) **Conveyance classification** flammable solid

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) bluegill sunfish 220 ppm static bioassay in fresh water, mild aeration applied after 24 hr, at 23°C (1).
LC_{50} (96 hr) inland silverside 66 ppm static bioassay in synthetic seawater, mild aeration applied after 24 hr, at 23°C (1).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Ammonium: guide level 0.05 mg l^{-1}, maximum admissible concentration 0.5 mg l^{-1} (2).
Included in the UK List of Classified and Authorised Explosives 1994. UK Class and Division 3.2. Competent Authority Reference GB32008 (3).

Other comments

Physiologic effects and protective measures in cases of exposure to ammonium picrate discussed (4).
Experimental toxicology and human health effects reviewed (5).
Explodes easily from heat or shock (6).

References

1. Dawson, G. W. et al *J. Haz. Mater.* 1975/77, **1**, 303-318.
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. *UK Explosives Acts, 1875 and 1923. The Classification and Labelling of Explosives Regulations 1983 (CLER). List of Classified and Authorised Explosives 1994 (LOCAE)* 1994, HSE.
4. *US Armed Forces Med. J.* 1953, **4**, 1425.
5. *Dangerous Prop. Ind. Mat. Rep.* 1988, **8**(2), 42-44.
6. *The Merck Index* 11th ed., 1989, Merck & Co. Inc, Rahway, NJ, USA

A183 ammonium polysulfide

$$(NH_4)_2S_3$$

$H_8N_2S_3$ **Mol. Wt.** 132.28 **CAS Registry No.** 9080-17-5; 12259-92-6 (trisulfide)
Synonyms ammonium trisulfide; AP-S; diammonium trisulfide
EINECS No. 232-989-1 **RTECS No.** BS 4027000
Uses Photography, chemical reagent.

Physical properties

Specific gravity 1.10
Solubility Water: miscible

Occupational exposure

UN No. 2818 (solution) **HAZCHEM Code** 2X (solution) **Conveyance classification** corrosive substance, toxic (solution)
Supply classification corrosive
Risk phrases Contact with acids liberates toxic gas – Causes burns (R31, R34)
Safety phrases Keep locked up and out of the reach of children (if sold to general public) – In case of contact with eyes, rinse immediately with plenty of water and seek medical advice – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S26, S45)

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 150 mg kg^{-1} (1).
LD_{50} dermal rabbit 1790 mg kg^{-1} (1).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Ammonium: guide level 0.05 mg l^{-1}, maximum admissible concentration 0.5 mg l^{-1} (2).

References

1. *NTIS Report* AD A062-138, National Technical Information Service, Springfield, VA, 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

A184 ammonium sulfamate

$$NH_2S(O_2)ONH_4$$

$H_6N_2O_3S$ **Mol. Wt.** 114.13 **CAS Registry No.** 7773-06-0
Synonyms AMS; ammonium sulfamidate; monoammonium sulfamate; ammonium amidosulfonate
EINECS No. 231-871-7 **RTECS No.** WO 6125000
Uses Non-selective herbicide. Fire-retardant for flame-proofing textiles and paper products. In electroplating solutions.

Physical properties

M. Pt. 131°C **B. Pt.** 160°C (decomp.)
Solubility Water: 684 g l^{-1} at 25°C. Organic solvents: formamide, glycerol

Occupational exposure

DE-MAK 15 mg m^{-3} (inhalable dust fraction)
FR-VME 10 mg m^{-3}
UK-LTEL 10 mg m^{-3} **UK-STEL** 20 mg m^{-3}
US-TWA 10 mg m^{-3}

Ecotoxicity

Fish toxicity

LC_{50} (48 hr) young carp 1000-2000 mg l^{-1} (1).

Exposure of threespine stickleback to 10 mg l^{-1} in a 24 hr bioassay resulted in death within 1 hr (2).

Environmental fate

Degradation studies

Microbially degraded in soil to ammonium sulfate within 6-8 weeks (1).

Mammalian & avian toxicity

Acute data

LC_{50} oral quail 3000 mg kg^{-1} (1).

LD_{50} oral rat 2000-3900 mg kg^{-1} (1,3).

LD_{Lo} intraperitoneal rat 800 mg kg^{-1} (4).

Sub-acute and sub-chronic data

In 105 day feeding trials in rats, no adverse effects were observed at 10,000 mg kg^{-1} diet, but growth inhibition was noted at 20,000 mg kg^{-1} diet (1).

Oral rat (27-42 day study) 1.7 g kg^{-1} day^{-1}. No gross pathological changes reported. Microscopic pathology indicated superficial damage to stomach mucosa, slight vacuolation of the cytoplasm of liver cells and moderate numbers of macrophages filled with hemosiderin in spleen (5).

Oral rat (90 days) 0, 100, 250 or 500 mg kg^{-1} 6 days wk^{-1}. Body weights in high-dose animals were significantly increased compared to controls (6).

Irritancy

Repeated application of 50% aqueous solutions to shaved skins of rats caused no irritation or systemic toxicity (4).

Other effects

Other adverse effects (human)

A cohort mortality study of 1225 workers who had worked ≥6 months during 1950-82 in the forestry trade at a public utility, using phenoxy acids, *s*-triazines, substituted urea and other herbicides including ammonium sulfamate showed no excess mortality relative to the reference population. There was a statistically significant increase in deaths due to suicide for the cohort as a whole. There were no deaths due to cancers such as soft-tissue sarcoma and non-Hodgkins lymphoma (7).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides and related products; maximum admissible concentration 0.1 mg l^{-1} (8).

Included in Schedule 6 (Release into Land: Prescribed Substances) of Statutory Instrument No. 472, 1991 (9).

Other comments

Reviews on experimental toxicology, physico-chemical properties and human health effects listed (10,11).

References

1. *The Pesticide Manual* 11th ed., 1997, The British Crop Protection Council, Farnham, UK.
2. *Lethal Effects of 2014 Chemicals upon Sockeye Salmon, Steelhead Trout and Threespine Stickleback* 1989, EPA 560/6-89-001.
3. *Arch. Ind. Health* 1956, **14**, 178.
4. *J. Ind. Hyg. Toxicol.* 1943, **25**, 26.
5. *USEPA Drinking Water Health Advisory: Pesticides* 1989, 35-42, Lewis Publishers, Chelsea, MI, USA.
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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.
11. *Dangerous Prop. Ind. Mater. Report* 1987, 7(5), 95-99

A185 ammonium sulfate

$$(NH_4)_2SO_4$$

$H_8N_2O_4S$ **Mol. Wt.** 132.14 **CAS Registry No.** 7783-20-2

Synonyms sulfuric acid, diammonium salt; diammonium sulfate

EINECS No. 231-984-1 **RTECS No.** BS 4500000

Uses Manufacture of ammonium alum. In analysis. Freezing mixtures. For flame-proofing fabrics and paper. In the manufacture of viscose silk. In the tanning industry. In the fractionation of proteins. The commercial grade is used as a fertiliser. Food additive in fermentation processes.
Occurrence In nature as mascagnite.

Physical properties

M. Pt. 280°C (decomp.) **Specific gravity** 1.77 at 20°C with respect to water at 4°C
Solubility Water: 1 g in 100 g

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) bleak 310 mg l^{-1} (1).
A 6-month exposure of snakehead fish to 100 ppm (considered a safe concentration) and 500 ppm (sublethal concentration) of ammonium sulfate caused hypertrophy, degranulation, nuclear pyknosis and focal necrosis in hepatocytes. Thyroid follicles exhibited various degrees of hypertrophy, hyperplasia, hyperaemia and a reduction in colloid content. The damage was more pronounced in high-dose fish (2).
Snakehead fish exposed to single concentrations of 100 and 500 ppm exhibited testicular abnormalities including disorganisation of lobules, degeneration of spermatogenic elements, necrosis of interstitial cells and proliferative fibrosis of lobule walls. The absence of intact germ cells in some lobules suggested irreversible damage in high-dose fish. The inhibition of testicular development and deleterious changes in spermatogenic elements result from direct action on the testis itself or indirectly via the hypothalamic-pituitary-testicular axis (3).

Invertebrate toxicity
LC_{50} (25-100 hr) *Daphnia magna* 423-292 mg l^{-1} (4).

Environmental fate

Nitrification inhibition
Inhibition of nitrification-threshold concentration 500 mg l^{-1} (5).
Ammonium sulfate was applied at 300 kg N ha^{-1} to highly calcareous soil with or without the nitrification inhibitor 1-carbamoyl-3(5)-methylpyrazol at 4 kg ha^{-1}. In the absence of the inhibitor, nitrification was completed in 3 wk. In the presence of the inhibitor only 10% of applied N was nitrified by the 3rd wk and 42% by the 8th wk (6).

Mammalian & avian toxicity

Acute data

TD_{Lo} oral man 1500 mg kg^{-1} (7).

LD_{50} oral rat 3000 mg kg^{-1} (8).

LD_{50} intraperitoneal mouse 610 mg kg^{-1} (9).

Sub-acute and sub-chronic data

Intratracheal (4 or 8 month) rat 0.5 mg m^{-3} 5 hr day^{-1}, 5 days wk^{-1}. At 4 months cellular immunological responsiveness was not impaired but physiological changes were detected. Effects included bronchiolar epithelial hyperplasia and changes in alveolar mean chord length (10).

The effects of ammonium sulfate aerosols on asthmatic dyspnoea (immediate type), induced in guinea pigs by repeated inhalation of a mixture of bovine serum and egg albumin, was investigated. Inhalation (38 wk) guinea pig 0.2, 0.4, and 2.0 mg m^{-3} ammonium sulfate aerosol for 2 hr day^{-1} 5 days wk^{-1}. Results show asthmatic dyspnoea was increased by exposure to aerosol (11).

Genotoxicity

Chinese hamster V-79 cells treated with a hypotonic solution of ammonium sulfate resulted in an increase of chromosomal aberrations. These can be attributed to direct DNA damage due to the hypotonic treatment or changes to internal pH or damage of chromosomal proteins (12).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Ammonium: guide level 0.05 mg l^{-1}, maximum admissible concentration 0.5 mg l^{-1} (13).

Other comments

A small scale ecosystem simulating hydrological isolated lentic soft waters was exposed to artificial rain pH 5.6 containing ammonium sulfate for 2 yrs. Remarkable changes in water quality and flora were observed. These included pH decrease to 3.5, accumulation of both ammonium and sulfate. Nitrification of ammonium appeared to be the dominant acidifying process resulting in increases in the concentrations of aluminium, cadmium, calcium, iron, magnesium, manganese, and zinc. In acidified systems exposed to high depositions of ammonium sulfate typical soft water plants such as *Littorella uniflora* disappeared and a luxuriant growth of *Sphagnum cuspidatum* and *Juncus bulbosas* occurred. The filamentous green algae *Oedogonium* spp. and *Mougeotic* spp. became dominant (14). Reviews on experimental toxicology, environmental effects, ecotoxicology and human health effects listed (15).

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2. Ram, R. N. et al *Ecotoxicol. Environ. Saf.* 1987, **13**(2), 185-190.
3. Ram, R. N. et al *Indian J. Exp. Biol.* 1987, **25**(10), 667-670.
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10. Smith, L. G. et al *Environ. Res.* 1989, **49**(1), 60-78.
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13. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
14. Schuurkes, J. A. A. R. et al *Aquat. Bot.* 1987, **28**(3-4), 199-226.
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

A186 ammonium sulfide

$(NH_4)_2S$

H_8N_2S **Mol. Wt.** 68.14 **CAS Registry No.** 12135-76-1

Synonyms diammonium sulfide; ammonium monosulfide

EINECS No. 235-223-4 **RTECS No.** BS 4920000

Uses To apply patina to bronze. In photography development. In textile manufacture. In chemical analysis. Fungicide.

Physical properties

M. Pt. –18°C

Solubility Organic solvents: ethanol

Occupational exposure

UN No. 2683 **HAZCHEM Code** 2X **Conveyance classification** corrosive substance, danger of fire (flammable liquid), toxic

Ecotoxicity

Fish toxicity

LC_{50} (48 hr) carp 6.6-109 mg l^{-1} total ammonia concentration in static bioassay, ammonium sulfide solution replaced every 24 hr (1).

LC_{50} (48 hr) carp 1.15-1.96 mg l^{-1} un-ionised ammonia in static bioassay (1).

LC_{50} (48 hr) mosquito fish 248 ppm in fresh water (2).

Environmental fate

Nitrification inhibition

Inhibition of NH_3 oxidation-activated sludge: 1 mg l^{-1} 28%; 5 mg l^{-1} 67%; 3.2 mg l^{-1} 100% (3).

Mammalian & avian toxicity

Acute data

LD_{Lo} oral mouse 80 mg kg^{-1} (3).

LD_{Lo} dermal mouse, rabbit 119-2460 mg kg^{-1} (4).

Metabolism and toxicokinetics

Alkali sulfides are rapidly absorbed from the intestine. Excretion occurs via three routes: the sulfide radical is excreted partially via the lung and kidney, is oxidised partially to sulfate and thiosulfate and excreted by the kidneys and it can also be incorporated into metallic sulfides, *e.g.* iron sulfide, which is excreted in the faeces (5).

Genotoxicity

Escherichia coli PQ37 SOS chromotest without metabolic activation negative (6).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides and related products: maximum admissible concentration 0.1 mg l^{-1} (7).

Included in Schedule 6 (Release Into Land: Prescribed Substances) of Statutory Instrument No. 472, 1991 (8).

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A187 ammonium sulfite

$$(NH_4)_2SO_3$$

$H_8N_2O_3S$ **Mol. Wt.** 116.14 **CAS Registry No.** 10196-04-0

EINECS No. 233-484-9

Uses In photography. As a reducing agent. In bricks for blast furnace linings. In lubricants for metal cold working.

Physical properties

M. Pt. 60-70°C (decomp.) **B. Pt.** 150°C (sublimes) **Specific gravity** 1.41 at 25°C
Solubility Water: 324 g l^{-1} at 0°C. Organic solvents: ethanol

Ecotoxicity

Fish toxicity
LC_{50} (48 hour) mosquito fish 240 ppm (1).

Invertebrate toxicity
LC_{50} (25-100 hr) *Daphnia magna* 300-200 mg l^{-1} (2).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Ammonium: guide level 0.05 mg l^{-1}, maximum admissible concentration 0.5 mg l^{-1} (3).

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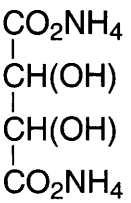
A188 ammonium tartrate



$C_4H_{12}N_2O_6$ **Mol. Wt.** 184.15 **CAS Registry No.** 3164-29-2

Synonyms butanedioic acid, 2,3-dihydroxy-, diammonium salt; 2,3-dihydroxybutanedioic acid, diammonium salt; ammonium threonate; 2,3-dihydroxysuccinic acid, diammonium salt

EINECS No. 221-618-9 **RTECS No.** WW 8050000

Physical properties

M. Pt. decomposes **Specific gravity** 1.601

Solubility Water: 580 g l^{-1} at 15°C. Organic solvents: ethanol

Mammalian & avian toxicity

Acute data

LD_{50} intravenous rabbit 113 mg kg^{-1} (1).

LD_{50} subcutaneous rabbit 1130 mg kg^{-1} (1).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Ammonium: guide level 0.05 mg l^{-1}, maximum admissible concentration 0.5 mg l^{-1} (2).

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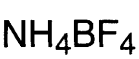
A189 ammonium tetrafluoroborate



H_4BF_4N **Mol. Wt.** 104.84 **CAS Registry No.** 13826-83-0

Synonyms ammonium borofluoride; ammonium fluoroborate

EINECS No. 237-531-4 **RTECS No.** BQ 6100000

Uses Flame retardant. Flux for inert atmosphere soldering.

Physical properties

M. Pt. 230°C **Specific gravity** 1.87

Solubility Water: 258 g l^{-1} at 25°C

Occupational exposure

SE-LEVL 2 mg m^{-3} (as F)
UK-LTEL 2.5 mg m^{-3} (as F)

UN No. 2811

Mammalian & avian toxicity

Metabolism and toxicokinetics

Following ingestion, soluble fluorides are rapidly absorbed from the gastrointestinal tract at least to the extent of 97%. Absorbed fluoride is distributed throughout the tissues of the body by the blood. Fluoride concentrations in soft tissues fall to pre-exposure levels within a few hours of exposure. Fluoride exchange with hydroxyl groups of hydroxyapatite (the inorganic constituent of bone) to form fluorohydroxyapatite. Fluoride that is not retained is excreted rapidly in urine (1).

Borates are rapidly absorbed from mucous membranes and abraded skin, but not from intact or unbroken skin. Borate excretion occurs mainly through kidneys; ~50% is excreted in first 12 hr and remainder is eliminated over a period of 5 to 7 days (2).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Ammonium: guide level 0.05 mg l^{-1}, maximum admissible concentration 0.5 mg l^{-1} (3).

Other comments

Reviews on human health effects, workplace experience and experimental toxicology listed (4).

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A190 ammonium thiocyanate

$$NH_4SCN$$

CH_4N_2S **Mol. Wt.** 76.12 **CAS Registry No.** 1762-95-4

Synonyms thiocyanic acid, ammonium salt; ammonium rhodanate; ammonium rhodanide; ammonium sulfocyanate; ammonium sulfocyanide

EINECS No. 217-175-6 **RTECS No.** XK 7875000

Uses In matches. Dyeing of fabrics, photography and coatings on zinc. In the manufacture of artificial resins, thiourea and pesticides. In rustproofing compositions. Detection and determination of iron, silver, mercury.

Physical properties

M. Pt. 149°C **B. Pt.** 170°C (decomp.) **Specific gravity** 1.305
Solubility Water: 128 g in 100 ml at 0°C. Organic solvents: acetone, ethanol, methanol

Occupational exposure

Supply classification harmful
Risk phrases Harmful by inhalation, in contact with skin and if swallowed – Contact with acids liberates very toxic gas (R20/21/22, R32)
Safety phrases Keep out of reach of children (if sold to general public) – Keep away from food, drink and animal feeding stuffs (S2, S13)

Ecotoxicity

Fish toxicity
Bluegill sunfish exposed to 280-300 ppm died within 1 hr (1).

Environmental fate

Nitrification inhibition
Ammonia oxidation inhibited by activated sludge concentration 100 mg l^{-1} (2).

Mammalian & avian toxicity

Acute data
LD_{Lo} oral mouse, guinea pig 330, 600 mg kg^{-1}, respectively (3,4).
TD_{Lo} oral human 375 mg kg^{-1} (5).
LD_{50} intragastric guinea pig, rat, mouse 500-750 mg kg^{-1} (5,6).
LD_{Lo} intraperitoneal mouse 500 mg kg^{-1} (7).

Metabolism and toxicokinetics
Thiocyanate readily diffuses into all tissues. It appears early in saliva and is excreted slowly via the urine. It is not decomposed to cyanide in appreciable quantities (8,9).
Intragastric rat (duration unspecified) 375 mg kg^{-1} uniform distribution throughout the body, except some accumulation in the thyroid gland and kidney. Excreted mainly in urine, $t_{1/2}$ 36 hr. During chronic aerosol inhalation by rats of maximum permissible concentration 5 mg m^{-3}, ammonium thiocyanate was rapidly excreted from the body within 24 hr (5).

Sensitisation
Subcutaneous guinea pig (concentration and duration unspecified) weak allergic reaction occurred (6).
In human subjects occupationally exposed the incidence of allergic dermatitis was above normal and phagocytic activity of neutrophils was impaired and the concentration of immunoglobulin A (IgA) was below controls (10).

Other effects

Any other adverse effects
In chronic inhalation studies in rats (duration unspecified) minimum toxic and maximum non-toxic concentrations were 20 and 5 mg m^{-3}, respectively (6).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Ammonium: guide level 0.05 mg l^{-1}, maximum admissible concentration 0.5 mg l^{-1} (11).

Other comments

Reviews on health effects, experimental toxicology and ecotoxicology listed (12).

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A191 ammonium thiosulfate

$$(NH_4)_2S_2O_3$$

$H_8N_2S_2O_3$ **Mol. Wt.** 148.21 **CAS Registry No.** 7783-18-8

Synonyms thiosulfuric acid, diammonium salt; ammonium hyposulfite

EINECS No. 231-982-0 **RTECS No.** XN 6465000

Uses Photographic chemicals. Metal refining. Fertilisers.

Physical properties

M. Pt. 150°C (decomp.) **Specific gravity** 1.679
Solubility Water: 1030 g l^{-1} at 100°C. Organic solvents: acetone

Environmental fate

Nitrification inhibition
Inhibits nitrite-to-nitrate conversion in soils (1).

Mammalian & avian toxicity

Acute data
Intraperitoneal or subcutaneous injections of 0.2 ml of an aqueous solution into 10 g mice caused convulsions and death (2).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Ammonium: guide level 0.05 mg l^{-1}, maximum admissible concentration 0.5 mg l^{-1} (3).

Other comments

A newly isolated bacterium, the strictly anaerobic, Gram-positive, motile rod, strain GKNTAU ferments taurine to thiosulfate quantitatively. The other fermentation products were ammonia and acetate. All could be formed by cell-free extracts (4).
The US Environmental Protection Agency has removed ammonium thiosulfate from its list of hazardous substances since the median lethal concentration is well above 500 mg l^{-1} for aquatic toxicity (5).
Reviews on experimental toxicology, ecotoxicology and human health effects listed (6).

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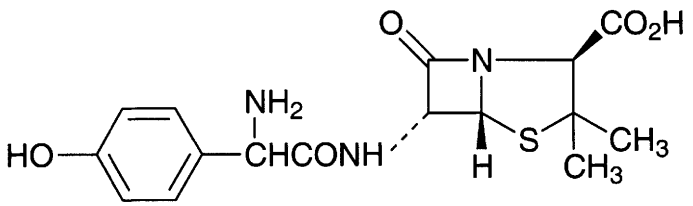
A192 amoxycillin



$C_{16}H_{19}N_3O_5S$ **Mol. Wt.** 365.41 **CAS Registry No.** 26787-78-0

Synonyms 4-thia-1-azabicyclo(3.2.0)heptane-2-carboxylic acid, 6-((amino(4-hydroxyphenyl)acetyl)amino)-3,3-dimethyl-7-oxo,(2*S*-(2α,5α,6β(*S*)+))-; BRL-2333; D-(–)-α-amino-*p*-hydroxybenzyl penicillin; (6*R*)-6-[α-D-(14-hydroxyphenyl)glycylamino]penicillanic acid; α-amino-*p*-hydroxyphenylacetamido]penicillanic acid; α-amino-*p*-hydroxybenzylpenicillin; Polymox; Trimox

EINECS No. 248-003-8 **RTECS No.** XH 8300000

Uses Antimicrobial. Antibacterial. Semi-synthetic antibiotic related to penicillin.

Ecotoxicity

Fish toxicity

Young yellowtail fish were exposed to 80 and 400 mg kg^{-1} amoxycillin for 10 days. At 400 mg kg^{-1} the fish showed no abnormal appetite, movement or haematological effects except an increased erythrophagocytosis by splenic macrophages (1).

Mammalian & avian toxicity

Acute data

LD_{50} intraperitoneal rat, mouse 2870-3590 mg kg^{-1} (as trihydrate) (2).

Teratogenicity and reproductive effects

LD_{Lo} (7-13 day pregnant) oral rat 2800 mg kg^{-1}.

LD_{Lo} (7-13 day pregnant) oral mouse 9100 mg kg^{-1} teratogenicity reported (2).

Metabolism and toxicokinetics

The bioavailability of amoxycillin was studied in healthy human volunteers. Single doses of 250, 500, 750 and 1000 mg were administered. The mean urinary recovery was 59.6, 55.9, 58.5 and 45.8%, respectively (3).

The serum $t_{1/2}$ of amoxycillin was 0.96 hr in humans given a single 500 mg oral dose of the drug (4).

Amoxycillin is more rapidly and completely absorbed from gastrointestinal tract than is ampicillin. After a single 250 mg dose (species unspecified) peak plasma concentrations are reached in 2 hr and average 4 μg ml^{-1}. Approximately 20% is bound to plasma proteins and 60% is excreted in active form via the urine (5).

Demonstrated *in vitro* to use the dipeptide carrier-mediated system as a transport mechanism in rodent small intestine (6).
Amoxycillin (2 × 250 mg capsules) was administered orally to healthy human ♂. Venous blood and urine were taken at intervals of 6 and 12 hr, respectively. Peak serum concentration measured 7.6 mg l^{-1} and was reached in 1.4 hr (7).

Irritancy
Analysis by the Boston Collaborative Drug Surveillance Program of data on 15,438 patients hospitalised between 1975 and 1982 detected 63 allergic skin reactions attributed to amoxycillin among 1225 recipients of the drug. This was the highest incidence of skin reactions among the drugs studied (8).
Photosensitivity reactions have been reported with amoxycillin (9).

Other effects

Other adverse effects (human)
Electron microscopy of a skin biopsy from an infant with neonatal adrenleukodystrophy detected numerous myelinic bodies within fibroblasts. These myelinic bodies were absent from skin fibroblasts from the same patient when examined approximately 1 yr later. The role of amoxycillin and gentamycin which had been administered for a urinary tract infection at the time of the first biopsy in inducing myelinic bodies was examined but the results were inconclusive (10).
Administration of amoxycillin (trihydrate) by mouth in three patients caused neutropenia 13-23 days after onset of treatment. It was considered to be immune-mediated (11).
Non-pseudomembranous colitis, presenting with abdominal pain and bloody diarrhoea was associated with the administration of amoxycillin by mouth in four patients (12).
Allergic response in breast-fed infants (13).

Any other adverse effects
Chlamydia trachomatis minimum inhibitory concentration 0.5 μg l^{-1} (14).

Other comments

Physiochemical properties, antibacterial pharmacology, pharmacokinetics and toxicity of amoxycillin for domestic animals reviewed (15).
Often administered as the sodium and trihydrate salts to enhance bioavailability (13).

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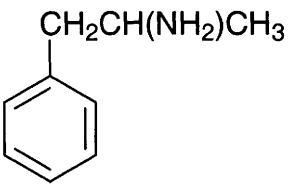
A193 amphetamine



$C_9H_{13}N$ **Mol. Wt.** 135.21 **CAS Registry No.** 300-62-9

Synonyms (±)-α-methylbenzene ethanamine; *dl*-α-methylphenethylamine; 1-phenyl-2-aminopropane; (phenylisopropyl)amine; β-aminopropylbenzene; Durophet

EINECS No. 206-096-2 **RTECS No.** SH 9450000

Uses Central nervous system stimulant.

Physical properties

B. Pt. 200-203°C **Flash point** <100°C (open cup) **Specific gravity** 0.913 at 25°C with respect to water at 4°C
Partition coefficient log P_{ow} 1.76 **Volatility** v.den. 4.7
Solubility Organic solvents: diethyl ether, ethanol

Ecotoxicity

Invertebrate toxicity
Tetrahymena pyriformis 2 hr exposure to 5 μg l^{-1} caused increased phagocytic activity (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 30 mg kg^{-1} (2).
LD_{50} subcutaneous rat 180 mg kg^{-1} (3).
LD_{50} intraperitoneal mouse 15 mg kg^{-1} (4).

Sub-acute and sub-chronic data
Injection mouse (duration unspecified) 0.4 mg kg^{-1} day^{-1} showed a reduction in thymus and spleen cellularity and in peripheral T-lymphocyte population. Inhibition of T-cell proliferation and a reduction in the capacity of mice to development and passive transfer of immunity to *Listeria monocytogenes* was observed (5).

Carcinogenicity and chronic effects
A COMPACT computer-optimised molecular parametric analysis of chemical toxicity was used to determine genotoxic and carcinogenic potential. The potential of amphetamine was negative (6).

Teratogenicity and reproductive effects
Wistar rat embryos explanted on day 10.5 of gestation exposed to 0.1, 0.4, 0.8, 1.2, or 1.6 mM amphetamine for 24 hr suffered malformations and abnormal histological changes at the two highest concentrations (7).

Metabolism and toxicokinetics
Metabolised to 4-hydroxyamphetamine and 4-hydroxynorephedrine (8).
A single dose 10-25 mg of amphetamine given to human volunteers produced peak plasma levels within 1-2 hr and was rapidly absorbed from gastrointestinal tract. Amphetamine absorption was usually complete within 4-6 hr (9).
Amphetamine concentrates in the kidney, lungs and brain (9).
Considerable species difference in biotransformation exists, but not in the excretion of ^{14}C after administration of ^{14}C-amphetamine. After intraperitoneal administration to dogs and oral administration to other species excretory percentages in urine were rats 86%, rabbits 86% and dogs 78% (10).

Genotoxicity

Amphetamine produced marked clastogenic activity and affected the cell proliferation in the bone marrow of mice. In mouse somatic cells, a dose-dependent increase in micronucleated polychromatic erythrocytes was observed (11).

Other effects

Other adverse effects (human)

An amphetamine-abusing mother, who had taken methamphetamine 5 hr prior to onset of labour confirmed previous findings of premature delivery and retarded intra-uterine development (12).
Behavioural effects include excitement, tremor, convulsions or effect on seizure threshold drug of abuse (13).

Any other adverse effects

In vitro horse liver alcohol dehydrogenase activity inhibited by amphetamine (14).
Respiration by rat brain homogenates was inhibited by 18% by 0.27 g l^{-1} amphetamine (15).
To assess the effects on independent feeding during development, pre-weanling rats were administered amphetamine and allowed to ingest milk through oral cannulas. In 1-hr milk-deprived pups, milk intake was stimulated at 3, 7 and 10 days of age and suppressed at 15 days. In 22-hr deprived pups, no effect observed at 3, 7 and 10 days but reliably suppressed intake at 15 days (16).

Other comments

Neurological and psychosis effects, toxicology and pharmacology, behavioural effects, biotransformation and metabolism have been extensively reviewed (17-27).
Structural features of amphetamine neurotoxicity in the brain have been reviewed (28).

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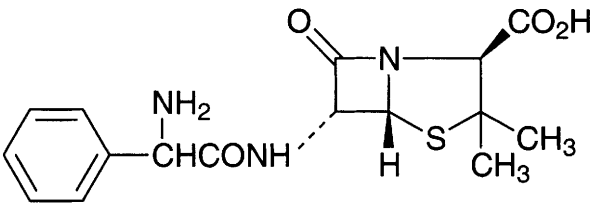
A194 ampicillin



$C_{16}H_{19}N_3O_4S$ **Mol. Wt.** 349.41 **CAS Registry No.** 69-53-4

Synonyms 4-thia-1-azabicyclo(3.2.0)heptane-2-carboxylic acid, 6-((aminophenylacetyl)amino)-3,3-dimethyl-7-oxo-2,*S*-12α,5α,6β7(*S*+)); amino benzylpenicillin; (6*R*)-6-(α-D-phenylglycylamino)penicillanic acid; Acillin; Ampen; Polycillin; Pentrexyl; Principen

EINECS No. 200-709-7 **RTECS No.** XH 8350000

Uses Broad spectrum antibiotic. Semi-synthetic derivative of penicillin.

Physical properties

M. Pt. 202°C (decomp.)

Ecotoxicity

Invertebrate toxicity

EC_{50} *Photobacterium phosphoreum* >100 ppm (1).

Mammalian & avian toxicity

Acute data

TD_{Lo} oral man 400 mg kg^{-1} (2).

LD_{50} oral rat, mouse 10, 15.2 g kg^{-1}, respectively (3).

LD_{50} intraperitoneal 1-day-old, 83-day-old rat 3300, 4500 mg kg^{-1}, respectively (4).

LD_{50} intraperitoneal, intravenous mouse 3250, 4990 mg kg^{-1}, respectively (5,6).

Sub-acute and sub-chronic data

Four-week old rats were administered 25 mg l^{-1} in drinking water for 4 wk. No toxic effects were noted but there was an increase in body weight gain (7).

Subcutaneous (5 day) guinea pig 6, 8, 10 mg kg^{-1} 3 × day^{-1}. Over a period of 12 days, the lowest ampicillin dose appeared to be tolerated well. However, significant body weight reduction and mortality occurred with the two higher dose regimens. Caecal cultures of dead animals confirmed the presence of *Clostridium difficile* associated with antibiotic-induced enterotoxaemia. Ampicillin accumulated in the urine and bile (8).

Carcinogenicity and chronic effects

Inadequate evidence for carcinogenicity in humans, limited evidence for carcinogenicity in animals, IARC classification group 3 (3).

The National Toxicology Program tested ampicillin trihydrate in rats and mice via gavage. No evidence of carcinogenicity was found in ♀ rats and ♂ and ♀ mice, and equivocal evidence was found in ♂ rats (9).

Metabolism and toxicokinetics

A penicillin amidase or acylase-type enzyme in fungi, yeasts, actinomycetes and bacteria causes hydrolysis to 6-aminopenicillanic acid (2).

Oral sheep, a single dose of 750 mg caused peak blood plasma concentration of 0.38 μg ml^{-1} within 1 hr. The biological $t_{1/2}$ was 110 min (10).

Studies of ampicillin pharmacokinetics in the pancreas of dogs and rats following intravenous administration of

50 mg kg^{-1} revealed an elimination $t_{1/2}$ of 50 min in dogs, whereby levels attained approximately 6% of that of blood serum levels in both rats and dogs, and the degree of permeation into the pancreatic secretion of dogs was 2%. In neither case did concentrations reach minimum inhibitory concentration required for *Escherichia coli* (11).
In humans, peak plasma concentrations are obtained in 1-2 hr, and following a dose of 500 mg are reported to range from 2-6 μg ml^{-1} (12).
After oral administration of 500 mg to human, serum $t_{1/2}$ was 0.92 hr (13).
The oral bioavailability of ampicillin when bound to sulbactam (sultamicillin) was compared with ampicillin alone in 16 healthy subjects using an open-label, multiple cross-over study. It was demonstrated that the bioavailability of ampicillin was increased by sulbactam (14).
Ampicillin is poorly bound to proteins which results in higher concentrations in foetal tissues and amniotic fluid than would occur with highly protein-bound penicillins. High foetal-to-maternal peak serum concentration ratios of between 0.3 and 0.9 have been reported for ampicillin (15).
In a study of 42 women, administration of 500 mg every 6 hr by mouth resulted in concentrations of 0.4-5.1 μg ml^{-1} in the amniotic fluid collected between 3.25 and 5.75 hr after the third dose and 0.24-2 μg ml^{-1} in cord sera collected of delivery after 2-13 doses (16).

Irritancy
Allergic reactions can occur in sensitised persons. Skin rashes are among the most common side-effects and are either urticaria or maculopapular (13).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA1535, TA1537 with and without metabolic activation negative (17).
Escherichia coli PQ37 cells with and without metabolic activation negative (18).
Chinese hamster ovary cells with and without metabolic activation, sister chromatid exchange and chromosomal aberrations negative (19).
Mouse lymphoma L5178Y with and without metabolic activation negative (20).
The *in vitro* and *in vivo* clastogenic potential of ampicillin was investigated using cultured human lymphocytes and the rat micronucleus test. No increase in chromosome damage *in vitro* up to test concentrations of 10 mg ml^{-1}. Negative in *in vivo* rat micronucleus test to 5 g kg^{-1} (21).

Other effects

Other adverse effects (human)
In humans symptomatic effects include diarrhoea, nausea and vomiting. Pseudomembranous colitis and supra-infections have been reported (13).
Neutropenia and thrombocytopenia in one patient has been reported following treatment with ampicillin (22).

Any other adverse effects
Intramuscular (7 days) rat 30 mg kg^{-1} day^{-1} some nephrotoxic effects (unspecified) reported (23).

Other comments

Human health effects and toxicity reviewed (3).
Pharmacokinetics, antibacterial activities and side-effects, and antiobiotic activity in veterinary medicine discussed (24,25).
Drug often administered as trihydrate or sodium salts to enhance bioavailability.

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A195 amyl acetate

$$CH_3CO_2(CH_2)_4CH_3$$

$C_7H_{14}O_2$ **Mol. Wt.** 130.19 **CAS Registry No.** 628-63-7

Synonyms pentyl acetate; acetic acid, amyl ester; amylacetic ester; 1-pentanol acetate; 1-pentyl acetate; primary amyl acetate; *n*-amyl acetate

EINECS No. 211-047-3 **RTECS No.** AJ 1925000

Uses Solvent and chemical intermediate. Used in the production of acrylic resins, photographic films, glass, polishes. Food flavouring agent.

Physical properties

M. Pt. –78.5°C **B. Pt.** 149°C **Flash point** 23°C **Specific gravity** 0.879 at 20°C with respect to water at 4°C
Partition coefficient log P_{ow} 2.258 (1) **Volatility** v.p. 5 mmHg at 25°C ; v.den. 4.5
Solubility Water: 800 mg l^{-1} at 20°C. Organic solvents: miscible with diethyl ether, ethanol

Occupational exposure

DE-MAK 50 ppm (270 mg m^{-3})
FR-VME 100 ppm (530 mg m^{-3}) **FR-VLE** 150 ppm (800 mg m^{-3})
JP-OEL 100 ppm (530 mg m^{-3})
SE-LEVL 100 ppm (500 mg m^{-3}) **SE-STEL** 150 ppm (800 mg m^{-3})
UK-LTEL 100 ppm (541 mg m^{-3}) **UK-STEL** 150 ppm (812 mg m^{-3})
US-TWA 100 ppm (532 mg m^{-3})

UN No. 1104 **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} (24-96 hr) mosquito fish 65 mg l^{-1} (2).

LC_{100} (24 hr) creek chub 120 mg l^{-1} in Detroit river water (3).

LC_{50} (96 hr) bluegill sunfish 650 ppm static bioassay in fresh water, mild aeration after 24 hr, at 23°C (4).

LC_{50} (96 hr) inland silverside 180 ppm static bioassay in synthetic seawater, mild aeration after 24 hr, at 23°C (4).

Invertebrate toxicity

Toxic threshold effect (48 hr) *Daphnia magna* 440 ppm (5).

Cell multiplication inhibition test *Pseudomonas putida* 145 mg l^{-1}, *Microcystis aeruginosa* 63 mg l^{-1}, *Scenedesmus quadricauda* 80 mg l^{-1}, *Entosiphon sulcatum* 226 mg l^{-1} (6,7).

Blocks muscle electrical activity in *Rana pipiens* (8).

Hydra sp. *in vitro* assay adult, embryo minimal effective ratio equals 1. This predicts that, when subject to standard testing in pregnant mammals, amyl acetate would be equally toxic to mother and embryo/foetus. However, the concentrations necessary to produce adverse effects in *Hydra* do not reliably predict the levels required to produce adverse effects in the standard mammalian species (9).

Bioaccumulation

Calculated bioconcentration factor 31 (10).

Environmental fate

Carbonaceous inhibition

Inhibition of glucose degradation by *Pseudomonas fluorescens* at 350 mg l^{-1} (11).

Inhibition of glucose degradation by *Escherichia coli* >1 g l^{-1} (11).

Degradation studies

BOD_5 0.9 at 440 mg l^{-1} standard dilution (12).

BOD_5 64 and 35% theoretical reduction in dissolved oxygen in fresh and salt water, respectively, using non-acclimated sewage sludge. After 20 days the respective values were 72 and 87% (13).

Abiotic removal

The calculated hydrolysis rate at pH >8 is 5.9×10^{-2} l^{-1} molecules sec^{-1} at 25°C, resulting in $t_{1/2}$ 13.5 days at pH 9 (14).

Activated carbon absorbability 0.175 g g^{-1} carbon, 88% reduction. Influent 985 mg l^{-1}, effluent 119 mg l^{-1} (15).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 6500 mg kg^{-1} (16).

LC_{Lo} (8 hr) inhalation rat 5200 ppm (17).

♂ CFW albino mice were exposed to 0-8000 ppm acetate vapour for 20 min. Amyl acetate had no effect on locomotor activity or observed functional behaviour (18). LD_{Lo} intraperitoneal guinea pig 1500 mg kg^{-1} (19).

Genotoxicity

Non-cytotoxic in Ehrlich-Landschuetz diploid ascites tumour cells (20,21).

Other effects

Other adverse effects (human)

TC_{Lo} inhalation human (30 min) 5000 mg m^{-3} central nervous system, eye and pulmonary effects (22).

Women exposed occupationally to amyl acetate (concentrations unspecified) showed deviations in haemoglobin and haematocrit values, erythrocyte, leukocyte, lymphocyte, monocyte, granulocyte counts, coagulation and bleeding times (23).

In humans, prolonged exposure may result in headache, fatigue and depression of the central nervous system. Irritation of mucous membranes may also occur (24).

A 27-yr-old man developed headache, nausea and vomiting after using a paint containing amyl acetate as the solvent in an unventilated room. Some days later chest pain and dyspnoea developed. He was admitted to hospital 2 wk after exposure with congestive heart failure which slowly responded to treatment (25).

Other comments

Has been reported in an effluent of the explosives industry and of the porcelain/enamelling industry (26).
Reviews on experimental toxicology, physico-chemical properties, exposure levels, epidemiology and human health effects listed (27).
In a survey of drinking water in the UK, amyl acetate was detected in the drinking water in (1/14) treatment plants tested. The source of water for this plant was groundwater (28).
Commercial amyl acetate is a mixture of isomers, the composition depending on its grade and derivation (29).

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A196 *tert*-amyl acetate

$$CH_3CO_2CH_2C(CH_3)_3$$

$C_7H_{14}O_2$ **Mol. Wt.** 130.19 **CAS Registry No.** 625-16-1

Synonyms 2-methyl-2-butanol acetate; *tert*-pentyl acetate

Uses Used as an industrial solvent.

Physical properties

M. Pt. −11.9°C **B. Pt.** 124-125°C **Specific gravity** 0.87 at 20°C with respect to water at 4°C

Solubility Water: 140 g l^{-1} at 30°C

Occupational exposure

DE-MAK 50 ppm (270 mg m^{-3})

SE-LEVL 100 ppm (500 mg m^{-3}) **SE-STEL** 150 ppm (800 mg m^{-3})

UN No. 1104 **HAZCHEM Code** 3Y **Conveyance classification** flammable liquid

Other comments

Reviews on experimental toxicology, physico-chemical properties, exposure levels, epidemiology and human health effects listed (1).

References

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

A197 amyl butyrate

$$CH_3CH_2CH_2CO_2CH_2(CH_2)_3CH_3$$

$C_9H_{18}O_2$ **Mol. Wt.** 158.24 **CAS Registry No.** 540-18-1

Synonyms butanoic acid, pentyl ester; butyric acid, pentyl ester; *m*-amyl butyrate; pentyl butyrate

EINECS No. 208-739-2 **RTECS No.** ET 5956000

Uses In flavours such as apricot, pineapple, pear, plum and sparingly in some perfume compositions.

Physical properties

M. Pt. −73.2°C **B. Pt.** 185°C **Flash point** 57°C **Specific gravity** 0.8713 at 15°C with respect to water at 4°C

Volatility v.den. 5.5

Solubility Water: 0.54 g l^{-1} at 50°C. Organic solvents: diethyl ether, ethanol

Occupational exposure

UN No. 2620 **HAZCHEM Code** 3Y **Conveyance classification** flammable liquid

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, guinea pig ~12 g kg^{-1} (1).

References

1. Jenner, P. M. et al *Food Cosmet. Toxicol.* 1964, **2**, 327

A198 amyl chloride

$$CH_3(CH_2)_4Cl$$

$C_5H_{11}Cl$ **Mol. Wt.** 106.60 **CAS Registry No.** 543-59-9

Synonyms pentyl chloride; 1-chloropentane; *n*-butylcarbonyl chloride

EINECS No. 208-846-4

Uses Solvent. Chemical intermediate.

Physical properties

M. Pt. -99°C **B. Pt.** 107.8°C **Flash point** 12.2°C **Specific gravity** 0.8818 at 20°C with respect to water at 4°C
Volatility v.den. 3.67
Solubility Organic solvents: miscible with diethyl ether, ethanol; soluble in benzene, chloroform

Occupational exposure

UN No. 1107 **HAZCHEM Code** 3[redacted]E **Conveyance classification** flammable liquid
Supply classification highly flammable
Supply classification harmful
Risk phrases Highly flammable – Harmful by inhalation, in contact with skin and if swallowed (R11, R20/21/22)
Safety phrases Keep out of reach of children (if sold to general public) – Keep container in a well ventilated place – Do not empty into drains (S2, S9, S29)

Ecotoxicity

Invertebrate toxicity

EC_{50} (5 min, 30 min) *Photobacterium phosphoreum* 244 mg l^{-1} Microtox test (1).
Aerobic heterotrophs, *Nitrosomonas* spp. and methanogens were tested for toxicity to amyl chloride. IC_{50} *Nitrosomonas* spp. 99 mg l^{-1}, methanogens 150 mg l^{-1} and aerobic heterotrophs 68 mg l^{-1} (2).

Environmental fate

Carbonaceous inhibition

A thermophilic obligate methane oxidising bacterium H-2 (type 1) can degrade liquid monochloro- and dichloro-*n*-alkanes (C5,C6) using the ribulose monophosphate and serine pathways. Compounds are oxidised yielding their corresponding acids or haloacids (3).

Degradation studies

Activated sludge from three operational waste treatment plants (Columbus, OH, Hilliard, OH, and Linworth, OH) were used to determine the extent of oxidation for a series of aliphatic compounds. ThOD (6, 12, 24 hr) were 1.5, 1.8 and 2.8%, respectively (4).

Acinetobacter sp. GJ70 isolated from activated study degraded amyl chloride; primary step was the release of the halide (5).

Genotoxicity

Aspergillus nidulans diploid strain P1 mitotic chromosome segregation negative (6).

Other effects

Any other adverse effects

Exposure to amyl chloride changes the structure of the myelin sheath of rat nerve tissue *in vitro* (7).

The effect of amyl chloride on hepatic triglyceride secretion was investigated *in vivo* and *in vitro* (species unspecified). A dose-related decrease in hepatic triglyceride secretion was reported (8).

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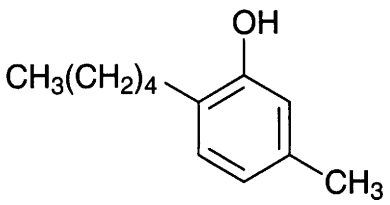
A199 amyl-*m*-cresol



$C_{12}H_{18}O$ **Mol. Wt.** 178.27 **CAS Registry No.** 1300-94-3

Synonyms 6-amyl-*m*-cresol; 6-*n*-amyl-*m*-cresol; 5-methyl-2-pentylphenol; 6-*n*-pentyl-*m*-cresol; amyl-3-cresol; amylmetacresol

EINECS No. 215-094-0 **RTECS No.** GP 3100000

Uses Phenolic antiseptic (1).

Physical properties

M. Pt. 24°C **B. Pt.** 137°C at 15 mmHg **Flash point** 115.6°C **Specific gravity** 0.97

Solubility Organic solvents: acetone, ethanol

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 1500 mg kg^{-1} (2).

References

1. *Martindale: The Extra Pharmacopoeia* 31st ed., 1996, The Royal Pharmaceutical Society, London, UK.
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A200 amylene

$$(CH_3)_2C{=}CHCH_3$$

C_5H_{10} **Mol. Wt.** 70.13 **CAS Registry No.** 513-35-9

Synonyms 2-methyl-2-butene; trimethylethylene; β-isoamylene

EINECS No. 208-156-3

Uses Organic synthesis. Polymerisation inhibition.

Physical properties

M. Pt. –124°C **B. Pt.** 37-39°C **Flash point** –18°C **Specific gravity** 0.66 at 15°C with respect to water at 4°C
Volatility v.den. 2.3
Solubility Organic solvents: miscible with diethyl ether, ethanol

Occupational exposure

UN No. 1108 **HAZCHEM Code** 3[redacted]E **Conveyance classification** flammable liquid

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537, TA1538 with and without metabolic activation negative (1).
Escherichia coli WP2, WP2 *uvrA* with and without metabolic activation negative (1).
Saccharomyces cerevisiae JD1 with and without metabolic activation negative (1).

Other effects

Other adverse effects (human)
A simple asphyxiant in humans (2).

Other comments

Critical evaluation of solubility data in water (3).

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A201 amyl mercaptan

$$CH_3(CH_2)_4SH$$

$C_5H_{12}S$ **Mol. Wt.** 104.22 **CAS Registry No.** 110-66-7

Synonyms pentylmercaptan; 1-pentanethiol

EINECS No. 203-789-1 **RTECS No.** SA 3150000

Uses Chemical intermediate.

Physical properties

M. Pt. –75.7°C **B. Pt.** 126°C **Flash point** 18°C **Specific gravity** 0.857 at 20°C with respect to water at 4°C
Volatility v.p. 13.8 mmHg at 25°C ; v.den. 3.59.
Solubility Organic solvents: miscible with diethyl ether, ethanol

Occupational exposure

UN No. 1111 **HAZCHEM Code** 3WE **Conveyance classification** flammable liquid

Mammalian & avian toxicity

Acute data
LC_{Lo} (4 hr) inhalation rat 2000 ppm (1).
LD_{50} intraperitoneal mouse 100 mg kg^{-1} (2).

Other effects

Any other adverse effects
Long-chain 1-mercapto-*n*-alkanes showed potent inhibitory effects with horse liver alcohol dehydrogenase. Results suggest that thiols interact simultaneously with ≥2 sites of the enzyme; it is thought the primary interaction could be with the zinc atom in the active site and the other with the hydrophobic binding site for alkyl carbon atoms (3).

Other comments

Reviews on experimental toxicology and human health effects listed (4).

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A202 amyl nitrate

$$CH_3(CH_2)_4NO_3$$

$C_5H_{11}NO_3$ **Mol. Wt.** 133.15 **CAS Registry No.** 1002-16-0

Synonyms nitric acid, pentyl ester; *n*-pentyl nitrate

EINECS No. 213-684-2 **RTECS No.** QU 0600000

Uses Additive for diesel fuel.

Physical properties

B. Pt. 153-157°C **Flash point** 48°C (open cup) **Specific gravity** 0.997 at 20°C with respect to water at 4°C
Solubility Organic solvents: alcohol, diethyl ether

Occupational exposure

UN No. 1112 **HAZCHEM Code** 3Y **Conveyance classification** flammable liquid

Mammalian & avian toxicity

Sub-acute and sub-chronic data
LC_{Lo} (3 × 7 hr) inhalation rat exposures 1703 ppm (1).

Other effects

Other adverse effects (human)
Human exposure during animal testing produced nausea and headaches (1).

References

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A203 1-amyl-1-nitrosourea

$$CH_3(CH_2)_4N(NO)CONH_2$$

$C_6H_{13}N_3O_2$ **Mol. Wt.** 159.19 **CAS Registry No.** 10589-74-9

Synonyms *N*-nitroso-*N*-pentylurea; *N*-amyl-*N*-nitrosourea; *N*-pentyl-*N*-nitrosourea; ANU

RTECS No. YT 9720000

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 570 mg kg^{-1} (1).
TD_{Lo} subcutaneous rat 510 mg kg^{-1} (1).

Sub-acute and sub-chronic data
LD_{50} (50 wk) dermal mouse 629 mg kg^{-1} (2).

Carcinogenicity and chronic effects

Gavage Fischer 344 rats (50 wk) administered as equimolar doses 2× wk^{-1}, induced tumours of the liver, forestomach, thyroid and nervous system in both sexes. Single sex tumours recorded: ♀ mammary gland, uterus, colon; ♂ ileum, jejunum, duodenum, mesothelioma, Zymbal gland, bladder and skin (3).

Dermal ♀ Swiss mice 6.4 g l^{-1} painted on 2 × wk^{-1} induced leukaemia, skin carcinomas, lung adenomas and adenocarcinomas, and tumours of the forestomach, mammary gland, uterus and ovary (4).

Dermal application to ♀ mice (40-50 weeks) 25 µl of a 0.04 ml solution in acetone. Animals were observed until death or 100 wk. Skin tumours were seen in 11/20 mice (2).

A single subcutaneous injection to rats (concentration unspecified) at 1 or 10 days of age induced tumours of the nervous system tissue and neurinomas of the heart. The carcinogenic potential was lower in older animals (5).

Genotoxicity

Salmonella typhimurium TA1535 without metabolic activation positive (6).

Escherichia coli BR339 λ positive (6).

In vitro Chinese hamster cells incubation for 48 hr with 0.25 mg ml^{-1} induced >50% chromosome aberrations (7).

References

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2. Lijinsky, W. et al *J. Cancer. Res. Clin. Oncol.* 1981, **102**(1), 13-20.
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6. Lijinsky, W. et al *Mutat. Res.* 1987, **178**(2), 157-165.
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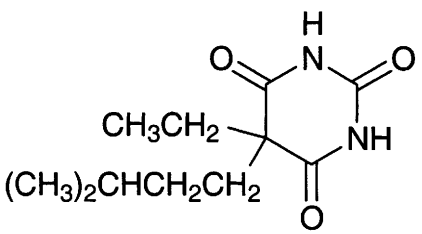
A204 amylobarbitone



$C_{11}H_{18}N_2O_3$ **Mol. Wt.** 226.28 **CAS Registry No.** 57-43-2

Synonyms Amobarbital; 5-ethyl-5-isopentylbarbituric acid; Pentymalum; 5-ethyl-5-(3-methylbutyl)-2,4,6-(1*H*,3*H*,5*H*)-pyrimidinetrione

EINECS No. 200-330-7 **RTECS No.** CQ 5075000

Uses Hypnotic and sedative.

Physical properties

M. Pt. 156-158°C

Solubility Water: 0.77 g l^{-1}. Organic solvents: benzene, chloroform, diethyl ether

Ecotoxicity

Invertebrate toxicity

EC_{50} (5 min) *Photobacterium phosphoreum* 1011 mg l^{-1} Microtox test (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse 345 mg kg^{-1} (2).

LD_{50} subcutaneous mouse 212 mg kg^{-1} (3).

LD_{50} intraperitoneal rat 115 mg kg^{-1} (4).

Metabolism and toxicokinetics

In humans, readily absorbed from gastrointestinal tract, 60% bound to plasma proteins. $t_{1/2}$ 20-25 hr, longer in neonates. 50% excreted in urine as 3'-hydroxyamylobarbitone and 30% as *N*-hydroxyamylobarbitone (5).

Readily absorbed from the gastrointestinal tract and following absorption, approximately 60% is bound to plasma proteins. $t_{1/2}$ 20-25 hr in adults. Metabolised in the liver with 50% excreted in the urine as 3'-hydroxyamylobarbitone, and 30% as *N*-hydroxyamylobarbitone. Less than 1% appears as unchanged parent compound. Approximately 5% is excreted in the faeces (6).

Significant urinary metabolite reported to be 5-(3'-carboxybutyl)-5-ethylbarbituric acid (7).

Intravenous injection 200 mg to nine healthy young human adults (4 ♂, 5 ♀). Blood samples were taken 48 hr after infusion, the mean values for clearance and apparent volume of distribution were 0.032 l hr^{-1} kg^{-1} and 1.08 l kg^{-1}, respectively (8).

One human subject ingested amylobarbitone (concentration unspecified) 7 × over 3 yr; plasma clearances 32.1 ml min^{-1} exhibited constancy, while the distribution volume 73.6 l showed some fluctuation (9).

Genotoxicity

In vivo Chinese hamster V-79 cells with and without metabolic activation positive (10).

Other effects

Other adverse effects (human)

In humans, adverse effects are similar to those for barbiturates and include respiratory depression, allergic skin rashes, hepatitis, cholestasis and photosensitivity. Erythema multiforme (Stevens-Johnson syndrome) and exfoliative dermatitis (sometimes fatal) have been reported. As with other sedatives, paradoxical excitement and irritability may occur. Nystagmus and ataxia may occur with excessive doses. Toxic effects of overdose result from profound central depression and include coma, respiratory and cardiovascular depression with hypotension and shock leading to renal failure (5).

Legislation

Controlled substance in the US (11).

Other comments

Often administered as the sodium salt to enhance bioavailability (7).

Properties, experimental toxicology and metabolism reviewed (12).

References

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3. Irrgang, K. *Arzneimittel. Forsch.* 1965, **15**, 688.
4. Knoll, J. et al *Arzneimittel. Forsch.* 1971, **21**, 719.
5. *Martindale: The Extra Pharmacopoeia* 31st ed., 1996, The Royal Pharmaceutical Society, London, UK.
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8. Bachmann, K. *Br. J. Clin. Pharmacol.* 1987, **23**(1), 95-98.
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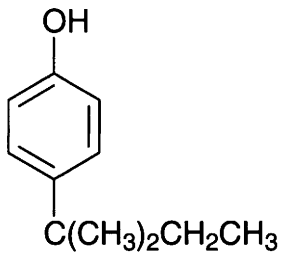
11. *US Code of Federal Regulations* 1987, **21**(329.1, 1308.12, 1308.13).
12. Mian, N. et al *Anal. Profiles Drug. Subst.* 1990, **19**, 27-58

A205 4-*tert*-amylphenol



$C_{11}H_{16}O$ **Mol. Wt.** 164.25 **CAS Registry No.** 80-46-6

Synonyms *p-tert*-pentylphenol; 2-methyl-2-*p*-hydroxyphenylbutane; *p-tert*-amylphenol; 4-(1,1-dimethylpropyl)phenol; 4-*tert*-pentylphenol; *p*-(α,α-dimethylpropyl)phenol; *p*-(1,1-dimethylpropyl)phenol; Pentaphen

EINECS No. 201-280-9 **RTECS No.** SM 6825000

Uses Manufacture of oil-soluble resins. Intermediate for organic mercury germicides and pesticides. Intermediate in the manufacture of chemicals used in the rubber and petroleum industries.

Physical properties

M. Pt. 94-95°C **B. Pt.** 262°C **Flash point** 112°C **Specific gravity** 0.96 at 20°C with respect to water at 4°C
Partition coefficient $\log P_{ow}$ 3.98
Solubility Organic solvents: chloroform, benzene, diethyl ether, ethanol

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) fathead minnow 2.5 mg l^{-1} (1).

A genetically ♂ population of common carp was exposed to 0.14 mg l^{-1} 4-*tert*-amylphenol for various periods during sexual differentiation. Exposure for three days during the embryo-larval period did not affect sexual differentiation or proliferation of primordial germ cells. Longer exposures, starting before and including sexual differentiation, induced the formation of an oviduct, which was incomplete or completely closed depending on exposure timing. This feature persisted in individuals that were returned to clean water for 59 days. Exposures for various durations before and during differentiation significantly reduced the number of primordial germ cells in a dose-related manner irrespective of timing (2).

Invertebrate toxicity

EC_{50} (48 hr) *Tetrahymena pyriformis* 9.6 mg l^{-1} (3).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 1830 mg kg^{-1} (4).

LD_{50} dermal rabbit 2000 mg kg^{-1} (5).

Irritancy

A 1% solution instilled into rabbit eye caused severe irritancy (5).

Application of 100 μg to rabbit skin for 24 hr caused irritancy (6).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA1535 with and without metabolic activation negative (7).

Other comments

Reviews on human health effects and experimental toxicology are listed (8).

References

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6. *Am. Ind. Hyg. Assoc. J.* 1962, **23**, 95.
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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

A206 amyltrichlorosilane

$$CH_3(CH_2)_4SiCl_3$$

$C_5H_{11}Cl_3Si$ **Mol. Wt.** 205.59 **CAS Registry No.** 107-72-2

Synonyms trichloropentylsilane; pentylsilicon trichloride; pentyltrichlorosilane; trichloroamylsilane

EINECS No. 203-515-0 **RTECS No.** VV 4725000

Uses Intermediate for silicone synthesis.

Physical properties

B. Pt. 160°C **Flash point** 62°C (open cup) **Specific gravity** 1.142

Occupational exposure

UN No. 1728 **HAZCHEM Code** 4XE **Conveyance classification** corrosive substance

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 2340 mg kg^{-1} (1).

LC_{50} (4 hr) inhalation rat 2000 ppm (2).

LD_{50} dermal rabbit 780 mg kg^{-1} (1).

Irritancy
100 µg applied to rabbit for 24 hr caused moderate irritancy (1).

Other comments

Readily hydrolysed with liberation of hydrogen chloride.

References

1. Smyth, H. F. et al *Am. Ind. Hyg. Assoc. J.* 1962, **23**, 95.
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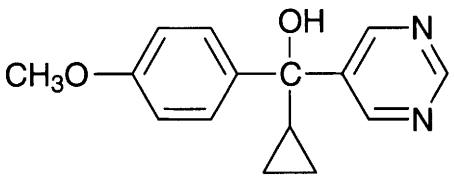
A207 ancymidol



$C_{15}H_{16}N_2O_2$ **Mol. Wt.** 256.30 **CAS Registry No.** 12771-68-5

Synonyms α-cyclopropyl-α-14-methoxyphenyl-5-pyrimidinemethanol; Reducymol

EINECS No. 235-814-7 **RTECS No.** UV 9280000

Uses Plant growth regulator and retardant.

Physical properties

M. Pt. 110-111°C **Volatility** v.p. 1.0×10^{-6} mmHg at 50°C
Solubility Water: 650 mg l^{-1}. Organic solvents: acetone, acetonitrile, chloroform, ethanol, hexane, methanol

Ecotoxicity

Fish toxicity
LC_{50} (fingerlings, duration unspecified) rainbow trout, goldfish, bluegill sunfish, 55, >100, 146 mg l^{-1}, respectively (1).

Invertebrate toxicity
Non-toxic to bees (1).

Environmental fate

Degradation studies
Undergoes microbial degradation in soil (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat, mouse 4500-5000 mg kg^{-1} (1,2).
LD_{50} oral dog >500 mg kg^{-1} (2).
LD_{50} oral chicken >500 mg kg^{-1} (1).
LD_{50} percutaneous rabbit >200 mg kg^{-1} (1).

Sub-acute and sub-chronic data

In 90-day feeding trials, rats and dogs receiving up to 8000 mg kg^{-1} diet showed no ill-effects (1).
Lowest-observed-effect level oral rat 200 mg kg^{-1} day^{-1} for non-developmental toxic effects based on decreased body-weight gain and food consumption (3).

Irritancy

Dermal rabbit (21 days) 1000 mg kg^{-1} showed no dermal irritation or systemic toxicity (3).

Genotoxicity

Non-mutagenic in a range of mutagenicity tests (3).

Legislation

Limited under EC Directive on Drinking Water Quality 80/77/EEC. Pesticides and related products: maximum admissible concentration 0.1 μg l^{-1} (4).
Included in Schedule 6 (Release into Land: Prescribed Substances) of Statutory Instrument No. 472, 1991 (5).
EPA Toxicity Class III. When applied to the skin it is practically non-toxic, Toxicity Class IV (3).

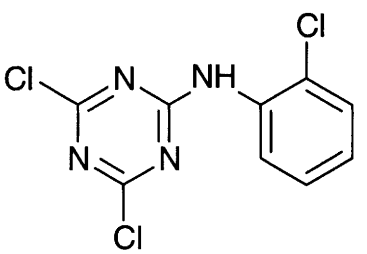
Other comments

Inhibitor of gibberellin biosynthesis (3).
Since environmental exposure to ancymidol is very limited and the compound has low toxicity, the EPA expects minimal adverse effects to birds, mammals, aquatic organisms and non-target plants (3).

References

1. *The Pesticide Manual* 11th ed., 1997, The British Crop Protection Council, Farnham, UK.
2. *European Directory of Agrochemical Products* 1990, Royal Society of Chemistry, London, UK.
3. *Prevention, Pesticides and Toxic Substances (7508W)*, United States Environmental Protection Agency, June 1995, EPA-738-F-95-027.
4. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/77/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

A208 anilazine



$C_9H_5Cl_3N_4$ **Mol. Wt.** 275.52 **CAS Registry No.** 101-05-3

Synonyms 4,6-dichloro-*N*-(2-chlorophenyl)-1,3,5-triazin-2-amine; 2,4-dichloro-6-(*o*-chloroanilino)-*s*-triazine; (*o*-choroanilino)dichlorotriazine; Dyrene; Triazine

EINECS No. 202-910-5 **RTECS No.** XY 7175000

Uses Superseded fungicide.

Physical properties

M. Pt. 159°C **Specific gravity** 1.8 at 20°C
Solubility Water: 8 mg l^{-1} at 20°C. Organic solvents: acetone, toluene, xylene

Occupational exposure

Supply classification irritant
Risk phrases Irritating to eyes and skin (R36/38)
Safety phrases Keep out of reach of children (if sold to general public) – Do not breathe dust (S2, S22)

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) rainbow trout, channel catfish, bluegill sunfish 140 μg l^{-1} (1).
LC_{50} (96 hr) rainbow trout, golden orfe 0.15 mg l^{-1} (2).

Invertebrate toxicity
EC_{50} (duration unspecified) *Daphnia pulex* 4.5 mg l^{-1} (3).
EC_{50} (48 hr) *Daphnia* 0.07 mg l^{-1} (2).
Not harmful to bees at recommended application rates (2).

Environmental fate

Degradation studies
$t_{1/2}$ in damp soil ~12 hr (2).

Adsorption and retention
Adsorption through exchange process to organic matter and clay minerals is dependent on pH of solution and acidity of adsorbent surface (4).

Mammalian & avian toxicity

Acute data
LD_{50} oral redwing blackbird 100 mg kg^{-1} (5).
LD_{50} rabbit 2700 mg kg^{-1} (6).
LD_{50} oral Virginia quail >2000 mg kg^{-1} (2).
LD_{50} oral rat >4000 mg kg^{-1} (2).
LC_{50} (4 hr) inhalation rat >0.25 mg l^{-1} (aerosol) (2).
LD_{50} intraperitoneal mouse, rat 25-50 mg kg^{-1} (7).
LD_{50} percutaneous rat >5000 mg kg^{-1} (2).

Carcinogenicity and chronic effects
National Toxicology Program tested rats and mice via dosed-feed. Negative evidence of carcinogenicity in ♂ and ♀ rats and mice (8).
No-observable-effect level (2 yr) rats, mice 2000, 1250 mg kg^{-1} diet, respectively; (18 months) dogs 40 mg kg^{-1} body weight (2).

Metabolism and toxicokinetics
20% of a dose was excreted in the faeces, 64% in urine and 16% remained in the carcass after 3 days (species unspecified) (9).

Irritancy
Dermal rabbit (duration unspecified) 500 mg caused severe irritancy (6).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA1535, TA1537 with and without metabolic activation negative (10).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides and related products: maximum admissible concentration 0.1 μg l^{-1} (11).
Included in Schedule 6 (Release into Land: Prescribed Substances) of Statutory Instrument No. 472, 1991 (12).
EPA Toxicity Class II (2).
WHO Toxicity Class Table 5 (13).
ADI 0.1 mg kg^{-1} body weight (2).

Other comments

Toxicity studied (14).
Incompatible with oils and alkaline materials.

References

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12. *S.I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
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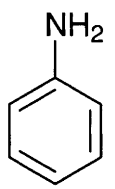
A209 aniline



C_6H_7N **Mol. Wt.** 93.13 **CAS Registry No.** 62-53-3

Synonyms benzenamine; phenylamine; aminobenzene; aminophen; Kyanol; Anyvim; Blue Oil; C.I. 76000; C.I. Oxidation Base; aniline oil; NCI-C03736

EINECS No. 200-539-3 **RTECS No.** BW 6650000

Uses In the manufacture of dyestuffs, medicinals, resins, varnishes and shoe blacks.

Physical properties

M. Pt. –6.2°C **B. Pt.** 184.4°C **Flash point** 70-76°C (closed cup) **Specific gravity** 1.02173 at 20°C with respect to water at 4°C **Partition coefficient** log P_{ow} 0.90 **Volatility** v.p. 0.3 mmHg at 20°C ; v.den. 3.22
Solubility Organic solvents: acetone, benzene, diethyl ether, ethanol

Occupational exposure

DE-MAK 2 ppm (7.7 mg m^{-3})
FR-VME 2 ppm (10 mg m^{-3})
JP-OEL 1 ppm (3.8 mg m^{-3})
SE-LEVL 1 ppm (4 mg m^{-3}) **SE-STEL** 2 ppm (8 mg m^{-3})
UK-LTEL MEL 1 ppm (4mg m^{-3})
US-TWA 2 ppm (7.6 mg m^{-3})

UN No. 1547 **HAZCHEM Code** 3X **Conveyance classification** toxic substance
Supply classification toxic, dangerous for the environment
Risk phrases Harmful 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, in contact with skin and if swallowed – Very toxic to aquatic organisms (R20/21/22, R40, R48/23/24/25, R50)
Safety phrases Keep locked up and out of the reach of children (if sold to general public) – After contact with skin, wash immediately with plenty of water – Wear suitable protective clothing and gloves – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) – Avoid release to the environment. Refer to special instructions/safety data sheet (S1/2, S28, S36/37, S45, S61)

Ecotoxicity

Fish toxicity
LC_{50} (0-8 day) bass, goldfish, catfish 47.3-4.4 mg l^{-1} (1).
LC_{50} (96 hr) fathead minnow 134 mg l^{-1} (2).
LC_{50} (7 day) rainbow trout 8.2 mg l^{-1} (3).
Embryotoxicity of aniline in zebra fish (*Brachydanio rerio*) is enhanced considerably by alkylation of the compound. NH_2-substitution of alkyl compounds leads to agents with less embryotoxicity (4).

Invertebrate toxicity
Inhibition of cell multiplication *Pseudomonas putida* 130 mg l^{-1} (5).
EC_{50} (48 hr) *Daphnia magna, Daphnia pulex, Daphnia cucullata* 0.10-0.68 mg l^{-1} (6).
EC_{50} (5-30 min) *Photobacterium phosphoreum* 70.6 mg l^{-1} Microtox test (7).
IC_{50} *Saccharomyces cerevisiae* 100 mg l^{-1} (8).

Bioaccumulation
Measured bioconcentration factor was ≤148, demonstrating that aniline does not accumulate in fish (9-11).

Environmental fate

Nitrification inhibition
Ammonia oxidation *Nitrosomonas* sp. 76% inhibition 2.5 mg l^{-1} (12).

Degradation studies
Achromobacter xylosoxidans and *Pseudomonas* spp. were isolated from an aniline-contaminated site. A mixed liquid culture of these bacteria grew on aniline as the only carbon source, demonstrating simultaneous oxygen uptake and aniline removal at concentrations of 700 mg l^{-1}. The optimum pH for biodegradation was 7-8 (13).
Nitrosomonas europaea ammonia monooxygenase catalysed aniline oxidation to nitrobenzene (and unidentified products) (14).
Biodegradable (15).
Decomposition by soil microflora 4 days (16).
Decomposition by *Aerobacter* 500 mg l^{-1} at 30°C; parent 100% ring disruption in 54 hr, mutant 100% ring disruption in 12 hr (17).

Degraded by many common species of bacteria and fungi found in soil; acetanilide, 2-hydroxyacetanilide, 4-hydroxyaniline and catechol are reported metabolites (18-21).
Desulfitobacterium anilini completely degraded aniline to carbon dioxide and ammonia with stoichiometric reduction of sulfate to sulfide (21).

Abiotic removal

Adsorption on Amberlite XAD 7 100% (22).
0.150 g g^{-1} carbon, 74.9% reduction (4).
Oxidised on exposure to sunlight in air forming products including hydrazobenzene, 4-aminodiphenylamine, 2-aminodiphenylamine, benzidine and azobenzene (23).
Photolytic $t_{1/2}$ in the atmosphere has been estimated to be 2.1 days based on a measured reaction rate constant of 0.32 l day^{-1} (24).
Estimated $t_{1/2}$ for aniline vapour reacting with photochemically generated hydroxyl radicals in the atmosphere is 3.3 hr (25).
Soil-catalysed oxidation occurs in sterilised soil with 9 products being detected after 2 days, including azobenzene, azoxybenzene, phenazine, formanilide and acetanilide (26).
$t_{1/2}$ in estuarine water was 27 and 173 hr in the light and dark (microbial), respectively. Photolysis rates decreased in winter due to decreased surface irradiation and temperature (27).

Adsorption and retention

Soil adsorption increases with the percent of organic carbon and decreases with the pH of the soil (28).
The soil adsorption coefficient in colloidal organic carbon from groundwater was 3900 which effectively increases aniline solubility and leaching into groundwater (29).

Mammalian & avian toxicity

Acute data

LD_{50} oral redwing blackbird 562 mg kg^{-1} (30).
LD_{50} oral rat 250 mg kg^{-1} (31).
LC_{50} (7 hr) inhalation mouse 175 ppm (32).
LD_{Lo} dermal rabbit 820 mg kg^{-1} (33).
LD_{50} dermal guinea pig 290 mg kg^{-1} (34).
LD_{50} intraperitoneal rat 420 mg kg^{-1} (35).

Sub-acute and sub-chronic data

Inhalation rat (4 day) 150 ppm methaemoglobinaemia, decreased haemocrit reported (36).

Carcinogenicity and chronic effects

Inadequate evidence for carcinogenicity to humans or animals, IARC classification group 3 (37).
Induced tumours in spleen of ♂ and ♀ rats, but not mice (38).

Metabolism and toxicokinetics

Converted via hepatic microsomal enzymes into aminophenols and *N*-hydroxylamines (39,40).
Following administration to rabbits, 80% of dose is excreted in urine as conjugates of 4-aminophenol (55%), 2-aminophenol (10%) and 3-aminophenol (0.1%), and as aniline (3.5%), aniline-*N*-glucuronide (6%), phenylsulfamic acid (8%) and acetanilide (0.2%). Traces of the metabolites (1%) were excreted in faeces and no aniline was exhaled (41).
In rats aniline is absorbed by simple diffusion from rectum at rates related to degree of ionisation and lipid-to-water Partition coefficient of compound (42).

Irritancy

Dermal rabbit (24 hr) 500 mg caused moderate irritation, while 102 mg instilled into rabbit eye caused severe irritation (43,44).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA102, TA104, TA1535, TA1537 Salmonella/mammalian microsome mutagenicity assay negative (45).

Escherichia coli PQ37 SOS-chromotest, with and without metabolic activation negative (45).
Escherichia coli WP2s(λ) negative induction of prophage in microscreen assay (46).
Mouse L5178Y tk+/tk– lymphoma cells with and without metabolic activation positive (47).
Positive response was obtained in the mouse bone marrow micronucleus test 24 hr after the second of two intraperitoneal injections of 80% of the median LD. Negative results were observed at low dose levels and at earlier and later sampling times (48).

Other effects

Other adverse effects (human)
Following exposure of two workers to aniline, methaemoglobin and urinary metabolites decreased while no significant change was observed for methaemoglobin reductase level. $t_{1/2}$ of methaemoglobin was 13 hr (49).
Inhalation, ingestion or cutaneous absorption results in methaemoglobinaemia, with cyanosis, headache, weakness, stupor and coma. Irritation, nausea, and cardiac arrhythmias may occur and haemolysis has been reported (50).

Other comments

The US government has alerted US companies using aniline to evidence that clearly associates exposure to aniline with an increased risk of bladder cancer, and that they should reduce workers' exposure to the chemical to the lowest feasible concentration. Other recommendations include: engineering controls and work practices to limit exposure, using personal protective equipment including special clothing, environmental monitoring and medical screening of workers (51).
Occupational exposure in organic synthesis and dyestuffs manufacturing, properties, risks, metabolism, toxicity, handling and storage, and first aid reviewed (52).
Analysis of air samples in school buildings containing self-levelling flooring material containing casein showed the presence of aniline, but at concentrations well below official threshold limits. The pollution was attributed to biodegradation of the casein by alkali-resistant *Clostridium* sp. People in these buildings reported sick building syndrome-type symptoms (53).
The main metabolic pathway of aniline in the larvae of arctic charr is *N*-acetylation (54).
Physical and chemical properties, toxicity, hazards and recommendations for storage and handling, and first aid in case of poisoning reviewed (55).
Reviews on physico-chemical properties, human health effects, experimental toxicology, epidemiology, environmental effects and workplace experience listed (56,57).
Incompatible with oxidisers, albumin, solutions of iron, zinc, aluminium, acids and alkalis.

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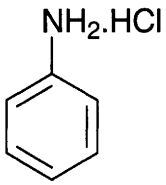
A210 aniline hydrochloride



C_6H_8ClN **Mol. Wt.** 129.59 **CAS Registry No.** 142-04-1

Synonyms aniline salt; benzenamine hydrochloride; anilinium chloride

EINECS No. 205-519-8 **RTECS No.** CY 0875000

Uses See aniline.

Physical properties

M. Pt. 189°C **B. Pt.** 245°C **Flash point** 193°C (open cup) **Specific gravity** 1.2215 **Volatility** v.den. 4.5
Solubility Organic solvents: ethanol

Occupational exposure

FR-VME 7.6 ppm

UN No. 1548 **HAZCHEM Code** 2Z **Conveyance classification** toxic substance
Supply classification toxic
Supply classification dangerous for the environment
Risk phrases Harmful 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, in contact with skin and if swallowed – Very toxic to aquatic organisms (R20/21/22, R40, R48/23/24/25, R50)
Safety phrases Keep locked up and out of the reach of children (if sold to general public) – After contact with skin, wash immediately with plenty of water – Wear suitable protective clothing and gloves – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) – Avoid release to the environment. Refer to special instructions/safety data sheet (S1/2, S28, S36/37, S45, S61)

Ecotoxicity

Fish toxicity
LC_{50} (48 hr) goldfish 5.5 mg l^{-1} (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat, mouse 840, 1070 mg kg^{-1}, respectively (2).
LD_{50} intraperitoneal mouse 300 mg kg^{-1} (3).
Oral rat 2 mmol kg^{-1}, euthanised at 0, 0.25, 0.5, 1, 3, 6, 12, 24 and 48 hr. Methaemoglobin levels peaked at 0.5 hr (37%), and then declined with time. Spleen weight to body weight ratio remained unchanged up to 24 hr, but increased 25% at 48 hr. Lipid peroxidation in the spleen increased by 39% at 24 hr. No changes were observed in splenic protein oxidation, however congestion of the blood vessels and expansion of red pulp was observed at 24 and 48 hr (4).

Sub-acute and sub-chronic data
Oral Sprague-Dawley ♂ rats 600 ppm in drinking water for 30, 60, or 90 days. Spleen organ-to-body weight ratio in treated animals was 56, 61, and 53% higher than controls at days 30, 60, and 90, respectively; liver showed a weight decrease at 30 days followed by an increase at 60 days; testes showed a significant decrease at 60 days.

Haematology: 65% increase in white blood cell count at 30 days, no change at later times; significant decrease in erythrocyte counts at all time points; Hb and haematocrit decreased at 30 and 90 days. Serum IgA showed 24 and 51% increase at days 60 and 90. Decreased numbers of splenic T-helper cells (CD+/CD8–) at 90 days. Spleen showed striking histopathological changes at all times, including marked red pulp expansion due to increased sinusoidal cells, fibroblasts, and markedly increased light brown pigment of haem origin. Focal pericapsular fibrosis was found at all times, with no evidence of neoplasia. These histological changes were greatly accentuated with the progression of exposure (5).

Carcinogenicity and chronic effects

After oral administration, no increase in tumour incidence was observed in mice, but fibrosarcomas, sarcomas and haemangiosarcomas of the spleen and peritoneal cavity occurred in rats (6).

National Toxicology Program tested rats and mice via dosed-feed. Positive evidence of carcinogenicity for ♂ and ♀ rats, negative for ♂ and ♀ mice (7).

Irritancy

Dermal rabbit (24 hr) 500 mg caused moderate irritation; 20 mg instilled into rabbit eye for 24 hr caused moderate irritation (8).

Genotoxicity

Vicia faba root cells induced chromosomal aberrations (9).

Oral ♂ CRH mouse (24 hr) 1000 mg kg^{-1} induced micronuclei in the bone marrow (10).

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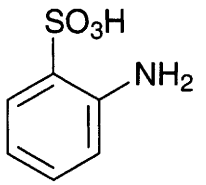
A211 aniline-2-sulfonic acid



$C_6H_7NO_3S$ **Mol. Wt.** 173.19 **CAS Registry No.** 88-21-1

Synonyms 2-aminobenzenesulfonic acid; orthanilic acid; *o*-sulfanilic acid; *o*-aminophenylsulfonic acid; benzenesulfonic acid, 2-amino; *o*-aniline sulfonic acid; anilino-*o*-sulfonic acid

EINECS No. 201-810-9 **RTECS No.** DB 4727700

Uses Manufacture of azo dyestuffs. Component of water-based hydraulic fluids.

Physical properties

M. Pt. >300°C

Environmental fate

Degradation studies

Decomposition by soil microflora in >64 days (1).

Mammalian & avian toxicity

Metabolism and toxicokinetics

2-Aminobenzenesulfonic acid interacts with rat liver glutathione *S*-transferase by direct binding (2).

Genotoxicity

Salmonella typhimurium TA98 without metabolic activation weakly positive (3).

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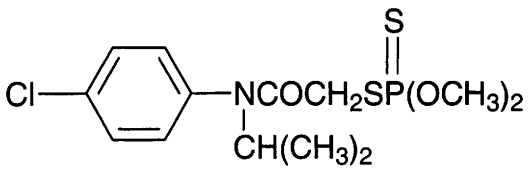
A212 anilofos



$C_{13}H_{19}ClNO_3PS_2$ **Mol. Wt.** 367.86 **CAS Registry No.** 64249-01-0

Synonyms *S*-[2-[4-chlorophenyl(1-methylethyl)amino]-2-oxo-ethyl]-*O*,*O*-dimethylphosphorodithioate; *S*-4-chloro-*N*-isopropylcarbaniloylmethyl-*O*,*O*-dimethyl phosphorodithioate

EINECS No. 264-756-5 **RTECS No.** TD 5185000

Uses Herbicide.

Physical properties

M. Pt. 50.5-52.5°C **B. Pt.** 150°C (decomp.) **Specific gravity** 1.27 at 25°C

Volatility v.p. 1.65×10^{-5} mmHg at 60°C

Solubility Water: 13.6 mg l^{-1}. Organic solvents: acetone, benzene, chloroform, dichloromethane, ethanol, hexane, toluene

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) goldfish, trout 2.8, 4.6 mg l^{-1}, respectively (1).

Invertebrate toxicity

EC_{50} (3 hr) *Daphnia* 756 mg l^{-1} (1).

Environmental fate

Degradation studies

$t_{1/2}$ in soil 30-45 days at 23°C (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral ♂, ♀ Japanese quail 3360, 2339 mg kg^{-1}, respectively (1).

LD_{50} oral ♂, ♀ rat 830, 472 mg kg^{-1}, respectively (1).

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

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides and related products: maximum admissible concentration 0.1 µg l^{-1} (2).

Included in Schedule 6 (Release into Land: Prescribed Substances) of Statutory Instrument No. 472, 1991 (3).

Other comments

Metabolic pathways reviewed (4).

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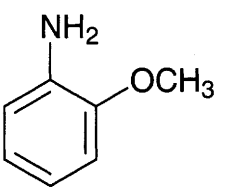
A213 2-anisidine



C_7H_9NO **Mol. Wt.** 123.15 **CAS Registry No.** 90-04-0

Synonyms *o*-methoxyaniline; 2-methoxyaniline; 2-methoxybenzenamine; *o*-aminoanisole; *o*-anisidine

EINECS No. 201-963-1 **RTECS No.** BZ 5410000

Uses Manufacture of azo dyestuffs.

Physical properties

M. Pt. 6.2°C **B. Pt.** 224°C **Flash point** 107°C (closed cup) **Specific gravity** 1.0923 at 20°C with respect to water at 4°C **Partition coefficient** log P_{ow} 0.95 **Volatility** v.p. <0.1 mmHg at 30°C ; v.den. 4.25

Solubility Organic solvents: acetone, benzene, diethyl ether (miscible), ethanol

Occupational exposure

FR-VME 0.1 ppm (0.5 mg m^{-3})
JP-OEL 0.1 ppm (0.5 mg m^{-3}) (provisional value)
UK-LTEL 0.1 ppm (0.51 mg m^{-3})
US-TWA 0.1 ppm (0.5 mg m^{-3})

UN No. 2431 **HAZCHEM Code** 3X **Conveyance classification** toxic substance
Supply classification very toxic, dangerous for the environment
Risk phrases May cause cancer – Very 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 (R45, R26/27/28, R33, 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

Bioaccumulation
Based on water solubility of 14 g l^{-1} and log K_{ow} of 1.18, the estimated bioconcentration factor is 3-5 which suggests bioaccumulation in aquatic organisms will be unlikely (1).

Environmental fate

Degradation studies
Japanese MITI test, initial 2-anisidine 100 ppm, initial activated sludge 30 mg l^{-1}, 14-day incubation period, 69.1% theoretical BOD (nitrate end-product), 81.7% theoretical BOD (ammonia end-product) (2).
20 μg l^{-1} inoculated with a mixed culture of soil microorganisms in an aqueous mineral salts media persisted for >64 days (3).
Escherichia coli converted 2-anisidine in the presence of nitrate into its corresponding (phenylazo)naphthol (4).

Abiotic removal
Atmospheric $t_{1/2}$ with photochemically generated hydroxyl radicals estimated as 3 hr (5).

Adsorption and retention
Relatively immobile in soil and strongly binds to humic material in suspended solids and sediments in water (6).

Mammalian & avian toxicity

Acute data
LD_{50} oral redwing blackbird 420 mg kg^{-1} (7).
LD_{50} oral mouse, rat 1400, 2000 mg kg^{-1}, respectively (8).
LD_{50} oral rabbit 870 mg kg^{-1} (8).

Carcinogenicity and chronic effects
No adequate evidence for carcinogenicity to humans, sufficient evidence for carcinogenicity in animals, IARC classification group 2B (8).
Oral B6C3F1 mice, maximum tolerated dose (750 mg kg^{-1}), yielded negative results in ^{32}P-post-labelling assays of bladder and liver DNA (24 hr after dosing). ^{14}C-ring-labelled 2-anisidine administered orally gave no evidence of DNA binding 6, 12, or 24 hr later. Oral transgenic lac I– mice (750 mg kg^{-1}) led to a small increase in mutation frequency in the bladder, but not in the liver. The possibility that 2-anisidine is mutagenic and carcinogenic to the rodent bladder via formation of radical species is suggested (9).

Genotoxicity

Salmonella typhimurium TA98, TA100 with metabolic activation positive (10).
Drosophila melanogaster chronic exposure gave positive white/white+ somatic assay (11).

Oral ♂ CD-1 mice (8-wk old) 690 mg kg^{-1}. Statistically significant DNA damage in bladder mucosa was seen at 3 and 24 hr after dosing and in the mucosa of colon after 3 but not 24 hr. No significant effects were seen in kidney, brain, bone marrow, or mucosa of stomach at 3 and 24 hr (12).

Other comments

Horseradish peroxidase metabolism yielded diimine, quinone imine, azo dimer, polymer metabolites (13). Reviews on physico-chemical properties, human health effects and experimental toxicology listed (14).

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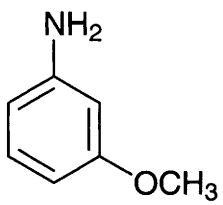
A214 3-anisidine



C_7H_9NO **Mol. Wt.** 123.15 **CAS Registry No.** 536-90-3

Synonyms *m*-methoxyaniline; 3-methoxybenzenamine; *m*-aminophenol methyl ether; *m*-aminoanisole; *m*-anisylamine; *m*-anisidine

EINECS No. 208-651-4 **RTECS No.** BZ 5408000

Uses Manufacture of azo dyestuffs.

Physical properties

M. Pt. –10°C **B. Pt.** 251°C **Specific gravity** 1.096 at 20°C with respect to water at 4°C **Partition coefficient** log P_{ow} 0.93

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

Occupational exposure

UN No. 2431 **HAZCHEM Code** 3X **Conveyance classification** toxic substance

Environmental fate

Degradation studies

Decomposition by a soil microflora >64 days (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral coturnix 560 mg kg^{-1} (2).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1538 with metabolic activation positive (3).

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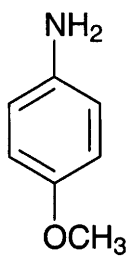
A215 4-anisidine



C_7H_9NO **Mol. Wt.** 123.15 **CAS Registry No.** 104-94-9

Synonyms 1-amino-4-methoxybenzene; benzenamine, 4-methoxy-; *p*-aminoanisole; *p*-anisidine; *p*-anisylamine; methoxyaniline; 4-methoxybenzenamine; *p*-methoxyphenylamine

EINECS No. 203-254-2 **RTECS No.** BZ 5450000

Uses Manufacture of azo dyestuffs.

Physical properties

M. Pt. 57°C **B. Pt.** 246°C **Flash point** 5°C (closed cup) **Specific gravity** 1.071 at 57°C with respect to water at 4°C **Partition coefficient** log P_{ow} 0.95 **Volatility** v.p. 0.1 mmHg at 20°C ; v.den. 4.25
Solubility Organic solvents: acetone, benzene, diethyl ether, ethanol, methanol

Occupational exposure

DE-MAK 0.1 ppm (0.51 mg m^{-3})
FR-VME 0.1 ppm (0.5 mg m^{-3})
JP-OEL 0.1 ppm (0.5 mg m^{-3}) (provisional value)

UK-LTEL 0.1 ppm (0.5 mg m^{-3})
US-TWA 0.1 ppm (0.5 mg m^{-3})

UN No. 2341 **HAZCHEM Code** 3X **Conveyance classification** toxic substance
Supply classification very toxic
Supply classification dangerous for the environment
Risk phrases Very toxic by inhalation, in contact with skin and if swallowed – Danger of cumulative effects – Very toxic to aquatic organisms (R26/27/28, R33, R50)
Safety phrases Keep locked up and out of the reach of children (if sold to general public) – After contact with skin, wash immediately with plenty of water – Wear suitable protective clothing and gloves – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) – Avoid release to the environment. Refer to special instructions/safety data sheet (S1/2, S28, S36/37, S45, S61)

Ecotoxicity

Invertebrate toxicity
EC_{50} (30 min) *Photobacterium phosphoreum* 14.5 mg l^{-1} Microtox test (1).

Bioaccumulation
Estimated bioconcentration factor of 3 which suggests bioaccumulation will be unlikely in aquatic organisms (2).

Environmental fate

Degradation studies
Escherichia coli converted 4-anisidine in the presence of nitrate into its corresponding (phenylazo)naphthol (3). Japanese MITI test, initial 4-anisidine concentration 100 ppm, initial activated sludge 30 mg l^{-1} 14-day incubation period, 65.3% theoretical BOD (nitrogen dioxide end-product), 78.5% theoretical BOD (ammonia end-product) (4). 25 μg l^{-1} of 4-anisidine inoculated with a mixed culture of soil microorganisms in an aqueous mineral salts media underwent complete degradation in 64 days (5).

Abiotic removal
Estimated $t_{1/2}$ 3 hr reacting with photochemically generated hydroxyl radicals (6).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 1400 mg kg^{-1} (7).
LD_{50} dermal rat 3200 mg kg^{-1} (7).
LD_{50} intraperitoneal rat 1400 mg kg^{-1} (7).
Intraperitoneal ♂ rats 120 mg kg^{-1} induced swelling of the tubular epithelial cells and a significant elevation in urinary *N*-acetyl-β-D-glucosaminidase activity (8).

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

Irritancy
Dermal New Zealand white rabbit (24 hr) 500 mg (abraded and intact sites); 2/3 abraded sites had slight erythema and one of these also had a slight amount of oedema. No effects present at 48 hr. 100 mg administered to left conjunctival sac of four New Zealand white rabbits produced conjunctival injection, chemosis, and colourless discharge. Ocular effects disappeared in 1/4 eyes at 72 hr, 2/4 appeared normal at 6 days, 1/4 remained irritated at the end of 14 days (10).

Genotoxicity

Salmonella typhimurium TA100 with metabolic activation positive (11).

Other comments

In vitro study, horseradish peroxidase metabolism yielded a diimine metabolite which subsequently hydrolysed to form a quinone imine; also observed was a dimeric metabolite with an azo bond (12).
Reviews on experimental toxicology and human health effects listed (13).

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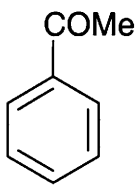
A216 anisole



C_7H_8O **Mol. Wt.** 108.14 **CAS Registry No.** 100-66-3

Synonyms methoxybenzene; phenyl methyl ether; methyl phenyl ether

EINECS No. 202-876-1 **RTECS No.** BZ 8050000

Uses Used in perfumery.

Physical properties

M. Pt. -37.3°C **B. Pt.** 153.8°C **Flash point** 52°C **Specific gravity** 0.9961 at 20°C with respect to water at 4°C
Partition coefficient log P_{ow} 2.11 **Volatility** v.p. 10 mmHg at 42.2°C ; v.den. 3.72
Solubility Organic solvents: acetone, benzene, diethyl ether, ethanol

Occupational exposure

UN No. 2222 **HAZCHEM Code** 3Y **Conveyance classification** flammable liquid

Ecotoxicity

Invertebrate toxicity
EC_{50} (30 min) *Photobacterium phosphoreum* 18.8 mg l^{-1} Microtox test (1).

Environmental fate

Degradation studies

Confirmed biodegradable (2).

Decomposition by soil microflora in 8 days (3).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 3700 mg kg^{-1} (4).

LD_{50} subcutaneous rat 3500-4000 mg kg^{-1} (5).

Mice exposed to an average concentration of 1880 mg m^{-3} anisole for 2 hr suffered damage to mucous membranes, exhibited slight excitation, then ataxia, and died within 2 days (6).

Metabolism and toxicokinetics

A major urinary metabolite is 4-hydroxyphenyl methyl ether which was excreted unconjugated (2%) and conjugated with glucuronic acid (48%) and sulfuric acid (29%). Administration of anisole to dogs caused increased excretion of ethereal sulfate (5).

Irritancy

Dermal rabbit (24 hr) 500 mg caused moderate irritation (7).

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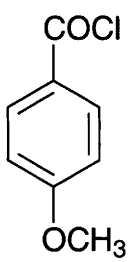
A217 4-anisoyl chloride



$C_8H_7ClO_2$ **Mol. Wt.** 170.60 **CAS Registry No.** 100-07-2

Synonyms *p*-anisoyl chloride; *p*-anisyl chloride; *p*-methoxybenzoyl chloride; 4-methoxybenzoyl chloride

EINECS No. 202-816-4 **RTECS No.** CA 0270000

Uses Chemical intermediate.

Physical properties

M. Pt. 22°C **B. Pt.** 262-263°C (decomp.) **Flash point** >107°C **Specific gravity** 1.261 at 20°C with respect to water at 4°C

Solubility Organic solvents: acetone, benzene, diethyl ether

Occupational exposure

UN No. 1729 **HAZCHEM Code** 2X **Conveyance classification** corrosive substance

Ecotoxicity

Invertebrate toxicity

EC_{50} (5 min) *Photobacterium phosphoreum* 1.91 mg l^{-1} Microtox test (1).

Other effects

Other adverse effects (human)

In humans exposure to vapours can cause serious eye burns (2).

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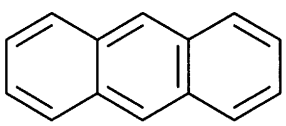
A218 anthracene



$C_{14}H_{10}$ **Mol. Wt.** 178.23 **CAS Registry No.** 120-12-7

Synonyms paranaphthalene

EINECS No. 204-371-1 **RTECS No.** CA 9350000

Uses Intermediate for anthraquinone dyestuffs.

Occurrence Urban air, incomplete combustion.

Obtained from coal tar.

Physical properties

M. Pt. 218°C **B. Pt.** 342°C **Flash point** 121°C **Specific gravity** 1.25 at 27°C with respect to water at 4°C

Partition coefficient log P_{ow} 4.45 **Volatility** v.den. 6.15

Solubility Water: 1.24 mg l^{-1}. Organic solvents: benzene, carbon disulfide, carbon tetrachloride, ethanol, toluene

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) bluegill sunfish 11.9 μg l^{-1} (1).

Fathead minnow (6 wk) 0, 6 or 12 μg l^{-1} followed by increases to 12 and 20 μg l^{-1} for 3 wk. Eggs were collected daily and placed into clean water. Significant bioconcentration of anthracene was observed in the eggs laid, in the gonads and carcasses of the spawning fish. Decreased reproductive output was observed in all anthracene-exposed fish and maternal exposure in the absence of solar UV radiation caused reduction in percent hatch and percent survival to 96 hr post-hatch. Teratogenic effects including internal haemorrhaging, oedema, eye and yolk deformities were observed in fry maternally exposed with subsequent solar UV radiation exposure (2).

Invertebrate toxicity

LC_{50} *Culicid* mosquito larvae 26.8 μg l^{-1} (1).

In the dark (16 hr), anthracene was not toxic at saturation to *Tetrahymena pyriformis*, but illumination with UVB radiation caused 100% mortality in 52 minutes (3).
The phototoxicity (as measured by LC_{50} and EC_{50}) of anthracene for the mysid *Mysidopsis bahia* and embryos and juveniles of the bivalve *Mulinia lateris* was greater under UV (UVA 397 ± 35.1, UVB 134 ± 22.8 μW cm^{-2}) than under fluorescent irradiation (UVA 9.70 ± 0.66, UVB 3.37 ± 0.22 μW cm^{-2}) by factors of 149, 658, and >193, respectively (4).

Bioaccumulation
Estimated bioconcentration factor in whole fish was 675, a lower value than that predicted by log P_{ow} 4.45 because of biotransformation (5).
Measured bioconcentration factor in goldfish exposed to 1 mg l^{-1} was 162 (6).
Rainbow trout were exposed for 72 hr to ^{14}C-anthracene alone and in an oil shale retort water. Tissues were analysed at 24, 48, and 96 hr, measured bioconcentration factor 9000-9200 (7).
Daphnia pulex bioconcentration factor measured as 759-912 (8).
Accumulation of anthracene administered to young coho salmon in food and by intraperitoneal injection was in key organs, e.g. liver and brain. After intraperitoneal injection the highest percent of metabolites occurred in the gall bladder, but significant amounts were also found in the liver, brain, flesh and carcass (9).

Environmental fate

Degradation studies
The $t_{1/2}$ in soil was 108-175 days (10).
Theoretical BOD_5 using inoculum from three polluted surface waters 2% (11).
Significant degradation with gradual adaptation reported for 5 and 10 mg l^{-1} anthracene incubated with sewage seed, 43% and 26% degradation after 7 days, 92% and 51% degradation after 28 days and 3 weekly subcultures (12).
Phanerochaete chrysosporium degraded anthracene to form the metabolite anthraquinone (13).
Alcaligenes denitrificans WW1 utilised anthracene as sole carbon source (14).
Slight degradation was reported with benzene acclimated sludge in 8 hr at 20°C (15).
The $t_{1/2}$ were 57-210 days in unacclimatised sediments and 5-7 days in oil-treated sediments (16).
Oil-polluted freshwater samples were screened for hydrocarbon-utilising ability using naphthalene and anthracene as sole source of carbon. *Micrococcus, Corynebacterium, Nocardia,* and *Pseudomonas* were recovered on basal medium supplemented with the hydrocarbons. *Aspergillus* (*A. flavus* var. *columnaris*) and *Scopulariopsis* (*S. brumptii*) were the most prevalent fungal genera (17).
Pseudomonas mendocina (NCIMB 13264) and *Pseudomonas 61* sp. (NCIMB 13262) isolated from soil polluted with crude oil degraded anthracene at 15 and 30°C. Additional nitrogen and phosphorus had no influence on the degradation process (18).
Proposed pathway for bacterial catabolism is via metabolites 1,2-dihydroxyanthracene, 2-hydroxy-3-naphthaldehyde, 2-hydroxy-3-naphthioic acid and 2,3-dihydroxynaphthalene salicylic acid (16).
Zygomycetes were shown to degrade 81% of anthracene (10 mg l^{-1}) in a liquid medium over a 4-day period (19).

Abiotic removal
$t_{1/2}$ 35 min in distilled water exposed to midday sunlight (20).
Estimated atmospheric $t_{1/2}$ is 1.67 days after reaction with photochemically produced hydroxyl radicals (21).

Adsorption and retention
Soil adsorption coefficient of 26,000 indicates strong adsorption to soil and anthracene may degrade before it reaches ground water (16).

Mammalian & avian toxicity

Carcinogenicity and chronic effects
No adequate evidence for carcinogenicity to humans, limited evidence for carcinogenicity to animals, IARC classification group 3 (22).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA102, TA104, TA1535, TA1537 with and without metabolic activation negative (23).
Escherichia coli PQ37 SOS induction negative (23).
Drosophila melanogaster DNA repair test negative (24). *Pleurodeles waltl* (Amphibia, Salamandridae) larval erythrocyte *in vivo* micronucleus test negative (25).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Polycyclic aromatic hydrocarbons: maximum admissible concentration 0.2 μg l^{-1} (26).

Other comments

Anthracene and related compounds were found in French alcoholic drinks at 1-10 ppb (27).
Reviews on experimental toxicology, human health effects, ecotoxicology and environmental effects listed (28).
Anthracene inhibits the electron transport system of plants at photosystem I causing inhibition of photosynthesis (29).

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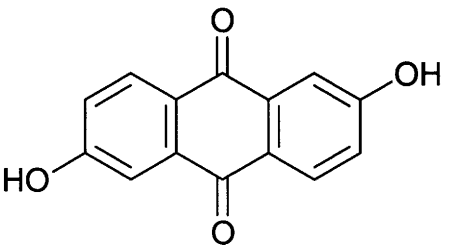
A219 anthraflavic acid



$C_{15}H_8O_4$ **Mol. Wt.** 252.23 **CAS Registry No.** 84-60-6

Synonyms 2,6-dihydroxyanthraquinone; 2,6-dihydroxy-9,10-anthracenedione; anthraflavin

EINECS No. 201-544-3 **RTECS No.** CB 6675000

Uses Dyestuffs.

Physical properties

M. Pt. >330°C

Solubility Organic solvents: ethanol

Mammalian & avian toxicity

Acute data

LD_{50} intravenous mouse 180 mg kg^{-1} (1,2).

Genotoxicity

Salmonella typhimurium TA102, TA1537 with and without metabolic activation negative (3).

In vitro V79-HGPRT mutagenicity assay negative (3).

Other comments

Administration of the antimutagen anthraflavic acid to rats gave rise to significant increases in the hepatic microsomal *O*-deethylations of ethoxyresorufin and ethoxycoumarin, but not in the *O*-dealkylation of pentoxyresorufin nor in cytosolic glutathione *S*-transfer activity. Immunoblot studies of solubilised microsomes from anthraflavic acid-treated rats revealed that anthraflavic acid induced the apoproteins P450 I, A1 and A2 but not P450 B1 and B2. Pre-treatment with anthraflavic acid resulted in a marked increase in the *in vitro* bioactivation of 2-amino-6-methyldipyrido[1,2-a:3',2'-d]imidazole and IQ to mutagenic intermediate(s). IQ is a carcinogen against which anthraflavic acid has displayed strong antimutagenic effect in the Ames test when incorporated into the metabolic activation system. The increase in mutagenicity of IQ was the result of enhancement of both the microsomal and cytosolic activation steps. Thus, anthraflavic acid is a specific inducer of P450 I proteins in the rat and this compound is not only unlikely to exhibit any anti-carcinogenic effect *in vivo* but may act as a co-carcinogen (4).

Caused a reduction in the binding of polycyclic aromatic hydrocarbons to DNA and protein following dermal application to mice (5).

Inhibited the mutagenicity of the cooked food mutagen IQ, by virtue of its ability to inhibit both the microsomal and cytosolic activation pathways (6).

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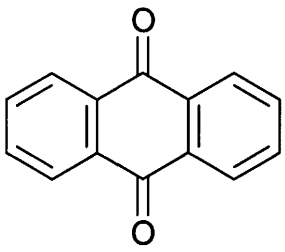
A220 anthraquinone



$C_{14}H_8O_2$ **Mol. Wt.** 208.22 **CAS Registry No.** 84-65-1

Synonyms 9,10-anthraquinone; 9,10-anthracenedione

EINECS No. 201-549-0 **RTECS No.** CB 4725000

Uses Intermediate for dyestuffs manufacture. Bird repellant.

Physical properties

M. Pt. 286°C (sublimes) **B. Pt.** 377°C **Flash point** 185°C **Specific gravity** 1.42-1.44 at 20°C with respect to water at 4°C **Volatility** v.p. 3.75×10^{-8} mmHg at 20°C ; v.den. 7.2
Solubility Water: 0.084 mg l^{-1} at 20°C. Organic solvents: benzene, diethyl ether, ethanol, toluene

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) rainbow trout, golden orfe 72, 44 mg l^{-1}, respectively (1).

Invertebrate toxicity
EC_{50} (48 hr) *Daphnia* >10 mg l^{-1} (1).

Environmental fate

Degradation studies
Confirmed biodegradable (2).

Adsorption and retention
Rapidly degraded in soil with very low mobility (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral Japanese quail >2000 mg kg^{-1} (1).
LD_{50} oral rat >5000 mg kg^{-1} (1).
LC_{50} (4 hr) inhalation rat >1.3 mg l^{-1} (1).
LD_{50} intraperitoneal rat 3500 mg kg^{-1} (3).
LD_{50} percutaneous rat >5000 mg kg^{-1} (1).

Sub-acute and sub-chronic data
In 90-day feeding trials, rats receiving up to 15 mg kg^{-1} diet showed no ill-effects (1).

Metabolism and toxicokinetics
In animals (species unspecified) elimination is quick with ~96% being excreted in the urine and faeces within 48 hr (1).

Genotoxicity

Salmonella typhimurium TA98, TA100 with and without metabolic activation positive (4).
Salmonella typhimurium TA98, TA100 with and without metabolic activation negative (5).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides and related products: maximum admissible concentration 0.1 $\mu g\ l^{-1}$ (6).
Included in Schedule 6 (Release Into Land: Prescribed Substances) of Statutory Instrument No. 472, 1991 (7).
WHO Toxicity Class Table 5 (8).
EPA Toxicity Class IV (1).

Other comments

Reviews on human health effects, experimental toxicology, workplace experience and ecotoxicology listed (9).

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A221 antimony

Sb

Sb **Mol. Wt.** 121.75 **CAS Registry No.** 7440-36-0

Synonyms antimony black; antimony regulus

EINECS No. 231-146-5 **RTECS No.** CC 4025000

Uses Manufacture of alloys, fireworks, thermoelectric piles, coating metals, paints, rubber, ceramics, medicines and semiconductors.
Occurrence In China, Mexico, Bolivia it is mined as stibnite Sb_2S_3.

Physical properties

M. Pt. 630°C **B. Pt.** 1635°C **Specific gravity** 6.68 at 25°C **Volatility** v.p. 1 mmHg at 886°C

Occupational exposure

DE-MAK 0.5 mg m^{-3} (inhalable dust fraction)
FR-VME 0.1 ppm (0.5 mg m^{-3})
JP-OEL 0.1 mg m^{-3}
SE-LEVL 0.5 mg m^{-3}
UK-LTEL MEL 0.5 mg m^{-3}
US-TWA 0.5 mg m^{-3}

UN No. 2871 **HAZCHEM Code** 2Z **Conveyance classification** toxic substance
Supply classification harmful

Ecotoxicity

Fish toxicity
LC_{50} (28 day) rainbow trout 0.66 mg l^{-1} (1).

Invertebrate toxicity
EC_{50} (48 hr) *Daphnia magna* 423 mg l^{-1} for trivalent antimony (2).
IC_{50} *Tetrahymena pyriformis* 16 and 6 mg l^{-1} using a flask or microplate technique, respectively (3).

Mammalian & avian toxicity

Acute data
LD_{50} intraperitoneal rat, guinea pig 100, 150 mg kg^{-1}, respectively (4).

Sub-acute and sub-chronic data
Oral ♂ and ♀ Sprague-Dawley rats (90 day) 0-500 ppm potassium antimony tartrate in drinking water. No-observed-adverse-effect level 0.5 ppm, equivalent to an average intake of 0.06 mg antimony kg^{-1} body weight day^{-1} based upon histological and biochemical changes (5).

Metabolism and toxicokinetics
Inorganic trivalent antimony is excreted in the bile after conjugation with glutathione and also in urine. A significant proportion of that excreted in bile undergoes an enterohepatic circulation. In workers exposed to pentavalent antimony, urinary antimony excretion is related to the intensity of exposure. After an 8 hr exposure to 500 μg m^{-3} the increase in urinary antimony at the end of the shift is on average 25 μg g^{-1} creatinine (6).
Rats were fed 40 mg kg^{-1} day^{-1} antimony for 7.5 months *ad libitum*; another group were fed similarly by increasing the dose to 1 g kg^{-1} day^{-1} or with 40 mg kg^{-1} day^{-1} for 4 months. An average of 1 mg of antimony was found in the carcasses of exposed rats regardless of the dose, indicating that accumulation in animals is insignificant (7).
Antimony may enter body through the lungs where it can then be absorbed and taken up by blood and tissues (8). Following six intraperitoneal injections of 50 mg kg^{-1} each to rats with grafted sarcoma 45 tumour, antimony was present in higher concentrations in the blood of sarcoma 45-bearing rats than in controls. Antimony did not selectively accumulate in the tumour tissue; highest levels were observed in muscles, lung and skin of the tumour-bearing rats and in the lung and skin of normal rats (9).

Irritancy
Following repeated antimony application to skin the intensity of skin responses and the number of animals affected were reduced gradually. Responsive animals may suffer from acute attacks of interstitial pneumonia and die after inhalation of antimony compound dust (10).

Other effects

Other adverse effects (human)
A survey of men employed on an antimony smelter in the North East of England showed a significant increase in deaths from lung cancer in men working on the smelter before 1961 (32 *vs.* 14.7 expected). A similar increase was seen among maintenance men (12 *vs.* 5.3 expected) but not in the cohort recruited after 1960 (5 *vs.* 9.2 expected, maintenance men 3 *vs.* 2.8 expected). There appeared to be a minimum latency period of 20 yr between first

exposure and death from lung cancer but there was no correlation between the length of time worked and mortality from lung cancer (11).
Lung tissue samples taken from 200 women aged over 40 yr with lung cancer and from urban areas were reported to contain traces of antimony due to air pollution (12).
Women exposed to unspecified amounts of antimony in an antimony metallurgical plant had blood antimony levels 10-times greater than in controls; levels in urine, breast milk, placental tissue, amniotic fluid and umbilical cord blood ranged from 21-126 mg l^{-1} (13).
Former smelter workers occupationally exposed to antimony had on average 12-times higher lung concentrations (315 μg kg^{-1}) than unexposed (26 μg kg^{-1}) (14).
Inhalation of dust and fumes in humans causes nose and throat irritation, inflamation of the respiratory tract, pneumonitis, ulceration and perforation of the nasal septum. Headaches, dyspnoea, nausea, vomiting and diarrhoea have been reported in smelters (15).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Antimony: maximum admissible concentration 10 μg l^{-1} (16).

Other comments

Antimony and its compounds reviewed (17).
Pollution by antimony, toxicity and health hazards reviewed (18).
Antimony content in human senile cataractous lenses was much lower that that in normal lenses (19).
Health effects assessment for antimony reported, suggesting tolerable exposure levels (20).
The acute and chronic toxicological properties of antimony with primary focus in relation to exposure in an industrial environment are reviewed (21).
Physico-chemical properties, epidemiology, workplace experience, exposure levels, environmental effects, experimental toxicology and human health effects reviewed (22,23).
Avoid conditions in which nascent hydrogen will react with antimony to form toxic stibine.
The toxicity of antimony is dependent on the ability of the organism to absorb it. Therefore toxicity data refers to bioavailable forms, such as the ion in solution or particulate matter.

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A222 antimonyl potassium tartrate hemihydrate

$C_8H_{10}K_2O_{15}Sb_2$ **Mol. Wt.** 667.86 **CAS Registry No.** 28300-74-5

Synonyms antimonate(2–), bis[μ-[2,3-dihydroxybutanedioato(4–)-O^1,O^2:O^3,O^4]]di-, dipotassium, trihydrate; potassium antimonyl tartrate; antimonyl potassium tartrate; tartar emetic

RTECS No. CC 6825000

Uses Mordant in textile and leather industry. Antischistomal drug. Formerly used as an emetic.

Physical properties

Specific gravity 2.607
Solubility Water: 83.33 g l^{-1}. Organic solvents: glycerol

Occupational exposure

JP-OEL 0.1 mg m^{-3} (as Sb)
UK-LTEL MEL 0.5 mg m^{-3} (as Sb)
US-TWA 0.5 mg m^{-3} (as Sb)

UN No. 1551 **HAZCHEM Code** 2X **Conveyance classification** toxic substance
Supply classification harmful
Risk phrases Harmful by inhalation and if swallowed (R20/22)
Safety phrases Keep out of reach of children (if sold to general public) – Do not breathe dust (S2, S22)

Mammalian & avian toxicity

Acute data

LD_{Lo} oral human 2 mg kg^{-1} (1).
LD_{50} oral rat, rabbit 115 mg kg^{-1} (2,3).
LD_{50} subcutaneous mouse 55 mg kg^{-1} (4).
LD_{50} intravenous mouse 65 mg kg^{-1} (4).

Sub-acute and sub-chronic data

Intraperitoneal F344 rats and B6C3F1 mice (90 day) 1.5, 3, 6, 12 and 24 mg kg^{-1} every other day. No clinical signs of toxicity nor gross or microscopic lesions in mice although elevated concentrations of antimony were detected in the liver and spleen of mice. Rats displayed dose-related mortality, body weight reduction and hepatoxicity. Hepatocellular degeneration and necrosis occurred in association with dose-related elevations in activities of the liver-specific serum enzymes sorbitol dehydrogenase and alanine aminotransferase (5).

Metabolism and toxicokinetics

Oral rat administration in drinking water for 1000 days at 13.7 mg l^{-1} (average daily dose 1.07 mg kg^{-1}); 12.1 μg g^{-1} in the heart, 10.14 μg g^{-1} in kidney, 11.57 μg g^{-1} in liver, 17.67 μg g^{-1} in lung and 5.97 μg g^{-1} in spleen were detected (6).
Following administration to rats, mice and monkeys, excretion was greater in faeces than urine, indicating poor absorption from intestinal tract and no persistent accumulation of antimony in the body (7).
Intravenous administration to monkey revealed >50% in liver, and detection in heart, kidney, thigh and thyroid. Maximum concentration in blood was reached at 8 hr after administration (8).

Rats were fed 8 mg kg^{-1} day^{-1} for 7.5 months (*ad libitum*); another group were fed for 6 months in doses increasing to 100 mg kg^{-1} day^{-1} antimony and maintained at that level for 6 months. Rabbits were fed at a dose of 8 mg kg^{-1} day^{-1} for 4 months. An average of 1 mg of antimony was found in the carcasses of exposed rats, regardless of the daily dose, indicating that accumulation in animals is insignificant (9).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA1535 with and without metabolic activation negative (10).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Antimony: maximum admissible concentration 10 μg l^{-1} (11).

Other comments

Reviews on physico-chemical properties, epidemiology, workplace experience, exposure levels, environmental effects, experimental toxicology and human health effects listed (12).
Incompatible with acids and alkalis, salts of heavy metals, albumin, soap and tannins (13).

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A223 antimony pentachloride

$$SbCl_5$$

Cl_5Sb **Mol. Wt.** 299.01 **CAS Registry No.** 7647-18-9

Synonyms antimonic chloride; antimony perchloride; antimony chloride; pentachloroantimony; antimony(v) chloride

EINECS No. 231-601-8 **RTECS No.** CC 5075000

Uses Catalyst, chemical reagent.

Physical properties

M. Pt. 2.8°C **B. Pt.** 79°C at 22 mmHg **Specific gravity** 2.336 at 20°C with respect to water at 4°C
Volatility v.p. 1 mmHg at 22.7°C
Solubility Water: decomp.. Organic solvents: carbon disulfide, carbon tetrachloride, chloroform

Occupational exposure

FR-VME 0.5 mg m^{-3} (as Sb)
JP-OEL 0.1 mg m^{-3} (as Sb)
UK-LTEL MEL 0.5 mg m^{-3} (as Sb)
US-TWA 0.5 mg m^{-3} (as Sb)

UN No. 1730 (liquid)

UN No. 1731 (solution) **HAZCHEM Code** 4X (liquid) **HAZCHEM Code** 2X (solution)
Conveyance classification corrosive substance
Supply classification corrosive
Risk phrases Causes burns – Irritating to the respiratory system (R34, R37)
Safety phrases Keep locked up and out of the reach of children (if sold to general public) – In case of contact with eyes, rinse immediately with plenty of water and seek medical advice – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S26, S45)

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 1120 mg kg^{-1} (1).
LD_{50} oral guinea pig 900 mg kg^{-1} (2).

Sub-acute and sub-chronic data
Inhalation by rats of 15 μg l^{-1} for 2 hr day^{-1} for 4 months caused general loss of weight and weight loss in the liver, kidneys and adrenal glands. Histological changes were also found in the heart, liver, kidneys and thyroid due to the irreversible accumulation of antimony (2).

Metabolism and toxicokinetics
Distribution in rats after chronic poisoning by inhalation of antimony pentachloride showed high antimony concentration in blood. Levels in liver, kidneys, spleen and pancreas were similar (3).

Genotoxicity

Bacillus subtilis rec assay positive (4).

Other effects

Any other adverse effects
Inhalation effects tested in mice and rats. Affected mucous membranes of respiratory tract and eyes (5).
Toxic effects in guinea pigs included weakness, drowsiness, adynamia and paresis of the hind limbs (1).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Antimony: maximum admissible concentration 10 μg l^{-1} (6).

Other comments

Reviews on physico-chemical properties, workplace experience, human health effects and experimental toxicology listed (7).
Reacts explosively with phosphorium iodide at ambient temperature.

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A224 antimony pentafluoride

SbF_5

F_5Sb **Mol. Wt.** 216.74 **CAS Registry No.** 7783-70-2

Synonyms antimony(v) fluoride

EINECS No. 232-021-8 **RTECS No.** CC 5800000

Uses Chemical intermediate in the fluorination of organic compounds.

Physical properties

M. Pt. 7°C **B. Pt.** 149.5°C **Specific gravity** 2.99 at 23°C **Volatility** v.p. 10 mmHg at 25°C ; v.den. 2.2

Occupational exposure

DE-MAK 2.5 mg m^{-3} (as F) (total dust)
FR-VME 0.5 mg m^{-3} (as Sb)
JP-OEL 0.1 mg m^{-3} (as Sb)
SE-LEVL 2 mg m^{-3} (as F)
UK-LTEL MEL 0.5 mg m^{-3} (as Sb)
US-TWA 0.5 mg m^{-3} (as Sb)

UN No. 1732 **HAZCHEM Code** 4WE **Conveyance classification** corrosive substance, toxic
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) – Do not breathe dust (S2, S22)

Mammalian & avian toxicity

Acute data

LC_{50} inhalation mice 0.27 mg l^{-1} (1).

Sub-acute and sub-chronic data

TD inhalation rats 0.015 mg l^{-1} 2 hr day^{-1} for 3.5 month, produced alterations in liver and thyroid function and changes in cardiac, renal and lung morphology (1).

Metabolism and toxicokinetics

Distribution in rats after chronic exposure by inhalation of antimony pentafluoride showed high antimony concentration in blood. Levels in liver, kidneys, spleen and pancreas were similar. Antimony was retained for a long time and could be detected in organs examined months after the study was discontinued (2).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Antimony: maximum admissible concentration 10 μg l^{-1} (3).

Other comments

Reviews on human health effects, experimental toxicology and workplace experience listed (4).
Soluble fluorides are rapidly absorbed from the gastrointestinal tract. Part is rapidly excreted via the urine, and the remainder is distributed to bone. Fluoride is a general protoplasmic poison, and poisoning can result from any soluble compound which dissociates fluoride ion. Effects include enzyme inhibition, hypocalcaemia, cardiovascular collapse and damage to the kidneys and brain (5,6).
Ignites on contact with phosphorus and reacts violently with water.

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A225 antimony trichloride

$SbCl_3$

Cl_3Sb **Mol. Wt.** 228.11 **CAS Registry No.** 10025-91-9

Synonyms antimonous chloride; antimony(III) chloride; trichlorostibine; stibine, trichloro-

EINECS No. 233-047-2 **RTECS No.** CC 4900000

Uses Chemical reagent, catalyst, mordant. Used as a mordant for patent leather and in dyeing, for bronzing iron, colouring zinc black, in the manufacture of other antimony salts, as a catalyst and in organic syntheses.

Physical properties

M. Pt. 73.4°C **B. Pt.** 283°C **Specific gravity** 3.14 at 20°C with respect to water at 4°C
Volatility v.p. 1 mmHg at 49.2°C
Solubility Water: 99.01 g l^{-1} at 25°C. Organic solvents: acetone, benzene, chloroform, ethanol

Occupational exposure

FR-VME 0.5 mg m^{-3} (as Sb)
JP-OEL 0.1 mg m^{-3} (as Sb)
UK-LTEL MEL 0.5 mg m^{-3} (as Sb)
US-TWA 0.5 mg m^{-3} (as Sb)

UN No. 1733 **HAZCHEM Code** 4WE **Conveyance classification** corrosive substance
Supply classification corrosive
Risk phrases Causes burns – Irritating to the respiratory system (R34, R37)
Safety phrases Keep locked up and out of the reach of children (if sold to general public) – In case of contact with

eyes, rinse immediately with plenty of water and seek medical advice – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S26, S45)

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 530 mg kg^{-1} (1).

LD_{50} oral guinea pig 570 mg kg^{-1} (2).

TC_{Lo} inhalation human 73 mg m^{-3} pulmonary and gastrointestinal effects (1).

Metabolism and toxicokinetics

Exposure of rats by inhalation resulted in about 10% of the body burden of antimony found in blood 14 days later. Intratracheal exposure in rabbits and dogs had <1% of the blood antimony concentrations found in rats (3).

Inhalation exposure of rats showed atypical, rapid loss from lung with somewhat longer biological $t_{1/2}$ of 100 days (4).

Part of intravenously administered antimony salts is absorbed by erythrocytes, and the rest is distributed to other tissues, predominantly liver, adrenals, spleen and thyroid (5).

Trivalent antimonials are excreted slowly by kidney because of low plasma concentration. Therefore, following single therapeutic dose, ~10% is recovered in urine within 24 hr and only 30% within 1 wk (6).

Genotoxicity

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

Bacillus subtilis M45(rec⁻), H17(rec⁺) positive (7).

V79 Chinese hamster cells sister chromatid exchange positive (7).

Other effects

Other adverse effects (human)

Chronic inhalation exposure may lead to olfactory disorders (8).

Inhalation causes irritation of the nose, throat and upper respiratory tract and may cause sore throat, dyspnoea and gastrointestinal symptoms such as abdominal pain and loss of appetite (9,10).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Antimony: maximum admissible concentration 10 $\mu g\ l^{-1}$ (11).

Other comments

Reviews on physico-chemical properties, workplace experience, human health effects and experimental toxicology listed (12).

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

A226 antimony trifluoride

SbF_3

F_3Sb **Mol. Wt.** 178.75 **CAS Registry No.** 7783-56-4

Synonyms antimonous fluoride; antimony(III) fluoride; trifluorostibine; stibine, trifluoro-

EINECS No. 232-009-2 **RTECS No.** CC 5150000

Uses Chemical reagent. Used in ceramics, dyeing, chlorofluoride manufacture and as a catalyst.

Physical properties

M. Pt. 292°C **B. Pt.** 319°C (sublimes) **Specific gravity** 4.379 at 21°C

Occupational exposure

DE-MAK 2.5 mg m^{-3} (as F) (total dust)
FR-VME 0.5 mg m^{-3} (as Sb)
JP-OEL 0.1 mg m^{-3} (as Sb)
SE-LEVL 2 mg m^{-3} (as F)
UK-LTEL MEL 0.5 mg m^{-3} (as Sb)
US-TWA 0.5 mg m^{-3} (as Sb)

UN No. 1549 **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) – Keep container tightly closed – In case of contact with eyes, rinse immediately with plenty of water and seek medical advice – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S7, S26, S45)

Mammalian & avian toxicity

Acute data
LD_{50} subcutaneous rat 23 mg kg^{-1} (1).

Sub-acute and sub-chronic data
In rats, doses of 30 g kg^{-1} day^{-1} for 14 days increased levels of citric acid in the liver and kidneys (2).

Metabolism and toxicokinetics
Part of intravenously administered trivalent antimony salts is absorbed by erythrocytes, and the rest is distributed to other tissues, predominantly liver, adrenals, spleen and thyroid (3).
Trivalent antimonials are excreted slowly by kidney because of low plasma concentration. Therefore, following single therapeutic dose, ~10% is recovered in urine within 24 hr and only 30% within 1 wk (4).

Other effects

Other adverse effects (human)
In humans, ingestion of antimony trifluoride may result in nausea, vomiting, diarrhoea, abdominal pain, weakness, dyspnoea, cyanosis, coma and convulsions. Weight loss and anaemia may also result from chronic exposure (5).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Antimony: maximum admissible concentration 10 $\mu g\ l^{-1}$ (6).

Other comments

Fluorides are absorbed from gastrointestinal tract, lung and skin and 95-96% of body burden of fluoride is in bones and teeth (7,8).
Reviews on physico-chemical properties, workplace experience, human health effects and experimental toxicology listed (9).

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A227 antimony trioxide

$$Sb_2O_3$$

O_3Sb_2 **Mol. Wt.** 291.50 **CAS Registry No.** 1309-64-4

Synonyms diantimony trioxide; flowers of antimony; antimony white; C.I. 77052; C.I. Pigment White 11

EINECS No. 215-175-0 **RTECS No.** CC 5650000

Uses Manufacture of tartar emetic, as mordant in paints, pigments, enamels, glasses, in flame-proofing canvas.
Occurrence Senartmontite, valentinite.

Physical properties

M. Pt. 655°C **B. Pt.** 1550°C **Specific gravity** 5.2

Occupational exposure

FR-VME 0.5 mg m^{-3} (as Sb)
JP-OEL 0.1 mg m^{-3} (as Sb)
SE-LEVL 0.5 mg m^{-3} (as Sb)
UK-LTEL MEL 0.5 mg m^{-3} (as Sb)

UN No. 1549 **Conveyance classification** toxic substance
Supply classification harmful
Risk phrases Possible risk of irreversible effects (R40)

Safety phrases Keep out of reach of children (if sold to general public) – Do not breathe dust – Wear suitable protective clothing and gloves (S2, S22, S36/37)

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) bluegill sunfish, fathead minnow 530-833 mg l^{-1} (1,2).

Environmental fate

Degradation studies

Pure cultural study using *Stibiobacter senarmontii* autotroph grown in a mineral medium containing antimony trioxide oxidised the chemical at 45-52 mg $month^{-1}$ for cubic and 13-20 mg $month^{-1}$ for rhombic forms. Little oxidation occurred in sterile medium (3).

Abiotic removal

Loss of antimony oxides from water by evaporation is very unlikely under normal conditions due to their very low concentration and low concentration of their hydrolysis products (3).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat >34.6 μg kg^{-1} (4).

LD_{50} percutaneous rabbit >2 μg kg^{-1} (4).

Sub-acute and sub-chronic data

Intragastric administration of 10 g kg^{-1} to rats caused no deaths, suggesting low toxicity. However, chronic toxic effects and effects on reproduction and other biochemical indexes via inhalation are reported (5).

Inhalation rat (13 wk) 0, 0.25, 1.08, 4.92 or 23.46 mg m^{-3}, 6 hr day^{-1}, 5 day wk^{-1} followed by a 27-wk observation period. Corneal irregularities were seen after ~2 wk of exposure which did not abate during the observation period. No other adverse effects were noted. Mean absolute and relative lung weights were significantly increased in the 4.92 and 23.46 mg m^{-3} groups; the lung weights of the latter group did not recover to control levels during the observation period (6).

Carcinogenicity and chronic effects

Inadequate evidence for carcinogenicity in humans, sufficient evidence for carcinogenicity in animals, IARC classification group 2B (7).

Inhalation (52 wk) Wistar rats 0 or 45 mg m^{-3}, 7 hr day^{-1}, 5 day wk^{-1}. No significant difference in survival was observed between treated and control rats. Non-neoplastic lesions of the lung were seen in both ♂ and ♀ rats but were less severe in ♂. Lung tumours were seen in treated ♀ but not treated ♂ or control animals. The incidence of other tumours was not different between treated and control rats (8).

Teratogenicity and reproductive effects

Inhalation (21 day) pregnant ♀ rats 0, 0.027, 0.082, 0.27 mg m^{-3} 24 hr day^{-1}. Maternal body weight was not affected. In the high-dose group an increase in pre- and post-implantation death of embryos was seen, and in the mid-dose group pre-implantation loss and foetal growth retardation were observed (9).

Inhalation ♀ rats 0 or 250 mg m^{-3} 4 hr day^{-1} for 1.5-2 months. The rats were then mated and exposures continued until 3-5 days before delivery. 16/24 treated ♀ became pregnant compared to 10/10 controls and litter weight and size of offspring at birth and weaning were not affected by the exposure (10).

Metabolism and toxicokinetics

Rats fed 1-2% in the diet showed antimony retention in the thyroid, liver, spleen, kidneys, heart, lungs and hair (7,11).

After single oral doses of 200 mg in 5 ml of water to rats, 3% was eliminated in urine. At a concentration of 2% for 8 months in the diet, antimony excretion in the faeces was much greater than in urine (11).

Part of intravenously administered trivalent antimony salts are absorbed by erythrocytes, and the rest are distributed to other tissues, predominantly liver, adrenals, spleen and thyroid (12).

Genotoxicity

Salmonella typhimurium TA98, TA100 with and without metabolic activation negative (13).
Bacillus subtilis gene conversion and mitotic recombination positive (14).
Bacillus subtilis M45(rec$^-$), H17(rec$^+$) positive (13).
V79 Chinese hamster cells sister chromatid exchange positive (13).

Other effects

Other adverse effects (human)

Skin lesions known as antimony spots are found in workers exposed to antimony trioxide and develop mainly in areas exposed to heat and where sweating occurs (7).
Women exposed to unspecified amounts of antimony trioxide in a metallurgical plant had antimony concentrations in blood 10-times greater than in controls; levels in urine, breast milk, placental tissue, amniotic fluid and umbilical cord blood were 3.3-126 mg l^{-1} (3).
Lung reticulomicronodular images among employees of an antimony oxide production plant revealed collagenous fibrosis with 600-3000 μg g^{-1} antimony in biopsies from two workers, showing there is a risk of pneumoconiosis due to dust inhalation in antimony trioxide plants (15).
Women occupationally exposed to antimony trioxide experienced increased rate of spontaneous late abortions, premature birth, gynaecological problems and reduced weight gain of children (10).

Any other adverse effects

Occasional exposure of rats did not cause chronic pneumonitis, but chronic inhalation caused pathological changes in the lungs of rats, pneumonitis and fatty degeneration of the liver in guinea pigs, and lipoid pneumonias in rats and rabbits (16-19).
Ingestion of 0.15 g kg^{-1} day^{-1} caused vomiting and gastrointestinal disturbances in dogs and cats and eventually significant weight loss (7).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Antimony: maximum admissible concentration 10 μg l^{-1} (20).

Other comments

Physico-chemical properties, human health effects, experimental toxicology, epidemiology, workplace experience and environmental effects reviewed (7,21).

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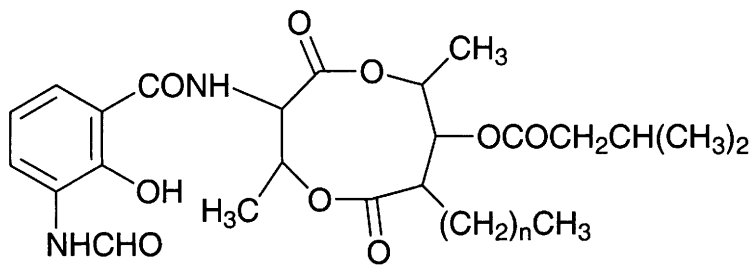
A228 antimycin A



$C_{28}H_{40}N_2O_9$ **Mol. Wt.** 548.63 **CAS Registry No.** 1397-94-0

RTECS No. CD 0350000

Uses Antibiotic.

Occurrence Produced by *Streptomyces* spp.

Physical properties

M. Pt. 149-150°C

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

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) northern pike, rainbow trout ≤55 μg l^{-1} (1).

LC_{50} (96 hr) guppy 1.14 μg l^{-1} (2).

Mammalian & avian toxicity

Acute data

LD_{50} oral pigeon, duck 2.0-2.9 mg kg^{-1} (3).

LD_{50} oral rat, guinea pig 1.8-28 mg kg^{-1} (4).

LD_{50} intraperitoneal rat 0.8 mg kg^{-1} (4).

LD_{50} subcutaneous mouse 21 mg kg^{-1} (5).

LD_{50} intravenous mouse 0.89 mg kg^{-1} (5).

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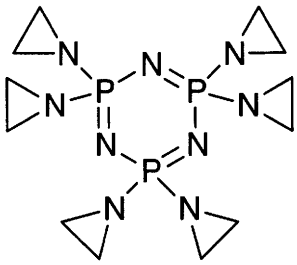
A229 apholate



$C_{12}H_{24}N_9P_3$ **Mol. Wt.** 387.30 **CAS Registry No.** 52-46-0

Synonyms 2,2,4,4,6,6-hexakis(1-aziridinyl)-2,2,4,4,6,6-hexahydro-1,3,5,2,4,6-triazatriphosphorine; hexakis(1-aziridinyl)phosphonitrile; 1-aziridinylphosphonitrile trimer; ENT 26,316; pholate

Uses Insect chemosterilant.

Physical properties

M. Pt. 147.5°C

Ecotoxicity

Invertebrate toxicity

Inhibited the development of the testis and ovary in the jute stem weevil *Apion corchori*. The bursa copulatrix and spermatheca in ♀s usually showed hypertrophy (1).

♂ Silkworms injected with 5-20 μg during the 5th larval instar did not suffer pronounced embryonic mortality, but the same dose injected during the periods from spinning to pupae caused reduced hatchability. The greatest embryonic deaths occurred when ♂s were injected at the time of pupation, indicating that young spermatozoa have the highest sensitivity to apholate (2).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat ♂ 98, ♀ 113 mg kg^{-1} (3).

LD_{50} oral mouse 110 mg kg^{-1} (4).

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

Carcinogenicity and chronic effects

No adequate data for human carcinogenicity, inadequate evidence for animal carcinogenicity, IARC classification group 3 (6).

Teratogenicity and reproductive effects

Chicken eggs injected with 25.0-250 μg egg^{-1} had a higher incidence of cumulative mortality and lower mean body weight of day 18 viable embryos than did controls. Beak, cranial, ocular, leg, and digit defects were common among treated embryos, and ectopic viscera, deformed digits, and general oedema were common among both treated and control groups (2).

Other effects

Any other adverse effects

♂ Albino rats, a single dose of 5 mg kg^{-1} (route not specified) interfered with the content of nucleic acids and protein content in the liver. Cellular atrophy was induced (although not major) and the mitotic index was lowered. The concentration and specific activities of glutamic-oxalacetic transaminase, alkaline phosphatase, and

5'-nucleotides were also affected but the normal levels were restored at 96 hr following treatment. The specific activity of glutamic-pyruvic transaminase was not affected (7).
Treatment with apholate (dose and route unspecified) caused degenerative changes in the testes of albino rats. No histological changes were seen in Leydig cells. Lactic dehydrogenase isoenzyme activity was present in the serum of treated rats but not in controls (8).

Other comments

Cytogenetic and other effects of apholate reviewed (9).

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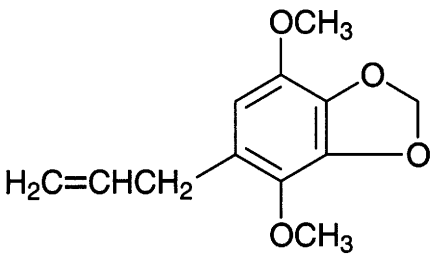
A230 apiole



$C_{12}H_{14}O_4$ **Mol. Wt.** 222.24 **CAS Registry No.** 523-80-8

Synonyms 4,7-dimethoxy-5-(2-propenyl)-1,3-benzodioxole; 1-allyl-2,5-dimethoxy-3,4-(methylenedioxy)benzene; parsley apiole; parsley camphor; petersilienapiole

EINECS No. 208-349-2 **RTECS No.** CY 2500000

Uses Synergistic agent for insecticides. Antipyretic. Emmenagogue.
Occurrence Isolated from the seed of *Petroselinum sativum* (1,2).
Occurs in dill and oil of parsley.

Physical properties

M. Pt. 29.5°C **B. Pt.** 294°C **Specific gravity** 1.015 at 20°C with respect to water at 4°C
Solubility Organic solvents: acetone, benzene, chloroform, diethyl ether, ethanol, vegetable oils

Mammalian & avian toxicity

Acute data
LD_{50} oral redwing blackbird, coturnix >316 mg kg^{-1} (1).
LD_{Lo} subcutaneous mouse 1000 mg kg^{-1} (2,3).

Carcinogenicity and chronic effects
Oral ♂ mice (1 yr) at the levels tested (unspecified) no detectable activity for the initiation of hepatic tumours prior to weaning (4).
Intraperitoneal ♀ CD-1 mice 2 or 10 mg per mouse. After 24 hr very low levels of DNA adducts were formed in the liver. The compound had not previously been shown to have any carcinogenic activity in rodent bioassays (5).

Legislation

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

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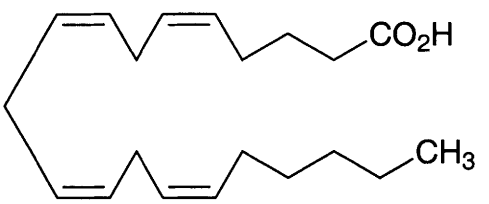
A231 arachidonic acid



$C_{20}H_{32}O_2$ **Mol. Wt.** 304.47 **CAS Registry No.** 506-32-1
Synonyms 5,8,11,14-eicosatetraenoic acid
EINECS No. 208-033-4 **RTECS No.** CE 6675000
Uses Essential fatty acid.
Occurrence Occurs in liver, brain, glandular organs, and depot fats in animals, and in small amounts in human depot fats. Constituent of animal phosphatides.

Physical properties

M. Pt. –49°C **B. Pt.** 169-171°C **Flash point** >110°C **Specific gravity** 1.4824 at 20°C
Partition coefficient log P_{ow} 6.98
Solubility Organic solvents: acetone, diethyl ether, ethanol

Mammalian & avian toxicity

Acute data
LD_{50} intravenous mouse 33 mg kg^{-1} (1).
LD_{Lo} intravenous rabbit, rat 1, 100 mg kg^{-1}, respectively (2).

Metabolism and toxicokinetics

The major metabolite found in the human placenta was 12-hydroxy-5,8,10,14-eicosatetraenoic acid with 5- and 15-hydroxy-5,8,10,14-eicosatetraenoic acid as minor metabolites (3).

Renal glomerular and cortical metabolism of endogenous arachidonic acid by cytochrome P-450 epoxygenase yields 8,9-, 11,12- and 14,15-epoxyeicosatrienoic acids (4).

Metabolites of 15(S)-hydroxy-5,8,11,13-eicosatetraenoic acid in human bronchi and in tissue specimens from three asthmatic patients were identified (5).

Irritancy

Application of arachidonic acid at 1 mg ear^{-1} day^{-1}, 5 day wk^{-1} for 3 wk caused a marked swelling of the ear which plateaued on day-10. This was accompanied by cellular infiltration and epidermal hyperplasia (6).

Other effects

Any other adverse effects

The production of eicosanoids by alveolar macrophages from the lungs of rats exposed to bituminous coal dust for 2 wk significantly altered arachidonic acid metabolism in a manner that promoted an inflammatory response which may be an important factor in the pathophysiology of coal workers' pneumoconiosis (7).

Other comments

Arachidonic acid metabolism and the role of its metabolites in blood vessel-platelet interactions, cytoprotection and tumour metastasis reviewed (8).

Cytochrome P-450 metabolism reviewed (9).

Chemistry, uses, biology, toxicology, mutagenicity, carcinogenicity and safety reviewed (10).

Generation of mutagens during arachidonic acid metabolism reviewed (11,12).

Metabolism of arachidonic acid in the biosynthesis of prostaglandins, prostacyclins and leukotrienes discussed (13).

Precursor in biosynthesis of prostaglandins, thromboxanes and leukotrienes.

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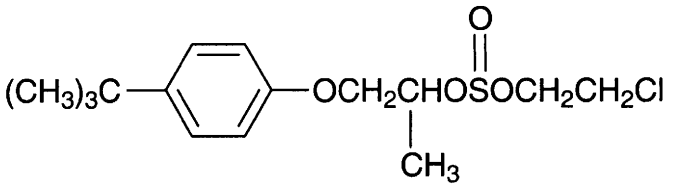
A232 aramite



$C_{15}H_{23}ClO_4S$ **Mol. Wt.** 334.86 **CAS Registry No.** 140-57-8

Synonyms sulfurous acid 2-chloroethyl 2-[4-(1,1-dimethylethyl)phenoxyl]-1-methylethyl ester; sulfurous acid 2-(*p-tert*-butylphenoxy)-1-methylethyl 2-chloroethyl ester; Compound 88R; ENT 16519; Araton; Niagaramite

RTECS No. WT 2975000

Uses Acaricide.

Physical properties

M. Pt. -37.3°C **B. Pt.** 175°C at 0.1 mmHg **Specific gravity** 1.145 at 20°C with respect to water at 20°C
Solubility Organic solvents: acetone, benzene, diethyl ether, miscible with ethanol

Ecotoxicity

Invertebrate toxicity
EC_{50} (48 hr) *Daphnia pulex, Simocephalus serrulatus* 0.16-0.18 mg l^{-1} (1).

Bioaccumulation
Estimated bioconcentration factor is 2265 based on water solubility of 0.1 ppm, which suggests bioconcentration in aquatic organisms is likely (2).

Environmental fate

Abiotic removal
Aramite does not absorb UV irradiation above 290 nm which suggests that it does not directly photolyse in the environment (3).

Adsorption and retention
Estimated soil adsorption coefficient is 15,500 which indicates soil immobility (4).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat, guinea pig 3900 mg kg^{-1} (5).
LD_{Lo} intraperitoneal mouse 200 mg kg^{-1} (6).

Sub-acute and sub-chronic data
LC_{50} (5 day) Japanese quail >5000 ppm in diet (7).

Carcinogenicity and chronic effects
No adequate evidence for carcinogenicity to humans, sufficient evidence for carcinogenicity to animals, IARC classification group 2B (8).
Experimental carcinogen in livers of rats and mice and of the liver and biliary tracts of dogs via ingestion and produces liver tumours in rats (9-12).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides and related products: maximum admissible concentration 0.1 μg l^{-1} (13).
Included in Schedule 6 (Release Into Land: Prescribed Substances) of Statutory Instrument No. 472, 1991 (14).

Other comments

Aramite is an animal carcinogen currently in commerical use. The US epidemiological studies of its use and production volume have not been carried out because of simultaneous exposure to other chemicals (15).

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A233 Aroclor 1016

CAS Registry No. 12674-11-2

Synonyms polychlorinated biphenyl; PCB

RTECS No. TQ 1351000

Uses Electrical insulator, heat transfer medium, hydraulic fluids and lubricants.

Occupational exposure

JP-OEL 0.1 mg m^{-3}
SE-LEVL 0.01 mg m^{-3} **SE-STEL** 0.03 mg m^{-3}
UK-LTEL MEL 0.1 mg m^{-3}

UN No. 2315 **HAZCHEM Code** 4X **Conveyance classification** other dangerous substance
Supply classification harmful, dangerous for the environment
Risk phrases Danger of cumulative effects – Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment (R33, R50/53)
Safety phrases Keep out of reach of children (if sold to general public) – This material and its container must be disposed of in a safe way – This material and/or its container must be disposed of as hazardous waste – Avoid release to the environment. Refer to special instructions/safety data sheet (S2, S35, S60, S61)

Ecotoxicity

Fish toxicity
LC_{Lo} (28 day) flow through bioassay intermittent sheepshead minnow 32 μg l^{-1} (1).
LD_{Lo} (42 day) *Lagodon rhomboides* 32 μg l^{-1} tissue damage found in pancreas (2).

LC_{50} (96 hr) rainbow trout, Atlantic salmon, brown trout, brook trout, fingerling longnose sucker, channel catfish, bluegill sunfish, yellow perch 134-800 μg l^{-1} (3).
Toxicity of Aroclor 1016 to different age groups of sheepshead minnows was studied in intermittent-flow bioassays lasting 26 days. 32 and 100 μg l^{-1} killed newly hatched fry and juveniles and adults. Accumulation was in proportion to concentration in test water. Fry contained 2500-8100 times the concentration added to the test water, adults 1700-15,000 times and juveniles 10,000-34,000 times. 77 μg l^{-1} of Aroclor 1016 in eggs from exposed adults did not affect survival of embryos and fry (1).

Invertebrate toxicity
LC_{50} (72 hr) *Hydra oligactis* 5 mg l^{-1} (4).

Bioaccumulation
Ambient concentration 0.1-10 μg l^{-1} sheepshead minnow fry bioconcentration factor 2500-8100, adults 4700-14,000 (1).
Bioaccumulation factor for pinfish exposed to 1 μg l^{-1} for 56 days was a 17,000-fold increase over the nominal test concentration (2).

Environmental fate

Degradation studies
Using BOD dilution water, settled domestic waste water inoculum and 5 and 10 ppm Aroclor 1016, after 28 days 48% degradation at 5 ppm and 13% degradation at 10 ppm occurred (5).

Adsorption and retention
Experimental soil adsorption coefficients of 52,100-171,000 suggest strong adsorption to sediments during a study of three ponds (6,7).

Mammalian & avian toxicity

Carcinogenicity and chronic effects
Limited evidence for carcinogenicity to humans, sufficient evidence for carcinogenicity to animals, IARC classification group 2A (8).
A NIOSH retrospective cohort study was conducted of 3588 men and women employed for ≥1 day between 1st January 1957 and 31st March 1977 manufacturing capacitors with known exposure to PCBs in the midwest US. Aroclor 1016 was used from 1970-1977 as a dielectric fluid. Results provided some evidence for an association between occupational PCB exposure and mortality from malignant melanoma. There was an increased incidence of brain cancer among workers who had more than twice the estimated cumulative PCB dose than the comparison group (9).

Metabolism and toxicokinetics
TD oral rat 3.6-6.9 mg kg^{-1} day^{-1} long-term feeding study showed PCB distributed throughout body, but mainly concentrated in adipose tissue. Steady-state concentration found in adipose tissue after 4 months. Only small levels of PCB found in urine. After exposure ceased, the elimination of the PCB was slow, with measurable amounts still present 5-6 months later. Pathological changes were found in liver cells (10).
Rats fed 100 ppm of Aroclor 1016 (6.6-3.5 mg kg^{-1} day^{-1}) revealed PCBs in plasma, kidneys, urine, brain, liver and adipose tissue at 0.5-10 months exposure. PCB tissue levels determined 2, 4, 5 and 6 months after exposure was discontinued were highest in adipose tissue; little residue was excreted in urine (11).
173 workers occupationally exposed to Aroclor 1016 revealed levels of serum lipid PCBs equal to the adipose fat PCB level (12).

Other effects

Other adverse effects (human)
Concentrations of 36 polychlorinated biphenyl (PCB) congeners were measured in 167 randomly sampled human milk samples from Finnish women. The levels of PCBs decreased with increasing number of children. The third child was exposed to about 70% of PCBs as compared with the first child, and the eighth to tenth children to about 20% (13).

Any other adverse effects

In vitro investigations on murine splenocytes showed that polychlorinated biphenyls (PCBs) exhibited immunotoxicity on the antibody forming response to T-dependent antigen of sheep erythrocytes, primary activation of T-cells by mixed lymphocytes, and lymphocyte proliferation induced by various mitogens (14).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides and related products: PCB maximum admissible concentration 0.1 $\mu g\ l^{-1}$ (15).

Included in Schedule 5 and 6 (Release Into Water and Land: Prescribed Substances) of Statutory Instrument No. 472, 1991 (16).

Other comments

In vivo testing of the aquatic salamander *Necturus maculosus* exposed to polychlorinated biphenyls and organochlorine pesticides in the wild suggested that these xenobiotics induced disruptions within the hypothalamo-pituitary-interrenal axis (17).

Reviews on human health effects, experimental toxicology, environmental effects and exposure levels listed (18).

Epidemiology, toxicity and waste disposal reviewed (19-21).

Long-term neurobehavioural effects in monkeys reviewed (22).

Teratogenic effects of polychlorinated biphenyls reviewed (23).

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A234 Aroclor 1221

CAS Registry No. 11104-28-2

Synonyms chlorodiphenyl (21% Cl)

RTECS No. TQ 1352000

Uses Electrical insulator, solvent, dispersants, lubricants.

Occupational exposure

SE-LEVL 0.01 mg m^{-3} **SE-STEL** 0.03 mg m^{-3}

UN No. 2315 **HAZCHEM Code** 4X **Conveyance classification** other dangerous substance
Supply classification harmful, dangerous for the environment
Risk phrases Danger of cumulative effects – Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment (R33, R50/53)
Safety phrases Keep out of reach of children (if sold to general public) – This material and its container must be disposed of in a safe way – This material and/or its container must be disposed of as hazardous waste – Avoid release to the environment. Refer to special instructions/safety data sheet (S2, S35, S60, S61)

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) constant flow harlequin fish 1.05 mg l^{-1} (1).
LC_{50} (96 hr) cutthroat trout 1.2 mg l^{-1} (2).

Bioaccumulation
Experimental bioconcentration factors of 955-13,804 have been reported for the dominant polychlorinated biphenyl (PCB) congeners present in Aroclor 1221 (3).

Environmental fate

Degradation studies
Mixed culture of *Pseudomonas* sp. HV3 and *Nocardia* sp. degraded 40-87% of Aroclor 1221 in 6-21 days releasing chlorobenzoic acid metabolites (4).
Using BOD dilution water, settled domestic waste water inoculum and 5 and 10 ppm Aroclor 1221, 100% was biodegraded during 28 days (5).

Abiotic removal
Processes such as hydrolysis and oxidation do not significantly degrade Aroclor 1221 in the aquatic environment (6,7).

Adsorption and retention
Estimated soil adsorption coefficients for the primary PCB congeners present in Aroclor 1221 were 10,965-75,858, suggesting that Aroclor 1221 is adsorbed onto solids and is often immobilised in sediment, although eventual re-solution can occur (8).
Removal by biological adsorption in activated sludge was 96.3% at an aeration time of 24 hr (9).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 3980 mg kg^{-1} (10).
LC_{50} oral Japanese quail 12,000 ppm (11).
LD_{50} dermal rabbit 2000 mg kg^{-1} (10).

Carcinogenicity and chronic effects

Limited evidence for carcinogenicity to humans, sufficient evidence for carcinogenicity to animals, IARC classification group 2A (12).

A NIOSH retrospective cohort study was conducted of 3588 men and women employed for ≥1 day between 1st January 1957 and 31st March 1977 manufacturing capacitors with known exposure to PCBs in the midwest US. Results provided some evidence for an association between occupational PCB exposure and mortality from malignant melanoma. There was an increased incidence of brain cancer among workers who had more than twice the estimated cumulative PCB dose than the comparison group (13).

Other effects

Other adverse effects (human)

Concentrations of 36 polychlorinated biphenyl (PCB) congeners were measured in 167 randomly sampled human milk samples from Finnish women. The levels of PCBs decreased with increasing number of children. The third child was exposed to about 70% of PCBs as compared with the first child, and the eighth to tenth children to about 20% (14).

Any other adverse effects

In vitro investigations on murine splenocytes showed that polychlorinated biphenyls (PCBs) exhibited immunotoxicity on the antibody forming response to T-dependent antigen of sheep erythrocytes, primary activation of T-cells by mixed lymphocytes, and lymphocyte proliferation induced by various mitogens (15).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides and related products: PCB maximum admissible concentration 0.1 $\mu g\ l^{-1}$ (16).

Included in Schedule 5 and 6 (Release Into Water and Land: Prescribed Substances) of Statutory Instrument No. 472, 1991 (17).

Other comments

In vivo testing of the aquatic salamander *Necturus maculosus* exposed to polychlorinated biphenyls and organochlorine pesticides in the wild suggested that these xenobiotics induced disruptions within the hypothalamo-pituitary-interrenal axis (18).

Reviews on human health effects, experimental toxicology, environmental effects and exposure levels listed (19).

Toxicity and waste disposal reviewed (20,21).

Teratogenic effects of polychlorinated biphenyls reviewed (22).

Pyrolysis at low temperatures (200-600°C) can produce even more toxic materials such as polychlorinated dibenzofuran and 2,3,7,8-tetrachlorodibenzodioxin (dioxin).

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A235 Aroclor 1232

CAS Registry No. 11141-16-5

Synonyms chlorodiphenyl (32% Cl)

RTECS No. TQ 1354000

Uses Electrical insulator, heat transfer medium, hydraulic fluids and lubricants.

Occupational exposure

SE-LEVL 0.01 mg m^{-3} **SE-STEL** 0.03 mg m^{-3}

UN No. 2315 **HAZCHEM Code** 4X **Conveyance classification** other dangerous substance
Supply classification harmful, dangerous for the environment
Risk phrases Danger of cumulative effects – Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment (R33, R50/53)
Safety phrases Keep out of reach of children (if sold to general public) – This material and its container must be disposed of in a safe way – This material and/or its container must be disposed of as hazardous waste – Avoid release to the environment. Refer to special instructions/safety data sheet (S2, S35, S60, S61)

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) constant flow harlequin fish 0.32 mg l^{-1} (1).
LC_{50} (96 hr) static assay cutthroat trout 2.5 mg l^{-1} (2).

Bioaccumulation
Bioconcentration factor for white sucker 5500 (3).

Environmental fate

Degradation studies
Using BOD dilution water, settled domestic wastewater inoculum and 5 and 10 ppm Aroclor 1232, after 28 days 100% was biodegraded (4).

Abiotic removal

Processes such as hydrolysis and oxidation do not significantly degrade Aroclor 1232 in the aquatic environment (5,6).

Adsorption and retention

Removal by biological adsorption in activated sludge, 94.2% at aeration time of 24 hr (7).

Estimated soil adsorption coefficients of primary polychlorinated biphenyl congeners in Aroclor 1232 are 10,965-177,828, suggesting Arochlor 1232 is readily adsorbed onto soils and is often immobilised in sediment, although eventual re-solution can occur (8).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 4470 mg kg^{-1} (9).

LD_{50} dermal rabbit >1260 mg kg^{-1} (9).

Sub-acute and sub-chronic data

LD_{50} oral Japanese quail, Northern bobwhite 5000, 3002 mg kg^{-1} diet, respectively (5 days on treated diet plus 3 days untreated) (10).

Immature ♂ Wistar rats were administered 10, 40, 160, 480 and 2000 mg kg^{-1} Aroclor 1232. Rats given the high dose showed a significant inhibition in body weight gain. A dose-dependent increase in hepatic microsomal aryl hydrocarbon hydroxylase, ethoxyresorufin *O*-deethylase and pentoxyresorufin *O*-deethylase activities was seen. Thymic atrophy was not observed (11).

Carcinogenicity and chronic effects

Limited evidence for carcinogenicity to humans, sufficient evidence for carcinogenicity to animals, IARC classification group 2A (12).

A NIOSH retrospective cohort study was conducted of 3588 men and women employed for ≥1 day between 1st January 1957 and 31st March 1977 manufacturing capacitors with known exposure to PCBs in the midwest US. Results provided some evidence for an association between occupational PCB exposure and mortality from malignant melanoma. There was an increased incidence of brain cancer among workers who had more than twice the estimated cumulative PCB dose than the comparison group (13).

Teratogenicity and reproductive effects

Diet containing 20 ppm fed to hens for 9 wk caused decreased hatchability and teratogenic effects in embryos (14).

Other effects

Other adverse effects (human)

Concentrations of 36 polychlorinated biphenyl (PCB) congeners were measured in 167 randomly sampled human milk samples from Finnish women. The levels of PCBs decreased with increasing number of children. The third child was exposed to about 70% of PCBs as compared with the first child, and the eighth to tenth children to about 20% (15).

Any other adverse effects

In vitro investigations on murine splenocytes showed that polychlorinated biphenyls (PCBs) exhibited immunotoxicity on the antibody forming response to T-dependent antigen of sheep erythrocytes, primary activation of T-cells by mixed lymphocytes, and lymphocyte proliferation induced by various mitogens (16).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides and related products: PCB maximum admissible concentration 0.1 μg l^{-1} (17).

Included in Schedule 5 and 6 (Release Into Water and Land: Prescribed Substances) of Statutory Instrument No. 472, 1991 (18).

Other comments

In vivo testing of the aquatic salamander *Necturus maculosus* exposed to polychlorinated biphenyls and organochlorine pesticides in the wild suggested that these xenobiotics induced disruptions within the hypothalamo-pituitary-interrenal axis (19).
Reviews on human health effects, experimental toxicology, environmental effects and exposure levels listed (20).
Toxicity and waste disposal reviewed (21-23).
Teratogenic effects of polychlorinated biphenyls reviewed (24).
Incomplete combustion can lead to the production of polychlorinated dibenzofurans and 2,3,7,8-tetrachlorodibenzodioxin, which are more toxic.

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A236 Aroclor 1242

CAS Registry No. 53469-21-9

Synonyms chlorodiphenyl (42% Cl); PCB 1242

RTECS No. TA 1356000

Uses In production of lubricants, plasticisers. Dielectric liquids (electrical insulators).

Physical properties

Specific gravity 1.41 at 15.5°C **Volatility** v.p. 55 mmHg at 225°C

Occupational exposure

DE-MAK 0.1 ppm (1.1 mg m^{-3})
FR-VME 1 mg m^{-3}
SE-LEVL 0.01 mg m^{-3} **SE-STEL** 0.03 mg m^{-3}
US-TWA 1 mg m^{-3}

UN No. 2315 **HAZCHEM Code** 4X **Conveyance classification** other dangerous substance
Supply classification harmful, dangerous for the environment
Risk phrases Danger of cumulative effects – Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment (R33, R50/53)
Safety phrases Keep out of reach of children (if sold to general public) – This material and its container must be disposed of in a safe way – This material and/or its container must be disposed of as hazardous waste – Avoid release to the environment. Refer to special instructions/safety data sheet (S2, S35, S60, S61)

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) harlequin fish 0.37 mg l^{-1} (1).
LC_{50} (96 hr) cutthroat trout, yellow perch, scud ≤5420 μg l^{-1} (2).
LC_{50} (5-15 day) rainbow trout, bluegill sunfish, channel catfish 54-125 μg l^{-1} (2).

Invertebrate toxicity
LC_{50} (96 hr) *Ischnura verticalis, Macromia* sp. 400-800 μg l^{-1} (2).
Water fleas (*Daphnia magna*) exposed to Aroclor 1242 took significantly more time to complete four moults than did controls. The authors suggest that some xenobiotics which are endocrine disruptors in vertebrates can also interfere with the hormonally regulated moulting process in arthropods by acting as antagonists of endogenous ecdysteroids by binding to and blocking the ecdysteroid receptor (3).

Bioaccumulation
Macoma balthica accumulated 60 ppm after 30 days of exposure (ambient concentration not reported) (4).
Bioconcentration factor fathead minnow 32,000- 274,000 (5).

Environmental fate

Degradation studies
Dechlorination was achieved by anaerobic microorganisms in lake sediments with the loss of *meta-* plus *para-* chlorines ranging from 15-85%. Maximum dechlorination rate was 0.3 μg-atoms of chlorine removed g^{-1} sediment wk^{-1} (6).
Pseudomonas putida LB400 degraded 50% of Aroclor 1242 in soil containing the transformed contaminant at 525 ppm in 15 wk (7).
Using BOD dilution water, settled domestic waste water inoculum and 5 and 10 ppm Arochlor 1242, after 28 days 66% of 5 ppm was degraded, and 0% of 10 ppm was degraded (8).
Experiments using samples of PCB-contaminated sediment from the upper Hudson River, spiked with Aroclor 1242, have demonstrated that low-temperature (4°C) microbial aerobic PCB degradation can occur in PCB-contaminated sediment (9).

Abiotic removal
90.9% removed by biological adsorption in activated sludge in aeration time of 24 hr (10).
Processes such as hydrolysis and oxidation do not significantly degrade Aroclor 1242 in the aquatic environment (11,12).
Evaporation rate is not rapid, but total loss from soil over time may be important because of the stability and persistence of Aroclor 1242 (13).

Adsorption and retention

Soil R_f values of 0.02-0.04, which are indicative of soil immobility, were measured for Aroclor 1252 in Ottawa sand, Catlin loam, Ara silty clay loam and Catlin silt loam using water and a landfill leachate (14).

Experimental soil adsorption coefficients of 2240-150,000 reported (13).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 794-1269 mg kg^{-1} (15).

LD_{50} dermal rabbit 8650 mg kg^{-1} (15).

Sub-acute and sub-chronic data

LC_{50} oral ring-necked pheasant 2078 mg kg^{-1} diet (5 days on treated diet plus 3 days untreated) (2).

LD_{50} oral mallard duck 3182 mg kg^{-1} diet (50 days on treated diet plus 3 days untreated) (2).

Immature ♂ Wistar rats were administered 10, 40, 160, 480 and 2000 mg kg^{-1} Aroclor 1242. A dose-dependent increase in hepatic microsomal aryl hydrocarbon hydroxylase, ethoxyresorufin *O*-deethylase and pentoxyresorufin *O*-deethylase activities was seen. Thymic atrophy was not observed (16).

Carcinogenicity and chronic effects

Limited evidence for carcinogenicity to humans, sufficient evidence for carcinogenicity to animals, IARC classification group 2A (17).

A NIOSH retrospective cohort study was conducted of 3588 men and women employed for ≥1 day between 1st January 1957 and 31st March 1977 manufacturing capacitors with known exposure to PCBs in the midwest US. Aroclor 1242 was used as a dielectric fluid until 1970. Results provided some evidence for an association between occupational PCB exposure and mortality from malignant melanoma. There was an increased incidence of brain cancer among workers who had more than twice the estimated cumulative PCB dose than the comparison group (18).

Teratogenicity and reproductive effects

TD oral mink ≥5 ppm diet complete reproductive failure (19).

TD oral ferrets ≥20 ppm diet complete reproductive failure (19).

Immature ♀ rats injected intraperitoneally with Aroclor 1242 (80 or 320 μg rat^{-1}) showed increased cell proliferation in the uterus (20).

Metabolism and toxicokinetics

PCBs (1016 and 1242) fed to rats over prolonged periods were metabolised into mono and dihydroxy derivatives of di-, tri-, and tetra-chlorobiphenyl (21).

Rats fed 3.89-6.6 mg kg^{-1} day^{-1} showed traces of PCB throughout body, but mainly in adipose tissue. Steady state reached in adipose tissue after 4 months. Little of PCB metabolites seen in urine. After administration ceased, elimination of PCB was slow; measurable traces found 5-6 months later. Pathological changes found in liver cells (22).

Other effects

Other adverse effects (human)

Workers exposed to 0.32-2.22 mg m^{-3} (air) complained of a burning sensation on face and hands, nausea and a persistent body odour. Chloracne and an eczematous rash on arms and legs was observed (23).

Fasting blood samples from 173 capacitor workers occupationally exposed to Aroclor 1242 detected 12-392 ppb which were dependent on serum concentration of lipids, but not albumin (24).

Concentrations of 36 polychlorinated biphenyl (PCB) congeners were measured in 167 randomly sampled human milk samples from Finnish women. The levels of PCBs decreased with increasing number of children. The third child was exposed to about 70% of PCBs as compared with the first children, and the eighth to tenth child to about 20% (25).

Any other adverse effects

In vitro investigations on murine splenocytes showed that polychlorinated biphenyls (PCBs) exhibited immunotoxicity on the antibody forming response to T-dependent antigen of sheep erythrocytes, primary activation of T-cells by mixed lymphocytes, and lymphocyte proliferation induced by various mitogens (26).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides and related products: PCB maximum admissible concentration 0.1 $\mu g\ l^{-1}$ (27).
Included in Schedule 5 and 6 (Release Into Water and Land: Prescribed Substances) of Statutory Instrument No. 472, 1991 (28).

Other comments

Aroclor 1242 is considered to have endocrine disrupting effects (29).
4-Hydroxy-2',4',6'-trichlorobiphenyl and 4-hydroxy-2',3',3',5'-tetrachlorobiphenyl, metabolites of Aroclor 1242 in the rat, caused significant sex reversal in eggs of the turtle *Trachemys scripta* at the temperature that normally produced males (30).
In vivo testing of the aquatic salamander *Necturus maculosus* exposed to polychlorinated biphenyls and organochlorine pesticides in the wild suggested that these xenobiotics induced disruptions within the hypothalamo-pituitary-interrenal axis (31).
Human health effects of PCB ingestion reviewed (17,32,33).
Reviews on human health effects, epidemiology, environmental effects, exposure levels, workplace experience and experimental toxicology listed (34).
Teratogenic effects of polychlorinated biphenyls reviewed (35).
14-49 ng g^{-1} detected in liver of cod collected in the Northwest Atlantic; not detected in muscles or ovaries (36).

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A237 Aroclor 1248

CAS Registry No. 12672-29-6

Synonyms chlorodiphenyl (48% Cl)

RTECS No. TQ 1358000

Uses Electrical insulator, heat transfer medium, hydraulic fluids and lubricants.

Occupational exposure

SE-LEVL 0.01 mg m^{-3} **SE-STEL** 0.03 mg m^{-3}

UN No. 2315 **HAZCHEM Code** 4X **Conveyance classification** other dangerous substance
Supply classification harmful, dangerous for the environment
Risk phrases Danger of cumulative effects – Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment (R33, R50/53)
Safety phrases Keep out of reach of children (if sold to general public) – This material and its container must be disposed of in a safe way – This material and/or its container must be disposed of as hazardous waste – Avoid release to the environment. Refer to special instructions/safety data sheet (S2, S35, S60, S61)

Ecotoxicity

Fish toxicity
LC_{50} (30 days, calculated) flow-through bioassay fathead minnow larvae (<8 hr old) 4.7 μg l^{-1} (1).
LC_{50} (96 hr) cutthroat trout, rainbow trout, channel catfish, bluegill sunfish, yellow perch ≤5750 μg l^{-1} (2).

Invertebrate toxicity
EC_{50} (2 wk) *Daphnia magna* 2.6 μg l^{-1} (3).
LC_{50} (48 hr) pink shrimp 32 μg l^{-1} (3).

Bioaccumulation
Bioconcentration factors: channel catfish 56,400; bluegill sunfish 52,000; scud 108,000; fathead minnow 120,000 (3).

Environmental fate

Degradation studies
Dechlorination was achieved by anaerobic microorganisms in lake sediments with the loss of *meta-* plus *para-*chlorines ranging from 15-85%. Maximum dechlorination rate was 0.3 μg-atoms of chlorine removed g^{-1} of sediment wk^{-1} (4).
Seven agricultural or forest soils degraded Aroclor 1248 at least 70% in 14 days and >90% in 112 days (5).
Removal by biological adsorption in activated sludge, 85.4% at aeration time of 24 hr (6).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 11 g kg^{-1} (7).

TD_{Lo} oral rhesus monkey 1500 mg kg^{-1}, single dose, produced anorexia and lethargy, increasing with time (8).

LD_{50} dermal rabbit >794 mg kg^{-1} (7).

Sub-acute and sub-chronic data

LC_{50} (5 day) oral bobwhite quail, Japanese quail 1175, 4844 ppm, respectively, in diet (8).

Carcinogenicity and chronic effects

Limited evidence for carcinogenicity to humans, sufficient evidence for carcinogenicity to animals, IARC classification group 2A (9).

A NIOSH retrospective cohort study was conducted of 3588 men and women employed for ≥1 day between 1st January 1957 and 31st March 1977 manufacturing capacitors with known exposure to PCBs in the midwest US. Results provided some evidence for an association between occupational PCB exposure and mortality from malignant melanoma. There was an increased incidence of brain cancer among workers who had more than twice the estimated cumulative PCB dose than the comparison group (10).

Teratogenicity and reproductive effects

TD_{Lo} oral rhesus monkey 2.5-5.0 ppm (diet) during gestation and lactation, caused death in some young and pathological changes in the others, e.g. to bone marrow and lymphoid tissue. Young also showed behavioural and learning difficulties. The PCBs were passed *in utero* and through breast feeding (11).

Metabolism and toxicokinetics

Pre-treatment of rats with Aroclor 1248 significantly increased microsomal protein concentrations and enzyme activities linked to cytochrome P450 (12).

Four weeks after intraperitoneal injection of 1 g of Aroclor 1248 into rats, adipose tissue contained 338 μg tetrachlorinated biphenyl residues g^{-1} and there was a shift to penta- and hexa-chlorobiphenyls (up to 63%) (13).

Over 90% of a single oral dose (1.5 or 3 g kg^{-1}) of Aroclor 1248 was absorbed from the gastrointestinal tract of monkeys, the major route via biliary excretion. By the 14th day after administration, 5.6% of the original dose had been eliminated in the urine and faeces (14).

Other effects

Other adverse effects (human)

Concentrations of 36 polychlorinated biphenyl (PCB) congeners were measured in 167 randomly sampled human milk samples from Finnish women. The levels of PCBs decreased with increasing number of children. The third child was exposed to about 70% of PCBs as compared with the first child, and the eighth to tenth children to about 20% (15).

Any other adverse effects

In vitro investigations on murine splenocytes showed that polychlorinated biphenyls (PCBs) exhibited immunotoxicity on the antibody forming response to T-dependent antigen of sheep erythrocytes, primary activation of T-cells by mixed lymphocytes, and lymphocyte proliferation induced by various mitogens (16).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides and related products: PCB maximum admissible concentration 0.1 μg l^{-1} (17).

Included in Schedule 5 and 6 (Release Into Water and Land: Prescribed Substances) of Statutory Instrument No. 472, 1991 (18).

Other comments

In vivo testing of the aquatic salamander *Necturus maculosus* exposed to polychlorinated biphenyls and organochlorine pesticides in the wild suggested that these xenobiotics induced disruptions within the hypothalamo-pituitary-interrenal axis (19).

Toxicity and waste disposal methods reviewed (20-22).
Long-term neurobehavioural effects in monkeys reviewed (23).
Teratogenic effects of polychlorinated biphenyls reviewed (24).
Incomplete combustion can lead to the production of the more toxic polychlorinated dibenzofurans and 2,3,7,8-tetrachlorodibenzodioxin.

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A238 Aroclor 1254

$C_{12}H_5Cl_5$ **Mol. Wt.** 326.44 **CAS Registry No.** 11097-69-1

Synonyms polychlorinated biphenyl; PCB 1254

RTECS No. TQ 1360000

Uses Dielectric liquids, transformers, capacitors, vacuum pumps, and gas turbines.

Physical properties

B. Pt. 365-390°C **Partition coefficient** log P_{ow} 6.9 (extrapolated) (1)

Occupational exposure

DE-MAK 0.05 ppm (0.70 mg m^{-3})
FR-VME 0.5 mg m^{-3}
JP-OEL 0.1 mg m^{-3}
SE-LEVL 0.01 mg m^{-3} **SE-STEL** 0.03 mg m^{-3}
UK-LTEL MEL 0.1 mg m^{-3}
US-TWA 0.5 mg m^{-3}

UN No. 2315 **HAZCHEM Code** 4X **Conveyance classification** other dangerous substance
Supply classification harmful, dangerous for the environment
Risk phrases Danger of cumulative effects – Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment (R33, R50/53)
Safety phrases Keep out of reach of children (if sold to general public) – This material and its container must be disposed of in a safe way – This material and/or its container must be disposed of as hazardous waste – Avoid release to the environment. Refer to special instructions/safety data sheet (S2, S35, S60, S61)

Ecotoxicity

Fish toxicity
Northwest Atlantic cod (November 1990), Aroclor 1254 mean levels: muscles, not detected; liver 154 ng g^{-1} wet weight; ovaries 5.1 mg g^{-1} wet weight. The total concentration of all organochlorines found in ovaries was below the level expected to affect egg and larval viability (2).
Sublethal effects on Atlantic cod 1-50 μg g^{-1} over 5.5 months. Abnormalities in testes, gills, livers (3).
LC_{50} (96 hr) crayfish, cutthroat trout, channel catfish, bluegill sunfish, yellow perch ≤42 mg l^{-1} (4).
Trout from Lake Michigan exposed to 20-times the ambient level of Aroclor 1254 showed no signs of reproductive failure (5).

Invertebrate toxicity
LC_{50} (96 hr) *Ischnura verticalis*, grass shrimp 200, 6.1-7.8 μg l^{-1}, respectively (4,6).
EC_{50} (14-21 day) *Daphnia magna* 24-1.3 mg l^{-1} (6).
LC_{50} house cricket (*Acheta domesticus*) (14 day laboratory soil bioassay) 1200 ppm (7).
LC_{50} manure worm (*Eisenia foetida*) 30.4 μg cm^{-1} (5 day filter paper contact exposure protocol); LD_{50} 4500 μg g^{-1} dry mass (8).
A refined microcosm technique was used to investigate the toxicity of Aroclor 1254 to trophic groups of nematodes and to the microarthropod community. Microarthropods were far more sensitive to Aroclor 1254 than were nematodes. Total microarthropod abundance declined at 2500 μg g^{-1} with prostigmatid and orbatid mites exhibiting the highest susceptibility (9).

Bioaccumulation
Small amounts accumulate in food chain. PCBs are fat-soluble and are stored in lipids of animals, resisting metabolic change and concentrating in animals high in the food chain (3).
Bioconcentration factors: American oyster 85,000; rotifer 340,000; crayfish 5100; scud 27,000; *Daphnia* sp. 3800 (6,10).
Bioconcentration factors *Sphaerium stratinum* 1000-25,118, fathead minnow 31,622-316,227 (11).
House crickets (*Acheta domesticus*) were exposed to Aroclor 1254 contaminated soil for 14 days. Mean whole-body concentrations were 11-149 ppm for soil test concentrations of 100-2000 ppm. Laboratory and field studies indicated that PCBs in soil can rapidly move into epigeic fauna but that the likelihood of acquiring sufficient body burdens to cause acute mortality is low (7).

Environmental fate

Nitrification inhibition
PCBs at >10 μg l^{-1} inhibited nitrification, principally ammonium oxidation (12).

Degradation studies

Dechlorination was achieved by anaerobic microorganisms in lake sediments with the loss of *meta-* plus *para-*chlorines ranging from 15-85%. Maximum dechlorination rate was 0.2 μg-atoms of chlorine removed g^{-1} of sediment wk^{-1} (13).

Using BOD dilution water, settled domestic wastewater inoculum and 5 and 10 ppm Aroclor 1254, no biodegradation occurred during 28 days (14).

Carbon dioxide evolution of Aroclor 1254 from 3 New Mexico soils over 240 days incubation in either unamended soil or soil amended with sewage sludge ranged from 1-11% with greatest carbon dioxide evolution occurring in the presence of sewage sludge (15).

208 mg of Aroclor 1254 in wastewater influent was diluted to a BOD of 200 ppm so that concentration was 1 ppm. After 17 hr wk treatment with a labscale biomass, 54% was recovered in effluent plus biomass and 30-39% was lost by evaporation (16).

Abiotic removal

Only destroyed by incineration at >1100°C with long residence time (2).

Calculated $t_{1/2}$ 10.3 hr based on evaporative loss for a water depth of 1 m at 25°C (17).

Transformation processes such as hydrolysis and oxidation do not significantly degrade Aroclor 1254 in aquatic environment (18,19).

Vapour loss of Aroclor 1254 from three soils was 40-50% over 2-4 months (20).

Evaporation was the major process by which Aroclor 1254 was lost from three untreated calcareous soils from New Mexico during 240 days; treating the soils with sewage sludge decreased the rate of evaporation (15).

Adsorption and retention

No effect on waste treatment efficiency nor toxicity to biomass although biomass accumulated 6.2 g kg^{-1} Aroclor 1254 (21).

Soil R_f values which are indicative of soil immobility are 0.02-0.04 in Ottawa sand, Catlin loam, Ava silty clay loam and Catlin silt loam using a water and landfill leachate (22).

Soil adsorption coefficients range from 110,000-1,330,000 (23).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 1300 mg kg^{-1} (24).

LD_{50} intravenous rat 358 mg kg^{-1} (24).

LD_{50} intraperitoneal mouse 2840 mg kg^{-1} (25).

Sub-acute and sub-chronic data

LC_{50} (5 day) oral bobwhite quail, Japanese quail 604, 2898 ppm, respectively, in diet (26).

Adult ♀ Japanese quails and American kestrels were administered oral doses of 7 mg kg^{-1} day^{-1} for 4-, 8-, and 12-wk periods. There were no effects on hepatic porphyrins in kestrels, aminopyrine *N*-demethylase (APND) and aldrin epoxidase (AE) were induced; renal ethoxyresorufin *O*-deethylase (EROD) was not induced. Chronic exposure of quail to Aroclor 1254 caused highly significant increases in mean hepatic porphyrin levels and in activity of EROD, APND, and 4-chlorobiphenyl hydroxylase. In both studies, Aroclor 1254 residues accumulated in tissues of both species, but there was no significant relationship between residue levels and effects (27).

Gavage adult ♂ mallards (5 wk) 0-500 mg kg^{-1} twice wk^{-1}. No immunotoxic effects were observed. Total cytochrome P450 activity was induced beginning at 100 mg kg^{-1} and peaked at 250 mg kg^{-1}. Birds treated with ≥100 mg kg^{-1} showed a dose-dependent increase in relative liver weights and significantly increased thyroid weights. No significant thyroid histological abnormalities were seen except at the highest dose. A dose-dependent decrease in plasma total triiodothyronine was observed with doses ≥20 mg kg^{-1}. The no-observed-adverse-effect level for decreased plasma triiodothyronine was 4 mg kg^{-1} (28). Intragastric ♂ Fischer 344 rat (5, 10 or 15 wk) 0-25 mg kg^{-1}. After 5, 10 and 15 wk urinary alkaline phosphatase and lactate dehydrogenase activities were elevated and the kidney-to-body weight ratios were elevated at the 10 and 25 mg kg^{-1} dose after 10- and 15-wk exposure indicating nephrotoxicity (29).

Five dose-groups of rhesus monkeys (menstruating 11-year-old ♀) self-ingested 0-80 μg kg^{-1} body weight daily for 25 months. Major findings included: decreased erythrocyte count, haematocrit, reticulocyte count and mean

platelet volume; decreased cholesterol and total bilirubin; decreased antibody production to sheep red blood cells and alterations in the percentage of T-helper and T-suppressor cells; significant reduction in the number of regions of sebaceous gland lobules; statistically significant, dose-related inflammation and/or prominence of the tarsal (Meibomian) glands, eye exudate, and various finger and toe nail changes (30).

Carcinogenicity and chronic effects

Limited evidence for carcinogenicity to humans, sufficient evidence for carcinogenicity to animals, IARC classification group 2A (31).

National Toxicology Program tested ♀ and ♂ rats via dosed-feed. Equivocal evidence of carcinogenicity in all animals (32).

A NIOSH retrospective cohort study was conducted of 3588 men and women employed for ≥1 day between 1st January 1957 and 31st March 1977 manufacturing capacitors with known exposure to PCBs in the midwest US. Results provided some evidence for an association between occupational PCB exposure and mortality from malignant melanoma. There was an increased incidence of brain cancer among workers who had more than twice the estimated cumulative PCB dose than the comparison group (33).

Teratogenicity and reproductive effects

Aroclor 1254 showed no *in vivo* estrogenic activity in rats (34).

Translactational ♀ rats (dams dosed orally on days 1, 3, 5, 7 and 9 of lactation, 8-64 μg g^{-1}). Translactational exposure that has little effect on the dams delays puberty in ♀ offspring and several months later results in decreased uterine response, impairment of fertility, and irregular cycle patterns. Reproductive ageing, however, is not hastened and may even be delayed. Many of these effects could be explained, in part, by interference with oestrogen (35).

Gavage Fischer rats (31-day-old ♂) 0-25 mg kg^{-1} day^{-1} for 5-15 wk. Testis is not a specific target organ. Serum thyroxine levels were reduced at a dose level 250-fold below the dose that failed to alter testicular function (36).

Exposure of ♀ mink to Aroclor 1254 did not prevent ovulation, fertilisation and implantation, but exposure during gestation caused foetal death. This was associated with an effect on placental development (37).

Five dose groups of rhesus monkeys (menstruating 11-year-old ♀) self-ingested 0-80 μg kg^{-1} body weight day^{-1}. At 37 months each ♀ was mated. Dosing of the dams was discontinued when a nursing infant was 7-wk old and restarted when it was weaned at 22-wk. Infants were killed humanely and autopsied at 122-wk old. The reproduction data obtained provided evidence for a significant increasing trend in foetal mortality. The major findings with the infants were some immunological test differences and mild clinical manifestations of PCB ingestion (38).

Metabolism and toxicokinetics

Sherman rats administered 10 or 50 mg kg^{-1} day^{-1} Aroclor 1254 on days 7-15 of pregnancy showed average PCB concentrations in foetuses taken by Caesarean section on day-20 of pregnancy as 0.63 and 1.38 mg kg^{-1}, respectively, compared with <0.12 mg kg^{-1} in controls (39).

In vivo percutaneous adsorption in the rhesus monkey was 14.1 ± 1.0% of dose (0.91 μg cm^{-2}) for a 5-wk period following topical dosing. With *in vitro* percutaneous adsorption through human skin, most of the Aroclor 1254 resided in the skin and the amounts depended on dosing vehicle (water > mineral oil > soil) (40).

Genotoxicity

Chinese hamster ovary cells with Aroclor 1254-induced metabolic activation caused chromosomal aberrations at exceptionally high levels up to 40 per 100 cells against a normal range of 0-10 (41).

Mouse lymphoma L5178Y tk+/tk– with metabolic activation induced DNA strand breaks (42).

Intraperitoneal common carp, tench, grass carp (48 hr) increased dose-response in micronucleus frequency and a species response dependency (43).

Other effects

Other adverse effects (human)

Excessive industrial exposure to PCBs often leads to symptoms including chloracne, brown pigmentation of the skin and nails, temporary visual disturbances, swelling of eyelids, eye discharge and some gastrointestinal symptoms with liver abnormalities and jaundice (44).

Evidence is given of two cases of Aroclor 1254 transmission from transformer maintenance workers to their wives whose household exposure occurred through contaminated clothes (45).

Fasting blood samples from 173 capacitor workers occupationally exposed to Aroclor 1254 revealed 4-129 ppb in serum, dependent on serum lipids but not albumin (46).
In a medical surveillance programme for persons potentially exposed to PCBs from an electrical transformer fire, about 820 litres of dielectric fluid containing 65% Aroclor 1254 leaked from a transformer. 450 subjects were monitored 6-12 months after the fire, 147 firemen and other persons in the building for ≥25 hr were questioned about symptoms and examined for physical abnormalities. Mean serum PCB concentrations were positively correlated with exposure extent and liver enzyme and lipid concentrations. About 50% of the subjects reported skin lesions (47).
Concentrations of 36 polychlorinated biphenyl (PCB) congeners were measured in 167 randomly sampled human milk samples from Finnish women. The levels of PCBs decreased with increasing number of children. The third child was exposed to about 70% of PCBs as compared with the first child, and the eighth to tenth children to about 20% (48).

Any other adverse effects

Oral Japanese quail 0.5 g kg^{-1} increased renal and hepatic concentrations of porphyrins, the activities of δ-aminolevulinate synthetase and uroporphyrinogen I synthetase, and faecal concentrations of δ-aminolevulinate and porphyrins, the main porphyrins being hepta-, octa-, penta-, hexa- and tetra-carboxyporphyrin (49).
The synthesis of cholesterol and cholesterol ethers by adult rat hepatocytes in primary culture was increased by 2-wk exposure to low concentrations of Aroclor 1254. The synthesis of triglycerides was unchanged. Long-term low concentrations (0.1-1.0 μg ml^{-1}) increased the secretion of cellular lipids but this was inhibited at higher concentrations (10-20 μg ml^{-1}) (50).
Pheasants fed either a single dose of 50 mg or 17 weekly doses of 12.5 or 50 mg showed up to 82% absorbed from the gastrointestinal tract and up to 50 mg kg^{-1} in their eggs (40).
Oral rat (4 day) 300 mg kg^{-1} day^{-1} caused weight loss and increased urinary nitrogen excretion as urea (51).
Aroclor 1254 fed to boars revealed PCBs in urine and faeces (52).
Aroclor 1254 pre-treatment induced P450IA1 in rabbit bone marrow microsomes 11-fold (53).
Intraperitoneal injection (dose unspecified) of Aroclor 1254 induced hepatic cytochrome P450 after 5 days in rats but not pigeons (54).
In vitro investigations on murine splenocytes showed that polychlorinated biphenyls (PCBs) exhibited immunotoxicity on the antibody forming response to T-dependent antigen of sheep erythrocytes, primary activation of T-cells by mixed lymphocytes, and lymphocyte proliferation induced by various mitogens (55).

Legislation

US Toxic Substances Control Act contains provision of discontinuance of use and eventual disposal (56-58).
US Regulations on Storage and Disposal of PCBs specify incineration as only acceptable method of disposal (59-61).
Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides and related products: PCB maximum admissible concentration 0.5 μg l^{-1} (62).
Included in Schedule 5 and 6 (Release into Water and Land: Prescribed Substances) of Statutory Instrument No. 472, 1991 (63).

Other comments

Reviews on human health effects, epidemiology, workplace experience, waste disposal and toxicology are listed (64,65).
Once widely used for high stability but now concern over long-term environmental and health effects.
Effects on the development of mouse embryos are discussed (66).

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A239 Aroclor 1260

CAS Registry No. 11096-82-5

Synonyms polychlorinated biphenyl; Santotherm; PCB 1260

RTECS No. TQ 1362000

Uses Dielectric liquids, thermostatic fluids, swelling agents for transmission seals, additives or base for lubricants, oils, greases, plasticiser for cellulosics, vinyls, chlorinated rubbers.

Physical properties

B. Pt. 385-420°C **Specific gravity** 1.41 at 15.5°C **Partition coefficient** log P_{ow} 7.7 (extrapolated) (1)
Volatility v.p. 50 mmHg at 225°C

Occupational exposure

JP-OEL 0.1 mg m^{-3}
SE-LEVL 0.01 mg m^{-3} **SE-STEL** 0.03 mg m^{-3}
UK-LTEL MEL 0.1 mg m^{-3}

UN No. 2315 **HAZCHEM Code** 4X **Conveyance classification** other dangerous substance
Supply classification harmful, dangerous for the environment
Risk phrases Danger of cumulative effects – Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment (R33, R50/53)
Safety phrases Keep out of reach of children (if sold to general public) – This material and its container must be disposed of in a safe way – This material and/or its container must be disposed of as hazardous waste – Avoid release to the environment. Refer to special instructions/safety data sheet (S2, S35, S60, S61)

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) cutthroat trout, yellow perch ≤61 mg l^{-1} (1).
LC_{50} (20 day) rainbow trout 21 μg l^{-1} (1).
LC_{50} (30 day) bluegill sunfish 150 μg l^{-1} (1).

Bioaccumulation
Bioconcentration factor for ♀ fathead minnow 270,000 (2).

Small amounts accumulate in food chain. PCBs are fat-soluble and stored in lipids of animals, resisting metabolic change and concentrating in animals high in the food chain (3).

Environmental fate

Nitrification inhibition

PCBs at >10 μg l^{-1} inhibited nitrification, principally ammonium oxidation (4).

Degradation studies

Dechlorination was achieved by anaerobic microorganisms in lake sediments with the loss of *meta-* plus *para-* chlorines ranging from 15-85%. Maximum dechlorination rates for Hudson River and Silver Lake organisms for Aroclor 1260 were 0.04 and 0.21 μg-atoms of chlorine removed g^{-1} of sediment wk^{-1}, respectively (5).
Results of a static flask screening procedure utilising BOD dilution water, settled domestic wastewater inoculum and 5 and 10 ppm of Aroclor 1260 found 0% biodegraded at the end of 28-day incubation (6).
Biological $t_{1/2}$ in *Rhabdosargus holubi* during depuration was estimated at 50 days (7).

Abiotic removal

Only destroyed by incineration at >1100°C with long residence time (3).
Calculated $t_{1/2}$ based on evaporative loss for a water depth of 1 m at 25°C: 10.2 hr (3).
Abiotic transformation processes, such as hydrolysis and oxidation, do not significantly degrade Aroclor 1260 in the aquatic environment (8).

Mammalian & avian toxicity

Acute data

LD_{50} oral mallard duck >2000 mg kg^{-1} (9).
LD_{50} oral rat 1320 mg kg^{-1} (10).
LD_{50} dermal rabbit 10 g kg^{-1} (11).

Sub-acute and sub-chronic data

LD_{50} oral northern bobwhite 747 mg kg^{-1} (5 days on treated diet plus 3 days untreated) (1).
♂ Wistar rats (120 day) fed 50 and 100 ppm significantly increased the activity of liver succinate dehydrogenase. Lactate dehydrogenase activity increased at 50 ppm level and decreased at 100 ppm. Alanine and aspartate aminotransferases and alkaline and acid aspartate aminotransferases and alkaline and acid phosphatases showed remarkable decrease in activity. In both Aroclor 1260-fed groups, the liver showed centrilobular hypertrophy, hepatocellular damage, hyperplasia, karyolysis and karyorrhexis. The kidney showed glomerulonephritis, degenerative changes in the proximal and distal tubules and increased cellularity of glomeruli whilst the thyroid showed degeneration of follicles, fibrosis of follicles and lymphocytic infiltration followed by thyroiditis (12).

Carcinogenicity and chronic effects

Limited evidence for carcinogenicity to humans, sufficient evidence for carcinogenicity to animals, IARC classification group 2A (13).
A NIOSH retrospective cohort study was conducted of 3588 men and women employed for ≥1 day between 1st January 1957 and 31st March 1977 manufacturing capacitors with known exposure to PCBs in the midwest US. Results provided some evidence for an association between occupational PCB exposure and mortality from malignant melanoma. There was an increased incidence of brain cancer among workers who had more than twice the estimated cumulative PCB dose than the comparison group (14).

Other effects

Other adverse effects (human)

Excessive industrial exposure to PCBs often leads to symptoms including chloracne, brown pigmentation of the skin and nails, temporary visual disturbances, swelling of eyelids, eye discharge and some gastrointestinal symptoms with liver abnormalities and jaundice (15).
Fasting blood samples obtained from 173 capacitor workers occupationally exposed to Aroclor 1260 revealed 4-129 ppb in serum, concentration being dependent on serum lipids but not of albumin (16).

Concentrations of 36 polychlorinated biphenyl (PCB) congeners were measured in 167 randomly sampled human milk samples from Finnish women. The levels of PCBs decreased with increasing number of children. The third child was exposed to about 70% of PCBs as compared with the first child, and the eighth to tenth children to about 20% (17).

Any other adverse effects

Hepatic changes, neoplastic modules and liver adenofibrosis in young rats in short time after exposure (18).
In vitro investigations on murine splenocytes showed that polychlorinated biphenyls (PCBs) exhibited immunotoxicity on the antibody forming response to T-dependent antigen of sheep erythrocytes, primary activation of T-cells by mixed lymphocytes, and lymphocyte proliferation induced by various mitogens (19).

Legislation

US Toxic Substances Control Act contains provision of discontinuance of use and eventual disposal (20-22).
US Regulations 1978 on Storage and Disposal of PCBs specify incineration as only acceptable method of disposal (23-25).
Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides and related products: PCB maximum admissible concentration 0.1 $\mu g\ l^{-1}$ (26).
Included in Schedule 5 and 6 (Release into Water and Land: Prescribed Substances) of Statutory Instrument No. 472, 1991 (27).

Other comments

Analysis of ready-to-eat foods collected in markets of 20 US cities as conducted by the US FDA found Aroclor 1260 in one of 360 food composites (positive in meat, fish and poultry category) in 1978 (28).
Toxicity and waste disposal methods reported (29).
Once widely used for high stability but now concern over long-term environmental and health effects.

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A240 arsenic

As

As **Mol. Wt.** 74.92 **CAS Registry No.** 7440-38-2

Synonyms arsenic-75; arsenic black; arsenicals; colloidal arsenic; grey arsenic; metallic arsenic

EINECS No. 231-148-6 **RTECS No.** CG 0525000

Uses Metallurgy, hardening copper, lead alloys, manufacture of glass.
Occurrence Occurrence in the earth's crust: 0.0005%. Found to a small extent as the element, mostly as an arsenide of true metals.

Physical properties

M. Pt. 814°C at 36 atm **B. Pt.** sublimes at 612°C **Specific gravity** black crystals 5.724 at 14°C, black amorphous 4.7

Occupational exposure

SE-LEVL 0.03 mg m^{-3}
UK-LTEL MEL 0.1 mg m^{-3}
US-TWA 0.01 mg m^{-3}

UN No. 1558 **HAZCHEM Code** 2Z **Conveyance classification** toxic substance
Supply classification toxic
Risk phrases Toxic by inhalation and if swallowed (R23/25)
Safety phrases Keep locked up and out of the reach of children (if sold to general public) – When using do not eat, drink or smoke – After contact with skin, wash immediately with plenty of water – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S20/21, S28, S45)

Ecotoxicity

Fish toxicity
EC_{50} (96 hr) fathead minnow 141-144 mg l^{-1} (1).
LC_{50} (96 hr) knifefish 31 mg l^{-1} (2).
Oral (24 wk) rainbow trout 0.52 mg kg^{-1} day^{-1} caused chronic inflammatory changes in subepithelial tissues of the gall bladder wall in 71% of group (3).
LC_{50} (96 hr) striped bass 30 mg l^{-1} (4).
LC_{50} (96 hr) striped catfish, barb 22-24 mg l^{-1} static bioassay (5).

Invertebrate toxicity
EC_{50} (96 hr) *Daphnia magna* 4.3 mg l^{-1} (with food), 1.5 mg l^{-1} (without food) (6).
LC_{50} (48 hr) *Daphnia magna* 47 mg l^{-1} (7).
LC_{50} (48 hr) *Aplexa hypnorum* 24.5 mg l^{-1} (8).

The manure worm (*Eisenia foetida*) tolerated 25 mg kg^{-1} in the wet substratum without lethal effect. Both juvenile mass gain and adult cocoon production were decreased significantly. No decrease of arsenic content could be observed at the end of the 8-wk recovery period (9).
Accumulation, biomethylation, and excretion of arsenic by an autotrophic freshwater alga, and the transport and transformation of the arsenic in the freshwater food chain [alga (autotroph) – moina (planktonic grazer) or shrimp (herbivore) – guppy (carnivore)] were investigated. Total arsenic concentrations in organisms after accumulation from food decreased one order of magnitude per elevation of the trophic level. Predominant methylated arsenic species in moina and guppy were di- and tri-methylarsenic compounds, respectively. Shrimp accumulated di- and tri-methylarsenic compounds in nearly equivalent quantities. No or little monomethylarsenic compound was detected in herbivores or carnivores (10).

Bioaccumulation
The arsenic content of clams collected during April-May 1991 along the Saudi Arabian coast of the Gulf was highest in those collected closest to Kuwait (11).

Mammalian & avian toxicity

Acute data
LD_{Lo} subcutaneous rabbit 300 mg kg^{-1} (12).
LD_{Lo} intraperitoneal guinea pig 10 mg kg^{-1} (13).

Carcinogenicity and chronic effects
Sufficient evidence for carcinogenicity to humans, sufficient evidence for carcinogenicity to animals, IARC classification group 1 for arsenic and arsenic compounds (14,15).
Intratracheal ♂ Syrian golden hamster total dose 3.75 mg arsenic 1 × wk^{-1} for 15 wk. Results concerning arsenic compounds inconclusive (16).
Low micromolar concentrations of sodium arsenite caused increased mRNA transcripts and secretion of keratinocyte growth factors in primary human epidermal keratinocyte cultures. Total cell numbers, as well as c-myc expression and incorporation of [3H]thymidine, both indicators of cell proliferation, were also elevated. As an *in vivo* model, the influence of arsenic on mouse skin tumour development was studied. Following low-dose application of 12-*O*-tetradecanoylphorbol-13-acetate (TPA) to transgenic TG.AC mice (which carry the V-Ha-ras oncogene and can serve as a genetically initiated model for carcinogenesis) a marked increase in the number of skin papillomas occurred in transgenic mice receiving arsenic in the drinking water as compared to control drinking water. Papillomas did not develop in arsenic-treated transgenic mice that had not received TPA or arsenic-treated wild-type FVB/N mice, suggesting that arsenic is neither a tumour indicator or promoter, but rather an enhancer. It is suggested that arsenic enhances papilloma development via the chronic stimulation of keratinocyte-derived growth factors (17).

Teratogenicity and reproductive effects
LD_{50} (14 day) chick embryo 9 μg egg^{-1}. The gross malformations observed were reduced body size, micromelia, twisted neck, haemorrhage, everted viscera and microphthalmia (18).
Mallard breeding pairs were fed 0-400 μg g^{-1} in diet in combination with selenium at 0-10 μg g^{-1}. Ducklings produced were placed on the same treatment combination as their parents. Arsenic accumulated in adult liver and egg, reduced the adult weight gain and liver weight, delayed the onset of egg laying, decreased whole egg weight, and caused eggshell thinning, but did not affect hatching success and was not teratogenic. In ducklings, arsenic accumulated in the liver and reduced body weight, growth, and liver weight. It did not increase duckling mortality but did decrease overall duckling production (19).
LD_{Lo} oral pregnant mouse 120 mg kg^{-1} reduced foetal weight and survival. Some gross and skeletal malformations reported. Effects of oral administration were less than those after intraperitoneal injection of 40 mg kg^{-1} (20).

Metabolism and toxicokinetics
Trivalent arsenic was metabolised by rat liver, kidney, lung slices to monomethylarsenic acid and dimethylarsenic acid; the liver had the greatest methylating capacity. GSH regulated trivalent arsenic metabolism. In contrast to trivalent arsenic, pentavalent arsenic was not extensively taken up by the hepatocyte and was poorly methylated (21).

Inhalation animals (species and dose unspecified) showed increased tissue levels of arsenic during the first week or month, but levels decreased with prolonged exposure. In rats after single exposure the biological $t_{1/2}$ is substantial due to the accumulation of arsenic in blood (22).
The ability of the rat to sequester arsenic is greater than that of humans (23).
Normal blood arsenic values for individuals are 1-5 μg l^{-1} whole blood. Cigarette smokers showed mean blood arsenic levels approximately 50% higher than non-smokers (24).
Organoarsenic compounds are bioaccumulated by human consumers of seafood products. The arsenic is excreted rapidly, mostly as organoarsenic compounds. Little of the organoarsenic accumulated by humans from seafood is converted into toxic inorganic arsenite (25).
Metabolites excreted in urine following human occupational acute intoxification with arsine were monomethylarsonate, dimethylarsinate, As^{3+}, arsenobetaine, and to a lesser extent As^{5+}. The highest elimination of total arsenic occurred during the first five days following intoxication. Arsenic clearance in urine was 7.8 ml hr^{-1} kg^{-1} and followed a triphasic model with periods of 28 hr, 59 hr, and 9 days, respectively (26).

Genotoxicity

In *in vivo* intraperitoneal ♂ Swiss Albino mice neither chromatid nor chromosome aberrations were observed in bone marrow cells and spermatogonia (27).
The L5178Y/TK+/– mouse lymphoma assay was used to determine the relative genotoxic potencies of sodium arsenite, sodium arsenate, monomethylarsenic acid (MMA), and dimethylarsinic acid (DMA). Sodium arsenite and sodium arsenate were active at concentrations of 1-2 μg ml^{-1} and 10-14 μg ml^{-1}, respectively. MMA was active between 2500-5000 μg ml^{-1} and DMA required almost 10,000 μg ml^{-1} to induce a genetic response. The organic arsenic compounds are thus much less potent as mutagenic agents than the inorganic compounds. All four compounds appear to act by mechanisms that cause chromosomal mutations (28).

Other effects

Other adverse effects (human)
Occupational studies in three countries have related quantitative estimates of arsenic exposure to lung cancer risks. Mine exposures in China appear to incur a higher relative risk than arsenic exposures elsewhere. All the studies with quantitative data are consistent with a supralinear dose-response relationship (29).
In comparison to controls, a significantly higher incidence of chromosomal aberrations was found in five women residing in an area heavily polluted by inorganic arsenic from the Srednogorie copper smelter, Bulgaria. The high arsenic exposure was verified by measuring arsenic concentrations in hair and nails (30).
The cytogenic effects of arsenic exposure were studied in two populations differing only in their exposure to inorganic arsenic via drinking water; exposed population 408.17 μg l^{-1} and control population 29.88 μg l^{-1} inorganic arsenic in drinking water. Exposed individuals showed a significant increase in the frequency of chromatid and isochromatid deletions in lymphocytes and of micronuclei in oral and urinary epithelial cells. Males were affected more than females, and a higher number of micronucleated oral cells were found among those individuals with skin lesions. The type of cytogenic damage observed gives evidence of arsenic as a clastogenic/aneugenic carcinogen (31).
The results of an 8-yr survey into arsenic poisoning in the Indian State of West Bengal has found at least 220,000 people have been poisoned via contaminated groundwater. Levels of arsenic have been determined at 5 to 370 times the maximum permitted levels in 26,000 groundwater wells. The permitted concentration is 0.01 mg l^{-1}. Health problems included: melanosis, spotted keratosis, oedema of the feet, hepatomegaly, splenomegaly, squamous cell carcinoma and intraepidermal carcinoma. Cancers of the bladder, genitourinary tract and lungs may also have been due to long-term exposure to arsenic. Often symptoms only appear 6 months to 2 yr following exposure. Arsenic groundwater contamination has also been reported in Argentina, Chile, Mexico, Taiwan, Thailand and the USA (32).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Arsenic: maximum admissible concentration 50 μg l^{-1} (33).

Other comments

The aquatic biota, Environmental fate, toxicology, neoplastic transformations, carcinogenicity, human health effects, occupational hazards, experimental toxicology and environmental effects have been extensively reviewed (34-49).

The average concentration of total arsenic in the ocean is about 1.7 $\mu g\ l^{-1}$ which is about two orders of magnitude higher than the US Environmental Protection Agency's human health criterion (fish consumption) value of 0.0175 $\mu g\ l^{-1}$. Arsenate is the dominant form of arsenic in oxygenated marine and brackish waters. The more toxic and potentially carcinogenic arsenite rarely accounts for more than 20% of total arsenic in seawater (25).

Ecotoxicology of arsenic in the marine environment reviewed (25).

Human and animal data on the reproductive toxicity of arsenic reviewed, with emphasis on its role in causing neural tube defects, and mechanisms thereof. In addition, literature concerning the presence of arsenic in the general environment and the workplace is discussed (50).

The toxicity of arsenic is dependent on the ability of the organism to absorb it. Therefore toxicity data refer to bioavailable forms such as the ion in solution or particulate matter. Found widely in nature.

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A241 arsenic acid

$$(HO)_3As{=}O$$

AsH_3O_4 **Mol. Wt.** 141.94 **CAS Registry No.** 7778-39-4

Synonyms ortho arsenic acid

EINECS No. 231-901-9 **RTECS No.** CG 0700000

Uses In the preparation of arsenate salts. Manufacture of insecticides.

Physical properties

M. Pt. 35.5°C **Specific gravity** 2.0-2.5
Solubility Organic solvents: ethanol, glycerol

Occupational exposure

SE-LEVL 0.03 mg m^{-3} (as As)
UK-LTEL MEL 0.1 mg m^{-3} (as As)
US-TWA 0.01 mg m^{-3} (as As)

UN No. 1553 (liquid)

UN No. 1554 (solid) **HAZCHEM Code** 2X **Conveyance classification** toxic substance
Supply classification toxic
Risk phrases May cause cancer – Toxic by inhalation and if swallowed (R45, R23/25)
Safety phrases 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 48 mg kg^{-1} (1).
LD_{Lo} oral rabbit, dog, chicken 5, 10, 125 mg kg^{-1}, respectively (1).
LD_{50} intravenous rabbit 6 mg kg^{-1} (2).

Carcinogenicity and chronic effects
Sufficient evidence for carcinogenicity to humans, limited evidence for carcinogenicity to animals, IARC classification group 1 for arsenic and arsenic compounds (3).

Two major studies have been carried out on the mortality of workers involved in the production of arsenical insecticides where arsenic acid was a starting material. In both cases arsenic acid was produced *in situ* from arsenic trioxide. In the first study, arsenic acid could not be confirmed as a contributory factor in the cancer mortality of workers. In the second, the mortality of workers who retired between 1960-1972 was investigated. Insufficient information was available to evaluate the reliability of reported results, but the authors stated that of 17 cancer deaths in men, 10 were respiratory tract and 3 lymphosarcomas (4-8).

Metabolism and toxicokinetics

Analysis of urine from treated hamsters showed the presence of inorganic arsenic and dimethylarsinic acid (9).
Oral ♂, ♀ hamster (single dose) 0.01 μg arsenic as arsenic acid. The $t_{1/2}$ for 1st component (98% of dose) was 0.29 days, and the $t_{1/2}$ for 2nd component (2% of dose) was 3-8 days (10).
Mice given radio-labelled arsenic acid and X-rayed for distribution revealed a high proportion of arsenic concentrated in the intestinal mucosa and the kidneys (11).

Other effects

Other adverse effects (human)

An organotypic culture of a human keratinocyte cell line over a human fibroblast-embedded collagen gel was used to model human epidermis in arsenicism. Acute or chronic exposure of keratinocytes to individual arsenic compounds [0.5 μM arsenate, 0.5 μM monomethylarsonic acid (MMA), 1.5 μM dimethylarsinic acid (DMA)] demonstrated that all arsenic mixture-induced changes could be duplicated by exposure to arsenate alone. In contrast, MMA and DMA were inactive, implicating inorganic arsenic as the ultimate carcinogen (12).

Any other adverse effects

Human leucocytes incubated with 1 mg l^{-1} cytotoxicity test positive (9).
Human fibroblasts incubated with 100 ppb cytotoxicity test positive (10).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Arsenic: maximum admissible concentration 50 μg l^{-1} (13).

Other comments

Toxicity reviewed under United Nations Environmental Programme (14).

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A242 arsenic disulfide

As_2S_2

As_2S_2 **Mol. Wt.** 213.98 **CAS Registry No.** 12044-79-0

Synonyms arsenic sulfide; arsine, thioxo-; arsenic monosulfide; arsenic sulfide red; C.I. 77085

Occurrence Arsenic ore. Realgar.

Physical properties

M. Pt. α 267°C, β 307°C **B. Pt.** 565°C **Specific gravity** α 3.506, β 3.254

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. 1577 **Conveyance classification** toxic substance
Supply classification toxic
Risk phrases May cause cancer – Toxic by inhalation and if swallowed (R45, R23/25)
Safety phrases Avoid exposure – obtain special instruction before use – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S53, S45)

Mammalian & avian toxicity

Carcinogenicity and chronic effects
Sufficient evidence for carcinogenicity to humans, limited evidence for carcinogenicity to animals, IARC classification group 1 for arsenic and arsenic compounds (1).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Arsenic: maximum admissible concentration 50 μg l^{-1} (2).

References

1. *IARC Monograph* 1987, **Suppl. 7**, 100-106.
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

A243 arsenic trichloride

$AsCl_3$

$AsCl_3$ **Mol. Wt.** 181.28 **CAS Registry No.** 7784-34-1

Synonyms arsenic chloride; arsenic(III) chloride; arsenous chloride; arsenious chloride; arsenious trichloride; trichloroarsine

EINECS No. 232-059-5 **RTECS No.** CG 1750000

Uses In specialised ceramic manufacture.

Physical properties

M. Pt. –16°C **B. Pt.** 130°C **Specific gravity** 2.163 at 20°C **Volatility** v.p. 10 mmHg at 23.5°C ; v.den. 6.25.
Solubility Organic solvents: carbon tetrachloride, chloroform, diethyl ether

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. 1560 **HAZCHEM Code** 2X **Conveyance classification** toxic substance
Supply classification toxic
Risk phrases May cause cancer – Toxic by inhalation and if swallowed (R45, R23/25)
Safety phrases Restricted to professional users – Avoid exposure – obtain special instruction before use – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S53, S45)

Mammalian & avian toxicity

Acute data
LC_{Lo} (10 min) inhalation mouse 338 ppm (1).
LD_{Lo} intravenous dog 120 mg kg^{-1} (2).

Carcinogenicity and chronic effects
Sufficient evidence for carcinogenicity in humans, limited evidence for carcinogenicity in animals, IARC classification group 1 for arsenic and arsenic compounds (3).

Genotoxicity

Bacillus subtilis rec+rec– positive (4).
Escherichia coli DNA damage repair test positive (5).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Arsenic: maximum admissible concentration 50 μg l^{-1} (6).

Other comments

Toxicity reviewed under the United Nations Environmental Programme (7).
Explodes on contact with sodium, potassium and aluminium.

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A244 arsenic trioxide

As_2O_3

As_2O_3 **Mol. Wt.** 197.84 **CAS Registry No.** 1327-53-3

Synonyms arsenic oxide; arsenic(III) oxide; arsenic sesquioxide; arsenious acid; arsenious oxide; arsenious trioxide; arsenous acid; arsenous acid anhydride; arsenous anhydride; arsenous oxide; arsenous oxide anhydride; crude arsenic; diarsenic trioxide; white arsenic

EINECS No. 215-481-4 **RTECS No.** CG 3325000

Uses In the manufacture of glass, Paris green and enamels. Used in weed killers. For preserving hides and in sheep dips. Used in rodenticides and insecticides.
Occurrence Occurs in nature as the mineral claudetite (As_2O_3).

Physical properties

M. Pt. claudetite (monoclinic crystal structure) 313°C, arsenolite (cubic crystal structure) 275°C **B. Pt.** 465°C
Specific gravity claudetite 3.865, arsenolite 4.15 at 25°C
Solubility Water: Slightly soluble (hot water) 65 g l^{-1}

Occupational exposure

FR-VME 0.2 mg m^{-3}
JP-OEL (pending)
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. 1561 **HAZCHEM Code** 2Z **Conveyance classification** toxic substance
Supply classification very toxic
Risk phrases May cause cancer – Very toxic if swallowed – Causes burns (R45, R28, R34)
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
Rainbow trout (8 wk) 1-137 μg arsenic g^{-1} in diet, no observed effects; at high exposures 137-1477 μg arsenic g^{-1} in diet, reduced growth and reduced feed behaviour have been reported (1).

Invertebrate toxicity
LC_{50} (24 hr) *Daphnia magna* 38 μM (2).
LC_{50} (24 hr) *Artemia salina* 1.2 μM (2).
LC_{50} (48 hr) *Channa punctatus* 14.7 mg (3).
IC_{50} *Geotrichum candidum* 0.9 mM inhibition of glucose uptake (4).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 20 mg kg^{-1} (5).
LD_{Lo} intravenous rabbit 4 mg kg^{-1} arsenic as arsenic trioxide (6).
LD_{Lo} subcutaneous guinea pig 6 mg kg^{-1} (7).

Sub-acute and sub-chronic data
Highly toxic. Effects of excess exposure include dermatitis, acute or chronic poisoning (6).
Subcutaneous ♂ guinea pig 2 × day^{-1} for 5 days (dose unspecified), had 3.3 μg arsenic g^{-1} in liver. Pyruvate

concentration was decreased, no correlation was found between metabolic changes and arsenic burden of liver after single and repeated treatment of arsenic oxide (7).
Highly toxic. Effects of excess exposure include dermatitis, acute or chronic poisoning (8).

Carcinogenicity and chronic effects
Sufficient evidence for carcinogenicity to humans, limited evidence for carcinogenicity to animals, IARC classification group 1 for arsenic and arsenic compounds (9).
Intratracheal installation Syrian golden hamster (15 wk) 3.75 mg total dose, tumour incidence 3.3% although arsenic trioxide had no apparent carcinogenicity or tumorigenicity (8).

Teratogenicity and reproductive effects
Intratracheal installation rats 1.3 mg kg^{-1} 2 × wk^{-1} for 8 wk. No reproductive toxicity was observed (10).
A woman who swallowed 30 ml of rat poison containing 1.32% elemental arsenic as the trioxide in the 30th wk of pregnancy gave birth 4 days later to a live baby weighing 1100 g, who died 11 hr later (11).
Smelter workers exposed to arsenic compounds during pregnancy had an excess of low birth weight babies, increased frequency of spontaneous abortion and increased occurrence of multiple malformations (11).

Metabolism and toxicokinetics
Oral rat (52 days) 215 ppm arsenic as arsenic trioxide, highest levels found in kidneys and liver and relatively lower levels in hair, brain, bone, muscle and skin (12).
Oral monkey (duration unspecified) 1 mg kg^{-1} arsenic as arsenic trioxide resulted in approximately 80% absorption from gut, 75% of dose excreted within 14 days (11).
In vivo hamster (single dose) methylated into methylarsenic acid and dimethylarsenic acid. Inorganic arsenic accounted for the major portion of total arsenic deposited in organs and tissues. The dose was followed by excretion of an amount of arsenic equivalent to approximately 60% of the administered dose (49% in urine, 11% in faeces) (13).

Genotoxicity

The frequency of sister chromatid exchanges in human peripheral lymphocytes exposed to 2 μg ml^{-1} was above that of controls (14).
Intraperitoneal ♂ mouse (12-48 hr) 0-12 mg arsenic kg^{-1}, neither chromatid nor chromosome aberrations were observed in spermatogonia and bone marrow cells (15).

Other effects

Other adverse effects (human)
In humans, symptoms of acute poisoning can occur from 30 min to several hours after ingestion, and include dryness and irritation of the mouth, difficulty in swallowing, vomiting, abdominal pain, diarrhoea, dehydration, fall in blood pressure, cyanosis and collapse (16).
Ulceration and perforation of the nasal septum is caused by airborne arsenic trioxide if proper precautions are not observed. However these injuries have not been associated with malignancy (17).
Highly toxic. Effects of excess exposure include dermatitis, acute or chronic poisoning (18).

Any other adverse effects
IC_{50} ascites sarcoma BP8 cells 5 μM inhibition of cell growth (19).
Single subcutaneous, unspecified dose ♂ guinea pig showed 18.5 μg arsenic g^{-1} in liver. An increase in the content of pyruvate, citrate and malate, and a decrease in hydroxybutyrate was found (20).
Subcutaneous ♂ guinea pig 2 × day^{-1} for 5 days (dose unspecified), had 3.3 μg arsenic g^{-1} in liver. Pyruvate concentration was decreased, no correlation was found between metabolic changes and arsenic burden of liver after single and repeated treatment of arsenic oxide (20).
The effect of trivalent arsenic oxide and pentavalent arsenic oxide on gluconeogenesis from various substrates in the liver and kidneys of rats was investigated. Decreased acetyl CoA, 3-hydroxybutyrate, and reduced glutathione was found in suspensions of isolated rat kidney tubes or hepatocytes incubated with trivalent arsenic oxide. About 10-times higher concentrations of pentavalent arsenic oxide were needed to induce a similar extent of inhibition of gluconeogenesis (21).

Results obtained using mice suggest that hypoglycaemia, following glycogen depletion and gluconeogenesis inhibition, represents a vital problem of acute trivalent arsenical poisoning and that glucose substitution should be considered as a treatment (22).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Arsenic: maximum admissible concentration 50 $\mu g\ l^{-1}$ (23).

Other comments

Chemical and physical properties, uses, risks, mutagenicity and carcinogenicity, human health effects, epidemiology and experimental toxicology reviewed (24-26).

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26. *International Registry of Potentially Toxic Chemicals* 1991, **20**, United Nations Environmental Programme, Geneva, Switzerland

A245 arsenic trisulfide

As_2S_3

As_2S_3 **Mol. Wt.** 246.04 **CAS Registry No.** 1303-33-9

Synonyms arsenic sesquisulfide; arsenic sulfide; arsenious sulfide; arsenous sulfide; diarsenic trisulfide; Kings gold

EINECS No. 215-117-4 **RTECS No.** CG 2638000

Uses Manufacture of specialist glasses, pyrotechnics, electronics.
Occurrence Ore: orpiment.

Physical properties

M. Pt. 300°C **B. Pt.** 707°C **Specific gravity** 3.43
Solubility Organic solvents: ethanol

Occupational exposure

SE-LEVL 0.03 mg m^{-3} (as As)
UK-LTEL MEL 0.1 mg m^{-3} (as As)
US-TWA 0.01 mg m^{-3} (as As)

UN No. 1577 **Conveyance classification** toxic substance
Supply classification toxic
Risk phrases May cause cancer – Toxic by inhalation and if swallowed (R45, R23/25)
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 135 mg l^{-1} (1).

Invertebrate toxicity
LC_{50} (96 hr) white shrimp 500 mg l^{-1} (2).

Mammalian & avian toxicity

Acute data
LD_{50} oral mouse, rat 185-255 mg kg^{-1} (3).
LD_{50} dermal rat 936 mg kg^{-1} (3).
LD_{50} intraperitoneal mouse, rat 86-215 mg kg^{-1} (3).
A single application of 0.05 LD_{50} to eye of rats caused severe keratoconjunctivitis leading to blindness (3).

Sub-acute and sub-chronic data
Oral doses totalling 570 mg kg^{-1} in rats caused hypoglycaemia, blood abnormalities and pathological changes in the kidneys, liver and spleen in the first 2 wk of the study (3).

Carcinogenicity and chronic effects
Sufficient evidence for carcinogenicity in humans, limited evidence for carcinogenicity in animals, IARC classification group 1 for arsenic and arsenic compounds (4).
Intratracheal ♂ Syrian golden hamsters 3 mg kg^{-1} (as As) of arsenic trisulfide induced lung adenoma in 1 of the 28 animals tested (5).
Intratracheal installation (15 wk) ♂ Syrian golden hamster weekly administration of arsenic sulfide equivalent to a total dose of 3.75 mg arsenic induced 1 lung adenoma in 22 hamsters in the arsenic sulfide group compared

with 1 lung adenosquamous carcinoma in 21 hamsters of the control group. The authors considered the results to be inconclusive (6).

Metabolism and toxicokinetics
Intratracheal (species unspecified) retention of arsenic trisulfide in lung 10 × higher than arsenic trioxide (7).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Arsenic: maximum admissible concentration 50 mg l^{-1} (8).

Other comments

Reviews on human health effects and experimental toxicology listed (9,10).

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10. *International Registry of Potentially Toxic Chemicals: Arsenic Compounds* 1991, **20**, United Nations Environmental Programme, Geneva, Switzerland

A246 arsine

AsH_3

AsH_3 **Mol. Wt.** 77.95 **CAS Registry No.** 7784-42-1

Synonyms arsenic hydride; arsenic trihydride; arseniuretted hydrogen; arsenous hydride; hydrogen arsenide

EINECS No. 232-066-3 **RTECS No.** CG 6475000

Uses Doping agent for semiconductors. Organic synthesis. Military poison gas. Transistor manufacture.

Physical properties

M. Pt. –116.3°C (decomp. at 300°C) **B. Pt.** –62.5°C **Specific gravity** 1.640 at –64.3°C (liquid)
Volatility v.p. >1 atm. ; v.den. 2.7
Solubility Water: 20 ml 100 g^{-1}. Organic solvents: benzene, chloroform

Occupational exposure

DE-MAK 0.05 ppm (0.16 mg m^{-3})
FR-VME 0.05 ppm (0.2 mg m^{-3}) **FR-VLE** 0.2 ppm (0.8 mg m^{-3})
JP-OEL 0.01 ppm (0.032 mg m^{-3}), ceiling limit 0.1 ppm (0.32 mg m^{-3})

SE-LEVL 0.02 ppm (0.05 mg m^{-3})
UK-LTEL 0.05 ppm (0.16 mg m^{-3})
US-TWA 0.05 ppm (0.16 mg m^{-3})

UN No. 2188 **Conveyance classification** toxic gas, danger of fire (flammable gas)
Supply classification very toxic
Supply classification extremely flammable
Supply classification dangerous for the environment
Risk phrases Extremely flammable – Very toxic by inhalation – Harmful: danger of serious damage to health by prolonged exposure through inhalation – Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment (R12, R26, R48/20, R50/53)
Safety phrases Keep locked up and out of the reach of children (if sold to general public) – Keep container in a well ventilated place – Keep away from sources of ignition – No smoking – After contact with skin, wash immediately with plenty of water – Take precautionary measures against static discharges – 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, S9, S16, S28, S33, S36/37, S45, S60, S61)

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) bluegill sunfish 1.1 μg l^{-1} (1).

Environmental fate

Abiotic removal
Rapid hydrolysis in water to arsenic acids and hydrides (2).

Mammalian & avian toxicity

Acute data
LC_{Lo} (15 min) inhalation rat 300 mg m^{-3} (3).
LC_{Lo} (15 min) inhalation rabbit 500 mg m^{-3} (3).
No effects on haematopoietic system observed following single exposure to 0.5 ppm (10 × threshold limit value set by American Conference of Governmental Industrial Hygienists), repeated exposure to 0.025 ppm caused significant anaemia in rats (4).

Sub-acute and sub-chronic data
Inhalation rat, mouse (28 day) 10 ppm produced 100% mortality within 4 days. Regenerative anaemia developed after prolonged exposure. Arsine-induced disturbances in haematopoietic system produce marked, specific changes in excretion of urinary proporphyrins (5).
Inhalation $B6C3F_1$ mouse, Fischer 344 rat (90 days) 0.5-5.0 ppm. No changes in body weight gain observed in mouse, decrease in body weight gain in ♂ rat exposed to 5.0 ppm for 28 days. Significant exposure-related increases in relative spleen weights occurred in both sexes of mouse and rat in all exposure groups. Decreased packed cell volumes, haematological profiles (in rats) and increased δ-aminolevulinic acid dehydratase activity in all species. Arsenic content measured in rat liver after 90 days increased in concentration. Histopathological changes include increased haemosiderosis, extramedullary haematopoiesis in spleen and intracanalicular bile stasis in liver (mice only). Additional bone marrow hyperplasia in rats observed (4).
Inhalation $B6C3F_1$ mouse, Fischer 344 rat (14 days), Fischer 344 rat, Syrian golden hamster (28 days) 0.5-5.0 ppm. No changes in body weight gain in either sex of mouse or hamster. Rat exposed to 5.0 ppm (28 days) incurred decrease in body weight gain. Significant exposure-related increases in relative spleen weight occurred in both sexes of mouse and rat in the 0.5 ppm (except 14-day ♀ rats), 2.5, 5.0 ppm exposure groups from all studies and in hamsters in 2.5, 5.0 ppm exposure groups. Decreased packed cell volumes and an increase in δ-aminolevulinic acid dehydratase activity observed in all species and haematological profiles in rats were also affected (4).

Carcinogenicity and chronic effects

Sufficient evidence for carcinogenicity in humans, limited evidence for carcinogenicity in animals, IARC classification group 1 for arsenic and arsenic compounds (6).

Teratogenicity and reproductive effects

Rats and mice (6-15 days pregnancy) 0.025-2.5 ppm. In rats, maternal spleens enlarged in 2.5 ppm group and packed red cell volume, decreased in pregnant rats. Arsine did not adversely affect end-points of developmental toxicity (7).

Metabolism and toxicokinetics

Inhalation mouse (duration unspecified) 0.025-2.5 mg l^{-1}, about 60% is absorbed. In rabbits, highest concentrations were found in liver, lungs and kidneys (8).

Metabolites excreted in urine following human occupational acute intoxification with arsine were monomethylarsonate, dimethylarsinate, As^{3+}, arsenobetaine, and to a lesser extent As^{5+}. The highest elimination of total arsenic occurred during the first five days following intoxication. Arsenic clearance in urine was 7.8 ml hr^{-1} kg^{-1} and followed a triphasic model with periods of 28 hr, 59 hr, and 9 days, respectively (9).

Other effects

Other adverse effects (human)

Acute arsine poisoning in an industrial metallurgy worker produced jaundice, vomiting and blood-stained urine (10).

Renal failure, fever, nausea, vomiting, diarrhoea, abdominal pain, haemoglobinuria, intravascular haemolysis in sailors exposed to leaking cylinder (11).

Arsine caused haemolysis of human erythrocytes *in vitro*, dependent on membrane disruption by a mechanism other than Hb oxidation (12).

Any other adverse effects

Inhalation of 250 ppm is instantly lethal. Exposure to 25-50 ppm for 30 min is lethal (species unspecified) (13).

Other comments

Human health effects, epidemiology and experimental toxicology reviewed (14,15).

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A247 asbestos

CAS Registry No. 1332-21-4

RTECS No. CI 6475000

Uses Heat resistant insulators, cements, furnace and hot pipe coverings, inert filler medium, fireproof gloves, clothing, brake linings.

Occurrence In two large groups of rock-forming minerals, the serpentines and the amphiboles as fibrous mineral silicates. Extensive deposits in Russia, China and South Africa.

The main commercial varieties are chrysotile (a serpentine mineral), and crocidolite and amosite (amphiboles) (1).

Physical properties

M. Pt. Decomposes to pyroxenes and silica **Specific gravity** chrysotile 2.55; anthophyllite 2.85-3.1; amosite 3.43; crocidolite 3.37; tremolite 2.9-3.2; actinolite 3.0-3.2

Occupational exposure

SE-LEVL 0.2 fibre ml^{-1}

UK-LTEL control limit 0.2 fibres ml^{-1} (4 hr) **UK-STEL** control limit 0.6 fibres ml^{-1} (10 min)

US-TWA 0.1 fibres cm^{-3} (all forms)

UN No. 2212 (blue or brown)

UN No. 2590 (white) **HAZCHEM Code** 2X **Conveyance classification** other dangerous substance

Supply classification toxic

Risk phrases May cause cancer – Toxic: danger of serious damage to health by prolonged exposure through inhalation (R45, R48/23)

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

Mammalian & avian toxicity

Sub-acute and sub-chronic data

Pulmonary fibrosis reported in rats, monkeys, hamsters, rabbits and guinea pigs following inhalation of chrysotile and amphiboles. Exposure was in the order of 10 mg m^{-3} for 6-12 months (1).

Carcinogenicity and chronic effects

Sufficient evidence for carcinogenicity in humans and animals, IARC classification group 1 (2).

Bronchial carcinomas and pleural mesotheliomas developed in rats following inhalation exposure to chrysotile and amphibole asbestos. Shorter fibres are less fibrogenic and carcinogenic; Potts hypothesis states that maximum carcinogenicity is from fibres 20 μm long and 0.125 μm in diameter (1).

Many cohort studies since 1955 in industrial populations showed excess lung cancer risk due to asbestos exposure (1).

Metabolism and toxicokinetics

Inhaled fibres deposit by sedimentation, diffusion, impaction and interception in airways of the respiratory system. Asbestos particles move through the epithelium to the lung interstitium where the fibres react with macrophages and fibroblasts. Two human studies gave evidence for the penetration and migration of asbestos. Amphibole asbestos has been detected in the urine of Minnesota residents who ingested drinking water contaminated with 5×10^7 fibres (3).

After intrapleural or subcutaneous inoculation (species unspecified), occasional asbestos fibres or bodies reported in other tissues, including pancreas, spleen and thyroid. There is no information on how fibres reach these sites (4).

Peritoneal mesothelioma in humans, excess cancer of the stomach, colon, rectum and cancers at other non-respiratory sites could result from the migration of fibres to and across the gastrointestinal mucosa, by transdiaphragmatic migration or lymphatic-haematogenous transport (5).
The ability of asbestos fibres to cross the gut wall is still debated; it seems likely that if it does occur it is very limited (1).
Oral rat (dose unspecified) for up to 1 yr. There was no evidence of asbestos retention within gut lumen, and no signs of cell penetration or damage to intestinal mucosa were observed (6).
Intraperitoneal Wistar rat (2-day intervals from day 10-14 of gestation) total dose 4-12 mg. Asbestos fibres were found to cross the placenta, but the extent of this occurrence was highly variable (7).

Genotoxicity

The induction of micronuclei, hyperdiploidy and chromosome breakage in human amniotic cells *in vitro* by amosite, chrysotile and crocidolite asbestos, and ceramic fibres has been investigated. The response of human (amniotic fluid cells) and rodent (Syrian hamster embryo fibroblasts, SHE) cells to fibre treatment was compared using the micronucleus assay. All types of mineral fibres caused a significant increase of micronucleated cells. The kinetochore analyses revealed that all three types of asbestos and ceramic fibres yielded similar effects. Approximately 50% of the induced micronuclei were kinetochore-negative, indicating formation through clastogenic events. Human amniotic cells were much less susceptible than SHE cells to the induction of micronuclei by mineral fibres. This again demonstrates that SHE cells are more susceptible to chromosomal changes than human amniotic fluid cells. The application of fluorescence *in situ* hybridization (FISH) with tandem DNA probes yielded more detailed information about specific structural chromosome aberrations in the 1 (cen-q12) and 9 (cen-q12) regions and about abnormal numbers of chromosomes in interphase human amniotic fluid cells. Using this FISH approach the authors found a statistically significant increase of chromosomal breakage in the pericentric heterochromatin regions of chromosomes 1 and 9 in interphase human amniotic cells after exposure to asbestos and ceramic fibres compared to control cells. The number of hyperdiploid cells was also significantly increased. These results show that asbestos fibres as well as ceramic fibres are inducers of structural and numerical chromosomal aberrations in human amniotic fluid cells (8).

Other effects

Any other adverse effects
Inhalation of asbestos dust causes the following pathological changes: asbestosis, carcinoma, mesothelioma, pleural plaques (9).

Legislation

Federally regulated carcinogen (NIOSH) in USA.
Use in UK controlled by legislation (10).
Included in Schedule 4 (Release into Air: Prescribed Substances) of Statutory Instrument No. 472, 1991 (11).

Other comments

Human health effects, epidemiology and experimental toxicology reviewed (1,4,12).

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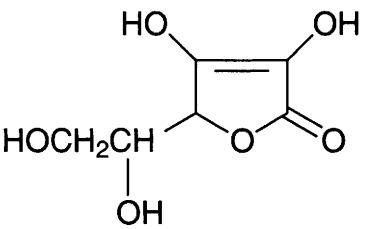
A248 ascorbic acid



$C_6H_8O_6$ **Mol. Wt.** 176.13 **CAS Registry No.** 50-81-7

Synonyms vitamin C; L-3-ketothreohexuronic acid lactone

EINECS No. 200-066-2 **RTECS No.** CI 7650000

Uses Vitamin supplement. Preservative and antioxidant in foodstuffs.
Occurrence Widely distributed in plant and animal kingdom. Good sources are citrus fruits and hip berries.

Physical properties

M. Pt. 193°C **Specific gravity** 1.65
Solubility Water: 333 g l^{-1}. Organic solvents: ethanol

Mammalian & avian toxicity

Acute data
LD_{50} intraperitoneal mouse, rat 2630, 3120 mg kg^{-1}, respectively (1,2).
LD_{50} intravenous mouse 518 mg kg^{-1} (3).

Sub-acute and sub-chronic data
Oral rabbit (10 days) 50 mg kg^{-1} day^{-1} induced immunostimulation by activating lymphocyte production through the facilitation of DNA and RNA formation (4).

Carcinogenicity and chronic effects
National Toxicology Program tested ♂, ♀ rats and mice via dosed-feed. Negative evidence of carcinogenicity in all animals (5).

Metabolism and toxicokinetics
Absorbed ascorbic acid is ubiquitously distributed in all body tissues. Highest concentrations found in glandular tissue, the lowest in muscle and stored fat (6).

Genotoxicity

Genetic alteration in *Neurospora crassa* at 350 mg l^{-1} (7).
Chromosomal abnormalities in cultivated hamster cells at 300 mg l^{-1} (8).
Chinese hamster lung V79 assay (6 hr) with metabolic activation increased the incidence of cells with chromosomal aberration (9).
Drosophila melanogaster 0-50,000 ppm feed, 0-10,600 ppm injection, SLRL assay negative (10).
Drosophila melanogaster 0-100 mM, (*white/white*$^+$) eye mosaic assay negative (11).

Other effects

Any other adverse effects

Using the Ames *Salmonella*/microsome assay, the antimutagenic activities of ascorbic acid against solvent extracts of coal dust, diesel emission particles, airborne particles, fried beef and tobacco snuff were compared. Ascorbic acid inhibited <39% of the activity of the complex mixtures studied, but enhanced the mutagenicity of airborne particles (12).

A single large dose of ethanol (5 g kg^{-1} of 25% w/v via incubation) to ♂ Donryu rats caused a decrease in renal and adrenal concentrations of ascorbic acid and an increase in the amount of ascorbic acid excreted in the urine (13).

The results of a series of studies in guinea pigs suggest that hepatic decarboxylation and gut microflora, in tandem, contribute to ascorbic acid decarboxylation in this species (14).

Other comments

Vitamin C has been shown to promote the *N*-acetylation of 2-aminofluorene in *Klebsiella pneumoniae*. There is thus the possibility that oral vitamin C may modify the mutagenicity/carcinogenicity of ingested arylamines through the enhancement of *N*-acetyltransferase activity of human enteric bacteria (15).

Ascorbic acid in the presence of copper has been shown to exert a strong killing effect on a number of prokaryotic cell species *in vitro* (16).

Pretreatment of mice with Vitamin C reduced by 90% the kidney DNA adduct formation caused by a single administration of the genotoxic mycotoxin ochratoxin (17).

Metabolism and toxicology in fish, cancer prevention, toxicity, human health effects, metabolism and experimental toxicology reviewed (18-25).

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A249 asphalt, fumes

CAS Registry No. 8052-42-4

Synonyms asphaltum; bitumen; Judgan pitch; mineral pitch; petroleum pitch; road tar

RTECS No. CI 9900000

Uses Making roads, roofing, waterproofing and insulating materials. Also an ingredient of some paints and varnishes.

Occurrence Consitituent of crude petroleum. Occurs in natural deposits in pits or lakes resulting from the evaporation and oxidation of liquid petroleum. Separated from petroleum by refining.

Physical properties

B. Pt. 470°C **Flash point** 204°C (closed cup) **Specific gravity** 0.95-1.1

Solubility Organic solvents: carbon disulfide, petroleum, turpentine oil

Occupational exposure

UK-LTEL 5 mg m^{-3} **UK-STEL** 10 mg m^{-3}

US-TWA 5 mg m^{-3}

Mammalian & avian toxicity

Acute data

LD_{50} intragastric rat 3-8 g kg^{-1} (1).

Carcinogenicity and chronic effects

Inadequate evidence for carcinogenicity in humans, limited to sufficient evidence for carcinogenicity in animals, IARC classification group 2B (for steam-refined and cracking-residue-; air-refined-; extracts of steam-refined and air-refined-bitumens) (2).

Other comments

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

A significant contribution to the PAH content of street dust from material associated with asphalt (4).

Experiments were conducted to find out whether the use of petroleum-asphalt seal coating in ductile-iron pipe would contribute significant concentrations of PAH in drinking water distribution systems. The results of the analyses were compared with the WHO recommendation for maximum allowable concentration of polycyclic aromatic hydrocarbons in drinking water of 200 ng l^{-1}. The highest concentration found in three experiments was 5 ng l^{-1} (5).

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A250 astatine

$_{85}At^{200}$-$_{85}At^{219}$

At **Mol. Wt.** 209.99 **CAS Registry No.** 7440-68-8

Uses Used in radiobiology, mainly ^{211}At. Cancer diagnostics and treatment.

Occurrence Minute quantities of ^{215}At, ^{218}At and ^{219}At exist, in nature, in equilibrium with uranium and thorium isotopes.

Physical properties

M. Pt. 302°C (estimated) **B. Pt.** 337°C (estimated)

Mammalian & avian toxicity

Sub-acute and sub-chronic data

Mice injected with a single dose containing 61 kBq ^{211}At showed pathological changes in spleen, lymph nodes, bone marrow, gonads, thyroid, salivary glands, and stomach, when killed at 14 or 56 days (1).

Other effects

Any other adverse effects

Thought to concentrate in the thyroid, similarly to iodine (1-3).

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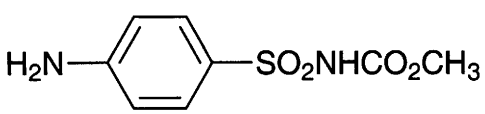
A251 asulam



$C_8H_{10}N_2O_4S$ **Mol. Wt.** 230.24 **CAS Registry No.** 3337-71-1

Synonyms methyl 4-aminophenylsulfonylcarbamate; methyl 4-aminobenzene sulfonylcarbamate; methyl sulfanilylcarbamate; methyl ((4-aminophenyl)sulfonyl)carbamate; carbamic acid, [(4-aminophenyl)sulfonyl]-, methyl ester

EINECS No. 222-077-1 **RTECS No.** ED 1190000

Uses Systemic herbicide.

Physical properties

M. Pt. 143-144°C (decomp.) **Volatility** v.p. $<7.5 \times 10^{-6}$ mmHg at 20°C

Solubility Water: 5 g l^{-1} at 20-25°C. Organic solvents: acetone, dimethyl formamide, ethanol, methanol

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) rainbow trout, channel catfish, goldfish, bluegill sunfish >3000 mg l^{-1} (1).

Invertebrate toxicity

Non-toxic to bees (2).

Environmental fate

Degradation studies

In soil $t_{1/2}$ 6-14 days. Metabolism is by loss of amino group, cleavage of carbamate group or acetylation of amino group (2).

Mammalian & avian toxicity

Acute data

LD_{50} oral mallard duck, pheasant, pigeon >4000 mg kg^{-1} (2).
LD_{50} oral rat, mouse, rabbit, dog >4000 mg kg^{-1} (2).
LC_{50} (6 hr) inhalation rat >1.8 mg l^{-1} (2).
LD_{50} percutaneous rat >1200 mg kg^{-1} (2).

Sub-acute and sub-chronic data

Oral rat (90 day) 400 mg kg^{-1} in diet. No significant ill-effects observed (2).
No effects observed when fed to cows at 800 ppm for 8 wk or to sheep at 50 mg kg^{-1} for 10 days (2).

Teratogenicity and reproductive effects

Considered non-teratogenic (species unspecified) (2).

Metabolism and toxicokinetics

Asulam administered by mouth or intravenously to rats was excreted within 24 hr. Excretory products consisted mainly of unchanged asulam, plus minor amounts of *N*-acetylasulam and *N*-acetylsulfanilamide (3).
Following oral administration to rats (dose unspecified), 85-96% of the dose is eliminated, predominantly in the urine, within 3 days (2).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides and related products: maximum admissible concentration 0.1 μg l^{-1} (4).
Included in Schedule 6 (Release into Land: Prescribed Substances) of Statutory Instrument No. 472, 1991 (5).

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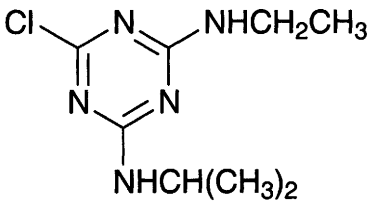
A252 atrazine



$C_8H_{14}ClN_5$ **Mol. Wt.** 215.69 **CAS Registry No.** 1912-24-9

Synonyms 2-chloro-4-ethylamino-6-isopropylamino-1,3,5-triazine; 6-chloro-*N*-2-ethyl-*N*-4-isopropyl-1,3,5-triazine-2,4-diamine; 6-chloro-*N*-ethyl-*N'*-(1-methylethyl)-1,3,5-triazine-2,4-diamine; 2-chloro-4-ethylamino-6-isopropylamino-*s*-triazine; Aatrex; Aktikon; Mebazine

EINECS No. 217-617-8 **RTECS No.** XY 5600000

Uses A selective herbicide and plant growth regulator.

Physical properties

M. Pt. 171-174°C **Specific gravity** 1.187 at 20°C **Partition coefficient** log P_{ow} 2.5 at 25°C (1)
Volatility v.p. 3.0×10^{-7} mmHg at 20°C
Solubility Water: 70 mg l^{-1} at 22°C. Organic solvents: acetone, chloroform, diethyl ether, dimethyl sulfoxide, ethanol, ethyl acetate

Occupational exposure

DE-MAK 2 mg m^{-3} (inhalable dust fraction)
FR-VME 5 mg m^{-3}
US-TWA 5 mg m^{-3}
Supply classification harmful
Risk phrases Harmful by inhalation and if swallowed – Irritating to the eyes – Possible risk of irreversible effects – May cause sensitisation by skin contact (R20/22, R36, R40, R43)
Safety phrases Keep out of reach of children (if sold to general public) – Wear suitable protective clothing and gloves – If swallowed seek medical advice immediately and show this container or label (S2, S36/37, S46)

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) rainbow trout 4.5-11.0 mg l^{-1}, bluegill sunfish 16 mg l^{-1}, carp 76 mg l^{-1}, catfish 7.6 mg l^{-1}, perch 16 mg l^{-1}, guppies 4.3 mg l^{-1} (1).
LC_{50} (96 hr) carp 18.8 mg l^{-1} (2).
Rainbow trout was exposed to 1.4-2.8 mg l^{-1} for 96 hr and 5-80 μg l^{-1} for 28 days. Necrosis of endothelial cells and renal tissue was observed at high doses for both time periods (3).
Significant changes in the body weight, hydration level and serum inorganic electrolytes of cichlid were observed following exposure to atrazine, suggesting disturbance of hydromineral balance (4).

Invertebrate toxicity
EC_{50} (48 hr) *Daphnia magna* >39 mg l^{-1} (5).
Chlamydomonas reinhardtii (24-48 hr) 21.6 μg l^{-1} caused change in cell number of algae species observed (6).
Cell multiplication inhibition test, *Pseudomonas putida* 10 mg l^{-1}, *Microcystis aeruginosa* 3 μg l^{-1} (7).
Southern armyworm larvae fed atrazine for three days showed cytochrome P 450-catalysed aldrin epoxidation and methoxyresorufin *o*-demethylation. Decreases in parathion and permethrin toxicity were observed (8).

EC_{50} (10 day) *Lemna minor* 56 μg l^{-1} (frond number), 60 μg l^{-1} (fresh weight), 62 μg l^{-1} (total chlorophyll) (9).
EC_{50} (96 hr) *Scenedesmus subspicatus* 21 μg l^{-1} (9).
Rhodococcus TE1 metabolised atrazine to deethylatrazine and deisopropylatrazine under aerobic conditions (10).
LD_{50} oral bee >97 μg bee^{-1} (1).

Toxicity to other species
LC_{50} (route unspecified) *Rana pipiens* larvae 47.6 mg l^{-1} (11).
LD_{Lo} bullfrog, leopard frog 0.41 mg l^{-1} (12).

Bioaccumulation
Bioconcentration factor values for snails 2-15, algae 10-83, fish 3-10 (7).
Calculated bioconcentration factors of 0.3-2 have been reported for mottled sculpin, golden ide, fathead minnow, whitefish and catfish. These values indicate environmental bioaccumulation of atrazine is unlikely (13-18).
Bioconcentration was determined for cichlid exposed to atrazine. Highest concentrations were found in ovaries (50.6 μg g^{-1}) and liver (40.1 μg g^{-1}). Bioconcentration factors for liver, muscle, heart, gonads and brain were 0.9-20.0 (19).

Environmental fate

Anaerobic effects
Under anaerobic conditions, 0.59% atrazine degraded to carbon dioxide (20).

Degradation studies
In soil, microbial degradation occurs with a $t_{1/2}$ of 6-10 wk (7).
Dealkylation is major mechanism of microbial degradation of atrazine, *s*-triazine ring is resistant to microbial degradation (21-23).
Soil metabolites include diethylatrazine, diisopropylatrazine, dealkylatrazine and hydroxyatrazine; $t_{1/2}$ 17-26 days (24).
Rapid mineralisation of the *s*-triazine and ethyl side chain of atrazine was accomplished by a mixed microbial consortium in soil. Degradation of atrazine by *Rhodococcus* sp. NI 86/21 produced deisopropylatrazine and deethylatrazine (25).
Atrazine (10 mg l^{-1}) disappeared within 15 days from sediment slurries obtained from two agricultural watersheds in the Great Lakes incubated aerobically at 30°C in the laboratory. Degradation was found in surface (0-10 cm) sediments, but not in sediments from a depth of 20 cm (26).
Atrazine supplied as sole carbon and energy source was mineralised by a microbial enrichment culture. Microorganisms were immobilised in a non-aerated fixed bed reactor with a sintered glass bed as carrier matrix. Elimination was rapid with a concentration of 7.5 mg l^{-1} atrazine and below 30 minute reactor retention time. Mineralisation was incomplete under oxygen-deficient conditions, but regained upon addition of 66 mg l^{-1} of NO_3^- ions to medium (27).
A bacterial culture isolated from soil previously impacted by herbicide spills was found to anaerobically degrade atrazine in media containing: atrazine only; atrazine and glucose; and atrazine, glucose and nitrate (28).
Two bacteria RK014 and RK016 were isolated from Japanese and Thai soils, respectively. RK014 was an unidentified Gram negative spore-forming rod, RK016 was identified as *Bacillus* sp. Both bacteria degraded atrazine (10 mg l^{-1}) at stationary phase. Degradation rates were higher at pH 8 than pH 5 with high density of bacterial inoculum. Deethylatrazine was the major metabolite (29).
Under unsaturated conditions atrazine is least persistent in top 30 cm of soil. Persistence increased with soil depth and $t_{1/2}$ ranged from 41 days to 231 days (at 120 cm) (30).

Abiotic removal
Evaporation is not significant for the removal of atrazine from the environment (31).
Chemical hydrolysis to hydroxyatrazine was the principal pathway of detoxification in soil. Biological dealkylation without dehalogenation occurs simultaneously leading to the formation of 2-chloro-4-amino-6-isopropyl-*s*-triazine (32).

Adsorption and retention

Moderately to highly mobile in soils ranging in texture from clay to gravelly sand, respectively. The metabolite hydroxyatrazine has low mobility in sandy loam and silty clay loam soils (33).

Atrazine binds strongly to soil and sediments, the process is reversible and dependent on factors such as temperature, moisture and pH (34,35).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, mouse, rabbit 750-3080 mg kg^{-1} (1,32,12,36).

LD_{50} oral bobwhite quail 940 mg kg^{-1} (1).

LD_{50} oral Japanese quail >10,000 mg kg^{-1} (1).

LC_{50} (4 hr) inhalation rat 5200 mg m^{-3} (37).

LD_{50} percutaneous rabbit 7500 mg kg^{-1} (1).

LD_{50} percutaneous rat >3100 mg kg^{-1} (1).

Sub-acute and sub-chronic data

LC_{50} (8 day dietary) bobwhite quail, mallard duck 5760-19,650 mg kg^{-1} as 80% wettable powder formulation (1).

Rabbits fed maize from treated fields (~2.5 kg ha^{-1}) for 6 months showed loss of appetite, general debility, depression and anaemia (38).

Oral ♀ pig (19 day) 2 mg kg^{-1} body weight in feed. Blood samples were collected 3 × day^{-1} for four days post-treatment. Serum activities of γ-glutamyltransferase, alanine aminotransferase, aspartate aminotransferase, and alkaline phosphatase were determined. Only γ-glutamyltransferase activity increased significantly. Livers of exposed pigs showed centrilobular parenchymatous degeneration (39).

Atrazine was administered to ♂ and ♀ Fischer rats (7 days for 120 mg kg^{-1} body weight day^{-1}). Significant decreases in body weight were observed (40).

Carcinogenicity and chronic effects

Inadequate evidence for carcinogenicity to humans, limited evidence for carcinogenicity to animals, IARC classification group 2B (41).

F344/LATI rats (126 wk) 0-750 ppm caused dose-dependent depression of body weight. Increased incidence of mammary tumours, uterine carcinomas and leukaemias/lymphomas (42).

Sprague-Dawley rats fed 0-50 mg kg^{-1} day^{-1}, high doses caused decreased body weight, hyperplastic changes to mammary gland, bladder, prostate, myeloid tissue of bone marrow and transitional epithelium of the kidney. Mammary gland tumour observed (43).

Teratogenicity and reproductive effects

Pregnant rats (6-15 day gestation) 0-1000 mg kg^{-1} day^{-1}. Increased number of embryonic and foetal deaths, decreased foetal weight and retarded skeletal development at high doses. No teratogenic effects observed. Induced 23% maternal mortality at 1000 mg kg^{-1} day^{-1} (42).

Atrazine (120 mg kg^{-1} body weight day^{-1}) was administered to ♂ and ♀ Fischer rats for 7 days. Increased pituitary and prostate weights were observed and a prolonged oestrous cycle, characterised by extended vaginal dioestrus. Rate of successful mating decreased for 1 wk after treatment between exposed ♂ and ♀ rats and unexposed ♂ and exposed ♀ rats. No alteration in mating was observed with exposed ♂ and unexposed ♀ rats (40).

Metabolism and toxicokinetics

Atrazine given orally to rats was excreted as atrazine and metabolites within 48 hr. Maximum excretion was at 24 hr and decreased steeply (44).

Oral rat (72 hr) 65% excreted in urine, 20% in faeces and 0.1% exhaled. Highest concentrations observed in muscle, tissue and fat (45).

Rats administered a single oral dose of 0.53 mg by gavage excreted 20% in faeces and 65% in urine. At 72 hr 16% of the administered dose was retained in the liver, kidneys and lungs (46).

A single 0.1 g dose was administered by gavage to 3-5 months old Pittman-Moore pigs. The major urinary products detected were the parent compound atrazine and its metabolite diethylatrazine (47).

In rats the major metabolic pathways for the detoxification of the compound were identified as dechlorination of the triazine ring and *N*-dealkylation. Secondary metabolic routes appeared to be oxidation of alkyl substituents (48).

In vitro hepatic microsomal systems from rats, goats, sheep, pigs, rabbits were used to investigate the metabolic action of atrazine. Phase I reactions were cytochrome P450 mediated and phase II products were reduced glutathione conjugates and monodealkylated products (49).
In rats (3 day) (unspecified route) 0.005-50 mg day^{-1}, major urinary metabolite was 2-chloro-4, 6-diamino-s-triazine (50).
Percutaneous absorption in human skin was studied. 16.4% of applied dose was absorbed. Two metabolites desisopropylatrazine and 2-chloro-4,6-diamino-s-triazine were found in the receptor fluid and skin supernates (51).
Exposure in six manufacturing workers was evaluated. Total exposure was 10-700 μmol $workshift^{-1}$. Urinary atrazine composition was bi-dealkylatrazine (80%), desisopropylatrazine (10%), deethylatrazine (8%), and unmodified atrazine (2%). Metabolites were excreted in just over 24 hr, 50% of this within the first 8 hr after workshift (52).

Irritancy
Dermal rabbit (duration unspecified) 38 mg caused mild irritation, while 6.3 mg instilled into rabbit eye caused severe irritation (53).
A farm worker exposed to an atrazine formulation was diagnosed with severe contact dermatitis. Clinical signs included red, swollen and blistered hands with haemorrhagic bullae between the fingers (54).
In a primary irritation study in rats 2800 mg kg^{-1} caused erythema but no systemic effects (46).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100 with and without metabolic activation negative (55).
Escherichia coli PQ37 with and without metabolic activation negative (56).
In vitro human bone marrow cells induced chromosome damage (57).
Atrazine is genotoxic in *Drosophila melanogaster* somatic and germ line cells (58).
Drosophila melanogaster wing spot test positive (59).
In vivo mouse bone marrow cells induced chromosome damage (57).
Vicia faba root tips induced micronuclei in soil poor in organic matter (60).
♀ Mice administered 1400 mg kg^{-1} showed an increase in micronuclei in the mouse bone marrow micronucleus test (61).

Other effects

Other adverse effects (human)
There is conflicting evidence for an increase in the incidence of non-Hodgkin's lymphoma attributable to agricultural use of atrazine (62,63).

Any other adverse effects
Rats administered a single dose of 3000 mg kg^{-1} by gavage and sacrificed 24-48 hr later showed evidence of pulmonary oedema, cardiac dilation and microscopic haemorrhages in the liver and spleen, cerebral oedema and histochemical alterations in lungs, liver and brain (64).
Moderate direct toxicity was observed with *in vitro* human granulomonocytic progenitor-cells, suggesting myelosuppressive activity (65).

Legislation

Included in Schedules 5 and 6 (Release Into Water and Land: Prescribed Substances) of Statutory Instrument No. 472, 1991 (66).
Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides and related products: maximum admissible concentration 0.1 μg l^{-1} (67).

Other comments

Considered to have endocrine disrupting effects. At high (ppm) doses atrazine can induce elevated testicular expression of the steroidogenic enzyme aromatase in ♂ alligators if exposure occurs *in ovo* (68).

Mammalian and aquatic toxicity reviewed (69,70,71).
Epidemiological, carcinogenicity and genotoxicity studies reported (42).
Genotoxicity reviewed (72).
Atrazine residues have been detected in numerous tapwater, groundwater and river samples.
Metabolic pathways reviewed (73).

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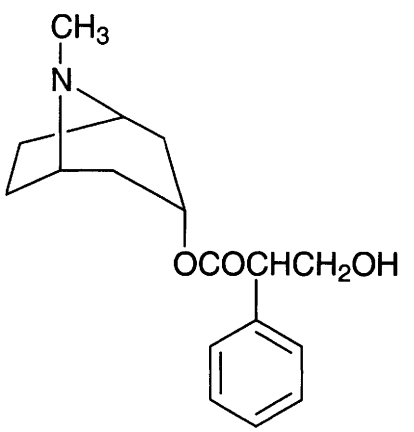
A253 atropine



$C_{17}H_{23}NO_3$ **Mol. Wt.** 289.37 **CAS Registry No.** 51-55-8

Synonyms benzeneacetic acid, α-(hydroxymethyl)-8-methyl-8-azobicyclo[3.2.1]oct-3-yl ester endo-(±)-; DL-hyoxyomene; DL-tropyl tropate

EINECS No. 200-104-8 **RTECS No.** CK 0700000

Uses Antimuscarinic drug. Antidote in poisoning cases. Treatment of gastro-intestinal disorders, bradycardia, and in ophthalmology as a cycloplegic and mydriatic (1).
Occurrence Obtained from *Atropase belladonna, Datura stramonium L.* and other Solanaceae.

Physical properties

M. Pt. 118-119°C
Solubility Organic solvents: benzene, chloroform, diethyl ether, ethanol

Occupational exposure

Supply classification very toxic
Risk phrases Very toxic by inhalation and if swallowed (R26/28)
Safety phrases Keep locked up and out of the reach of children (if sold to general public) – Avoid contact with the eyes – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S25, S45)

Mammalian & avian toxicity

Acute data
LD_{50} oral mouse 75 mg kg^{-1} (2).
LD_{50} intraperitoneal rat 280 mg kg^{-1} (3).
LD_{50} intravenous rabbit 50 mg kg^{-1} (2).
LD_{Lo} subcutaneous guinea pig 450 mg kg^{-1} (4).
Human lethal concentration 0.302 μmol l^{-1} (as sulfate) (5).

Sub-acute and sub-chronic data
Rat (90 day) in feed, 0.5, 1.58, 5.0% jimson weed seed. The alkaloid content was 2.71 mg atropine and 0.66 mg scopolamine g^{-1} of seed. Decreased body weight gain, serum albumin and serum calcium, increased liver and testes weights (as percentage of body weight), serum alkaline phosphatase, and blood urea nitrogen. ♀ developed decreased serum total protein and cholesterol, and increased serum glutamic-pyruvic transaminase activity, red blood cell count, haemoglobin concentration and packed red cell volume. No histological lesions associated with ingestion of jimson weed seed at 5% (6).

Irritancy
Dermatitis from the use of eyedrops containing atropine has been reported (7).

Other effects

Other adverse effects (human)
Symptoms of atropine poisoning are dryness of skin, mouth and throat, tachycardia, flushed skin and face, irritability and restlessness (8).

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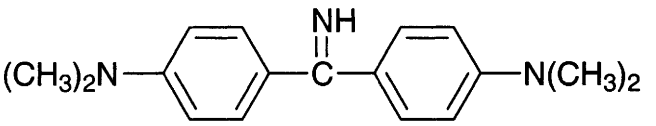
A254 auramine



$C_{17}H_{22}ClN_3$ **Mol. Wt.** 267.37 **CAS Registry No.** 2465-27-2

Synonyms bis(*p*-dimethylaminophenyl)methyleneimine; 4,4'-carbonimidoylbis(*N*,*N*-dimethylbenzenamine); 4,4'-dimethylaminobenzophenonimide; 4,4'-(imidocarbonyl)bis(*N*,*N*-dimethylaniline); tetramethyldiaminodiphenylacetimine; aniline, 4,4-(imidocarbonyl)bis(*N*,*N*-dimethyl)-; 4,4-bisdimethylaminobenzophenoneimide; C.I. Solvent Yellow 34

EINECS No. 219-567-2 **RTECS No.** BY 3500000

Uses Dyestuff for paper, textiles and leather.

Physical properties

M. Pt. 136°C

Solubility Organic solvents: acetone, dimethylformamide, ethanol

Occupational exposure

Supply classification harmful

Risk phrases Harmful if swallowed – Irritating to the eyes – Possible risk of irreversible effects (R22, R36, R40)

Safety phrases Keep out of reach of children (if sold to general public) – Wear suitable protective clothing and gloves (S2, S36/37)

Ecotoxicity

Bioaccumulation

Calculated bioconcentration factor 288 (1).

Environmental fate

Degradation studies

BOD_5 1.5% reduction of dissolved oxygen concentration using standard dilution techniques (2).

Abiotic removal

Calculated hydrolytic $t_{1/2}$ 65 days at pH 5, increasing to 74 days at pH 9. Michler's ketone has been detected as a product of hydrolysis (3).

Mammalian & avian toxicity

Acute data

LD_{50} intraperitoneal mouse 103 mg kg^{-1} (4).

Carcinogenicity and chronic effects

Sufficient evidence for carcinogenicity to humans, IARC classification group 1 for the manufacture of auramine (5).

Inadequate evidence for carcinogenicity to humans, sufficient evidence for carcinogenicity to animals, IARC classification group 2B for technical grade auramine (5).

Oral mice (1 yr) 0.1% in diet, total dose 728 mg administered as 14 mg wk^{-1}, induced hepatomas, lymphomas, especially lymphosarcoma and reticulum-cell sarcoma and intestinal tumours (6).

Subcutaneous rat (21 wk) 0.1 ml of 2.5% suspension in arachis oil 5 day wk^{-1} induced hepatomas, intestinal carcinoma and subcutaneous sarcoma at injection site (7).

Irritancy
Absorption through skin may result in dermatitis and burns (8).

Genotoxicity

Salmonella typhimurium, TA98, TA100, TA1535, TA1537, TA1538 with and without metabolic activation positive (9). *In vitro* rat and human hepatocytes, exposed to 10-32 μM for 20 hr, showed a dose-dependent increase in DNA fragmentation (10).

Other comments

Human health effects, epidemiology, workplace experience, and experimental toxicology reviewed (11-12).

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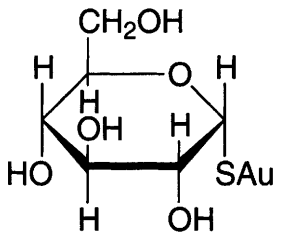
A255 aurothioglucose



$C_6H_{11}AuO_5S$ **Mol. Wt.** 392.18 **CAS Registry No.** 12192-57-3

Synonyms (1-thio-D-glucopyranosato)-gold; (1-D-glucosylthio)gold; gold thioglucose; 1-aurothio-D-glucopyranose; (D-glucopyranosylthio)gold; 1-thio-glucopyranose, monogold(I) salt

RTECS No. MD 6475000

Uses In the treatment of severe rheumatoid arthritis. Less commonly, to treat non-disseminated lupus erythematosus (1).

Physical properties

Solubility Water: soluble (decomp.). Organic solvents: propylene glycol

Mammalian & avian toxicity

Acute data

LD_{50} intravenous chicken 1000 mg kg^{-1} (2).
LD_{50} intraperitoneal mouse 2000-2500 mg kg^{-1} (3).
LD_{Lo} intramuscular chicken 300 mg kg^{-1} (4).
LD_{Lo} subcutaneous mouse 1650 mg kg^{-1} (5).
LD_{Lo} (unspecified route) man 3 mg kg^{-1} (6).

Carcinogenicity and chronic effects

No adequate data for carcinogenicity to humans, limited evidence for carcinogenicity to animals, IARC classification group 3 (7).
Intraperitoneal injection of 400 mg aurothioglucose kg^{-1} virgin ♀ RIIIxCBA mice (70-80 days old) caused mammary tumours in 38/38 mice that became obese, compared with 29/34 controls and 10/10 untreated breeders. Fifty percent of each group of mice had developed mammary tumours by 240, 350 and 250 days, respectively. The average number of tumours was 3.2, 1.9 and 2.2 in treated virgin mice, controls and breeders, respectively (8). Intraperitoneal injection ♂ and ♀ AKR mice, thymectomised at 4-wk old, 750 mg aurothioglucose kg^{-1} given at 10-wk old resulted in 1/9 (11%) ♂ and 5/12 (41%) ♀ mice developing benign osteomas of the skull, compared with 0/15 ♂ and 1/23 (4%) ♀ controls (9).

Metabolism and toxicokinetics

Daily intramuscular injection in rats (14 days), total dose 14 mg aurothioglucose per animal, resulted in greatest retention of absorbed gold in the kidneys, followed by the liver and the spleen. After 85 days, 15% of the dose was retained in the body (10). In humans, readily absorbed after intramuscular injection in the treatment of arthritic disorders, with 85 to 95% binding to plasma proteins. A dose of 50 mg wk^{-1} for 5 to 8 wk results in a serum gold concentration of 3 to 5 μg ml^{-1}, with wide distribution throughout the body tissues and fluids, including synovial fluid. The serum half-life of gold increases with successive doses; after a course of treatment, gold may be detected in the urine for up to 1 yr, owing to its accumulation in the body. In pregnant women receiving treatment, gold has been detected in the foetus (11).

Other effects

Other adverse effects (human)

A wide range of adverse effects to treatment have been reported, with skin and mucous membrane effects, such as pruritus and stomatitis, being the most common. Other such effects include erythema, urticaria, eczema, maculopapular eruptions, lichenoid eruptions, exfoliative and seborrhoeic dermatitis, alopecia, glossitis, pharyngitis, vaginitis, photosensitivity reactions and pigmentation. Toxic effects on the blood include eosinophilia, thrombocytopenia, leucopenia, agranulocytosis and aplastic anaemia. Effects on the kidneys include mild to heavy proteinuria, haematuria and nephrosis. Other effects include pulmonary fibrosis, hepatitis, encephalitis, psychoses, gastro-intestinal disorders and vasomotor reactions (11).

Any other adverse effects

Damage to the medulla oblongata was observed in C57BL mice (30 days old) which had become obese after being given 800 mg aurothioglucose kg^{-1}. Neurons were destroyed in the dorsal motor nucleus of the vagus (DMX), and tissue loss was seen in the nucleus of the solitary tract (NST). Cell numbers in the hypoglossal nucleus were unaffected, and the volume of the area postrema was not reduced. Statistical evaluation of the relative contributions of hypothalamic, DMX and NST damage to the development of obesity suggests that obesity primarily correlates with the hypothalamic lesions caused by aurothioglucose (12).
Eight months after administration to mice, examination of the brains of non-obese mice showed that there was a single, irregular net of fibrocysts and their fibres, and reduced numbers of ganglion cells in the area around the hypothalamic ventromedial nucleus. The third ventricle was distorted and dilated, increased epithelial cells were seen in one case, and encephalitic foci were found in the area ventral from the hypothalamic ventromedial nucleus in three cases (13).
Administration to mice caused the death of all structures in an area of the ventromedial hypothalamus due to loss of blood supply. This occurred as a result of damage by aurothioglucose to neural processes adjacent to capillaries

in the area, which caused abnormal capillary permeability. Damage to the pericapillary neural processes was insulin-dependent and prevented by glucocorticoids (14).

Legislation

Included in Schedule 6 (Release into Land: Prescribed Substances) of Statutory Instrument No. 472, 1991 (15).

Other comments

Human health effects and experimental toxicology reviewed (16).

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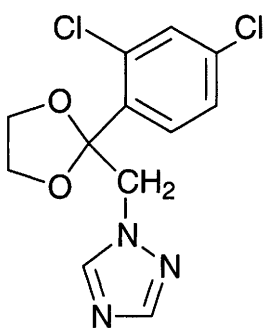
A256 azaconazole



$C_{12}H_{11}Cl_2N_3O_2$ **Mol. Wt.** 300.14 **CAS Registry No.** 60207-31-0

Synonyms 1-[[2-(2,4-dichlorophenyl)-1,3-dioxolan-2-yl]methyl]-1*H*-1,2,4-triazole

Uses Fungicide. Particularly active against wood-destroying and sapstain fungi.

Physical properties

M. Pt. 112.6°C **Flash point** 180°C **Specific gravity** 1.511 at 23°C **Partition coefficient** log P 2.17 (pH 6.4, 23±1°C) **Volatility** v.p. 6.5×10^{-8} mmHg (20°C)

Solubility Water: 0.3 g l^{-1} at 20°C. Organic solvents: acetone 160, hexane 0.8, methanol 150, toluene 79 g l^{-1}, 20°C

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) rainbow trout 42 mg l^{-1} (1).

Invertebrate toxicity

EC_{50} *Daphnia magna* 86 mg l^{-1} (1).

Mammalian & avian toxicity

Acute data

LC_{50} (5 days) oral ring-necked pheasants >5000 mg kg^{-1} (1).

LD_{50} oral rats, mice, dogs 308, 1123, 114-136 mg kg^{-1}, respectively (1).

LC_{50} (4 hr) inhalation rat >0.84 mg l^{-1} air (5% and 1% formulations) (1).

LD_{50} dermal rat >2560 mg kg^{-1} in diet (1).

♂Fischer 344 rats administered a single intraperitoneal dose of ≥0.6 mmol kg^{-1} suffered acute, reversible renal effects and altered organic ion transport both *in vivo* and *in vitro* (2).

Carcinogenicity and chronic effects

No-observed-adverse-effect level for rats 2.5 mg kg^{-1} body weight daily (duration unspecified) (1).

Irritancy

Slightly irritating to eyes and skin of rabbits (1).

Sensitisation

Non-sensitising to skin of guinea pigs (1).

Legislation

WHO Toxicity Class I (3).

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

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

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

Other comments

Stable to hydrolysis between pH 4 and pH 9.

References

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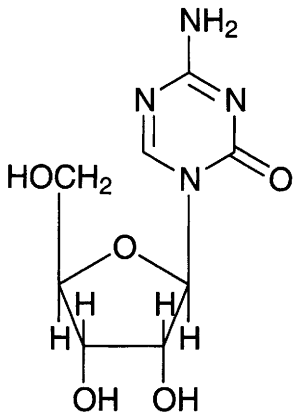
A257 5-azacytidine



$C_8H_{12}N_4O_5$ **Mol. Wt.** 244.21 **CAS Registry No.** 320-67-2

Synonyms 4-amino-1-β-D-ribofuranosyl-*s*-triazin-2(1*H*)-one; 4-amino-1-β-D-ribofuranosyl-1,3,5-triazin-2(1*H*)-one; azacytidine

EINECS No. 206-280-2 **RTECS No.** XZ 3017500

Uses Antineoplastic agent.

Occurrence Obtained from *Streptoverticillium ladakanus*.

Physical properties

M. Pt. 228-230°C

Solubility Organic solvents: methanol

Mammalian & avian toxicity

Acute data

LD_{50} oral starling 100 mg kg^{-1} (1).

LD_{50} oral mouse 572 mg kg^{-1} (2).

LD_{50} intraperitoneal mouse 68 mg kg^{-1} (3).

Sub-acute and sub-chronic data

Repeated doses of ≥0.55 mg kg^{-1} (5 days) produced bone marrow depression and liver degeneration in dogs (2).

LD_{50} (14 days) intravenous rhesus monkey 2.2 mg kg^{-1} (4).

Carcinogenicity and chronic effects

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

National Toxicology Program tested ♂, ♀ rats and mice with 5-azacytidine via intraperitoneal injection. Results were positive in ♀ mice, but the study was inadequate to achieve valid results for other species (6).

National Toxicology Program classification: reasonably anticipated to be a human carcinogen (7).

Intraperitoneal ♂ rat (12 months) 10 mg kg^{-1} 2 × wk^{-1} induced multiple tumour; sites included the testis, skin, bronchus. Acute leukaemia and malignant reticuloendotheliosis also occurred. No hepatic tumours were found unless a prior initiating dose of *N*-nitrosodiethylamine was given (8).

40 ♀ AKR mice were given six intraperitoneal injections of 5-azacytidine (1.5 mg kg^{-1} body weight) over 20 days and six injections of 5-azacytidine at 0.8 mg kg^{-1} body weight over the following 30 days. All treated mice died of leukaemia by 60 days (5).

35 ♂ and 35 ♀ B6C3F1 mice received intraperitoneal injections of 2.2 and 4.4 mg kg^{-1} body weight 3 × wk^{-1} for 52 wk. Surviving mice were killed at 81 or 82 wk. All high-dose ♀ mice died before 62 days with no significant increase in tumour incidence, 17/35 ♀ mice in low-dose group survived until termination of the experiment. In the high-dose group 7/35 ♂ mice survived until termination of the study and 13/35 in the low-dose group. Lymphocytic and granulocytic neoplasms of the haematopoietic system were observed in 17/29 ♀ mice in the low-dose group. Ten treated animals had granulocytic tumours. No increase in tumours was observed in ♂ mice (5).
♂ and ♀ BALB/C/Cb/Se mice were given 2.0 mg kg^{-1} body weight of 5-azacytidine intraperitoneally once a week for 50 weeks. Lymphoreticular neoplasms occurred in 12/50 ♂ and 36/50 ♀. Lung adenomas increased in ♂ mice (27/50) but not ♀ mice. Increases in skin tumours in both sexes were noted (5).
Two groups of ♂ Fischer rats were given 2.5 or 10 mg kg^{-1} body weight 5-azacytidine intraperitoneally twice a week for nine months. Interstitial-cell testicular tumours were found in 1/8 high-dose rats and 9/12 low-dose rats (0/12 in controls). Two squamous-cell carcinomas of the skin and one skin appendage tumour at the injection site were found in the high-dose group (5).
Adult ♂ Fischer rats were injected intraperitoneally with 0.025, 0.25 or 2.5 mg kg^{-1} body weight 5-azacytidine 3 × wk^{-1} for one year. Testicular interstitial-cell tumours increased in the high-dose group. Four lymphomas, four renal tumours, one lung tumour, three skin tumours, two mesotheliomas, and two sarcomas were also detected in the high-dose group (5).
Target organs of carcinogenicity: mouse hematopoietic system, mouselung, mouse mammary gland, rat testes (9).

Teratogenicity and reproductive effects

Pregnant mouse (route unspecified) 1 mg kg^{-1} after 7.5-8.5 days of pregnancy development of malformed foetuses (10).
Intraperitoneal administration of 1.5-2.5 mg kg^{-1} body weight to mice during the pre-implantation period of pregnancy induced very high or total resorption of conceptuses. Administration after day-6 of pregnancy induced resorptions at a level only slightly higher than the control level (5).
Single intraperitoneal doses of 1-2 mg kg^{-1} to mice during embryogenesis can cause high resorption rate and malformations in the majority of surviving foetuses including central nervous system defects, facial clefts and limb defects (5).
Intraperitoneal injection of 1-4 mg kg^{-1} to mice in the later stages of pregnancy (especially on day-15) can result in morphological changes in the brains of offspring, resulting in behavioural changes when tested as adults (5).
The primary mechanisms of teratogenicity in rats is thought to be induction of cell death, however inhibition of some of the effects of 5-azacytidine by caffeine suggests that more than one mechanism may be involved (5).

Metabolism and toxicokinetics

After intravenous injection of radiolabelled 5-azacytidine the α-phase $t_{1/2}$ was 16-33 mins, the β-phase $t_{1/2}$ was 3.4-6.2 hr. After 30 min <2% of plasma radioactivity cochromatographed with 5-azacytidine, at least two different metabolites were detected by thin-layer chromatography. 73-98% of injected radioactivity was detected in the urine within three days (5).
<1% of radiolabelled 5-azacytidine was bound to human serum albumin *in vitro* (5).
It has been shown to be capable of incorporation into DNA and RNA, and is an inhibitor of uridine kinase and of orotidylic acid decarboxylase (11,12). Blood levels of 5-azacytidine (determined by biological activity) peaked 0.5 hr after oral or intraperitoneal administration to mice. Maximal concentrations after administration of 50 mg kg^{-1} body weight were 2μg ml^{-1} (oral) and 43 μg ml^{-1} (intraperitoneal) (5).
In a study using a microbiological assay, maximal blood concentrations were found 15 min after intraperitoneal injection of 9.5 or 4.75 mg kg^{-1} body weight. Elimination was rapid and no 5-azacytidine was detected in the blood 1 hr after high-dose injection and 30 min after low-dose injection (5).
Calculated $t_{1/2}$ is 3.8 hr (5).
50% of a dose of 5-azacytidine given to mice (route and amount unspecified) was excreted in the urine within 8 hr. The excreted material consisted of 4% unchanged 5-azacytidine and six additional metabolites. In beagle dogs given 0.5 mg kg^{-1} body weight intravenous 5-azacytidine, 33% of the administered dose was excreted in the urine within 4 hr; 5-azacytidine, 5-azacytosine, urea and guanidine were observed (5).

Genotoxicity

Salmonella typhimurium TA98, TA100 with and without metabolic activation positive (13).
Salmonella typhimurium TA98 with and without metabolic activation negative (14).
Salmonella typhimurium TA100 with and without metabolic activation positive (14).
Saccharomyces cerevisiae induced mitotic recombinations, mitotic gene conversions and reverse mutations (5).
C3H IOTI/2 mouse embryo fibroblasts positive chromosome aberrations in DNA methylation (15).
Human lymphoblast TK6 induced mutation at thymidine kinase (TK) locus and the hypoxanthine-guanine phosphoribosyltransferase (HGPRT) locus (13).
In vitro human peripheral lymphocytes induced sister chromatid exchange and chromosomal aberrations (5).
5-Azacytidine can reactivate genes on the inactive human X-chromosome. May act by causing demethylation of the DNA at specific sites (16).
Exposure to 5-azacytidine in Chinese hamster ovary cells increased the incidence of sister chromatid exchange (17).
Drosophila melanogaster wing spot assay induced mitotic recombinations, deletions and gene mutations (5).
Drosophila melanogaster eye mosaic assay positive (18).

Other effects

Other adverse effects (human)
Nausea, vomiting and bone marrow suppression found in patients treated with 5-azacytidine (19).
The major toxic effects of clinical use of 5-azacytidine are gastrointestinal, haematological and hepatic. Leucopenia is dose related (5).

Other comments

Reviews on human health effects and experimental toxicology listed (20).
Toxicity, cytostatic activity and mechanism of action reviewed (5).

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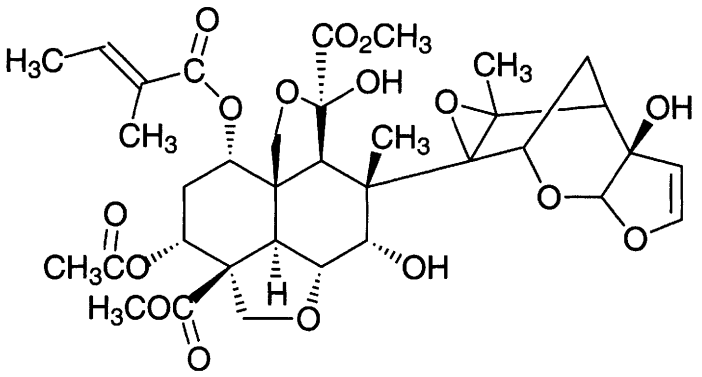
A258 azadirachtin



$C_{35}H_{44}O_{16}$ **Mol. Wt.** 720.72 **CAS Registry No.** 11141-17-6

Synonyms Align; Azatin; Bio Neem; Margosan-O; Meen; Neemix; Turplex

Uses Insect feeding deterrent and growth regulator.

Occurrence A tetranortriterpenoid isolated from the seeds of the neem and chinaberry trees.

Physical properties

M. Pt. 154-158°C (microcrystalline powder from carbon tetrachloride) **Flash point** >60°C (Tag closed cup)

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) azadirachtin (49% purity) juvenile salmon >4 mg l^{-1} (1).

Invertebrate toxicity

Azadirachtin (0.125 μg) injected into newly hatched adults of the heteropteran *Oncopeltus fasciatus* caused impotency in ♂s (2).

Azadirachtin applied to Kentucky Bluegrass turf at the rate used by the turfgrass industry of 0.0264 kg ha^{-1} caused no significant mortality to earthworms 1 week or 3 weeks after treatment, for spring or summer application (3).

Topical application of azadirachtin to final instar larvae of the African armyworm *Spodoptera exempta* adversely affected oogenesis and reproductive maturation in subsequent ♀ moths. Protein levels as well as fat body development in ♀ moths were suppressed (4).

Chlorophyll and protein contents of freshwater algae were inhibited at treatment levels of 3.0–4.5 μg ml^{-1} azadirachtin. Chlorophyll production was stimulated at 1.5 μg ml^{-1} (5).

Other comments

Structural analyses of azadirachtin indicate that it has the potential for acting as a genotoxic carcinogen. The authors suggest that as genotoxic carcinogens are regarded as presenting a potential carcinogenic risk to humans, the possible metabolism of azadirachtin to DNA-reactive products should be evaluated experimentally (6).

Endocrine disruption effects in wildlife. Arthropod moult inhibition (7).

Azadirachtins are insect growth inhibitors which interfere with the neuroendocrine regulation of juvenile and moulting hormone titres. The main cellular targets are the Malpighian tubules and the corpus cardiacum (8).

Effects of neem and azadirachtin on aphids and their natural enemies reviewed (9).

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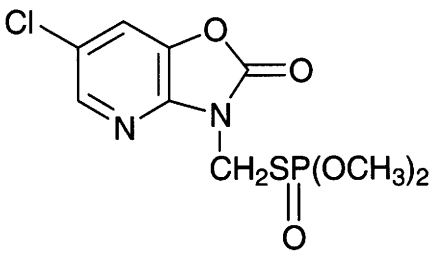
A259 azamethiphos



$C_9H_{10}ClN_2O_5PS$ **Mol. Wt.** 324.68 **CAS Registry No.** 35575-96-3

Synonyms *S*-6-chloro-2,3-dihydro-2-oxo-1,3-oxazolo[4,5-*b*]pyridin-3-ylmethyl *O*,*O*-dimethyl phosphorothioate; *S*-6-chloro-2-oxooxazolo[4,5-*b*]pyridin-3-ylmethyl *O*,*O*-dimethyl phosphorothioate; 6-chloro-3-dimethoxyphosphinoylthiomethyl-1,3-oxazolo[4,5-*b*]pyridin-2(3*H*)-one; *S*-[(6-chloro-2-oxooxazolo[4,5-b]pyridin-3(2*H*)-yl)methyl]*O*,*O*-dimethyl phosphorothioate; Alfacron; Alficron; Dymox; Rubidor; Snip

EINECS No. 252-626-0 **RTECS No.** TE 8070000

Uses Insecticide and acaricide.

Physical properties

M. Pt. 89°C **Specific gravity** 1.6 at 20°C **Volatility** v.p. 3.69×10^{-7} mmHg at 20°C
Solubility Water: 1.1 g l^{-1} at 20°C. Organic solvents: benzene, dichloromethane, methanol, octanol

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) channel catfish 3 mg l^{-1}, crucian carp 6 mg l^{-1}, guppy 8 mg l^{-1}, rainbow trout 0.115-0.2 mg l^{-1}, sheepshead minnow 2.22 mg l^{-1} (1).

Invertebrate toxicity
EC_{50} (48 hr) *Daphnia* 0.67 μg l^{-1} (1).
Toxic to bees (1).
LD_{50} (24 hr) oral bee <0.1 μg bee^{-1} (1).
LD_{50} (24 hr) contact bee 10 μg bee^{-1} (1).

Environmental fate

Degradation studies
In loamy soil, $t_{1/2}$ ~6 hr (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 1180 mg kg^{-1} (2).
LD_{50} oral bobwhite quail 30.2 mg kg^{-1}, mallard duck 48.4 mg kg^{-1} (1).
LC_{50} (4 hr) inhalation rat >560 mg m^{-3} (1).
LD_{50} percutaneous rat >2150 mg kg^{-1} (1).

Sub-acute and sub-chronic data
LC_{50} (8 day dietary) bobwhite quail, Japanese quail, mallard duck 860, >1000, 700 ppm, respectively (1).
Oral rat (90 day) 20 mg kg^{-1} in diet, no adverse effects reported (1).
Oral dog (90 day) 10 mg kg^{-1} in diet, no adverse effects reported (1).

Metabolism and toxicokinetics
In rats and goats the glucuronic acid conjugate of 2-amino-3-hydroxy-5-chloropyridine represents the major metabolite (27-48% of the dose), followed by the corresponding sulfuric acid conjugate (3-20% of the dose) (1).

Irritancy
Mild eye irritant, non-irritating to skin in rabbits (1).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides and related products: maximum admissible concentration 0.1 μg l^{-1} (3).
Included in Schedule 6 (Release into Land: Prescribed Substances) of Statutory Instrument No. 472, 1991 (4).
WHO Toxicity Class III (5).
EPA Toxicity Class III (1).

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A260 azaserine

$$HO_2CCH(NH_2)CH_2O_2CCHN_2$$

$C_5H_7N_3O_4$ **Mol. Wt.** 173.13 **CAS Registry No.** 115-02-6

Synonyms azaserin; *O*-diazoacetyl-L-serine; L-serine diazoacetate (ester); 2-amino-3-hydroxypropionic acid

EINECS No. 204-061-6 **RTECS No.** VT 9625000

Uses Glutamine antagonist which inhibits purine biosynthesis.
Antifungal and antitumour agent.
Occurrence Present in cultures of *Streptomyces fragilis*.

Physical properties

M. Pt. 153-155°C (decomp.)
Solubility Organic solvents: acetone, ethanol

Environmental fate

Abiotic removal

Hydrolysis in aqueous solution at pHs of 3, 7 and 11 at 25°C corresponds to $t_{1/2}$ 2.1 hr, 111 days and 425 days, respectively. Photochemical reaction with atmospheric hydroxyl radicals corresponds to an atmospheric $t_{1/2}$ of 10 hr at an atmospheric concentration of 5×10^{-5} hydroxyl radicals cm^{-3} (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse, rat 150, 170 mg kg^{-1}, respectively (2).
LD_{50} intraperitoneal rat, mouse 70, 100 mg kg^{-1}, respectively (2,3).
LD_{50} subcutaneous mouse 50 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 (5,6).
Intraperitoneal single dose (7-wk old) ♂ rat 30 mg kg^{-1}. After 6-18 months all treated rats had acidophilic and basophilic foci and nodules present in pancreas. At 9 months, incidence of carcinoma *in situ* was 30%; by 18 months, 100% incidence of pancreatic cancers (58% *in situ*, 42% carcinoma) (7).
Target organ of carcinogenicity: rat pancreas (8).

Genotoxicity

Salmonella typhimurium TA100 without metabolic activation positive (9).
Escherichia coli PQ37 without metabolic activation positive (9).
A 50% reduction in colony formation and unscheduled DNA synthesis was observed in rat pancreatic epithelial cells exposed to 52 mg l^{-1} without metabolic activation (10).
In vitro mouse L1210 leukaemia cells, inhibition of *N*-formylglycineamidine ribotide synthetase and glucosamine-6-phosphate isomerase and large accumulations of *N*-formylglycineamide ribotide and its di- and tri-phosphate derivatives, which could interfere with the biosynthesis of nucleic acids, have been reported (11).
In vitro Chinese hamster ovary V-79 cells without metabolic activation positive (12).
Drosophila melanogaster eye mosaic assay positive (13).
In vivo heterozygous soybean plants (Y11y11) mutational leaf spots found at 0.1 mg ml^{-1} (14).

Other comments

Human health effects and experimental toxicology reviewed (6,15,16).

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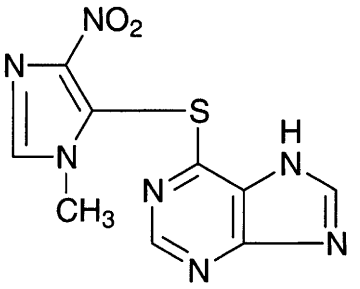
A261 azathioprine



$C_9H_7N_7O_2S$ **Mol. Wt.** 277.27 **CAS Registry No.** 446-86-6

Synonyms 6-[(1-methyl-4-nitro-1*H*-imidazol-5-yl)thio]-1*H*-purine; 6-(1[1]-methyl-4[1]-nitro-5[1]-imidazolyl)-mercaptopurine; 6-(methyl-*p*-nitro-5-imidazolyl)-thiopurine; 6-[(1-methyl-4-nitroimidazol-5-yl)thio]purine

EINECS No. 207-175-4 **RTECS No.** UO 8925000

Uses Immunosuppressive drug. Antirheumatic.

Physical properties

M. Pt. 243-244°C (decomp.)
Solubility Organic solvents: acetone, chloroform, ethanol, methanol

Mammalian & avian toxicity

Acute data
LD_{50} oral mouse, rat 535, 1389 mg kg^{-1}, respectively (1).
LD_{50} intraperitoneal rat 300 mg kg^{-1} (2).
LD_{50} subcutaneous mouse 350 mg kg^{-1} (3).

Carcinogenicity and chronic effects
Sufficient evidence of carcinogenicity to humans, limited evidence of carcinogenicity to animals, IARC classification group 1 (4,5).
Intraperitoneal ♂ and ♀ Sprague-Dawley (CD strain) rat and Swiss-Webster mouse 7.5-37 mg kg^{-1} $dose^{-1}$ induced lymphosarcoma and lung tumours in both ♂ and ♀ mice and uterus tumours in ♀ mice. Skin, pituitary and sarcomas tumours induced in both ♂ and ♀ rats, lymphosarcoma in ♂ rats and breast tumours and leukaemia in ♀ rats (6).

Teratogenicity and reproductive effects
C57BL and C3H mice were examined 1, 4 and 10 wk after treatment with 500 mg kg^{-1} for 5 days. A 1.2-3.4% increase in sperm abnormalities was seen (7).

Metabolism and toxicokinetics

In rats, presence of glutathione lead to formation of 1-methyl-4-nitro-5-(*S*-glutathionyl)-imidazole, then to 1-methyl-4-nitro-5-(*N*-acetyl-*S*-cysteinyl) imidazole and 1-methyl-4-nitro-5-thioimidazole (8).
Metabolised to the purine antagonist 6-mercaptopurine and to 5-substituted 1-methyl-4-nitro-5-thioimidazoles or aminoimidazoles (9).

Sensitisation

A 51 yr old production worker developed dermatitis on his hands, the onset coinciding with his starting work on the production line for azathioprine tablets. Patch testing showed a positive allergic reaction only to azathioprine diluted in petrolatum (10).

Genotoxicity

Salmonella typhimurium TA98 with and without metabolic activation negative (11).
Salmonella typhimurium TA100 with and without metabolic activation positive (11).
Salmonella typhimurium TA100, TA1535 with and without metabolic activation positive (12).
Mutation in microorganisms *Klebsiella pneumoniae* 0.277 mg l^{-1} (13).
Induced chromosome aberrations but not sister chromatid exchanges in human lymphocytes *in vitro*. Induced dominant lethal mutations in mice, chromosome aberrations but not sister chromatid exhanges in Chinese hamster bone marrow cells, and induced micronuclei in mice, rabbits and hamsters *in vivo* (13).

Other effects

Other adverse effects (human)

Dose-related bone-marrow depression may be manifested as leucopenia or thrombocytopenia or less often anaemia. Other side-effects include gastro-intestinal disturbances, reversible alopecia, rashes, muscle pain, fever, rigors, pneumonitis, pancreatitis, meningitis, arrhythmias and hypotension (14).

Any other adverse effects

Isolated rat hepatocytes exposed to the immunosuppressant azathioprine showed a marked decrease in both oxygen uptake and cell viability (15).

Other comments

Renal transplant patients were at high risk from non-Hodgkins lymphoma, squamous cell cancers, hepatobiliary carcinomas and mesenchymal tumours (5).
Toxicity and genotoxicity reviewed (16,17).

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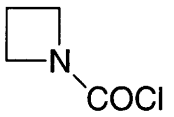
A262 1-azetidinecarbonyl chloride



C_4H_6ClNO **Mol. Wt.** 119.55 **CAS Registry No.** 75485-12-0

Uses Chemical intermediate (1,2).

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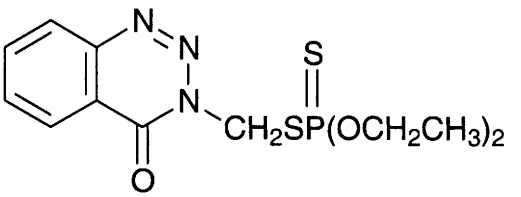
A263 azinphos-ethyl



$C_{12}H_{16}N_3O_3PS_2$ **Mol. Wt.** 345.38 **CAS Registry No.** 2642-71-9

Synonyms *S*-(3,4-dihydro-4-oxobenzo-[*d*]-[1,2,3]-triazin-3-ylmethyl)*O*,*O*-diethyl phosphorodithioate; *O*,*O*-diethyl *S*-(4-oxobenzotriazino-3-methyl)phosphorodithioate; *O*,*O*-diethyl *S*-[(4-oxo-1,2,3-benzotriazin-3(4*H*)-yl)methyl]phosphorodithioic acid ester; ethyl guthion; Aithulphos; Azin; Azinfos; Azinos

EINECS No. 220-147-6 **RTECS No.** TD 8400000

Uses Insecticide and acaricide.

Physical properties

M. Pt. 53°C **B. Pt.** 111°C **Specific gravity** 1.284 at 20°C with respect to water at 4°C
Partition coefficient log P_{ow} 3.18 (1) **Volatility** v.p. $<2.2 \times 10^{-7}$ mmHg at 20°C
Solubility Water: 4-5 mg l^{-1}. Organic solvents: dichloromethane, *n*-hexane, isopropanol, toluene

Occupational exposure

Supply classification very toxic
Risk phrases Toxic in contact with skin – Very toxic if swallowed (R24, R28)
Safety phrases Keep locked up and out of the reach of children (if sold to general public) – After contact with skin, wash immediately with plenty of water – Wear suitable protective clothing and gloves – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S28, S36/37, S45)

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) golden orfe, rainbow trout 0.03, 0.08 mg l^{-1}, respectively (1).
LC_{50} (96 hr) rainbow trout 0.019 mg l^{-1} (2).

Invertebrate toxicity

LC_{50} (96 hr) *Penaeus monodon* 120 ppb. *Penaeus monodon* exposed to 1.5-150 ppb had 27-53% shell softening. Histopathological changes in gills and hepatopancreas included slight hyperplasia of the gill epithelium, delamination of the hepatopancreatocytes and general necrosis and degeneration of these tissues (3).

LC_{50} (48 hr) *Daphnia pulex* 3.2 μg l^{-1} (4).

EC_{50} (48 hr) *Daphnia* 0.2 μg l^{-1} (1).

EC_{50} (24 hr) *Artemia* sp. (Artoxkit M) 3.3 mg l^{-1}, *Brachionus plicatilis* (Rotoxkit M) >5.2 mg l^{-1} (5).

Not toxic to bees (depends on application method) (1).

Environmental fate

Degradation studies

$t_{1/2}$ is several weeks. Metabolites formed in soil under aerobic and anaerobic conditions are: desethyl azinphos-ethyl, sulfonmethylbenzazimide, bis(benzazimidmethyl)ether, methylthiomethylsulfoxide and methylthiomethylsulfone (1).

In plants, metabolised to azinphos-ethyl-oxon, benzazimide, and dimethyl benzazimide sulfide and disulfide (1).

Adsorption and retention

K_{oc} values and leaching studies indicate low mobility in soil (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral Japanese quail 12.5-20 mg kg^{-1} (1).

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

LC_{50} (4 hr) inhalation rat 0.15 mg l^{-1} (1).

LC_{50} (duration unspecified) inhalation rat 390 mg m^{-3} (6).

LD_{50} dermal rat 250 mg kg^{-1} (7).

LD_{50} intraperitoneal rat 7500 μg kg^{-1} (1,8).

Carcinogenicity and chronic effects

Oral rats, dogs, mice (2 yr) 2, 0.1 and 1.4 mg kg^{-1} diet, respectively. No adverse effects reported (1).

Metabolism and toxicokinetics

Oral mammal (species unspecified) >90% eliminated in faeces and urine in two days, mostly as the monodesethyl compound and benzazimide (1).

Genotoxicity

Salmonella typhimurium TA100 without metabolic activation positive (7).

Legislation

Included in Schedule 6 (Release into Land: Prescribed Substances) of Statutory Instrument No. 472, 1991 (9). Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides and related products: maximum admissible concentration 0.1 μg l^{-1} (10).

Other comments

Rapidly hydrolysed in alkaline conditions.

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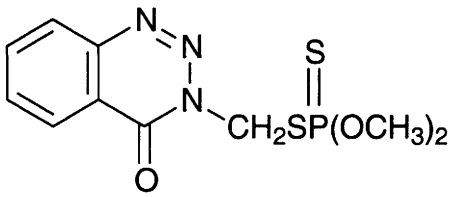
A264 azinphos-methyl



$C_{10}H_{12}N_3O_3PS_2$ **Mol. Wt.** 317.33 **CAS Registry No.** 86-50-0

Synonyms *S*-3,4-dihydro-4-oxobenzo-[d]-1,2,3-triazin-3-ylmethyl *O,O*-dimethyl phosphorodithioate; Acifon; Aziflo; Azimet; Azimil; Azin; Cotnion-methyl; Gusathion

EINECS No. 201-676-1 **RTECS No.** TE 1925000

Uses Insecticide and acaricide.

Physical properties

M. Pt. 73-74°C **Specific gravity** 1.44 at 20°C with respect to water at 4°C **Partition coefficient** log P_{ow} 2.96 (1)
Volatility v.p. 0.18 mPa at 20°C
Solubility Water: 33 mg l^{-1} at 25°C. Organic solvents: ethanol, methanol, propylene glycol, xylene

Occupational exposure

DE-MAK 0.2 mg m^{-3} (inhalable fraction of the aerosol)
FR-VME 0.2 mg m^{-3}
UK-LTEL 0.2 mg m^{-3} **UK-STEL** 0.6 mg m^{-3}
US-TWA 0.2 mg m^{-3}
Supply classification very toxic
Risk phrases Toxic in contact with skin – Very toxic if swallowed (R24, R28)
Safety phrases Keep locked up and out of the reach of children (if sold to general public) – After contact with skin, wash immediately with plenty of water – Wear suitable protective clothing and gloves – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S28, S36/37, S45)

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) rainbow trout 0.02 mg l^{-1}, golden orfe 0.12 mg l^{-1} (1).
LC_{50} (96 hr) channel catfish, goldfish 3.3, 4.3 mg l^{-1}, respectively (2,3).
LC_{50} (96 hr) rainbow trout, bluegill sunfish, fathead minnow 14, 20, 65 μg l^{-1}, respectively (2-4).
LC_{50} (96 hr) sheepshead minnow 2.0 μg l^{-1} (5).
LC_{50} (96 hr, static renewal) juvenile red drum, mummichog 6.3-7.1 μg l^{-1}, 65-84 μg l^{-1}, respectively. Behavioural response studies indicated that neither species avoided pesticide-laden water, which may increase their

vulnerability to azinphos-methyl run-off. After 6-hr exposure to 12 μg l^{-1} juvenile red drum experienced a decreased ability to swim. Mummichogs were less sensitive with respect to the effects of azinphos-methyl on swimming ability at concentrations as high as 24 μg l^{-1} (6).
Adult bluegills were exposed to a single application of 1 or 4 μg l^{-1} of azinphos-methyl. $t_{1/2}$ was 2.3 and 2.4 days, respectively. Quantifiable residues remained after 8 days. Neither concentration caused any significant long-term (63-day) effects in reproduction, embryo hatchability, larval survival, growth or biomass (7).

Invertebrate toxicity
EC_{50} (48 hr) *Daphnia* 0.0011 mg l^{-1} (1).
LC_{50} (30 days) *Pteronarcys dorsata* 5 μg l^{-1} (8).
LC_{50} (96 hr) *Aplexa hypnorum* 3.7 mg l^{-1} (4).
LC_{50} (96 hr) *Mysidopsis bahia* 0.29 μg l^{-1} (5).
LC_{50} (48 hr) American oyster eggs 620 ppb in a static laboratory bioassay (8).
LC_{50} (12 hr) hard clam larvae 860 ppb in a static laboratory bioassay (8).
LC_{50} (96 hr) *Gammarus fasciatus, Gammarus lacustris* 0.10, 0.15 μg l^{-1} , respectively (8).
EC_{50} (24 hr) *Artemia* sp. (Artoxkit M) 23 mg l^{-1}, *Brachionus plicatilis* (Rotoxkit M) 85 mg l^{-1} (9).
EC_{50} (96 hr) *Palaemonetes pugio* 18-day-old larvae 0.38 μg l^{-1}, adults 1.64 μg l^{-1} (10).
Natural zooplankton communities in littoral ecosystem enclosures were exposed to 0.2, 1.0, 4.0, or 20 μg l^{-1} azinphos-methyl. Analyses of population abundance were more sensitive to the effects of azinphos-methyl than were analyses of major zooplankton groups. The zooplankton communities showed concentration-dependent effects and recovery through time, with the communities exposed to the highest treatment concentration still not having fully recovered by the last sampling date, 78 days after treatment (11).
Toxic to bees (1).

Toxicity to other species
Xenopus laevis (clawed frog) embryos were exposed for 96 hr to six increasing concentrations in 10 ml and 100 ml exposure volumes (6.1-6.3 mg l^{-1} and 10.6-11.9 mg l^{-1}, respectively). LC_{50} in 100 ml exposure volumes was 1.6 mg l^{-1} (technical grade). No-observed-adverse-effect levels were 0.48-7.96 mg l^{-1} (12).

Bioaccumulation
Calculated bioconcentration factor 72 (13).

Environmental fate

Degradation studies
Degradation involves oxidation, demethylation, and hydrolysis (1).
After 44 and 197 days incubation of ^{14}C-labelled compound in soil, about 50 and 93%, respectively, was degraded and after 222 days incubation, 18.6% of the radiolabel was recovered (14).
The main degradation products in soil and selected by soil microorganisms are benzazimide, thiomethylbenzazimide, bis(benzozimidyl-methyl)disulfide and anthranilic acid (15).
In plants, major metabolites identified include oxon, benzazimide, mercaptomethyl benzazimide, and cysteinmethyl benzazimide derivatives (1).

Abiotic removal
Hydrolysis $t_{1/2}$ in water at pH 8.6 was 36.4, 27.9, 7.2 days at 6, 25, 40°C, respectively (16).

Adsorption and retention
K_{oc} values and leaching studies indicate low mobility in soil (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral bobwhite quail 32 mg kg^{-1} (17).
LD_{50} oral rat 9 mg kg^{-1} (16).
LD_{50} oral ♂ guinea pig 80 mg kg^{-1} (1).
LD_{50} oral mouse 11-20 mg kg^{-1} (1).
LD_{50} oral dog >10 mg kg^{-1} (1).

LC_{50} (4 hr) inhalation rat 0.15 mg l^{-1} (1).
LD_{50} percutaneous rat 220 mg kg^{-1} (18).

Sub-acute and sub-chronic data
Dogs given 5 mg kg^{-1} in diet for 1 yr showed no observable effects (1).

Carcinogenicity and chronic effects
In 2-year feeding trials, rats and mice receiving 5 mg kg^{-1} in the diet showed no ill-effects (1).
Intraperitoneal mouse (4-64 hr) 2.08 mg kg^{-1} caused changes in liver tissue after 4 hr. In liver parenchyma cells, granular endoplasmic reticulum increased in the liver, whereas glycogen decreased. In the liver parenchyma cells, one of the ribosomes dissociated from the endoplasmic reticulum and scattered in the cytoplasm (19).
National Toxicology Program tested ♂, ♀ rats and mice via dosed-feed. Results showed equivocal evidence of carcinogenicity in ♂ rat and negative in mice and ♀ rat (20).

Metabolism and toxicokinetics
In mammals following oral administration >95% is eliminated in the urine and faeces within 2 days. The major metabolites are the monodesmethyl compound and benzazimide (1).
In vivo percutaneous absorption in humans is 16%. Occulsion 56% dose absorbed (21).
Intravenous human (dose unspecified), radioactivity equivalent to about 1.5% of administered dose hr^{-1} recovered in urine during the first 12 hr. Recovery decreased gradually but still slightly over 0.1% 96-120 hr after injection. Total recovery during 120 hr was 69% of the dose following intravenous administration and 15.9% following dermal application (22).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537 with and without metabolic activation weakly positive (18).
Saccharomyces pombe without metabolic activation positive (23).
Saccharomyces cerevisiae D7 with and without metabolic activation caused reversion and gene conversion (24).
Failed to induce sister chromatid exchanges in cultured human lymphocytes (25).

Legislation

Included in Schedules 5 and 6 (Release Into Water and Land: Prescribed Substances) of Statutory Instrument No. 472, 1991 (26).
Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides and related products: maximum admissible concentration 0.1 µg l^{-1} (27).
ADI 0.005 mg kg^{-1} body weight (1).
WHO Toxicity Class Ib (28).
EPA Toxicity Class I (1).

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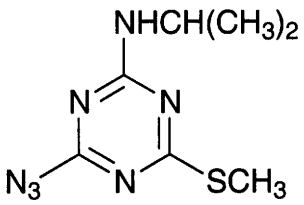
28. *The WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification 1998-1999* WHO/PCS/98.2

A265 aziprotryne



$C_7H_{11}N_7S$ **Mol. Wt.** 225.28 **CAS Registry No.** 4658-28-0

Synonyms aziprotryn; 4-azido-*N*-(1-methylethyl)-6-methylthio-1,3,5-triazin-2-amine; 2-azido-4-(isopropylamino)-6-(methylthio)-*s*-triazine; 4-azido-4-isopropylamino-6-methylthio-1,3,5-triazine; Brasoran

EINECS No. 225-101-9 **RTECS No.** XY 3280000

Uses Superseded herbicide and fungicide.

Physical properties

M. Pt. 94.5-95.5°C **Specific gravity** 1.4 at 20°C **Volatility** v.p. 2.67×10^{-5} mmHg at 20°C
Solubility Organic solvents: acetone, benzene, dichloromethane, ethyl acetate

Ecotoxicity

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

Mammalian & avian toxicity

Acute data
LD_{50} oral rat, mouse 2970, 3600 mg kg^{-1}, respectively (2).
LD_{50} (6 hr) inhalation rat >208 mg m^{-3} (1).
LD_{50} dermal rat >3000 mg kg^{-1} (3).
LD_{50} intraperitoneal mouse 265 mg kg^{-1} (2).

Sub-acute and sub-chronic data
LD_{50} (8 day) oral mallard duck, quail >4000 mg kg^{-1} in diet (4).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides and related products: maximum admissible concentration 0.1 μg l^{-1} (5).
Included in Schedule 6 (Release into Land: Prescribed Substances) of Statutory Instrument No. 472, 1991 (6).

References

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

A266 aziridine

C_2H_5N **Mol. Wt.** 43.07 **CAS Registry No.** 151-56-4

Synonyms ethylenimine; aminoethylene; dihydroazirene; azacyclopropane; azirane; dimethyleneimine; ethylimine; ENT-50324; RCRA Waste No. P054; TL 337; dihydro-1*H*-azirine; Chemitte

EINECS No. 205-793-9 **RTECS No.** XX 5075000

Uses Chemical intermediate.

Physical properties

M. Pt. –71.5°C **B. Pt.** 56.72°C **Flash point** –11°C (closed cup) **Specific gravity** 0.832 at 20°C with respect to water at 4°C **Volatility** v.p. 160 mmHg at 20°C ; v.den. 1.48
Solubility Water: miscible. Organic solvents: acetone, benzene, diethyl ether, ethanol

Occupational exposure

JP-OEL 0.5 ppm (0.88 mg m^{-3})
US-TWA 0.5 ppm (0.88 mg m^{-3})

UN No. 1185 **Conveyance classification** toxic substance, flammable liquid
Supply classification highly flammable, very toxic, dangerous for the environment
Risk phrases May cause cancer – May cause heritable genetic damage – Highly flammable – Very toxic by inhalation, in contact with skin and if swallowed – Causes burns – Toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment (R45, R46, R11, R26/27/28, R34, 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)

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 15 mg kg^{-1} (1).

LC_{50} (2 hr) inhalation rat, rabbit, mouse 100, 100, 400 mg m^{-3}, respectively (2).
LD_{Lo} (8 hr) inhalation rat, guinea pig 25 ppm (3).

Carcinogenicity and chronic effects

No adequate data for carcinogenicity to humans, limited evidence for carcinogenicity to animals, IARC classification group 3 (4).
Oral ♂ and ♀ mouse 4.64 mg kg^{-1} day^{-1} from 7-28 days old, subsequently 13 mg kg^{-1} diet 77-78 wk. The number of hepatomas and pulmonary tumours combined was significantly greater than that in controls (5).
Subcutaneous ♂ and ♀ albino rat 2 × wk^{-1} total dose 20 mg kg^{-1} over 67 injections. Total number of tumours at injection site greater than that in controls (6).
Target organs of carcinogenicity: mouse liver, mouse lung (7).

Genotoxicity

Inhibits DNA transformation by *Bacillus subtilis* at 86 mg l^{-1} (8).
Chromosomal aberrations in Syrian hamster cells induced by 43 mg l^{-1} (9).
Chinese hamster ovary cells at 2 mg l^{-1} positive at five independent genetic loci (Emt^r, Drb^R, Oua^R, Mbg^r and Thg^r) (10).
Drosophila melanogaster induction of sex-linked recessive lethals and ring-X loss in ♂ adult (11).

Other effects

Other adverse effects (human)

Symptomatic effects, which appeared 3-7 hr after a 2-hr exposure to aziridine, included vomiting, irritation of eyes and respiratory tract (12).

Any other adverse effects

Inhalation rat 0.01 mg l^{-1} (4 hr for 1.5 months) caused catarrhal bronchitis, diminishing of lymphatic elements in lymph glands and degenerative changes in liver and kidney (13).

Other comments

Human health effects, experimental toxicology, ecotoxicology, physico-chemical properties, epidemiology, and workplace experience reviewed (14-17).

References

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6. Walpole, A. L. et al *Br. J. Pharmacol.* 1954, **9**, 306-323.
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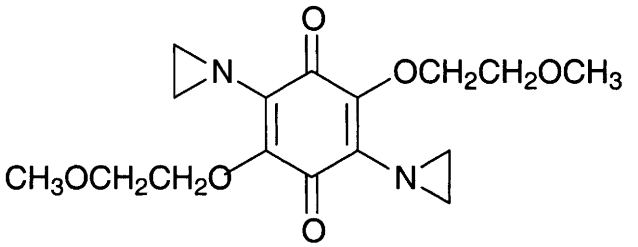
17. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

A267 aziridyl-*p*-benzoquinone



$C_{16}H_{22}N_2O_6$ **Mol. Wt.** 338.36 **CAS Registry No.** 800-24-8

Synonyms aziridyl benzoquinone; 2,5-bis(1-aziridinyl)-3,6-bis(2-methoxyethoxy)-1,4-benzoquinone; 2,5-bis(1-aziridinyl)-3,6-bis(2-methoxyethoxy)-2,5-cyclohexadiene-1,4-dione; 2,5-bismethoxyethoxy-3,6-bisethyleneimino-1,4-benzoquinone; 3,6-bis(β-methoxyethoxy)-2,5-bis(ethyleneimino)-*p*-benzoquinone; benzoquinone aziridine; aziridinylbenzoquinone

RTECS No. DK 3325000

Physical properties

M. Pt. 79-80.5°C

Mammalian & avian toxicity

Acute data

LD_{Lo} intravenous dog 250 μg kg^{-1} (1).

LD_{Lo} intravenous monkey 500 μg kg^{-1} (1).

Carcinogenicity and chronic effects

No adequate data for carcinogenicity to humans, limited evidence for carcinogenicity to animals, IARC classification group 3 (2).

Four groups of 15 ♂ and 15 ♀ A/J mice (4-6 wk old) were injected intraperitoneally with 0.2 ml of an aziridyl benzoquinone aqueous solution 3 × wk^{-1} for 4 wk, to a total dose of 0.47, 1.87, 7.5 or 30 mg kg^{-1}. After 39 wk, lung tumours were found in 18/29 (62%), 8/22 (36%), 16/25 (64%) and 24/28 (86%) treated mice, compared with 39.5% and 31.4% of 385 ♂ and 392 ♀ controls, respectively. The numbers of lung tumours per mouse were 0.8, 0.4, 1.4 and 2.9 in treated mice, compared with 0.50 and 0.36 in the control groups (3).

Genotoxicity

Drosophila melanogaster dominant lethal mutation assay positive (4).

Drosophila interchromosomal mitotic recombination assay positive (5).

In vitro human leukocyte cultures chromosome aberrations positive (6,7).

Other effects

Other adverse effects (human)

Adverse effects include alopecia, gastro-intestinal disturbances and bone marrow suppression, mainly as leucopenia and thrombocytopenia (8).

Other comments

Physico-chemical properties, human health effects, exposure levels, experimental toxicology, workplace experience and epidemiology reviewed (9).

References

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2. *IARC Monograph* 1987, **Suppl. 7**, 58.
3. Shimkin, M. B. et al *J. Natl. Cancer Inst.* 1966, **36**, 915-935.
4. *Mutat. Res.*1972, **14**, 250.
5. Vogel, E. W. et al *Mutagenesis* 1993, **8**(1), 57-81.
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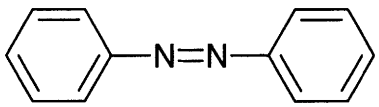
A268 azobenzene



$C_{12}H_{10}N_2$ **Mol. Wt.** 182.22 **CAS Registry No.** 103-33-3

Synonyms diphenyl diazine; azobisbenzene; azodibenzene; azodibenzeneazofume; benzenazobenzene; diazobenzene

EINECS No. 203-102-5 **RTECS No.** CN 1400000

Uses Acaricide. Chemical and dyestuff intermediate.

Physical properties

M. Pt. 68°C **B. Pt.** 297°C **Specific gravity** 1.203 at 20°C with respect to water at 4°C
Partition coefficient log P_{ow} 3.82 (1) **Volatility** v.p. 1 mmHg at 103.5°C
Solubility Organic solvents: acetone, benzene, diethyl ether, ethanol

Occupational exposure

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) – After contact with skin, wash immediately with plenty of water (S2, S28)

Environmental fate

Nitrification inhibition
Nitrosomonas spp. no inhibition of ammonia oxidation at concentrations of 100 mg l^{-1} (2).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 1000 mg kg^{-1} (3).
LD_{50} intraperitoneal mouse 500 mg kg^{-1} (4).

Carcinogenicity and chronic effects
No adequate evidence for carcinogenicity to humans, limited evidence for carcinogenicity to animals, IARC classification group 3 (5).
National Toxicology Program tested ♂, ♀ rats and mice via dosed-feed. Positive evidence of carcinogenicity in rats, negative in mice (6). Target organs of carcinogenicity: rat spleen, rat vascular system (7).

Metabolism and toxicokinetics
Rabbit (route unspecified) 500 mg kg^{-1}, 30% appeared in faeces, 23% excreted in urine (8).

Genotoxicity

Salmonella typhimurium TA100 with metabolic activation positive (9).
Escherichia coli K-12 *uvrB/recA* DNA repair host-mediated assay without metabolic activation positive, with metabolite activation negative (10).
Drosophila melanogaster eye mosaic assay weakly positive (11).

Other comments

Human health effects, experimental toxicology, ecotoxicology and physico-chemical properties reviewed (8,12-13).

References

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A269 azobis(isobutyronitrile)

$$NCC(CH_3)_2N{=}NC(CH_3)_2CN$$

$C_8H_{12}N_4$ **Mol. Wt.** 164.21 **CAS Registry No.** 78-67-1

Synonyms propanenitrile, 2,2'-azobis(2-methyl)-; 2,2'-azobisisobutyronitrile; α,α'-azobisisobutyronitrile; Porofor 57; Genitron

EINECS No. 201-132-3 **RTECS No.** UG 0800000

Uses Initiator for free radical reactions, blowing agent for elastomers and plastics.

Physical properties

M. Pt. 107°C (decomp.)
Solubility Organic solvents: ethanol, methanol

Occupational exposure

Supply classification explosive, harmful
Risk phrases Risk of explosion by shock, friction, fire or other sources of ignition – Highly flammable – Harmful by inhalation and if swallowed (R2, R11, R20/22)

Safety phrases Keep out of reach of children (if sold to general public) – Wear eye/face protection – In case of fire and/or explosion do not breathe fumes – Keep at temperature not exceeding 54°C (S2, S39, S41, S47)

Mammalian & avian toxicity

Acute data

LD_{Lo} oral rat 670 mg kg^{-1} (1).

LD_{50} oral mouse 700 mg kg^{-1} (2).

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

Metabolism and toxicokinetics

After oral administration to mice 700 mg kg^{-1} (duration unspecified) azobis(isobutyronitrile) formed hydrogen cyanide which was detected in the blood, liver and brain. It was not absorbed through the skin (2).

Other comments

Reviews on human health effects, experimental toxicology, ecotoxicology, and physico-chemical properties listed (4). Explosive decomposition can occur.

References

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2. Rusin, V. Y. *Trudy Nauch. Sessii Leningrad. Nauch.-Issledovatel. Inst. GigieNew York Truda i Profzabolev.* 1958, 247-251 (Russ.) (*Chem. Abstr.* **56**, 2682f).
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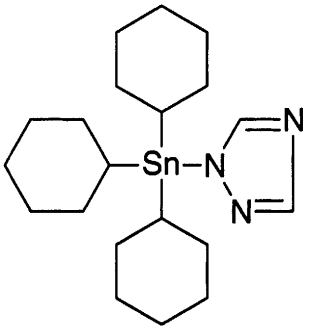
A270 azocyclotin



$C_{20}H_{35}N_3Sn$ **Mol. Wt.** 436.23 **CAS Registry No.** 41083-11-8

Synonyms tri(cyclohexyl)-1*H*-1,2,4-triazol-1-yltin; (1*H*-1,2,4-triazolyl-1-yl)tricyclohexyl stannane; (1*H*-1,2,4-triazolyl)tricyclohexyl stannane; 1-(tricyclohexylstannyl)-1*H*-1,2,4-triazole; Peropal

EINECS No. 255-209-1 **RTECS No.** WH 8637700

Uses Acaricide.

Physical properties

M. Pt. 218.8°C **Volatility** v.p. $<3.76 \times 10^{-6}$ mmHg

Solubility Water: <1 mg l^{-1} at 20°C. Organic solvents: dichloromethane, isopropanol

Occupational exposure

SE-LEVL 0.1 mg m^{-3} (as Sn) **SE-STEL** 0.2 mg m^{-3} (as Sn)
UK-LTEL 0.1 mg m^{-3} (as Sn) **UK-STEL** 0.2 mg m^{-3} (as Sn)
US-TWA 0.1 mg m^{-3} (as Sn) **US-STEL** 0.2 mg m^{-3} (as Sn)

Supply classification very toxic, dangerous for the environment

Risk phrases Toxic if swallowed – Very toxic by inhalation – Irritating to respiratory system and skin – Risk of serious damage to eyes – Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment (R25, R26, R37/38, R41, R50/53)

Safety phrases Keep locked up and out of the reach of children (if sold to general public) – In case of contact with eyes, rinse immediately with plenty of water and seek medical advice – After contact with skin, wash immediately with plenty of water. Wear suitable protective clothing, gloves and eye/face protection – In case of insufficient ventilation, wear suitable respiratory equipment – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) – This material and/or its container must be disposed of as hazardous waste – Avoid release to the environment. Refer to special instructions/safety data sheet (S1/2, S26, S28, S36/37/39, S38, S45, S60, S61)

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) rainbow trout 0.004 mg l^{-1}, golden orfe 0.0093 mg l^{-1} (1).

Invertebrate toxicity

EC_{50} (48 hr) *Daphnia* 0.04 mg l^{-1} (1).
Non-toxic to bees (1).

Environmental fate

Degradation studies

$t_{1/2}$ in soil ranges from a few days to many weeks, depending on soil type (1).
Metabolites identified in plants include 1,2,4-triazole, tricyclohexyl tin hydroxide and dicyclohexyl tin hydroxide (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral ♂, ♀ rat 209, 363 mg kg^{-1}, respectively (1).
LD_{50} oral guinea pig 261 mg kg^{-1} (1).
LD_{50} oral mouse 870-980 mg kg^{-1} (1).
LD_{50} oral Japanese quail 144-250 mg kg^{-1} (1).
LC_{50} (4 hr) inhalation rat 0.02 mg l^{-1} (1).
LD_{50} percutaneous rat >5000 mg kg^{-1} (1).
LD_{50} dermal rat 1000 mg kg^{-1} (2).

Carcinogenicity and chronic effects

Oral rat, mouse, dog (2 yr) 5, 15 and 10 mg kg^{-1} diet, respectively. No adverse effects reported (1).

Metabolism and toxicokinetics

Metabolised by hydrolysis, forming 1,2,4-triazole and tricyclohexyl tin hydroxide, which is further oxidized to form dicyclohexyl tin hydroxide (species unspecified) (1).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides and related products: maximum admissible concentration 0.1 μg l^{-1} (3).
Included in Schedule 6 (Release into Land: Prescribed Substances) of Statutory Instrument No. 472, 1991 (4).
ADI 0.001 mg kg^{-1} body weight (1).
WHO Toxicity Class II (5).
EPA Toxicity Class II (1).

References

1. *The Pesticide Manual* 11th ed., 1997, The British Crop Protection Council, Farnham, UK.
2. *Farm Chemicals Handbook* 1983, C182, Meister Publishing Co, Willoughby, OH, USA.
3. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
4. *S.I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
5. *The WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification 1998-1999* WHO/PCS/98.21

A271 azodicarbonamide

$$H_2NCON{=}NCONH_2$$

$C_2H_4N_4O_2$ **Mol. Wt.** 116.08 **CAS Registry No.** 123-77-3

Synonyms azoformamide; 1,1-azobisformamide; azobiscarbonamide; azodicarboxylic acid diamide; azodicarboxamide; diazenedicarboxamide

EINECS No. 204-650-8 **RTECS No.** LQ 1040000

Uses Blowing agent for foams, plastics and rubbers. Maturing agent for flour. Food additive No. E927 (UK).

Physical properties

M. Pt. 225°C (decomp.) **B. Pt.** decomposes above 195°C **Specific gravity** 1.65 at 20°C with respect to water at 20°C
Solubility Organic solvents: diethyl ether

Occupational exposure

UK-LTEL MEL 1.0 mg m^{-3} **UK-STEL** MEL 3.0 mg m^{-3}
Supply classification harmful
Risk phrases May cause sensitisation by inhalation – Risk of explosion if heated under confinement (R42, R44)
Safety phrases Keep out of reach of children (if sold to general public) – Do not breathe dust – Avoid contact with the skin – Wear suitable gloves (S2, S22, S24, S37)

Mammalian & avian toxicity

Sub-acute and sub-chronic data
Inhalation rat, mouse (2 wk) 2-207 mg m^{-3} caused no exposure-related mortality or abnormal clinical signs in rats or mice during or after exposure. No lesions noted, on either gross or histological evaluation of rats or mice (1). Inhalation rat, mouse (13 wk) 50-204 mg m^{-3} no exposure-related mortality or abnormal clinical signs were observed. No histopathological lesions reported in mice. In rats exposed to 50 mg m^{-3}, lung weights increased and enlarged mediastinal and/or tracheobronchial lymph nodes were observed. No exposure-related lesions observed microscopically in rats exposed to 100 or 200 mg m^{-3} (1).

Other effects

Other adverse effects (human)
Inhalation of azodicarbonamide dust at levels of 2-5 mg m^{-3} during its manufacture were found to cause sensitisation and asthma in workers. Symptoms ceased on removal from source of irritancy (2).

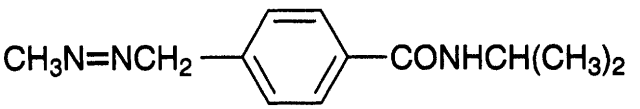
Other comments

Reviews on human health effects, experimental toxicology workplace experience, and ecotoxicology listed (3). British Rubber Manufacturers' Association recommends exposure should be reduced to <1 mg m^{-3} (4).

References

1. Medinsky, M. A. et al *Fundam. Appl. Toxicol.* 1990, **15**(2), 308-319.
2. Slovak, A. J. M. *Thorax* 1981, **36**(12), 906-909.
3. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium.
4. *Occup. Health* 1986, **38**(3), 72

A272 azoprocarbazine



$C_{12}N_{17}N_3O$ **Mol. Wt.** 440.27 **CAS Registry No.** 2235-59-8

Synonyms 4-[(methylazo)methyl]-*N*-(1-methylethyl)-benzamide; *N*-isopropyl-1α-(2-methylazo)-*p*-toluamide

RTECS No. XS 4375000

Mammalian & avian toxicity

Metabolism and toxicokinetics

Metabolised by rat liver microsomes to azoxy metabolites (1).

Other comments

Found as the primary oxidative metabolite of the drug procarbazine (1).

Found to be active as procarbazine in increasing the lifespan of mice implanted with leukaemia cells (2).

References

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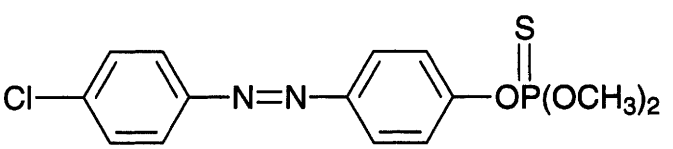
A273 azothoate



$C_{14}H_{14}ClN_2O_3PS$ **Mol. Wt.** 356.77 **CAS Registry No.** 5834-96-8

Synonyms *O*-4-(4-chlorophenylazo)phenyl *O,O*-dimethylphosphorothioate; *O*-[4-[(4-chlorophenyl)azo]phenyl]-*O,O*-dimethylphosphorothioate; O-[*p*-[(*p*-chlorophenyl)azo]phenyl]-*O,O*-dimethyl phosphorothioate; Slam C

EINECS No. 227-419-3 **RTECS No.** TE 8183000

Uses Superseded insecticide and acaricide.

Physical properties

M. Pt. 76.5-78°C
Solubility Organic solvents: methanol

Occupational exposure

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) – Keep away from food, drink and animal feeding stuffs (S2, S13)

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides and related products: maximum admissible concentration 0.1 $\mu g\ l^{-1}$ (1).
Included in Schedule 6 (Release into Land: Prescribed Substances) of Statutory Instrument No. 472, 1991 (2).

References

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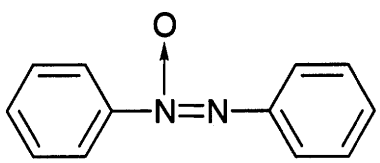
A274 azoxybenzene



$C_{12}H_{10}N_2O$ **Mol. Wt.** 198.22 **CAS Registry No.** 495-48-7

Synonyms diazene, diphenyl 1-oxide; azobenzene oxide; azoxybenzide; azoxydibenzene; diphenyldiazene 1-oxide

EINECS No. 207-802-1 **RTECS No.** CO 4025000

Uses Acaricide. Chemical intermediate.

Physical properties

M. Pt. 36°C **B. Pt.** decomp. **Specific gravity** 1.1590 at 26°C with respect to water at 4°C
Solubility Organic solvents: acetone, diethyl ether, ethanol

Occupational exposure

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) – After contact with skin, wash immediately with plenty of water (S2, S28)

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, mouse 515, 700 mg kg^{-1}, respectively (1,2).
LD_{50} dermal rabbit 1090 mg kg^{-1} (1).
LD_{Lo} intraperitoneal mouse 500 mg kg^{-1} (3).
LD_{Lo} subcutaneous rabbit 250 mg kg^{-1} (3).

Irritancy

10 mg applied to rabbit skin for 24 hr caused mild irritation (1).

Genotoxicity

Salmonella typhimurium TA98 and TA100 without metabolic activation negative, with metabolic activation positive (4).
Escherichia coli without metabolic activation positive (5).
Escherichia coli PQ37 with and without metabolic activation negative (6).

Other effects

Any other adverse effects

Caused swelling of spleen and liver, icteritious skin, methaemoglobinemia, and atrophy of the testes and epididymis in rats and mice after oral administration of LD_{50} (2).
Oral administration to ♂ and ♀ rat, 0-100 mg kg^{-1} daily for ≤7 days caused time and dose-dependent decrease in cytochrome P450 and in the activity of aminopyrine-*N*-demethylase and aniline hydroxylase in the hepatic microsomes of both sexes. Retardation and body-weight gain, increase in relative liver weight and increases in microsomal cytochrome b_5 were reported (7).

Other comments

Reviews on human health effects, experimental toxicology, ecotoxicology and physico-chemical properties listed (8).

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B1 bacitracin

$C_{66}H_{103}N_{17}O_{16}S$ **Mol. Wt.** 1422.71 **CAS Registry No.** 1405-87-4

Synonyms Baciguent

EINECS No. 215-786-2 **RTECS No.** CP 0175000

Uses Antibiotic applied topically to treat infections of the skin, nose or eye.

Occurrence Antimicrobial polypeptide produced by certain strains of *Bacillus licheniformis* and *Bacillus subtilis*.

Physical properties

Solubility Water: freely soluble in water. Organic solvents: cyclohexanol, ethanol, methanol

Ecotoxicity

Invertebrate toxicity

EC_{50} (24, 48 hr) *Daphnia magna* 126.36, 30.48 mg l^{-1}, respectively (1).
EC_{50} (24, 48 hr) *Artemia salina* 34.06, 21.82 mg l^{-1}, respectively (1).
IC_{50} *Saccharomyces cerevisiae* 31 mg l^{-1} (2).

Mammalian & avian toxicity

Acute data

LD_{50} oral red-winged blackbird >100 mg kg^{-1} (3).
LD_{50} oral Japanese quail >316 mg kg^{-1} (3).
LD_{50} oral guinea pig 2000 mg kg^{-1} (4).
LD_{50} oral rat, mouse 7.5, 28 mg kg^{-1}, respectively (2).
LD_{50} intraperitoneal, intravenous rat, mouse 190-360 mg kg^{-1} (5).
LD_{50} subcutaneous mouse 1300 mg kg^{-1} (5).

Metabolism and toxicokinetics

There is no appreciable absorption from the gastro intestinal tract. Following a single intramuscular injection 10-40% was excreted in urine within 24 hr. Bacitracin readily diffuses into the pleural and ascitic fluids but little passes into the cerebrospinal fluid. Absorption is negligible following topical application (6).
Following parenteral administration of large single doses, significant concentrations of the drug persisted in the blood stream for as long as 7-8 hr (7).

Other effects

Other adverse effects (human)

May produce severe nephrotoxicity when administered systemically. Hypersensitivity reactions, including rashes and anaphylaxis, have occurred with both systemic and topical administration (6).

Other comments

Physico-chemical properties, experimental toxicology and health effects reviewed (8,9).
Commercial bacitracin is a mixture of at least nine bacitracins.

References

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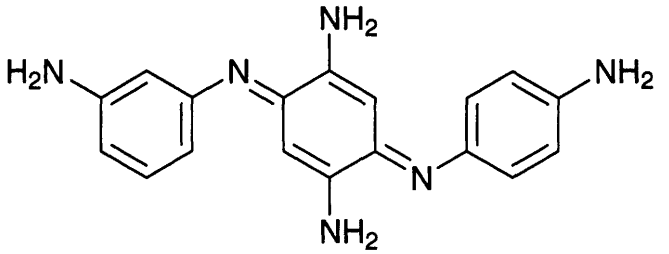
B2 Bandrowski's base



$C_{18}H_{18}N_6$ **Mol. Wt.** 318.38 **CAS Registry No.** 20048-27-5

Synonyms *N,N''*-(2,5-diamino-2,5-cyclohexadiene-1,4-diylidene)bis-1,4-benzenediamine

RTECS No. GU 4805000

Genotoxicity

Salmonella typhimurium TA1538 without metabolic activation positive (1).
Salmonella typhimurium TA98, TA1538 with and without metabolic activation induced frameshift mutations (2).
Salmonella typhimurium TA98 without metabolic activation highly mutagenic on exposure to ultra violet light (3).

References

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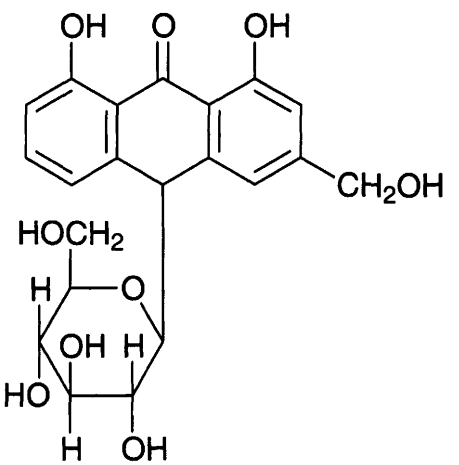
B3 barbaloin



$C_{21}H_{22}O_9$ **Mol. Wt.** 418.40 **CAS Registry No.** 1415-73-2

Synonyms (*R*)-10-β-D-glucopyranosyl-1,8-dihydroxy-3-(hydroxymethyl)-9(10*H*)-anthracenone

EINECS No. 215-808-0 **RTECS No.** LZ 6520000

Uses Laxative.

Occurrence Various species of aloe.

Physical properties

M. Pt. 148-149°C
Solubility Organic solvents: methanol, pyridine

Mammalian & avian toxicity

Acute data
LD_{Lo} oral cat 500 mg kg^{-1} (1).
LD_{50} intravenous mouse 200 mg kg^{-1} (2).
LD_{Lo} subcutaneous rabbit 200 mg kg^{-1} (1).

Metabolism and toxicokinetics
Under anaerobic conditions the C-glucosyl bond of barbaloin, a major purgative principle of aloe, was cleaved with human intestinal bacteria, yielding aloe-emodin anthrone and aloe-emodin bianthrone. The faecal flora of humans had the most potent transforming activity, whereas those of rats and mice had less or no activity (3).

Other comments

Has been replaced by safer purgatives (4).

References

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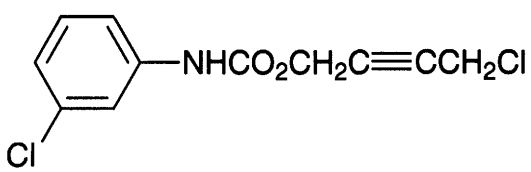
B4 barban



$C_{11}H_9Cl_2NO_2$ **Mol. Wt.** 258.10 **CAS Registry No.** 101-27-9

Synonyms Barbamat; Chlorinat; 4-chlorobut-2-ynyl 3-chlorocarbanilate; 4-chloro-2-butynyl-(3-chlorophenyl)carbamate; (3-chlorophenyl)carbamic acid 4-chloro-2-butynyl ester; Barbane

EINECS No. 202-930-4 **RTECS No.** FD 7700000

Uses Superseded post-emergence herbicide.

Physical properties

M. Pt. 75-76°C **Flash point** 81°C **Specific gravity** 1.403 at 25°C **Volatility** v.p. 3.76×10^{-5} mmHg
Solubility Water: 11 mg l^{-1} at 25°C. Organic solvents: benzene, ethylene dichloride, hexane, kerosene

Occupational exposure

Supply classification harmful
Risk phrases Harmful if swallowed – May cause sensitisation by skin contact (R22, R43)
Safety phrases Keep out of reach of children (if sold to general public) – Avoid contact with the skin – Wear suitable protective clothing and gloves (S2, S24, S36/37)

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) rainbow trout, bluegill sunfish, goldfish, guppy 0.6-1.3 mg l^{-1} (1).

Invertebrate toxicity

Non-toxic to bees (1).

Environmental fate

Degradation studies

Degrades in soil to give 3-chloroaniline. Residual activity in soil ~2-3 months (1).

Adsorption and retention

Carbanilates resist leaching into the soil profile. Immobile in soil and activated by adsorption to soil organic matter (2).

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse, rat, rabbit 322-600 mg kg^{-1} (3,4).

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

Sub-acute and sub-chronic data

LC_{50} (8 day) mallard duck, bobwhite quail >1000 mg kg^{-1} (1).

Daily oral administration to guinea pigs and rabbits for 4-6 months caused fatty dystrophy of the liver and kidneys, haemosiderosis of the spleen and vascular hyperaemia of the liver, brain, kidneys, spleen and gastric mucosa. Daily doses of 20-40 mg kg^{-1} for 4-6 months to rabbits caused a significant decrease in liver glycogen content (5).

Carcinogenicity and chronic effects

In 2-yr feeding trials the no-effect levels in rats and dogs were 150 and 5 mg kg^{-1} diet, respectively (6).

Metabolism and toxicokinetics

Following oral administration to rats, chloroaniline, 2-amino-4-chlorophenol and 4-amino-2-chlorophenol were excreted free and in conjugated form. In addition to aniline and *m*-chloroaniline, hydroxycarbamate was found in blood and in all organs; the urine contained *p*-aminophenol (7).

Genotoxicity

Salmonella typhimurium TA100, TA1535 with metabolic activation positive (8).

Other effects

Any other adverse effects

Effects on blood cholinesterase activity were reported in rats following inhalation exposure to 80 mg m^{-3} for 4 hr (5).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides and related products: maximum admissible concentration 0.1 μg l^{-1} (9).

Included in Schedule 6 (Release into Land: Prescribed Substances) of Statutory Instrument No. 472, 1991 (10).

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B5 barium

Ba

Ba **Mol. Wt.** 137.33 **CAS Registry No.** 7440-39-3

EINECS No. 231-149-1 **RTECS No.** CQ 8370000

Uses Used in the radio, ceramics, glass, electronics and computer industries. In the manufacture of alloys and valves. Extinguisher for uranium and plutonium fires.
Occurrence A relatively abundant element found in soils, rocks and minerals, also in plant and animal tissue. Some surface and sea waters also contain barium. Occurs in lead and zinc ore deposits.

Physical properties

M. Pt. 725°C (metal) **B. Pt.** 1640°C **Specific gravity** 3.51 at 20°C **Volatility** v.p. 10 mmHg at 1049°C
Solubility Organic solvents: ethanol (decomp.)

Occupational exposure

US-TWA 0.5 mg m^{-3}

UN No. 1400 **HAZCHEM Code** 4W **Conveyance classification** substance which in contact with water emits flammable gas

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) sheepshead minnow >500 mg l^{-1} (1).
LC_{50} (96 hr) salmon 78 mg l^{-1} (2).

Invertebrate toxicity
LC_{50} (48 hr) *Daphnia magna* >530 mg l^{-1} (3).
IC_{50} *Tetrahymena pyriformis* 350 mg l^{-1} using a flask technique (4).

Mammalian & avian toxicity

Sub-acute and sub-chronic data
Guinea pigs administered 12 mg kg^{-1} day^{-1} subcutaneously for 26 wk developed myeloid hyperplasia of the spleen, liver and bone marrow (5).

Carcinogenicity and chronic effects

Rats exposed to 100 ppm barium in drinking water for 16 months exhibited depressed rates of cardiac contraction and depressed excitability in the heart. Barium-induced increase in the blood pressure of rats was modest but a comparable mild hypertension in humans would have major health implications (6).

Metabolism and toxicokinetics

In humans, a major part of this element is concentrated in the bones (~91%), remainder being in soft tissues such as the brain, heart, kidney, spleen, pancreas and lungs. The skeletal metabolism of barium in humans is qualitatively similar to calcium although the incorporation of these two elements is quantitatively different. The $t_{1/2}$ of barium in bones is 50 days (7).

During the first 4 hr after administration, barium absorption from the nasal passages was ~61% compared with 11% gastric absorption (8).

Excretion of barium following intravenous injection in a 60-yr-old man was 0.22-0.33 and 0.181% in saliva and seminal fluid, respectively, after 3-6 hr. The percentage of the injected dose eliminated via the faeces and urine was 20% after 24 hr, 70% after 3 days and 85% after 10 days (9).

Rats were fed a basal diet containing 25% Brazil nuts (containing 996 ppm barium) and a basal diet to which a concentration of barium as barium chloride was added at 249 ppm equivalent to that in the Brazil nut diet. Corresponding total skeletal deposition of barium was 72.8 and 91.3 ppm, respectively. Excretion of barium in the faeces was 10-20-fold greater than that in urine (10).

Other effects

Other adverse effects (human)

Negative results were obtained for *in vitro* human lymphocyte testing of barium by (phytohaemagglutinin) PHA-induced blastogenesis using [3H]thymidine incorporation (11).

A study of the association between age and sex-adjusted cardiovascular death rates and barium levels in drinking water in 16 Illinois communities was reported (12).

Four cases of pneumonoconiosis were reported in barium miners in Scotland, three of whom developed progressive massive fibrosis, from which two died, and one developed a nodular simple pneumonoconiosis after leaving the industry. There was a complete absence of barium in the lungs, suggesting that much of the barium inhaled is not taken into pulmonary tissues, but remains in alveolar macrophages and is eventually removed by the mucociliary mechanism (13).

Toxic effects from doses as low as 0.2-0.5 mg kg^{-1} in adult humans include acute gastroenteritis, loss of deep reflexes with onset of muscular paralysis and progressive muscular paralysis (14).

Workers occupationally exposed to soluble barium compounds in welding fumes revealed 31-234 $\mu g\ l^{-1}$ barium in urine after 3 hr and 20-110 $\mu g\ l^{-1}$ in 12 hr (14).

Any other adverse effects

Acute effects of barium ingestion in experimental animals include salivation, nausea, diarrhoea, tachycardia, hypokalaemia, twitching, flaccid paralysis of sketetal muscle, respiratory muscle paralysis and ventricular fibrillation (14).

Barium ion contracture tonically activates myocardium while preserving cellular integrity. Myocardium in barium ion contracture is metabolically stable for 30 min (species unspecified) (15).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Barium: guide level 100 $\mu g\ l^{-1}$ (16).

Included in Schedule 6 (Release into Land: Prescribed Substances) of Statutory Instrument No. 472, 1991 (17).

Other comments

Barium has been reported to inhibit growth and cellular process in microorganisms. It has also been observed to affect the development of germinating bacterial spores (14).

Physico-chemical properties, human health effects, experimental toxicology, ecotoxicology, environmental effects, exposure levels, workplace experience and epidemiology reviewed (14,18).

Industrial hygiene and toxicology during use of barium compounds discussed (19).
General information and properties, pharmacokinetics, health effects in humans and animals, quantification of toxicological effects and other criterial guidance and standards summarised (20).
Gastrointestinal absorption of barium relating to physiological differences between infant rats and infant humans reviewed (21).
Variability occurred in the barium concentration in bottled waters (7-660 $\mu g\ l^{-1}$) and groundwaters (7-1160 $\mu g\ l^{-1}$), while concentrations were homogeneous in treated waters (13-140 $\mu g\ l^{-1}$). The median value for groundwater was higher than the maximum allowed concentration according to EEC Guidelines. Barium levels were not altered significantly during water transportation. Barium drinking water standards appear to have been developed in the absence of studies examining the human health effects associated with drinking water intake (22).
The toxicity of barium is dependent on the ability of the organism to absorb it. Therefore toxicity data refer to bioavailable forms, such as the ion in solution or particulate matter.
Emissions of barium into the air from mining, refining and processing barium ore can occur during loading and unloading, stockpiling, materials handling and grinding and refining the ore.
Fossil fuel combustion may also release barium into the air.
The detonation of nuclear devices in the atmosphere is a source of radioactive barium.
Forty-seven popular red lipsticks were analysed for barium content. The soluble barium content ranged from 8 to 2104 ppm (23).

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B6 barium acetate

$$Ba(O_2CCH_3)_2$$

$C_4H_6BaO_4$ **Mol. Wt.** 255.42 **CAS Registry No.** 543-80-6

Synonyms acetic acid, barium salt; barium diacetate

EINECS No. 208-849-0 **RTECS No.** AF 4550000

Uses In fabric printing, lubricating oils. Catalyst in organic synthesis. Paint and varnish drier.

Physical properties

Specific gravity 2.468

Solubility Water: 588 g l^{-1} at 0°C. Organic solvents: ethanol

Occupational exposure

DE-MAK 0.5 mg m^{-3} (as Ba) (inhalable dust fraction)

FR-VME 0.5 mg m^{-3} (as Ba)

SE-LEVL 0.5 mg m^{-3} (as Ba)

UK-LTEL 0.5 mg m^{-3} (as Ba)

US-TWA 0.5 mg m^{-3} (as Ba)

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) – After contact with skin, wash immediately with plenty of water (S2, S28)

Ecotoxicity

Fish toxicity

Listed as negative in tests on trout, bluegill sunfish and goldfish. However the authors state that the high mineral content of the water used in these studies adds an additional source of error. Therefore the compounds listed as negative might be toxic in softer water supplies (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral rabbit, rat 240, 920 mg kg^{-1}, respectively (2,3).

LD_{50} intravenous mouse 23 mg kg^{-1} (4).

LD_{Lo} intravenous rabbit 12 mg kg^{-1} (3).

LD_{Lo} subcutaneous rabbit 96 mg kg^{-1} (3).

Carcinogenicity and chronic effects

Lifetime exposure to barium acetate 0 or 5 mg l^{-1} in drinking water of rat. After 540 days slight increased mortality in ♀ rat. After 150 days increased growth rate in exposed rats over controls (5).

Other effects

Other adverse effects (human)

The symptoms of barium poisoning from soluble barium salts arise from stimulation of all forms of muscle and include vomiting, colic, diarrhoea, hypertension, convulsive tremors and muscular paralysis. Hypokalaemia is common. Death from cardiac or respiratory failure may occur (6).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Barium: guide level 100 μg l^{-1} (7).

Other comments

Experimental toxicology, Environmental fate, physico-chemical properties, ecotoxicology, environmental effects, exposure levels, workplace experience, epidemiology and human health effects reviewed (8,9).

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B7 barium bromate

$$Ba(BrO_3)_2$$

$BaBr_2O_6$ **Mol. Wt.** 393.13 **CAS Registry No.** 13967-90-3

Synonyms bromic acid, barium salt

EINECS No. 237-750-5 **RTECS No.** EF 8715000

Uses Analytical reagent. Oxidation agent. Corrosion inhibitor in low-carbon steel. Used to prepare rare-earth bromates.

Physical properties

M. Pt. 260°C (decomp.) **Specific gravity** 3.99 at 18°C
Solubility Water: 9.6 g l^{-1} at 30°C. Organic solvents: acetone

Occupational exposure

DE-MAK 0.5 mg m^{-3} (as Ba) (inhalable dust fraction)
FR-VME 0.5 mg m^{-3} (as Ba)
SE-LEVL 0.5 mg m^{-3} (as Ba)
UK-LTEL 0.5 mg m^{-3} (as Ba)
US-TWA 0.5 mg m^{-3} (as Ba)

UN No. 2719 **HAZCHEM Code** 2YE **Conveyance classification** oxidising substance, toxic
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) – After contact with skin, wash immediately with plenty of water (S2, S28)

Ecotoxicity

Bioaccumulation
Barium obtained from soluble salts in soil accumulates in some plants and algae (1,2).

Other effects

Other adverse effects (human)

In humans, symptoms of barium poisoning from soluble barium salts arise from stimulation of all forms of muscle and include vomiting, colic, diarrhoea, hypertension, convulsive tremors and muscular paralysis. Hypokalaemia is common. Death from cardiac or respiratory failure may occur (3).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Barium: guide level 100 $\mu g\ l^{-1}$ (4).
Included in Schedule 6 (Release into Land: Prescribed Substances) of Statutory Instrument No. 472, 1991 (5).

Other comments

Experimental toxicology, Environmental fate, physico-chemical properties, ecotoxicology, environmental effects, exposure levels, workplace experience, epidemiology and human health effects reviewed (6,7).

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B8 barium bromide

$$BaBr_2$$

$BaBr_2$ **Mol. Wt.** 297.13 **CAS Registry No.** 10553-31-8

EINECS No. 234-140-0

Uses As an intermediate to prepare bromide compounds and phosphors. In photographic compounds.

Physical properties

M. Pt. 847°C **B. Pt.** 1835°C **Specific gravity** 4.781
Solubility Water: 1041 g l^{-1} at 25°C. Organic solvents: methanol

Occupational exposure

DE-MAK 0.5 mg m^{-3} (as Ba) (inhalable dust fraction)
FR-VME 0.5 mg m^{-3} (as Ba)
SE-LEVL 0.5 mg m^{-3} (as Ba)
UK-LTEL 0.5 mg m^{-3} (as Ba)
US-TWA 0.5 mg m^{-3} (as Ba)
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) – After contact with skin, wash immediately with plenty of water (S2, S28)

Ecotoxicity

Bioaccumulation
Barium obtained from soluble salts in soil accumulates in some plants and algae (1,2).

Other effects

Other adverse effects (human)
In humans, symptoms of barium poisoning from soluble barium salts arise from stimulation of all forms of muscle and include vomiting, colic, diarrhoea, hypertension, convulsive tremors and muscular paralysis. Hypokalaemia is common. Death from cardiac or respiratory failure may occur (3).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Barium: guide level 100 $\mu g\ l^{-1}$ (4).

Other comments

Soluble barium salts are readily absorbed in mammals (5).
In general, the Ba^{2+} ion is toxic or inhibitory to cellular processes in bacteria, fungi, mosses and algae (6).
Environmental fate, experimental toxicology, physico-chemical properties, ecotoxicology, environmental effects, exposure levels, workplace experience, epidemiology and human health effects reviewed (6,7).

References

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B9 barium carbonate

$$BaCO_3$$

$BaCO_3$ **Mol. Wt.** 197.34 **CAS Registry No.** 513-77-9

Synonyms carbonic acid, barium salt (1:1); C.I. 77099; C.I. Pigment White 10

EINECS No. 208-167-3 **RTECS No.** CQ 8600000

Uses A rodenticide. Used in ceramics, paints, enamels, marble substitutes and rubber. In the manufacture of paper, barium salts, electrodes and optical glasses. An analytical reagent.
Occurrence In nature as the mineral Witherite.

Physical properties

M. Pt. 1300°C (decomp.) **B. Pt.** decomposes **Specific gravity** 4.43 at 20°C **Volatility** v.p. not available
Solubility Water: 0.022 g l^{-1} at 20°C. Organic solvents: ethanol

Occupational exposure

DE-MAK 0.5 mg m^{-3} (as Ba) (inhalable dust fraction)
FR-VME 0.5 mg m^{-3} (as Ba)
UK-LTEL 0.5 mg m^{-3} (as Ba)

UN No. 1564 **HAZCHEM Code** 2Z **Conveyance classification** toxic substance
Supply classification harmful
Risk phrases Harmful if swallowed (R22)
Safety phrases Keep out of reach of children (if sold to general public) – Avoid contact with skin and eyes (S2, S24/25)

Ecotoxicity

Invertebrate toxicity
IC_{50} *Saccharomyces cerevisiae* 342 mg l^{-1} (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral ♂, ♀ rat 630-750 mg kg^{-1} (2).
LD_{50} oral rat 1480 mg kg^{-1} (1).
LD_{50} oral mouse, rat 200-420 mg kg^{-1} (3).
Oral rabbit, mouse lethal dose 170, 300 mg kg^{-1}, respectively (4).
LD_{50} intraperitoneal mouse 50 mg kg^{-1} (3).
LD_{Lo} oral human 57 mg kg^{-1} (5).
TD_{Lo} oral human 11 mg kg^{-1} gastro-intestinal tract effects (6).
TD_{Lo} oral human 29 mg kg^{-1} peripheral and central nervous system effects (7).
Classified as harmful by the acute-toxic-class method, an alternative to the LD_{50} test (2).

Sub-acute and sub-chronic data
♂ rats exposed to 1.15 and 5.2 mg m^{-3} 4 hr day^{-1} 6 days wk^{-1} for 4 months experienced decreased weight gain, low blood sugar and haemoglobin, as well as leucocytosis and thrombopenia in the high-dose group (8).

Teratogenicity and reproductive effects
TC_{Lo} oral ♀ rat 26 mg kg^{-1} 29 days before conception and throughout pregnancy caused increased mortality of offspring, low birth weights but no teratogenesis (9).

Metabolism and toxicokinetics
Following intramuscular injection into hind leg of rats, aerosolised barium carbonate dissolved rapidly leaving injection site within 3 days (10).

Irritancy
Can cause dermatitis in humans (11).

Other effects

Other adverse effects (human)
A benign pneumoconiosis (baritosis) may result from the inhalation of barium carbonate dust (12).
In a reported case of an attempted suicide, the ingestion of 40 g barium carbonate resulted in a 30% reduction in normal plasma potassium level and induced muscle weakness, respiratory failure and complete paralysis. Normal muscular and renal function was regained within 7 days (13).
Out of >100 people who had consumed sausages made with barium carbonate instead of potato meal, 19 people

were hospitalised with symptoms ranging from mild vomiting and diarrhoea to partial paralysis. One patient died suddenly after developing right facial paralysis and left hemiplegia (14,15).
Poison to humans by ingestion, systemic effects include stomach ulcers, muscle weakness, paresthesias and paralysis (16).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Barium: guide level 100 $\mu g\ l^{-1}$ (17).
Included in Schedule 6 (Release into Land: Prescribed Substances) of Statutory Instrument No. 472, 1991 (18).

Other comments

In vivo solubility of the carbonate salt was studied in rats after intramuscular injection. It was found the carbonate and chloride salts were equally soluble in the soft tissues and were absorbed from the injection site very rapidly (19).
Experimental toxicology, human health effects, physico-chemical properties, ecotoxicology, environmental effects, exposure levels, workplace experience, epidemiology and Environmental fate reviewed (8,20).

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B10 barium chlorate

$$Ba(ClO_3)_2$$

$BaCl_2O_6$ **Mol. Wt.** 304.23 **CAS Registry No.** 13477-00-4

Synonyms chloric acid, barium salt

EINECS No. 236-760-7 **RTECS No.** FN 9770000

Uses In pyrotechnics. A textile mordant. In the manufacture of other chlorates and of explosives and matches.

Physical properties

M. Pt. 414°C **Specific gravity** 3.18
Solubility Water: 274 g l^{-1} at 15°C. Organic solvents: acetone, ethanol, ethylamine

Occupational exposure

DE-MAK 0.5 mg m^{-3} (as Ba) (inhalable dust fraction)
FR-VME 0.5 m m^{-3} (as Ba)
SE-LEVL 0.5 mg m^{-3} (as Ba)
UK-LTEL 0.5 mg m^{-3} (as Ba)
US-TWA 0.5 mg m^{-3} (as Ba)

UN No. 1445 **HAZCHEM Code** 2YE **Conveyance classification** oxidising substance, toxic
Supply classification oxidising, harmful
Risk phrases Explosive when mixed with combustible material – Harmful by inhalation and if swallowed (R9, R20/22)
Safety phrases Keep out of reach of children (if sold to general public) – Keep away from food, drink and animal feeding stuffs – Take off immediately all contaminated clothing (S2, S13, S27)

Ecotoxicity

Bioaccumulation
Barium obtained from soluble salts in soil accumlates in some plants and algae (1,2).

Mammalian & avian toxicity

Irritancy
An eye, skin and respiratory tract irritant (3).

Other effects

Other adverse effects (human)
In humans, symptoms of barium poisoning from soluble barium salts arise from stimulation of all forms of muscle and include vomiting, colic, diarrhoea, hypertension, convulsive tremors and muscular paralysis. Hypokalaemia is common. Death from cardiac or respiratory failure may occur (4).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Barium: guide level 100 μg l^{-1} (5).
Included in Schedule 6 (Release into Land: Prescribed Substances) of Statutory Instrument No. 472, 1991 (6).

Other comments

In general the Ba^{2+} ion is toxic or inhibitory to cellular processes in bacteria, fungi, mosses and algae (3).
Principal toxic effects of chlorates are the production of methaemoglobin in the blood and destruction of red blood corpuscles. Damage to heart muscle and kidney has been reported. Soluble barium salts are readily absorbed in mammals (7).
Chlorates are absorbed by ingestion or by inhalation of dust (8).
Physico-chemical properties, Environmental fate, experimental toxicology, ecotoxicology, environmental effects, exposure levels, workplace experience, epidemiology and human health effects reviewed (3,9).

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B11 barium chloride

$BaCl_2$

$BaCl_2$ **Mol. Wt.** 208.23 **CAS Registry No.** 10361-37-2

Synonyms barium dichloride; SBa 0108E; NCI-C61

EINECS No. 233-788-1 **RTECS No.** CQ 8750000

Uses In the manufacture of pigments, colour lakes, glass. A mordant for acid dyestuffs. Used in the manufacture of pesticides, lube oil additives, boiler compounds and aluminium refining. In leather tanning and finishing. In photographic paper and textiles. A flux in the manufacture of magnesium metal. Formerly used as purgative in horses and in cattle.

Physical properties

M. Pt. 962°C **B. Pt.** 1560°C **Specific gravity** 3.856 at 24°C
Solubility Water: 375 g l^{-1} at 26°C

Occupational exposure

DE-MAK 0.5 mg m^{-3} (as Ba) (inhalable dust fraction)
FR-VME 0.5 mg m^{-3} (as Ba)
SE-LEVL 0.5 mg m^{-3} (as Ba)
UK-LTEL 0.5 mg m^{-3} (as Ba)
US-TWA 0.5 mg m^{-3} (as Ba)

UN No. 1564 **HAZCHEM Code** 2Z **Conveyance classification** toxic substance
Supply classification harmful
Risk phrases Harmful by inhalation and if swallowed (R20/22)
Safety phrases Keep out of reach of children (if sold to general public) – After contact with skin, wash immediately with plenty of water (S2, S28)

Mammalian & avian toxicity

Acute data
LD_{50} oral guinea pig, rat 76-188 mg kg^{-1} (1,2).
LD_{Lo} oral mouse, dog, rabbit 70, 90, 170 mg kg^{-1}, respectively (3-5).
LD_{50} subcutaneous rat 178 mg kg^{-1} (3).
LD_{Lo} subcutaneous guinea pig 55 mg kg^{-1} (4).
LD_{50} intravenous mouse 8.2-19.2 mg kg^{-1} (6-8).
LD_{50} intravenous cat 40 mg kg^{-1} (5).
LD_{Lo} ingestion human 11.4 mg kg^{-1} (9).

Sub-acute and sub-chronic data

♂ and ♀ B6C3F1 mice and Fischer 344/N rats were given 0-4000 ppm barium chloride dihydrate in their drinking water for 92 days. Mortality was 60-70% in mice and 10-30% in rats administered 4000 ppm. Deaths in mice were associated with treatment-related renal toxicity, renal lesions in rats were less severe than in mice and did not contribute to treatment-related deaths. Body weights of all animals in the 4000 ppm group were lower than controls after 92 days, and motor activity, grip strengh and thermal sensitivity were slightly affected. Treated ♂ and ♀ rats showed higher serum phosphorus levels than controls; serum sodium, potassium and calcium levels were unchanged by the treatment (10).

Teratogenicity and reproductive effects

♂ and ♀ B6C3F1 mice and Fischer 344/N rats were given 0-4000 ppm barium chloride dihydrate in their drinking water for 92 days. No anatomical effects on offspring of rats or mice were seen, and reproductive indexes were unaffected. Rats administered 4000 ppm showed a marginal reduction in pup weights (10).

TD_{Lo} (1 day) intratesticular rat 16 mg kg^{-1} caused reproductive effects to testes, epididymis and sperm-duct (11).

Metabolism and toxicokinetics

In rats, nasal absorption of barium chloride was estimated at 60-80% after 4 hr and alveolar absorption may be of a similar magnitude. In hamsters receiving barium chloride by intragastric intubation, 11-32% of the dose was absorbed (12).

Following intramuscular injection of barium chloride solution into five children and two adults, the concentration of barium in serum fell rapidly during the first 6 days and then more slowly. The amount detected on day-6 was <0.0002% of the initial dose (13).

After a single oral dose (1, 5, 25 or 125 mg kg^{-1}) to ♂ weanling rats and sacrificed 0.5, 2, 4, 8, 16 and 24 hr after exposure, results indicated rapid absorption of barium from the gastrointestinal tract. Peak barium concentrations occurred 30 min post-administration in blood and soft tissues and 2 hr in the femur (14).

Pigmented and albino ♂ mice and late-gestation ♀ were intravenously administered 63 μg kg^{-1} barium containing barium chloride and sacrificed. The calcified tissues, cartilage, kidney and melanin-containing tissues of the ♂ and ♀ pigmented animals had highest barium activity at 20 minutes. The calcified and cartilage tissues retained activity even at the longest survival time, 32 days. After four days the only sites other than bone, cartilage and melanin-containing tissue positive for barium were gastrointestinal contents, urinary tract and salivary gland (15).

Genotoxicity

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

Salmonella typhimurium TA97, TA100, TA1535, TA1537, TA1538 with and without metabolic activation negative (17).

Saccharomyces cerevisiae gene conversion and mitotic recombination positive (18).

Other effects

Other adverse effects (human)

In humans, symptoms of barium poisoning from soluble barium salts arise from stimulation of all forms of muscle and include vomiting, colic, diarrhoea, hypertension, convulsion and muscular paralysis. Hypokalaemia is common. Death from cardiac or respiratory failure may occur (19).

A patient suffered acute renal failure associated with barium chloride poisoning (20).

In a 10-wk study barium chloride was administered in the drinking water of 11 healthy ♂ volunteers at concentrations of 0 mg l^{-1} (1-2 wk), 5 mg l^{-1} (3-6 wk) and 10 mg l^{-1} (7-10 wk). The levels corresponded to levels found in drinking water of some communities in the US. Subjects ranged in age from 27-61 yr and had no previous history of diabetes, hypertension or cardiovascular disease of any kind. No change was reported in blood pressure, total cholesterol, triglycerides, high-density lipoprotein or low-density lipoprotein cholesterol levels. Serum potassium and glucose levels and urinary metanephrine levels were also unchanged. No significant arrhythmias were noted during the barium exposure period (21).

Any other adverse effects

Rats exposed to 250 ppm barium ion for 5 months were challenged with an arrhythmagenic dose of 1-norepinephrine administered intravenously as 5 mg kg^{-1}. No significant ECG changes occurred (22).
Oral rat (16 months) 1, 10, 100 mg l^{-1} caused depressed cardiac rates and excitabiity, and increased systolic pressure, while decreasing conductivity and conduction (23).
Infusion of barium chloride in conscious rabbits caused severe ventricular dysrhythmias (24).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Barium: guide level 100 $\mu g\ l^{-1}$ (25).

Other comments

Experimental toxicology, human health effects, physico-chemical properties, exposure levels, workplace experience, epidemiology and Environmental fate reviewed (9,26).

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B12 barium cyanide

$Ba(CN)_2$

BaC_2N_2 **Mol. Wt.** 189.36 **CAS Registry No.** 542-62-1

Synonyms barium dicyanide; RCRA Waste No. PO13

EINECS No. 208-822-3 **RTECS No.** CQ 8785000

Uses In metallurgy and electroplating processes.

Physical properties

Solubility Water: 800 g l^{-1} at 14°C. Organic solvents: ethanol

Occupational exposure

DE-MAK 0.5 mg m^{-3} (as Ba) (inhalable dust fraction)
FR-VME 0.5 mg m^{-3} (as Ba)
SE-LEVL 0.5 mg m^{-3} (as Ba)
UK-LTEL 0.5 mg m^{-3} (as Ba)
US-TWA 0.5 mg m^{-3} (as Ba)

UN No. 1565 **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
Threshold concentrations for fish 5 ppm Ba^{2+}; threshold concentration for fresh and sea water fish 0.02 ppm CN^- (1).
LC_{100} (120 hr) trout 0.05 mg l^{-1} (1).
LC_{50} (24 hr) bluegill sunfish 0.18 mg l^{-1} (1).
LC_{50} (1.5 hr) carp 10 mg l^{-1} (1).

Invertebrate toxicity
Cyanides are moderate chronic poisons and may have accumulative effects. Marine waters should not exceed concentrations of 1:20 LD_{50} (1).

Bioaccumulation
Bioconcentration factor goldfish 150. Bioconcentration factors in marine and fresh water plants 500, fish 10, invertebrates 100. Barium was toxic to Eurasian water milfoil at 40-100 ppm. Cyanide is the more toxic ion, it is toxic by all routes (1).
Ba^{2+} accumulates in the soil from the dissolution of soluble barium salts and can accumulate in some plants (2).

Other effects

Other adverse effects (human)
Workers such as electroplaters and picklers can develop a cyanide rash characterised by itching, and muscular, papular and vesicular eruptions. Case studies and epidemiological studies have reported symptoms of cyanide poisoning to include headache, dizziness and thyroid enlargement (3).

A blood cyanide level of >1.0 μg ml^{-1} is lethal (species unspecified) (1).
In humans, symptoms of barium poisoning from soluble barium salts arise from stimulation of all forms of muscle and include vomiting, colic, diarrhoea, hypertension, convulsive tremors and muscular paralysis. Hypokalaemia is common. Death from cardiac or respiratory failure may occur (4).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Cyanides: maximum admissible concentration 50 μg l^{-1} (5).

Other comments

Soluble barium salts are readily absorbed in mammals (6).
The Ba^{2+} ion is toxic or inhibitory to cellular processes in bacteria, fungi, mosses and algae (7).
Cyanide ions are rapidly absorbed after oral or parenteral administration, from skin and mucosal surfaces and are extremely dangerous when inhaled (8,9).
Experimental toxicology, Environmental fate, physico-chemical properties, ecotoxicology, environmental effects, exposure levels, workplace experience, epidemiology and human health effects reviewed (7,10).

References

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B13 barium nitrate

$$Ba(NO_3)_2$$

BaN_2O_6 **Mol. Wt.** 261.34 **CAS Registry No.** 10022-31-8

Synonyms nitrobarite; barium dinitrate; nitric acid, barium salt

EINECS No. 233-020-5 **RTECS No.** CQ 9625000

Uses In pyrotechnics, for green signal lights. In vacuum tubes. In the manufacture of barium oxides. Incendary devices. Ceramic glazes. Rodenticide.

Physical properties

M. Pt. 592°C **B. Pt.** decomp. **Specific gravity** 3.24 at 23°C
Solubility Water: 87 g l^{-1} at 20°C

Occupational exposure

DE-MAK 0.5 mg m^{-3} (as Ba) (inhalable dust fraction)
FR-VME 0.5 mg m^{-3} (as Ba)
SE-LEVL 0.5 mg m^{-3} (as Ba)
UK-LTEL 0.5 mg m^{-3} (as Ba)
US-TWA 0.5 mg m^{-3} (as Ba)

UN No. 1446 **HAZCHEM Code** 2W **Conveyance classification** oxidising substance, toxic
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) – After contact with skin, wash immediately with plenty of water (S2, S28)

Ecotoxicity

Fish toxicity
Listed as negative in tests on trout, bluegill sunfish and goldfish. However the authors state that the high mineral content of the water used in these studies adds an additional source of error. Therefore the compounds listed as negative might be toxic in softer water supplies (1).

Invertebrate toxicity
EC_{50} *Artemia salina, Streptocephalus proboscideus, Daphnia magna, Brachionus calyciflorus* 34.7, 2.57, 0.79, 2.69 mmol l^{-1}, respectively (2).

Bioaccumulation
Barium obtained from soluble salts accumulates in some plants and algae (3,4).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 355 mg kg^{-1} (5).
LD_{Lo} oral dog 800 mg kg^{-1} (6).
LD_{Lo} oral rabbit 150 mg kg^{-1} (6).
LD_{50} intravenous mouse 8 mg kg^{-1} (7).

Irritancy
Dermal rabbit (24 hr) 500 mg caused mild irritation and 100 mg instilled into rabbit eye caused moderate irritation (5).

Other effects

Other adverse effects (human)
In humans symptoms of barium poisoning from soluble barium salts arise from stimulation of all forms of muscle and include vomiting, colic, diarrhoea, hypertension, convulsive tremors and muscular paralysis. Hypokalaemia is common. Death from cardiac or respiratory failure may occur (8).

Any other adverse effects
IC_{50} Ascites sarcoma BP8 cells 1.29 mM (9).
CT_{50} rat hepatocytes, Madin-Darbin bovine kidney cells, human McCoy epithelial cells 0.470, 0.788, 0.593 mM, respectively; CT_{100} 0.593, 1.098, 1.083 mM, respectively (10).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Nitrates: guide level 25 mg l^{-1}, maximum admissible concentration 50 mg l^{-1} (11).
Included in Schedule 6 (Release into Land: Prescribed Substances) of Statutory Instrument No. 472, 1991 (12).

Other comments

In general the Ba^{2+} ion is toxic or inhibitory to cellular processes in bacteria, fungi, mosses and algae (13).
Soluble barium salts are readily absorbed in mammals (14).
Experimental toxicology, Environmental fate, physico-chemical properties, ecotoxicology, environmental effects, exposure levels, workplace experience, epidemiology and human health effects reviewed (13,15).

References

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

B14 barium oxide

BaO

BaO **Mol. Wt.** 153.33 **CAS Registry No.** 1304-28-5

Synonyms barium monoxide; barium protoxide; baryta; calcined baryta

EINECS No. 215-127-9 **RTECS No.** CQ 9800000

Uses For drying solvents and gases. In the manufacture of lubricating oil detergents. Chemical intermediate in the production of barium methoxide.

Physical properties

M. Pt. 1923°C **B. Pt.** 2000°C **Specific gravity** 5.7
Solubility Water: 34.8 g l^{-1} at 20°C. Organic solvents: methanol

Occupational exposure

DE-MAK 0.5 mg m^{-3} (as Ba) (inhalable dust fraction)
FR-VME 0.5 mg m^{-3} (as Ba)
SE-LEVL 0.5 mg m^{-3} (as Ba)
UK-LTEL 0.5 mg m^{-3} (as Ba)
US-TWA 0.5 mg m^{-3} (as Ba)

UN No. 1884 **HAZCHEM Code** 2Z **Conveyance classification** toxic substance
Supply classification harmful

Risk phrases Harmful by inhalation and if swallowed (R20/22)
Safety phrases Keep out of reach of children (if sold to general public) – After contact with skin, wash immediately with plenty of water (S2, S28)

Ecotoxicity

Fish toxicity
Threshold concentration for toxicity to young sturgeon 50 mg l^{-1} (1).

Mammalian & avian toxicity

Carcinogenicity and chronic effects
The long-term effects of barium was investigated in Long-Evans rats and CD mice given 0 or 5 mg barium l^{-1} (administered as soluble salts) in drinking water throughout their lifetime. The incidence of tumours in treated animals was not significantly different from that of controls. It was concluded that under these conditions barium was not carcinogenic (2).

Irritancy
Dusts of barium oxide are potential dermal and nasal irritants (3).

Other effects

Other adverse effects (human)
Heavy exposure to dust may cause baritosis (4).
In humans symptoms of barium poisoning from soluble barium salts arise from stimulation of all forms of muscle and include vomiting, colic, diarrhoea, hypertension, convulsive tremors and muscular paralysis. Hypokalaemia is common. Death from cardiac or respiratory failure may occur (5).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Barium: guide level 100 μg l^{-1} (6).
Included in Schedule 6 (Release into Land: Prescribed Substances) of Statutory Instrument No. 472, 1991 (7).

Other comments

Experimental toxicology, Environmental fate, physico-chemical properties, ecotoxicology, environmental effects, exposure levels, workplace experience, epidemiology and human health effects reviewed (8,9).

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7. *S.I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
8. *Environmental Health Criteria 107: Barium* 1990, World Health Organisation, Geneva, Switzerland.
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

B15 barium perchlorate

$Ba(ClO_4)_2$

$BaCl_2O_8$ **Mol. Wt.** 336.23 **CAS Registry No.** 13465-95-7

Synonyms perchloric acid, barium salt

EINECS No. 236-710-4 **RTECS No.** SC 7550000

Uses Used in the determination of ribonuclease. Desiccant. Used in explosives and as an experimental rocket fuel.

Physical properties

M. Pt. 505°C **Specific gravity** 3.20

Solubility Water: 1985 g l^{-1} at 25°C. Organic solvents: ethanol

Occupational exposure

DE-MAK 0.5 mg m^{-3} (as Ba) (inhalable dust fraction)

FR-VME 0.5 mg m^{-3} (as Ba)

SE-LEVL 0.5 mg m^{-3} (as Ba)

UK-LTEL 0.5 mg m^{-3} (as Ba)

US-TWA 0.5 mg m^{-3} (as Ba)

UN No. 1447 **HAZCHEM Code** 2W **Conveyance classification** oxidising substance, toxic

Supply classification oxidising, harmful

Risk phrases Explosive when mixed with combustible material – Harmful by inhalation and if swallowed (R9, R20/22)

Safety phrases Keep out of reach of children (if sold to general public) – Take off immediately all contaminated clothing (S2, S27)

Other effects

Other adverse effects (human)

In humans symptoms of barium poisoning from soluble barium salts arise from stimulation of all forms of muscle and include vomiting, colic, diarrhoea, hypertension, convulsive tremors and muscular paralysis. Hypokalaemia is common. Death from cardiac or respiratory failure may occur (1).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Barium: guide level 100 μg l^{-1} (2).
Included in Schedule 6 (Release Into Land: Prescribed Substances) of Statutory Instrument No. 472, 1991 (3).

Other comments

Physico-chemical properties, Environmental fate, experimental toxicology, ecotoxicology, exposure levels, workplace experience, epidemiology and human health effects reviewed (4,5).

References

1. *Martindale: The Extra Pharmacopoeia* 31st ed., 1996, The Royal Pharmaceutical Society, London, UK.
2. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
3. *S.I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
4. *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 107: Barium* 1990, World Health Organisation, Geneva, Switzerland

B16 barium permanganate

$$Ba(MnO_4)_2$$

$BaMn_2O_8$ **Mol. Wt.** 375.20 **CAS Registry No.** 7787-36-2

Synonyms permanganic acid, barium salt

EINECS No. 232-110-1

Uses Dry cell depolariser. A strong disinfectant.

Physical properties

M. Pt. 200°C (decomp.) **Specific gravity** 3.77

Solubility Water: 625 g l^{-1} at 11°C. Organic solvents: ethanol (decomp.)

Occupational exposure

DE-MAK 0.5 mg m^{-3} (as Ba) (inhalable dust fraction)

FR-VME 0.5 mg m^{-3} (as Ba)

SE-LEVL 0.5 mg m^{-3} (as Ba)

UK-LTEL 0.5 mg m^{-3} (as Ba)

US-TWA 0.5 mg m^{-3} (as Ba)

UN No. 1448 **HAZCHEM Code** 2X **Conveyance classification** oxidising substance, toxic

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) – After contact with skin, wash immediately with plenty of water (S2, S28)

Other effects

Other adverse effects (human)

In humans symptoms of barium poisoning from soluble barium salts arise from stimulation of all forms of muscle and include vomiting, colic, diarrhoea, hypertension, convulsive tremors and muscular paralysis. Hypokalaemia is common. Death from cardiac or respiratory failure may occur (1).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Barium: guide level 100 μg l^{-1} (2).

Included in Schedule 6 (Release into Land: Prescribed Substances) of Statutory Instrument No. 472, 1991 (3).

Other comments

Environmental fate, experimental toxicology, physico-chemical properties, ecotoxicology, exposure levels, workplace experience, epidemiology and human health effects reviewed (4,5).

References

1. *Martindale: The Extra Pharmacopoeia* 31st ed., 1996, The Royal Pharmaceutical Society, London, UK.
2. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
3. *S.I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
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5. *Environmental Health Criteria 107: Barium* 1990, World Health Organisation, Geneva, Switzerland

B17 barium peroxide

BaO_2

BaO_2 **Mol. Wt.** 169.33 **CAS Registry No.** 1304-29-6

Synonyms barium dioxide; barium superoxide

EINECS No. 215-128-4 **RTECS No.** CR 0175000

Uses For bleaching, in textile dyeing and printing. In hydrogen peroxide and oxygen manufacture. Glass decoloriser.

Physical properties

M. Pt. 450°C **B. Pt.** 800°C (decomp.) **Specific gravity** 4.96

Occupational exposure

UN No. 1449 **HAZCHEM Code** 2Y **Conveyance classification** oxidising substance, toxic

Supply classification oxidising, harmful

Risk phrases Contact with combustible material may cause fire – Harmful by inhalation and if swallowed (R8, R20/22)

Safety phrases Keep out of reach of children (if sold to general public) – Keep away from food, drink and animal feeding stuffs – Take off immediately all contaminated clothing (S2, S13, S27)

Mammalian & avian toxicity

Acute data

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

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Barium: guide level 100 μg l^{-1} (2). Included in Schedule 6 (Release into Land: Prescribed Substances) of Statutory Instrument No. 472, 1991 (3).

Other comments

Physico-chemical properties, Environmental fate, experimental toxicology, ecotoxicology, exposure levels, workplace experience, epidemiology and human health effects reviewed (4,5).

References

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5. *Environmental Health Criteria 107: Barium* 1990, World Health Organisation, Geneva, Switzerland

B18 barium polysulfides (BaS_2)

BaS_2

BaS_2 **Mol. Wt.** 201.46 **CAS Registry No.** 12230-99-8

Synonyms barium disulfide

Physical properties

M. Pt. 925°C **Specific gravity** 3.84 (calculated)

Occupational exposure

Supply classification irritant

Risk phrases Contact with acids liberates toxic gas – Irritating to eyes, respiratory system and skin (R31, R36/37/38)

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)

Other effects

Other adverse effects (human)

In humans symptoms of barium poisoning from soluble barium salts arise from stimulation of all forms of muscle and include vomiting, colic, diarrhoea, hypertension, convulsive tremors and muscular paralysis. Hypokalaemia is common. Death from cardiac or respiratory failure may occur (1).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Barium: guide level 100 $\mu g\ l^{-1}$ (2).

Other comments

Physico-chemical and spectral properties reviewed (3).

Reviews on experimental toxicology, Environmental fate, physico-chemical properties, ecotoxicology, environmental effects, exposure levels, workplace experience, epidemiology and human health effects listed (4).

References

1. *Martindale: The Extra Pharmacopoeia* 31st ed., 1996, The Royal Pharmaceutical Society, London, UK.
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B19 barium polysulfides (BaS_3)

BaS_3

BaS_3 **Mol. Wt.** 233.53 **CAS Registry No.** 12231-01-5

Synonyms barium trisulfide (BaS_3)

Physical properties

M. Pt. 554-555°C **Specific gravity** 3.94

Occupational exposure

Supply classification irritant

Risk phrases Contact with acids liberates toxic gas – Irritating to eyes, respiratory system and skin (R31, R36/37/38)

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)

Other effects

Other adverse effects (human)

In humans symptoms of barium poisoning from soluble barium salts arise from stimulation of all forms of muscle and include vomiting, colic, diarrhoea, hypertension, convulsive tremors and muscular paralysis. Hypokalaemia is common. Death from cardiac or respiratory failure may occur (1).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Barium: guide level 100 $\mu g\ l^{-1}$ (2).

Other comments

Reviews on physico-chemical properties, human health effects, experimental toxicology, ecotoxicology, environmental effects, exposure levels, workplace experience and epidemiology listed (3).

Decomposes at >400°C to barium disulfide (4,5).

Oxidised in air to barium carbonate and barium sulfite. Oxidised in aqueous solution to barium hexahydrate (6). Stable to 250°C.

Evaporation of aqueous solution gives barium hexahydrate and barium tetrahydrate.

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1. *Martindale: The Extra Pharmacopoeia* 31st ed., 1996, The Royal Pharmaceutical Society, 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.
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B20 barium polysulfides (BaS_4)

BaS_4

BaS_4 **Mol. Wt.** 265.59 **CAS Registry No.** 12448-67-8

Synonyms barium tetrasulfide

Physical properties

Specific gravity 3.11
Solubility Water: 410 g l^{-1} at 15°C

Occupational exposure

UK-LTEL 0.5 mg m^{-3} (as Ba)
Supply classification irritant
Risk phrases Contact with acids liberates toxic gas – Irritating to eyes, respiratory system and skin (R31, R36/37/38)
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)

Other effects

Other adverse effects (human)
In humans symptoms of barium poisoning from soluble barium salts arise from stimulation of all forms of muscle and include vomiting, colic, diarrhoea, hypertension, convulsive tremors and muscular paralysis. Hypokalaemia is common. Death from cardiac or respiratory failure may occur (1).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Barium: guide level 100 μg l^{-1} (2).

Other comments

Reviews on physico-chemical properties, human health effects, experimental toxicology, ecotoxicology, environmental effects, exposure levels, workplace experience and epidemiology listed (3).
Piezoelectric (4).
Decomposes at >200-300°C to sulfur, water, hydrogen sulfide and barium trisulfide.

References

1. *Martindale: The Extra Pharmacopoeia* 31st ed., 1996, The Royal Pharmaceutical Society, 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.
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4. Abrahams, S. C. et al *Acta Crystallogr.* 1954, **7**, 423-429

B21 barium polysulfides (BaS_5)

$$BaS_5$$

BaS_5 **Mol. Wt.** 297.66 **CAS Registry No.** 12448-68-9

Synonyms barium pentasulfide

Occupational exposure

Supply classification irritant

Risk phrases Contact with acids liberates toxic gas – Irritating to eyes, respiratory system and skin (R31, R36/37/38)

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)

Other effects

Other adverse effects (human)

In humans symptoms of barium poisoning from soluble barium salts arise from stimulation of all forms of muscle and include vomiting, colic, diarrhoea, hypertension, convulsive tremors and muscular paralysis. Hypokalaemia is common. Death from cardiac or respiratory failure may occur (1).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Barium: guide level 100 $\mu g\ l^{-1}$ (2).

Other comments

Reviews on physico-chemical properties, human health effects, experimental toxicology, ecotoxicology, environmental effects, exposure levels, workplace experience and epidemiology listed (3).

Appears to exist only in solution. Decomposes to barium tetrasulfide, barium sulfite, hydrogen sulfide, sulfur and water (4).

References

1. *Martindale: The Extra Pharmacopoeia* 31st ed., 1996, The Royal Pharmaceutical Society, London, UK.
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B22 barium polysulfides (Ba_2S_3)

$$Ba_2S_3$$

Ba_2S_3 **Mol. Wt.** 370.85 **CAS Registry No.** 53111-28-7

Synonyms dibarium trisulfide

Physical properties

Specific gravity 4.13 at 25°C with respect to water at 4°C

Occupational exposure

Supply classification irritant
Risk phrases Contact with acids liberates toxic gas – Irritating to eyes, respiratory system and skin (R31, R36/37/38)
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)

Other effects

Other adverse effects (human)
In humans symptoms of barium poisoning from soluble barium salts arise from stimulation of all forms of muscle and include vomiting, colic, diarrhoea, hypertension, convulsive tremors and muscular paralysis. Hypokalaemia is common. Death from cardiac or respiratory failure may occur (1).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Barium: guide level 100 $\mu g\ l^{-1}$ (2).

Other comments

Reviews on physico-chemical properties, human health effects, experimental toxicology, ecotoxicology, environmental effects, exposure levels, workplace experience and epidemiology listed (3).

References

1. *Martindale: The Extra Pharmacopoeia* 31st ed., 1996, The Royal Pharmaceutical Society, 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. *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

B23 barium polysulfides (Ba_4S_7)

$$Ba_4S_7$$

Ba_4S_7 **Mol. Wt.** 773.77 **CAS Registry No.** 50864-67-0
Synonyms tetrabarium heptasulfide
EINECS No. 256-814-3 **RTECS No.** CR 0270000
Uses Superseded insecticide and fungicide.

Occupational exposure

Supply classification irritant
Risk phrases Contact with acids liberates toxic gas – Irritating to eyes, respiratory system and skin (R31, R36/37/38)
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)

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 375 mg kg^{-1} (1).
TD_{Lo} oral human 226 mg kg^{-1} (2).

Other effects

Other adverse effects (human)

In humans symptoms of barium poisoning from soluble barium salts arise from stimulation of all forms of muscle and include vomiting, colic, diarrhoea, hypertension, convulsive tremors and muscular paralysis. Hypokalaemia is common. Death from cardiac or respiratory failure may occur (3,4).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Barium: guide level 100 μg l^{-1} (5).
Included in Schedule 6 (Release into Land: Prescribed Substances) of Statutory Instrument No. 472, 1991 (6).

Other comments

Reviews on physico-chemical properties, human health effects, experimental toxicology, ecotoxicology, environmental effects, exposure levels, workplace experience and epidemiology listed (7).
Oxidised in air to barium sulfite. Loses water of crystallisation at 100°C-230°C to give hydrogen sulfide and barium sulfite (8).

References

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3. *Environmental Health Criteria 107: Barium* 1990, World Health Organisation, Geneva, Switzerland.
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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.
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B24 barium sulfate

$$BaSO_4$$

BaO_4S **Mol. Wt.** 233.39 **CAS Registry No.** 7727-43-7

Synonyms Blanc Fixe; Barosperse; Barotrast; Oratrast; sulfuric acid, barium salt (1:1)

EINECS No. 231-784-4 (natural) **RTECS No.** CR 0600000

Uses In the manufacture of photographic paper and cellophane. A filler for rubber, lino, oil cloth. Pigment in white paint. Diagnostic aid (radio-opaque medium).
Occurrence In nature as the mineral barite.

Physical properties

M. Pt. 1350°C **B. Pt.** 1580°C (decomp.) **Specific gravity** 4.500 at 15°C
Solubility Water: 2.23 mg l^{-1} at 25°C

Occupational exposure

UK-LTEL 10 mg m^{-3} (total inhalable dust), 4 mg m^{-3} (respirable dust)
US-TWA 10 mg m^{-3}

UN No. 1564 **HAZCHEM Code** 2Z

Ecotoxicity

Fish toxicity

Barium sulfate used to weight drilling fluid was not toxic to fish at concentrations up to 100,000 ppm in fresh or sea water. Therefore does not constitute the introduction of a toxic material into the environment (1).

Mammalian & avian toxicity

Metabolism and toxicokinetics

In ♀ beagle dog, barium sulfate was cleared from lung with $t_{1/2}$ 8-9 days indicating some solubility in body fluids, possibly in colloidal form (2).

After rat inhalation of barium sulfate 40 mg m^{-3} 5 hr day^{-1} for 2 months, lymphatic transport was slight. Skeletal concentration of barium was 0.8-1.5 mg day^{-1} and skeletal uptake decreased with advancing age (2).

In patients with a normal gastrointestinal tract barium sulfate is excreted unchanged within 24 hr after oral administration. After rectal administration the compound is usually excreted when the enema is expelled, however some may remain in the colon for several wk (3).

Sensitisation

Patients with history of atopy may be susceptible to allergic reactions if exposed to barium sulfate (4).

Other effects

Other adverse effects (human)

A benign pneumoconiosis (baritosis) may result from the inhalation of barium sulfate dust (5-7).

Baritosis was reported among workers exposed to finely ground barium sulfate in the US, Germany and Czechoslovakia, but no firm conclusions could be drawn (8).

Constipation may occur after oral or rectal barium sulfate administration. Impaction, obstruction and appendicitis have occurred. Cramping and diarrhoea have also been reported. Intravasation has led to the formation of emboli; deaths have occurred. Perforation of the bowel has led to peritonitis, adhesions, granulomas and death. The use of barium sulfate for bronchography by aspiration into the lungs has led to pneumonitis or granuloma formation. Cardiac arrhythmias have occurred during the use of barium sulfate enemas (9).

Any other adverse effects

Intra-uterine subcutaneous injection into rabbit foetuses caused acute inflammatory response in both vascular and cellular components (10).

In vitro mouse peritoneal macrophages exposed to barium sulfate for up to 144 hr showed marked cytoplasmic vacuolisation with only partial recovery (11).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Barium: guide level 100 µg l^{-1} (12).

Other comments

In systems having pH ≤5 barium sulfate did not dissolve even in anaerobic conditions (13).

Experimental toxicology, Environmental fate, workplace experience, physico-chemical properties, ecotoxicology, exposure levels, epidemiology and human effects reviewed (14-16).

References

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3. *American Hospital Formulary Service – Drug Information 88* 1988, 1317, American Society of Hospital Pharmacists, Bethesda, MD, USA.
4. Feczko, P. J. et al *Am. J. Roetenology* 1989, **153**, 275.
5. *Br. Med. J.* 1972, **2**, 5813.
6. Browning, E. *Toxicity of Industrial Metals* 2nd ed., 1969, 61-66, Butterworth and Co, London, UK.
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8. Pendergrass, E. P. et al *Arch. Ind. Health* 1953, **7**, 44.
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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.
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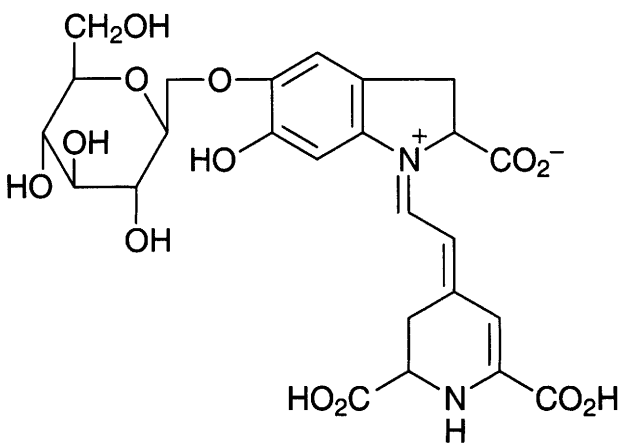
B25 Beetroot Red



$C_{24}H_{26}N_2O_{13}$ **Mol. Wt.** 550.48 **CAS Registry No.** 57917-55-2

Synonyms C.I. Natural Red 33; E162; 2,6-piperidinedicarboxylic acid 4-[2-[2-carboxy-5-(β-D-glucopyranosyloxy)-2,3-dihydro-6-hydroxy-1*H*-indol-1-yl]ethylidene

RTECS No. CT 3400000

Uses Food dyestuff.

Occurrence Extract from red beetroot (*Beta vulgaris*) consists of red and yellow quaternary ammonium amino acid pigments of the betalamino class.

Genotoxicity

Salmonella typhimurium TA100 with and without metabolic activation positive (1).
In vitro Chinese hamster fibroblast cells negative (1).

Other comments

Experimental toxicology and human health effects reviewed (2).
The chemistry, manufacture and safety, of beetroot red used as a food additive reviewed (3).
Nitrate levels in liquid and powdered beet red varied from 391-34,181 mg kg^{-1}. Acceptable daily intake was not established for beetroot red as the compound was not considered hazardous to health (4).

References

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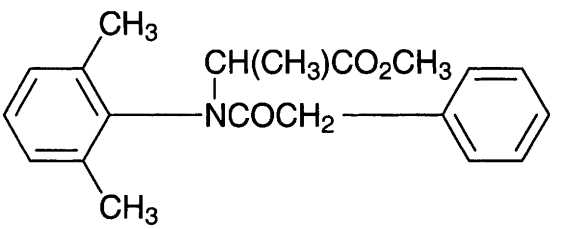
B26 benalaxyl



$C_{20}H_{23}NO_3$ **Mol. Wt.** 325.41 **CAS Registry No.** 71626-11-4

Synonyms methyl *N*-phenylacetyl-*N*-2,6-xylyl-DL-alaninate; methyl *N*-(2,6-dimethylphenyl)-*N*-(phenylacetyl)-DL-alaninate; Galben Tairel

EINECS No. 275-728-7 **RTECS No.** AY 5993200

Uses Fungicide.

Physical properties

M. Pt. 78-80°C **Flash point** 195°C (open cup) **Specific gravity** 1.27 at 25°C **Volatility** v.p. 5.0×10^{-6} mmHg at 25°C
Solubility Water: 37 mg l^{-1} at 25°C. Organic solvents: acetone, chloroform, cyclohexanone, dichloromethane, DMF, hexane, xylene

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) rainbow trout, carp, guppy, goldfish 3.75, 6.0, 7.0, 7.6 mg l^{-1}, respectively (1).

Invertebrate toxicity
LC_{50} (48 hr) earthworm 0.0035 mg cm^{-2} (1).
Non-toxic to bees; LD_{50} >100 μg bee^{-1} (1).

Environmental fate

Degradation studies
$t_{1/2}$ in soil 20-71 days (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral mallard duck >6000 mg kg^{-1} (1).
LD_{50} oral bobwhite, Japanese quail >5000 mg kg^{-1} (1).
LD_{50} oral rat 4200 mg kg^{-1} (1).
LD_{50} oral mouse 680 mg kg^{-1} (1).
LC_{50} (4 hr) inhalation rat >10 mg l^{-1} (1).
LD_{50} percutaneous rat >5000 mg kg^{-1} (1).
LD_{50} intraperitoneal rat 1100 mg kg^{-1} (1).

Sub-acute and sub-chronic data

LD_{50} (5-day) oral bobwhite quail >5000 mg kg^{-1} diet (1).
No-effect level for rats in 90-day feeding trials 1000 mg kg^{-1} diet (1).
No-effect level for dogs in 1-yr feeding trials 200 mg kg^{-1} diet (1).

Carcinogenicity and chronic effects

Considered non-carcinogenic (1).

Teratogenicity and reproductive effects

Considered non-teratogenic (1).

Metabolism and toxicokinetics

Oral rat, rapidly metabolised and eliminated in urine (23%) and faeces (75%) within 2 days (1).

Irritancy

Non-irritating to skin and eyes of rabbits (1).

Sensitisation

Non-sensitising to skin of guinea-pigs (1).

Genotoxicity

Considered non-mutagenic (1).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides and related products: maximum admissible concentration 0.1 µg l^{-1} (2).
Included in Schedule 6 (Release into Land: Prescribed Substances) of Statutory Instrument No. 472, 1991 (3).
Human ADI 0.05 mg kg^{-1} body weight (1).
WHO Toxicity Class Table 5 (4).
EPA Toxicity Class III (1).

References

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2. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
3. *S.I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
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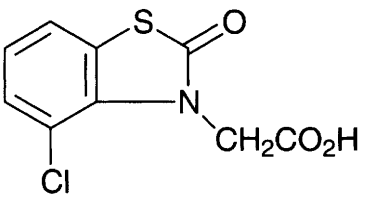
B27 benazolin



$C_9H_6ClNO_3S$ **Mol. Wt.** 243.67 **CAS Registry No.** 3813-05-6

Synonyms benazoline; 4-chloro-2-oxobenzothiazolin-3-ylacetic acid; 4-chloro-2,3-dihydro-2-oxobenzothiazol-3-ylacetic acid; 4-chloro-2-oxo-3(2*H*)-benzothiazoleacetic acid; 4-chloro-2-oxo-3-benzothiazolineacetic acid; Asepta Brazolin; Benasalox; Benazalox; Benazolinester; Cornox CWK

EINECS No. 223-297-0 **RTECS No.** AF 9700000

Uses Herbicide.

Physical properties

M. Pt. 193°C **Volatility** v.p. 0.003 mmHg at 20°C

Solubility Water: 500 mg l^{-1} at 20°C. Organic solvents: acetone, ethanol, ethyl acetate, isopropanol

Occupational exposure

Supply classification irritant

Risk phrases Irritating to eyes and skin (R36/38)

Safety phrases Keep out of reach of children (if sold to general public) – Do not breathe dust (S2, S22)

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) bluegill sunfish 27 mg l^{-1} (1).

LC_{50} (96 hr) trout 31.3 mg l^{-1} (1).

LC_{50} (24 hr) harlequin fish 360 ppm (2).

Invertebrate toxicity

EC_{50} (48 hr) *Daphnia* 233.4 mg l^{-1} (1).

Non-toxic to bees; LD_{50} 480 µg bee^{-1} (1).

Environmental fate

Degradation studies

Degrades principally to bound residues. $t_{1/2}$ *ca.* 14-28 days (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat >5000 mg kg^{-1} (1).

LD_{50} oral mouse >4000 mg kg^{-1} (1).

LD_{50} percutaneous rat >5000 mg kg^{-1} (1).

LD_{50} oral Japanese quail >10,200 mg kg^{-1} (1).

Sub-acute and sub-chronic data

No-observable-effect level (90 days) rats 300-1000 mg kg^{-1} day^{-1}, dogs 300 mg kg^{-1} day^{-1} (1).

Metabolism and toxicokinetics

In urine, major metabolites are *N*-[2-chloro-6-(methylsulfinyl)phenyl]glycine and *N*-[*N*-[2-chloro-6-(methylthio)phenyl]glycinyl]aniline. There are also small amounts of other acid-labile polar conjugates of benazolin acid, and *N*-[2-chloro-6-(methylthio)phenylglycine]. Faecal metabolites are similar to those in urine (species unspecified) (1).

Irritancy

Mild skin and eye irritant in rabbits (1).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides and related products: maximum admissible concentration 0.1 $\mu g\ l^{-1}$ (3).

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

Toxicity Class EPA III (1).

Other comments

The alkali-metal and diethanolamine salts are readily soluble in water (2).

References

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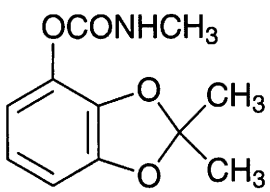
B28 bendiocarb



$C_{11}H_{13}NO_4$ **Mol. Wt.** 223.23 **CAS Registry No.** 22781-23-3

Synonyms 2,2-dimethyl-1,3-benzodioxol-4-yl methylcarbamate; methylcarbamic acid, 2,3-(isopropylidenedioxy)phenyl ester; bencarbate; 2,2-dimethyl-4-[(*N*-methylamino)carboxylato]-1,3-benzodioxole; 1,3-benzodioxol-4-ol, 2,2-dimethyl-, methylcarbamate; carbamic acid, methyl-, 2,3-(isopropylidenedioxy)phenyl ester; 2,3-(dimethylmethylenedioxy)-phenyl methylcarbamate; Ficam; Rotate

EINECS No. 245-216-8 **RTECS No.** FC 1140000

Uses Contact and systemic insecticide.

Physical properties

M. Pt. 124.6-128.7°C **Partition coefficient** log P_{ow} 1.72 (pH 6.55)

Solubility Water: 0.2 $g\ l^{-1}$ (pH 7.0, 20°C). Organic solvents: acetone, chloroform, dichloromethane, dioxane, hexane

Occupational exposure

Supply classification toxic
Risk phrases Harmful in contact with skin – Toxic if swallowed (R21, R25)
Safety phrases Keep locked up and out of the reach of children (if sold to general public) – 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

Invertebrate toxicity
Oral LD_{50} honeybees, 0.1 μg bee^{-1} (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 40-156 mg kg^{-1} (2).
LD_{50} dermal rat 1000 mg kg^{-1} (3).
LC_{50} (4 hr) inhalation rat 0.55 mg l^{-1} (1).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (4).
ADI (JMPR) 0.004 mg kg^{-1} body weight (1).
WHO Toxicity Class II (5).
EPA Toxicity Class II (1).

References

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2. *Farm Chemicals Handbook* 1991, **29**, 83, Meister Publ. Co., Willoughby, OH, USA.
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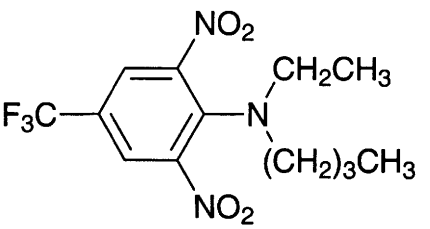
B29 benfluralin



$C_{13}H_{16}F_3N_3O_4$ **Mol. Wt.** 335.28 **CAS Registry No.** 1861-40-1
Synonyms *N*-butyl-*N*-ethyl-α,α,α-trifluoro-2,6-dinitro-*p*-toluidine; *N*-butyl-*N*-ethyl-2,6-dinitro-4-(trifluoromethyl)benzenamine; *N*-butyl-*N*-ethyl-2,6-dinitro-4-trifluoromethylaniline; Balfin; Benafine; Benefex; Bonalan; Flubalex; Flural; Quilan

EINECS No. 217-465-2 **RTECS No.** XU 4550000

Uses Herbicide.

Physical properties

M. Pt. 65-66°C **B. Pt.** 121-122°C at 0.5 mmHg, 148-149°C at 7 mmHg **Flash point** 25.6°C
Specific gravity 1.28 (technical grade) at 20°C **Partition coefficient** log P_{ow} 5.29 at 20°C and pH 7 (1)
Volatility v.p. 2.78×10^{-5} mmHg at 25°C
Solubility Water: 0.1 mg l^{-1} at 25°C. Organic solvents: acetone, acetonitrile, chloroform, dichloromethane, ethyl acetate, toluene

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) bluegill sunfish, rainbow trout, 6.0, 0.081 mg l^{-1}, respectively (1).

Invertebrate toxicity
LC_{50} (96 hr) freshwater shrimp 1.1 mg l^{-1} (2).
EC_{50} (48 hr) *Daphnia* >0.1 mg l^{-1} (1).
Selenastrum capricornutum (7 days) 3.68 mg l^{-1} reduced specific growth rate and terminal biomass by 16.6% and 34.3%, respectively (1).

Environmental fate

Degradation studies
Residual activity in soil 4-8 months (1).
Estimated degradation in soil at 30°C, $t_{1/2}$ 0.4-1.8 months (3).

Adsorption and retention
Strongly adsorbed on soil with negligible leaching; surface material was removed by photodecomposition (4).

Mammalian & avian toxicity

Acute data
LD_{50} oral mallard duck, chicken, bobwhite quail >2000 mg kg^{-1} (1).
LD_{50} oral rat, mouse >10,000, >5000 mg kg^{-1}, respectively (1).
LD_{50} oral dog, rabbit >2000 mg kg^{-1} (1).
LD_{50} percutaneous rabbit >5000 mg kg^{-1} (1).

Carcinogenicity and chronic effects
In 2-yr feeding trial with rats the no-effect level was 1 g kg^{-1} diet and with mice 6.5 mg kg^{-1} body weight day^{-1} (1).

Metabolism and toxicokinetics
Oral goat (5 day) after administration of an unspecified dose 90% and 10% were excreted in faeces and urine, respectively (5).

Irritancy
Skin and eye irritation reported in humans (6).
Non-irritating to eyes and skin of rabbits (1).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides and related products: maximum admissible concentration 0.1 μg l^{-1} (7).
Included in Schedule 6 (Release into Land: Prescribed Substances) of Statutory Instrument No. 472, 1991 (8).
Human ADI 0.065 mg kg^{-1} (1).
WHO Toxicity Class Table 5 (9).
EPA Toxicity Class IV (1).

Other comments

Hazardous properties reviewed (10).
Decomposes in ultra-violet light.
Metabolic pathways reviewed (11).

References

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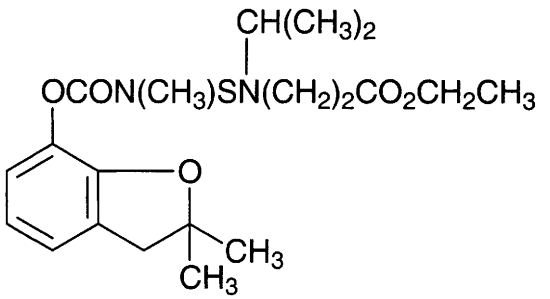
B30 benfuracarb



$C_{20}H_{30}N_2O_5S$ **Mol. Wt.** 410.53 **CAS Registry No.** 82560-54-1

Synonyms ethyl *N*-[2,3-dihydro-2,2-dimethylbenzofuran-7-yloxycarbonyl(methyl)aminothio]-*N*-isopropyl-β-alaninate; 2,3-dihydro-2,2-dimethyl-7-benzofuranyl, 2-methyl-4-(1-methylethyl)-7-oxo-8-oxa-3-thia-2,4-diazadecanoate; 2-methyl-4-(1-methylethyl)-7-oxo-8-oxa-3-thia-2,4-diazadecanoic acid 2,3-dihydro-2,2-dimethyl-7-benzofuranyl ester; Benfuracarbe; Oncol; Furacon; Nakar

RTECS No. AY 5088000

Uses Insecticide.

Physical properties

B. Pt. 110°C at 0.03 mmHg **Flash point** 114°C (closed cup) **Specific gravity** 1.142 at 20°C
Partition coefficient log P_{ow} 4.30 at 20°C and pH 7 (1) **Volatility** v.p. 2×10^{-7} mmHg at 20°C
Solubility Water: 8 mg l^{-1} at 20°C. Organic solvents: acetone, benzene, dichloromethane, ethyl acetate, hexane, methanol, xylene

Ecotoxicity

Fish toxicity

LC_{50} (48 hr) carp 0.65 mg l^{-1} (1).

Invertebrate toxicity

EC_{50} (3 hr) *Daphnia magna* >10 mg l^{-1} (1).

LD_{50} topical bee 0.29 μg g^{-1} (1).

Environmental fate

Degradation studies

$t_{1/2}$ in soil is *ca.* 4-28 hr. Under upland conditions benfuracarb is decomposed to carbofuran, while under flooded conditions carbofuran phenol is also found as a major degradation product (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral hen 92 mg kg^{-1} (1).

LD_{50} oral rat ~30 mg kg^{-1} (2).

LD_{50} oral rat, mouse 138, 175 mg kg^{-1}, respectively (1).

LD_{50} oral dog 300 mg kg^{-1} (1).

LC_{50} (duration unspecified) inhalation ♂ rats 0.61 mg l^{-1} (1).

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

Carcinogenicity and chronic effects

No-observable-effect level (2 yr) for rats 25 mg kg^{-1} diet (1).

Considered non-carcinogenic in rats and mice (1).

Teratogenicity and reproductive effects

Considered non-teratogenic in rats and rabbits (1).

Metabolism and toxicokinetics

In rats, benfucarb is metabolised rapidly and almost completely excreted in the urine and faeces with 7 days. Major metabolites in the faeces are carbofuran, carbofuran phenol, 3-hydroxycarbofuran, 3-hydroxyphenol, and 3-ketophenol. Urinary metabolites are β-glucuronide conjugates of these metabolites (1).

Irritancy

Non-irritating to skin but slightly irritating to the eyes of rabbits (1).

Sensitisation

Non-sensitising to guinea pig skin (1).

Genotoxicity

Considered non-mutagenic in rats and rabbits (1).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides and related products: maximum admissible concentration 0.1 μg l^{-1} (2).

Included in Schedule 6 (Release into Land: Prescribed Substances) of Statutory Instrument No. 472, 1991 (3).

WHO Toxicity Class Ib (4).

Other comments

Cholinesterase inhibitor. IC_{50} human erythrocyte acetylcholinesterase, human serum butyrylcholinesterase, *Drosophila* nervous system cholinesterase 117.5, 2540, 42 μM, respectively (5).

The metabolism of ring 14C-labelled benfuracarb was examined in cotton, bean and corn. Initial degradation step

is N-S bond cleavage giving rise to carbofuran as the first major metabolite. Carbofuran is further metabolised to 3-hydroxy carbofuran which is in turn conjugated. Carbofuran is significant in the early period after treatment while 3-hydroxycarbofuran is important during later stages (6).

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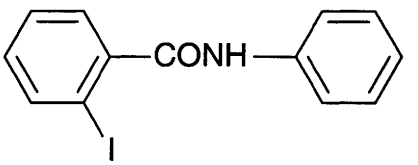
B31 benodanil



$C_{13}H_{10}INO$ **Mol. Wt.** 323.13 **CAS Registry No.** 15310-01-7

Synonyms 2-iodobenzanilide; 2-iodo-*N*-phenylbenzamide; calirus; BAS 3170F

EINECS No. 239-352-7 **RTECS No.** CV 8710000

Uses Superseded fungicide for rust diseases.

Physical properties

M. Pt. 137°C **Volatility** v.p. $<7.52 \times 10^{-8}$ mmHg at 20°C

Solubility Water: 20 mg l^{-1} at 20°C. Organic solvents: acetone, chloroform, ethanol, ethyl acetate

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) trout 6.4 mg l^{-1} (1).

Invertebrate toxicity

Non-toxic to bees (1).

Environmental fate

Degradation studies

$t_{1/2}$ in loamy and humous sandy soil 3-4 wk (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, guinea pig >6400 mg kg^{-1} (1).

LD_{50} percutaneous rats >2000 mg kg^{-1} (1).

Sub-acute and sub-chronic data

No-effect-level for rats in 90-day feeding trials was 100 mg kg^{-1} diet (1).

Metabolism and toxicokinetics
After oral administration to rats 80% is excreted in faeces and 16% in urine within 6 days. Principal metabolites are the 4-hydroxy-derivative and its glucuronide and sulfate conjugates (1).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides and related products: maximum admissible concentration 0.1 μg l^{-1} (2).
Included in Schedule 6 (Release into Land: Prescribed Substances) of Statutory Instrument No. 472, 1991 (3).

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1. *The Agrochemicals Handbook* 3rd ed., 1991, The Royal Society of Chemistry, London, UK.
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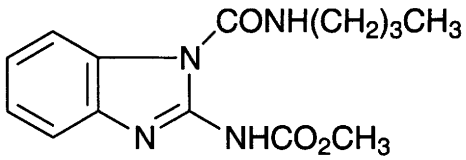
B32 benomyl



$C_{14}H_{18}N_4O_3$ **Mol. Wt.** 290.32 **CAS Registry No.** 17804-35-2

Synonyms methyl 1-(butylcarbamomyl)benzimidazol-2-ylcarbamate; methyl 1-[(butylamino)carbonyl]-1*H*-benzimidazol-2-ylcarbamate; methyl 1-(butylcarbamoyl)-2-benzimidazolecarbamate; Benlate; Benex; Fundazol

EINECS No. 241-775-7 **RTECS No.** DD 6475000

Uses Fungicide. Acaricide. Used to increase the biological oxidation rate of sewage and fertilisers.

Physical properties

Solubility Water: 4 mg l^{-1} at 25°C (pH 3-10). Organic solvents: acetone, chloroform, dimethylformamide, ethanol, xylene

Occupational exposure

FR-VME 0.8 ppm (10 mg m^{-3})
UK-LTEL 10 mg m^{-3} **UK-STEL** 15 mg m^{-3}
US-TWA 10 mg m^{-3}
Supply classification harmful
Risk phrases Possible risk of irreversible effects (R40)
Safety phrases Keep out of reach of children (if sold to general public) – Wear suitable protective clothing and gloves (S2, S36/37)

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) rainbow trout 170 μg l^{-1} at 12°C – technical material (1).
LC_{50} (96 hr) fathead minnow 2200 μg l^{-1} at 22°C – technical material (1).
LC_{50} (96 hr) channel catfish 29 μg l^{-1} at 22°C – technical material (1).
LC_{50} (96 hr) fathead minnow, bluegill sunfish 1200-1900 μg l^{-1} at 22°C – wettable powder (1).
LC_{50} (96 hr) channel catfish 28 μg l^{-1} at 22°C – wettable powder (1).

Invertebrate toxicity

LC_{50} (96 hr) crayfish 1032 mg l^{-1} (2).
Highly toxic to earthworms (3).
Suppresses earthworm feeding and is toxic on contact (4).
The toxicity of benomyl to a small *Enchytraeus* sp. worm decreased with increasing soil moisture (5).
Non-toxic to *Apis mellifera* (6).

Environmental fate

Nitrification inhibition

Nitrobacter agilis effect of 0 ppm benomyl addition, 289.5 μg nitrite ml^{-1}, 10 ppm addition (513.2 days) and 100 ppm addition (440.5 days) 444.2 μg nitrite ml^{-1} (7).
Nitrosomonas spp. effect of 0 ppm benomyl addition 3.8 μg nitrite ml^{-1}, 10 ppm addition (2.1 days) 2.0 μg nitrite ml^{-1}, 100 ppm addition (2 days) 1.7 μg nitrite ml^{-1} (7).
Symbiotic interactions between nitrogen fixing bacteria and three strains of *Rhizobium* (*R. leguminosarum, R. Meliloti and R. loti*) were adversely affected by the presence of benomyl (amount unspecified). Nodule formation decreased (8).
1000 ppm benomyl inhibited nitrification in a simulated oxidised surface of a flooded soil during a 30-day incubation period. Nitrification was not strongly inhibited at ≤100 ppm. Hydrolysis products detected were methyl-2-benzimidazolecarbamate and 2-aminobenzimidazole; both were less inhibitory of nitrification than benomyl (9).

Degradation studies

$t_{1/2}$ in soil and water 2 and 19 hr, respectively (6).
Mixed bacterial cultures grew with benomyl as sole carbon source, but rates of breakdown to methyl benzimidazol-2-ylcarbamate were small and 2-aminobenzimidazole did not support growth (10).

Abiotic removal

In aqueous solutions under acidic conditions, benomyl is hydrolysed to methyl 2-benzimidazole carbamate and butyl isocyanate. In water, the conversion of benomyl into methylbenzimidazole-2-yl carbamate (carbendazim) is completed within 1 wk (11).

Adsorption and retention

Laboratory and greenhouse experiments showed that benomyl and its two soil metabolites, methyl 2-benzimidazole carbamate and 2-aminobenzimidazole were immobile in soils (organic content ranged from 0.7-83.5%). No leaching or significant movement from the site of application (12).
Calculated bioconcentration factor 290 (13).

Mammalian & avian toxicity

Acute data

LD_{50} oral starling >100 mg kg^{-1} (6).
LD_{50} oral rat >9590 mg kg^{-1} (14).
LC_{50} (4 hr) inhalation rat >2 mg l^{-1} in air (6).
LD_{50} percutaneous rabbit >10,000 mg kg^{-1} (6).

Sub-acute and sub-chronic data

LC_{50} (8-day) dietary mallard duck, bobwhite quail >500 mg kg^{-1} (6).

Inhalation ♂, ♀ rat (90 day) ≤200 mg m^{-3} 6 hr day^{-1} 5 day wk^{-1} caused degeneration of the olfactory epithelium in all animals exposed to 200 mg m^{-3} (15).
Oral rat (7-day) 0-600 mg kg^{-1}. Cellular swelling and oedema in liver, kidney, and spleen (16).

Carcinogenicity and chronic effects
No-effect level for rats in 2-yr feeding trials >2500 mg kg^{-1} diet and for dogs 500 mg kg^{-1} diet (6).

Teratogenicity and reproductive effects
Gavage pregnant Sprague-Dawley rats (7-21 day gestation) 31.2-125 mg kg^{-1}. Malformations increased in incidence and severity with increasing benomyl dosage and nearly doubled with a protein-deficient diet. Effects included foetal resorptions and late foetal death, anomalies included hydrocephalus, exencephaly and periventricular overgrowth. Common systemic malformations included cleft palate, micromelia, hydroureter and misshapen tails (17).
Oral gravid CD1 mice (5 day) 200 mg kg^{-1} in corn oil. Positive teratogenic effects included reduced litter size and viability (18).
Four-day-old *Drosophila melanogaster* pairs were maintained on a nutritive media treated with benomyl (amount unspecified) for 1-6 wk. There was an overall reduction in egg mass which returned to normal on termination of the treatment (19).
Adult ♂ Sprague-Dawley rats were given single oral doses of 25-800 mg kg^{-1} benomyl. Primary effects were testicular swelling and occlusions of the efferent ductules. Premature release of germ cells was detected even with lowest dosage. Ductule occlusions were dose-dependent and correlated with testicular weight. Long-term effects were decreased testicular weight and dose-dependent seminiferous tubular atrophy (20).

Metabolism and toxicokinetics
In animals, the butylcarbamoyl group is split off to give the relatively stable carbendazim, followed by slow degradation to non-toxic 2-aminobenzimidazole. Hydroxylation also occurs, and the principal metabolite 5-hydroxybenzimidazolecarbamate is converted into the *O*- and *N*-conjugates. In rats and dogs, following a single oral dose, 99% of benomyl and its metabolites are excreted in the urine and faeces within 72 hr. There is no accumulation of benomyl or its metabolites in animal tissue (6).

Sensitisation
Extreme sensitisation observed in guinea pig maximisation test (21).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537 with and without metabolic activation negative (22).
Salmonella typhimurium TA98, TA100, TA1535, TA1537, and *Escherichia coli* WP2 hcr with and without metabolic activation negative (23).
Saccharomyces cerevisiae D7 with and without metabolic activation negative (24).
In vitro human lymphocytes, 0.5-2.0 μg ml^{-1} caused decreases in the number of cells undergoing third division, 0.25-4.0 μg ml^{-1} strongly increased the number of aneuploid cells and increased sister chromatid exchange (25).
In vitro mouse bone marrow cells induced micronuclei, polyploidy and hyperdiploidy (26).

Other effects

Any other adverse effects
Exposure of cucumber seedlings to a suspension of benomyl severely inhibited primary and secondary root development (27).
The effect of benomyl on the DNA turnover in various organs of the mouse was evaluated by measuring the incorporation of [3H]thymidine 24 hr after administration of single oral doses of 377, 740 or 1480 mg kg^{-1}. Mice were sacrificed at 24 hr and inhibition of [3H]thymidine was observed in liver and kidney at the lowest dose while at the higher doses inhibition of [3H]thymidine occurred in the thymus, spleen and testis (28).

Legislation

Included in Schedule 6 (Release into Land: Prescribed Substances) of Statutory Instrument No. 472, 1991 (29).
Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides and related products: maximum admissible concentration 0.1 μg l^{-1} (30).

Other comments

Considered to have endocrine disruptive effects. Caused impaired fish growth and reduced embryo survival.
Mysid reproduction impaired (31).
Experimental toxicology, genotoxicity, teratogenicity and carcinogenicity reviewed (23,32-33).
Toxicity and hazards reviewed (34).
Health risks from Occupational exposure reviewed (35,36).

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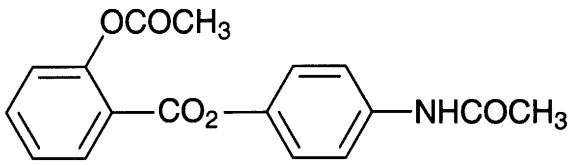
B33 benorylate



$C_{17}H_{15}NO_5$ **Mol. Wt.** 313.31 **CAS Registry No.** 5003-48-5

Synonyms 4-acetamidophenyl acetylsalicylate; 4-(acetamido)phenyl 2-acetoxybenzoate; 2-(acetyloxy)benzoic acid 4-(acetylamino)phenyl ester

EINECS No. 225-674-5 **RTECS No.** VO 7200000

Uses Analgesic. Anti-inflammatory and antipyretic.

Physical properties

M. Pt. 175-176°C

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse 2000 mg kg^{-1} (1).
LD_{50} intraperitoneal mouse, rat 1260, 1830 mg kg^{-1}, respectively (1).
LD_{50} oral mouse 2700 mg kg^{-1} death due to respiratory arrest (2).

Sub-acute and sub-chronic data

TD_{Lo} (8-day) ingestion woman 1280 mg kg^{-1} caused central nervous system and pulmonary effects (3).
Oral rat (4-day) 300 mg kg^{-1} every 6 hr caused no detrimental effect on stomach mucosa. A dose of 435 mg kg^{-1} showed better kidney tolerance in rat than equimolar dose of aspirin (2).

Metabolism and toxicokinetics

Metabolised in humans to salicylic acid and paracetamol which are then excreted in the urine (4-6).
Benorylate was hydrolysed *in vitro* to paracetamol and salicylate by human liver cytosol (7).
Following administration of 4 g to healthy volunteers benorylate was eliminated in the urine within 21 hr. The urinary metabolites detected were similar to those observed for aspirin and paracetamol (2).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537, TA1538 with and without metabolic activation negative (8).

Other effects

Other adverse effects (human)

Human systemic effects by unspecified route include respiratory stimulation, dehydration and distorted perception (1).
Benorylate may cause nausea, indigestion, heartburn, constipation, drowsiness, dizziness, diarrhoea and skin rashes (9).

Any other adverse effects

The humoral response in benorylate-treated mice was 40-50% lower than the controls. Mitogen-induced proliferation of spleen lymphocytes was also inhibited in treated mice, slight inhibition was observed where cells were activated by bacterial lipo-polysaccharide. When lymphocytes from drug-treated animals were further cultured in the presence of the same drug a variable inhibition of mitogen-induced proliferation was observed (10).

Other comments

Review of benorylate as a antirheumatic drug (11).

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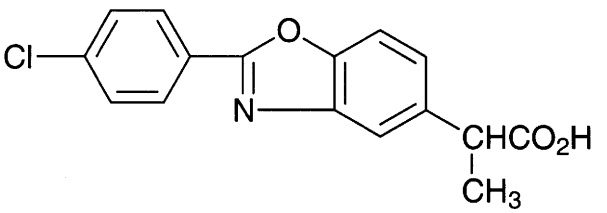
B34 benoxaprofen



$C_{16}H_{12}ClNO_3$ **Mol. Wt.** 301.73 **CAS Registry No.** 51234-28-7

Synonyms 2-(4-chlorophenyl)-α-methyl-5-benzoxazoleacetic acid

EINECS No. 257-069-7 **RTECS No.** DM 4447000

Uses Anti-inflammatory, analgesic and antipyretic drug.

Physical properties

M. Pt. 189-190°C

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse 800 mg kg^{-1} (1).

LD_{50} oral rat 118 mg kg^{-1} observed behavioural change in motor activity, ataxia, and aplastic anaemia in blood (2).

LD_{50} intraperitoneal rat, mouse 129, 398 mg kg^{-1}, respectively (2).

LD_{50} subcutaneous rat, mouse 121, 482 mg kg^{-1}, respectively (2).

Metabolism and toxicokinetics

Well absorbed after oral administration of 1-10 mg kg^{-1} in dog, mouse, rat, rabbit, rhesus monkey, and human. Only unchanged drug was detected in plasma, bound to plasma proteins; highest binding occurred in humans. Plasma elimination: human (33 hr); rat and mouse (28 and 24 hr respectively); all other species <13 hr. Oral dose of ^{14}C benoxaprofen 20 mg kg^{-1} to ♀ rats, tissue concentration was highest in liver, kidney, lungs, adrenals and ovaries (3).

Sensitisation

Skin disorders have been reported including photosensitivity reactions, erythema multiforme (the Stevens-Johnson syndrome) (4).

Patients receiving 600 mg day^{-1} reported photosensitisation (5).

Genotoxicity

Human leukocyte 15 mg l^{-1} induced DNA damage (6).

Other effects

Other adverse effects (human)

Onycholysis and other nail disorders, gastrointestinal disturbances including peptic ulceration and bleeding, blood disorders, liver disorders and heart failure have been reported (4,7).

Three hundred patients received 600 mg day^{-1} in the course of their treatment reported side-effects included cutaneous, gastrointestinal and central nervous system disorders (5).

In vitro 3.75 μg ml^{-1} caused dose-related spontaneous activation of luminol- and lucigenin- enhanced chemiluminescence in human polymorphonuclear leukocytes (8).

Any other adverse effects

Administration (dose, route unspecified) to rat induced the cytochrome P450 I and IV families and peroxisomal proliferation in the liver (9).

Other comments

Benoxaprofen's association with a variety of adverse reactions and fatalities in elderly people caused the drug to be withdrawn in 1982 (9).

Benoxaprofen is discussed in a retrospective study (10).

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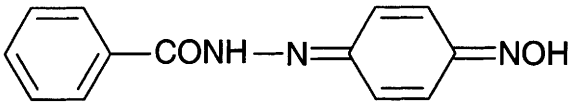
B35 benquinox



$C_{13}H_{11}N_3O_2$ **Mol. Wt.** 241.25 **CAS Registry No.** 495-73-8

Synonyms 1,4-Benzoquinone-*N'*-benzoylhydrazone oxime; 4-benzoyl-hydrazona-1,4-benzoquinone oxime; benzoic acid [4-hydroxyimino)-2,5-cyclohexadien-1-ylidene)hydrazide

EINECS No. 207-807-9 **RTECS No.** DH 6125000

Uses Fungicide. Modifier for isoprene rubber. Superseded as a fungicide (1).

Physical properties

M. Pt. 209-210°C

Occupational exposure

Supply classification toxic

Risk phrases Harmful in contact with skin – Toxic if swallowed (R21, R25)

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

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, mouse 100 mg kg^{-1} (2,3).

Legislation

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

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

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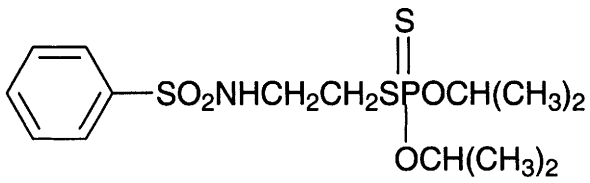
5. *S.I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK

B36 bensulide



$C_{14}H_{24}NO_4PS_3$ **Mol. Wt.** 397.52 **CAS Registry No.** 741-58-2

Synonyms (*N*-(2-ethylthio)benzene sulfonamido-*S*,*O*,*O*-diisopropylphosphorodithioate; *S*-*O*,*O*-diisopropylphosphorodithioate) of *N*-(2-mercaptoethyl)benzenesufonamide; *O*,*O*-bis(1-methylethyl)*S*-[2-[(phenylsulfonyl)amino]ethyl]phosphorodithoate; phosphorodithioic acid, *O*,*O*-diisopropylester *S*-ester with *N*-(2-mercaptoethyl)benzenesulfonamide; Bensumec; Betasan; Disan; Prefar; Pre-san

EINECS No. 212-010-4 **RTECS No.** TE 0250000

Uses Herbicide.

Physical properties

M. Pt. 34.4°C **Partition coefficient** log P_{ow} 4.2 (1) **Volatility** v.p. < 0.133 mPa at 20°C (1).
Solubility Water: 25 mg l^{-1} at 20°C. Organic solvents: kerosene, miscible with acetone, ethanol, methyl isobutyl ketone, 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 – Wear suitable protective clothing (S2, S24, S36)

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) rainbow trout 1.1 mg l^{-1} (1).
LC_{50} (96 hr) goldfish 1-2 mg l^{-1} (1).
LC_{50} (96 hr) bluegill sunfish 1.4 mg l^{-1} (1).
LC_{50} (96 hr) channel catfish 0.379 mg l^{-1} (2).
LC_{50} (96 hr) bluegill sunfish 0.8 mg l^{-1} at 24°C (3).

Invertebrate toxicity
EC_{50} (48 hr) *Daphnia* 0.58 ppm (1).
LC_{50} (96 hr) water shrimp 1.4 mg l^{-1} at 15°C (3).
LD_{50} 0.0016 mg bee^{-1} (1).

Environmental fate

Degradation studies
Slowly degraded by microbial action. Residual activity in soil 4-6 months at 21-27°C (1).
Bensulide is degraded slowly in soil by microorganisms (4).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 270 mg kg^{-1} (5).
LD_{50} oral ♂, ♀ rat 360, 270 mg kg^{-1}, respectively (1).
LD_{50} oral bobwhite quail 1390 mg kg^{-1} (1).
LD_{50} oral ♂ rat 1080 mg kg^{-1} (6).
LC_{50} (4 hr) inhalation rat >1.75 mg l^{-1} (1).
LD_{50} percutaneous rat > 2000 mg kg^{-1} (1).

Sub-acute and sub-chronic data

Oral rat, dog, mice (90 day) 25, 2.5, 30 mg kg^{-1} daily. No observed adverse effects (1).

Irritancy

Mild skin and eye irritant in rabbits (1).

Genotoxicity

Salmonella typhimurium TA100, TA98, TA1535, TA1537, TA1538 with and without metabolic activation negative (7).
Escherichia coli WP2 hcr with and without metabolic activation negative (7).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides and related products: maximum admissible concentration 0.1 μg l^{-1} (7).
Included in Schedule 6 (Release into Land Prescribed Substances) of Statutory Instrument No. 472, 1991 (8).

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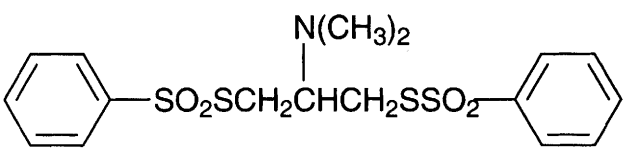
7. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
8. *S.I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK

B37 bensultap



$C_{17}H_{21}NO_4S_4$ **Mol. Wt.** 431.62 **CAS Registry No.** 17606-31-4

Synonyms *S,S'*-2-dimethylaminotrimethylene di(benzenethiosulfonate); *S,S'*-[2-(dimethylamino)-1,3-propanediyl] benzenesulfonothionate; *S,S'*-[2-(dimethylamino)trimethylene]bis(benzenethiosulfonate); benzenesulfonic acid, thio-*S,S'*-(2-(dimethylamino)trimethylene)ester; Bancol; Victenon; ZZ-Doricide; Malice; Ruban

RTECS No. DB 8000000

Uses Insecticide.

Physical properties

M. Pt. 83-84°C **B. Pt.** 150°C (decomp.)
Solubility Water: 0.7-0.8 mg l^{-1} (30°C). Organic solvents: acetone, acetonitrile, chloroform, *N,N*-dimethylformamide, ethanol, methanol, xylene

Occupational Exposure

Supply classification harmful, dangerous for the environment
Risk phrases Harmful if swallowed – Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment (R22, R50/53)
Safety phrases Keep out of reach of children (if sold to general public) – This material and/or its container must be disposed of as hazardous waste – Avoid release to the environment. Refer to special instructions/safety data sheet (S2, S60, S61)

Ecotoxicity

Fish toxicity
LC_{50} (48 hr) carp, guppy, rainbow trout 15, 17 and 0.76 mg l^{-2}, respectively (1).
LC_{50} (72 hr) carp, guppy, rainbow trout 8, 16, 0.76 mg l^{-1}, respectively (1).

Invertebrate toxicity
EC_{50} (6 hr) *Daphnia* 40 mg l^{-1} (1).
LD_{50} (24 hr) topical application *Apis melliferra* 14.75 mg bee^{-1} (1).
LD_{50} (24 hr) oral *Apis mellifera* 25.9 mg bee^{-1} (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral Japanese quail 60 mg kg^{-1} (1).
LD_{50} oral ♂ rat 1110 mg kg^{-1} (2).
LD_{50} oral ♂ mouse 415 mg kg^{-1} (3).
LD_{50} percutaneous rabbit >2000 mg kg^{-1} (1).
LD_{50} intraperitoneal ♂, ♀ rat 503, 438 mg kg^{-1}, respectively (1).
LD_{50} intraperitoneal ♂, ♀ mice 442, 343 mg kg^{-1}, respectively (1).

Sub-acute and sub-chronic data
LD_{50} (8-day) oral pheasant 2730 mg kg^{-1} diet (1).

Carcinogenicity and chronic effects
In 2-yr feeding trials the no-effect level for rat was 10 mg kg^{-1} day^{-1} and for mice 3.6 mg kg^{-1} day^{-1}. Reported to be non-oncogenic (1).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides and related products: maximum admissible concentration 0.1 μg l^{-1} (4).
Included in Schedule 6 (Release into Land: Prescribed Substances) of Statutory Instrument No. 472, 1991 (5).

Other comments

Incompatible with alkaline pesticides (1).

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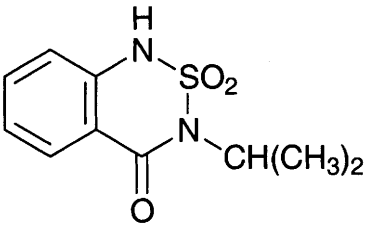
B38 bentazone



$C_{10}H_{12}N_2O_3S$ **Mol. Wt.** 240.28 **CAS Registry No.** 25057-89-0

Synonyms 3-isopropyl-(1*H*)-benzo-2,1,3-thiadiazin-4-one 2,2-dioxide; 3-(1-methylethyl)-(1*H*)-2,1,3-benzothiadiazin-4(3*H*)-one 2,2-dioxide; 3-isopropyl-2,1,3-benzothiadiazin-4-one 2,2-dioxide; Bentazon; Basagran; 1*H*-2,1,3-benzthiadiazin-4(3*H*)-one, 3-isopropyl-2,2-dioxide-

EINECS No. 246-585-8 **RTECS No.** DK 9900000

Uses Post-emergence herbicide.

Physical properties

M. Pt. 137-139°C **Specific gravity** 1.47 **Partition coefficient** K_{ow} 0.35 (pH 7) (1)
Volatility v.p. 3.459×10^{-6} mmHg at 20°C
Solubility Water: 570 mg l^{-1} at 20°C (pH 7). Organic solvents: acetone, benzene, chloroform, cyclohexane, diethyl ether, ethanol, ethyl acetate

Occupational exposure

Supply classification harmful
Risk phrases Harmful if swallowed – Irritating to the eyes (R22, R36)
Safety phrases Keep out of reach of children (if sold to general public) – In case of contact with eyes, rinse immediately with plenty of water and seek medical advice (S2, S26)

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) rainbow trout >100 mg l^{-1} (1).
LC_{50} (96 hr) bluegill sunfish >100 mg l^{-1} (1).

Invertebrate toxicity
EC_{50} (48 hr) *Daphnia* 125 mg l^{-1} (1).
EC_{50} (72 hr) *Ankistrodesmus* 62 mg l^{-1} (1).
Chronic study *Daphnia magna* 0.25-1.0 mg l^{-1} affected post-embryonic growth period, which was delayed by 2.3-2.7 days compared with control (2).
Non-toxic to bees (3).

Bioaccumulation
Calculated bioconcentration factor 19 (4).

Environmental fate

Degradation studies

Bentazone has low soil persistence. Aerobic $t_{1/2}$ (at 20°C) was 13.6 day. $t_{1/2}$ (field) was ~ 12 days (1).
Rapidly metabolised in tolerant plants to extractable conjugates which are incorporated into plant components.
Potential to contaminate surface waters as result of its mobility in run-off water and application to rice fields (5).

Abiotic removal

In sunlight bentazone undergoes oxidation and dimerisation with loss of SO_2 (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, dog, rabbit, cat >1000, >500, 750, 500 mg kg^{-1}, respectively (1).
LD_{50} oral rat, mouse, rabbit, cat, quail 400-1100 mg kg^{-1} (6).
LC_{50} (4 hr) inhalation rat >5.1 mg l^{-1} (1).
LD_{50} percutaneous rat >2500 mg kg^{-1} (1).
Acute inhalation studies were conducted on saturated air containing bentazone volatiles at 1.2 mg l^{-1} at 20°C.
Inhalation rat (8 hr) did not result in any mortality (7).
LD_{50} dermal rat, rabbit 2500, 4000 mg kg^{-1}, respectively (6).

Carcinogenicity and chronic effects

In 2-yr feeding trials the no-effect level in rat was 350 mg kg^{-1} (1).
Oral ♂, ♀ rat (2 yr) 4000 ppm lesions observed included testicular Leydig cell adenomas, urinary bladder transitional cell papilloma and mesenchymal tumour in the thoracic cavity. The authors conclude there was no evidence of bentazone-related tumour induction or of induced non-neoplastic histopathological changes. The no-observed-adverse-effect level was 200 ppm (7).

Teratogenicity and reproductive effects

TD_{Lo} (6 days) pregnant oral rat 25 mg kg^{-1} caused both reduced fertility and foetotoxic effects including implantation mortality and specific developmental abnormalities to musculoskeletal system (8).
Administration of 0, 2.5, 7.5, 25 and 75 mg kg day^{-1} of bentazone at different times in gestation (6-16 days) to beagle dogs caused prostatis in ♂ animals at highest dose and 1/3 ♂ and 2/3 ♀ animals died (8).
Oral pregnant ♀ albino rat (6-16 days gestation) 25-200 mg kg^{-1}. Foetus sizes below normal, absence of coccygeal vertebrae recorded in all groups. Metacarpal and metatarsal phalanges absent in all but one group (8).
In studies on rabbits no external malformations were noted in the 118 (control), 114 (low-dose), 129 (mid-dose) or 114 (high-dose) foetuses examined. No abnormalities of the abdominal or thoracic soft tissues, or of the skull skeletal structures were observed. A single foetus exhibited hydrocephaly at 150 mg kg^{-1} dose. In the absence of any dose-effect relationship, this observation was not considered to be compound- related. Skeletal variants were observed in a number of foetuses, but there was no evidence of a dose or compound relationship in their incidence. A no-observed-adverse-effect level of 150 mg kg^{-1} was determined based on the total litter loss occurring in one female at 375 mg kg^{-1}. There was no evidence of teratogenicity at dose levels up to 375 mg kg^{-1} (7).
Hen eggs were immersed in 50% bentazone before incubation and on the 4th and 19th of day of incubation for 30 sec. High mortality of embryos was reported (9).

Metabolism and toxicokinetics

Gavage ♂, ♀ rats received 0.8 mg ^{14}C-bentazone in 1 ml of 50% ethanol. Of the administered dose 91% was excreted in urine as parent compound within 24 hr, faeces contained 1% of administered dose (10,11).
Whole body autoradiography of rats indicated high levels of radioactivity in the stomach, liver, heart, kidneys after 1 hr of dosing with ^{14}C-bentazone. Radioactivity was not observed in brain or spinal cord (10).

Irritancy

Three white Vienna rabbits had 33 mg bentazone instilled into the conjunctival sac of one eye. Corneal opacity, iris congestion, conjunctival redness, chemosis and discharge were observed. Symptoms cleared by day 15 post-dosing (7).

Sensitisation

Sensitisation tests in guinea pigs using the Magnusson and Kligman Maximisation Test and the Open Epicutaneous Test indicated that bentazone has sensitising potential (7).

Genotoxicity

Salmonella typhimurium TA100, TA98, TA1535, TA1537, TA1538 and *Escherichia coli* WP2 hcr with and without metabolic activation negative (12).

In vitro Chinese hamster ovary HGPRT (hypoxanthine-guanine phosphoribosyl-transferase) point mutation negative (8).

Chinese hamster ovary chromosomal aberrations negative (8).

In vivo mouse bone marrow micronuclei negative (8).

In vivo rat, mouse dominant lethal assay single 195 mg kg^{-1} (mouse) and 13-wk 20-180 ppm in diet (rat) negative (8).

Other effects

Any other adverse effects

After oral dosing to rats, guinea pigs, rabbits, cats and dogs (dose unspecified), signs of toxicity included dyspnoea, apathy, staggering gait and, in cats and dogs, vomiting. Convulsions were also observed in cats (7).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides and Related Products: maximum admissible concentration 0.1 μg l^{-1} (13).

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

Other comments

Comprehensive report on toxicity of bentazone (7).

Resistant to hydrolysis in acid and alkali. Bentazone 1 ppm was stable to hydrolysis for up to 122 days in unbuffered water (pH 5, 7, 9) at 22°C (8).

Spraying of *Xanthium strumarium* affected both vegetative growth and reproduction (15).

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B39 bentonite

CAS Registry No. 1302-78-9

Synonyms Albagel premium USP4444; Bentopharm; Bregel; Brebent; Laundrosil; Carmago White

EINECS No. 215-108-5 **RTECS No.** CT 9450000

Uses General purpose food additive (UK Additive No. 558). Pharmaceutical aid. Suspending and stabilising agent. Adsorbent or clarifying agent (1).
Occurrence In clay, predominantly montmorillonite.

Physical properties

Solubility Water: Absorbs water to form insoluble gel (1)

Mammalian & avian toxicity

Acute data
LD_{50} intravenous rat 35 mg kg^{-1} (2).

Carcinogenicity and chronic effects
TD_{Lo} oral mouse 12000 g kg^{-1} administered over 28 wk caused equivocal tumorigenic effects (3).

Other comments

Human health effects and experimental toxicology reviewed (4,5).

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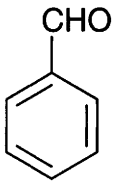
B40 benzaldehyde



C_7H_6O **Mol. Wt.** 106.12 **CAS Registry No.** 100-52-7

Synonyms benzene aldehyde; artificial essential oil of almond; benzenecarbonal

EINECS No. 202-860-4 **RTECS No.** CU 4375000

Uses In the manufacture of dyestuffs. Used in the perfume and flavouring industries. Reducing agent. Solvent.
Occurrence In kernels of bitter almonds.

Physical properties

M. Pt. –26°C **B. Pt.** 179°C **Flash point** 62°C **Specific gravity** 1.050 at 15°C with respect to water at 4°C
Partition coefficient log P_{ow} 1.48 **Volatility** v.p. 1 mmHg at 26.2°C ; v.den. 3.66
Solubility Water: 2.86 g l^{-1}. Organic solvents: miscible ethanol

Occupational exposure

UN No. 1990 **Conveyance classification** other dangerous substance
Supply classification harmful
Risk phrases Harmful if swallowed (R22)
Safety phrases Keep out of reach of children (if sold to general public) – Avoid contact with the skin (S2, S24)

Ecotoxicity

Fish toxicity
Exposure to 14.5 mg l^{-1} caused growth to stop early in *Phoxinus phoxinus* (1).
LC_{50} (96 hr) rainbow trout 11 mg l^{-1} (2).
LC_{50} (96 hr) bluegill sunfish 1.1 mg l^{-1} (2).

Invertebrate toxicity
Cell multiplication test *Microcystis aeruginosa* 20 mg l^{-1}, *Pseudomonas putida* 132 mg l^{-1}, *Entosiphon sulcatum* 0.29 mg l^{-1} (3,4).
EC_{50} (5, 15, 30 min) *Photobacterium phosphoreum* 5.32 mg l^{-1} Microtox test (5).
IC_{50} (30, 90, 120 min) *Saccharomyces cerevisiae* 204 mg l^{-1} (6).

Environmental fate

Nitrification inhibition
Benzaldehyde inhibited ammonia oxidation, by ammonia monooxygenase in *Nitrosomonas europaea* (concentration unspecified). Inhibition was accompanied by conversion into benzyl alcohol (7).

Degradation studies
99% degradation in adapted activated sludge (8).
ThOD: 2.4 g g^{-1}; DOC: 0.79 g g^{-1} (9).
BOD_5 150% reduction in dissolved oxygen (10).
Confirmed biodegradable (11).
Converted into alcohol by *Euglena gracilis* Z in culture (12).

Abiotic removal
Adsorbability 0.188 g g^{-1} carbon 94% reduction (13).

Mammalian & avian toxicity

Acute data
LD_{50} oral guinea pig 1000 mg kg^{-1} (14).
LD_{Lo} subcutaneous rat 5000 mg kg^{-1} (15).

Sub-acute and sub-chronic data
Inhalation rat (14 day) 500, 750 and 1000 ppm. Hypothermia and reduction in motor activity were observed in all rats, and severe impairment of the central nervous system in high level rats (16).

Carcinogenicity and chronic effects
National Toxicology Program tested ♂, ♀ rat and mice with benzaldehyde via oral gavage (dose unspecified). No evidence of carcinogenic activity in rats, some evidence of carcinogenic activity in mice (17).
Gavage ♂, ♀ F344/N rat and B6C3F1 mouse (2 yr) 0-400 mg kg^{-1}. No evidence of carcinogenic activity in rats, some evidence of carcinogenic activity in mice, indicated by increased incidences of squamous cell papillomas and hyperplasia of the forestomach (18).

Metabolism and toxicokinetics

Metabolised by the liver, aromatic aldehydes, such as benzaldehyde, are oxidised to the corresponding acids (19). Intraperitoneal rat, approximately 30% was excreted in urine as hippuric acid (20).

Genotoxicity

Bacillus subtilis M45, H17 liquid microsome rec-assay without metabolic activation DNA damaging potential negative (21).

In vitro Chinese hamster ovary cells with and without metabolic activation sister chromatid exchange positive (22).

Mouse lymphoma L5178Y cell forward mutation assay without metabolic activation positive (23).

Other effects

Any other adverse effects

LC_{50} (48 hr) *Ambystoma mexicanum* mexican axolotl (3-4 wk after hatching) 370 mg l^{-1} (24).

Other comments

Human health and effects experimental toxicology, ecotoxicology and physico-chemical properties reviewed (25,26).

Estimated acceptable daily intake from all food additive sources ≤5 mg kg^{-1} (27).

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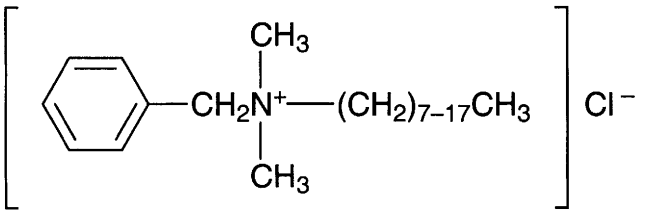
B41 benzalkonium chloride



CAS Registry No. 8001-54-5

Synonyms *N*-alkyl(C_8-C_{18})dimethylbenzylammonium chloride; cetalkonium chloride

RTECS No. BO 3150000

Uses Cationic surfactant, germicide and fungicide. Used in leather processing and textile dyeing industries. As a general antibacterial agent.

Physical properties

Specific gravity 0.988 at 20°C

Solubility Organic solvents: acetone, carbon tetrachloride, diethyl ether, ethanol

Ecotoxicity

Fish toxicity

Threespine stickleback exposed to 2 mg l^{-1} died within 4-6 hr and steelhead trout died within 2-4 hr (1).

Mammalian & avian toxicity

Sensitisation

An allergic reaction was reported in one patient to benzalkonium chloride used as a preservative in nose drops and confirmed by a challenge which produced nasal congestion and irritation of the eyes and throat lasting 48 hr (2). At a 0.01-0.1% concentration no allergenic activity was observed in rabbits, guinea pigs and dogs and skin irritating action was dependent on the nature, concentration and number of applications (3).

Other effects

Other adverse effects (human)

Reported to be toxic in humans (4).

Inflammation of the eye and deterioration of vision occurred three days after change of soaking solution for a soft contact lens to one containing benzalkonium chloride (5).

In addition to inhibiting sperm motility there is evidence that benzalkonium chloride disturbs the electrolyte balance in the aqueous phase of cervical mucous, making it hostile to sperm (6).

A woman occupationally exposed to disinfectant containing the compound developed asthmatic symptoms and a skin test and bronchial provocation test proved her sensitivity which could be blocked by sodium chromoglycate (7).

Any other adverse effects

Intramuscular rat induced myofascial edematous swelling with increased succinate oxidation and Na^+, K^+, Mg^{2+} ATPase activity 30 min after administration (8).

Dermal application of 13% and 15% caused death in 9 of 48 and 20 of 48 mice, respectively. Survivors developed skin lesions and lost weight. Applications of 0.08% or 3% had minor effects (8).

Other comments

Incompatible with soaps and other anionic surfactants, citrates, iodides, nitrates, permanganates, salicylates, silver salts and tartrates. Incompatible with some commercial rubber mixes or plastics, aluminium, cotton

dressings, fluorescein sodium, hydrogen peroxide, kaolin, hydrous wool fat and some sulfonamides (9). Reviews on exposure, experimental and environmental toxicology, and human health effects listed (10).

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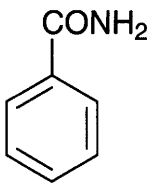
B42 benzamide



C_7H_7NO **Mol. Wt.** 121.14 **CAS Registry No.** 55-21-0

Synonyms benzoic acid amide; benzoyl amide; phenylcarboxy amide

EINECS No. 200-227-7 **RTECS No.** CU 8700000

Uses Intermediate in organic synthesis. Antiviral agent.

Physical properties

M. Pt. 128-129°C **B. Pt.** 288°C **Specific gravity** 1.341 at -4°C **Partition coefficient** log P_{ow} 0.64
Solubility Water: <1 mg ml^{-1} at 22°C. Organic solvents: acetone, dimethyl sulfoxide, ethanol

Ecotoxicity

Invertebrate toxicity
EC_{50} (5, 15, 30 min) *Photobacterium phosphoreum* 59.3 mg l^{-1} Microtox test (1).

Environmental fate

Degradation studies
Biodegradable (2).

Mammalian & avian toxicity

Acute data
LD_{50} oral mouse 1160 mg kg^{-1} (3).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA1535, TA1537 with and without metabolic activation negative (4-6).
In vitro Chinese hamster ovary cells sister chromatid exchange positive (7).
Mouse lymphoma cell line L1210 sister chromatid exchange positive (8).

Other effects

Any other adverse effects
Benzamide exhibited antitransforming action to human fibroblasts exposed to increasing ultraviolet radiation at low intracellular drug concentration (9).
Phorbol-ester-induced promotion of initiated mouse skin keratinocytes to papillomas was largely prevented by the administration of benzamide and other nicotinamide analogues (10).
Chronic administration oral mouse 200 mg kg^{-1} inhibits poly-ADP-ribose synthetase (11).

Other comments

Central nervous system effects of benzamides are reviewed (12).

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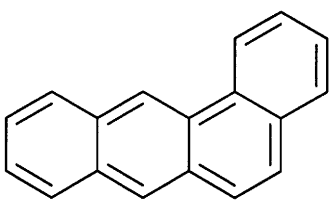
B43 benz[*a*]anthracene



$C_{18}H_{12}$ **Mol. Wt.** 228.29 **CAS Registry No.** 56-55-3

Synonyms 1,2-benzanthracene; benzanthrene; naphthanthracene; tetraphene; 2,3-benzphenanthrene

EINECS No. 200-280-6 **RTECS No.** CV 9275000

Occurrence In gasoline, bitumen, crude oil, oil and waxes (1).

Physical properties

M. Pt. 157-159°C **B. Pt.** 435°C
Solubility Water: 9-14 μg l^{-1}. Organic solvents: acetone, benzene, diethyl ether, dimethyl sulfoxide, ethanol

Occupational exposure

Supply classification toxic, dangerous for the environment
Risk phrases May cause cancer – Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment (R45, 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)

Ecotoxicity

Fish toxicity
Skin and liver tumours observed in brown bullhead fish inhabiting the Black River, an industrialised tributary of Lake Erie. The river was particularly contaminated with benz[*a*]anthracene and benzo[*a*]pyrene (2).

Invertebrate toxicity
Eastern oyster (2 day) 4.1 $\mu g\ g^{-1}$ $t_{1/2}$ depuration 9 days (3).

Bioaccumulation
Bioconcentration factor for *Daphnia* sp. 54 and oysters 20 (4-6).
Shrimp exposed to 2.8 ppb benz[*a*]anthracene showed rapid uptake during the first 6 hr. At 96 hr exposure shrimp exhibited continual accumulation. Accumulation in the tissues was in the order stomach, intestine, hepatopancreas, cephalothorax and abdomen. When transferred to fresh seawater, shrimp appeared to depurate benz[*a*]anthracene rapidly (7).

Environmental fate

Degradation studies
Soil contaminated with benz[*a*]anthracene showed losses of 22-88% in 400 days (8).
Degraded to CO_2 in estuarine water (9).
In seawater-sediment slurry, 1.4-1.8% degradation was observed wk^{-1} which indicated $t_{1/2}$ of 199-252 days (10,11).
$t_{1/2}$ of 290 days in sediment from an oil-contaminated stream, but $t_{1/2}$ 10-400 times longer in an uncontaminated stream (12).
Microbial degradation is faster in the upper layers of sediment (10).
97.7% was degraded by *Pseudomonas paucimobilis* when incubated for 17 hr with 10 ppm benz[*a*]anthracene and fluoranthene as a sole carbon source for energy and growth (13).
Degraded by *Cunninghamella elegans*, grown in dextrose broth, to *trans*-8,9-dihydrodiol (90%), to *trans*-10,11-dihydrodiol (6%) and *trans*-3,4-dihydrodiol (4%) derivatives. A tetraol derivative was also discovered by HPLC and may be the result of a further oxidation of the 8,9- or 10,11-dihydrodiol derivatives (14).

Abiotic removal
Photolytic $t_{1/2}$ in early March is 5 hr. Based on seasonal variations, $t_{1/2}$ would be 2.9 and 7.8 hr in summer and winter, respectively (15).
Photolytic $t_{1/2}$ in an oligotrophic lake is 10 hr, in a stream 20 hr and eutrophic pond or lake 50 hr (16).

Adsorption and retention
Adsorption in estuarine waters of 3 $\mu g\ l^{-1}$ recorded, 59% adsorbed on particles after 3 hr (3).
Benzoanthracene is strongly adsorbed on sediments with a soil adsorption coefficient of $0.55 \times 10^{-6} - 1.87 \times 10^{-6}$ in three sediments (16).

Mammalian & avian toxicity

Acute data
LD_{Lo} intravenous mouse 10 $mg\ kg^{-1}$ (17).

Sub-acute and sub-chronic data

LD_{50} (72-hr) chick embryo 79 μg kg^{-1} following injection into 7 day pre-incubated air sacs (18).

Carcinogenicity and chronic effects

No adequate evidence for carcinogenicity to humans, sufficient evidence of carcinogenicity to animals, IARC classification group 2A (19).

In a CASE-SAR analysis of polycyclic aromatic hydrocarbon carcinogenicity, benz[*a*]anthracene was classified as a suspect carcinogen with low to moderate potency (20).

Application to exposed mammary gland of ♀ Sprague-Dawley rats, inactive (21).

In ♂ mice administered 0.6 mg of benz[*a*]anthracene the hepatic tumour incidence was 79% (duration unspecified) (22).

♂ Syrian golden hamster buccal pouch surfaces painted for ≤20 wk with benzo[*a*]anthracene dissolved in paraffin oil developed carcinomas of the buccal pouch (23).

Metabolism and toxicokinetics

Benz[*a*]anthracene is metabolised by human liver microsomes to the 8,9-dihydrodiol (42.4%) 5,6-dihydrodiol (25%), 10,11-dihydrodiol (24.8%), 3,4-dihydrodiol (5.3%) and 1,2-dihydrodiol (<1.5%) derivatives. No tetrahydrotetrols were detected (24).

In mammals benz[*a*]anthracene appears to be metabolized via 3,4-epoxide to 3,4-diol 3,4-diol, 1,2-epoxide, or 8,9-dihydroxybenz[a]anthracene-10,11-epoxide (25-27).

Benzoanthracene was not detected in human liver, but was present in fatty tissues (28).

Induces cytochrome P450 activity in rats. Benz[*a*]anthracene also has a self-inducing effect on its own metabolism as well as other polycyclic aromatic hydrocarbons e.g. pyrene and fluoroanthene (29).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1537, TA1538 with metabolic activation positive (30).

Escherichia coli PQ37 SOS chromotest with metabolic activation positive (30,31).

Rat bone marrow cells limited ability to induce chromosomal aberrations (32).

In vitro human peripheral blood lymphocytes benz[*a*]anthracene caused the formation of readily measurable levels of DNA adducts (33).

The frequency of sister chromatid exchanges in rat mammary epithelial cells was 0.4. Exposure of rat mammary epithelial cells to 5 μg ml^{-1} for 24 hr resulted in a 45-62% reduction in the ^{3}HTdR labelling index of rat cells; human mammary epithelial cells resulted in a 50-90% depression. In mammary epithelial cell mediated assays for rat and humans, frequencies of sister chromatid exchange per chromosome were 3 and 4.5, respectively (34).

Pleurodeles waltl micronuclei observed in blood smears (35).

Drosophila melanogaster eye mosaic assay negative (36).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Polycyclic aromatic hydrocarbons: maximum admissible concentration 0.2 μg l^{-1} (37).

Other comments

Content in domestic effluent 0.191-0.319 ppb (1).

Air pollution emissions, values for Europe using leaded and unleaded petrol 32.4 μg l^{-1} fuel burnt (38).

Metabolism, toxicity and carcinogenic potential of benz[*a*]anthracene reviewed (39,40).

Human health effects, experimental toxicology, ecotoxicology, physico-chemical properties, environmental effects, safety test data and exposure conditions reviewed (41-44).

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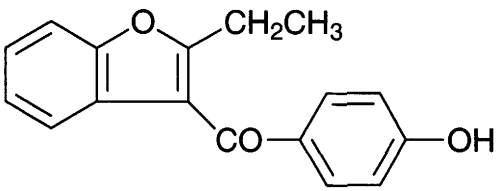
B44 benzarone



$C_{17}H_{14}O_3$ **Mol. Wt.** 266.30 **CAS Registry No.** 1477-19-6

Synonyms (2-ethyl-3-benzofuranyl)(4-hydroxyphenyl)methanone; 2-ethyl-3-benzofuranyl-*p*-hydroxyphenyl ketone; 2-ethyl-4'-hydroxy-3-benzoylbenzofuran

EINECS No. 216-026-2 **RTECS No.** OB 2975000

Uses Therapeutically for increased capillary fragility, thrombolytic agent. Treatment of various peripheral vascular disorders (1).

Physical properties

M. Pt. 124.3°C

Mammalian & avian toxicity

Acute data

LD_{50} intraperitoneal mouse 200 mg kg^{-1} (2).

Teratogenicity and reproductive effects

TD_{Lo} (9-14 days) oral ♀ pregnant rat 1020 mg kg^{-1} both maternal toxicity to ovaries, fallopian tubes and abnormal musculoskeletal development in foetus (3).

TD_{Lo} (7-12 days) oral ♀ pregnant mouse specific development abnormalities musculoskeletal system (3).

Metabolism and toxicokinetics

In man 70% dose eliminated in urine, the metabolites present as conjugates (mainly glucuronides). The two major aglycones were the hydroxylated metabolites 2-(1-hydroxyethyl)-3-(4-hydroxybenzoyl)benzofuran and 2-(1-hydroxyethyl)-3-(4-hydroxybenzoyl)-hydroxyben zofuran, 26% and 8%, respectively. Small amounts (2-3% dose) of benzarone and metabolites 2-ethyl-3-(4-hydroxybenzoyl)-hydroxybenzofuran and 2-(1, 2-dihydroxyethyl)-3-(4-hydroxybenzoyl)benzofuran were detected. The same conjugated components were present in human plasma and metabolites 2-(1-hydroxyethyl)-3-(4-hydroxybenzoyl)benzofuran and 2-ethyl-3-(4-hydroxybenzoyl)-hydroxybenzofuran were the major components in the faeces. Metabolism was less extensive in rat and dog, benzarone (free and conjugated) representing >70% of the total material in bile, urine and faecal extracts from dogs and in bile from rats (4).

The metabolic fate of benzarone in rat 2 mg kg^{-1}, dog 0-5 mg kg^{-1}, and human 100 mg, all taken orally, was compared. Humans excreted 73% in urine, 19% in faeces, dog and rat excreted >80% in faeces, mostly during first 48 hr (5).

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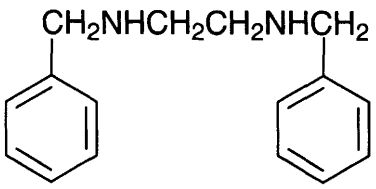
B45 benzathine



$C_{16}H_{20}N_2$ **Mol. Wt.** 240.35 **CAS Registry No.** 140-28-3

Synonyms 1,2-bis(benzylamino)ethane; DBED; *N,N'*-dibenzylethylenediamine
1,2-ethanediamine-*N,N*-bis(phenylmethyl)-

EINECS No. 205-408-4 **RTECS No.** KV 3325000

Uses Precursor for benzathine penicillin.

Physical properties

M. Pt. 26°C **B. Pt.** 212-213 at 12 mmHg **Specific gravity** 1.024 at 20°C with respect to water at 4°C

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse 388 mg kg^{-1} (1).

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

References

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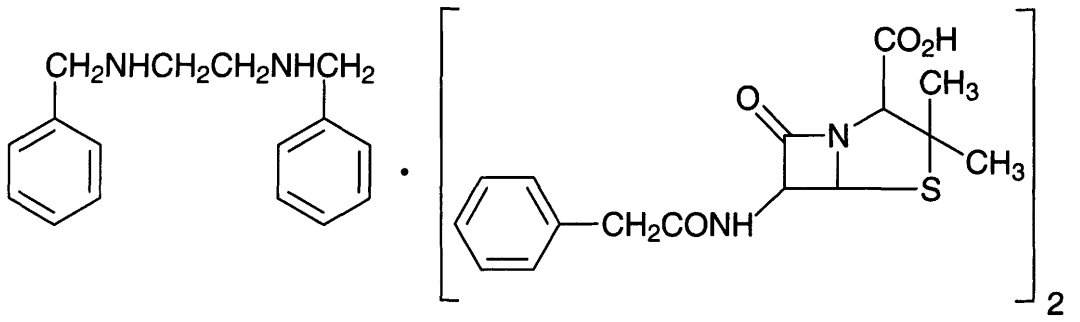
B46 benzathine penicillin



$C_{48}H_{56}N_6O_8S_2$ **Mol. Wt.** 909.14 **CAS Registry No.** 1538-09-6

Synonyms 4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid, 3,3-dimethyl-7-oxo-6-[(phenylacetyl)amino]-[2*S*(2α6β]-, compound with *N,N'*-bis(phenylmethyl)-1,2-ethanediamine (2:1)

EINECS No. 216-260-5 **RTECS No.** XH 9425000

Uses Antibacterial agent. Used in the treatment of syphilis, diptheria, pharyngitis, rheumatic fever and spleen disorders (1).

Physical properties

M. Pt. 123-124°C
Solubility Water: 0.15 mg ml^{-1}. Organic solvents: acetone, benzene, formamide

Mammalian & avian toxicity

Acute data
LD_{50} oral mouse 2000 mg kg^{-1} (2).
LD_{50} intraperitoneal mouse 460 mg kg^{-1} (2).

Teratogenicity and reproductive effects
TD_{Lo} (4 day) ♀ rat 23 mg kg^{-1} caused post-implantation mortality (3).

Metabolism and toxicokinetics
In humans it is hydrolysed to benzylpenicillin. Major excretory route via urine (1).

Other effects

Any other adverse effects
Administered to guinea pigs at 100,000-400,000 U kg^{-1} can alter erythrocyte membrane functions and may lead to haemolysis. Highest dose increased membrane cholesterol and decreased phospholipid levels. All doses decreased Na, K ATPase activity (4).

Other comments

Converts to benzylpenicillin and benzathine (5).
Toxicity reviewed (6).

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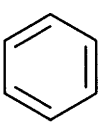
B47 benzene



C_6H_6 **Mol. Wt.** 78.11 **CAS Registry No.** 71-43-2

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

EINECS No. 200-753-7 **RTECS No.** CY 1400000

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

Physical properties

M. Pt. 5.5°C **B. Pt.** 80.1°C **Flash point** –11°C **Specific gravity** 0.8786 at 20°C with respect to water at 4°C
Partition coefficient log P_{ow} 2.15 **Volatility** v.p. 76 mmHg at 20°C ; v.den. 2.77
Solubility Water: 1780 mg l^{-1} at 20°C. Organic solvents: diethyl ether, ethanol, miscible acetone

Occupational exposure

FR-VME 5 ppm (16 mg m^{-3})
JP-OEL 10 ppm (32 mg m^{-3})
SE-LEVL 0.5 ppm (1.5 mg m^{-3}) **SE-STEL** 3 ppm (9 mg m^{-3})
UK-LTEL MEL 5 ppm (16 mg m^{-3})
US-TWA 0.5 ppm (1.6 mg m^{-3}) **US-STEL** 2.5 ppm (8 mg m^{-3})

UN No. 1114 **HAZCHEM Code** 3WE **Conveyance classification** flammable liquid
Supply classification highly flammable, toxic
Risk phrases May cause cancer – Highly flammable – Toxic: danger of serious damage to health by prolonged exposure through inhalation, in contact with skin and if swallowed (R45, R11, R48/23/24/25)
Safety phrases Restricted to professional users – Avoid exposure – obtain special instruction before use – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S53, S45)

Ecotoxicity

Fish toxicity
LC_{50} (24-96 hr) fathead minnow, bluegill sunfish, goldfish 36-22 mg l^{-1} (1).
LC_{50} (96 hr) bass 6-11 ppm (1).

Invertebrate toxicity
LC_{50} (96 hr) grass shrimp 20-27 ppm (1,2).
Cell multiplication inhibition test, *Pseudomonas putida* 92 mg l^{-1}, *Microcystis aeruginosa* >1400 mg l^{-1}, *Entosiphon sulcatum* >700 mg l^{-1} (1).
LC_{50} *Brachionus calyciflorus* and *Brachionus plicatilis* > 1000 mg l^{-1} (3).
EC_{50} (8 day) *Selenastrum capricornutum* 41 mg l^{-1} (4).

Toxicity to other species
LC_{50} (48 hr) Mexican axolotl (3-4 wk after hatching) 370 mg l^{-1} (5).

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

Environmental fate

Nitrification inhibition
Not inhibited at 500 mg l^{-1} (6).
Benzene inhibited ammonia oxidation, by ammonia monooxygenase, in *Nitrosomonas europaea* (concentration unspecified) (7).

Degradation studies
ThOD 3.07 g g^{-1}, COD 0.92 7 g^{-1} (8).
BOD_{10} 67% reduction of dissolved oxygen in acclimatised sludge (1).
Benzene is subject to rapid volatilisation in water and from soil surfaces, and is very mobile in soil.
Biodegradation may occur in shallow aerobic ground water, but not under anaerobic conditions (9).
Confirmed biodegradable (10).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat, mouse 3400, 4700 mg kg^{-1}, respectively (11,12).

Short-term acute exposure in humans may cause initial exhilaration, followed by dizziness, headache, nausea, drowsiness and pulmonary irritation. 7500 ppm and above for approximately 30 min may produce narcosis and death (13).

Sub-acute and sub-chronic data

Exposure of rats to 50 ppm benzene vapour for several wk, led to a reduction in red and white blood cells and platelets; exposure to concentrations >100 ppm produced leucopenia and aplasia (13).

♂ mice were fed 0-790 mg l^{-1} in drinking water for 28 days. Stimulation of the hypothalamic-pituitary-adrenocortical axis and increased circulatory levels of corticosterone were observed at high dose levels (14).

Oral mouse (3 day) 660 mg kg^{-1} 1× day^{-1} in feed. Increase in the number of mature activated macrophages in the bone marrow, and enhanced production of hydrogen peroxide by bone marrow granulocytes and mononuclear phagocytes (15).

Carcinogenicity and chronic effects

Sufficient evidence for carcinogenicity to humans and animals, IARC classification group 1 (16). Chronic exposure to benzene, in humans, at concentrations that produce changes in the blood may result in leukaemia, especially acute myelogenous leukaemia (13).

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

Tumours have been reported in various tissues including adrenals, lung, liver, ovary, oral cavity, stomach and skin (17).

Benzene administered by gavage produced ovarian atrophy, cysts, hyperplasia and neoplasia in mice (18).

National Toxicology Program tested ♂ and ♀ rats and mice via gavage. Clear evidence of carcinogenicity in ♂ and ♀ rats and mice (19).

Rat Zymbal glands, nasal and oral cavities, mammary gland and bone marrow all have higher peroxidase activity than non-target tissue for benzene carcinogenicity. This ability to oxidise benzene to phenolic metabolites could explain the greater susceptibility of these tissues to benzene-induced tumourigenesis (20).

Target organs of carcinogenicity: mouse and rat Zymbal's gland, mouse Harderian gland, mouse lung, mouse mammary gland, rat oral cavity, rat skin, rat stomach, and rat vascular system (21).

Teratogenicity and reproductive effects

Teratogenicity has been reported at high concentrations in rats, but there is no evidence of foetal malformations at concentrations which produce no maternal toxicity. Women are considered hypersusceptible to benzene, particularly during pregnancy and breast feeding, however there are no reports of teratogenic effects or any increase in spontaneous abortion in women occupationally exposed to benzene (18,22).

Benzene shows concentration-dependent embryotoxicity in rats. Lowest embryotoxic concentration is 1.5 μ mol ml^{-1} (23).

Metabolism and toxicokinetics

Benzene is partly eliminated unchanged in the breath and urine of humans. Oxidation occurs producing benzene epoxide, phenols and diphenols, including catechol, hydroquinone, benzoquinone and 1,2,4-benzenetriol, which are in turn conjugated in the liver and excreted in the urine (13,24).

Toxic amounts of benzene can readily be absorbed through the skin (13).

Cytochrome P450 (CYP) 2E1 activity in human liver microsomes metabolises benzene to hydroquinone and catechol (25).

EC_{50} mitochondrial respiration 525 ppm (species unspecified) (26).

Cynomolgus monkeys were given 5, 50 or 500 mg of radiolabelled benzene intraperitoneally. Urine was collected for up to 24 h. The proportion of excreted radiolabel decreased from 50 to 15% with increasing dose. The proportion of hydroquinone derivatives and muconic acid in the urine also decreased with increasing dose. Catechol conjugates were not detected (27).

The *in vitro* penetration of ^{14}C-benzene was studied using freshly prepared human skin. The permeability coefficient under standard conditions (26°C) was 0.14 cm hr^{-1}. This increased to 0.26 cm hr^{-1} at 50°C. Application of baby oil, moisturiser or insect repellent had no effect, however pre-treatment with sunscreen caused an increase to 0.24 cm hr^{-1} (28).

Benzene oxide has been shown to be a product of hepatic benzene metabolism in man, rats, and mice *in vitro*.

After 18 minutes of incubation of mouse liver microsomes with 1 mM benzene, 7% of the total benzene metabolites were benzene oxide (29).

Irritancy

Dermal rabbit (24 hr) 15 mg caused mild irritation, and 2 mg instilled into rabbit eye caused severe irritation (30,31).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA1535, TA1537 with and without metabolic activation negative (17,32).
Salmonella typhimurium TA102 with metabolic activation negative (33).
Escherichia coli K-12 *uvrB/recA* DNA repair host-mediated assay with and without metabolic activation negative (34).
In vitro human lymphoblastoid MCL-5 cells induced micronucleus formation (35).
In vitro rat bone marrow cells, induced micronucleated polychromatic erythrocytes and sister-chromatid exchange (36).
In vitro rat spleen lymphocytes, induced micronucleated polychromatic erythrocytes and sister-chromatid exchange (36).
In vivo rodent bone marrow autogenetic test positive induction of micronuclei and chromosomal aberrations (32).
Chromosomal aberrations in white blood cells and bone marrow in humans which could initiate leukaemia have been reported, but there is no evidence of aberrations at exposure levels of 25 ppm or less (13).
Inhalation ♂ mice 1 ppm induced chromosomal aberrations in spermatocytes and sister chromatid exchange in spermatogonia (37,38).

Other effects

Other adverse effects (human)

Thirteen published population-based and hospital-based case-control studies of multiple myeloma up to 1995 were examined for any relationship between this cancer and exposure to benzene or to surrogates for benzene exposure. No increased association was found between multiple myeloma and benzene or groups of chemicals that included benzene. Exposure to petroleum products, employment in petroleum-related occupations and cigarette smoking were not risk factors for multiple myeloma. However, there was a significant association with exposure to combustion products in engine exhaust (39).
Haematological and immunochemical investigation of 270 workers with chronic exposure to benzene evidenced changes to lymphocyte nuclei and disorders of the humoral immune response (40).
A cohort of 74,828 benzene-exposed and 35,805 non-exposed workers employed during 1972-1987 in 12 cities in China was studied to determine mortality from all causes. Demographic and occupational data were examined. Mortality was slightly increased in workers with greater cumulative exposure to benzene, the excess being largely due to cancer deaths. Mortality from lymphatic and haematopoietic malignancies, lung cancer and occupational injuries increased in direct relation to cumulative benzene exposure. Suggestive assocations were also noted for nasopharyngeal and oesophageal cancer (41).

Legislation

Included in Schedule 6 (Release into Land: Prescribed Substances) of Statutory Instrument No. 472, 1991 (42).

Other comments

Originally produced by coal carbonisation, but now largely derived from petroleum or by cyclisation and aromatisation of paraffinic hydrocarbons.
Benzene exposure, experimental toxicology, epidemiology studies, human health and environmental effects have been extensively reviewed (43-68).
Epidemiological evidence on benzene and lymphatic and haematopoietic cancers reviewed (69).
World Health Organisation guidelines on drinking water, provisional limit 10 $\mu g\ l^{-1}$.

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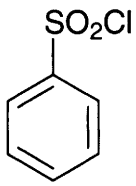
B48 benzenesulfonyl chloride



$C_6H_5ClO_2S$ **Mol. Wt.** 176.62 **CAS Registry No.** 98-09-9

Synonyms benzenesulfochloride; benzenesulfonchloride; benzenesulfonic (acid) chloride; phenylsulfonyl chloride

EINECS No. 202-636-6 **RTECS No.** DB 8750000

Uses Intermediate for dyestuff manufacture. Accelerator in alkyl resin formation. Intermediate in manufacture of phenol and resorcinol.

Physical properties

M. Pt. 14.5°C **B. Pt.** 246°C (decomp.) **Flash point** 110°C **Specific gravity** 1.378 at 23°C with respect to water at 4°C

Solubility Organic solvents: diethyl ether, ethanol

Occupational exposure

UN No. 2225 **HAZCHEM Code** 2X **Conveyance classification** corrosive substance

Ecotoxicity

Fish toxicity

LC_{50} (48 hr) brown trout yearlings 3 mg l^{-1} static bioassay (1).

Trout, bluegill sunfish, yellow perch and goldfish exposed to 5 ppm died within 2-6 hr (2).

Bioaccumulation

Since benzenesulfonyl chloride rapidly hydrolyses in water, bioconcentration in aquatic organisms is not expected to be significant (3).

Environmental fate

Degradation studies

Since benzenesulfonyl chloride rapidly hydrolyses in water, biodegradation probably will not be an important process in the environment (3).

Abiotic removal

Hydrolytic $t_{1/2}$ 5.1 min at 21°C. Calculated hydrolytic $t_{1/2}$ 12.9 min at 10°C, producing benzenesulfonic acid and hydrogen chloride (3).

Atmospheric $t_{1/2}$ 7.9 days (4).

Based upon an estimated vapour pressure of 0.068 mmHg at 25°C, volatilisation from surfaces and near-surface dry soil may be a significant process (5).

Adsorption and retention

Adsorption to soil is not expected to be a significant removal process (3).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 1960 mg kg^{-1} (6).

LC_{50} (1 hr) inhalation rat 32 ppm (7).

LD_{50} intraperitoneal rat 76 mg kg^{-1} (6).

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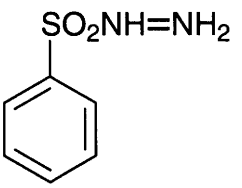
B49 benzenesulfonyl hydrazide



$C_6H_8N_2O_2S$ **Mol. Wt.** 172.21 **CAS Registry No.** 80-17-1

Synonyms benzene sulfohydrazide; phenyl sulfohydrazide; phenylsulfonyl hydrazide

EINECS No. 201-255-2 **RTECS No.** DB 6888000

Uses Gas-generating agent for use in making foam rubber and foam plastics. Blowing agent in rubber industry.

Physical properties

M. Pt. 101-103°C **Flash point** 110°C **Specific gravity** 1.369

Solubility Organic solvents: diethyl ether

Mammalian & avian toxicity

Acute data

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

Sensitisation

Eczema reported in humans from contact with benzenesulfonyl hydrazide (2).

Other comments

ED_{50} 3-day chicken embryos 15-560 μg egg^{-1} positive embryo toxic effect (3).
Reviews on human health effects and experimental toxicology listed (4).

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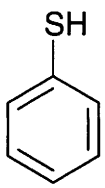
B50 benzenethiol



C_6H_6S **Mol. Wt.** 110.18 **CAS Registry No.** 108-98-5

Synonyms thiophenol; phenylmercaptan

EINECS No. 203-635-3 **RTECS No.** DC 0525000

Uses In the manufacture of pharmaceuticals. Chemical intermediate. Mosquito larvicide.

Physical properties

M. Pt. –15°C **B. Pt.** 168-169°C **Flash point** 50°C **Specific gravity** 1.078 at 25°C with respect to water at 4°C
Partition coefficient log P_{ow} 2.52 **Volatility** v.p. 1 mmHg at 18.6°C
Solubility Organic solvents: miscible with benzene, carbon disulfide and diethyl ether, soluble in ethanol

Occupational exposure

FR-VME 0.5 ppm (2 mg m^{-3})
UK-LTEL 0.5 ppm (2.3 mg m^{-3})
US-TWA 0.5 ppm (2.3 mg m^{-3})

UN No. 2337 **HAZCHEM Code** 3WE **Conveyance classification** toxic substance, danger of fire (flammable liquid)

Ecotoxicity

Fish toxicity

Trout exposed to 5 ppm benzenethiol died within 1 hr, bluegill sunfish died within 6 hr, yellow perch within 3 hr, and goldfish within 23 hr (1).

Invertebrate toxicity

EC_{50} (5, 15, 30 min) *Photobacterium phosphoreum* 0.875 mg l^{-1} Microtox test (2).

Bioaccumulation

Estimated bioconcentration factors 14-48 based on a log K_{ow} of 2.52 and water solubility of 836 mg l^{-1} suggest accumulation in aquatic organisms will not be significant (3-5).

Environmental fate

Degradation studies

$ThOD_6$ 30-42% in activated sludge inocula (6).
Benzenethiol was oxidised by isolated cells of *Thiobacillus thiooxidans* (7).

Abiotic removal

At 19.8 mg l^{-1} in cyclohexane solution, very slight absorption of ultraviolet light at >290 nm occurs which suggests benzenethiol is not susceptible to direct photolysis in air or water, or on soil surfaces (8).
Atmospheric $t_{1/2}$ 8.8 hr (9).
A vapour pressure of 2 mmHg at 25°C suggests benzenethiol would volatilise rapidly from dry soil surfaces (10).

Adsorption and retention

Estimated soil adsorption coefficients of 108-560 suggest moderate adsorption to suspended solids and sediments in water and moderate mobility in soil. However, benzenethiol is an acidic compound which should exist predominantly in its ionised form under neutral and alkaline conditions. Significance of adsorption is therefore uncertain since ionisation could cause more or less mobility than its estimated value indicates (11).

Mammalian & avian toxicity

Acute data

LD_{50} oral redwing blackbird, starling 24, 32 mg kg^{-1}, respectively (12).
LD_{50} oral rat 46 mg kg^{-1} (13).
LC_{50} (4 hr) inhalation rat 149 mg m^{-3} (14).
LD_{50} dermal rat 300 mg kg^{-1} (13).
LD_{Lo} intraperitoneal mouse 25 mg kg^{-1} (15).

Sub-acute and sub-chronic data

Subacute inhalation studies in mice (duration and concentration unspecified) showed systemic effects, including kidney damage, liver necrosis and lung haemorrhages, in exposed animals (14).

Metabolism and toxicokinetics

Rapidly metabolised via thiomethane and sulfone. Further biotransformation occurred to yield diphenyl disulfide (species unspecified) (15).

Irritancy

108 mg instilled into rabbit eye caused severe irritation (16).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537 with and without metabolic activation negative (17).

Other effects

Other adverse effects (human)

Methaemoglobin formation increased as a result of oxidative stress following exposure of 27.5-55 mg l^{-1} benzenethiol in human erythrocytes (18).

Glycolysis was inhibited following administration of 55 mg l^{-1} and at the lowest dose the erythrocyte response appears to represent a level of oxidative stress to which the cell is capable of an adaptive metabolic response (18). Inhalation may be fatal as a result of spasm. Systemic effects include inflammation and oedema of the larynx and bronchi and pneumonitis (16).

Legislation

Federal Republic of Germany regulates air emissions of benzenethiol according to class 1 organic compounds (19).

Other comments

Human health effects and experimental and industrial toxicology reviewed (20,21).

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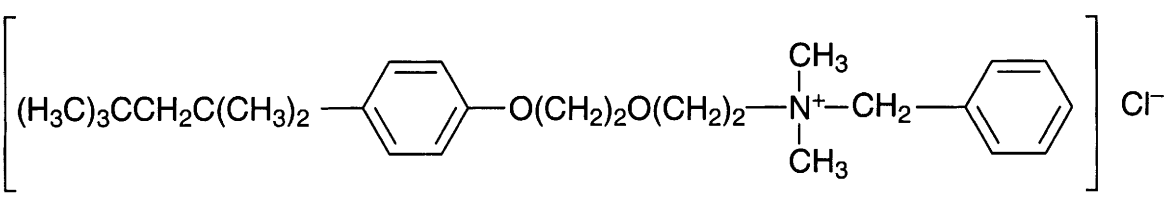
B51 benzethonium chloride



$C_{27}H_{42}NO_2Cl$ **Mol. Wt.** 448.09 **CAS Registry No.** 121-54-0

Synonyms *N,N*-dimethyl *N*-[2-[2-[4-[1,1,3,3-tetramethylbutyl]phenoxy]ethoxy]ethyl]benzenemethanaminium chloride; phemerol chloride; Hyamine 1622; Antiseptol; BZT

EINECS No. 204-479-9 **RTECS No.** BO 7175000

Uses Topical anti-infective agent. Antiseptic. Cationic detergent.

Physical properties

M. Pt. 164-166 °C
Solubility Organic solvents: acetone, chloroform, ethanol

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) fathead minnow, bluegill sunfish 1.4-1.6 mg l^{-1} (1).
LC_{50} (96 hr) coho salmon 53 mg l^{-1} (1).

Invertebrate toxicity
EC_{50} (24 hr) *Colpoda aspera* 4.31 mg l^{-1} (2).

Environmental fate

Degradation studies
Non-biodegradable (3).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat, mouse 338, 368 mg kg^{-1}, respectively (4).
LD_{50} intraperitoneal rat 119 mg kg^{-1} (5).

Carcinogenicity and chronic effects
The National Toxicology Program carried out a 2-yr skin painting study on rats and mice. No evidence of carcinogenicity was found (6).

Irritancy
100 µl instilled in rabbit eye caused severe irritation in a modified Draize test (7).
Mild skin irritation at 5% or lower. Not considered to be a sensitiser and is considered to be safe at 0.5% in cosmetics applied to the skin and at a maximum concentration of 0.02% in cosmetics used in the eye area (8).

Other effects

Other adverse effects (human)
Ingestion may cause vomiting, collapse, convulsions and coma in humans (9).

Legislation

Limited under EEC Directive on Drinking Water Quality 80/778/EEC. Chlorides: guide level 25 mg l^{-1} (10).

Other comments

Incompatible with soap and anionic detergents (9).

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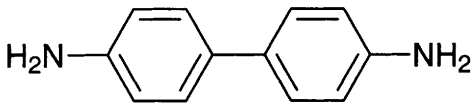
B52 benzidine



$C_{12}H_{12}N_2$ **Mol. Wt.** 184.24 **CAS Registry No.** 92-87-5

Synonyms biphenyl-4,4'-enediamine; 4,4'-diaminobiphenyl; *p,p'*-bianiline; [1,1'-biphenyl]-4,4'-diamine

EINECS No. 202-199-1 **RTECS No.** DC 9625000

Uses Intermediate for dyestuffs. Reagent for hydrogen peroxide.

Physical properties

M. Pt. 128°C **B. Pt.** 400°C at 740 mmHg **Specific gravity** 1.250 at 20°C with respect to water at 4°C
Partition coefficient log P_{ow} 2.007
Solubility Water: 400 mg l^{-1} at 12°C. Organic solvents: diethyl ether, dimethyl sulfoxide, ethanol

Occupational exposure

FR-VME 0.001 ppm (0.008 mg m^{-3})

UN No. 1885 **HAZCHEM Code** 4X **Conveyance classification** toxic substance
Supply classification toxic
Supply classification dangerous for the environment
Risk phrases May cause cancer – Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment – Harmful if swallowed (R45, R50/53, 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) – This material and/or its container must be disposed of as hazardous waste – Avoid release to the environment. Refer to special instructions/safety data sheet – Restricted to professional users (S53, S45, S60, S61)

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) sheepshead minnow 64 ppm. 1 ppm caused proliferative liver lesions and ≥50 ppm caused various anomalies in embryos in sheepshead minnows in a 1-wk study period (1,2).
LC_{50} (24 hr) red killifish 16.5 mg l^{-1} (2).

Environmental fate

Degradation studies
Initial benzidine concentration of 20 mg l^{-1} in activated sludge from mixed industrial and domestic treatment plants was depleted by 85-93% after 6 hr at 25°C. (3).
Benzidine in sludge applied to a sandy loam soil in a biological soil reactor, $t_{1/2}$ averaged 76 days (4).
Benzidine has a low decomposition rate in natural soils due to its strong adsorption to clay soils and its toxicity to microorganisms at high concentrations (5,6).
Biodegradable (7).

Abiotic removal
Removed from the environment by photolysis. Benzidine is rapidly oxidised by ferric ions and by complexing fulvic acids and clay minerals in water. Removal by evaporation and hydrolysis are insignificant (8,9).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, mouse 214, 309 mg kg^{-1}, respectively (10).

LD_{50} intraperitoneal mouse 110 mg kg^{-1} (11).

Carcinogenicity and chronic effects

Sufficient evidence of carcinogenicity to both humans and animals, IARC classification group 1 (12).

0-160 ppm administered to BALB/c and C57BL mice in drinking water for 33 months produced treatment-related lung tumours, reticulum-cell sarcomas and hepatocellular carcinomas. Other dose-related effects included pigmentation of the spleen, hepatic cytological alterations, hyperplasia of the bile ducts, megakaryocytosis of the bone marrow, vacuolisation of the brain, adenoma of the Harderian gland, atrophy of the ovaries and angioma of the uterus (13).

Oral administration of benzidine to mouse, hamster and dog induced liver and bladder carcinomas while administration to rat by oral, subcutaneous and intraperitoneal routes caused mammary and Zymbal gland neoplasms (14-18).

Dose-response data in rats showed that old animals were more susceptible to benzidine hydrochloride than young and adult animals (19).

Metabolism and toxicokinetics

Metabolites of benzidine include *N,N'*-diacetylbenzidine, *N*-hydroxy-*N,N'*-diacetylbenzidine, *N*-hydroxy-*N*-acetylbenzidine, *N,N'*-dodecylbenzidine, 3-hydroxybenzidine and 4-amino-4-hydroxybiphenyl (12,20).

Intravenous dog 1 mg kg^{-1}, plasma $t_{1/2}$ of benzidine and metabolites 3 hr, $t_{1/2}$ measured for benzidine 30 minutes. A significant amount of binding observed in DNA from liver, kidney and bladder (21).

50% of an unspecified concentration of benzidine in acetone solution was absorbed through the skin of rats in 24 hr (22).

Genotoxicity

Salmonella typhimurium TA1538 with metabolic activation positive (23).

Non-mutagenic, but induced aneuploidy, gene conversion and DNA damage in yeast. *In vitro*, rodent cells induced chromosomal aberrations, sister chromatid exchanges, unscheduled DNA synthesis and DNA strand breaks. *In vivo*, rodent cells induced micronuclei, sister chromatid exchange, DNA strand breaks and unscheduled DNA synthesis (24).

Induced transformation in Syrian hamster embryo and BALB/c 3T3 cells (12,25).

In vitro L51178Y mouse lymphoma cells with and without metabolic activation positive mutagenic response (26).

Chinese hamster V-79 cells *in vitro* with and without metabolic activation negative (27-29).

Chinese hamster V-79 (PTA) cells with rat hepatocytes metabolic activation positive, V-79/HGPRT test negative (30).

Drosophila melanogaster strongly positive in the (*w/w*$^+$) test (31).

Intraperitoneal mouse 73 and 220 mg kg^{-1}, *E. coli* K12 DNA repair host-mediated assay positive (32).

Other effects

Other adverse effects (human)

A study of workers exposed to benzidine between 1945-1979 showed a significant excess of bladder cancer incidence (33).

Of 25 benzidine workers at a US plant, 13 developed bladder cancer; all cases had been exposed to benzidine for a minimum of 6 yr (34).

An investigation of 244 workers in a Japanese dyestuffs manufacturing plant revealed nine cases of bladder cancer occurring between 1968-1981, all had been working in benzidine production (35).

Of 1601 workers in the chemical industry in China exposed to benzidine, 21 cases of bladder carcinoma were confirmed (36).

The acetylation phenotypes of 38 bladder cancer cases and 43 controls from subjects occupationally exposed to benzidine were determined and provided evidence that the NAT2-related slow *N*-acetylation polymorphism is

not associated with an increased risk of bladder cancer in workers exposed to benzidine, and may have a protective effect (37).
Workers exposed to benzidine exhibit specific benzidine-DNA adducts in exfoliated urothelial cells and peripheral white blood cells (38).

Legislation

Use prohibited in UK, controlled in US (39-41).
The FDA has declared this substance and its salts as carcinogens.
An EC Directive on the protection of the health and safety or workers from the risks related to chemical agents at work has been adopted. It prohibits the production, manufacture or use at work of benzidine and its salts. Member states must implement the Directive by 5 May 2001 (42).

Other comments

Released as emissions and in wastewater during its production. Reviews on experimental toxicology, environmental and human health effects are listed (43,44).

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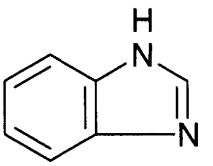
B53 benzimidazole



$C_7H_6N_2$ **Mol. Wt.** 118.14 **CAS Registry No.** 51-17-2

Synonyms benzoimidazole; BZI; NSC 759; 3-azindole; 1,3-diazaindene; *N,N'*-methyenyl-*o*-phenylenediamine; benziminazole; benzoglyoxaline

EINECS No. 200-081-4 **RTECS No.** DD 5425000

Physical properties

M. Pt. 170.5°C **B. Pt.** >360°C
Solubility Organic solvents: ethanol, boiling xylene

Mammalian & avian toxicity

Acute data
LD_{Lo} oral rat 500 mg kg^{-1} (1).
LD_{50} intravenous mouse 280 mg kg^{-1} (2).
LD_{50} intraperitoneal mouse 445 mg kg^{-1} (3).

Teratogenicity and reproductive effects
Treatment of rats with 80 mg kg^{-1} day^{-1} for 30 days caused severe testicular atrophy and arrest of spermatogenesis. Plasma follicle stimulating hormone was markedly increased by 40 and 80 mg kg^{-1} day^{-1} doses administered for 30 days and remained high for 90 days after discontinuation of the drug (4).

Other comments

A constituent of tobacco smoke.

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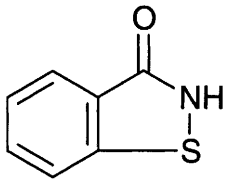
B54 1,2-benzisothiazolin-3-one



$C_7H_5NO_5$ **Mol. Wt.** 183.12 **CAS Registry No.** 2634-33-5

Synonyms 1,2-benzisothiazol-3(2*H*)-one; benzoisothiazolin-3-one

EINECS No. 220-120-9 **RTECS No.** DE 4620000

Uses Antibacterial agent. Slimicide.

Physical properties

M. Pt. 157-158°C

Occupational exposure

Supply classification harmful

Risk phrases Harmful if swallowed – Irritating to the skin – May cause sensitisation by skin contact (R22, R38, R43)

Safety phrases Keep out of reach of children (if sold to general public) – Avoid contact with the skin – Wear suitable gloves (S2, S24, S37)

Ecotoxicity

Invertebrate toxicity

LC_{50} (96 hr) shrimp 25 mg l^{-1} (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, mouse 1020, 1150 mg kg^{-1}, respectively (2).

Sensitisation

Weak sensitiser in guinea pig maximisation test (3).

A case of occupational asthma and rhinitis caused by inhalation of 1,2-benzisothiazolin-3-one in a 26-year-old man employed in a chemical factory producing detergents has been reported. To the authors' knowledge this is the first case of occupational asthma and rhinitis caused by this compound (4).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides and related products: maximum admissible concentration 0.1 μg l^{-1} (5).

Other comments

Allergic effects of paint preservatives containing 1,2-benzisothiazolin-3-one reviewed and recommendations are made not to use it as a preservative in water-based paints (6).

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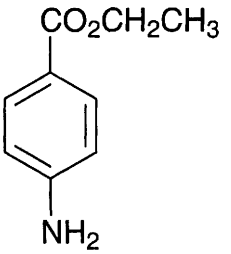
B55 benzocaine



$C_9H_{11}NO_2$ **Mol. Wt.** 165.19 **CAS Registry No.** 94-09-7

Synonyms ethyl *p*-aminobenzoate; Americaine; *p*-aminobenzoic acid, ethyl ester

EINECS No. 202-303-5 **RTECS No.** DG 2450000

Uses Topical anaesthetic. Suntan preparations.

Physical properties

M. Pt. 88-90°C **Partition coefficient** $\log P_{ow}$ 1.96
Solubility Organic solvents: chloroform, diethyl ether, ethanol

Environmental fate

Nitrification inhibition
Nitrosomonas sp. exposure to 100 mg l^{-1} resulted in 20-50 % inhibition of ammonia oxidation (1).
Nitrosomonas sp. 10 mg l^{-1} 0% inhibition of ammonia oxidation (2).

Mammalian & avian toxicity

Acute data
LD_{50} oral starling 316 mg kg^{-1} (3).
LD_{50} intraperitoneal mouse 216 mg kg^{-1} (4).

Irritancy
Dermal (24 hr) guinea pig 2% solution caused mild irritation (5).

Other effects

Other adverse effects (human)
Methaemoglobinaemia has been reported following the use of benzocaine (6).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Substances extractable in chloroform: guide level 0.1 mgl^{-1} dry residue (7).

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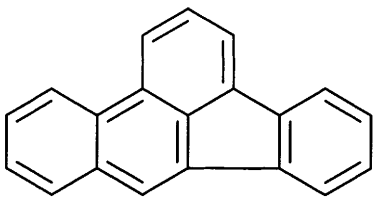
B56 benzo[*b*]fluoranthene



$C_{20}H_{12}$ **Mol. Wt.** 252.32 **CAS Registry No.** 205-99-2

Synonyms 3,4-benz[*e*]acephenanthrylene; 2,3-benzfluoranthene; 3,4-benzfluoranthene; benzo[*e*]fluoranthene; B(*b*)F

EINECS No. 205-911-9 **RTECS No.** CU 1400000

Occurrence In crude oil (1,2).

Physical properties

M. Pt. 168°C

Solubility Organic solvents: acetone, benzene

Occupational exposure

Supply classification toxic, dangerous for the environment

Risk phrases May cause cancer – Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment (R45, 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)

Ecotoxicity

Bioaccumulation

The high estimated log P_{ow} 6.124 suggests that it will bioconcentrate appreciably in aquatic organisms. The presence of microsomal oxidase in fish, however, suggests that benzo[*b*]fluroanthene will not accumulate in fish due to the anticipated rapid metabolism (1,2).

Environmental fate

Degradation studies

Subject to co-metabolism, but as a sole carbon source is not expected to biodegrade (3).

After 17 hr of incubation with 10 ppm benzo[*b*]fluoranthene resting cells of *Pseudomonas paucimobilis* (grown on fluoranthane) degraded 70% to a major, highly polar metabolite (4).

Abiotic removal

Ozonolytic $t_{1/2}$ were 52.7, 10.8 and 2.9 hrs for ozone concentrations of 0.19, 0.70 and 2.28 ppm, respectively.
Photolytic $t_{1/2}$ irradiated with 290-400 nm light in the absence of ozone was 8.7 hr, and in the presence of ozone at above concentrations was 4.2, 3.6 and 1.9 hr, respectively (5).
Photolysis in the presence of oxygen is likely to produce quinone (6).
Volatilisation $t_{1/2}$ in streams, rivers and lakes were 10, 14 and 5586 hr, respectively. Volatilisation from soil is not expected to be significant (7).

Adsorption and retention

Estimated soil adsorption coefficient 358 suggests immobility in soil. Leaching to groundwater is therefore expected to be very slow and it is also expected to partition to sediments (7,8).

Mammalian & avian toxicity

Carcinogenicity and chronic effects

No adequate data for evidence of carcinogenicity to humans, sufficient evidence for carcinogenicity to animals, IARC classification group 2B (9).
Dermal ♀ CD-1 mice 0.25-1.0 μg l^{-1} per mouse, 10 subdoses administered every other day. Induced a 100% incidence of tumour-bearing mice averaging 8.5 tumours per mouse at a total initiation dose of 0.25 μg l^{-1} (10).

Metabolism and toxicokinetics

Highly soluble in adipose tissue and lipids (11).
Topical administration of benzo[*b*]fluoranthene (B*b*F) to mice caused death at various intervals. Metabolites detected in the epidermis were 4-, 5- and 6-hydroxy B*b*F. Sulfate and glucuronide conjugates of these hydroxy B*b*F were also detected. Minor metabolites included 12-hydroxy-B*b*F, B*b*F-1,2-diol and B*b*F-11, 12-diol (12).

Genotoxicity

Salmonella typhimurium TA98, TA100 with and without metabolic activation positive (13).
Escherichia coli PQ37 (SOS chromotest) with metabolic activation positive (14).

Other effects

Other adverse effects (human)

A case-control study was undertaken in Montreal to investigate the possible associations between Occupational exposures and cancer of oesophagus, stomach, colorectum, liver, pancreas, lung, prostate, bladder, kidney, melanoma and lymphoid tissue. In total 3726 cancer patients were interviewed, between 1979 and 1985, to obtain lifetime job histories, which were translated into a history of Occupational exposures to polycyclic aromatic hydrocarbons (PAHs). 75% of all subjects had some exposure to PAHs. At the levels of exposure experienced, the preliminary analysis reported here revealed no clear evidence of an increased risk of any type of cancer among exposed workers (15).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Polycyclic aromatic hydrocarbons: maximum admissible concentration 0.2 μg l^{-1} (16).

Other comments

Human health effects, experimental toxicology and environmental effects reviewed (17,18).

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17. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium.
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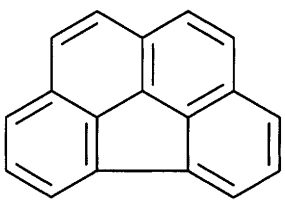
B57 benzo[*ghi*]fluoranthene



$C_{18}H_{10}$ **Mol. Wt.** 226.28 **CAS Registry No.** 203-12-3

Synonyms benzo[*mno*]fluoranthene; 2,13-benzofluoranthene; 7,10-benzofluoranthene

EINECS No. 205-903-5 **RTECS No.** DF 6140000

Physical properties

M. Pt. 147-149°C

Solubility Organic solvents: petroleum ether

Mammalian & avian toxicity

Carcinogenicity and chronic effects

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

Genotoxicity

Escherichia coli PQ37 (SOS chromotest) with metabolic activation positive (2).

Other effects

Other adverse effects (human)

A case-control study was undertaken in Montreal to investigate the possible associations between Occupational exposures and cancers of oesophagus, stomach, colorectum, liver, pancreas, lung, prostate, bladder, kidney, melanoma and lymphoid tissue. In total, 3726 cancer patients were interviewed, between 1979 and 1985, to obtain detailed lifetime job histories, which were translated into a history of Occupational exposures to polycyclic aromatic hydrocarbons (PAHs). 75% of all subjects had some exposure to PAHs. At the levels of exposure experienced, the preliminary analysis reported here revealed no clear evidence of an increased risk of any type of cancer among exposed workers (3).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Polycyclic aromatic hydrocarbons: maximum admissible concentration 0.2 $\mu g\ l^{-1}$ (4).

Other comments

Found in exhaust condensate of gasoline engines, wood preservative sludge and water sediment (5-7). Reviews on human health effects and experimental toxicology listed (8).

References

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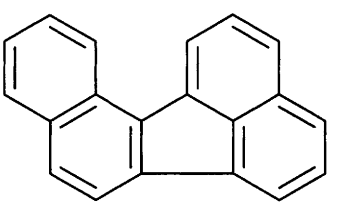
B58 benzo[*j*]fluoranthene



$C_{20}H_{12}$ **Mol. Wt.** 252.32 **CAS Registry No.** 205-82-3

Synonyms 10,11-benzofluoranthene; 7,8-benzofluoranthene; benz[*j*]fluoranthene; benzo(1)fluoranthene; dibenzo[*a,j,k*]fluorene

EINECS No. 205-910-3 **RTECS No.** DF 6300000

Physical properties

M. Pt. 165.5°C

Solubility Organic solvents: ethanol

Occupational exposure

Supply classification toxic, dangerous for the environment
Risk phrases May cause cancer – Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment (R45, 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)

Ecotoxicity

Bioaccumulation
Calculated bioconcentration factor was 55.1-83.1 which suggests potential accumulation in aquatic systems (1).

Environmental fate

Degradation studies
After 1280 days in soil treated with oil sludge, 79% of the original benzo[*j*]fluoranthene was recovered (1).

Abiotic removal
May potentially undergo photolysis in sunlit media since absorbs ultraviolet light at >290 nm. Atmospheric $t_{1/2}$ was 7 hr (2,3).
Volatilisation $t_{1/2}$ estimated as >400 yr (4).

Adsorption and retention
Based on water solubility of 6.76 μg l^{-1} and an estimated log K_{ow} of 6.12, the calculated soil adsorption coefficient of 51, 000-68,000 suggests strong adsorption to soils and sediments (5).

Mammalian & avian toxicity

Carcinogenicity and chronic effects
No adequate data for carcinogenicity to humans, sufficient evidence for carcinogenicity to animals, IARC classification group 2B (6).
Dermal mouse 0.1 and 0.5% benzo[*j*]fluoranthene solutions applied 2× wk^{-1} for life. At 9 months all animals had died. Incidence of skin papillomas was 70-95% and skin carcinomas 75-100% in low- and high-dose groups, respectively (7).

Genotoxicity

Escherichia coli PQ437 (SOS chromotest) with metabolic activation positive (8).

Other effects

Other adverse effects (human)
A case-control study was undertaken in Montreal to investigate the possible associations between Occupational exposures and cancers of oesophagus, stomach, colorectum, liver, pancreas, lung, prostate, bladder, kidney, melanoma and lymphoid tissue. In total 3726 cancer patients were interviewed, between 1979 and 1985, to obtain detailed lifetime job histories, which were translated into a history of Occupational exposures to polycyclic aromatic hydrocarbons (PAHs). 75% of all subjects had some exposure to PAHs. At the levels of exposure experienced, the preliminary analysis reported here revealed no clear evidence of an increased risk of any type of cancer among exposed workers (9).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Polycyclic aromatic hydrocarbons: maximum admissible concentration 0.2 μg l^{-1} (10).

Other comments

Present in man-made pollution sources including gasoline exhausts, cigarette smoke, soot and sewage sludge effluent (1-4).
Reviews on human health effects and experiment toxicology listed (11).

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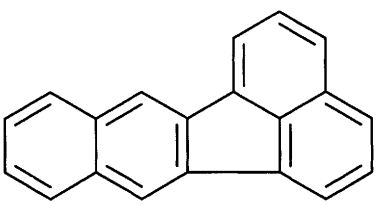
11. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

B59 benzo[*k*]fluoranthene



$C_{20}H_{12}$ **Mol. Wt.** 252.32 **CAS Registry No.** 207-08-9

Synonyms 8,9-benzofluoranthene; 2,3,1'8'-binaphthylene; 11,12-benzofluoranthene; dibenzo[*bjk*]fluorene

EINECS No. 205-916-6 **RTECS No.** DF 6350000

Physical properties

M. Pt. 217°C **B. Pt.** 480°C
Solubility Organic solvents: acetic acid, benzene, ethanol

Occupational exposure

Supply classification toxic, dangerous for the environment
Risk phrases May cause cancer – Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment (R45, 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)

Ecotoxicity

Bioaccumulation

From calculated log K_{ow} of 6.84, the estimated bioconcentration factor for fish is 144. However, no accumulation is likely due to the presence of microsomal mixed-function oxidases which enables it to be metabolised (1,2).
Short-necked clam cultured in artificial seawater at 21-25°C for 10 days revealed a decrease in benzo[*k*]fluoranthene of ~20% on day-8. When clams were placed in a basket and kept in harbour water, initially only a small increase in polycyclic aromatic hydrocarbons was found. After 1 month, a 2.5-9-fold increase was observed (3).

Environmental fate

Degradation studies

When soil treated with seven applications of oil sludge containing polynucleated aromatic hydrocarbons over a 2-yr period was monitored for an additional 18 months the benzo[*k*]fluoranthene residue in the soil decreased by 57%. In a static biodegradability test employing a domestic wastewater inoculum, 50-70% of benzo[*k*]fluoranthene was degraded in four successive weekly subcultures (4).

Abiotic removal

Demonstrates considerable atmospheric stability. Pollution resulting from emissions can be found far from source (5).
Atmospheric $t_{1/2}$ 14 hr in sunlight without ozone, $t_{1/2}$ 3-9 hr with ozone and $t_{1/2}$ 35 hr with ozone in the dark (5).
Very reactive with chlorine and ozone in solution which suggests that the levels of these chemicals will be lowered considerably in treated drinking water (6,7).
Generally resistant to hydrolysis (1).
Under ultraviolet irradiation $t_{1/2}$ was 111 min (8).

Adsorption and retention

Volatilistion from soil is expected to be low due to its low vapour pressure (9).
Estimated soil adsorption coefficient of 678 suggests strong adsorption to soils and sediments will occur (10).
Leaching may occur from soils with low organic content or high porosity (sand), or from sites that have been exposed to spills or chemical wastes containing benzo[*k*]fluoranthene (11).

Mammalian & avian toxicity

Sub-acute and sub-chronic data

LD_{50} (72 hr) chick embryo 14 μg kg^{-1} following injection into 7-day pre-incubated air sacs (12).

Carcinogenicity and chronic effects

No adequate data for carcinogenicity to humans, sufficient evidence for carcinogenicity to animals, IARC classification group 2B (13).

Metabolism and toxicokinetics

Readily absorbed from the gastrointestinal tract and lung (species unspecified) (11).
Major metabolites of benzo[*k*]fluoranthene (B*k*F) formed *in vitro* by incubation with rat liver S9 metabolic fraction were 8,9-dihydro-8,9-dihydro-B*k*F, the 2,3-quinone of B*k*F and 3-, 8- and 9-hydroxy-B*k*F (14).

Other effects

Other adverse effects (human)

A case-control study was undertaken in Montreal to investigate the possible associations between Occupational exposures and cancers of the oesophagus, stomach, colorectum, liver, pancreas, lung, prostate, bladder, kidney, melanoma and lymphoid tissue. In total 3726 cancer patients were interviewed, between 1979 and 1985, to obtain detailed lifetime job histories, which were translated into a history of Occupational exposure to polycyclic hydrocarbons (PAHs). 75% of all subjects had some Occupational exposure to PAHs. At the levels of exposure experienced, the preliminary analysis reported here revealed no clear evidence of an increased risk of any type of cancer among exposed workers (15).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Polycyclic aromatic hydrocarbons: maximum admissible concentration 0.2 $\mu g\ l^{-1}$ (16).

Other comments

Present in man-made pollution sources including gasoline exhausts and sewage sludge (17-21).
Occurs as a pollutant in tapwater and groundwater (22).
Reviews on human health effects, experimental toxicology and environmental effects listed (23).

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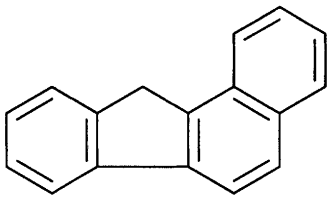
23. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

B60 benzo[a]fluorene



$C_{17}H_{12}$ **Mol. Wt.** 216.28 **CAS Registry No.** 30777-18-5

Synonyms 1,2-benzofluorene; 11*H*-benzo[*a*]fluorene; chrysofluorene; α-naphthofluorene

EINECS No. 250-335-3

Physical properties

M. Pt. 189-190°C **B. Pt.** 413°C

Solubility Organic solvents: hot benzene, chloroform, diethyl ether

Mammalian & avian toxicity

Carcinogenicity and chronic effects

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

Other effects

Other adverse effects (human)

A case-control study was undertaken in Montreal to investigate the possible associations between Occupational exposures and cancers of oesophagus, stomach, colorectum, liver, pancreas, lung, prostate, bladder, kidney, melanoma and lymphoid tissue. In total 3726 cancer patients were interviewed, between 1979 and 1985, to obtain detailed lifetime job histories, which were translated into a history of Occupational exposure to polycyclic aromatic hydrocarbons (PAHs). 75% of all subjects had some Occupational exposure to PAHs. At levels of exposure experienced, the preliminary analysis reported here revealed no clear evidence of an increased risk of any type of cancer among exposed workers (2).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Polycyclic aromatic hydrocarbons: maximum admissible concentration 0.2 μg l^{-1} (3).

Other comments

Present in man-made pollution sources including bitumen, coal tar, gasoline and cigarette smoke (4).

References

1. *IARC Monograph* 1987, **Suppl. 7**, 58.
2. Krewski, D. et al *Environ. Sci. Res.* 1990, **39**, 343-352.
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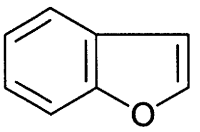
B61 benzofuran



C_8H_6O **Mol. Wt.** 118.14 **CAS Registry No.** 271-89-6

Synonyms benzo[*b*]furan; 2,3-benzofuran; coumarone; benzofurfuran; NCI-C56166; 1-oxindene

EINECS No. 205-982-6 **RTECS No.** DF 6423800

Uses Manufacture of coumarone and indene resins.

Physical properties

M. Pt. <–18°C **B. Pt.** 170-173°C **Specific gravity** 1.0913 at 22.7°C with respect to water at 4°C **Partition coefficient** log P_{ow} 2.67

Solubility Organic solvents: miscible with acetone, benzene, diethyl ether, ethanol, petroleum ether

Mammalian & avian toxicity

Acute data

LD_{50} intraperitoneal mouse 500 mg kg^{-1} (1).

Carcinogenicity and chronic effects

National Toxicology Program tested ♂ and ♀ rats and mice with benzofuran via gavage (dose unspecified). Results showed no evidence of carcinogenic activity in ♂ rat, some evidence of carcinogenic activity in ♀ rat and clear evidence of carcinogenic activity in both ♂ and ♀ mice (2).

Other comments

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

References

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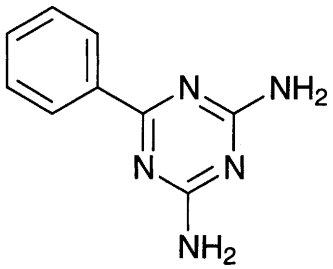
2. *National Toxicology Program, Research and Testing Div.* 1992, Report No. TR-370, NIEHS, Research Triangle Park, NC, USA.
3. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

B62 benzoguanamine



$C_9H_9N_5$ **Mol. Wt.** 187.20 **CAS Registry No.** 91-76-9

Synonyms 6-phenyl-1,3,5-triazine-2,4-diamine; benzochinamide; benzquinamide; Quantril

EINECS No. 202-095-6 **RTECS No.** XY 7000000

Uses In the manufacture of thermosetting resins, pesticides, pharmaceuticals and dyestuffs.

Physical properties

M. Pt. 227°C **Specific gravity** 1.40 at 25°C with respect to water at 4°C
Solubility Organic solvents: diethyl ether, ethanol

Occupational exposure

Supply classification harmful
Risk phrases Harmful if swallowed (R22)
Safety phrases Keep out of reach of children (if sold to general public) (S2)

Mammalian & avian toxicity

Acute data
LD_{50} oral redwing blackbird 100 mg kg^{-1} (1).
LD_{50} oral rat 1050 mg kg^{-1} (2).
LD_{50} intraperitoneal mouse 320 mg kg^{-1} (3).

Other comments

Reviews on human health effects, experimental toxicology and environmental effects listed (4).

References

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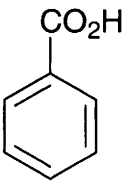
B63 benzoic acid



$C_7H_6O_2$ **Mol. Wt.** 122.12 **CAS Registry No.** 65-85-0

Synonyms benzenecarboxylic acid; phenylformic acid; Dow Corning Q7-2587; Retarder BAX; Retarder BA

EINECS No. 200-618-2 **RTECS No.** DG 0875000

Uses Permitted foodstuff preservative in fats and fruit juices. In the manufacture of dyestuffs. Antifungal agent.
Occurrence Component of berries, fruits and vegetables.

Physical properties

M. Pt. 122.4°C **B. Pt.** 249°C **Flash point** 121-131°C **Specific gravity** 1.27 **Partition coefficient** log P_{ow} 1.87 at 20°C **Volatility** v.p. 1 mmHg at 96° (sublimes)
Solubility Water: 2.9 g l^{-1} at 20°C. Organic solvents: acetone, benzene, carbon disulfide, carbon tetrachloride, chloroform, diethyl ether, ethanol

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) mosquito fish 180 mg l^{-1} (1).

Invertebrate toxicity
Cell multiplication inhibition test, *Pseudomonas putida* 480 mg l^{-1}, *Microcystis aeruginosa* 55 mg l^{-1}, *Scenedesmus quadricauda* 1630 mg l^{-1}, *Entosiphon sulcatum* 218 mg l^{-1}, *Uronema parduczi* 31 mg l^{-1} (2-4).

Bioaccumulation
Bioconcentration factor in golden ide and *Chlorella fusca* <10 (5).
Bioconcentration factors of mosquito fish, algae, mosquito larvae are 21, 100 and 138, respectively, and of *Daphnia* and snail are 1800 and 2800, respectively (6).

Environmental fate

Degradation studies
99% removal within 24 hr using adapted activated sludge (7).
ThOD 1.97 g g^{-1}; COD 0.69 g g^{-1} (8).
BOD_5 at 20°C 1.34-1.4 using normal sewage seed and 1.36 using acclimated sewage seed. BOD_{10} at 20°C 1.4 using normal sewage seed. BOD_{20} 1.45 at 20°C (9).
The $t_{1/2}$ for mineralisation using a Captina silt loam inoculum was 4.5 hr after a 30-min lag (10).
$t_{1/2}$ of 0.85 and 3.6 days in a polluted river and reservoir, respectively (11).
$t_{1/2}$ of 0.22 days for mineralisation in eutrophic water in a range of 32 ng l^{-1} to 50 µg l^{-1}. From 63-83% was lost in 6 hr and >94% in 58 hr (12).
Under anaerobic conditions, 91% of benzoic acid was converted into methane and carbon dioxide in 18 days including an 8-day lag period (13).
86-93% conversion into methane and carbon dioxide occurred in 14 days with a sewage sludge inoculum (14).
Benzoic acid is biodegradable under aerobic conditions by bacteria present in crude municipal wastewater at ≤200 g m^{-3} (15).

$t_{1/2}$ for carboxyl and ring-labelled benzoic acid was 3.9 and 7.2 hr, respectively (16).
Confirmed biodegradable (17).

Abiotic removal

The pK_a of 4.2 suggests almost exclusive existence in the dissociated form at environmental pHs (18).
In the vapour phase, estimated $t_{1/2}$ with photochemically produced hydroxyl radicals 2 days (19).

Adsorption and retention

Benzoic acid did not adsorb appreciably to two different sandy soils, a clay subsoil and montmorillonite clay (20,21).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 1700 mg kg^{-1} (22).
LD_{Lo} subcutaneous rabbit 2000 mg kg^{-1} (23).
LD_{Lo} oral human 500 mg kg^{-1} (22).

Metabolism and toxicokinetics

Following intravenous administration to weaning Yorkshire sows of benzoic acid in physiological saline (200 μg, 10 μCi), collection of excrement over 6 days revealed >80% in urine. In ethanol (200 μg, 10 μCi), topical doses applied at a surface concentration of 40 μg cm^{-2} penetrated at 25.7%; faecal clearance of radiolabel, expressed as a percentage of total excretion was greater after topical administration (24).
Human clearance time 9-15 hr (25).
When administered orally, benzoic acid is rapidly absorbed from the gastrointestinal tract, conjugated with glycine in the liver to form hippuric acid which is rapidly excreted in the urine within 12 hr (up to 97% within the first 4 hr). When taken in large doses, some benzoic acid may be excreted as benzoylglucuronic acid (26).
Ruminants excrete much larger quantities of aromatic acids, such as benzoic acid, in their urine than do non-ruminants, particularly when fed a high-roughage diet (27).
In 3 hr, biliary excretion as percentage dose excreted is 1.2 in rat, 1.7 in guinea pig, 0.7 in rabbit, 0.8 in dog, 1.2 in cat and 0.5 in hen (28).

Irritancy

Dermal rabbit (24 hr) 500 mg caused mild irritation and 100 mg instilled into rabbit eye caused severe irritation (29).

Sensitisation

Asthmatics or urticaria sufferers may be sensitive to benzoic acid (25).

Genotoxicity

Salmonella typhimurium TA98, TA100 with and without metabolic activation negative (30).

Other effects

Other adverse effects (human)

Immediate irritant skin reactions to benzoic acid were stronger in areas of skin washed with a diluted dishwashing liquid 2 × day^{-1} for 6 days compared with controls (31).
Neonates with fatal toxic syndrome attributable to benzyl alcohol have been reported to have elevated urinary concentrations of its metabolite, benzoic acid. The accumulation of benzoic acid in blood, possibly due to the liver's diminished metabolic capacity in premature infants, might be responsible for the metabolic acidosis observed (32,33).

Other comments

Earlier reports that benzoic acid is uterotrophic to the rat and mouse have not been confirmed in studies involving a range of test protocols and dose levels. The compound was also inactive in a human oestrogen receptor (hERα) yeast estrogenicity test (34).
Reacts with the preservative sodium hydrogen sulfite (*E222*) (25).

Found in groundwater in Australia underlying an area where acid wastes from a manufacturing process of a chemical company was stored in unlined ponds. Since the chemical was only found in the aquifer down stream from the believed source of pollution and not close to this source, it was either formed by bacterial action or came from another source (35).

Biochemistry and toxicology of benzoic acid metabolism reviewed (36).

Hazardous properties, human health effects and experimental toxicology reviewed (37,38).

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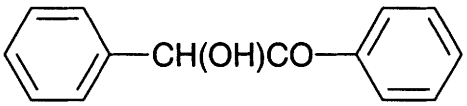
B64 benzoin



$C_{14}H_{12}O_2$ **Mol. Wt.** 212.25 **CAS Registry No.** 579-44-2

Synonyms benzoylphenylcarbinol; bitter almond oil camphor; α-hydroxybenzyl phenyl ketone; α-hydroxy-α-phenylacetophenone; 2-hydroxy-2-phenylacetophenone; NCI-CS011

EINECS No. 204-331-3 **RTECS No.** DI 1590000

Uses Organic synthesis.

Physical properties

M. Pt. 133-135°C **B. Pt.** 344°C at 768 mmHg
Solubility Organic solvents: acetone, boiling ethanol

Environmental fate

Degradation studies
Confirmed biodegradable (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 10 g kg^{-1} (2).
LD_{50} dermal rabbit 8870 mg kg^{-1} (2).

Carcinogenicity and chronic effects
National Toxicolgy Program tested rats and mice via feed. Negative results obtained in both species (3).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA1535 without metabolic activation positive (4).
In vitro mouse lymphoma cell L51787/tk+/– mutation assay positive.
In vitro Chinese hamster ovary cell HGPRT+ mutation assay negative (5).

Other comments

Human health effects, genotoxicity and experimental toxicology reviewed (6-8).

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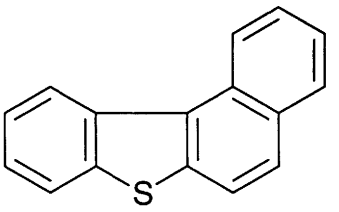
B65 benzo[*b*]naphtho[1,2-*d*]thiophene



$C_{16}H_{10}S$ **Mol. Wt.** 234.32 **CAS Registry No.** 205-43-6

Synonyms 3,4-benzo-9-thiafluorene; 7-thia-7(H)-benzo[*c*]fluorene; naphtho[2,1-*b*]thianaphthene

RTECS No. DI 2340000

Physical properties

M. Pt. 103-4°C

Mammalian & avian toxicity

Metabolism and toxicokinetics

Metabolised by rat liver microsomes, preferentially undergoing S-oxidation, to form the sulfone as the major metabolite and the sulfoxide as the minor metabolite (1).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1538 with metabolic activation positive (2).

Other comments

Combustion product from fossil fuels, particularly from diesel engines. Found in metal working oils and machine oils (3).

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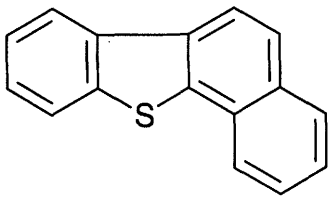
B66 benzo[*b*]naphtho[2,1-*d*]thiophene



$C_{16}H_{10}S$ **Mol. Wt.** 234.32 **CAS Registry No.** 239-35-0

Synonyms naphtho[1,2-*b*]thianaphthene

EINECS No. 205-948-0

Physical properties

M. Pt. 185-186°C

Mammalian & avian toxicity

Carcinogenicity and chronic effects

Using a beeswax/trioctanoin mixture as vehicle, 6, 3 and 1 mg were injected into the lungs of 35 ♀ rabbits per group. A dose-dependent tumour incidence was found, but an increasing incidence of neoplasms was not seen between the median and high dose. Estimated ED_{10} value is 1.65 mg (1).

Metabolism and toxicokinetics

Metabolism by F344 rat liver 9000 g supernatant (S-9), from Aroclor 1254-treated rats, produced six metabolites: *trans*-1,2-dihydroxy-1,2-dihydrobenzo[*b*]- naphtho[2,1-*d*]thiophene, benzo[*b*]naphtho[2,1-*d*] thiophene sulfoxide, *trans*-3,4-dihydroxy-3,4-dihydrobenzo[*b*]naphtho[2,1-*d*]thiophene, 8- or 9-hydroxybenzo[*b*]naphtho[2,1-*d*]thiophene and 7-hydroxybenzo[*b*]naphtho[2,1-*d*]thiophene (2).

Other comments

Combustion product from fossil fuels, especially diesel engines.
Major impurity in materials related to coal tar fractions 2-3 wt%.

References

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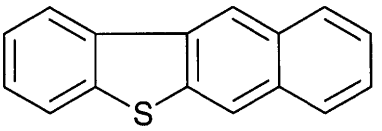
B67 benzo[*b*]naphtho[2,3-*d*]thiophene



$C_{16}H_{10}S$ **Mol. Wt.** 234.32 **CAS Registry No.** 243-46-9

Synonyms naphtho[3,2-*b*]thianaphthene

EINECS No. 205-956-4

Physical properties

M. Pt. 158-9°C

Occupational exposure

Safety phrases 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 (S16, S26, S29)

Mammalian & avian toxicity

Metabolism and toxicokinetics

Metabolised by liver microsomes of untreated rats to form the sulfone as the major metabolite, and the sulfoxide as the minor metabolite. Pretreatment of rats with phenobarbitol resulted in enhanced sulfone formation. Pretreatment with 5,6-benzoflavone caused the sulfone to be formed as the major metabolite and a dihydrodiol as the minor metabolite (1).

Other comments

Combustion product from fossil fuels especially from diesel engines. Found in metal working oils, engine sump oils, quenching oils.

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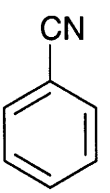
B68 benzonitrile



C_7H_5N **Mol. Wt.** 103.12 **CAS Registry No.** 100-47-0

Synonyms benzenenitrile; cyanobenzene; benzoic acid nitrile; phenyl cyanide

EINECS No. 202-855-7 **RTECS No.** DI 2450000

Uses Solvent.

Physical properties

M. Pt. –13°C **B. Pt.** 191°C **Specific gravity** 1.01 at 15°C with respect to water at 15°C
Partition coefficient log P_{ow} 1.56
Solubility Organic solvents: acetone, benzene, diethyl ether, ethanol

Occupational exposure

UN No. 2224 **HAZCHEM Code** 3X **Conveyance classification** toxic substance
Supply classification harmful
Risk phrases Harmful in contact with skin and if swallowed (R21/22)
Safety phrases Keep out of reach of children (if sold to general public) – Do not breathe vapour (S2, S23)

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) fathead minnow 78-135 mg l^{-1} range dependent on pH (1).
LC_{50} (96 hr) bluegill sunfish, guppy 78-400 mg l^{-1} (1,2).
Trout and bluegill sunfish exposed to 5 ppm died in 22 hr (3).

Invertebrate toxicity
Cell multiplication inhibition test *Pseudomonas putida* 11 mg l^{-1}, *Microcystis aeruginosa* 3.4 mg l^{-1}, *Scenedesmus quadricauda* 75 mg l^{-1}, *Entosiphon sulcatum* 30 mg l^{-1}, *Uronema parduczi* 119 mg l^{-1} (4-6).
EC_{50} (5-30 min) *Photobacterium phosphoreum* 11.6 mg l^{-1} Microtox test (7).

Environmental fate

Degradation studies
Klebsiella pneumoniae, adapted to use benzonitrile as the sole source of carbon and nitrogen, metabolised 8.4 mM to 4 mM benzoic acid and 2.7 mM ammonia. Mixtures of benzonitrile and aliphatic nitriles were also degraded (8).
Confirmed biodegradable (9).

Mammalian & avian toxicity

Acute data
LD_{50} oral mouse 970 mg kg^{-1} (10).
LD_{50} intraperitoneal rabbit 1250 mg kg^{-1} (11).

Sub-acute and sub-chronic data
Intraperitoneal mouse, a single dose of 0.58 or 0.145 m mol kg^{-1} caused no histopathological changes in the olfactory mucosa or in the liver (12).

Irritancy
Dermal rabbit (24 hr) 500 mg caused moderate irritation (13).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Cyanides maximum admissible concentration 50 μg l^{-1} (14).

Other comments

Reviews on physico-chemical properties, human health effects and experimental toxicology listed (15).

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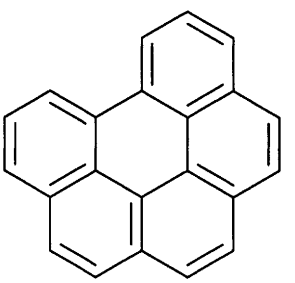
B69 benzo[*ghi*]perylene



$C_{22}H_{12}$ **Mol. Wt.** 276.34 **CAS Registry No.** 191-24-2

Synonyms 1,12-benzperylene; 1,12-benzoperylene

EINECS No. 205-883-8 **RTECS No.** DI 6200500

Physical properties

M. Pt. 278-280°C **Partition coefficient** log P_{ow} 6.90

Solubility Water: 0.26 μg l^{-1} at 25°C

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) fathead minnow 78-135 mg l^{-1}, dependent on pH (1).

LC_{50} (96 hr) bluegill sunfish, guppy 400 mg l^{-1} in soft water (1,2).

Invertebrate toxicity

EC_{50} (48 hr) *Daphnia magna* 0.2 μg l^{-1} (3).

Bioaccumulation

Based on a water solubility of 0.26 μg l^{-1} at 25°C and an estimated log K_{ow} of 6.58, calculated bioconcentration factors were 85-110 which indicates potential accumulation in aquatic systems (4,5).

Environmental fate

Degradation studies

Bacillus megaterium metabolises benzo[*ghi*]perylene, but, data are insufficient to predict the significance of soil biodegradation (6).

If released to the atmosphere, may be susceptible to slow biodegradation under aerobic conditions. It is not expected to leach or volatilise from soils (6).

Benzo[*ghi*]perylene was not biodegraded in the presence of sodium dodecyl sulfate (SDS), an anionic surfactant (10, 100 and 500 mg kg^{-1} creosote-contaminated soil), but was mobilised from soil samples in high concentration solutions of SDS (0.005 to 1% wt./vol.) (7).

Within 7 days, an aerobic aqueous screening test inoculated with sewage showed a 60% loss of an initial 1 ppm benzo[*ghi*]perylene concentration (8).

After 240 days, in an unacclimated agricultural sandy loam soil incubated at 10 and 20°C, 81 and 76%, respectively, of an initial concentration of 9.96 μg g^{-1} remained. Corresponding estimated $t_{1/2}$ were 650 and 600 days (9).

After 1280 days, 78.3% of an inital 3.1 μg g^{-1} remained in a soil treated with oil sludge at 17.0 μg g^{-1} (10).

Abiotic removal

Photolytic $t_{1/2}$ on silica gel, alumina, fly ash and carbon black were 7, 22, 29 and >1000 hr, respectively (11).

Atmospheric $t_{1/2}$ using photochemically produced hydroxyl radicals was estimated to be 2 hr (12).

Volatilisation $t_{1/2}$ from a model river 1 m deep, flow rate 1 m sec^{-1} with a windspeed of 3 m sec^{-1} has been estimated to be 38 days (4).

Adsorption and retention

Estimated soil adsorption coefficients of >1 million and the widespread detection of benzo[*ghi*]perylene in various USA sediments indicate that adsorption to suspended particulate matter and sediments is an important environmental process (6).

Estimated soil adsorption coefficients of 90,000-400,000 indicate high immobility in soil (13).

Mammalian & avian toxicity

Carcinogenicity and chronic effects

No adequate data for carcinogenicity to humans, inadequate evidence for carcinogenicity to animals, IARC classification group 3 (14).

Dermal mouse (1 yr) 0.05 or 0.1% solution applied 3× wk^{-1} induced a low tumour incidence (15).

Metabolism and toxicokinetics

Absorbed readily from the gastrointestinal tract and lung, is highly lipid soluble and can pass across epithelial membranes (6).

Genotoxicity

Escherichia coli PQ37 (SOS chromotest) with metabolic activation positive (16).

Other effects

Other adverse effects (human)

A case-control study was undertaken in Montreal to investigate the possible associations between Occupational exposures and cancers of oesophagus, stomach, colorectum, liver, pancreas, lung, prostate, bladder, kidney, melanoma and lymphoid tissue. In total 3726 cancer patients were interviewed between 1979 and 1985, to obtain detailed lifetime job histories, which were translated into a history of Occupational exposures to polycyclic aromatic hydrocarbons (PAHs). 75% of all subjects had some Occupational exposure to PAHs. At levels of exposure experienced, the preliminary analysis reported here revealed no clear evidence of an increased risk of any type of cancer among exposed workers (17).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Polycyclic aromatic hydrocarbons maximum admissible concentration 0.2 μg l^{-1} (18).

Other comments

Present in coal tar. Gasoline engine exhausts. Contaminant in tap water, groundwater and sediment. Occurs in domestic effluent (1,2,19,20).
Reviews on human health effects, experimental toxicology and environmental effects listed (21).

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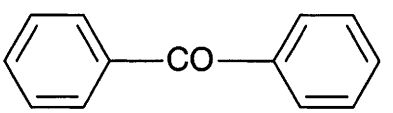
B70 benzophenone



$C_{13}H_{10}O$ **Mol. Wt.** 182.22 **CAS Registry No.** 119-61-9

Synonyms diphenyl ketone; benzoylbenzene; diphenylmethanone

EINECS No. 204-337-6 **RTECS No.** DI 9950000

Uses Used in the manufacture of antihistamines, hypnotics and insecticides. Used as a fixative for heavy perfumes, especially when used in soaps.
Occurrence In Baltic Sea shale tar.

Physical properties

M. Pt. 48.5°C **B. Pt.** 305°C **Specific gravity** 1.1108 at 18°C with respect to water at 4°C
Solubility Organic solvents: acetone, benzene, chloroform, diethyl ether, ethanol

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) fathead minnow 15.3 mg l^{-1} (1).

Invertebrate toxicity
EC_{50} (30 min) *Photobacterium phosphoreum* 8.92 mg l^{-1} Microtox test (2).

Bioaccumulation
Non-accumulative or low accumulative (3).

Environmental fate

Degradation studies
Biodegradable (3).

Mammalian & avian toxicity

Acute data
LD_{50} oral mouse 2900 mg kg^{-1} (4).
LD_{50} intraperitoneal mouse 727 mg kg^{-1} (4).

Sub-acute and sub-chronic data
Oral rat (90 day) no-effect level 20 mg kg^{-1} day^{-1} in diet (5). Oral rat (28 day) 100-500 mg kg^{-1} day^{-1} hepatocellular enlargement with an associated clumping of cytoplasmic basophilic material around the central vein. Treatment-related changes also occurred in erythrocyte count, Hb, haematocrit, bilirubin, total protein and albumin, although all changes did not occur in both groups (100 and 500 mg dose day^{-1}) in both sexes (5). Intraperitoneal guinea pig (15 day) 5 mg kg^{-1} day^{-1}, histopathological studies showed benzophenone to be hepatotoxic (6).

Carcinogenicity and chronic effects
Selected for general toxicology study by National Toxicology Program (7).

Genotoxicity

Escherichia coli polA without metabolic activation negative (8).
Salmonella typhimurium TA98, TA100 with and without metabolic activation negative (9).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Substances extractable in chloroform: guide level 0.1 mg l^{-1} dry residue (10).

Other comments

On the basis of the calculated Possible Average Daily Intake of 0.33 mg day^{-1}, a safety factor of >3600 is demonstrated. The safety factor based on the more realistic per capita consumption of 0.32 µg day^{-1} would be approximately 3.7 million (5).
Reviews on human health effects and experimental toxicology listed (11).

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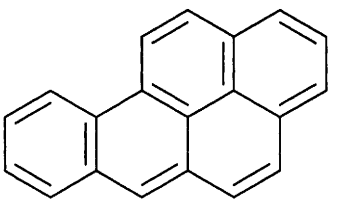
B71 benzo[a]pyrene



$C_{20}H_{12}$ **Mol. Wt.** 252.32 **CAS Registry No.** 50-32-8

Synonyms benzo[*d,e,f*]chrysene; 3,4-benzopyrene; 6,7-benzopyrene; 3,4-benzpyrene; benz[*a*]pyrene; benzo[*d,e,f*]chrysene; 3,4-benzopyrene; 6,7-benzopyrene; 3,4-benzpyrene; benz[*a*]pyrene

EINECS No. 200-028-5 **RTECS No.** DJ 3675000

Physical properties

M. Pt. 179°C **B. Pt.** 495°C **Partition coefficient** log P_{ow} 6.35
Solubility Organic solvents: benzene, toluene, xylene

Occupational exposure

SE-LEVL 0.002 mg m^{-3} **SE-STEL** 0.02 mg m^{-3}
Supply classification toxic, dangerous for the environment
Risk phrases May cause cancer – May cause heritable genetic damage – May impair fertility – May cause harm to the unborn child – Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment (R45, R46, R60, R61, 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)

Ecotoxicity

Fish toxicity
Sea bass were intoxicated with benzo[*a*]pyrene by two different routes. In force-fed fish the intestinal epithelium was the first injured tissue, in intraperitoneally toxified fish the liver. In both hepatocytes and enterocytes the main structural perturbations concerned a large development of rough and smooth endoplasmic reticulum and a great increase in the number of vacuoles and lysosomes. After 17 days of contamination some nuclear changes

were observed indicating the high reactivity of benzo[*a*]pyrene metabolites which form covalent adducts with DNA and the long-term toxicity of this compound (1).
After intragastric administration of ^{14}C-labelled benzo[*a*]pyrene to sea bass only 25% of the injected radioactivity was detected and it was found only in the liver, gallbladder, intestine and kidney; 85% of this was found in the gallbladder. The calculated half-lives in these tissues were 8.2, 3.5, 3.3 and 0.8 days, respectively (2).
Sheepshead minnows (6-10 days old) were exposed to benzo[*a*]pyrene (0-200 ppb) for periods of 6 or 24 hours 1 × wk^{-1} for 1 or 2 wk. Neoplastic lesions were not seen in control or experimental fish. (3).
Primary cultures of rainbow trout hepatocytes were exposed to 0.1-10 μM benzo[*a*]pyrene in the alkaline comet assay. A significant increase in DNA single-strand breaks was observed after 4 hr of exposure. After 48 hr of exposure the level of DNA strand breaks was lower than that of the control (4).
Coho salmon parr and smolts are able to metabolise benzo[*a*]pyrene via phase I and II biotransformation reactions to glucuronide, sulfate and other conjugated metabolites (5).
Intraperitoneal injection of 20 μg g^{-1} into sea bass caused a reduction in liver metallothionein content (6).

Invertebrate toxicity
LD_{50} (96 hr) ragworm *Neanthes arenaceodentata* in seawater at 22°C <1 ppm (in static bioassay) (7).
EC_{50} (96 hr) *Daphnia pulex* 0.05 mg l^{-1} (8).
Incubation of intertidal sea anenome (*Bunodosoma cavernata*) microsomes with benzo[*a*]pyrene and either NAD(P)H or *tert*-butylhydroperoxide resulted in several oxidative metabolites including: 3-hydroxybenzo[*a*]pyrene, 4,5-, 7,8-, and 9,10-benzo[*a*]pyrenediols; 1,6-, 3,6-, and 6,12-benzo[*a*]pyrenediones; benzo[*a*]pyrenetetrols; and benzo[*a*]pyrenediol epoxides. *tert*-Butylhydroperoxide-dependent reactions proceeded ~67-fold faster than NAD(P)H-dependent reactions and produced primarily diols (9).

Bioaccumulation
Administered to northern pike via the diet or water at levels found in moderately polluted water, fish were observed for 10 hr to 21 days after initial exposure. Uptake was through the gastrointestinal system and the gills, and the compound was metabolised in the liver and excreted in urine and bile. Benzo[*a*]pyrene and its metabolites were heterogeneously distributed in the kidneys with little accumulation in adipose tissue. Since recovery of the compounds in different organs after 8.5 days of exposure was in the form of metabolites, metabolism is thought to play an important role in the bioaccumulation and disposition in fish (10).
Studies on the American lobster, *Homarus americanus*, administered benzo[*a*]pyrene (50 μg kg^{-1}) orally or intravenously (*sic*) showed that benzo[*a*]pyrene from dietary sources is retained for long periods in the tissues and suggest that a major reason for the resistance of American lobsters to polycyclic aromatic hydrocarbon induced cancers is the very slow phase 1 metabolism to reactive metabolites (11).
Bioconcentration factors in oysters 3000, rainbow trout 920, bluegill sunfish 2657, *Daphnia magna* 1000, *Daphnia pulex* 13,000 (12-17).

Environmental fate

Degradation studies
50-80% degradation occurred in soil inoculated with N5 and N13 bacterial strains. After 8 days the highest degradation occurred in soil inoculated with pretreated bacteria (18,19).
Degradation of 56-67% was observed in nutrient/benzo[*a*]pyrene solutions seeded with acclimated sewage and incubated for 4-7 day periods (20).
Soil biodegradation is temperature-dependent, $t_{1/2}$ 2-694 days from <15->25°C (21).

Abiotic removal
Absorbs light at >290 nm and may undergo direct photolysis (22).
Calculated photolytic $t_{1/2}$ is 0.54 hr in surface waters (23).
Estimated $t_{1/2}$ with photochemically produced hydroxyl radicals is 21 hr (24).
Reported estimated theoretical maximum $t_{1/2}$ for volatilisation from a model river 1 m deep, flowing at 1 m sec^{-1} with a wind velocity of 4 m sec^{-1} was 18 days. It is concluded that vaporisation will be significant (25).
Adsorption of benzo[*a*]pyrene on kaolinite clay inhibited photolysis, and adsorption on fly ash showed 17% degradation when exposed to sunlight for 3-4 hr (26).

Adsorption and retention

Soil adsorption coefficient, binding to dissolved organic carbon in three natural waters 18,000-52,000 and to Aldrich humates 890,000 (27).

Mammalian & avian toxicity

Acute data

LD_{Lo} intraperitoneal mouse 500 mg kg^{-1} (28).

LD_{50} subcutaneous rat 50 mg kg^{-1} (29).

Carcinogenicity and chronic effects

No adequate data for carcinogenicity to humans, sufficient evidence for carcinogenicity to animals, IARC classification group 2A (30).

Dermal ♀ mouse (9 wk) 8, 16, 32, 64 μg wk^{-1} caused initial linear increase in DNA adducts with dose in the epidermis, but the increase was much less steep above 32 μg wk^{-1}. This did not correlate with the sharp rise in tumour response above 32 μg wk^{-1}. There was little epidermal hyperplasia but an associated dose-dependent increase in incidence of pyknotic and dark cells at 64 μg wk^{-1} indicated that benzo[*a*]pyrene produced extensive cytotoxicity and cell death with regenerative proliferation. Giant keratinocytes occurred in all dose groups. Tumours were initially papillomas and required an average of 8 wk to convert to carcinomas (31).

Benzo[*a*]pyrene is a weak mammary carcinogen in mice and rats (32).

Metabolism and toxicokinetics

Eight pregnant rats were exposed (day-17 of gestation) for 95 min to a microcondensation aerosol of benzo[*a*]pyrene at five different atmospheric concentrations (200-800 m^{-3}). Five were killed immediately following the exposure and three at 6-hr post-dosing. Distribution to the foetus did not appear to be related to its position on the uterine horn and the uptake of benzo[*a*]pyrene was non-linear with increasing exposure concentrations, which was similar to the observations previously reported for pyrene. The levels of benzo[*a*]pyrene were much higher in the foetus, especially in the lung, than those observed in the pyrene study, as also were the levels of total metabolites, which might account in part for the carcinogenic potency of the compound (33).

A single oral or topical dose was administered to ♂ SENCAR mice. After 6-48 hr, high concentrations were found in skin following topical applications but very little material reached the organs after oral doses. The internal organs contained more material after oral administration (34).

Following a single dose of tritiated benzo[*a*]pyrene (BaP) instilled in dog trachea, just anterior to the carina, $t_{1/2}$ for absorption into the trachea mucosa was determined to be ~ 73 minutes, consistent with diffusion-limited passage through the epithelium, and led to local doses in the tracheal epithelium which were more than 1000-fold higher than those of other tissues. The long retention of BaP in the epithelium provided the local metabolising enzymes with high substrate levels over a long period, resulting in extensive metabolism. These results explain the tendency of highly lipophilic carcinogens such as BaP to induce tumours at the site of entry (35).

Urine samples of pitch-coke plant workers showed increased levels of benzo[*a*]pyrene both before and after work shifts, which indicated slow excretion (36).

Intraperitoneal administration in rats showed maximum uptake of benzo[*a*]pyrene after 1 hr in aortic media and liver; levels in kidney and urine continued to increase. Smooth arterial muscle cells in culture incubated with tritium-benzo[*a*]pyrene took up the radioactivity. This was inversely related to extracellular lipid content and ^{3}H release was increased by proteins (37).

In rats, benzo[*a*]pyrene is readily absorbed from the intestinal tract, and localised primarily in body fat and fatty tissues. After a single intravenous injection it was detected in blood and liver, $t_{1/2}$ <5 min and 10 min, respectively (38).

♂ rats, with cannulated bile duct, received intravenous injections of radiolabelled benzo[*a*]pyrene non-covalently bound to lipoproteins in equimolar amounts. Cumulative biliary excretions were 39.6, 24.6 and 21.2% for very-low-, low- and high-density lipoproteins complexed to benzo[*a*]pyrene, respectively. 60-80% of injected benzo[*a*]pyrene, and 50-60% of injected benzo[*a*]pyrene metabolites were not excreted immediately in control or induced animals (39).

Investigations on B6C3F1 mice showed that macrophages were the splenic cell types which metabolised

benzo[*a*]pyrene and that as a result they may be the cell type targeted by this compound resulting in suppression of splenic humoral immune responses (40).

Genotoxicity

Escherichia coli PQ37 with metabolic activation positive (41).
Salmonella typhimurium TA98, TA100, TA1535, TA1538 with metabolic activation positive (42).
Benzo[*a*]pyrene in the absence of a metabolic activation system induced aneuploidy at 2.5-10 μg ml^{-1} in Chinese hamster cell line V79-MZ. Higher concentrations caused cell cycle delay and, therefore, did not effect ploidy. No significant increase in SCE frequency occurred at the above concentrations (43).

Other effects

Other adverse effects (human)
A case-control study of 3730 cancer patients and 533 population controls was carried out in Montreal to investigate associations between a large variety of environmental and Occupational exposures to PAHs, including benzo[*a*]pyrene, and different types of cancer. Associations between 14 cancer types and 6 PAH exposures were analysed using logistic regression methods. For most types of cancer evaluated there was no evidence of excess risk due to PAHs at the levels encountered in the occupations in which PAH exposure has been prevalent in the Montreal area. For a few cancer sites – the oesophagus, pancreas and the prostate gland – there were suggestions of excessive risk (44).
The respiratory health of 726 workers in a rubber processing factory have been investigated. Chest X-rays showed that 16% of the group of workers most exposed to benzo[*a*]pyrene and total suspended particulate matter exhibited radiological abnormalities. Of seven possible factors thought likely to be related to the effects on pulmonary function, only total suspended particulate matter and the concentration of benzo[*a*]pyrene in the respirable fraction of particulates resulted in a statistically significant association in a multiple regression analysis (45).

Any other adverse effects
Intramammillary injection of 0.25 μmol $gland^{-1}$ in rats produced one major and two minor DNA adducts in mammary epithelial cells. Non-target tissues showed a similar adduct pattern, however none were detected in the pancreas and bladder (32).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Polycyclic aromatic hydrocarbons: maximum admissible concentration 0.2 μg l^{-1} (46).

Other comments

Occurs in cigarette smoke and from the combustion of fuels (47-49).
The influence of anti-initiators upon the metabolic pattern of benzo[*a*]pyrene *in vitro* reviewed (50).
The *in vitro* metabolism of benzo[*a*]pyrene by microsomes from the hepatopancreas and antennal gland of *Procambarus clarkii* compared and contrasted with reports on other crustacean systems in the literature (51).
The *in vivo* metabolism of benzo[*a*]pyrene in the newt *Pleurodeles walt* is rapid (52).
Benzo[*a*]pyrene metabolism was studied in the pyloric caecum microsomes of the sea star *Asterias rubens*. Benzo[*a*]pyrene was metabolised into phenols, quinones and dihydrodiols. Monohydroxylated benzo[*a*]pyrene comprised approximately 40% of the total metabolites produced. Protein adducts of benzo[*a*]pyrene appeared to be formed (53).
F344/DuCrj ♂ rats were given a subcutaneous injection of benzo[*a*]pyrene. Thereafter they received water extracts of six Chinese medicinal herbs for 50 weeks and were then examined for tumours. *Polygonum multiflorum* extract significantly reduced the tumour incidence (54).
Green tea extracts at the concentrations customarily consumed by humans caused a very marked and concentration-dependent inhibition of the Aroclor 1254-hepatic S9-mediated mutagenicity of benzo[*a*]pyrene (55).
Methanol and hot-water extracts of glossy privet (*Ligustrum lucidum Ait.*) inhibited the mutagenic activity of benzo[*a*]pyrene in *Salmonella typhimurium* TA98 with S9 mix (56).

Murine α/β interferons inhibit benzo[*a*]pyrene activation and mutagenesis in mice, as scored in the bone marrow chromosome aberration assay (57).
The reverse mutations of *Salmonella typhimurium* TA98 and TA100 induced by benzo[*a*]pyrene were suppressed by about 90% by vitamin C (1500 $\mu g\ plate^{-1}$) (58).
Salmonella typhimurium TA97a, TA98, TA100, TA102 were exposed to benzo[*a*]pyrene (15 $\mu g\ plate^{-1}$) in the presence of different dosage levels of iron (0-1000 $\mu g\ plate^{-1}$) and germanium (0-600 $\mu g\ plate^{-1}$). Iron at concentrations of 100$\mu g\ plate^{-1}$ and higher significantly reduced the mutagenicity of benzo[*a*]pyrene in strain TA98. In strains TA97a and TA100 iron concentrations had to reach 250 $\mu g\ plate^{-1}$ to produce significant effects. Iron was much less effective in reducing benzo[*a*]pyrene mutagenicity in strain TA102. In general, germanium was not as effective in reducing the mutagenic potential of benzo[*a*]pyrene (59).
Risk assessment review (60).
Comparative genotoxicites with pyrene reviewed (61).
Reviews on physico-chemical properties, human health effects, experimental toxicology, environmental effects, ecotoxicology, epidemiology and workplace experience listed (62).

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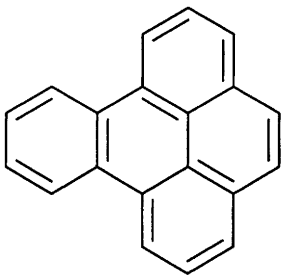
B72 benzo[*e*]pyrene



$C_{20}H_{12}$ **Mol. Wt.** 252.32 **CAS Registry No.** 192-97-2

Synonyms 1,2-benzpyrene; 4,5-benzpyrene; B(e)P

EINECS No. 205-892-7 **RTECS No.** DJ 4200000

Occurrence Constituent of coal tar.

Physical properties

M. Pt. 178.7°C **B. Pt.** 310-312°C

Solubility Water: 2.9×10^{-8} mol l^{-1} at 25°C. Organic solvents: acetone

Mammalian & avian toxicity

Carcinogenicity and chronic effects

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

Dermal ♀ CD-1 mice 7-8 wk old single application 1.0, 2.5, or 6.0 μmol in acetone/DMSO followed after 7 days by 16 nmol 12-*O*-tetradecanoylphorbol-13-acetate (TPA) in acetone 2 × wk^{-1} for 25 wk. Percentages of mice with papillomas (number of papillomas per mouse) in the three experimental groups were 15 (0.15), 11 (0.1), 14 (0.14), respectively. The corresponding values for control mice receiving only the TPA treatment were 7 (0.07) (2).

Dermal ♀ Swiss mice 0.1% benzo[*e*]pyrene 3 × wk^{-1} for life. 5/20 Animals survived 13 months after start of treatment. Of those 2/5 had skin papillomas 3/5 had carcinomas. No animals survived more than 14 months (3).

Perinatal Swiss-Webster BLU:Ha (ICR) mice injected intraperitoneally at 1, 8, and 15 days old with 0.4, 0.8, and 1.6 μmol (total dose 2.8 μmol) in DMSO. Another group was injected intraperitoneally on the same days with 0.8, 1.6, and 3.2 μmol (total dose 5.6 μmol). No treatment-related tumours were seen in ♂ or ♀ animals at any dose 62-66 wk after the end of treatment (2).

Metabolism and toxicokinetics

In rat liver preparations incubated with benzo[*e*]pyrene, the 4,5-dihydrodiol was the major metabolite and the 9,10-dihydrodiol was a minor metabolite (4).

The major identified metabolites during 12-96-hr incubations of benzo[*e*]pyrene (4 μM) with hamster embryo cells were 4,5-dihydro-4,5-dihydroxy-benzo[*e*]pyrene and its glucuronide conjugate and the glucuronide conjugate of 3-hydroxy-benzo[*e*]pyrene (5).

Genotoxicity

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

Other effects

Any other adverse effects

Inbred C57 and C3H mice preimmunised with P815 tumour cells were administered a single intraperitoneal dose of 5 or 50 mg kg^{-1} benzo[*e*]pyrene in corn oil. At different post-injection times antigen-sensitised splenic lymphocytes and peritoneal exudate lymphocytes were measured for binding and killing rates using a single-cell assay. Both binding and killing rates were inconsistent and of borderline significance compared with controls (7).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Polycyclic aromatic hydrocarbons: maximum and admissible concentration 0.2 μg l^{-1} (8).

Other comments

Widespread in products of incomplete combustion. Found in car exhausts. Occurs in cigarette smoke condensate. Concentrations in the air depend upon location, presence of nearby sources of pollution such as traffic highways or industries, and the season, i.e. concentrations are generally higher in winter than in summer and greater in urban than rural areas. Exposure also occurs through ingestion of food and drink contaminated by combustion effluents.

Carcinogenic risk to humans evaluated (9,10).

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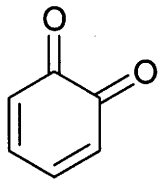
B73 o-benzoquinone



$C_6H_4O_2$ **Mol. Wt.** 108.10 **CAS Registry No.** 583-63-1

Synonyms 3,5-cyclohexadiene-1,2-dione; 1,2-benzoquinone; 2-benzoquinone

RTECS No. DK 2490000

Uses Oxidising agent.

Physical properties

M. Pt. 67-70°C

Occupational exposure

UN No. 2587 **HAZCHEM Code** 2Z **Conveyance classification** toxic substance

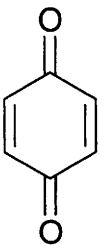
Genotoxicity

Salmonella typhimurium TA100 without metabolic activation positive (1).

References

1. Nazar, M. A. et al *Mutat. Res.* 1981, **89** (1), 45-55

B74 *p*-benzoquinone



$C_6H_4O_2$ **Mol. Wt.** 108.10 **CAS Registry No.** 106-51-4

Synonyms quinone; 2,5-cyclohexadiene-1,4-dione; 1,4-benzoquinone; 1,4-cyclohexadienedione; USAF P-220; NCI-C55845; 4-benzoquinone

EINECS No. 203-405-2 **RTECS No.** DK 2625000

Uses Manufacture of dyestuffs and hydroquinone. Used in photography and the tannery industry. Oxidising agent.

Occurrence Occurs naturally in a variety of arthropods (1).

Physical properties

M. Pt. 113-115°C **B. Pt.** sublimes **Flash point** 38.93°C **Specific gravity** 1.318 at 20°C
Partition coefficient log P_{ow} 0.20 **Volatility** v.p. 0.09 mmHg at 20°C ; v.den. 3.7
Solubility Water: 10 g l^{-1} at 25°C. Organic solvents: ethanol, diethyl ether

Occupational exposure

DE-MAK 0.1 ppm (0.45 mg m^{-3})
FR-VME 0.1 ppm (0.4 mg m^{-3}) **FR-VLE** 0.3 ppm (1.5 mg m^{-3})
SE-LEVL 0.1 ppm (0.4 mg m^{-3}) **SE-STEL** 0.3 ppm (1.3 mg m^{-3})
UK-LTEL 0.1 ppm (0.45 mg m^{-3}) **UK-STEL** 0.3 ppm (1.3 mg m^{-3})
US-TWA 0.1 ppm (0.44 mg m^{-3})

UN No. 2587 **HAZCHEM Code** 2Z **Conveyance classification** toxic substance
Supply classification toxic
Risk phrases Toxic by inhalation and if swallowed – Irritating to eyes, respiratory system and skin (R23/25, R36/37/38)
Safety phrases Keep locked up and out of the reach of children (if sold to general public) – 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 accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S26, S28, S45)

Ecotoxicity

Fish toxicity
Exposure to 1 mg l^{-1} caused death in 1-2 hr in rainbow trout and steelhead trout, and in 3-4 hr in bridgelip sucker (2).
LC_{50} (96 hr) fathead minnow, rainbow trout 0.045, 0.125 mg l^{-1}, respectively (3).

Invertebrate toxicity
Cell multiplication inhibition test, *Escherichia coli* 55 mg l^{-1}, *Scenedemus quadricauda* 6 mg l^{-1} (4).
Inhibited Calvin cycle in *Chlorella pyrenoidosa* (5).
EC_{50} (5-30 min) *Photobacterium phosphoreum* 2.09 mg l^{-1} Microtox test (6).

Bioaccumulation

Based an a log K_{ow} of 0.20, estimated bioconcentration factor is 0.84 (7).

Environmental fate

Nitrification inhibition

Inhibition of photosynthesis of freshwater *Selenastrum capricornutum* 0.1 mg l^{-1} 37% ^{14}C fixation, 1 mg l^{-1} 17% ^{14}C fixation, 10 mg l^{-1} 7-13% ^{14}C fixation, 100 mg l^{-1} 1% ^{14}C fixation (8).

Degradation studies

Concentration of 0.2 mg l^{-1} inhibited degradation of glucose by *Pseudomonas fluorescens* and 55 mg l^{-1} inhibited degradation of glucose by *Escherichia coli* (9).

Fourteen strains of phenol-utilising bacteria from soil did not grow visibly when using *p*-benzoquinone as a carbon source in an aqueous mineral salt media over an incubation period 5 days (10).

Abiotic removal

Estimated $t_{1/2}$ is 110 min with photochemically produced hydroxyl radicals in the atmosphere (11).

Combined atmospheric $t_{1/2}$ due to reaction with both hydroxyl radicals and ozone is 33 min (11).

Estimated $t_{1/2}$ for the vapour-phase reaction with ozone in the atmosphere is 48 min (11).

Photolysis of *p*-benzoquinone in aqueous solution using natural sunlight and artifical light in excess of 290 nm has yielded unidentifiable polar products (12).

Based on its vapour pressure of 0.09 mmHg at 20°C and ability to sublime, volatilisation of solid particles from soil surfaces may be a significant transfer mechanism (13).

Adsorption and retention

Estimated soil adsorption coefficient of 30 indicates high mobility in soil (7).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 130 mg kg^{-1} (14).

LD_{50} intravenous rat 25 mg kg^{-1} (14).

LD_{50} intraperitoneal mouse 8.5 mg kg^{-1} (15).

Carcinogenicity and chronic effects

No adequate data for carcinogenicity to humans, inadequate evidence for carcinogenicity to animals, IARC classification group 3 (16).

Metabolism and toxicokinetics

Readily absorbed from gastrointestinal tract and subcutaneous tissues of animals, partially excreted unchanged in urine, but bulk is eliminated in conjugation with hexuronic, sulfuric and other acids (17).

Irritancy

Exposure to 0.1 ppm caused irritation to human eye (duration unspecified) (18).

Genotoxicity

Salmonella typhimurium TA100 with metabolic activation positive (19).

Treatment of HL-60 cells produced DNA adducts (0.05-10 adducts per 10^7 nucleotides) (20).

In vitro human lymphocytes resulted in 2- and 5-fold increases in micronuclei (21).

Other effects

Any other adverse effects

Reported to cause dermatitis in humans. Inhibitor of sulfhydryl enzymes (22).

Readily absorbed from the gastroenteric tract and subcutaneous tissues, but no systemic poisonings reported in humans (23).

Poisoning (species unspecified) caused convulsions, breathing difficulties and death due to medullary paralysis. Lung damage from excretion into alveoli and effects on haemoglobin also played a role in death from asphyxia (24).

Other comments

Physico-chemical properties, human health effects and experimental toxicology reviewed (25).
Enzymic activation of quinones by DT-diaphorase reviewed (26).

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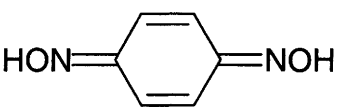
B75 *p*-benzoquinone dioxime



$C_6H_6N_2O_2$ **Mol. Wt.** 138.13 **CAS Registry No.** 105-11-3

Synonyms 1,4-benzoquinone dioxime; 2,5-cyclohexadiene-1,4-dione dioxime; dibenzo PQD; *p*-quinone dioxime; G-M-F; NCI-C03850

EINECS No. 203-271-5 **RTECS No.** DK 4900000

Uses Vulcanising agent in the production of rubber. Chemical intermediate in the synthesis of poly-*p*-dinitrosobenzene and dibenzoyl-*p*-quinone dioxime.

Physical properties

M. Pt. 243°C (decomp.)
Solubility Water: soluble in hot water

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 464 mg kg^{-1} (1).
LD_{50} oral mouse 1542 mg kg^{-1} (2).

Sub-acute and sub-chronic data
Inhalation rat 340-400 mg m^{-3} 2 hr day^{-1} for 15 days (60-71 ppm; particle size not given). No local or systemic effects produced (2).
Rabbits given 20 mg kg^{-1} body weight every second day for two months and every day for a further two months by gavage revealed a decrease in prothrombin activity and an increase in serum alkaline phosphatase and aldolase activities, without gross signs of toxicity (3).
Rat chronic feeding studies, 375 and 750 mg kg^{-1}. Slight increase in chronic inflammation and epithelial hyperplasia in kidney, haemosiderosis of the spleen of both sexes (1).
Mice chronic feeding studies, 750 and 1500 mg kg^{-1}. Slight increase in chronic inflammation and epithelial hyperplasia in the kidneys. Minimal inflammatory responses of the lungs (1).

Carcinogenicity and chronic effects
No adequate data for carcinogenicity to humans, limited evidence for carcinogenicity to animals, IARC classification group 3 (3).
National Toxicology Program tested rats and mice via dosed-feed. Positive evidence for carcinogenicity in ♀ rats. Negative evidence for carcinogenicity in ♂ rats and ♂, ♀ mice (4).
Target organs of carcinogenicity: rat urinary bladder/urethra (5).

Genotoxicity

p-Benzoquinone dioxime (BQD) is a direct-acting mutagen in *Salmonella typhimurium* TA98. In contrast to these *in vitro* data, negative results were obtained after oral administration to ♀ rats in both the bone marrow micronucleus test and the *in vivo* liver unscheduled DNA synthesis test. BQD did, however, induce a marked effect upon S-phase synthesis in the livers of ♀ rats between 14 and 48 hr after a single oral dose of 250 mg kg^{-1}. A similar effect was also observed in the livers of ♂ rats (6).
L5178Y tk+/tk- mouse lymphoma cell forward mutation assay. No S9 activation was required for the demonstration of mutagenicity at a lowest observed effective dose of 25 μg ml^{-1} (7).

Other comments

A review of *p*-benzoquinone dioxime appears in IARC Monograph Volume 29, 1982 (8).
When heated to decomposition it emits toxic fumes of NO_x.

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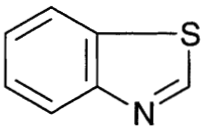
B76 benzothiazole



C_7H_5NS **Mol. Wt.** 135.19 **CAS Registry No.** 95-16-9

Synonyms benzosulfonazole; 1-thia-3-azaindene; 0-2857; USAF EK-4812

EINECS No. 202-396-2 **RTECS No.** DL 0875000

Uses In organic synthesis.

Occurrence In flowers and fruit.

Physical properties

M. Pt. 2°C **B. Pt.** 233-235°C **Specific gravity** 1.246 at 20°C with respect to water at 4°C

Solubility Organic solvents: carbon disulfide, ethanol

Ecotoxicity

Invertebrate toxicity

EC_{50} (5-30 min) *Photobacterium phosphoreum* 1.81-1.87 mg l^{-1} Microtox test (1).

Environmental fate

Degradation studies

Benzothiazole is oxidised by activated sludge. The sulfur and nitrogen moieties are converted into sulfate and ammonium ions (2,3).

Mammalian & avian toxicity

Acute data

LD_{50} oral redwing blackbird 96 mg kg^{-1} (4).

LD_{50} oral rat 479 mg kg^{-1} (5).

LD_{50} oral mouse 900 mg kg^{-1} (6).

LD_{50} intravenous mouse 95 mg kg^{-1} (7).

LD_{50} intraperitoneal mouse 100 mg kg^{-1} (8).

Metabolism and toxicokinetics

Benzothiazole and 2-hydroxybenzothiazole were metabolised to 2-methylmercaptoaniline, 2-methylsulfinylaniline and 2-methylsulfonylaniline in guinea pigs indicating that aldehyde oxidase may have a role in the *in vivo* metabolism of benzothiazole (9).

Other comments

Provides fungal resistance to cedar, red pine and beech trees (10).

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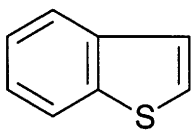
B77 benzo[*b*]thiophene



C_8H_6S **Mol. Wt.** 134.20 **CAS Registry No.** 95-15-8

Synonyms benzothiofuran; 1-benzothiophene; thionaphthene; thionaphthalene

EINECS No. 202-395-7

Uses Manufacture of pharmaceuticals, thio-indigo.
Occurrence In lignite tar.

Physical properties

M. Pt. 29-32°C **B. Pt.** 221-222°C **Partition coefficient** log P_{ow} 3.12
Solubility Organic solvents: acetone, benzene, diethyl ether, ethanol

Ecotoxicity

Invertebrate toxicity
Artemia salina egg hatchability 0% at 500 ppm (1).

Bioaccumulation
Daphnia magna bioconcentration factor 794 (2).
Poecilia reticulata bioconcentration factor 340 (3).

Mammalian & avian toxicity

Sub-acute and sub-chronic data
Rats were treated, by gavage, with 2, 20 or 200 mg kg^{-1} body weight for 21 days. Rats exposed to 200 mg kg^{-1} by gavage exhibited depressed weight gains, increased relative liver and kidney weights, decreased relative thymus weight and elevated levels of a number of enzymes. A 4-5-fold increase in urine volume was observed on days 14-21 and a transient 4-fold increase in urinary ascorbic acid on day-1. Additional groups were fed with 100 or 500 mg kg^{-1} body weight of BTP by diet for 28 days. Rats fed 500 mg kg^{-1} by diet exhibited absolute and relative liver weight, elevated enzymic levels, decreased red blood cell counts and minor increases in serum urea nitrogen and glucose (4).

Metabolism and toxicokinetics
BTP residues were not detected in adipose tissue, liver and serum of rats fed with 200 mg kg^{-1} but a small quantity was observed in urine (4).

Other comments

Inhibition of photosynthesis of a freshwater, non-axenic uni-algal culture of *Selenastrum capricornutum* at 1% saturation, 89% ^{14}C fixation reported, at 10% saturation ^{14}C fixation was 82% ^{14}C fixation and at 100% saturation 4% ^{14}C fixation occurred (5).

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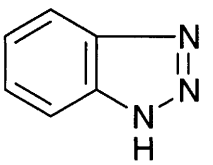
B78 benzotriazole



$C_6H_5N_3$ **Mol. Wt.** 119.13 **CAS Registry No.** 95-14-7

Synonyms 1*H*-benzotriazole; 1,2-aminozophenylene; azimidobenzene; benzene azimide; NCI-C03521; U-6233

EINECS No. 202-394-1 **RTECS No.** DM 1225000

Uses Anticorrosive in metal working.

Physical properties

M. Pt. 98.5°C **B. Pt.** 205°C at 15 mmHg

Solubility Water: 20 g l^{-1}. Organic solvents: benzene, chloroform, ethanol, toluene

Environmental fate

Degradation studies

Benzotriazole was biologically stable as a source of organic carbon in an activated sludge inoculum (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 500 mg kg^{-1} (2).

LD_{50} intravenous mouse 240 mg kg^{-1} (3).

LD_{50} intraperitoneal mouse 860 mg kg^{-1} (4).

Carcinogenicity and chronic effects

National Toxicology Program tested rats and mice via feed. Equivocal results in ♂ and ♀ rats and ♀ mice, negative results in ♂ mice (5).

Genotoxicity

Escherichia coli without metabolic activation positive (6).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Substances extractable in chloroform: guide level 0.1 mg l^{-1} dry residue (7).

Other comments

Reviews on human health effects and experimental toxicology listed (8).

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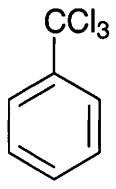
B79 benzotrichloride



$C_7H_5Cl_3$ **Mol. Wt.** 195.47 **CAS Registry No.** 98-07-7

Synonyms α,α,α-trichlorotoluene; (trichloromethyl)benzene; phenylchloroform; benzenyltrichloride; benzoic trichloride; benzyl trichloride

EINECS No. 202-634-5 **RTECS No.** XT 9275000

Uses In dyestuff chemistry. In organic synthesis (as source of benzenyl group).

Physical properties

M. Pt. -3 to -5°C **B. Pt.** 90-91°C at 15 mmHg **Specific gravity** 1.3756 at 20°C with respect to water at 4°C
Solubility Organic solvents: benzene, diethyl ether, ethanol

Occupational exposure

US-STEL ceiling limit 0.1 ppm (0.8 mg m^{-3})

UN No. 2226 **HAZCHEM Code** 2X **Conveyance classification** corrosive substance
Supply classification toxic
Risk phrases May cause cancer – Harmful if swallowed – Toxic by inhalation – Irritating to respiratory system and skin – Risk of serious damage to eyes (R45, R22, R23, R37/38, 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

Fish toxicity
LC_{50} (48 hr) golden orfe 4140 mg l^{-1} (1).

Invertebrate toxicity

Cell multiplication inhibition test, *Pseudomonas putida* >100 mg l^{-1}, *Entosiphon sulcatum* 56 mg l^{-1}, *Uronema parduczi* >80 mg l^{-1} (2,3).

EC_{50} (48 hr) *Daphnia magna* >100 mg l^{-1} (4).

EC_{50} (5-30 min) *Photobacterium phosphoreum* 17.8 mg l^{-1} Microtox test (5).

Bioaccumulation

Based on a log K_{ow} of 2.92, bioconcentration factor is estimated to be 98. Due to rapid hydrolysis in water, accumulation in aquatic organisms is not expected to occur (6).

Environmental fate

Abiotic removal

Hydrolysed in the presence of moisture to form benzoic acid and hydrochloric acid (7).

At 25°C hydrolytic $t_{1/2}$ is 11 sec, at 5.1°C $t_{1/2}$ is 3 min (8,9). Virtually no absorption occurs above 290 nm, therefore direct photolysis in the environment is not expected to occur (10).

Reacts with photochemically produced hydroxyl radicals in the atmosphere, estimated $t_{1/2}$ 2 day (11).

Due to rapid hydrolysis in water, volatilisation is not expected to be important. Evaporation from dry surfaces may be expected owing to its fuming in air and estimated vapour pressure of 0.23 mmHg at 20°C (7,12).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 6000 mg kg^{-1} (13).

Sub-acute and sub-chronic data

LD_{50} (14 day) oral mouse 770 mg kg^{-1} (14).

LD_{50} (14 day) dermal rabbit 4 g kg^{-1} (14).

Carcinogenicity and chronic effects

Inadequate evidence for carcinogenicity to humans, sufficient evidence for carcinogenicity in animals, IARC classification group 2B (15,16).

Gastric intubation ♀ ICR mice administered benzotrichloride, 2.0-0.0315 µl $mouse^{-1}$ (4 doses), 2× wk^{-1} for 25 weeks, produced forestomach tumours (squamous cell carcinoma and papilloma), lung tumours (adenocarcinoma and adenoma) and tumours of the haematopoietic system (thymic lymphosarcoma and lymphatic leukaemia) with dose-related response by 18 months (17).

Irritancy

Benzotrichloride has been reported to be highly irritating to skin and mucous membranes (18).

Dermal rabbit (24 hr) 10 mg caused severe irritation and 50 µg instilled into rabbit eye caused severe irritation (19).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535 and *Escherichia coli* WP2 hcr with and without metabolic activation positive (18).

Bacillus subtilis differential toxicity assay without metabolic activation positive (18,20).

Other effects

Other adverse effects (human)

The standard mortality ratios for all causes, i.e. all cancers and all non-cancers in 1961-1984 were 138, 163 and 129, respectively, for a group of 951 workers exposed to benzotrichloride and chlorinated toluenes in England and Wales. Statistically significant excesses were found for lung cancer and for Hodgkin's disease (standardised mortality ratios 180 and 741, respectively). However, 95% confidence intervals were large and the authors conclude that risks did not approach statistical significance, but that chlorinated toluenes should continue to be considered potential carcinogens until further research is carried out (21).

Other comments

Reviews on physico-chemical properties, human health effects, experimental toxicology, workplace experience, epidemiology and environmental effects listed (22).

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20. *IARC Monograph* 1987, **Suppl. 6**, 101.
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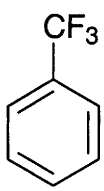
B80 benzotrifluoride



$C_7H_5F_3$ **Mol. Wt.** 146.11 **CAS Registry No.** 98-08-8

Synonyms α,α,α-trifluorotoluene; (trifluoromethyl)benzene; phenylfluoroform; benzenyl fluoride; benzylidyne fluoride; o-trifluorotoluene

EINECS No. 202-635-0 **RTECS No.** XT 9450000

Uses In dyestuff chemistry. Manufacture of substituted benzotrifluorides containing an ethylenic group. Used in dielectric fluids such as transformer oils.

Physical properties

M. Pt. –29.05°C **B. Pt.** 104°C **Flash point** 12°C **Specific gravity** 1.1886 at 20°C
Volatility v.p. 4.0×10^{-5} mmHg ; v.den. 5.0
Solubility Organic solvents: acetone, benzene

Occupational exposure

UN No. 2338 **HAZCHEM Code** 2YE **Conveyance classification** flammable liquid
Supply classification highly flammable, dangerous for the environment
Risk phrases Highly flammable – Toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment (R11, R51/53)
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 – Avoid release to the environment. Refer to special instructions/safety data sheet (S2, S16, S23, S61)

Ecotoxicity

Invertebrate toxicity
EC_{50} (5-30 min) *Photobacterium phosphoreum* 32.0 mg l^{-1} Microtox test (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral mouse, rat 10, 15 g kg^{-1}, respectively (2).
LC_{50} (4 hr) inhalation rat 71 g m^{-3} (3).
LC_{50} (2 hr) inhalation mouse 92 g m^{-3} (3).
LD_{50} intraperitoneal mouse 100 mg kg^{-1} (3).

Other comments

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

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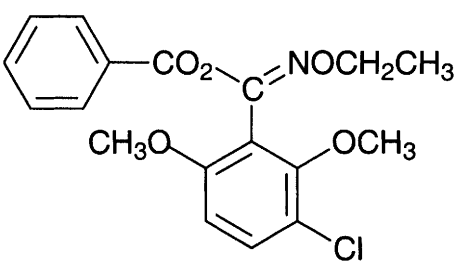
B81 benzoximate



$C_{18}H_{18}ClNO_5$ **Mol. Wt.** 363.80 **CAS Registry No.** 29104-30-1

Synonyms Benzomate; Citrazon; Azomate; Artaban; Acarmate; ethyl *O*-benzol-3-chloro-2,6-dimethoxybenzohydroximate

EINECS No. 249-439-1 **RTECS No.** DF 9700000

Uses A non-systemic acaricide.

Physical properties

M. Pt. 73°C **Partition coefficient** $\log P_{ow}$ 2.4 **Volatility** v.p. 3.4×10^{-6} mmHg
Solubility Water: 30 mg l^{-1} at 25°C. Organic solvents: benzene, dimethyl formamide, *n*-hexane, xylene

Ecotoxicity

Fish toxicity
LC_{50} (48 hr) carp 1.75 mg l^{-1} (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat >10 g kg^{-1} (1-3).
LD_{50} percutaneous rat >15 g kg^{-1} (1).
LD_{50} intraperitoneal rat, mouse 4220, 4260 mg kg^{-1}, respectively (1-3).

Carcinogenicity and chronic effects
In 2-yr feeding trials, rats receiving up to 400 mg kg^{-1} diet showed no ill-effects (1).

Legislation

WHO Toxicity Class Table 5 (4).
EPA Toxicity Class IV (1).
Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides and related products: maximum admissible concentration 0.1 μg l^{-1} (5).
Included in Schedule 6 (Release into Land Prescribed Substances) of Statutory Instrument No. 472, 1991 (6).

References

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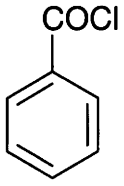
B82 benzoyl chloride



C_7H_5ClO **Mol. Wt.** 140.57 **CAS Registry No.** 98-88-4
Synonyms benzenecarbonyl chloride; benzoic acid chloride; α-chlorobenzaldehyde
EINECS No. 202-710-8 **RTECS No.** DM 6600000
Uses Used in acylation reactions. Manufacture of benzoyl peroxide. Production of dyestuff intermediates, drugs and agrochemicals. Inorganic analysis for preparation of benzoyl derivatives for identification purposes.

Physical properties

M. Pt. –1.0°C **B. Pt.** 197.2°C **Flash point** 88°C **Specific gravity** 1.207 at 25°C with respect to water at 4°C
Volatility v.p. 3.8×10^{-7} mmHg at 20°C ; v.den. 4.9
Solubility Organic solvents: miscible with benzene, carbon disulfide, diethyl ether, dimethyl sulfoxide

Occupational exposure

US-STEL ceiling limit 0.5 ppm (2.8 mg m^{-3})

UN No. 1736 **HAZCHEM Code** 2X **Conveyance classification** corrosive substance
Supply classification corrosive
Risk phrases Causes burns (R34)
Safety phrases Keep locked up and out of the reach of children (if sold to general public) – In case of contact with eyes, rinse immediately with plenty of water and seek medical advice – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S26, S45)

Ecotoxicity

Fish toxicity
LC_{50} (24-96 hr) fathead minnow 43-35 mg l^{-1} (1).

Invertebrate toxicity
LC_{50} (96 hr) *Palomonetes pugio* 180 mg l^{-1} (2).
EC_{50} (5-30 min) *Photobacterium phosphoreum* 12.2 mg l^{-1} Microtox test (3).

Bioaccumulation
Owing to the rapid rate of hydrolysis, bioconcentration is not expected to be an important factor (4).

Environmental fate

Degradation studies
Hydrolysis is so rapid that biodegradation is not expected to be an important factor in the fate of benzoyl chloride (4).

Abiotic removal
Using photochemically produced hydroxyl radicals, estimated atmospheric $t_{1/2}$ is 2-10 days (4).
Hydrolytic $t_{1/2}$ 16 sec; products detected benzoic acid and hydrochloric acid (5,6).

Adsorption and retention
Owing to the rapid rate of hydrolysis, benzoyl chloride is not expected to persist in the soil (4).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 2460 mg kg^{-1} (7).
LC_{50} (2 hr) inhalation rat 1870 mg m^{-3} (8).
TC_{Lo} (1 min) inhalation human 2 ppm, affects sense organs. Causes olfactory effects and damage to lungs, thorax and respiration (8).
TD_{Lo} dermal mouse 9200 mg kg^{-1} (9).
LD_{50} dermal rabbit 790 mg kg^{-1} (7).

Carcinogenicity and chronic effects
Inadequate evidence for carcinogenicity to humans, inadequate evidence for carcinogenicity to animals, IARC classification group 3 (10).
Dermal mouse (50 wk intermittently) caused equivocal tumorigenic effects to lungs, thorax or respiration system (9,11).

Genotoxicity

Salmonella typhimurium TA100 with and without metabolic activation negative.
Escherichia coli WP2 hcr with and without metabolic activation positive (12).

Other effects

Other adverse effects (human)
Six cases of respiratory cancer reported among workers in two small factories where benzoyl chloride and its chlorinated precursors were produced. Epidemiological data provided limited evidence that employment in the production of chlorinated toluenes presented carcinogenic risk to man (13).

Legislation

Limited under EC Directive on Drinking Water 80/778/EEC. Organochlorine compounds: guide level 1 $\mu g\ l^{-1}$ (14).

Other comments

Reviews on physico-chemical properties, human health effects, experimental toxicology and workplace experience listed (15).
Corrosive. Lachrymatory. Decomposes violently with water.

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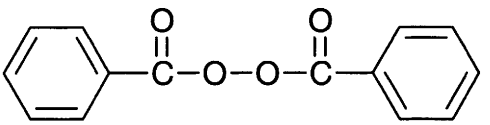
B83 benzoyl peroxide



$C_{14}H_{10}O_4$ **Mol. Wt.** 242.23 **CAS Registry No.** 94-36-0

Synonyms dibenzoyl peroxide; benzoyl superoxide; Benzac; Dermoxyl; Eloxyl; Persadox

EINECS No. 202-327-6 **RTECS No.** DM 8575000

Uses Bleaching agent for flour, fats, oils, waxes. Drying agent for unsaturated oils. Pharmaceutical and cosmetic ingredient. Rubber vulcaniser without sulfur. Production of embossed vinyl flooring. Burnout agent for acetate yarns, radical reactions. Polymerisation catalyst.

Physical properties

M. Pt. 104-106°C (decomp.)

Solubility Water: <1 g l^{-1}. Organic solvents: acetone, benzene, chloroform, diethyl ether, ethanol

Occupational exposure

DE-MAK 5 mg m^{-3} (inhalable fraction or aerosol)

FR-VME 5 mg m^{-3}

UK-LTEL 5 mg m^{-3}

US-TWA 5 mg m^{-3}

Supply classification explosive, irritant

Risk phrases Risk of explosion by shock, friction, fire or other sources of ignition – May cause fire – Irritating to the eyes – May cause sensitisation by skin contact (R2, R7, R36, R43)

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

Acute data

LD_{50} oral rat 7710 mg kg^{-1} (1).

LD_{Lo} intraperitoneal mouse 250 mg kg^{-1} (2).

Carcinogenicity and chronic effects

Inadequate evidence for carcinogenicity to humans, inadequate evidence for carcinogenicity to animals, IARC classification group 3 (3).

Metabolism and toxicokinetics

Approximately 50% of a dose was absorbed following topical application to the forearm of primates (4).

Percutaneous penetration and metabolism on human skin *in vivo* and *in vitro* on five patients with leg ulcers revealed absorption by the skin *in vitro* with conversion into benzoic acid principally in the dermis (5).

Irritancy

Applications to human skin may produce an initial stinging effect (6).

500 mg instilled into rabbit eye caused mild irritation within 24 hr (1).

Sensitisation

Some patients were sensitised after repeated applications for acne therapy (7,8).

A case of purpuric contact dermatitis has been reported (9).

A number of cases of skin reactions to formulations used in the treatment of acne have been described (10).

Contact reactions are not linked to susceptibility to skin irritants in atopic dermatitis patients, but tend to increase with time (11).

Other effects

Any other adverse effects

Decreased glucose utilisation was observed in isolated perfused porcine skin treated with benzoyl peroxide compared to controls. Statistically significant changes in vascular resistance were not observed in dose or control flaps (12).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Substances extractable in chloroform: guide level 0.1 mg l^{-1} dry residue (13).

Other comments

Hazards and legislation in France, recommendations for its storage and handling, and medical treatment in case of accidents reviewed (14).

Human safety assessment for carcinogenicity reviewed (15).

Physico-chemical properties, human health effects, experimental toxicology, epidemiology, workplace experience and exposure reviewed (16,17).

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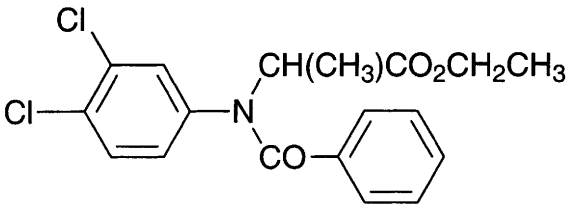
B84 benzoylprop-ethyl



$C_{18}H_{17}Cl_2NO_3$ **Mol. Wt.** 366.24 **CAS Registry No.** 22212-55-1

Synonyms *N*-benzoyl-*N*-(3,4-dichlorophenyl)-L-alanine ethyl ester; propionic acid, 2-(*N*-benzoyl-*N*-(3,4-dichlorophenyl)amino ethyl ester; ethyl *N*-benzoyl-*N*-(3,4-dichlorophenyl)-2-aminopropionate; Suffix

EINECS No. 244-845-5 **RTECS No.** UE 7550000

Uses A selective systemic herbicide. Believed to be no longer manufactured, or marketed for crop protection use (1).

Physical properties

M. Pt. 71°C (rhombic crystals);55°C (needles) **Volatility** v.p. 3.5×10^{-8} mmHg at 20°C
Solubility Water: 20 mg l^{-1} at 25°C. Organic solvents: acetone, ethanol

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) rainbow trout, harlequin fish 2.2, 5 mg l^{-1}, respectively (2).

Invertebrate toxicity
Non-toxic to bees(2).

Environmental fate

Abiotic removal
Photochemically and hydrolytically stable range pH 3-6 (2).

Mammalian & avian toxicity

Acute data
LD_{50} oral hen >1000 mg kg^{-1} (1).
LD_{50} oral rat, guinea pig, rabbit 1000-1550 mg kg^{-1} (3,4).
LD_{50} oral mouse 716 mg kg^{-1} (5).
LD_{50} percutaneous rat >1000 mg kg^{-1} (4).

Sub-acute and sub-chronic data
In 90-day feeding trials, rats receiving up to 1000 mg kg^{-1} diet and dogs 300 mg kg^{-1} diet showed no ill effects (2).

Other comments

In plants, metabolism involves hydrolysis of the ester group to give the benzoyl moiety which is ultimately converted into a biologically inactive conjugate (6).
Effects on total arthropod populations, soil invertebrate biosmass, earthworm numbers and biomass, and predatory beetle populations reviewed (7).

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2. *The Agrochemicals Handbook* 2nd ed., 1987, The Royal Society of Chemistry, London, UK.
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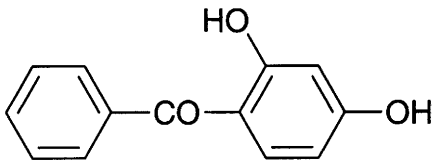
B85 4-benzoylresorcinol



$C_{13}H_{10}O_3$ **Mol. Wt.** 214.22 **CAS Registry No.** 131-56-6

Synonyms Benzoresorcinol; resbenzophenone; benzophenone-1; 2,4-dihydroxybenzophenone; (2,4-dihydroxyphenyl)phenylmethanone

EINECS No. 205-029-4 **RTECS No.** DJ 0700000

Uses Ultraviolet light absorber, especially in paints and plastics. Cosmetics.

Physical properties

M. Pt. 144.5-147°C

Solubility Organic solvents: diethyl ether, ethanol, glacial acetic acid

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 7200 mg kg^{-1} (1).

LD_{50} intraperitoneal mouse 100 mg kg^{-1} (2).

LD_{50} intravenous mouse 85 mg kg^{-1} (3).

Irritancy

100 mg instilled into rabbit eye for 24 hr caused moderate irritation (1).

References

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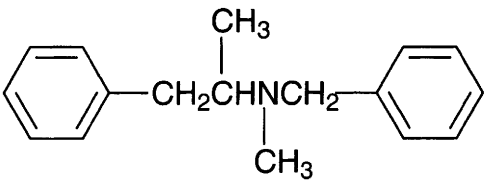
B86 benzphetamine



$C_{17}H_{21}N$ **Mol. Wt.** 239.36 **CAS Registry No.** 156-08-1

Synonyms *N*,α-dimethy-*N*-(phenylmethyl)benzeneethanamine; *N*-benzyl-*N*,α-dimethylphenethylamine

RTECS No. SG 9602000

Uses Anorexic used in obesity treatment.

Physical properties

B. Pt. 127°C at 0.02 mmHg

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

Mammalian & avian toxicity

Acute data

LD_{50} intraperitoneal mouse 32 mg kg^{-1} (1).

Metabolism and toxicokinetics

Methylbenzylamine derived from benzphetamine, could in the nitrosating environment of the gastrointestinal tract yield the carcinogenic compound methylbenzylnitrosamine (2).

In vitro metabolism studied using rat liver microsomal preparation. Five metabolites were isolated and identified as benzylamphetamine, 1-(*p*-hydroxyphenyl)-2-(*N*-methyl-*N*-benzylamino) propane, 1-(*p*-hydroxyphenyl)-2-(*N*-benzylamino)propane, methamphetamine and amphetamine. Their formation was catalysed by the microsomal mixed function oxidase system. *In vitro* metabolism was mediated by three different types of cytochrome P450 enzymes (3).

In vivo studies in rats showed the major metabolite formed by aromatic hydroxylation and *N*-demethylation, was 1-(*p*-hydroxyphenyl)-2-(*N*-benzylamino)propane. Of the eight other metabolites obtained, one was methamphetamine. After administration, 40% of the dose was recovered as urinary metabolites during three days (4).

Nine metabolites and traces of the unchanged drug were excreted in the urine of human volunteers. The major metabolite was 1-(*p*-hydroxyphenyl)-2-(*N*-benzylamino)propane. Minor metabolites included methamphetamine, amphetamine and their hydroxylated products. Identified urinary metabolites excreted during three days following administration accounted for 30-44% of the dose (5).

Legislation

Controlled substance (stimulant) listed in the US Code of Federal Regulations (6).

Other comments

Excessive use may lead to tolerance and physical dependence (7).

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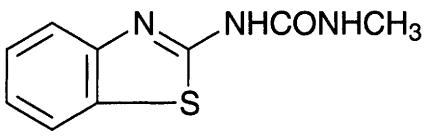
B87 benzthiazuron



$C_9H_9N_3OS$ **Mol. Wt.** 207.26 **CAS Registry No.** 1929-88-0

Synonyms 1-(2-benzothiazoyl)-3-methylurea

EINECS No. 217-685-9 **RTECS No.** YR 8985000

Uses Herbicide. Believed to be no longer manufactured, or marketed for crop protection use (1).

Physical properties

M. Pt. 287°C (decomp.)
Solubility Water: 12 mg l^{-1} at 20°C. Organic solvents: acetone, 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 skin and eyes (S2, S24/25)

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) harlequin fish 400 mg l^{-1} (2).

Environmental fate

Degradation studies
$t_{1/2}$ in soil is 10-12 wk (3).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 1280 mg kg^{-1} (3).

Sub-acute and sub-chronic data
60-day feeding trials rats at 130 mg kg^{-1} daily dose, no adverse effects reported (3).

Genotoxicity

Environmental Protection Agency Genotox Program 1988, *Saccharomyces cerevisiae* gene conversion negative (4).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides and related products: maximum admissible concentration 0.1 μg l^{-1} (5).
Included in Schedule 6 (Release Into Land: Prescribed Substances) of Statutory Instrument No. 472, 1991 (6).

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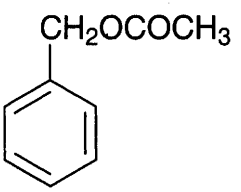
B88 benzyl acetate



$C_9H_{10}O_2$ **Mol. Wt.** 150.18 **CAS Registry No.** 140-11-4

Synonyms acetic acid, phenylmethyl ester; acetic acid, benzyl ester; benzyl ethanoate; α-acetoxytoluene

EINECS No. 205-399-7 **RTECS No.** AF 5075000

Uses In perfumery. In the manufacture of lacquers, polishes, printing ink and varnish removers. Solvent for cellulose acetate and cellulose nitrate.
Occurrence In jasmine, gardenia and other essential oils (1,2).

Physical properties

M. Pt. –51.5°C **B. Pt.** 213°C **Flash point** 102°C **Specific gravity** 1.05 at 25°C with respect to water at 4°C
Volatility v.p. 1.0×10^{-6} mmHg at 45°C ; v.den. 5.2
Solubility Water: <1 mg ml^{-1} at 25°C. Organic solvents: acetone, dimethyl sulfoxide, ethanol

Occupational exposure

US-TWA 10 ppm (61 mg m^{-3})

Ecotoxicity

Invertebrate toxicity
EC_{50} (30 min) *Photobacterium phosphoreum* 4.54 mg l^{-1} Microtox test (3).

Environmental fate

Degradation studies
Readily biodegradable (4).

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse 830 mg kg^{-1} (5).
LD_{50} oral rat, rabbit, guinea pig 2200-2490 mg kg^{-1} (6,7).
LC_{Lo} (22 hr) inhalation mouse 1300 mg m^{-3} (7).

Sub-acute and sub-chronic data

Oral B6C3F1 mice (13 wk) 3130 – 50,000 ppm in diet decreased absolute weight (increased relative weight) of reproductive organs (testis, epididymis and cauda epididymis). There was no effect on sperm motility, density or normality (8).

Carcinogenicity and chronic effects

No adequate data for carcinogenicity to humans, limited evidence for carcinogenicity to animals, IARC classification group 3 (9).
National Toxicology Program evaluation of benzyl acetate in rats and mice by gavage. Equivocal evidence of carcinogenic activity in ♂ rats (target organs not specified), no evidence of carcinogenicity in ♀ rats, some evidence of carcinogenicity in ♂ and ♀ mice (10).
Gavage F344 rats 0, 250 and 500 mg kg^{-1} and B6C3F1 mice 0, 500 and 1000 mg kg^{-1}. Dosed 1 × day^{-1}, 5 days wk^{-1} for 103 wk. No evidence of carcinogenicity in ♀ rats. Increased incidence of acinar cell adenoma of the exocrine pancreas in ♂ rats. Increased incidence of hepatocellular neoplasms and squamous cell neoplasms of the forestomach in ♂ and ♀ rats (11).

Metabolism and toxicokinetics

The major urinary metabolite in rats and mice was hippuric acid; other metabolites detected in minor quantities included benzoyl glucuronide, benzoic acid and benzylmercapturic acid (12).
Changes in minor routes of metabolism and excretion occur with age, but formation of hippuric acid from benzyl acetate is unaffected by ageing (13).

Irritancy

The skin irritation potential of benzyl acetate presented as a Primary Irritation Index (maximum possible value 8) has a value of 0.83-1.56, calculated from erythema and oedema grades, using data from dermal rabbit irritancy tests (14).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA1535 and TA1537 with and without metabolic activation negative (15).
Mouse lymphoma L5178Y cell forward mutation assay without metabolic activation negative, with metabolic activation positive (16).
Chinese hamster ovary cells with and without metabolic activation did not produce chromosome aberrations or sister chromatid exchange (17).

Other effects

Other adverse effects (human)

In humans if ingested can cause gastrointestinal irritation with vomiting and diarrhoea. Skin, eye and respiratory tract irritant (18).

Other comments

Reviews on experimental toxicology and human health effects listed (19).

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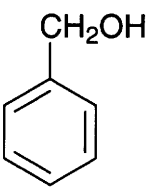
B89 benzyl alcohol



C_7H_8O **Mol. Wt.** 108.14 **CAS Registry No.** 100-51-6

Synonyms benzenemethanol; α-hydroxytoluene; phenylcarbinol; phenylmethanol; 2-hydroxytoluene

EINECS No. 202-859-9 **RTECS No.** DN 3150000

Uses Manufacture of other benzyl compounds. In perfumery and flavourings. Pharmaceutical aid. Bacteriostat. Solvent for inks. Surfactant.

Occurrence Constituent of jasmine, hyacinth, ylang ylang oils.

Physical properties

M. Pt. –15°C **B. Pt.** 205°C **Flash point** 100°C (closed cup) **Specific gravity** 1.045 at 20°C with respect to water at 4°C **Partition coefficient** log P_{ow} 1.10 **Volatility** v.p. 1 mmHg at 58°C ; v.den. 3.72

Solubility Water: 35 g l^{-1} at 20°C. Organic solvents: acetone, aromatic hydrocarbons, benzene, chloroform, diethyl ether, ethanol

Occupational exposure

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) – In case of contact with eyes, rinse immediately with plenty of water and seek medical advice (S2, S26)

Ecotoxicity

Fish toxicity

LC_{50} (48-96 hr) fathead minnow 770-460 mg l^{-1}, static bioassay at 18-22°C (1).
LC_{50} (96 hr) bluegill sunfish 10 ppm, static bioassay in fresh water at 23°C with mild aeration after 24 hr (1).
LC_{50} (96 hr) tidewater silverside fish 15 ppm, static bioassay in synthetic seawater at 23°C with mild aeration after 24 hr (1).
Trout, bluegill sunfish and goldfish exposed to 5 ppm benzyl alcohol died within 2-6 hr (2).

Invertebrate toxicity

EC_{50} (5, 15, 30 min) *Photobacterium phosphoreum* 71.4 mg l^{-1} Microtox test (3).
EC_{50}(48 hr) *Daphnia magna* 400 mg l^{-1} (4).
EC_{100} (48 hr) *Daphnia magna* 500 mg l^{-1} (4).
EC_{10} (48 hr) *Pseudomonas putida* 658 mg l^{-1} (4).
EC_{50} (24 hr) *Haematococcus pluvialis* 2600 mg l^{-1} (4).
Cell multiplication inhibition test, *Pseudomonas fluorescens* 350 mg l^{-1} (5).

Bioaccumulation

Calculated bioconcentration factor 4 (6).

Environmental fate

Degradation studies

Initial concentration of 50 ppm benzyl alcohol underwent >75% degradation to carbon dioxide and methane within 8 wk using municipal sewage sludge inocula under anaerobic conditions (7).
Using sediment from anoxic salt marsh, 1080 mg l^{-1} benzyl alcohol underwent degradation to carbon dioxide and methane after a 2-month incubation period (8).
ThOD 2.52 g g^{-1}, COD 0.78 g g^{-1} (9).
BOD_5 70% degradation under aerobic conditions with an acclimated mixed microbial culture (10).
At an initial concentration of 500 ppm ThOD (12 hr) 52%, 42% and 43% using settled sewage sludge acclimated to phenol, benzoic acid and catechol, respectively, under aerobic conditions (11).

Abiotic removal

Exposure of benzyl alcohol in natural water to sunlight showed that photochemically induced oxidation did not occur within 4 hr (12).

Mammalian & avian toxicity

Acute data

LD_{50} oral starling >100 mg kg^{-1} (13).
LD_{50} oral rat 1230 mg kg^{-1} (14).
LC_{50} (2 hr) inhalation rat 200-300 ppm (15).
LD_{Lo} intravenous dog 50 mg kg^{-1} (16).
LD_{50} intraperitoneal mouse 650 mg kg^{-1} (17).

Carcinogenicity and chronic effects

National Toxicology Program evaluation of benzyl alcohol in rats and mice by gavage. No evidence of carcinogenicity (18).

Teratogenicity and reproductive effects

TD_{Lo} oral mouse (6-13 day gestation) 6 g kg^{-1} (total dose) reduced birth weight and maternal weight gain (19).
No evidence of developmental toxicity (20).

Metabolism and toxicokinetics

Oxidised to benzoic acid and excreted as hippuric acid (21).
Rabbits given 1 g benzyl alcohol subcutaneously eliminated 300-400 mg hippuric acid within 24 hr. Rabbits given 0.4 g kg^{-1} orally eliminated 65.7% as hippuric acid in the urine (22).

Irritancy

16 mg applied to human skin caused mild irritation within 24 hr (23). The skin irritation potential of benzyl alcohol, presented as a Primary Irritation Index (maximum possible value 8), has a value of 1.56-1.83, calculated from erythema and oedema grades, using data from dermal rabbit irritancy tests (24).

Sensitisation

Human hypersensitivity to benzyl alcohol reported (25).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, and TA1537, with and without metabolic activation negative (26).
Chinese hamster ovary cells chromosome aberration without metabolic activation negative, with metabolic activation positive; sister chromatid exchange with or without metabolic activation weakly positive (27).
Mouse lymphoma L5178Y cell forward mutation assay with or without metabolic activation equivocal responses (28).
Did not induce micronuclei in mice after single intraperitoneal injection (29).

Other effects

Any other adverse effects

In humans prolonged exposure may cause lung damage, gastrointestinal disturbances and narcotic effects (30).
Can cause death in neonates. Systemic effects include central nervous system depression, respiratory distress and renal failure (31).
Aseptic meningitis observed following intrathecal administration of radio-pharmaceuticals containing benzyl alcohol as preservative (32).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Substances extractable in chloroform guide level 0.1 mg l^{-1} dry residue (33).

Other comments

Identified in wastewater effluent from photographic processing industry, paper mills, secondary effluent from wastewater treatment plants, and wastewater of a petrochemical plant (34-37).
Also found in a test waste incinerator and as a volatile flavour component of baked potatoes, cheese and roast nuts (38-41).
Gasoline exhaust content >0.1 to 47 ppm (42).
Catabolism of benzene compounds by ascomycetous and basidiomycetous yeasts and yeast-like fungi reviewed (43). Toxicology reviewed (44,45).
Reviews on human health effects, experimental toxicology, environmental effects, physico-chemical properties and exposure levels listed (46).
Hygroscopic.

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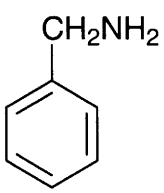
B90 benzylamine



C_7H_9N **Mol. Wt.** 107.16 **CAS Registry No.** 100-46-9

Synonyms aminotoluene; benzenemethanamine; phenylmethylamine

EINECS No. 202-854-1 **RTECS No.** DP 1488500

Uses Chemical intermediate for dyestuffs, pharmaceuticals and polymers.

Physical properties

M. Pt. 10°C **B. Pt.** 184-185°C **Flash point** 60°C (closed cup) **Specific gravity** 0.983 at 19°C with respect to water at 4°C **Partition coefficient** log P_{ow} 1.09
Solubility Water: miscible. Organic solvents: diethyl ether, ethanol

Occupational exposure

Supply classification corrosive
Risk phrases Causes burns – Harmful in contact with skin and if swallowed (R34, R21/22)
Safety phrases Keep locked up and out of the reach of children (if sold to general public) – In case of contact with eyes, rinse immediately with plenty of water and seek medical advice – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) – Wear suitable protective clothing, gloves and eye/face protection (S1/2, S26, S45, S36/37/39)

Ecotoxicity

Fish toxicity
Steelhead trout exposed to 6 mg l^{-1} died within 6-8 hr (1).

Invertebrate toxicity
Toxic dose *Daphnia magna* 60 mg l^{-1}. Toxic dose *Scenedesmus quadricauda* 6 mg l^{-1} (2).
EC_{50} (30 min) *Photobacterium phosphoreum* 17 mg l^{-1} Microtox test (3).

Environmental fate

Nitrification inhibition
Nitrosomonas sp. 100 mg l^{-1} inhibited ammonia oxidation by 26%, 50 mg l^{-1} inhibited 10%, 10 mg l^{-1} inhibited 0% (4).

Carbonaceous inhibition
Pseudomonas fluorescens 400 mg l^{-1} inhibited glucose degradation. *Escherichia coli* >1000 mg l^{-1} inhibited glucose degradation (5).
Confirmed biodegradable (6).

Genotoxicity

Mouse lymphoma L5178Y cell forward mutation assay without metabolic activation negative (7).

Other effects

Other adverse effects (human)
Metabolic inactivation of benzylamine in myometrium from women at term, with normal labour and with uterine inertia was studied. Benzylamine deamination was highest in uterine inertia. Possible pathogenic implications of the selective changes in the myometrial activity associated with uterine inertia are discussed (8).

Other comments

Pollution properties, toxicity and Environmental fate reviewed (9).
General literature review of toxicity of aromatic amino and nitro compounds (10).
Reviews on physico-chemical properties, human health effects and experimental toxicology listed (11).
Corrosive. Lachrymatory. Incompatible with *N*-chlorosuccinimide.

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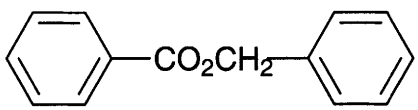
B91 benzyl benzoate



$C_{14}H_{12}O_2$ **Mol. Wt.** 212.25 **CAS Registry No.** 120-51-4

Synonyms benzoic acid benzyl ester; benzoic acid phenylmethyl ester; benzyl benzenecarboxylate; Ascabiol; Unichem BZBM

EINECS No. 204-402-9 **RTECS No.** DG 4200000

Uses Scabicide, pediculicide. Component in dyestuffs, perfume fixatives. Solvent for cellulose acetate, nitrocellulose and artificial musk. Camphor substitute in celluloid and plastic pyroxylin compounds. Flavour for confectionery and chewing gum.

Occurrence Natural substance in the volatile bark oils of cinnamon, and in Peru and Tolu balsams (1,2).

Physical properties

M. Pt. 18-20°C **B. Pt.** 323°C **Flash point** 147°C **Specific gravity** 1.118 at 25°C with respect to water at 4°C
Partition coefficient log P_{ow} 3.97 **Volatility** v.p. 1.3 mmHg at 44°C ; v.den. 7.31
Solubility Organic solvents: miscible with chloroform, diethyl ether, ethanol

Occupational exposure

Supply classification harmful
Risk phrases Harmful if swallowed (R22)
Safety phrases Keep out of reach of children (if sold to general public) – Avoid contact with the eyes (S2, S25)

Mammalian & avian toxicity

Acute data
LD_{50} oral guinea pig, mouse, rabbit, rat 1000-1700 mg kg^{-1} (3-5).
LD_{50} dermal rabbit 4000 mg kg^{-1} (5).

Irritancy
In humans, irritant to eyes and mucous membranes and may be an irritant to skin (6).

Sensitisation
Hypersensitivity reactions have been reported in humans (6).
The dyestuffs residue associated with benzyl benzoate was detected in cloth samples. The skin test of these cloth samples revealed irritating and sensitising effects (7).

Other effects

Other adverse effects (human)

Blood pressure lowering capabilities (8). Expectorant, respiratory sedative and mild local anaesthetic (9). Diuretic (10).

Any other adverse effects

In experimental animals ingestion causes progressive incoordination, excitation, convulsions and death (11).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Substances extractable in chloroform: guide level 0.1 mg l^{-1} dry residue (12).

Other comments

Toxicity and sensitisation effects of benzyl benzoate reviewed (13-16).
Reviews on physico-chemical properties, human health effects and experimental toxicology listed (17).

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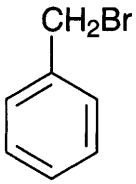
B92 benzyl bromide



C_7H_7Br **Mol. Wt.** 171.04 **CAS Registry No.** 100-39-0

Synonyms (bromomethyl)benzene; bromophenylmethane; o-bromotoluene; α-bromotoluene; benzene, bromomethyl-

EINECS No. 202-847-3 **RTECS No.** XS 7965000

Uses In tear gas. Foaming and frothing agent. Intermediate in organic synthesis. Filling for fire system sprinkler heads.

Physical properties

M. Pt. –4.0°C **B. Pt.** 198°C **Flash point** 86°C **Specific gravity** 1.438 at 22°C with respect to water at 0°C
Partition coefficient log P_{ow} 2.92 **Volatility** v.den. 5.8
Solubility Organic solvents: diethyl ether, ethanol

Occupational exposure

UN No. 1737 **HAZCHEM Code** 2X **Conveyance classification** toxic substance, corrosive
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) – Wear eye/face protection (S2, S39)

Environmental fate

Abiotic removal
Estimated hydrolytic $t_{1/2}$ 79 min (1).
At high concentration, 297 mg l^{-1} benzyl bromide in methanol, absorbs ultraviolet light >290 nm which suggests direct photolysis is unlikely (2).
Photochemical reaction with atmospheric hydroxyl radicals estimated $t_{1/2}$ 6-7 days (3).
Due to its high vapour pressure, volatilisation is expected to be fairly rapid from dry soil surfaces (4).

Adsorption and retention
Estimated soil adsorption coefficients of 154-923 suggests benzyl bromides would not be susceptible to significant leaching in soil and that adsorption to suspended solids and sediments in water would be negligible (5).

Other effects

Any other adverse effects
Narcotic (6).

Legislation

Included in Schedule 6 (Release into Land: Prescribed Substances) of Statutory Instrument No. 472, 1991 (7).

Other comments

Reviews on physico-chemical properties, human health effects and experimental toxicology listed (8).
Corrosive. Lachrymatory.

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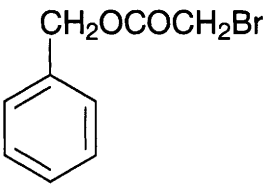
B93 benzyl bromoacetate



$C_9H_9BrO_2$ **Mol. Wt.** 229.07 **CAS Registry No.** 5437-45-6

Synonyms acetic acid, bromo-, benzyl ester; acetic acid, bromo-, phenylmethyl ester

EINECS No. 226-611-4 **RTECS No.** AF 5957215

Uses Plastics additive. Antimicrobial agent. Active ingredient in pesticides.

Physical properties

B. Pt. 166-170°C at 22 mmHg **Flash point** >110°C **Specific gravity** 1.446

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides and related products: maximum admissible concentration 0.1 μg l^{-1} (1).
Included in Schedule 6 (Release into Land: Prescribed Substances) of Statutory Instrument No. 472, 1991 (2).

Other comments

Benzyl bromoacetate may be used under the US Federal, Food, Drug and Cosmetic Act as an antimicrobial preservative (3).

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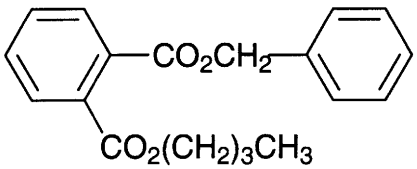
B94 benzyl butyl phthalate



$C_{19}H_{20}O_4$ **Mol. Wt.** 312.37 **CAS Registry No.** 85-68-7

Synonyms 1,2-benzenedicarboxylic acid, butyl phenylmethyl ester; butyl benzyl phthalate; phthalic acid, benzyl butyl ester; Saniticiser 160; Unimoll BB (BBP)

EINECS No. 201-622-7 **RTECS No.** TH 9990000

Uses Plasticiser for synthetic resins, chiefly polyvinylchloride and cellulose resins.

Physical properties

M. Pt. –35°C **B. Pt.** 370°C **Flash point** 199°C (closed cup) **Specific gravity** 1.100 at 25°C with respect to water at 25°C **Partition coefficient** log P_{ow} 4.91 (1) **Volatility** v.p. 8.6×10^{-6} mmHg at 20°C ; v.den. 10.8 **Solubility** Water: 2.7 mg l^{-1} (2)

Occupational exposure

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

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) bluegill sunfish, fathead minnow, sheepshead minnow, rainbow trout 1.7-5.3 mg l^{-1} (3).
LC_{50} (24 hr, 96 hr) bluegill sunfish 62 mg l^{-1} and 43 mg l^{-1}, respectively (4).

Invertebrate toxicity

EC_{50} (96 hr) *Selenastrum capricornutum, Skeletonema costatum* 110-170 μg l^{-1} (5).
Tetrahymena pyriformis growth inhibition, NOEC 50 mg l^{-1} (6).
LC_{50} (48 hr) *Daphnia magna* flow-through 1.8 mg l^{-1}, static >0.96 mg l^{-1}; NOEC flow-through 0.82 mg l^{-1}, static 0.96 mg l^{-1} (7-9).

Bioaccumulation

Bluegill sunfish (21 day) 9.73 mg l^{-1} bioconcentration factor 663 (10).
Bluegill sunfish (3.27 days) exposed to [^{14}C]benzyl butyl phthalate (BBP) in a dynamic system. Bioconcentration factors for intact BBP (normalised to 6% lipid) were 9.4 (whole fish), 8.7 (viscera), and 1.7 (fillet). These are considerably lower than previously published values, which were based upon total radioactive residues in whole fish (11).
Uptake efficiency 42.2 % in English sole gills exposed to 20-250 mg l^{-1} for 3 hr (12).

Environmental fate

Degradation studies

Degraded >90% of 20 mg ml^{-1} in 1 wk under anaerobic conditions with 10% sludge (13).
Undiluted anaerobic sludge, neutralised 20 μg ml^{-1} in >7 days. In sludge diluted to 10% in an anaerobic salt medium, 76-103% of the phthalate ester carbon expected as methane was found as methane within 30 days.
Degradation pathway apparently butyl benzyl phthalate forming monobutyl phthalate forming phthalic acid (13).
Benzyl butyl phthalate is readily degraded in water and sediment, $t_{1/2} \leq 2$ days (14).

93% primary degradation rate and 5 mg-cycle addition rate in a semi-continuous activated sludge test (15). Phthalate esters undergo ≥ 50% ultimate degradation within 28 days in standardised aerobic biodegradation tests with sewage sludge inocula. Biodegradation is expected to be the dominant loss mechanism in surface water, soils and sediments (16).

Adsorption and retention

Insoluble in water, tends to partition to soil, sediment and biota in aqueous environments (3).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 2330 mg kg^{-1} (17).
LD_{50} oral mouse 4170 mg kg^{-1} (17).
LD_{50} intraperitoneal mouse 3160 mg kg^{-1} (18).

Carcinogenicity and chronic effects

No adequate data for carcinogenicity to humans, inadequate evidence for carcinogenicity to animals, IARC classification group 3 (19). National Toxicology Program evaluation of benzyl butyl phthalate in feed. Positive ♀ rats, some evidence for carcinogenicity in ♂ rats and negative ♂, ♀ mice (20).
Fed in diet at 0, 6000 and 12,000 ppm to rats and mice for 102-106 wk. Benzyl butyl phthalate did not induce tumours in ♂ or ♀ mice. Significantly increased incidence of myelomonocytic leukaemia in ♀ rats (21).

Teratogenicity and reproductive effects

Gastric intubation pregnant rats (days 7-15 of gestation) 0-1.0 g kg^{-1}. 0.5 g kg^{-1} produced decreased food consumption, but no adverse effects on the embryo/foetus. 0.75 g kg^{-1} caused reduced maternal food consumption and weight gain, reduced foetal weight, increased embryo/foetal mortality and foetal malformations, predominantly cleft palate, fusion of sternebrae and dilation of the renal pelvis. 1.0 g kg^{-1} resulted in high maternal lethality and complete resorption of implanted embryos in all surviving dams (22).
A similar study to the above found that benzyl butyl phthalate is embryolethal and teratogenic in the first and second half of pregnancy, respectively (23).
14-day dietary study in adult ♂ Fischer 344 rats at 0, 0.625, 1.25 and 5.0% benzyl butyl phthalate; 2.5% and 5% reduced total body, thymus, testis, epididymis, prostate and seminal vesicle weights, and reduced plasma testosterone. Dose-dependent atrophy of testis, prostate and seminal vesicles at 2.5% and 5%. Atrophy of thymus and epididymis at 5% (24).
Fed in diet of ♂ F334 rats at 25,000 ppm for 10 wk benzyl butyl phthalate caused aspermia (25). Fed in diet of ♀ Sprague-Dawley rats on day-6 of pregnancy at 0, 0.5, 1.25, and 2%. No-observed-adverse-effect level 0.5% for maternal and development toxicity. Significant maternal toxicity and minimal developmental toxicity at 1.25%. Significant maternal and developmental toxicity at 2%. Increased incidence of malformations reported (26).
Oral ♀ rats (0-20 day gestation) 0, 0.25, 0.5, 1.0 or 2%. No significant effect on preimplantation loss. Complete resorption of all embryos at 2%. No-observable-effect levels were 0.5% and 1% for maternal and embryo-foetal toxicity respectively. Teratogenic effects, cleft palate and fusion of sternebrae detected in foetuses of high dose animals (27).

Metabolism and toxicokinetics

Male Fischer-344 rats were dosed with ^{14}C-labelled benzyl butyl phthalate (BPP) at 2, 20, 200, or 2000 mg kg orally or 20 mg kg^{-1} intravenously to detect the effects of dose on rates and routes of excretion. In 24 hr, 61-74% of the dose was excreted in the urine and 13-19% in the faeces at 2-200 mg kg^{-1}. At 2000 mg kg^{-1}, 16% of the ^{14}C was excreted in the urine and 57% in the faeces. Urinary ^{14}C was composed of monophthalate glucuronide derivatives (10-42% of the dose) and monophthalate glucuronides (2-21% of the dose). At 4 hr after intravenous administration of BBP (20 mg kg^{-1}), 53-58% of the dose was excreted in the bile of anaesthetised rats. BBP was not found in the bile, but monobutyl glucuronide and monobenzyl phthalate glucuronide (26 and 13% of the dose, respectively) and trace amounts of free monoesters (2% of the dose) were detected. The half-lives of BBP, monophthalates, and total ^{14}C in blood (20 mg kg^{-1} intravenous) were 10 min, 5.9 hr, and 6.3 hr, respectively (28).

Irritancy

Rabbit skin (intact and abraded) 0.5 ml benzyl butyl phthalate held in continuous contact for 24 hr no irritation.

Fifteen daily applications of undiluted benzyl butyl phthalate (dose unspecified) over 3 wk in 200 humans caused no primary irritation or sensitisation. 0.1 ml undiluted benzyl butyl phthalate instilled into rabbits' eyes caused slight irritation, subsiding within 48 hr (29).

Genotoxicity

Mouse lymphoma L5178Y cell forward mutation assay with or without metabolic activation negative (30).
Chinese hamster ovary cells without metabolic activation sister chromatid exchange equivocal (31).
Salmonella typhimurium TA98 with metabolic activation, no enhancement of mutagenicity of Trp-P-2 by benzyl butyl phalate was observed (32).

Other effects

Other adverse effects (human)
Exposure of dialysis patients to benzyl butyl phthalate can cause sodium wastage and polyuria; defect is resistant to arginine vasopression (33).

Any other adverse effects
In a 21-day feeding study, in F344 rats 25,000 ppm induced a moderate increase in peroxisomes in the liver (29).

Other comments

Benzyl butyl phthalate is a xenoestrogen (34).
Present in effluent from industrial and sewage plants (35,36).
Published research on toxicity and environmental effects of phthalic acid esters, since 1978, has been reviewed (37).
Potential occupational hazards, experimental toxicology and carcinogenicity reviewed (17,29,38,39).
Extensive studies have been carried out under a variety of laboratory conditions, including activated sludge, static flask, anaerobic microrganisms in river, lake and seawater (40-49).
Reviews on human health effects and experimental toxicology listed (50).
Aquatic toxicity of eighteen phthalate esters reviewed (2).
The Environmental fate of eighteen phthalate esters reviewed (16).

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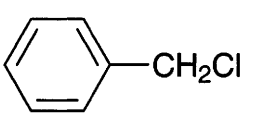
B95 benzyl chloride



C_7H_7Cl **Mol. Wt.** 126.59 **CAS Registry No.** 100-44-7

Synonyms (chloromethyl)benzene; α-chlorotoluene; tolyl chloride

EINECS No. 202-853-6 **RTECS No.** XS 8925000

Uses A dye intermediate. Pharmaceutical precursor. Manufacture of perfumes, synthetic tannins and artificial resins.

Physical properties

M. Pt. –43-48°C **B. Pt.** 177-181°C **Flash point** 73°C **Specific gravity** 1.100 at 20°C with respect to water at 20°C **Partition coefficient** log P_{ow} 2.30 (1) **Volatility** v.p. 1 mmHg at 22°C
Solubility Water: 493mg l^{-1} 20°C. Organic solvents: acetone, dimethyl sulfoxide; ethanol

Occupational exposure

FR-VME 1 ppm (5 mg m^{-3})
FR-VLE 2 ppm (11 mg m^{-3})
SE-LEVL 1 ppm (5 mg m^{-3})
SE-STEL 2 ppm (11 mg m^{-3})
US-TWA 1 ppm (5.2 mg m^{-3})

UN No. 1738 **HAZCHEM Code** 2W **Conveyance classification** toxic substance, corrosive
Supply classification toxic
Risk phrases Harmful if swallowed – Toxic by inhalation – Irritating to respiratory system and skin – Possible risk of irreversible effects – Risk of serious damage to eyes (R22, R23, R37/38, R40, R41)
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) fathead minnow, trout, carp 6-17 mg l^{-1}. Exposed fish suffered paralysis (2).

Invertebrate toxicity
LC_{50} (24-96 hr) white shrimp 7-4 mg l^{-1} (3).
EC_{50} (5-30 min) *Photobacterium phosphoreum* 2.97 mg l^{-1} Microtox test (4).
Cell multiplication inhibition test, *Pseudomonas putida* 4.8 mg l^{-1}, *Scenedesmus quadricauda* 50 mg l^{-1}, *Entosiphon sulcatum* 25 mg l^{-1} (5).

Bioaccumulation
Based on a log P_{ow} 2.30 and water solubility 493 ppm at 20°C, estimated bioconcentration factor range 16-33 (6-8).

Environmental fate

Degradation studies
Readily biodegradable under the Japanese MITI test (9,10).
During a 2-day incubation period using raw sewage and raw sewage acclimated to non-chlorinated compounds, biodegradation was significant with the formation of dechlorinated products (11).
Confirmed biodegradable (12).

Abiotic removal
Aqueous hydrolysis products are benzyl alcohol and hydrogen chloride (13).
Hydrolytic $t_{1/2}$ 14 hr-19 day independent of pH up to pH 13.0 (14).
Atmospheric residence time due to vapour-phase reaction with hydroxyl radicals estimated at 3 days (15).

Adsorption and retention
Soil sorption coefficient estimated at 123-482 which indicates medium to high mobility in soil (16).

Mammalian & avian toxicity

Acute data
LD_{50} oral mouse, rat 1500, 1231 mg kg^{-1}, respectively (17,18).
LC_{50} (2 hr) inhalation rat 150 ppm (19).

Sub-acute and sub-chronic data
Inhalation mouse 6 hr day^{-1} 5 days wk^{-1} (4, 9, 14 day exposure), 46.0 ppm (approx. 3 × RD_{50} value of 17 ppm) resulted in lesions in the respiratory epithelium and olfactory epithelium. Lesions were graded on a four-point scale of "no change" to "very severe change". 4-day exposure resulted in "severe change", 9-day exposure in "very severe change", and 14-day exposure showed some improvement with a "severe change" grading (20).

Carcinogenicity and chronic effects
Inadequate evidence for carcinogenicity to humans, limited evidence for carcinogenicity to animals, IARC classification group 2B (21).

Maximum tolerated dose by gavage 3 doses wk^{-1} for 104 wk for mice and rats was 100 mg kg^{-1} and 30 mg kg^{-1}, respectively. Exposure induced papillomas and carcinomas of forestomach, alveolar and bronchiolar adenomas, carcinomas of lung, haemangiosarcomas, liver carcinomas and thyroid cell adenomas (22).
Application to skin of mice (560 day) caused 15% incidence of skin cancer (23).

Teratogenicity and reproductive effects
Oral ♀ Sprague-Dawley rat (day 6-15 of gestation) 100 mg kg^{-1} positive foetotoxic effect, but reported to be non-teratogenic (24).

Metabolism and toxicokinetics
Absorbed through the lung and gut (25).
After a single oral dose of 25 mg kg^{-1} to adult ♂ and ♀ rats elimination was predominantly in the urine. Excretion was faster in ♀ rats and slightly lower tissue concentration was maintained with the exception of blood and kidneys. Recovery was 90% in urine and faeces of ♀ rats at 24 hr compared with 80% in ♂ rats (26).

Genotoxicity

Salmonella typhimurium TA100 without metabolic activation weakly positive (27).
Salmonella typhimurium TA97, TA98, TA100, TA1535, TA1537 with and without metabolic activation weakly positive (28).
Salmonella typhimurium TA100 and *Escherichia coli* WP2 with and without metabolic activation negative (29).
Saccharomyces cerevisiae induced mitotic gene conversion (30).
Mouse lymphoma L5178V tk+/tk– without metabolic activation positive (31).

Other effects

Other adverse effects (human)
Intensely irritating to skin, eyes and mucous membranes. Large doses cause central nervous system depression (32).

Any other adverse effects
Intradermal injection mice caused depigmentation of hair (33).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Organochlorine compounds: guide level 1 $\mu g\ l^{-1}$ (34).
Included in Schedule 6 (Release into Land: Prescribed Substances) of Statutory Instrument No. 472, 1991 (35).

Other comments

Toxicological and skin corrosion effects and safety handling practices discussed (36,37).
Applications, physico-chemical properties, genotoxicity, carcinogenicity, pathology, fire risk and toxicity of benzyl chloride reviewed (38-40).
Reviews on human health effects, experimental toxicology and exposure levels listed (41).

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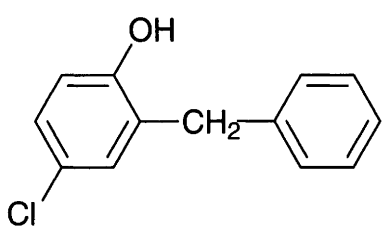
B96 2-benzyl-4-chlorophenol



$C_{13}H_{11}ClO$ **Mol. Wt.** 218.68 **CAS Registry No.** 120-32-1

Synonyms 4-chloro-α-phenyl-*o*-cresol; *o*-benzyl-*p*-chlorophenol; 5-chloro-2-hydroxydiphenylmethane; chlorophene; Nipacide BCP

EINECS No. 204-385-8 **RTECS No.** GO 7175000

Uses Germicide. Hard surface cleaner. Used in disinfectant solutions and soaps.

Physical properties

M. Pt. 49°C **B. Pt.** 175°C at 5 mmHg **Specific gravity** 1.2 at 55°C with respect to water at 25°C
Solubility Organic solvents: acetone, dimethyl sulfoxide, ethanol

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 1700 mg kg^{-1} (1).
LD_{50} oral mouse 65 mg kg^{-1} (2).

Sub-acute and sub-chronic data

Oral rats, mice (12 exposures) 0-1000 mg kg^{-1} resulted in dose-related rectal dilation and nephrosis (3).
Oral gavage in corn oil rats 0-480 mg kg^{-1} mice 0-1000 mg kg^{-1} (13 wk) 5 days wk^{-1} caused urogenital staining in rats and rough/oily haircoats in mice. Main target organ: kidney (3).
Gavage ♂ F344/N rats (13 wk) 240 mg kg^{-1} caused increased nephropathy (4).

Carcinogenicity and chronic effects

The National Toxicology Program tested rats and mice via gavage. No evidence of carcinogenicity in ♂ rats and ♀ mice, equivocal evidence in ♀ rats and some evidence in ♂ mice (5). Oral ♂ F344/N rats (2 yr) 30, 60 or 120 mg kg^{-1}, oral ♀ F344/N rats (2 yr) 60, 120 or 240 mg kg^{-1}, oral ♂ and ♀ B6C3F1 mice (2 yr) 120, 240 or 480 mg kg^{-1}, in corn oil. Survival rate and body weights of dosed rats were comparable to those of controls; survival rates of high-dose ♂ and ♀ mice, and body weights of all ♂ and mid- and high-dose ♀ mice, were below those of controls. Greater incidence and severity of nephropathy was noted with increasing dosage and length of treatment in ♂ and ♀ rats and mice. The mid- and high-dose ♂ mice showed an increased incidence of renal tubule adenomas or carcinomas. No increased incidence of neoplasms in ♀ mice or in ♂ or ♀ rats was observed; therefore, factors other than nephrotoxicity of 2-benzyl-4-chlorophenol are likely to have played a part in the renal carcinogenesis in ♂ mice (4).

Irritancy

Formulations containing 10% or more 2-benzyl-4-chlorophenol are primary skin irritants (6).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537 with or without metabolic activation (preincubation modification) negative (7).
Mouse lymphoma cell L5178Y forward mutation assay without metabolic activation positive. Human lymphoblast TK6 cells without metabolic activation positive. Chinese hamster ovary cells with or without metabolic activation chromosome aberration, sister chromatid exchange negative (8).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Organochlorine compounds: guide level 1 $\mu g\ l^{-1}$ (9).
Included in Schedule 6 (Release into Land: Prescribed Substances) of Statutory Instrument No. 472, 1991 (10).

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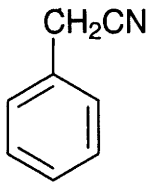
B97 benzyl cyanide



C_8H_7N **Mol. Wt.** 117.15 **CAS Registry No.** 140-29-4

Synonyms benzenacetonitrile; α-cyanotoluene; phenylacetonitrile; α-tolunitrile

EINECS No. 205-410-5 **RTECS No.** AM 1400000

Uses Manufacture of rubber. Chemical intermediate.

Occurrence In garden cress and other plants.

Physical properties

M. Pt. –24°C **B. Pt.** 233-234°C **Flash point** 101°C (closed cup) **Specific gravity** 1.021 at 15°C with respect to water at 15°C **Volatility** v.p. 0.1 mmHg at 20°C

Solubility Organic solvents: diethyl ether, ethanol

Occupational exposure

FR-VME 5 mg m^{-3} (as HCN) **SE-CEIL** 5 mg m^{-3} (as CN)

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

UN No. 2470 **HAZCHEM Code** 3X **Conveyance classification** toxic substance

Ecotoxicity

Invertebrate toxicity

EC_{50} (30 min) *Photobacterium phosphoreum* 1.35 mg l^{-1} Microtox test (1).

Toxicity to other species

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

Environmental fate

Degradation studies

Microbial degradation occurs in water, initial concentration 500 mg l^{-1} at 20°C, 84% degraded within 24 hr (3).

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse 45 mg kg^{-1} (4).

LC_{50} (2 hr) inhalation mouse 100 mg m^{-3} (5).

LD_{50} dermal rabbit 270 mg kg^{-1} (6).

LD_{Lo} intraperitoneal rat 25 mg kg^{-1} (7). LD_{Lo} ♂ and ♀ rats 0.2-0.3 g kg^{-1} by gavage. Sub-lethal oral doses were nephrotoxic (5).

Sub-acute and sub-chronic data

Subcutaneous injection to rabbits (21 day) 0.01-0.5 ml day^{-1} produced thyroid hyperplasia (8).

Metabolism and toxicokinetics

Metabolised to cyanide by rat liver and nasal microsomes (9,10).

Irritancy

Dermal rabbit (24 hr) 500 mg caused mild irritation (5).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA1535, TA1537 with and without metabolic activation negative (11). Exposure to concentrations between 15 ppm and 180 ppm induced mitotic aneuploidy in yeast (strain unspecified) (12).

Other effects

Any other adverse effects

Reported to cause damage to liver, kidney, heart, spleen, lungs, brain and cerebral tissue respiration in experimental animals (species unspecified) (13).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Cyanides: maximum admissible concentration 50 $\mu g\ l^{-1}$ (14).

Other comments

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

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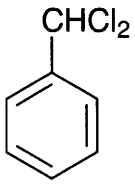
B98 benzylidene chloride



$C_7H_6Cl_2$ **Mol. Wt.** 161.03 **CAS Registry No.** 98-87-3

Synonyms (dichloromethyl)benzene; benzyl dichloride; α,α-dichlorotoluene; benzal chloride; benzylene chloride

EINECS No. 202-709-2 **RTECS No.** CZ 5075000

Uses In manufacture of benzaldehyde and cinnamic acid.

Physical properties

M. Pt. –16°C **B. Pt.** 205°C **Flash point** 85°C **Specific gravity** 1.26
Solubility Organic solvents: diethyl ether, ethanol

Occupational exposure

UN No. 1886 **HAZCHEM Code** 2X **Conveyance classification** toxic substance
Supply classification toxic
Risk phrases Harmful if swallowed – Toxic by inhalation – Irritating to respiratory system and skin – Possible risk of irreversible effects – Risk of serious damage to eyes (R22, R23, R37/38, R40, R41)
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

Invertebrate toxicity
EC_{50} (30 min) *Photobacterium phosphoreum* 5.85 mg l^{-1} Microtox test (1).

Bioaccumulation
Calculated bioconcentration factor 164 (2).

Environmental fate

Abiotic removal
Readily biodegrades in water (3).
Hydrolyses to benzaldehyde under both acid and alkaline conditions (4).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 3250 mg kg^{-1} (5).
LC_{50} (2 hr) inhalation mouse, rat 32, 61 ppm, respectively (6).

Carcinogenicity and chronic effects
Evidence for carcinogenicity to humans inadequate, evidence for carcinogenicity to animals limited, IARC classification group 2B (7).
Dermal mice (560 day) dose unspecified induced 15% incidence of skin cancers (8).

Genotoxicity

Salmonella typhimurium TA100 with and without metabolic activation positive.
Escherichia coli WP2 with and without metabolic activation positive (9).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Organochlorine compounds: guide level 1 $\mu g\ l^{-1}$ (10).
Included in Schedule 6 (Release into Land: Prescribed Substances) of Statutory Instrument No. 472, 1991 (11).

Other comments

Reviews on experimental toxicology and human health effects listed (12).
Lachrymatory.

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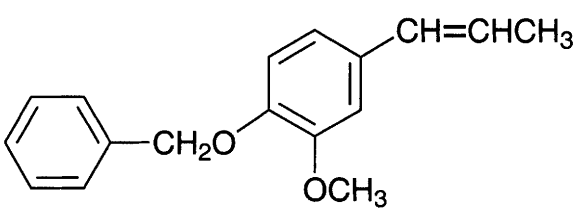
B99 benzyl isoeugenol



$C_{17}H_{18}O_2$ **Mol. Wt.** 254.33 **CAS Registry No.** 120-11-6

Synonyms benzyl isoeugenol ether; benzyl 2-methoxy-4-proprenylphenyl ether

EINECS No. 204-370-6 **RTECS No.** CY 8885000

Uses Intermediate in perfume manufacture.

Physical properties

M. Pt. 58-60°C

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 4900 kg^{-1} (1).

Sub-acute and sub-chronic data

Gavage rat (28 day) 240 mg kg^{-1} caused significant decreases in body weight, blood glucose, blood urea and liver weight. No dose-related histopathological changes were observed in any organs. The no-observed-effect level was 60 mg kg^{-1} day^{-1} (2).

Irritancy

Dermal rat (24 hr) 500 mg caused irritation (1).

Sensitisation

A 5% concentration of benzyl isoeugenol in petrolatum applied to the skin of 25 volunteers produced no sensitisation reactions (1).

Genotoxicity

Salmonella typhimurium TA98 with and without metabolic activation reduced mutation frequency 30-80% (3).

Other comments

Human health effects and experimental toxicology reviewed (4,5).

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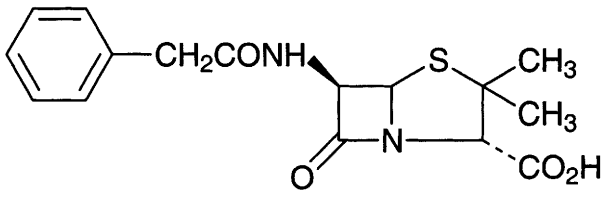
B100 benzylpenicillin



$C_{16}H_{18}N_2O_4S$ **Mol. Wt.** 334.40 **CAS Registry No.** 61-33-6

Synonyms 3,3-dimethyl-7-oxo-6-phenylacetamido-4-thia-1-azabicyclo[3,2,0]heptane-2-carboxylic acid; benzylpenicillinic acid; 6-phenylacetamidopenicillinic acid

EINECS No. 200-506-3

Uses Antibacterial.

Physical properties

Solubility Water: sparingly soluble in water. Organic solvents: benzene, ethanol, ether, ethyl acetate, methanol

Mammalian & avian toxicity

Acute data

LD_{50} oral hamster 24 mg kg^{-1} (1).
LD_{50} intracerebral mouse 7500 mg kg^{-1} (2).
LD_{50} intracerebral rabbit 653-1118 mg kg^{-1} (2).
LD_{50} intraspinal dog 4940 mg kg^{-1} (2).
LD_{50} intravenous mouse 329 mg kg^{-1} (3).

Teratogenicity and reproductive effects

Post-implantation rat embryo culture system negative (4).

Metabolism and toxicokinetics

Degradation products include penillic, penicillenic and penicillic acids (5).
Widely distributed in the body; apparent volume of distribution is in 50% total body water. >90% in blood is in plasma; <10% in erythrocytes; 65% reversibly bound to plasma albumin (6).
Significant amounts appear in liver, bile, kidney, semen, lymph and intestine, but benzylpenicillin does not readily enter cerebrospinal fluid when meninges normal (4).
Oral doses of 500 mg potassium penicillin to humans. Urinary concentrations 2 and 4 hr after dosing 600 μg ml^{-1} and 300 μg ml^{-1}, respectively. Poor placental transfer due to low lipid solubility and low ionisation constant of benzylpencillin (7).

Sensitisation

Allergic reactions include exfoliative dermatitis, interstitial nephritis and vasculitis (5).
Sodium and potassium salts cause allergic sensitisation reactions in some patients due to penicillin metabolites. Desensitisation has been attempted where appropriate (8).
Sensitised patients may also react to cephalosporins (5).

Genotoxicity

Bacillus subtilis: H17/M45 agar incorporation test (AT) and spot test (ST) negative; HLL3 g/HJ15 AT equivocal, ST negative (9).
Escherichia coli: AB1157/JC5547 AT negative, ST positive; AB1157/JC2921 AT negative, ST positive; AB1157/JC2926 AT negative, ST positive; AB1157/JC5519 AT negative (9).

Other effects

Other adverse effects (human)

TD_{Lo} child 15,000 units kg^{-1} change in cochlear structure or function. Convulsions or effect on seizure threshold, lungs, thorax, respiration (dyspnoea) (10).
Administration of benzylpenicillin to a hypersensitive patient may result in anaphylactic shock with collapse and death occurring within minutes. Angioedema or bronchospasm may also occur. Generalised sensitivity reaction with urticaria, fever, joint pains and eosinophilia can develop within a few hours to several weeks after starting treatment with penicillin. Haemolytic anaemia and leucopenia have been reported, usually following high intravenous doses of benzylpenicillin. Prolongation of bleeding time and defective platelet function has also been observed. Convulsions and other signs of toxicity to the central nervous system may occur with very high doses of benzylpenicillin, particularly when administered intravenously or to patients with renal failure.
Encephalopathy may also follow intrathecal administration. Disturbances of blood electrolytes may follow the administration of large doses of the potassium and sodium salts of benzylpenicillin. Patients with syphilis may experience a Jarisch-Herxheimer reaction: symptoms are fever, chills, headache and reactions at lesion sites shortly after treatment with penicillin. Benzylpenicillin may produce diarrhoea, nausea and heartburn following oral administration. A sore mouth or tongue or a black hairy tongue have occasionally been reported (5).

Other comments

Produced by growing certain strains of *Penicillium notatum* (5).

Benzylpenicillin is commonly used to describe either benzylpenicillin potassium or benzylpenicillin sodium as these are the forms in which benzylpenicillin is used. Incompatible with metal ions, some acid and alkaline drugs and some rubber products (5).

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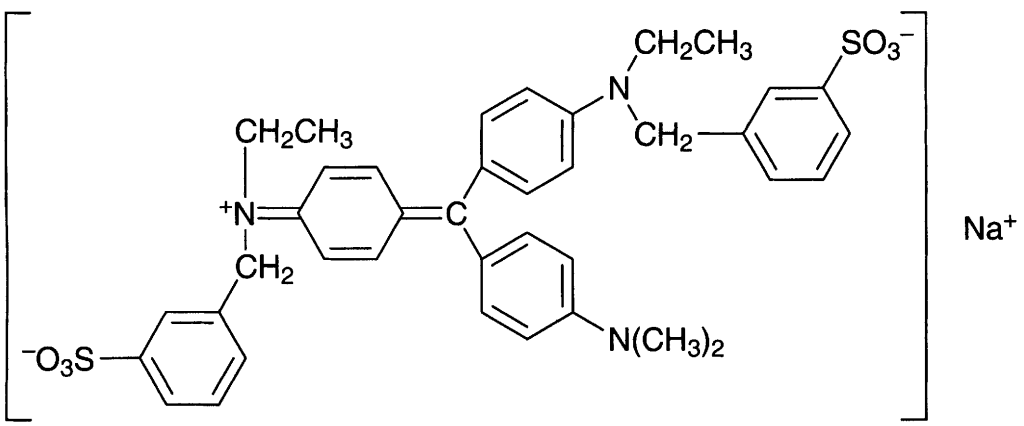
B101 Benzyl Violet 4B



$C_{39}H_{40}N_3O_6S_2Na$ **Mol. Wt.** 733.88 **CAS Registry No.** 1694-09-3

Synonyms benzenemethanaminium, *N*-[4-[[4-(dimethylamino)phenyl][4-[ethyl[(3-sulfophenyl)methyl]amino]phenyl]methylene]-2,5-cycl ohexadien-1-ylidene]-*N*-ethyl-3-sulfo-, hydroxide, inner salt, sodium salt; C.I. Acid Violet 49; A.F. Violet No 1; Benzyl Violet 3B; Food Violet 2; Wool Violet 4BN

EINECS No. 216-901-9 **RTECS No.** BQ 1140000

Uses In dyestuffs for wool, silk, nylon, leather and paper. Used as biological and wood stain.

Occupational exposure

Supply classification harmful

Risk phrases Possible risk of irreversible effects (R40)

Safety phrases Keep out of reach of children (if sold to general public) – Wear suitable protective clothing and gloves (S2, S36/37)

Mammalian & avian toxicity

Carcinogenicity and chronic effects

No adequate data for carcinogenicity to humans, sufficient evidence for carcinogenicity in animals, IARC classification group 2B (1).

Oral or subcutaneous administration to ♀ rats (unspecified dose) induced mammary and squamous carcinomas and local fibrosarcomas following subcutaneous injection in ♂ and ♀ rats (2).

Metabolism and toxicokinetics

Oral administration to rats and dogs, less than 5% absorbed, mainly excreted in faeces (2).

Levels of colour in liver, kidney, abdominal muscle and blood serum ranged from 1 to 3 $\mu g\ g^{-1}$ tissue in rats fed 5% in the diet (3).

Genotoxicity

Salmonella typhimurium TA1535 without metabolic activation positive (4).

Other comments

Withdrawn as food colorant, drug and cosmetics additive US 1973, Europe 1978 (2).

Toxicity reviewed (5).

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B102 beryllium

Be

Be **Mol. Wt.** 9.01 **CAS Registry No.** 7440-41-7

EINECS No. 231-150-7 **RTECS No.** DS 1750000

Uses Used in alloys, applications in the electrical, nuclear and aerospace industries.

Occurrence In nature, beryllium occurs in the minerals beryl, phenacite, bertrandite, bromellite and chrysoberyl. Estimates of abundance in Earth's crust vary from 2 to 10 ppm.

Physical properties

M. Pt. 1278°C **B. Pt.** 2970°C at 3335 mm Hg **Specific gravity** 1.85 at 20°C **Volatility** v.p. 7.6 mmHg at 1810°C

Occupational exposure

FR-VME 0.002 mg m^{-3}
JP-OEL 0.002 mg m^{-3}
SE-LEVL 0.002 mg m^{-3}
UK-LTEL MEL 0.002 mg m^{-3}
US-TWA 0.002 mg m^{-3} **US-STEL** 0.01 mg m^{-3}

UN No. 1567 **HAZCHEM Code** 2X **Conveyance classification** toxic substance, danger of fire (flammable solid)

Supply classification very toxic

Risk phrases May cause cancer by inhalation – Toxic if swallowed – Very toxic by inhalation – Irritating to eyes, respiratory system and skin – May cause sensitisation by skin contact – Toxic: danger of serious damage to health by prolonged exposure through inhalation (R49, R25, R26, R36/37/38, R43, R48/23)

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

Acute toxicity range to fish (24-96 hr) (species unspecified) in fresh water 87-0.87 $\mu g\ l^{-1}$ (1).

LC_{50} (96 hr) fathead minnow 150 $\mu g\ l^{-1}$ (2).

Beryllium concentrations of ≥10 $\mu g\ l^{-1}$ caused increased mortality at pH 4.5 in perch but only higher concentrations, >50 $\mu g\ l^{-1}$, were lethal at pH 5.5. In roach, beryllium concentrations ≥100 $\mu g\ l^{-1}$ killed most fish within 96 hr, regardless of pH. Beryllium also produced gill abnormalities at concentrations as low as 10 $\mu g\ l^{-1}$ similar to those caused by aluminium (3).

Invertebrate toxicity

EC_{50} (48 hr) *Daphnia magna* 1.88 $mg\ l^{-1}$ (4).

Bioaccumulation

Bioconcentration factor for marine and freshwater fish, invertebrates and plants is 100 (1).

Mammalian & avian toxicity

Acute data

Single exposure (50 min) inhalation rat 800 $\mu g\ m^{-3}$ beryllium resulted in severe, acute, chemical pneumonitis progressing to chronic-active fibrosing pneumonitis. The authors conclude that induced lung lesions in rats appear to be due to direct chemical toxicity and foreign-body-type reactions in contrast to the immunological mediated granulomatous lung disease in humans (5).

LD_{50} intravenous rat 496 $mg\ kg^{-1}$ (6).

TC_{Lo} inhalation human 300 $mg\ m^{-3}$ pulmonary effects include bronchitis, pneumonitis and oedema (7).

Sub-acute and sub-chronic data

Groups of ♂ F344/N rats were sacrificed at 8, 16, 40, 90, 210 and 365 days after single, nose-only exposure to a mixed aerosol of beryllium metal and radioactive tracer particles. No lesions were observed in animals receiving lung burdens of 0.32 μg beryllium. Only late-occurring, minimal chronic inflammation and alveolar epithelial hyperplasia was observed in animals receiving lung burdens of 1.8 μg beryllium. Lung burdens of 10 and 100 μg beryllium induced minimal to mild acute and chronic inflammation, alveolar epithelial hyperplasia, and early-occurring fibrosis; the early- and late-phase clearance of the tracer particles through 365 days was significantly reduced compared to controls. A reduced ability of the lungs to clear the tracer particles was among the most sensitive indications of lung toxic response to inhaled beryllium (8).

Cynomolgus monkeys exposed to beryllium metal by bronchoscopic, intrabronchiolar instillation underwent bronchoalveolar lavage of the right and left diaphragmatic lobes at 14, 30, 60, 90 and 120 days post-exposure (dpe). Monkeys were sacrificed at 80 and 180 dpe. Numbers of lymphocytes from beryllium metal exposed lung lobes increased at 14, 30 and 90 dpe. *In vitro*, beryllium-specific, lung lymphocyte proliferation occurred at 14, 60 and 90 dpe. Lung lesions were characterised by focally intense, interstitial fibrosis, marked Type II cell hyperplasia and variable lymphocytes infiltration. Some monkeys had discrete immune granulomas consisting of lightly organised lymphocyte cuffs surrounding nodular aggregates of epitheloid macrophages (9).

Carcinogenicity and chronic effects

Sufficient evidence for carcinogenicity to humans and animals, IARC classification 1 (10-12).

TD_{Lo} intratracheal rat 13 $mg\ kg^{-1}$ can cause bronchogenic carcinoma (13).

TD_{Lo} intravenous rabbit 20 $mg\ kg^{-1}$ muscular skeletal tumours (14).

Teratogenicity and reproductive effects

Teratogenic in the developing chick embryo. The effect was organ-specific and simultaneously dependent on the stage of embryonic development at which beryllium was administered (15).

Metabolism and toxicokinetics

Unabsorbed beryllium is excreted in the faeces of rats and other animals; 96% of a single dietary dose is excreted within 24 hr, while only 1% of absorbed beryllium is excreted in urine and faeces in 24 hr (16).

$t_{1/2}$ in total human body 180 days (1).

Beryllium salts are readily precipitated in the tissues and are transported in the blood predominantly as colloidal phosphate-hydroxide complexes weakly associated with plasma globulins; these may be taken up by macrophages. Beryllium accumulates in bone, and to a lesser extent, in the liver. Absorbed beryllium is excreted mostly in the urine (12).

Elevated beryllium levels (e.g. 0.32 $\mu g\ g^{-1}$ in metastinal node) were found in lung tissue of subjects >20 years after termination of short-term exposure to beryllium (17).

Sensitisation

Cutaneous hypersensitivity to beryllium observed in guinea pigs may be significant for humans exposed to beryllium (18,19).

Genotoxicity

Escherichia coli, HeLa cells and Ehrlich ascites tumour cells, DNA cell binding assays positive (20).

Chinese hamster ovary and rat lung epithelial cells, 20-hr exposure, positive cytotoxic effects (21).

Oral rat (6 month) in drinking water, caused cytotoxicity at the toxic dose level and induced chromosomal aberrations, but was negative in dominant lethal assays (22).

Other effects

Other adverse effects (human)

Beryllium dermatitis, granulomatous ulcerations of the skin and conjunctivitis reported (23).

Concentrations of beryllium were determined in human breast milk; implications for childhealth are highlighted (24).

Workers occupationally exposed to beryllium exhibit the amino acid glutamate in a potentially critical location in a cell-surface glycoprotein that participates in antigen recognition (25).

In a nested case-control study of cancers of the central nervous system among workers employed at some time during 1973-1977 at two nuclear facilities in Oak Ridge, Tennessee the deaths of 72 white males and 17 white females from cancer of the CNS were identified. A weak association between exposure to beryllium and cancers of the CNS was observed, but confidence limits were wide and included the null value (26).

When all cancers were considered, no association between childhood cancer and parental exposure to beryllium or its compounds was found in a case-control study carried out in Denver, Colorado. The study included 252 cases of childhood cancer diagnosed during 1976-1983 and 222 population controls. When exposures of the fathers were analysed for specific types of cancer, an elevated odds ratio was found for brain cancer (2.1; 0.6-7.6; 5 cases) but not for acute lymphocytic leukaemia (1.3; 0.3-5.9; 5 cases) (27).

Beryllium exposure in humans may cause acute chemical pneumonitis, tracheobronchitis, conjunctivitis, dermatitis and chronic granulomatous pulmonary disease with systemic manifestations (28,29).

Any other adverse effects

Ionic beryllium has been shown to inhibit a number of enzymes *in vitro* including phosphatases, phosphoglutamase, hexokinase, deoxythymidine kinase, lactate dehydrogenase and amylase (30).

Legislation

Included in Schedules 4 and 6 (Release into Air/Land Prescribed Substances) of Statutory Instrument No. 472, 1991 (31).

Other comments

The toxicity of beryllium is dependent on the ability of the organism to absorb it. Therefore toxicity data refer to bioavailable forms, such as the ion in solution or particulate matter.
Exposure levels, ecotoxicology, experimental toxicology, human health and environmental effects have been extensively reviewed (1,11,12,32-40).
Chronic beryllium disease reviewed (41).
Toxicity of inhaled beryllium dust reviewed (42).
The results of chelation therapy with some polyaminocarboxylic acids in the rat suggest that HEDTA is a promising chelator for beryllium toxicity while DTPA enhances the toxic manifestation of beryllium (43).
Incompatible with halocarbons, causes flash or spark on impact. Reacts violently with trichloroethylene.
Moderate fire and explosion hazard.

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B103 beryllium chloride

$BeCl_2$

$BeCl_2$ **Mol. Wt.** 79.92 **CAS Registry No.** 7787-47-5

Synonyms beryllium dichloride

EINECS No. 232-116-4 **RTECS No.** DS 2625000

Uses Manufacture of beryllium catalysts.

Physical properties

M. Pt. 399°C **B. Pt.** 482°C **Specific gravity** 1.899 at 25°C with respect to water at 4°C
Volatility v.p. 1 mmHg at 291°C
Solubility Water: very soluble. Organic solvents: diethyl ether, ethanol, pyridine

Occupational exposure

FR-VME 0.002 mg m^{-3} (as Be)
JP-OEL 0.002 mg m^{-3} (as Be)
SE-LEVL 0.002 mg m^{-3} (as Be)
UK-LTEL MEL 0.002 mg m^{-3} (as Be)
US-TWA 0.002 mg m^{-3} (as Be) **US-STEL** 0.01 mg m^{-3} (as Be)

UN No. 1566 **HAZCHEM Code** 2X **Conveyance classification** toxic substance
Supply classification very toxic
Risk phrases May cause cancer by inhalation – Toxic if swallowed – Very toxic by inhalation – Irritating to eyes, respiratory system and skin – May cause sensitisation by skin contact – Toxic: danger of serious damage to health by prolonged exposure through inhalation (R49, R25, R26, R36/37/38, R43, R48/23)
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 150 μg l^{-1} (soft water), 20,000 μg l^{-1} (hard water) static bioassay (1).
LC_{50} (96 hr) bluegill sunfish 1300 μg l^{-1} (soft water) 12,000 μg l^{-1} (hard water) static bioassay (2).

Invertebrate toxicity
EC_{50} (48 hr) *Daphnia magna* 7.9 mg Be l^{-1} (hardness: 180 mg l^{-1} as $CaCO_3$) (2).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 86 mg kg^{-1}.
LD_{50} intraperitoneal rat 4.4 mg kg^{-1}.
LD_{50} intramuscular mouse 12 mg kg^{-1}.
LD_{50} intraperitoneal guinea pig 50 mg kg^{-1} (3).

Carcinogenicity and chronic effects

Sufficient evidence for carcinogenicity to humans and animals, IARC classification group 1, for beryllium and beryllium compounds (4-6).

Inhalation exposure of rats to 0.2 or 0.4 mg m^{-3} for 1 hr daily 5 days wk^{-1} for 4 months. Adenocarcinomas and trabecular adenomas found 18 months after termination of exposure (7).

Inhalation (4 months) ♀ rat 0.8, 4, 30 or 400 μg m^{-3} 1 hr day^{-1} 5 day wk^{-1}, only malignant epithelial lung tumours were considered and these occurred in 1/44, 2/42, 8/24 and 11/19, respectively, of the treated groups. No tumours were found in control rats (7).

Teratogenicity and reproductive effects

A single injection of 3-300 μg into chicken embryos killed most of the embryos and caused severe damage to those surviving. Embryos treated with 0.03-0.3 μg survived but showed malformations; defects included cardiac malformations, malpositions and caudal regression (8).

Metabolism and toxicokinetics

Intravenous ICR mice administered before fertilisation and on days 7-14 of pregnancy. Beryllium permeates placenta with difficulty. Part of administered dose circulated in blood long enough to penetrate foetuses (9).

Intraperitoneal injection into rats at 1.2 mg kg^{-1} every other day for 3 months; accumulated in liver and spleen > kidney > heart > lung (10).

Mice were administered 0.5 μg $^{7}BeCl_2$ by various routes (subcutaneously, intraperitoneally, intramuscularly, intrathoracically and intravenously) and distribution was observed for periods up to 1 wk. Within the limits of 1 wk of exposure the skeleton appears to be a critical organ (11).

Sensitisation

0.5% challenge caused skin sensitisation in guinea pigs at 24 hr and 48 hr (12).

Genotoxicity

Salmonella typhimurium TA98, TA100 with and without metabolic activation negative. Mild positive effect in the *rec* assay. Induced sister chromatid exchanges in V79 Chinese hamster cells (13).

In vitro domestic pig peripheral lymphocytes and primary kidney cells mitotic delay and chromosomal aberrations positive (14,15).

Beryllium dichloride did not induce aberrations of chromosomes in *Vicia faba* (16).

Other effects

Other adverse effects (human)

Respiratory diseases from inhalation of soluble beryllium compounds include rhinitis, pharyngitis, tracheobronchitis and pneumonitis (17).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Chlorides : guide level 25 mg l^{-1} (18).

Other comments

Human health effects, experimental toxicology and environmental effects reviewed (19,20).

Beryllium has been measured in 59 samples of surface water from 15 US/Canadian rivers. Highest concentration was less than 0.22 μg l^{-1}. Beryllium was found in 85% of samples from 15 major river basins in the USA at concentrations of 0.01-1.22 μg l^{-1}. Beryllium has been reported to occur in US drinking water at 0.01-0.7 μg l^{-1} with a mean of 0.013 μg l^{-1} total beryllium (21).

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B104 beryllium fluoride

BeF_2

BeF_2 **Mol. Wt.** 47.01 **CAS Registry No.** 7787-49-7

Synonyms beryllium difluoride

EINECS No. 232-118-5 **RTECS No.** DS 2800000

Uses Commercial production of beryllium metals and glass. Used in nuclear reactors.

Physical properties

M. Pt. 555°C **B. Pt.** 1160°C **Specific gravity** 1.986 at 25°C

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

Occupational exposure

DE-MAK 2.5 mg m^{-3} (as F) (inhalable dust fraction)

FR-VME 0.002 mg m^{-3} (as Be)

JP-OEL 0.002 mg m^{-3} (as Be)

SE-LEVL 0.002 mg m^{-3} (as Be)

UK-LTEL MEL 0.002 mg m^{-3} (as Be)

US-TWA 0.002 mg m^{-3} (as Be) **US-STEL** 0.01 mg m^{-3} (as Be)

UN No. 1566 **HAZCHEM Code** 2X **Conveyance classification** toxic substance

Supply classification very toxic

Risk phrases May cause cancer by inhalation – Toxic if swallowed – Very toxic by inhalation – Irritating to eyes, respiratory system and skin – May cause sensitisation by skin contact – Toxic: danger of serious damage to health by prolonged exposure through inhalation (R49, R25, R26, R36/37/38, R43, R48/23)

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 150 μg l^{-1} (soft water); 20,000 μg l^{-1} (hard water) static bioassay (1).
LD_{50} (96 hr) bluegill sunfish 1300 μg l^{-1} (soft water); 12,000 μg l^{-1} (hard water) static bioassay (1).

Invertebrate toxicity

EC_{50} (48 hr) *Daphnia magna* 2500 μg l^{-1} (2).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, mouse 98, 100 mg kg^{-1}, respectively (3).
LD_{50} subcutaneous mouse 20 mg kg^{-1} (3).
LD_{50} intraperitoneal hamster 21 mg kg^{-1} (3).

Carcinogenicity and chronic effects

Sufficient evidence for carcinogenicity to humans and animals, IARC classification group 1, for beryllium and its compounds (4).
Inhalation (1 hr) or intratracheal (single instillation) ♂ rats, neoplasms in the lung observed after 16 months (5).
Inhalation rat (4 month) 0.2 mg m^{-3} 1 hr daily, 5 × wk, induced the development of large foci of catharal pneumonia, atelectasis and fields of emphysema. Twelve months after termination, chronic intestitial pneumonia, interspersed with emphysema, occurred. In a number of cases hyperplasia with polymorphism of rapidly reproducing cells was observed. Flat-cell cancer infiltrating surrounding tissue, and adenocarcinomas were observed in several cases. Eighteen months after termination of the inhalation, trabecular adenoma and adenocarcinomas with infiltrating growth and hepatic metastic foci were found (6).

Metabolism and toxicokinetics

Humans exposed to 3 μg Be m^{-3} inhaled air (duration unspecified), excretion mainly in urine. Urinary excretion is prolonged with detection of beryllium in urine for 10 yr after exposure (7).
Accumulation, distribution and excretion of inhaled aerosol beryllium fluoride in rats depends on age of rat. Beryllium clearance from nose, oral cavity, and trachea was slower, retention in stomach and small intestine longer in 1-wk-old than adult rats (8).

Sensitisation

Hartley strain II and III guinea pigs were sensitised to beryllium fluoride by painting a 20% solution of beryllium fluoride in detergent each day for 3 days on the left ear. Fourteen days after starting sensitisation treatment, they were skin painted with 1% beryllium fluoride in 1% Triton X 100 on the flank to determine sensitivity. Only strain II animals could be sensitised to beryllium fluoride (9).

Other effects

Any other adverse effects

Inhalation monkey (7-16 day) 27 μg ft^{-3} 6 hr day^{-1} beryllium fluoride (corresponds to 5.2 μg ft^{-3} beryllium) caused severe pulmonary reactions and changes to liver, kidney, adrenals, pancreas, thyroid and spleen (10).
Symptoms of acute inhalation (species unspecified) include rhinitis, pharyngitis, tracheobronchitis and pneumonitis (11).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Fluorides: maximum admissible concentration 1500 μg l^{-1} (8-12°C); 700 μg l^{-1} (25-30°C) (12).

Other comments

Human health effects, experimental toxicology and environmental effects reviewed (13,14).
Beryllium and beryllium compounds reviewed (4).

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B105 beryllium nitrate

$$Be(NO_3)_2$$

BeN_2O_6 **Mol. Wt.** 133.02 **CAS Registry No.** 13597-99-4

EINECS No. 237-062-5 **RTECS No.** DS 3675000

Uses Used to stiffen mantles in gas and acetylene lamps.

Physical properties

M. Pt. ~60°C **B. Pt.** 100-200°C (decomp.)
Solubility Water: very soluble. Organic solvents: ethanol

Occupational exposure

FR-VME 0.002 mg m^{-3} (as Be)
JP-OEL 0.002 mg m^{-3} (as Be)
SE-LEVL 0.002 mg m^{-3} (as Be)
UK-LTEL MEL 0.002 mg m^{-3} (as Be)
US-TWA 0.002 mg m^{-3} (as Be) **US-STEL** 0.01 mg m^{-3} (as Be)

UN No. 2464 **HAZCHEM Code** 2WE **Conveyance classification** oxidising substance, toxic
Supply classification very toxic
Risk phrases May cause cancer by inhalation – Toxic if swallowed – Very toxic by inhalation – Irritating to eyes, respiratory system and skin – May cause sensitisation by skin contact – Toxic: danger of serious damage to health by prolonged exposure through inhalation (R49, R25, R26, R36/37/38, R43, R48/23)
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 150 μg l^{-1} (soft water) 20,000 μg l^{-1} (hard water) static bioassay (1).
LC_{50} (96 hr) bluegill sunfish 1300 μg l^{-1} (soft water) 12,000 μg l^{-1} (hard water) static bioassay (1).

Invertebrate toxicity

LC_{50} (24 hr) *Daphnia magna* 18 mg Be l^{-1} (hardness: 300 mg l^{-1} as $CaCO_3$) (2).

Toxicity to other species

LD_{Lo} subcutaneous frog 1041 mg kg^{-1} (3).

Bioaccumulation

Bioconcentration of 100-fold can occur under constant exposure. Not significant in spill conditions (4).

Mammalian & avian toxicity

Acute data

LD_{50} intraperitoneal, intravenous mouse 0.5, 3.0 mg kg^{-1}, respectively (5,6).
LD_{Lo} intraperitoneal guinea pig 100 mg kg^{-1} (5).

Carcinogenicity and chronic effects

Sufficient evidence for carcinogenicity to humans and animals, IARC classification group 1, for beryllium and its compounds (7).

Metabolism and toxicokinetics

Intravenous rat (dose unspecified) circulating beryllium carried to all tissues. Analysis 2.5 hr after administration gave measurable levels in most organs. Distribution to organs was dose-dependent, the skeleton was favoured for smaller doses and the liver for larger doses (8).

Genotoxicity

Salmonella typhimurium TA100 and TA98 with and without metabolic activation negative. Mild positive effect in *rec* assay. Induced sister chromatid exchanges in V79 Chinese hamster cells (9).

Other effects

Any other adverse effects

Intratesticular injections (7 days) caused decrease of testis weight from 651 mg in control to 580 mg in treated rat. Partial necrosis occurred in 2 days and total necrosis occurred within 7 days (10).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Nitrates : guide level 25 mg l^{-1}, maximum admissible concentration 50 mg l^{-1} (11).

Other comments

Beryllium has been measured in 59 samples of surface water from 15 US/Canadian rivers. Highest concentration was less than 0.22 μg l^{-1}. Beryllium was found in 85% of samples from 15 major river basins in the USA at concentrations of 0.01-1.22 μg l^{-1}. Beryllium has been reported to occur in US drinking water at 0.1-0.7 μg l^{-1} with a mean of 0.013 μg l^{-1} total beryllium (12).
Human health effects, experimental toxicology and environmental effects reviewed (13,14).
Beryllium and beryllium compounds reviewed (7).

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B106 beryllium sulfate

$BeSO_4$

BeO_4S **Mol. Wt.** 105.08 **CAS Registry No.** 13510-49-1

Synonyms sulfuric acid, beryllium salt

EINECS No. 236-842-2 **RTECS No.** DS 4800000

Uses In X-ray media.

Physical properties

M. Pt. 550-600°C (decomp.) **Specific gravity** 2.443 at 25°C
Solubility Water: very soluble

Occupational exposure

FR-VME 0.002 mg m^{-3} (as Be)
JP-OEL 0.002 mg m^{-3} (as Be)
SE-LEVL 0.002 mg m^{-3} (as Be)
UK-LTEL MEL 0.002 mg m^{-3} (as Be)
US-TWA 0.002 mg m^{-3} (as Be) **US-STEL** 0.01 mg m^{-3} (as Be)

UN No. 1566 **HAZCHEM Code** 2X **Conveyance classification** toxic substance
Supply classification very toxic
Risk phrases May cause cancer by inhalation – Toxic if swallowed – Very toxic by inhalation – Irritating to eyes, respiratory system and skin – May cause sensitisation by skin contact – Toxic: danger of serious damage to health by prolonged exposure through inhalation (R49, R25, R26, R36/37/38, R43, R48/23)
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, rat 80 mg kg^{-1} (1).
LD_{50} subcutaneous rat 1.5 mg kg^{-1} (1).
LD_{50} intravenous, intraperitoneal rat 7, 18 mg kg^{-1}, respectively (1).

LD_{50} intravenous monkey 0.6 mg kg^{-1} (1).
Intravenous rats, rabbits, 0.5 or 0.75 mg Be^{-1} kg^{-1} (injected as sulfate solution) caused death within 72 hr. Symptomatic effects included low blood-sugar levels and necrotic liver lesions (2).

Carcinogenicity and chronic effects
Sufficient evidence for carcinogenicity to humans and animals IARC classification group 1, beryllium and its compounds (3).
TC_{Lo} (26 wk) inhalation rat 432 μg m^{-3} induced tumours of lungs, thorax or respiratory system (4).
TD_{Lo} (2 wk) intratracheal rat 17 mg kg^{-1} intermittent doses induced tumours of lungs, thorax or respiratory system (5).

Metabolism and toxicokinetics
Oral rat (dose unspecified) in drinking water, most of the beryllium precipated as phosphate in the gut lumen and was excreted in the faeces. Ultimate site of accumulation of beryllium was in the skeleton (6).
Intravenous rat (dose unspecified) circulating beryllium carried to all tissues. Analysis 2.5 hr after administration gave measurable levels in most organs. Distribution to organs was dose-dependent, the skeleton was favoured for smaller doses and the liver for larger doses (7).
Beryllium sulfate forms beryllium phosphate in plasma. Uptake by liver cells in rats (8).

Irritancy
Beryllium dermatitis, granulomatous ulcerations and conjunctivitis reported (9).

Sensitisation
Depressed lymphocyte stimulation in sensitised animals demonstrated delayed skin reactivity and macrophage migration inhibition (9).
Animals immunised with beryllium sulfate developed skin reactivity as well as antigen-specific alveolar macrophage migration inhibition (10).

Genotoxicity

Salmonella typhimurium TA1530, TA1535, TA1538 and *Saccharomyces cerevisiae* D3 host mediated assay using Swiss-Webster mice negative (11).
Bacillus subtilis H17, M45 without metabolic activation weekly positive (12).
Mouse embryo cell line C3H/10T1/2 equivocal mutagen, transformation assay negative (13).
Syrian hamster embryo cells exposure to 59 μg l^{-1} induced morphological transformation (14).

Other effects

Any other adverse effects
In vitro pulmonary alveolar macrophages of dogs exposed to beryllium sulfate cytotoxic (15).
On nose-only inhalation rat (1 hr) beryllium sulfate aerosol caused granulomatosis and a high prevalence of pneumonitis (8).
A single exposure inhalation rat (21 day) 3.3 or 7.0 μg Be l^{-1} (administered as beryllium sulfate) caused lung injury enhanced by lactate dehydrogenase and alkaline phosphatase activity (16).
Rats exposed to 66 μg ft^{-3} 6 hr day^{-1} beryllium sulfate (corresponds to 5.6 μg ft^{-3} beryllium) caused malaise and apathy, anorexia and dyspnoea (17).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Sulfates: guide level 25 mg l^{-1}, maximum admissible concentration 250 mg l^{-1} (18).

Other comments

Beryllium has been measured in 59 samples of surface water from 15 US and Canadian rivers. Highest concentration was less than 0.22 μg l^{-1}. Beryllium was found in 85% of samples from 15 major river basins in the

US at concentrations of 0.01-1.22 μg l^{-1}. Beryllium has been reported to occur in US drinking water at 0.1-0.7 μg l^{-1} with a mean of 0.013 μg l^{-1} total beryllium (19).
Experimental toxicology, human health and environmental effects reviewed (20,21).
Beryllium and beryllium compounds reviewed (3).
Insoluble in cold water, converts to tetrahydrate in hot water (1).

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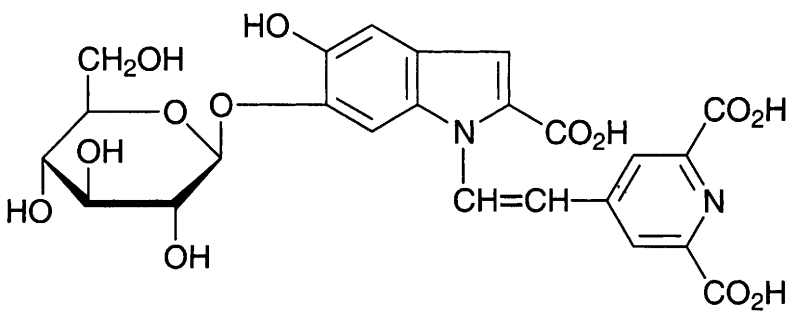
B107 betanin



$C_{24}H_{26}N_2O_{13}$ **Mol. Wt.** 550.48 **CAS Registry No.** 7659-95-2

Synonyms 5-β-D-glucoside; E162; phytolaccanin; 2,6-pyridinedicarboxylic acid, 4-[2-[2-carboxy-5-(β-D-glucopyranosyloxy)-2,3-dihydro-6-hydroxy-1*H*-indol-1-yl]ethenyl]-2,3-dihydro-, [5-(*R*,*R*)]-

EINECS No. 231-628-5 **RTECS No.** US 7968100

Uses Natural dyestuff. Taxonomically important.
Occurrence Obtained from red beet extracts, *Beta vulgaris* (1).

Mammalian & avian toxicity

Carcinogenicity and chronic effects

50 mg kg^{-1} pure or degraded betanin administered to partially hepatectomised Sprague-Dawley rats pretreated with phenobarbital for 6 months showed no cancer initiating activity (2).

Other comments

Red beetroot contains both red and yellow pigments of the class betaines. Used in food to replace delisted FD&C Reds 2 and 4 (1).

Principal colouring compound is β-D-glucopyranoside of betanidine. Colour is unstable in many food processing conditions (most stable at pH 4.0-5.0). May contain sodium nitrate E251 up to 25 mg kg^{-1} so may need to be eliminated from the diets of babies and young children (3).

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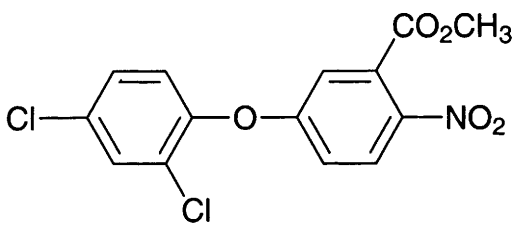
B108 bifenox



$C_{14}H_9Cl_2NO_5$ **Mol. Wt.** 342.13 **CAS Registry No.** 42576-02-3

Synonyms methyl 5-(2,4-dichlorophenoxy)-2-nitrobenzoate; 5-(2,4-dichlorophenoxy)-2-nitrobenzoic acid methyl ester; 2,4-dichlorophenyl-3-(methoxycarbonyl)-4-nitrophenyl ether

EINECS No. 255-894-7 **RTECS No.** DG 7890000

Uses Pre-emergence herbicide.

Physical properties

M. Pt. 84-86°C **Partition coefficient** log P_{ow} 4.5 **Volatility** v.p. 2.4×10^{-6} mmHg at 30°C

Solubility Water: 0.35 mg l^{-1} at 25°C. Organic solvents: acetone, chlorobenzene, ethanol, xylene

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) bluegill sunfish, rainbow trout > 0.27, > 0.18 mg l^{-1}, respectively (1).

Invertebrate toxicity

EC_{50}(48 hr) *Daphnia magna* 0.66 mg l^{-1} (1).

LD_{50} (contact) >1000 μg bee^{-1} (1).

Environmental fate

Degradation studies

In soil $t_{1/2}$ 5-7 days. Duration of residual activity 7-8 wk (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat >6400 mg kg^{-1} (2).
LD_{50} oral mouse 4556 mg kg^{-1} (2).
LC_{50} inhalation rat >0.91 mg l^{-1} air (1).
LD_{50} dermal rabbit >2000 mg kg^{-1} (1).

Sub-acute and sub-chronic data

LD_{50} (8 day) dietary duck, pheasant >5000 mg kg^{-1} (1).
Oral American Kestrel nestlings (dosed for the 10 consecutive days after hatching) 10, 50, 250 or 500 mg kg^{-1} in corn oil. 500 mg kg^{-1} resulted in 66% mortality. Crown-rump, humerus, radius-ulna and femur of nestlings dosed with 250 mg kg^{-1} were significantly shorter than controls. Bifenox ingestion resulted in increased hepatic GSH peroxidase activity in the 50 and 250 mg kg^{-1} groups (3).

Carcinogenicity and chronic effects

In 2-yr feeding trials the no-effect levels for rats, dogs and mice were 80, 145 and 30 mg kg^{-1} daily, respectively (1).
Oral ♂, ♀ B6C3F1 mice (18 month, dose unspecified) induced liver adenomas and carcinomas in ♂ mice only (4).

Teratogenicity and reproductive effects

In rats bifenox caused low incidence of bloody tears but did not decrease survival to term or to weaning in rats or mice. Did not reduce Harderian gland weight in mice. The authors concluded bifenox is non-teratogenic (5).

Metabolism and toxicokinetics

In animals (species unspecified) bifenox is relatively rapidly absorbed and eliminated from the body. 5-(2, 4-dichlorophenyl)-2-nitrobenzoic acid was the major urinary metabolite, with no bifenox detected. Bifenox together with 5-(2,4-dichlorophenyl)anthranilate were detected in faeces (1).

Irritancy

Non-irritating to skin and eyes of rabbit (1).

Genotoxicity

Salmonella typhimurium TA98 and TA100 with and without metabolic activation negative. *Salmonella typhimurium* YG1026 with metabolic activation positive (3.0 revertants μg^{-1}) (6).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides and related products: maximum admissible concentration 0.1 $\mu g\ l^{-1}$ (7).
Included in Schedule 6 (Release Into Land Prescribed Substances) of Statutory Instrument No. 472, 1991 (8).

Other comments

Structurally related to the probable human carcinogen acifluorfen (4).
Metabolic pathways reviewed (9).

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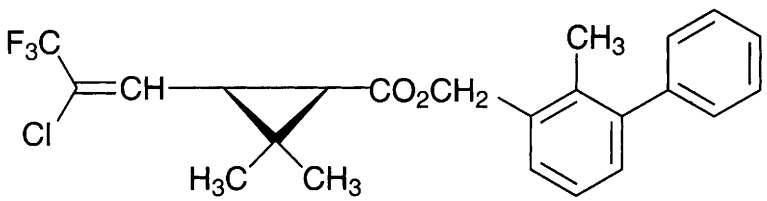
B109 bifenthrin



$C_{23}H_{22}ClF_3O_2$ **Mol. Wt.** 422.87 **CAS Registry No.** 82657-04-3

Synonyms 2-methylbiphenyl-3-ylmethyl Z-(1*RS*,3*RS*)-3-(2-chloro-3,3,3-trifluoroprop-1-enyl)-2,2-dimethylcyclopropanecarboxylate; [1α,3αZ]-(±)-(2-methyl[1,1'-biphenyl]-3-yl)methyl 3-(2-chloro-3,3,3-trifluoro-1-propenyl)-2,2-dimethylcyclopropanecarboxylate; Brigade; Talstar; Biflex; Capture; Kiros; Polysect

RTECS No. GZ 1227800

Uses Contact insecticide and acaricide. Synthetic pyrethroid.

Physical properties

M. Pt. 51-66°C **Flash point** 165°C (open cup) **Specific gravity** 1.21 at 25°C **Volatility** v.p. 1.81×10^{-7} mmHg at 25°C

Solubility Water: 0.1 mg l^{-1}. Organic solvents: acetone, chloroform, dichloromethane, diethyl ether, toluene

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) rainbow trout, bluegill sunfish 150, 350 mg l^{-1}, respectively (1).

Blood serum proteins of the freshwater fish *Tilapia mossambica* were decreased or degraded by low concentrations of bifenthrin. Higher doses degraded the proteins and also caused the synthesis of new defensive proteins to withstand the environmental stress. If the toxicant did not persist then the fish serum proteins regained their normal levels (2).

LC_{50} (8 day) gizzard shad, concentration in water 1 hr after the addition of sediment-bound bifenthrin and average concentration during the 8-day study, 521 and 207 ng l^{-1}, respectively (3).

Invertebrate toxicity

EC_{50} (48 hr) *Daphnia magna* 160 mg l^{-1} (1).

The residual life and toxicity to foraging honey bees, *Apis mellifera*, of bifenthrin applied to cotton, *Gossypium hirsutum*, in Arizona were examined. Residues on cotton leaf surfaces dropped to <5% at 5 days after application. Honey bee mortalities from leaves freshly treated with bifenthrin were 100% (emulsifiable concentrate) and 95% (wettable powder) (4).

Bifenthrin applied to Kentucky bluegrass turf at the rate used by the turfgrass industry of 0.11 kg ha^{-1} caused no significant mortality to earthworms 1 wk or 3 wk after treatment, for spring or autumn application (5).

Bioaccumulation
Its low solubility in water and high affinity for soil contribute to produce little impact in aquatic systems under field conditions (1).

Environmental fate

Degradation studies
In soil $t_{1/2}$ 65-125 days (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral mallard duck >4450 mg kg^{-1} (1).
LD_{50} oral rat 54 mg kg^{-1} (1).
LD_{50} dermal rabbit >2000 mg kg^{-1} (1).

Sub-acute and sub-chronic data
LD_{50} (8 day) bobwhite quail 4450 mg kg^{-1} in diet (1).

Teratogenicity and reproductive effects
Non-teratogenic in rats given <2 mg kg^{-1} day^{-1}. Non-teratogenic in rabbits given 8 mg kg^{-1} day^{-1} (1).

Legislation

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

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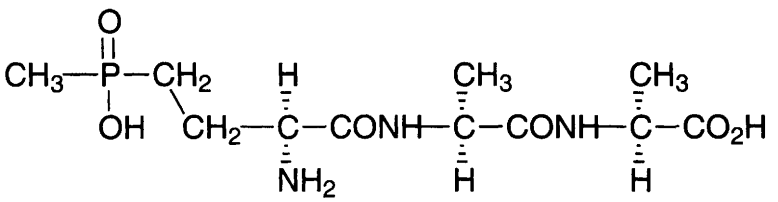
B110 bilanafos



$C_{11}H_{22}N_3O_6P$ **Mol. Wt.** 323.29 **CAS Registry No.** 35597-43-4
Synonyms 4-[hydroxy(methyl)phosphinoyl]-L-homoalanyl-L-alanyl-L-alanine; 4-(hydroxymethylphosphinyl)-L-2-aminobutanoyl-L-alanyl-L-alanine; Meiji Herbiace
Uses Herbicide used for post-emergence control of annual weeds.
Occurrence Bilanafos-sodium is produced by *Streptomyces hygroscopicus* during fermentation.

Physical properties

M. Pt. *c.* 160°C (decomp.) (sodium salt)
Solubility Water: 1 kg l^{-1}. Organic solvents: 250 g l^{-1} ethanol, 500 g l^{-1} methanol

Ecotoxicity

Fish toxicity
LC_{50} (48 hr) carp 1000 mg l^{-1} (1).

Invertebrate toxicity
EC_{50} (48 hr) *Daphnia magna* 1000 mg l^{-1} (1).
10 mg l^{-1} caused a transient reduction in live phytoplankton cells, which was particularly apparent in the small (1-2 and 2-3 μm) classes. The impact on live cell numbers was mirrored by a reduction in dissolved oxygen content in the treated enclosures (2).

Mammalian & avian toxicity

Acute data
LD_{50} oral ♂ rat 268, oral ♀ rat 404 mg sodium salt kg^{-1} (1).
LD_{50} dermal rat >5000 mg kg^{-1} (1).

Carcinogenicity and chronic effects
In sub-acute and chronic toxicity studies, no adverse effects were observed; non-carcinogenic (1).

Teratogenicity and reproductive effects
Non-teratogenic (1).

Metabolism and toxicokinetics
♂ Mice administered a single oral dose of 1.85 mg kg^{-1} ^{14}C-labelled bilanafos excreted 7.9 and 89.2% of the applied ^{14}C into the urine and faeces, respectively, within 24 hr. The major metabolite was L-2-amino-4-[(hydroxy)(methyl)phosphinyl]butyric acid (3).

Irritancy
Non-irritating to skin and eyes of rabbits (1).

Genotoxicity

Not mutagenic in Ames and Rec assays (1).

Legislation

WHO Toxicity Class II (4).
Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticide: maximum admissible concentration 0.1 μg l^{-1} (5).
Included in Schedule 6 (Release into Land: Prescribed Substances) of Statutory Instrument No. 472, 1991 (6).

Other comments

Bilanafos rapidly inhibits photosynthesis of mustard under atmospheric conditions (400 ppm CO_2, 21% O_2, but under conditions where no photorespiration can occur (1000 ppm CO_2, 2% O_2, there is no inhibition of photosynthesis. Bilanafos is split in plants into phosphinothricin and alanine and freed phosphinothricin inhibits glutamine synthetase and causes NH_4^+ accumulation and a decrease in glutamine levels, but this NH_4^+ accumulation has been shown not to be the primary cause for the inhibition of photosynthesis by bilanafos – a process connected with photorespiration is thought to play a considerable role in this inhibition (7).
Bilanafos did not inhibit glutamine synthetase, extracted from the shoots of the rice plant, at concentrations of 0.1 – 3 mM. However, L-2-amino-4-[(hydroxy)(methyl)phosphinyl]butyric acid, a metabolite of bilanafos, completely inhibited glutamine synthetase activity at a concentration of 1 mM (8).

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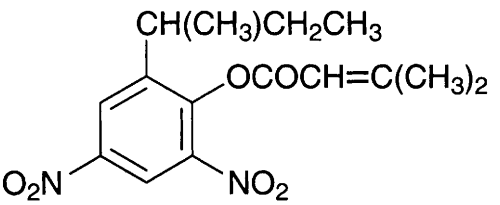
B111 binapacryl



$C_{15}H_{18}N_2O_6$ **Mol. Wt.** 322.32 **CAS Registry No.** 485-31-4

Synonyms 2-butenoic acid, 3-methyl-2-(1-methylpropyl)-4,6-dinitrophenyl ester; 2-*sec*-butyl-4,6-dinitrophenyl 3-methylcrotonate; 2-(1-methylpropyl)-4,6-dinitrophenyl 3-methyl-2-butenoate; crotonic acid, 3-methyl-2-*sec*-butyl-4,6-dinitrophenyl ester

EINECS No. 207-612-9 **RTECS No.** GQ 5600000

Uses Acaricide. Fungicide. Believed to be no longer manufactured, or marketed for crop protection use (1).

Physical properties

M. Pt. 66-67°C **Specific gravity** 1.2 at 20°C **Volatility** v.p. 1×10^{-4} mmHg at 60°C
Solubility Water: 1 mg l^{-1} at 20°C. Organic solvents: acetone, dichloromethane, ethanol, ethyl acetate, isophorone, methanol, toluene, xylene

Occupational exposure

Supply classification harmful
Risk phrases May cause harm to the unborn child – Harmful in contact with skin and if swallowed (R61, R21/22)
Safety phrases Restricted to professional users – Avoid exposure – obtain special instruction before use – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S53, S45)

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) channel catfish, bluegill sunfish, rainbow trout 15-50 μg l^{-1} as the technical material (2).

Invertebrate toxicity
Asellus brevicaudus (96 hr) 29 μg l^{-1} at 16°C as the technical material (2).
Non-toxic to bees (3).

Environmental fate

Degradation studies

Residual activity in soil 15-25 days. Degraded in the environment to the amine and carboxylic acid (3).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, guinea pig, rabbit, dog 150-640 mg kg^{-1} (3).

LD_{50} oral mice 1600-3200 mg kg^{-1} (3).

LD_{50} percutaneous rat 750 mg kg^{-1} (in acetone) (3).

Carcinogenicity and chronic effects

Rats administered 500 mg kg^{-1} in diet for 2 yr and dogs receiving 50 mg kg^{-1} in diet for 2 yr showed no ill-effects (3).

Metabolism and toxicokinetics

In mammals (species unspecified) after oral administration binapacryl was eliminated as the glucuronic acid conjugate (3).

Cytochrome P450, lipoperoxidase and xanthine oxidase in liver and blood glutathione levels were altered by an unspecified concentration of binapacryl (4).

After a single dose of binapacryl, 17% was excreted in the urine of rats and rabbits within 48 hr. 0.12% could still be detected in the urine of rats after 10 days (5).

Genotoxicity

Salmonella typhimurium TA100 without metabolic activation positive (6).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides and related products: maximum admissible concentration 0.1 μg l^{-1} (7).

Included in Schedule 6 (Release Into Land Prescribed Substances) of Statutory Instrument No. 472, 1991 (8).

References

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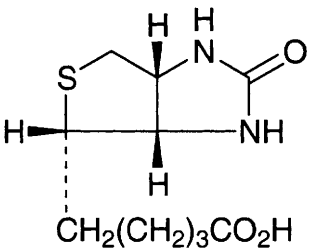
B112 biotin



$C_{10}H_{16}N_2O_3S$ **Mol. Wt.** 244.31 **CAS Registry No.** 58-85-5

Synonyms *d*-(+)-biotin; coenzyme R; Factor S; (3*aS*-(3*a*-α-4-β,6*a*-α)-hexahydro-2-oxo-1*H*-thieno[3,4-*d*]imidazole-4 -pentanoic acid; vitamin H; vitamin B_7; Ritatin

EINECS No. 200-399-3 **RTECS No.** XJ 9088200

Uses In immunoassays. DNA labelling. Dietary supplement.

Occurrence Richest sources are animal liver, kidney, pancreas, milk and yeasts.

Physical properties

M. Pt. 232-233°C

Solubility Water: 220 mg l^{-1} at 25°C. Organic solvents: chloroform, ethanol

Mammalian & avian toxicity

Carcinogenicity and chronic effects

CASE prediction of carcinogenicity negative (1).

Teratogenicity and reproductive effects

An acute dose to rats 10 mg per 100 g body weight on days 14-15 of gestation inhibited foetal and placental growth; in some dams resorption of foetuses and placentae occurred. Oestrogen therapy established normal pregnancy but treatment with progesterone failed to correct B_7-induced effects (2).

Subcutaneous ♀ rat (5 mg per 100 g body weight) on days 7, 14 and 21 prior to mating failed to maintain pregnancy, suggesting the induced infertility may be the result of oestrogen deficiency (3).

Metabolism and toxicokinetics

In rats, intestinal absorption proceeded by a saturable process at ≤ 10 ppm, whereas at higher concentrations uptake by passive diffusion predominated (4).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA537, TA538 with and without metabolic activation negative (5).

In vitro Chinese hamster ovary cells sister chromatid exchanges positive, chromosomal aberrations negative (6).

Other comments

Dietary and hormonal control of vitamin B_7 reviewed (7).

Plays an indispensable role in carboxylation reactions (8).

Dietary deficiency causes characteristic skin lesions and retarded growth (8).

References

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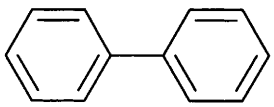
B113 biphenyl



$C_{12}H_{10}$ **Mol. Wt.** 154.21 **CAS Registry No.** 92-52-4

Synonyms diphenyl; phenylbenzene

EINECS No. 202-163-5 **RTECS No.** DU 8050000

Uses In organic synthesis. Heat transfer medium. Formerly fumigant for oranges during shipment.

Physical properties

M. Pt. 69-71°C **B. Pt.** 254-255°C **Flash point** 113°C **Specific gravity** 1.041 **Partition coefficient** log P_{ow} 3.98

Solubility Water: 17.5 mg l^{-1}. Organic solvents: diethyl ether, ethanol

Occupational exposure

DE-MAK 0.16 ppm (1 mg m^{-3})
FR-VME 0.2 ppm (1.5 mg m^{-3})
SE-LEVL 0.2 ppm (1.3 mg m^{-3}) **SE-STEL** 0.4 ppm (2.5 mg m^{-3})
UK-LTEL 0.2 ppm (1.3 mg m^{-3}) **UK-STEL** 0.6 ppm (3.8 mg m^{-3})
US-TWA 0.2 ppm (1.3 mg m^{-3})

Supply classification irritant, dangerous for the environment

Risk phrases Irritating to eyes, respiratory system and skin – Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment (R36/37/38, R50/53)

Safety phrases Keep out of reach of children (if sold to general public) – Do not breathe vapour – 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, S23, S60, S61)

Ecotoxicity

Invertebrate toxicity

EC_{50} (24,48 hr) *Daphnia magna* 1.3-0.36 mg l^{-1} (1).

Paracentrotus lividus and *Sphaerechinus granularis* (sea urchins) ≥1.5 mg l^{-1} caused developmental defects and mitotic abnormalities, following exposure of embryos or by pretreatment of sperm or eggs (2).

Environmental fate

Degradation studies

After 24 hr incubation with normal sewage sludge 0% degradation, 135 hr incubation 79% degradation. Incubation with acclimated sewage sludge, 24 hr 87% degradation and 135 hr 100% degradation (3).

Pseudomonas sp. and Gram-negative isolate degrade 1,1'-biphenyl to yield a variety of products. Metabolites include 2,3-dihydroxy-2, 3-dihydroxybiphenyl; 2,3-dihydroxybiphenyl; 2-hydroxy-6-oxo-6-phenylhexa-2,4-dienoate; 2-hydroxy-3-phenyl-6-oxohexa-2,4-dienoate; benzoic acid, 2-oxopenta-4-enoate and phenylpyruvic acid (4,5).

Abiotic removal

Calculated $t_{1/2}$ in water at 25°C and 1 m depth 7.5 hr, based on an evaporation rate of 0.092 m hr^{-1} (6).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, rabbit 2400, 3280 mg kg^{-1}, respectively (7,8).

Carcinogenicity and chronic effects

Oral mice (2 yr) 0.25% in feed induced tumours of mammary glands, lungs, lymphocytic tissue, liver, stomach, skin, ovary, uterus, pituitary gland (9).

Metabolism and toxicokinetics

Metabolised in isolated rat hepatocytes, predominantly to *p*-phenylphenol with smaller amounts of *m*-phenylphenol and *o*-phenylphenol (10).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100 with and without metabolic activation negative (11).
Saccharomyces cerevisiae D7 with and without metabolic activation positive (2).
Oral ♂ CD-1 mice administered 200 or 2000 mg kg^{-1} biphenyl were sacrificed 3, 8, or 24 hr after dosing. Using a modified Comet assay it was found that 2000 mg kg^{-1} induced DNA damage in the stomach, liver, kidney, bladder and lung. Increased DNA migration peaked at 24 hr (12).

Other effects

Any other adverse effects

Central nervous system depression, paralysis, convulsions have been observed in rats (8).

Other comments

Reviews on human health effects, experimental toxicology and environmental effects listed (13).
Microbial degradation reviewed (14,15).

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B114 1,4-bis(bromoacetoxy)-2-butene

$$BrCH_2CO_2CH_2CH{=}CHCH_2CO_2CH_2Br$$

$C_8H_{10}Br_2O_4$ **Mol. Wt.** 329.97 **CAS Registry No.** 20679-58-7

Synonyms acetic acid, bromo-, 2-butene-1,4-diyl ester

EINECS No. 243-962-9 **RTECS No.** AF 5957265

Uses Control of slime in the water systems of paper mills.

Physical properties

M. Pt. (*E*) form 56-58°C **B. Pt.** 135-136°C at 0.005 mmHg ((Z) form)

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) bleak 520 μg l^{-1} (1).

Invertebrate toxicity

EC_{50} (24 hr) *Chlorella kessleri* 0.1-3.0 mg l^{-1} but more effective against *Monoraphidium griffithii* and *Selenastrum capricornutum* in lower water levels (2).

LC_{50} (96 hr) *Nitocra spinipes* 0.24 mg l^{-1} (1).

Environmental fate

Degradation studies

Biodegradation in fresh water $t_{1/2}$ 6-10 hr and in sea water $t_{1/2}$ ~24 hr (3).

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse 125 mg kg^{-1} (4,5).

Genotoxicity

Salmonella typhimurium TA98, TA100 with and without metabolic activation negative (4).

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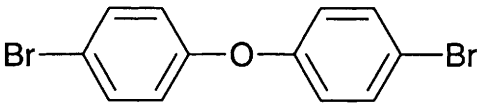
B115 bis(4-bromophenyl) ether



$C_{12}H_8Br_2O$ **Mol. Wt.** 328.00 **CAS Registry No.** 2050-47-7

Synonyms 4,4'-dibromodiphenyl ether; 1,1'-oxybis(4-bromobenzene); di-4-bromophenyl ether

EINECS No. 218-090-7 **RTECS No.** KN 0175000

Physical properties

M. Pt. 58.5°C **B. Pt.** 338-340°C

Mammalian & avian toxicity

Acute data

LD_{50} intraperitoneal mouse 125 mg kg^{-1} (1).

Sub-acute and sub-chronic data

Oral ♂ rat (14 day) 33 mg kg^{-1} increased liver weight and increased activity of cytochrome C reductase and cytochrome P450 content (2).

Other comments

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

References

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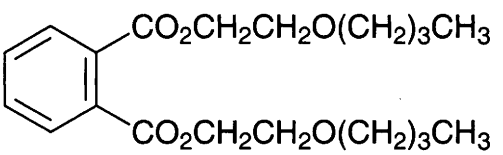
B116 bis(2-butoxyethyl) phthalate



$C_{20}H_{30}O_6$ **Mol. Wt.** 366.45 **CAS Registry No.** 117-83-9

Synonyms 1,2-benzenedicarboxylic acid, bis(2-butoxyethyl) ester; dibutylcellusolve phthalate

EINECS No. 204-213-1 **RTECS No.** TI 0175000

Uses Solvent and plasticiser for polyvinyl chloride, polyvinyl acetate and other resins.

Physical properties

M. Pt. –55°C **B. Pt.** 270°C
Solubility Water: 30 mg l^{-1} at 25°C

Occupational exposure

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

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 8,380 mg kg^{-1} (1).

Teratogenicity and reproductive effects
Reported to cause congenital malformations in chick embryos (2).
When injected into egg yolk at 2½ to 3 days of incubation was associated with cranial bifida and anophthalmia in the chick embryos (3).
Damage to chick central nervous system also reported (4).
Reported to be teratogenic to rats following intraperitoneal injection (5).

Metabolism and toxicokinetics
Phthalate diesters are rapidly metabolised to the monoester both in the intestine and following absorption (6).

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

References

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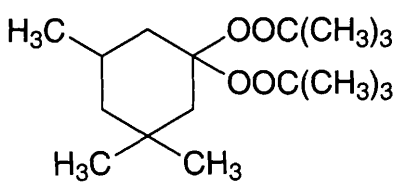
B117 1,1-bis(*tert*-butylperoxy)-3,3,5-trimethylcyclohexane



$C_{17}H_{34}O_4$ **Mol. Wt.** 302.45 **CAS Registry No.** 6731-36-8
Synonyms 1,1-bis(*tert*-butyldioxy)-3,3,5-trimethylcyclohexane; 3,3,5-trimethylcyclohexylidene bis(1,1-dimethylethyl peroxide); DIGIF; 3,3,5-trimethylcyclohexylidene bis(*tert*-butyl peroxide)
EINECS No. 229-782-3 **RTECS No.** SD 8600000
Uses Catalyst in cross-linking rubber manufacture. Vulcanisation agent.

Mammalian & avian toxicity

Irritancy

Causes local skin irritation, affects eye mucosa and upper respiratory tract in humans. No apparent cumulative action (1).

Other comments

IC_{50} *Plasmodium falciparum* clone D-G 50 mg l^{-1} antimalarial activity positive. Mice treated with *Plasmodium berghei* at concentrations of 40, 160 and 640 mg kg^{-1}, survived 0.9, 0.3 and 0.3 days longer, respectively, than the control group. The compound is considered active if mice survive 6.2 days longer than controls (2).
Explosion hazards reviewed (3).

References

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B118 bis(2-chloroethoxy)methane

$$(ClCH_2CH_2O)_2CH_2$$

$C_5H_{10}Cl_2O_2$ **Mol. Wt.** 173.04 **CAS Registry No.** 111-91-1

Synonyms bis(β-chloroethyl)formal; dichloroethyl formal; formaldehyde bis(β-chloroethyl)acetal; 1,1′-methylenebis(oxy)bis(2-chloroethane)

EINECS No. 203-920-2 **RTECS No.** PA 3675000

Uses Solvent. Intermediate for polysulfide rubber.

Physical properties

M. Pt. –32.8°C **B. Pt.** 217.5°C **Flash point** 110°C (open cup) **Specific gravity** 1.2339 at 20°C with respect to water at 20°C **Volatility** v.den. 5.9

Ecotoxicity

Bioaccumulation

Calculated bioconcentration factor 0.84 – 2.2 (1).

Environmental fate

Degradation studies

No biodegradation occurred using settled domestic wastewater inoculum under aerobic conditions through three successive subcultures (2).

Abiotic removal

Estimated hydrolytic $t_{1/2}$ 6 month-2 yr independent of pH (3).
Estimated $t_{1/2}$ for atmospheric reaction with photochemically produced hydroxyl radicals 10 hr (4).
Direct degradation is not as important a fate process as bis(2-chloroetoxy)methane does not have chromophores that absorb visible or near ultraviolet radiation (3).

Adsorption and retention

Based on estimated $\log P_{ow}$ (K_{ow}) of 0.75 and estimated water solubility of 1.2×10^5 mg l^{-1} at 25°C, K_{oc} values are 7-61, suggesting high to very high mobility in soil (5).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 65 mg kg^{-1} (6).

LC_{50} (4 hr) inhalation rat 62 ppm (7).

LD_{50} dermal guinea pig 170 mg kg^{-1} (6).

Irritancy

Dermal rabbit (24 hr) 10 mg caused irritation and 500 mg administered into rabbit eye caused irritation (8).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Organochlorine compounds: guide level 1 μg l^{-1} (9).

Included in Schedule 6 (Release into Land: Prescribed Substances) of Statutory Instrument No. 472, 1991 (10).

Other comments

Contaminant in industrial effluent (11,12).

Human health effects and experimental toxicology reviewed (13,14).

Decomposed by mineral acids.

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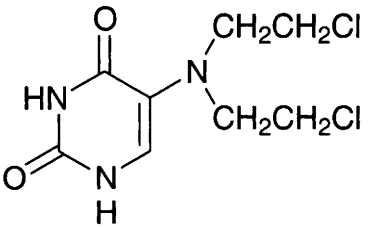
B119 5-bis(2-chloroethyl)aminouracil



$C_8H_{11}Cl_2N_3O_2$ **Mol. Wt.** 252.10 **CAS Registry No.** 66-75-1

Synonyms aminouracil mustard; 5-(bis(2-chloroethyl)amino)-2,4(1*H*,3*H*)pyrimidinedione; 5-*N*,*N*-bis(2-chloroethyl)-aminouracil; 2,6-dihydroxy-5-bis(2-chloroethyl)aminopyrimidine; 2,4-1*H*,3*H*-pyrimidinedione, 5-bis(2-chloroethylamino); uracil mustard

EINECS No. 200-631-3 **RTECS No.** YQ 8925000

Uses Antineoplastic agent. Used in treatment of chronic lymphocytic leukaemia and malignant lymphomas. Occasionally used to treat mycosis fungoides, polycythaemia, thrombocytosis. Adjunct in treatment of carcinoma of ovary and lung.

Physical properties

M. Pt. 206°C (decomp.)
Solubility Water: <1 g l^{-1} at 20°C. Organic solvents: acetone, dimethyl sulfoxide, ethanol

Ecotoxicity

Bioaccumulation
Calculated bioconcentration factor 0.783 (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 7.5 mg kg^{-1} (2).
LD_{50} intraperitoneal rat 1250 µg kg^{-1} (3).
LD_{Lo} intraperitoneal mouse 3 mg kg^{-1} (4).

Carcinogenicity and chronic effects
Inadequate evidence of carcinogenicity to humans, sufficient evidence of carcinogenicity to animals, IARC classification group 2B (5).
Intravenous mice (24 wk) 40, 20 and 8 mg kg^{-1} all developed lung adenomas and adenocarcinomas (6).

Teratogenicity and reproductive effects
TD_{Lo} (21 day) intraperitoneal pregnant rat 0.3-0.6 mg kg^{-1} reported malformations in surviving offspring including exencephaly, retarded and club appendages and deformed paws and tails (7).

Metabolism and toxicokinetics
Oral administration of 2 mg kg^{-1} or intravenous injection of 1 mg kg^{-1} in dogs. No evidence of the drug detected at 2 hr. Less than 1% dose recovered unchanged in urine (8).

Genotoxicity

Salmonella typhimurium TA1535 without metabolic activation positive (9).

Other effects

Other adverse effects (human)

Symptoms of poisoning include nausea, vomiting, diarrhoea, bone marrow depression (7).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Organochlorine compounds: guide level 1 $\mu g\ l^{-1}$ (10).

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

Other comments

Chemical and physical properties, human health effects, carcinogenicity and experimental toxicology reviewed (12-14).

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B120 bis(2-chloroethyl) ether

$$ClCH_2CH_2OCH_2CH_2Cl$$

$C_4H_8Cl_2O$ **Mol. Wt.** 143.01 **CAS Registry No.** 111-44-4

Synonyms bis(β-chloroethyl) ether; 1-chloro-2-(β-chloroethoxy)ethane; 2,2'-dichlorethyl ether; 1,1'-oxybis(2-chloro)ethane; *sym*-dichloroethyl ether

EINECS No. 203-870-1 **RTECS No.** KN 0875000

Uses Soil fumigant. Used to make polysulfide polymers. Solvent for resins, rubbers, cellulox posters in paints industry. Extracting agent in petroleum industry.

Physical properties

M. Pt. –50°C **B. Pt.** 178.5°C **Flash point** 55°C (closed cup) **Specific gravity** 1.222 at 20°C with respect to water at 20°C **Partition coefficient** log P_{ow} 1.29 (1) **Volatility** v.p. 0.7 mmHg at 20°C ; v.den. 4.93. **Solubility** Water: 10.2 g l^{-1} at 20°C. Organic solvents: miscible with aromatics

Occupational exposure

DE-MAK 10 ppm (59 mg m^{-3})
FR-VME 5 ppm (30 mg m^{-3})
JP-OEL 15 ppm (88 mg m^{-3})
US-TWA 5 ppm (29 mg m^{-3}) **US-STEL** 10 ppm (58 mg m^{-3})

UN No. 1916 **HAZCHEM Code** 2W **Conveyance classification** toxic substance
Supply classification very toxic
Risk phrases Flammable – Very toxic by inhalation, in contact with skin and if swallowed – Possible risk of irreversible effects (R10, R26/27/28, R40)
Safety phrases Keep locked up and out of the reach of children (if sold to general public) – Keep container tightly closed and in a well ventilated place – Take off immediately all contaminated clothing – In case of insufficient ventilation, wear suitable respiratory equipment – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S7/9, S27, S38, S45)

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) bluegill sunfish 600 mg l^{-1} (2).

Invertebrate toxicity
EC_{50} (48 hr) *Daphnia magna* 238-240 mg l^{-1} static assay (3,4). IC_{50} (concentration of chemical causing 50% inhibition of microorganisms) using activated sludge 21.38 mM (5).

Bioaccumulation
Bioconcentration factor of 11 observed in bluegill sunfish 14 day exposure (6).

Environmental fate

Anaerobic effects
Does not inhibit anaerobic digestion, laboratory scale at 100 mg l^{-1} (7).

Degradation studies
Concentrations of ≥300 mg l^{-1} significantly inhibited overall biodegradation during treatment of wastewater from an organic chemical manufacturing plant (8).
Abiotic removal
Estimated hydrolysis $t_{1/2}$ 20 yr at 25°C (8).
Estimated atmospheric $t_{1/2}$ 13.44 hr for reaction of bis(2-chloroethyl) ether with hydroxy radicals (9).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 144 mg kg^{-1} (10).
LD_{50} oral mouse 211 mg kg^{-1} (10).
LC_{50} (4 hr) inhalation rat 330 mg m^{-3} (11).
LC_{50} (2 hr) inhalation mouse 650 mg m^{-3} (11).
LD_{50} dermal guinea pig 300 mg kg^{-1} (12).

Carcinogenicity and chronic effects
No adequate data for carcinogenicity to humans, limited evidence for carcinogenicity to animals, IARC classification group 3 (13).

Metabolism and toxicokinetics
Rapidly absorbed through skin although skin itself showed no marked irritation (14).
Rapidly distributed throughout body tissues, with the kidney and lung taking up greatest amounts (species unspecified) (15).

After injection of 5 mg into rats the metabolites thiodiglycolic acid and hydroxyethyl mercapturic acid were detected in 24 hr urine samples (16).
Oral ♂ rat 40 mg kg^{-1} dose ^{14}C-labelled bis (2-chloroethyl) ether. Excreted in urine and respired air for 48 hr. Expired $^{14}CO_2$ accounted for 11.5% of dose, urinary ^{14}C 64.7% and faeces 2.4% $t_{1/2}$ for elimination 12 hr.
Inhalation exposure ♂ rat (8 hr) 10, 50, 100 and 500 ppm. Metabolites hydroxymethyl mercapturic acid and thiodiglycolic acid detect in 24 hr urine samples (16).

Irritancy
Dermal rabbit (24 hr) 10 mg caused irritation (12).
20 mg instilled into rabbit eye caused irritation (17).
In humans, vapour is highly irritant to eyes, nose and respiratory passages (15).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA1535, TA1537 with and without metabolic activation positive (18).

Other effects

Other adverse effects (human)
Narcotic at high concentrations (15).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Organochlorine compounds: guide level 1 $\mu g\ l^{-1}$ (19).
Included in Schedule 6 (Release into Land: Prescribed Substances) of Statutory Instrument No. 472, 1991 (20).

Other comments

Found in water samples probably as an artifact in chemical analysis procedures (21).
Bis (2-chloroethyl) ether residues found in treated wastewater effluent of organic chemicals manufacturing, plastics industry, paint and ink formulation and synthetic rubber plants (1,22). Discontinued by Union Carbide for use as a soil fumigant (23).
Toxicity of bis(2-chloroethyl)ether reviewed (24).
Adverse health implications of bis(2-chloroethyl)ether and other compounds reported (25).
Human health effects and experimental toxicology reviewed (26,27).

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B121 1,3-bis(chloroethyl)-1-nitrosourea

$$Cl(CH_2)_2N(NO)CONH(CH_2)_2Cl$$

$C_5H_9Cl_2N_3O_2$ **Mol. Wt.** 214.05 **CAS Registry No.** 154-93-8

Synonyms 1,3-bis(β-chloroethyl)-1-nitrosourea; urea, *N,N'*-bis(2-chloroethyl)-*N*-nitroso-

EINECS No. 205-838-2 **RTECS No.** YS 2625000

Uses Anticancer drug.

Physical properties

M. Pt. 27-32°C

Solubility Water: 4 g l^{-1} at 18°C. Organic solvents: dimethyl sulfoxide, diethyl ether, ethanol

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse, rat 19, 20 mg kg^{-1}, respectively (1,2).
LD_{50} intravenous rat, mouse 13.8, 45 mg kg^{-1}, respectively (3,4).
LD_{50} intraperitoneal rat, mouse 17.42, 21.26 mg kg^{-1}, respectively (5).
LD_{Lo} parenteral woman 1566 mg kg^{-1} (6).

Sub-acute and sub-chronic data

LD_{Lo} (52 wk intermittently) intravenous child 78 mg kg^{-1} (7).
Treatment with 1,3-bis(chloroethyl)-1-nitrosourea can cause acute interstitial pneumonitis in children with rhabdomyosarcoma or brain tumour (dose unspecified). A review of lung damage is included (8).

Carcinogenicity and chronic effects

Limited evidence for carcinogenicity to humans, sufficient evidence for carcinogenicity in experimental animals, IARC classification group 2A (9).
Intravenous rat (2 yr) dose unspecified induced malignant lung tumours (10).
Skin painting of mouse (23 wk, dose unspecified) induced papilloma (11).

Teratogenicity and reproductive effects

Intravenous rat 0.25-1.5 mg kg^{-1} prior to breeding and during gestation decreased implantations and 1-4 mg kg^{-1} during organogenesis was teratogenic. Intravenous rabbit 0.5-4 mg kg^{-1} day^{-1} on days 6-18 of gestation caused weight loss and abortion; maximum dose increased mortality but was not teratogenic (12).

Metabolism and toxicokinetics

1,3-bis(chloroethyl)-1-nitrosourea is readily absorbed from the gastrointestinal tract. It is rapidly metabolised, $t_{1/2}$ <15 min, excreted in urine and exhaled as carbon dioxide (13).

Sensitive to oxidation and hydrolysis, forms alkylating and carbamoylating intermediates, $t_{1/2}$ 1 hr at neutral pH (14).

Genotoxicity

Salmonella typhimurium TA1535 with and without metabolic activation positive (15).

Escherichia coli multitest negative. Recombinogenic and SOS inducing (16).

Saccharomyces cerevisiae strain D5 mitotic crossing over and recombinogenic activity positive (17).

Saccharomyces cerevisiae diploid homozygous *rad18*, showed enhanced mutagenic and recombination potential (18).

Human lymphocytes (1 hr) induced sister chromatid exchange and chromosomal aberrations (19).

C6B3F1 mice single and repeated dose caused proliferation of bone marrow stem cells. DNA cross-linking and myelotoxicity (20).

Direct acting, bifunctional alkylating agent which induced chromosomal aberrations, micronuclei and sister chromatid exchanges in cells of mice treated *in vivo*. *In vitro* human cells, rodents, bacteria, caused DNA damage and mutation. Induced gene conversion in yeast and sex-linked recessive lethal mutations in *Drosophila melanogaster* (21).

Other effects

Other adverse effects (human)

Two cases of non-lymphoblastic leukaemia reported among 1628 patients treated with the drug for brain tumours. Considered leukaemogenic in humans (22,23).

In humans, systemic effects include nausea, vomiting, diarrhoea, dyspnoea, flushing of skin, oesophagitis, cytotoxic effect in liver, kidneys and central nervous system, leucopenia and thrombocytopenia (24).

Delayed and cumulative bone marrow depression has been reported in humans. A potentially fatal pulmonary toxin, serious risk occurs at cumulative doses of 1.2-1.5 g m^{-2} body $surface^{-1}$ (25).

Any other adverse effects

Rats given a single intraperitoneal injection of 20 mg kg^{-1} and sacrificed at day 14 showed decreased cytochrome P450, ethylmorphine *N*-demethylase activity and hepatic delta aminolevulinic acid synthetase activity. Produced cholestasis which preceded its effect on microsomal mixed-function oxygenase activity (26).

Single injection ♂ mice (unspecified dose) inhibited differential spermatogenesis and caused some stem cell death (27).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Organochlorine compounds: guide level 1 $\mu g\ l^{-1}$ (28).

Included in Schedule 6 (Release into Land: Prescribed Substances) of Statutory Instrument No. 472, 1991 (29).

Other comments

The pharmacokinetics of 1,3-bis(chloroethyl)-1-nitrosourea reviewed (30).

Antiviral, antibacterial and antifungal activity reported (31-33).

Can cross the blood/brain barrier (34).

Human health effects and experimental toxicology reviewed (35,36).

Very soluble in lipids. Store between 2-8°C, above 27°C the drug liquefies and decomposes.

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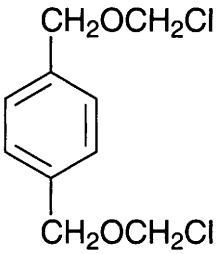
B122 bis-1,4-(chloromethoxy)-*p*-xylene



$C_{10}H_{12}Cl_2O_2$ **Mol. Wt.** 235.11 **CAS Registry No.** 56894-91-8

Synonyms 1,4-bis(chloromethoxymethyl)benzene; benzene, 1,4-bis[(chloromethoxy)methyl]-; terephthalyl alcohol bis(chloromethyl) ether

RTECS No. CY 8420000

Uses In the preparation of ion-exchange resins.

Mammalian & avian toxicity

Carcinogenicity and chronic effects

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

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Organochlorine compounds: guide level 1 $\mu g\ l^{-1}$ (2).

Included in Schedule 6 (Release into Land: Prescribed Substances) of Statutory Instrument No. 472, 1991 (3).

Other comments

Experimental toxicology, human health and environmental effects are reviewed (4,5).

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B123 bis(chloromethyl) ether

$$(ClCH_2)_2O$$

$C_2H_4Cl_2O$ **Mol. Wt.** 114.96 **CAS Registry No.** 542-88-1

Synonyms *sym*-dichloromethyl ether; chloromethyl ether; dichlorodimethyl ether; monochloromethyl ether; oxybis[chloromethane]; α,α'-dichlorodimethyl ether

EINECS No. 208-832-8 **RTECS No.** KN 1575000

Uses Formerly used as an alkylating agent in organic synthesis, but now more commonly found as a contaminant (1-8%) in chloromethyl methyl ether.

Physical properties

M. Pt. –41.5°C **B. Pt.** 105°C **Flash point** <19°C **Specific gravity** 1.315 at 20°C

Volatility v.p. 30 mmHg at 22°C ; v.den. 4.0

Solubility Organic solvents: benzene, diethyl ether, ethanol

Occupational exposure

FR-VME 0.001 ppm (0.005 mg m^{-3})

UK-LTEL MEL 0.001 ppm (0.005 mg m^{-3})

US-TWA 0.001 ppm (0.0047 mg m^{-3})

Supply classification very toxic

Risk phrases May cause cancer – Flammable – Harmful if swallowed – Toxic in contact with skin – Very toxic by inhalation (R45, R10, R22, R24, R26)

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

Hydrolysis $t_{1/2}$ is sufficiently fast to preclude any possibility of bioconcentration in the food chain. Reported bioconcentration factor for bluegill sunfish 11 (1).

Environmental fate

Degradation studies

The fate of chloromethyl ether in soil is unknown. However, due to its rapid hydrolysis it would be expected to disappear rapidly from moist soil (2).

Abiotic removal

Rapid hydrolysis $t_{1/2}$ 10-38 sec (3).
Hydrolysis $t_{1/2}$; in humid air >25 hr (3).
Degradation reaction with photochemically produced hydroxyl radicals, $t_{1/2}$ >4.1 days (2).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 210 mg kg^{-1} (4).
Lowest lethal concentration for humans (3 min) 100 ppm (5).
LC_{50} (7 hr) inhalation rat, hamster 7 ppm (6).
LC_{50} (6 hr) inhalation mouse 25 mg m^{-3} (7).
LD_{50} dermal rabbit 280 mg kg^{-1} (4).

Carcinogenicity and chronic effects

Sufficient evidence for carcinogenicity to humans and animals, IARC classification group 1 (8).
Induces tumours in lung and nasal cavity of test animals (9).
Induces tumours in the lungs of humans (9).
Dermal Charles River CD1 mice single topical application 1034 μg l^{-1} and 2068 μg l^{-1}, followed 1 wk later by 2 applications of 0.25% croton oil wkly for the duration of the experiment, resulted in 0.4 and 0.9 papilloma, respectively, per mouse, at 15 wk (10).
Subcutaneous implantation into dorso-lumbar region of two-month-old Alderley Park Swiss mice. Mice were killed after three months. Malignant tumour observed at the implant site, with cells infiltrating and replacing surrounding tissue (11).
Inhalation mice (27 wk) 0.005 mg l^{-1} 6 hr day^{-1} 5 day wk^{-1} (total number of exposures 82) induced lung tumours (12).

Irritancy

Strong skin and eye irritant (13).

Genotoxicity

Salmonella typhimurium TA100 with metabolic activation positive; TA98, TA1535, TA1538 with metabolic activation negative (11).
Salmonella typhimurium TA1535 without metabolic activation positive (14).
Induced unscheduled DNA synthesis in human fibroblasts with metabolic activation *in vitro* (15).
Did not induce chromosome aberrations in bone marrow of rats treated *in vivo* (16).
A slight increase in chromosomal aberrations observed in peripheral lymphocytes of exposed workers (17).

Other effects

Other adverse effects (human)

A study on a small group of workers exposed to chloromethyl ether between 1956 and 1962 revealed six cases of lung cancer (18).

Reports from five countries cite 117 respiratory cancer deaths in 3024 exposed workers (19).

Respiratory tract cancer mortality was significantly greater in 737 exposed workers than in 1210 unexposed (32 observed versus 11.5 expected). There was a clear dose-response relationship, with risk elevated >10-fold at the highest doses. A latency period of 10-19 yr was reported (20).

Excess lung cancer mortality reported in dyestuff factories using chloromethyl ether; 13 cases of lung cancer occurred in a group of 35 exposed workers with a mean latency of 87 (but as low as 23) months (21).

Legislation

Covered in the UK by the Control of Carcinogenic substances, Control of Substances Hazardous to Health Regulations, 1988 (22).

Included in Schedule 6 (Release into Land: Prescribed Substances) of Statutory Instrument No. 472, 1991 (23).

Other comments

Physicochemical properties, industrial applications and carcinogenicity reviewed (24).

Reviews on human health effects, experimental toxicology, physico-chemical properties and environmental effects listed (25).

Toxicology and carcinogenicity reviewed (12,26,27).

Carcinogenicity in relation to Occupational exposure standards reviewed (28).

Reports of the spontaneous formation of chloromethyl ether in air from the reaction of formaldehyde and hydrogen chloride in textile plants have been contested (1).

Possibly present in exhaust gases from factories where it was used as a chemical intermediate; however, it would not be expected to occur in waste water effluent discharges (2).

Hydrolyses rapidly in water to hydrochloric acid and formaldehyde.

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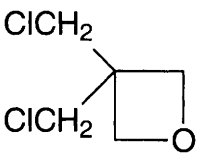
B124 3,3-bis(chloromethyl)oxetane



$C_5H_8Cl_2O$ **Mol. Wt.** 155.02 **CAS Registry No.** 78-71-7

Synonyms 3,3-dichloromethyloxacyclobutane

EINECS No. 201-136-5 **RTECS No.** RQ 6826000

Physical properties

M. Pt. 18-19°C **B. Pt.** 200°C **Specific gravity** 1.4

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse 420 mg kg^{-1} (1).

LC_{50} (2 hr) inhalation mouse 200 mg m^{-3} (1).

References

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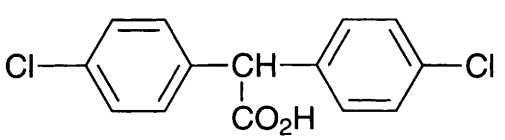
B125 bis(4-chlorophenyl)acetic acid



$C_{14}H_{10}Cl_2O_2$ **Mol. Wt.** 281.14 **CAS Registry No.** 83-05-6

Synonyms bis(*p*-chorophenyl)acetic acid; dichlorodiphenylacetic acid; *p,p'*-dichlorodiphenylacetic acid; 4-chloro-α-(4-chlorophenyl)benzeneacetic acid

EINECS No. 201-451-8 **RTECS No.** AF 5475000

Occurrence Metabolite of DDT.

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse 590 mg kg^{-1} (1).

Metabolism and toxicokinetics

Compound is a major urinary metabolite of DDT. In 11 human volunteers with no known exposure to DDT the levels of bis(*p*-chlorophenyl)acetic acid ranged from 0.025-0.120 μg ml^{-1} of urine (2).

Genotoxicity

Drosophila melanogaster sex chromosome loss and non-disjunction positive (3).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Organochlorine compounds: guide level 1 μg l^{-1} (4).

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

Other comments

Reviews on human health effects and experimental toxicology listed (6).

References

1. *Archives Internationales Pharmacodynamie Therapie* 1946, **73**, 128.
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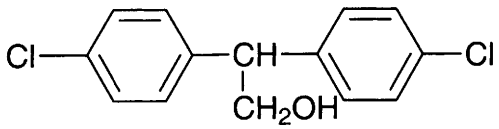
6. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

B126 2,2-bis(4-chlorophenyl)ethanol



$C_{14}H_{12}Cl_2O$ **Mol. Wt.** 267.15 **CAS Registry No.** 2642-82-2

Synonyms benzeneethanol, 4-chloro-β-(4-chlorophenyl)-; 2,2-bis(*p*-chlorophenyl)ethanol; 2,2-bis(4-chlorophenyl)-1-hydroxyethane

EINECS No. 220-148-1 **RTECS No.** DA 0470000

Occurrence Metabolite of DDT (1).

Physical properties

M. Pt. 100-102°C

Mammalian & avian toxicity

Metabolism and toxicokinetics

Metabolite of DDT; detoxified in rat kidney (2,3).

Genotoxicity

Salmonella typhimurium TA98, TA100 with and without metabolic activation negative (4).
Drosophila melanogaster genotoxicity research into sex-linked lethal mutations inconclusive (5).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Organochlorine compounds: guide level 1 $\mu g\ l^{-1}$ (6).
Included in Schedule 6 (Release into Land: Prescribed Substances) of Statutory Instrument No. 472, 1991 (7).

Other comments

Details of DDT metabolism and effects on the environment reported (8,9).
Reviews on human health effects and experimental toxicology listed (10).

References

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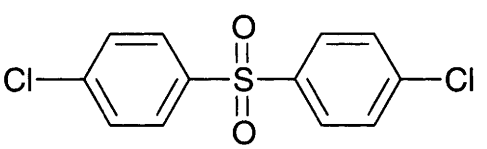
B127 bis(4-chlorophenyl) sulfone



$C_{12}H_8Cl_2O_2S$ **Mol. Wt.** 287.17 **CAS Registry No.** 80-07-9

Synonyms 4-chlorophenyl sulfone; 1,1'-sulfonylbis(4-chlorobenzene); 4,4'-dichlorodiphenyl sulfone; 4-chloro-1-(4-chlorophenylsulfonyl)benzene; *p*-chlorophenyl sulfone; di-*p*-chlorophenyl sulfone

EINECS No. 201-247-9 **RTECS No.** WR 3450000

Physical properties

M. Pt. 145-148°C **B. Pt.** 250°C at 10 mmHg
Solubility Water: <1 mg ml^{-1} at 20°C. Organic solvents: acetone, DMSO

Mammalian & avian toxicity

Acute data
LD_{50} oral mouse 24 g kg^{-1} (1).

Metabolism and toxicokinetics
Rapidly absorbed in the rat following gavage dosing, with a biphasic diminution of blood level. Evidence found that clearance is primarily via the urine, in a dose-dependent manner, conjugated as water-soluble metabolites (1). Readily absorbed from the gastrointestinal tract in rats and distributed to all tissues examined. Concentrated in the adipose tissues. Intravenous administration of 10 mg kg^{-1} [^{14}C]bis(4-chlorophenyl) sulfone to rats resulted in increasing accumulation of radiolabel in adipose tissues for up to 24 hr followed by slow elimination with $t_{1/2}$ ~12 days. Repeat oral dosing at 10 mg kg^{-1} resulted in a steady-state concentration in the adipose tissues of 265 μg g^{-1} tissue after ~2 wk. Bis(4-chlorophenyl) sulfone-derived radioactivity was excreted primarily in faeces and to a lesser extent in urine as a phenolic metabolite and its glucuronide. The aglycon of this glucuronide was identified as 3-hydroxy-4,4'-dichlorodiphenyl sulfone (2).

Irritancy
May cause irritation in humans (3).

Other effects

Other adverse effects (human)
May be harmful by ingestion or inhalation (3).

Any other adverse effects
Hepatomegaly was observed in sub-chronic studies on rats (4)

Legislation

Included in Schedule 6 (Release into Land: Prescribed Substances) of Statutory Instrument No. 272, 1991 (5).

Other comments

Decreased hexobarbital sleep times were observed in rats administered a 3-day oral treatment with 50 mg kg^{-1}, suggesting induction of hepatic microsomal enzymes (4).

References

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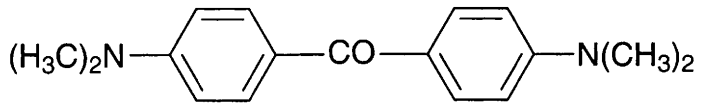
B128 4,4′-bis(dimethylamino)benzophenone



$C_{17}H_{20}N_2O$ **Mol. Wt.** 268.36 **CAS Registry No.** 90-94-8

Synonyms bis-[4-(dimethylamino)phenyl]methanone; Michler's ketone; di-*p*-dimethylaminophenyl ketone; *p,p'*-bis(*N,N*-dimethylamino)benzophenone; NCI-C02006; tetramethyldiaminobenzophenone

EINECS No. 202-027-5 **RTECS No.** DJ 0250000

Uses Manufacture of dyestuffs and photosensitiser.

Physical properties

M. Pt. 172°C **B. Pt.** >360°C (decomp.)
Solubility Water: 0.4 g l^{-1} 20-25°C. Organic solvents: ethanol, quinoline, pyridine

Ecotoxicity

Bioaccumulation
Non-accumulative or low accumulative (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral redwing blackbird 100 mg kg^{-1} (2).

Carcinogenicity and chronic effects
Oral rat, mouse (2 yr) 250-1000 ppm and 1250-2500 ppm, respectively, induced hepatocellular carcinomas and hemangiosarcomas (3).
Positive correlation between rats fed 4,4′-bis(dimethylamino)benzophenone and hepatocarcinogenic effects in food in rats and binding of metabolites to liver DNA and RNA (4).
National Toxicology Program evaluation of 4,4-bis(dimethylamine)benzene rat and mouse in feed positive (5).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537, TA1538 with and without metabolic activation negative (6).
Escherichia coli PQ37 SOS chromotest negative (7).
In vitro rat hepatocyte DNA repair test positive (5).
In vitro Chinese hamster fibroblasts chromosome damage positive (8).

Other comments

Contaminant in drinking water (9).
Reviews on human health effects and experimental toxicology listed (10).

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4. Scribner, J. D. et al *Cancer Lett. (Shannon, Irel.)* 1980, **9**(2), 117-121.
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8. Lafi, A. et al *Mutagenesis* 1986, **1**(1), 17-20.
9. Noordsij, A. et al *Sci. Total Environ.* 1985 **47**, 273-292.
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B129 bis(2-hexyloxyethyl) adipate

$$[CH_3(CH_2)_5OCH_2CH_2OC(O)CH_2CH_2]_2$$

$C_{22}H_{42}O_6$ **Mol. Wt.** 402.57 **CAS Registry No.** 110-32-7

Synonyms di(2-hexyloxyethyl) adipate; adipic acid, bis(2-hexyloxyethyl) ester

RTECS No. AU 9800000

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 4290 mg kg^{-1} (1).

LD_{50} dermal rabbit 12,310 mg kg^{-1} (1).

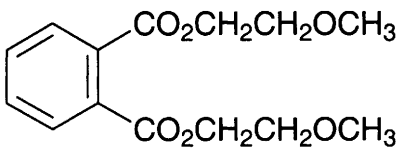
Irritancy

Dermal rabbit (24 hr) 500 mg produced mild effect. 500 mg instilled into rabbit eye for 24 hr produced mild effect (2).

References

1. *AMA Arch. Ind. Hyg. Occup. Med.* 1954, **10**, 61.
2. Marhold, J. V. *Prehled Prumyslove Toxikologie: Organicke Latky* 1986, 717, Prague, Czechoslovakia

B130 bis(2-methoxyethyl) phthalate



$C_{14}H_{18}O_6$ **Mol. Wt.** 282.29 **CAS Registry No.** 117-82-8

Synonyms 1,2-benzenedicarboxylic acid, bis(2-methoxyethyl) ester

EINECS No. 204-212-6 **RTECS No.** TI 1400000

Uses Plasticiser in polyvinyl chloride.

Physical properties

M. Pt. –40°C **B. Pt.** 190-210°C at 4 mmHg **Specific gravity** 1.171 at 20°C with respect to water at 20°C
Volatility v.p. 0.3 mmHg at 150°C; 0.01 mmHg at 20°C
Solubility Water: 0.8% at 20°C. Organic solvents: ethanol

Occupational exposure

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

Supply classification toxic

Risk phrases May cause harm to the unborn child – Possible risk of impaired fertility (R61, R62)

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

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse 3200 mg kg^{-1} (1).

LD_{50} oral guinea pig 1600 mg kg^{-1} (1).

LD_{50} intraperitoneal rat 3740 mg kg^{-1} (2).

LD_{50} intraperitoneal mouse 2510 mg kg^{-1} (3).

LD_{50} dermal guinea pig 10 g kg^{-1} (4).

Teratogenicity and reproductive effects

Intraperitoneal administration to rats of doses up to one-third the LD_{50} induced dose-related skeletal and gross abnormalities in foetuses (2).

Affected the central nervous system of developing chick embryos. After hatching, tremor, non-purposeful movement and inability to stand or walk normally were observed (5).

Metabolism and toxicokinetics

Rapidly metabolised to the monoester both in the intestine and following absorption (6).

Irritancy

Dermal guinea pig (duration unspecified) 500 mg produced mild effect. 100 mg instilled into rabbit eye produced mild effect (7).

Genotoxicity

Dominant lethal mutagenic assay in mice positive (8).

Other comments

May leach out of pvc plastics.

References

1. Patty, F. A. (Ed.) *Industrial Hygiene and Toxicology* 2nd ed., 1963, **2**, 1904, John Wiley, New York, NY, USA.
2. Singh, A. R. et al *J. Pharm. Sci.* 1972, **61**, 51.
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5. Bower, R. K. et al *J. Pharmacol. Exp. Ther.* 1970, **171**(2), 314-324.
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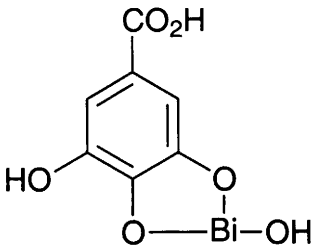
B131 bismuth subgallate



$C_7H_5BiO_6$ **Mol. Wt.** 394.09 **CAS Registry No.** 99-26-3

Synonyms bismuth gallate, basic; gallic acid bismuth basic salt; bismuth oxygallate; 2,7-dihydroxy-1,3,2-benzodioxabismole-5-carboxylic acid

EINECS No. 202-742-2

Uses Astringent. Antacid. Suppository in the treatment of haemorrhoids. Used as a treatment for gastrointestinal disorders.

Physical properties

M. Pt. 100°C (decomp.)

Ecotoxicity

Bioaccumulation

Predicted concentration for the River Lee, UK, 0.15 μg l^{-1} (1).

Other effects

Other adverse effects (human)

Can reduce clotting time of whole blood (2).

Systemic effects include ulcerative stomatitis, anorexia, headache, kidney tubule damage and mild jaundice (3).

Other comments

Major active ingredient of Bungast (4).

Has an inhibitory effect on *Campylobacter pylori* (5).

Combined with gallic acid is used as a dusting powder in dermatology (6).

Thermolabile compound (7).

References

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B132 bismuth telluride

Bi_2Te_3

Bi_2Te_3 **Mol. Wt.** 800.76 **CAS Registry No.** 1304-82-1

Synonyms bismuth sesquitelluride; tellurobismuthite; bismuth tritelluride; dibismuth tritelluride

EINECS No. 215-135-2 **RTECS No.** EB 3110000

Uses In electronics as semiconductor and for thermoelectric cooling. Power generation applications.

Physical properties

M. Pt. 585°C **Specific gravity** 7.7 at 20°C

Occupational exposure

FR-VME 10 mg m^{-3}, selenium-doped 5 mg m^{-3}
SE-LEVL 0.1 mg m^{-3} (as Te)
UK-LTEL 10 mg m^{-3}; 5 mg m^{-3} (selenium doped) **UK-STEL** 20 mg m^{-3}; 10 mg m^{-3} (selenium doped)
US-TWA 10 mg m^{-3} (undoped); 5 mg m^{-3} (Se-doped)

UN No. 3284 **HAZCHEM Code** 2X **Conveyance classification** toxic substance

Other effects

Other adverse effects (human)

Symptoms of poisoning include vomiting, reduced appetite, insomnia, unconsciousness, liver and kidney damage (1).

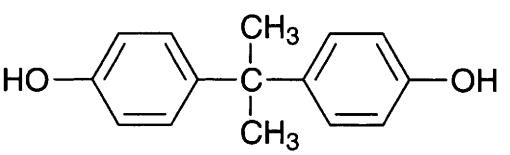
Other comments

Reveiw on human health effects, experimental toxicology and workplace experience listed (2).

References

1. *Chemical Safety Data Sheets* 1989, **2**, 110-112, The Royal Society of Chemistry, London, UK.
2. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

B133 bisphenol A



$C_{15}H_{16}O_2$ **Mol. Wt.** 228.29 **CAS Registry No.** 80-05-7

Synonyms 4,4'-isopropylidenediphenol; 4,4'-(1-methylethylidene)bisphenol; *p,p'*-dihydroxydiphenylpropane; diphenylolpropane

EINECS No. 201-245-8 **RTECS No.** SL 6300000

Uses Fungicide. Manufacture of epoxy resins and polycarbonates.

Physical properties

M. Pt. 158-159°C (99+% purity) **B. Pt.** 220°C at 4 mmHg **Partition coefficient** log P_{ow} 3.32
Solubility Water: 120 mg l^{-1}. Organic solvents: acetone, ethanol

Occupational exposure

DE-MAK 5 mg m^{-3} (inhalable fraction of aerosol)
Supply classification irritant
Risk phrases Irritating to eyes, respiratory system and skin – May cause sensitisation by skin contact (R36/37/38, R43)
Safety phrases Keep out of reach of children (if sold to general public) – Avoid contact with the skin – In case of contact with eyes, rinse immediately with plenty of water and seek medical advice – Wear suitable gloves (S2, S24, S26, S37)

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) fathead minnow 4.7 mg l^{-1} static test and 4.6 mg l^{-1} flow through test (1).
LC_{50} (96 hr) Atlantic silverside 9.4 mg l^{-1} (1).

Invertebrate toxicity
EC_{50} (96 hr) *Selenastrum capricornutum* 2.7 mg l^{-1} (1).
EC_{50} (96 hr) *Skeletonema costatum* 1.0 mg l^{-1} (1).
LC_{50} (96 hr) *Mysidopsis bahia* 1.1 mg l^{-1} (1).
EC_{50} (48 hr) *Daphnia magna* 10 mg l^{-1} (1).

Bioaccumulation
Bioconcentration factors of 42 and 196 were estimated, based on the water solubility and log K_{ow}, respectively (2).

Environmental fate

Nitrification inhibition
At 50 mg l^{-1} does not inhibit nitrification (activated sludge) (3).

Degradation studies
Acclimated activated sludge innocula, 72% COD removal in 24 hr, initial concentration 105 mg l^{-1} (4).
Acclimated activated sludge, 72% COD and 57% TOC removal in 24 hr, initial concentration 58 mg l^{-1} (5).
Rapidly biodegraded in acclimated wastewater treatment plants and receiving waters ($t_{1/2}$ 2.5 to 4 days) (6).

Abiotic removal
The $t_{1/2}$ for bisphenol A vapour reacting with photochemically generated hydroxyl radicals is estimated as 4 hr (7).
It is not expected to undergo chemical hydrolysis under environmental conditions, since it contains no hydrolysable functional groups (2).
Photodecomposition products of the vapour are phenol; 4-isopropylphenol; and a semiquinone derivative (8).

Adsorption and retention
Estimated soil adsorption coefficients of 314 and 1524 indicate moderate to low mobility in soil and moderate to extensive mobility in suspended solids (2,9).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 3250 mg kg^{-1} (10).
LD_{50} oral mouse 2500 mg kg^{-1} (10).
LD_{50} oral rabbit 2230 mg kg^{-1} (10).
LC_{50} inhalation rat 200 ppm (duration unspecified) (11).
LD_{50} dermal rabbit 3000 mg kg^{-1} (12).

Sub-acute and sub-chronic data
Oral ♂ or ♀ mice (14 day) 0.0, 0.31, 0.62, 1.25, 2.5 and 5.0%. No clinical signs of toxicity were observed in either ♂ or ♀ (13).

Carcinogenicity and chronic effects
Oral feed ♂ or ♀ rats and mice (103 wk) 2000-10,000 ppm. ♂ rat equivocal, ♀ rat, ♂ and ♀ mice negative. Tumour site was in the haematopoietic system (14-16).

Teratogenicity and reproductive effects
Oral administration to ♀ mice of 2 ng g^{-1} day^{-1} during gestation days 11-17 resulted in a permanent increase in size of preputial glands, but reduced size of epididymes in ♂ offspring. 20 ng doses for the same period resulted in ♂ offspring with significantly decreased efficiency of sperm production, lower by 20%, relative to control ♂s (17).
Pregnant mice were fed bisphenol A at 2 and 20 μg kg^{-1} day^{-1} on days 13-19 of pregnancy. Increased prostate weights were seen in ♂ offspring at 6-8 months after exposure. The lower dose is within the reported range of some current human exposures (18). CD rats (6-15 day gestation) 0, 160, 320 or 640 mg kg^{-1} day^{-1}, CD-1 mice (6-15 day gestation) 0, 500, 750, 1000 or 1250 mg kg^{-1} day^{-1}. In rats gravid uterine weight and average foetal body weight $litter^{-1}$ was not affected, no increase in percentage resorptions $litter^{-1}$ or percentage foetuses malformed $litter^{-1}$. In mice, there was a reduction in gravid uterine weight and average foetal body weight and increase in the percentage of resorptions per litter with 1250 mg kg^{-1} day^{-1} dose. No alteration in the incidence of malformations was observed in mice (19).
Treatment of ovariectomised rats (route unspecified) with single high doses, from 37.5-150 mg kg^{-1}, caused cell proliferation in the uterus and vagina in a dose-dependent manner (20).

Irritancy
Dermal (duration unspecified) rabbit 250 mg, exposed to atmosphere, caused mild irritation and 20 mg instilled into rabbit eye (24 hr) caused severe irritation (21,22).

Sensitisation
Reported induction of contact and allergic dermatitis and sensitisation in humans (23).
Dermal mice, photoallergic contact dermatitis was induced; sites of photochallenge reactions flared when tested with UVA. Attempts to induce photoallergy in guinea pigs failed (24).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA97/TA1537 with and without metabolic activation negative (15,25).
In vitro mouse lymphoma L5178Y cells with and without metabolic activation negative (26).
In vitro Chinese hamster ovary cells, sister chromatid exchange with and without metabolic activation, negative (27).
In vitro Chinese hamster ovary cells, chromosomal aberration assays, with or without metabolic activation, negative (27).
In vivo human leukocytes chromosomal aberrations positive in occupationally exposed workers (28).

Other effects

Any other adverse effects
Bisphenol A (250 μmol kg^{-1}) administered intramuscularly to white leghorn roosters had antioestrogenic activity as measured by its effect on oestrogen-regulated mRNA stabilising factor. Even at higher concentrations (876 μmol kg^{-1}) bisphenol A did not have oestrogen agonist activity (29).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Phenol compounds: maximum admissible concentration 0.5 C_6H_5OH mg l^{-1}, excluding natural phenols which do not react to chlorine (30).
Included in Schedule 6 (Release into Land: Prescribed Substances) Statutory Instrument No. 472, 1991 (31).
The log P_{ow} value exceeds the European Community recommended level 3.0 (6th and 7th amendments) (32).

Other comments

Suspected environmental endocrine disruptor (33).
A constituent leached from polycarbonate flasks during autoclaving, bisphenol A has been shown to be oestrogenic in *in vivo* tests (34).
Reviews on experimental toxicology, human health effects and exposure listed (35).
Toxicity reviewed (36).
Environmental fate, effects, and exposures of bisphenol A reviewed (6).

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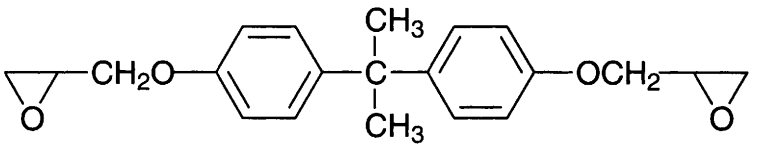
B134 bisphenyl A diglycidyl ether



$C_{21}H_{24}O_4$ **Mol. Wt.** 340.42 **CAS Registry No.** 1675-54-3

Synonyms bisphenol A diglycidyl ether; 2,2'-[(1-methylethylidene)bis(4,1-phenyleneoxymethylene)]bisoxirane]; diphenylolpropane glycidyl ether; 4,4'-isopropylidenediphenol diglycidyl ether

EINECS No. 216-823-5 **RTECS No.** TX 3800000

Uses Manufacture of adhesives and epoxy resins. Photopolymers as a co-polymer and cross-linking agent. Plasticiser for vinyl polymers.

Physical properties

M. Pt. 43°C

Occupational exposure

Supply classification irritant
Risk phrases Irritating to eyes and skin – May cause sensitisation by skin contact (R36/38, R43)
Safety phrases Keep out of reach of children (if sold to general public) – After contact with skin, wash immediately with plenty of water – Wear suitable gloves and eye/face protection (S2, S28, S37/39)

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 11 g kg^{-1} (1).

Carcinogenicity and chronic effects
No adequate data for carcinogenicity to humans, limited evidence for carcinogenicity in experimental animals, IARC classification group 3 (2).
Total dose (2 yr, intermittent) dermal mouse 16.4 g kg^{-1} induced tumours of lymphatic system and kidney adenomas. 0.2 ml of a 1 or 10% (w/v) solution applied in acetone to skin of ♂ and ♀ mice 2 × wk^{-1} for 1 yr. Mild irritation, very low incidence of benign and malignant skin tumours. Increased incidence of lymphoreticular/haematopoietic tumours in ♀ mice (3,4).

Teratogenicity and reproductive effects
Applied daily to skin of rabbits for 6 hr day^{-1} at 0, 30, 100 or 300 mg kg^{-1} day^{-1} on days 6 to 18 of pregnancy. 300 and 100 mg kg^{-1} doses were maternally toxic, but there was no embryo/foetal toxicity or teratogenicity (5).

Metabolism and toxicokinetics
Dermal mouse (3 day): 56 mg kg^{-1} 20% eliminated in faeces, 3% in urine, 66% recovered from application site.
Oral ♂ mice (3 day): 55 mg kg^{-1} 80% in faeces, 11% in urine (6).

Sensitisation
Conclusive allergen in guinea pig, sensitises 80-100% of animals challenged (7).
Skin of humans gave positive reaction in 3 out of 12 men tested; 1% w/w causes rashes of eyelids, face, forearms and hands (8).

Genotoxicity

Salmonella typhimurium TA100 with and without metabolic activation positive (9,10).
Escherichia coli with and without metabolic activation positive (11).

Other comments

Found in drinking water from pipes sealed with its resins and polymers (12,13).
Reviews on human health effects and experimental toxicology listed (14).

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B135 *trans*-1,2-bis(propylsulfonyl)ethylene

$$CH_3(CH_2)_2S(O)_2CH{=}CHS(O)_2(CH_2)_2CH_3$$

$C_8H_{16}O_4S_2$ **Mol. Wt.** 240.34 **CAS Registry No.** 1113-14-0

Synonyms propane, 1,1-[1,2-ethenediylbis(sulfonyl)]bis-*E*-; *trans*-1,2-bis-(*n*-propylsulfonyl)ethylene

EINECS No. 214-200-2 **RTECS No.** KU 8085000

Uses Fungicide.

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 200 mg kg^{-1} (1).
LD_{50} intraperitoneal rat 11,500 μg kg^{-1} (2).
LD_{Lo} intraperitoneal guinea pig 11,500 mg kg^{-1} (2).

Sub-acute and sub-chronic data

LC_{50} (8 day) Japanese quail (14-day-old) >5000 ppm in food, based on active ingredient (3).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides and related products: maximum admissible concentration 0.1μg l^{-1} (4).
Included in Schedule 6 (Release into Land: Prescribed Substances) of Statutory Instrument No. 472, 1991 (5).

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B136 bis(2,3,3,3-tetrachloropropyl) ether

$$(Cl_3CCHClCH_2)_2O$$

$C_6H_6Cl_8O$ **Mol. Wt.** 377.73 **CAS Registry No.** 127-90-2

Synonyms octachlorodipropyl ether; 1,1'-oxybis[2,3,3,3-tetrachloropropane]

EINECS No. 204-870-4 **RTECS No.** KN 3600000

Uses Lubricant additive. Insect repellent. Synergist for DDT, carbamates, pyrethrin and organophosphorus insecticides.

Physical properties

B. Pt. 296-298°C **Flash point** 177°C **Specific gravity** 1.65

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) guppy 1.7 mg l^{-1} (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral rabbit 2500-3630 mg kg^{-1} (2,3).

LD_{50} oral rat (24 h, 8 day) 8, 2.5 ml kg^{-1}, respectively (4).

LD_{50} oral mouse (24 h, 8 day) 12, 3.5 ml kg^{-1}, respectively (4).

Sub-acute and sub-chronic data

Rats fed 400-2500 mg kg^{-1} in diet for 13 wk showed increase in absolute weight of liver, kidney and thyroid (♂), and hypophysis (♀) (5).

ED oral rat 10-60 mg kg^{-1} via feed increased kidney weight (5).

ED oral rat 3200-7812 mg kg^{-1} disturbed circulatory system (6).

ED (28 day) oral rat 30-3000 mg kg^{-1} liver and kidney degeneration (6).

Metabolism and toxicokinetics

Oral rat (24 hr) 37.8 mg kg^{-1} formed 0.014-0.018% trichloroacrylic acid in urine (7).

Other effects

Other adverse effects (human)

Found as a residue in human milk (0.5 ppb in women) (~14 ppb fat-milk basis) or 1.5 ppb in 9712 women (~32 ppb fat-milk basis) (1).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Organochlorine compounds: guide level 1 $\mu g\ l^{-1}$ (8).
Included in Schedule 6 (Release into Land: Prescribed Substances) of Statutory Instrument No. 472, 1991 (9).

Other comments

Toxicity reviewed (10).

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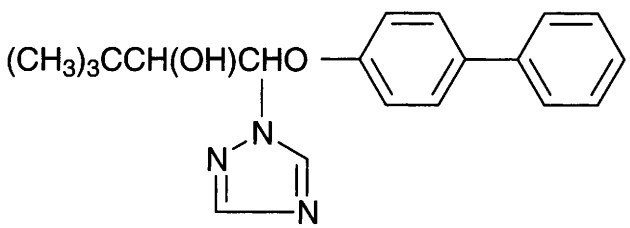
B137 bitertanol



$C_{20}H_{23}N_3O_2$ **Mol. Wt.** 337.42 **CAS Registry No.** 55179-31-2

Synonyms Baycor; 1-(4-biphenyloxy)-3,3-dimethyl-1-(1*H*-1,2,4-triazol-1-yl)butan-2-ol [20:80 ratio of (1*RS*,2*RS* and (1*RS*,2*SR*) isomers; β-[(1,1′-biphenyl)-4-yloxy]-α-(1-1-dimethylethyl)-1*H*-1,2,4-triazole-1-ethanol; Baycoral; Baykor; Compo Rosen-Spray; Delros; Zaron

EINECS No. 259-513-5 **RTECS No.** XZ 4803050

Uses Fungicide. Steroid demethylation inhibitor.

Physical properties

M. Pt. 136.7°C (diastereomer A); 145.2°C (diastereomer B); 118°C (eutectic of A and B)
Volatility v.p. 2.857×10^{-5} mmHg at 100°C (diastereomer A), 2.406×10^{-5} mmHg at 100°C (diastereomer B)
Solubility Water: 2.9 mg l^{-1} (A), 1.6 mg l^{-1} (B), 5 mg l^{-1} (A + B). Organic solvents: cyclohexanone, isopropanol, methylene chloride, toluene.

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) rainbow trout 2.2-2.7 mg l^{-1} (1).
LC_{50} (48 hr) carp 2.5 mg l^{-1} (2).

Invertebrate toxicity

Non-toxic to bees (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat >5000 mg kg^{-1} (technical grade) (1).
LC_{50} (4 hr) inhalation rat >0.55 mg l^{-1} air (aerosol) (2).
LC_{50} (4 hr) inhalation rat >1.2 mg l^{-1} air (dust) (2).
LD_{50} dermal rat >5000 mg kg^{-1} (technical grade) (1).

Carcinogenicity and chronic effects

In 2-yr feeding trials the no-effect level for rats was 100 mg kg^{-1} in diet (2).

Other effects

Other adverse effects (human)

A study of 55 people working with bitertanol was undertaken. From the results no conclusions could be drawn regarding the effects on workers' health (3).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides and related products: maximum admissible concentration 0.1 μg l^{-1} (4).
Included in Schedule 6 (Release into Land: Prescribed Substances) of Statutory Instrument No. 472, 1991 (5).

Other comments

Calculated allowable daily intake for humans 0.01 mg kg^{-1} (2).

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B138 bitoscanate

$C_8H_4N_2S_2$ **Mol. Wt.** 192.27 **CAS Registry No.** 4044-65-9

Synonyms benzene, 1,4-diisothiocyanato-; Biscomate; isothiocyanic acid, *p*-phenylene ester; 1,4-phenylenediisothiocyanic acid; phenylene thiocyanate; WM 842

EINECS No. 223-741-3 **RTECS No.** NX 9150000

Uses Anthelmintic used in the treatment of hookworm.

Physical properties

M. Pt. 132°C

Ecotoxicity

Invertebrate toxicity

EC_{50} (30 min) *Photobacterium phosphoreum* 0.0179 mg l^{-1} Microtox test (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 21 mg kg^{-1}(2).

LD_{50} intraperitoneal mouse 21 mg kg^{-1}(3).

TD_{Lo} oral human 3 mg kg^{-1} reported central nervous system and gastrointestinal tract effects (2).

Metabolism and toxicokinetics

After oral administration to dogs, renal elimination and fall-off of blood concentrations were biphasic. Similar results were obtained in humans except that urinary excretion was more delayed and more was excreted renally. Excretion was mostly complete in 5 days from both species, but excretion of the remainder was protracted. After 3 wk, the dogs had excreted 80% in the faeces and 12% in urine, and after 5 wk, humans had excreted 55% and 28%, respectively, by these routes; 3% still circulated in blood. Foetuses contained 3% of the dose 16 hr after administration to a pregnant dog (4).

Bitoscanate is partly absorbed from the gastrointestinal tract and slowly excreted (5).

Other effects

Other adverse effects (human)

Can cause gastrointestinal disturbance and dizziness (5).

Ingestion causes hallucinations and nausea (6).

Other comments

5 mg ml^{-1} in ethylene glycol showed inhibition against western equine encephalomyelitis viruses (7). Reacts with albumin and red blood cells (3).

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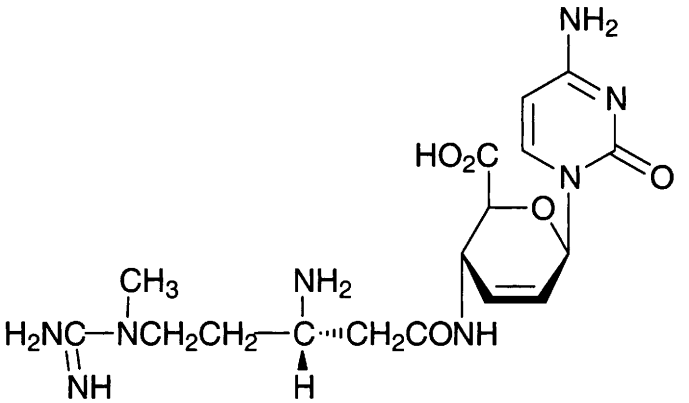
B139 blasticidin-S



$C_{17}H_{26}N_8O_5$ **Mol. Wt.** 422.44 **CAS Registry No.** 2079-00-7

Synonyms 4-[[3-amino-5-[(aminoiminomethyl)methylamino]-1-oxopentyl]amino]-1-(4-amino-2-oxo-1(2*H*)-pyrimidinyl)-1,2,3,4-tetradeoxy-β-D-*erythro*-hex-2-enopyranuronic acid; 4-[3-amino-5-(1-methylguanidino)-valeramido]-1-(4-amino-2-oxo-1(2*H*)-pyrimidinyl-1,2,3,4-tetradeoxy-β-D-*erythro*-hex-2-enopyranuronic acid; 1-(1'-cytosinyl)-4-[L-3'-amino-5'-(1''-*N*-methylguanidino)-valerylamino]-1,2, 3,4-tetradeoxy-β-*erythro*-hex-2-enuronic acid; Bla-S

Uses Antibiotic. Antifungal against rice blast disease in Japan.

Occurrence Produced by *Streptomyces griseochromogenes*.

Physical properties

M. Pt. 235-236°C (decomp.) (needles from water)

Solubility Water: >30 g l^{-1} (20°C). Organic solvents: acetic acid, practically insoluble in acetone, benzene, carbon tetrachloride, chloroform, cyclohexane, ethanol, ether, ethyl acetate, pyridine, xylene

Ecotoxicity

Fish toxicity

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

Invertebrate toxicity

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

Mammalian & avian toxicity

Acute data

LD_{50} orat rat, mouse 16, 38 mg kg^{-1}, respectively (2,3).

LD_{50} intravenous mouse 2.8 mg kg^{-1} (4).

LD_{50} dermal mouse, rat 220, 3100 mg kg^{-1}, respectively (5).

LD_{50} dermal mouse, rat 220, 3100 mg kg^{-1}, respectively (6).

Carcinogenicity and chronic effects
No-observed-effect level (2 yr) rat 1 mg kg^{-1} in diet (6).

Irritancy
Severe eye irritant (6).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537 and TA1538 and *Escherichia coli* WP2 *hcr* mutagenicity in reversion-assay systems negative (7).

Other effects

Other adverse effects (human)
Poison by ingestion, skin contact, and intravenous routes.

Legislation

WHO Toxicity Class Ib (8).
EPA Toxicity Class II (6).

Other comments

Contact fungicide with protective and curative action. Acts by inhibiting protein synthesis (6).
Blasticidin-S is more phytotoxic to dicotyledonous than to monocotyledenous plants. It inhibits [14C]amino acid incorporation into proteins of rice and carrot cell cultures (9).

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B140 bleomycin

CAS Registry No. 11056-06-7

RTECS No. EC 5988000

Uses Bleomycin (as the sulfate or hydrochloride) is used as an antineoplastic agent, either alone or in combination with other drugs, in the treatment of squamous cell carcinoma, Hodgkin's disease, non-Hodgkin's lymphoma and malignant neoplasms of the testis.
Occurrence Bleomycin is a generic term for a mixture of antineoplastic glycopeptide antibiotics isolated from *Streptomyces verticillus*.

Physical properties

Solubility Water: very soluble. Organic solvents: very soluble in methanol, slightly soluble in ethanol, practically insoluble in acetone, butylacetate, ether and ethylacetate

Mammalian & avian toxicity

Acute data

LD_{50} intraperitoneal mouse, rat 35, 168 mg kg^{-1}, respectively (1,2).
LD_{50} intravenous mouse 53 mg kg^{-1} (3).

Sub-acute and sub-chronic data

The cellular stage of bleomycin lung toxicity in rabbits administered endotracheally with 10 μg kg^{-1} resulted in small, stiff lungs with impaired diffusing capacity (4).
LD_{50} intraperitoneal (young) mouse 15 mg kg^{-1} daily for 14 days. Bleomycin was more toxic in older mice. Toxic effects included bad hair-condition, nail deformations and salivation (5).

Carcinogenicity and chronic effects

Inadequate evidence for carcinogenicity to humans, limited evidence for carcinogenicity to animals, IARC classification group 2B (6).

Metabolism and toxicokinetics

Bleomycin administered to humans (large, single intramuscular or intravenous injections) has a short half-life of ~115 min. It is excreted in the urine, 50% in 4 hr and >70% by 24 hr, but renal clearance is probably not the only route of elimination; it may be partly metabolised (7).

Irritancy

1 mg instilled into rabbit eye caused mild irritation (8).

Genotoxicity

Sprague-Dawley rats were administered 50, 100 and 150 mg kg^{-1} bleomycin by gavage in the alkaline COMET assay. Two wk after treatment, testicular and bone marrow cells showed only occasional slight increases in damage over controls (9).
Bleomycin treatment (4 μg ml^{-1}) of the purple sulfur bacterium *Thiocapsa roseopersicina* sharply increased the frequency of ampicillin-resistant mutants from 10^{-8} (spontaneous) to 4×10^{-4} (induced) in 17 h (10).
Patients receiving bleomycin treatment (cumulative intravenous doses of 30-80 mg per patient) showed significant increases in the number of chromosomal aberrations in bone-marrow cells and in peripheral lymphocytes (11,12).

Other effects

Other adverse effects (human)

The most frequent side-effects involve the skin and mucous membranes and include rash, erythema, pruritus, vesiculation, hyperkeratosis, nail changes, alopecia, hyperpigmentation, striae, and stomatitis. Fever is also common. Acute anaphylactoid reactions with hyperoxia and cardiorespiratory collapse have been reported in about 1% of patients. The most serious delayed effect is pulmonary toxicity (13).

Any other adverse effects

Hamsters given 0.5 U kg^{-1} bleomycin intratracheally and exposed for 24 hr to 80% oxygen developed acute respiratory failure 72 hr after treatment, coinciding in time with a significant decrease in broncheoalveolar dipalmitoyl phosphatidylcholine/sphingomyelin ratio. This decreased ratio may reflect type II cell damage and inhibition of surfactant function by the oedema fluid (14).

Other comments

Simultaneous treatment of *Aspergillus nidulans* with hyperthermia (43 °C) and bleomycin results in greater cytotoxic activity in spores and in a higher induction rate of point mutations (15).

Post-treatment with sodium arsenite has no effect on the cytotoxicity of bleomycin in CHO cells, human skin fibroblasts, and HeLa cells. Pre-treatment with sodium arsenite potentiated the cytotoxicity of bleomycin in CHO cells (16).
Pre-treatment, simultaneous treatment, and pre-plus-simultaneous treatment with β-carotene potentiated the clastogenicity of bleomycin to Chinese hamster ovary cells (17).
Seventeen injectable anticancer drugs, including bleomycin, have been classified according to the level of potential risk to medical personnel involved in their preparation and administration (18).
Oxidation with potassium permanganate or 5.25% sodium hypochlorite solution (bleach) completely degraded and inactivated bleomycin (19).
Mode of action of DNA and resulting effects reviewed (20).
Bleomycin exposure in the operating theatre reviewed (21).
Genetic toxicology reviewed (22).

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B141 borax

$$Na_2B_4O_7 \cdot 10H_2O$$

$B_4H_{20}Na_2O_{17}$ **Mol. Wt.** 381.37 **CAS Registry No.** 1303-96-4

Synonyms borax decahydrate; sodium tetraborate; Polybor; sodium pyroborate; sodium biborate; sodium borate decahydrate

RTECS No. VZ 2275000

Uses Mild antiseptic. Fungicide and herbicide. In ant poisons and for fly control. Larvicide. In the manufacture of glazes, enamels, cleaning compounds, and in soldering metals.

Physical properties

M. Pt. 75°C (when rapidly heated) **Specific gravity** 1.73 at 20°C with respect to water at 4°C
Solubility Water: 51.4 g l^{-1} at 20°C. Organic solvents: glycerol, ethylene glycerol

Occupational exposure

FR-VME 5 mg m^{-3}
SE-LEVL 2 mg m^{-3} **SE-STEL** 5 mg m^{-3}
UK-LTEL 5 mg m^{-3}
US-TWA 5 mg m^{-3}

Ecotoxicity

Invertebrate toxicity
Non-toxic to bees (1).

Environmental fate

Degradation studies
No microbial degradation. Washed out of soil but may persist for ≥2 yr depending on rainfall and soil structure (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 2660 mg kg^{-1} (2).
LD_{50} oral mouse 2000 mg kg^{-1} (3).
LD_{50} oral guinea pig 5330 mg kg^{-1} (3).
LD_{50} intraperitoneal mouse 2711 mg kg^{-1} (4).
LD_{50} intravenous mouse 1320 mg kg^{-1} (3).
LD_{Lo} subcutaneous rabbit 150 mg kg^{-1} (5).
LD_{Lo} oral ♂ human 709 mg kg^{-1} (6).
LD_{Lo} oral infant 1000 mg kg^{-1} (7).

Teratogenicity and reproductive effects
Oral rats (duration unspecified) 5250 ppm caused growth suppression, decreased food utilisation efficiency, degeneration of gonads and skin desquamation on the paws and tails (8).
Oral rats fed both borax and boric acid at 1170 ppm body equivalent, sterility and testicular degeneration were observed (8).
Oral rats, dogs 350 ppm body equivalent, no adverse effects to fertility, lactation, litter size, weight and appearance (8).

Irritancy
A polishing powder containing borax caused medium irritation action and weak allergic effects when applied dermally to ten volunteers (9).
Caused irritation of the upper respiratory tract in animals and high levels of dust caused nasal irritation in humans. Irritating to skin and percutaneous absorption can cause gastro-intestinal irritation, kidney damage and may be fatal due to vascular collapse or central nervous system depression (10).

Other effects

Other adverse effects (human)
Chronic exposure to small amounts can cause gastroenteritis (dose unspecified) (11).
Toxic if swallowed and severe vomiting, diarrhoea, and shock and death of young children has been reported on ingestion of 5-10 g (12).
Can cause nausea, vomiting and diarrhoea. Exposure to concentrations ≤4.0 mg m^{-3} caused symptoms of acute respiratory irritation and chest tightness (13).

Any other adverse effects

A polishing powder containing borax was administered intratracheally to rats; increased content of hydroxyproline and reactive lesions in the form of granulomas were found in rat lungs (9).

Legislation

EPA Toxicity Class III (1).

WHO Class Table 5 (14).

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Sodium: guide level 20 mg l^{-1} (15).

Other comments

Incompatible with acids, alkali and metallic salts. Aqueous solution is alkaline and so is incompatible with some herbicides (16).

Toxicity of borax used as a preservative reviewed (17).

Borax is used as an ingredient in some cosmetics, soap, and acne preparations, and in a homeopathic compound for sleep disorders (18).

Hazards and toxicity data reviewed (19).

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B142 Bordeaux mixture

$$CuSO_4.3Cu(OH)_2.3CaSO_4$$

$H_2Ca_3Cu_4S_2O_{10}$ **Mol. Wt.** 600.56 **CAS Registry No.** 8011-63-0

Synonyms basic cupric sulfate; tribasic copper mixture; Comac; BBS; Bordocure; Bordolex; Cofol; Cuprix; Cuprocal; Idrorame; Poltan

Uses Foliar fungicide. Insect repellent.

Occupational exposure

SE-LEVL 1 mg m^{-3} (as Cu) (total dust); 0.2 mg m^{-3} (as Cu) (respirable dust)

UN No. 2775 **HAZCHEM Code** 2X **Conveyance classification** toxic substance

Mammalian & avian toxicity

Acute data

LD_{50} oral rat >4000 mg kg^{-1} as wettable powder (1).

Other effects

Other adverse effects (human)

Humans exposed to high copper sulfate content, 392-555 g kg^{-1}, by repeated administration of Bordeaux mixture suffered systemic effects including gastroenteritis, haemolysis, jaundice, albuminuria, haemoglobinuria and delayed sudden increase in the blood bilirubin, both free and conjugated with glucuronic acid. Uremia indicated injury of the glomerular apparatus in kidney. Haemolytic crises were associated with hypercupraemia. Liver copper content increased 8-10-fold (2).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Copper: maximum admissible concentration 100 µg l^{-1} (3).

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

Other comments

Dissolves in ammonium hydroxide to form a cuprammonium complex.

Incompatible with alkali-sensitive pesticides such as organophosphorus compounds and carbamates and strongly alkaline pesticides such as lime sulfur (1).

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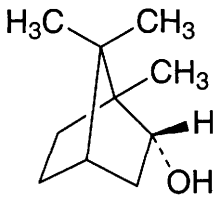
B143 borneol



$C_{10}H_{18}O$ **Mol. Wt.** 154.25 **CAS Registry No.** 507-70-0

Synonyms 1,7,7-trimethylbicyclo[2.2.1]heptan-2-ol; endo-2-bornanol; bornyl alcohol; camphol; endo-2-camphanol; endo-2-hydroxybornane

EINECS No. 208-080-0 **RTECS No.** ED 7000000

Uses In textile industry. Solvent and bactericide in soap manufacture. Flotation agent. Preservative in paints. Perfumes, flavourings and medicinals.

Occurrence Dextrorotatory form occurs in the oil from *Dryobalanops aromatica* Gaertn., and in many other plants. Laevorotatory form is found in *Blumea balsamifera*.

Physical properties

M. Pt. 208°C (+form), 204°C (–form), 206-207°C (±form) **B. Pt.** 212°C (sublimes) (+form), 210°C (–form)
Flash point 65°C (closed cup) **Specific gravity** 1.011 at 25°C with respect to water at 4°C
Volatility v.den. 5.31
Solubility Organic solvents: acetone, benzene, decalin, diethyl ether, ethanol, petroleum ether, toluene

Occupational exposure

UN No. 1312 **HAZCHEM Code** 1Z **Conveyance classification** flammable solid

Environmental fate

Degradation studies
Biodegradable (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat, mouse, rabbit 500-2000 mg kg^{-1} (2-4).

Other effects

Other adverse effects (human)
In humans systemic effects include nausea, vomiting, mental confusion, dizziness and convulsions (5).

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B144 boron oxide

B_2O_3

B_2O_3 **Mol. Wt.** 69.62 **CAS Registry No.** 1303-86-2

Synonyms boric anhydride; boron sesquioxide; diboron trioxide

EINECS No. 215-125-8 **RTECS No.** ED 7900000

Uses Herbicide. Metallurgy. Analysis for silicates and blowpipe analysis.

Physical properties

M. Pt. 450°C **B. Pt.** 1860°C **Specific gravity** 2.460
Solubility Organic solvents: ethanol

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}

Mammalian & avian toxicity

Acute data
LD_{50} oral mouse 3136 mg kg^{-1} (1).
LD_{50} intraperitoneal mouse 1868 mg kg^{-1} (1).

Other effects

Any other adverse effects
Irritant to eye and skin (2).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Boron: guide level 1000 μg l^{-1} (3).
Included in Schedule 6 (Release into Land: Prescribed Substances) of Statutory Instrument No. 472, 1991 (4).

Other comments

Toxicity and hazards reviewed (5).
Hygroscopic. Mixed with CaO and fused into $CaCl_2$ the mixture incandesces.
Reviews on human health effects, experimental toxicology, epidemiology and workplace experience listed (6).

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B145 boron tribromide

BBr_3

BBr_3 **Mol. Wt.** 250.52 **CAS Registry No.** 10294-33-4

Synonyms boron bromide; tribromoborane; tribromoboron; Trona Boron Tribromide 99

EINECS No. 233-657-9 **RTECS No.** ED 7400000

Uses In the manufacture of diborane and of ultra-high purity boron. In the manufacture of anhydrous metal bromides. Catalyst. Doping agent for semiconductors.

Physical properties

M. Pt. –46°C **B. Pt.** 90°C **Specific gravity** 2.698 at 0°C **Volatility** v.p. 40 mmHg at 14°C
Solubility Water: (decomp.). Organic solvents: ethanol (decomp.)

Occupational exposure

UK-STEL 1 ppm (10 mg m^{-3})
US-STEL ceiling limit 1 ppm (10 mg m^{-3})

UN No. 2692 **HAZCHEM Code** 4WE **Conveyance classification** corrosive substance
Supply classification very toxic, corrosive
Risk phrases Reacts violently with water – Very toxic by inhalation and if swallowed – Causes severe burns (R14, R26/28, R35)
Safety phrases Keep locked up and out of the reach of children (if sold to general public) – Keep container in a well ventilated place – In case of contact with eyes, rinse immediately with plenty of water and seek medical advice – 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)

Environmental fate

Adsorption and retention
Some boron is adsorbed by iron and aluminium hydroxy compounds and clay minerals, maximum sorption in the range pH 7-9 (1).

Mammalian & avian toxicity

Irritancy
Corrosive to tissues of mucous membranes, upper respiratory tract, eyes and skin (2).

Other effects

Other adverse effects (human)
In humans systemic effects include vomiting and abdominal pain. Burns on contact and can be absorbed through the skin. Exposure to vapour causes pain, redness, watering, blurred vision in eyes and coughing and shortness of breath. Can cause pulmonary oedema, severe vomiting and diarrhoea (3).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Boron: guide level 1000 μg l^{-1} (4).

Other comments

Toxicity and hazards reviewed (5).

Reviews on physico-chemical properties, human health effects, experimental toxicology and workplace experience listed (6).
Mixtures are shock sensitive and liable to explode on impact (7).
Corrosive. Light and moisture sensitive. Incompatible with sodium and potassium. Hydrolyses to boric acid and hydrogen bromide.

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B146 boron trichloride

BCl_3

BCl_3 **Mol. Wt.** 117.17 **CAS Registry No.** 10294-34-5

Synonyms boron chloride; trichloroborane; trichloroboron

EINECS No. 233-658-4 **RTECS No.** ED 1925000

Uses Manufacture and purification of boron. Catalyst for organic reactions. Semiconductors. Bonding of iron and steels. Purification of metal alloys to remove nitrides and carbides.

Physical properties

M. Pt. –107°C **B. Pt.** 12.5°C **Specific gravity** 1.35 at 15°C **Volatility** v.p. 1128 mmHg at 20°C ; v.den. 4.05
Solubility Water: (decomp.). Organic solvents: ethanol (decomp.)

Occupational exposure

UN No. 1741 **Conveyance classification** toxic gas, corrosive
Supply classification very toxic
Risk phrases Reacts violently with water – Very toxic by inhalation and if swallowed – Causes burns (R14, R26/28, 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)

Environmental fate

Adsorption and retention
Some boron is adsorbed by iron and aluminium hydroxy compounds and clay minerals, maximum sorption ranging from pH 7-9 (1).

Mammalian & avian toxicity

Acute data

LC_{Lo} (7 hr) inhalation mouse, rat 20 ppm (2).
LC_{50} (1 hr) inhalation ♂ rat 2541 ppm (3).

Irritancy

Exposure can cause dermatitis in humans (4).

Other effects

Other adverse effects (human)

Destructive to tissues of the mucous membranes and upper respiratory tract, eyes and skin. In humans, inhalation can be fatal as a result of spasm, inflammation, and oedema of larynx and bronchi, chemical pneumonitis and pulmonary oedema. Symptoms of exposure may include burning sensation, coughing, laryngitis, shortness of breath, wheezing, headache, nausea and vomiting. Can cause nervous system disturbance (5).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Boron: guide level 1000 $\mu g\ l^{-1}$ (6).
Included in Schedule 6 (Release into Land: Prescribed Substances) of Statutory Instrument No. 472, 1991 (7).

Other comments

Reacts with hydrogen at 1200°C (8).
Hydrolyses to hydrochloric and boric acids (9).
Toxicity and hazards reviewed (10).
Physico-chemical properties, human health effects and experimental toxicology reviewed (5,11).
Non-flammable gas. Corrosive.

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B147 boron trifluoride

BF_3

BF_3 **Mol. Wt.** 67.81 **CAS Registry No.** 7637-07-2

Synonyms boron fluoride; trifluoroborane; trifluoroboron; Leecure B Series

EINECS No. 231-569-5 **RTECS No.** ED 2275000

Uses Initiation and polymerisation catalyst. Catalyst in organic synthesis. Fumigant. Protects molten magnesium and its alloys from oxidation. Detection of weak neutrons in ionisation chambers.

Physical properties

M. Pt. –127°C **B. Pt.** –100°C **Specific gravity** 2.99 **Volatility** v.p. >1 mmHg at 20°C ; v.den. 2.4
Solubility Water: 3320 g l^{-1} at 0°C. Organic solvents: most saturated and halogenated hydrocarbons and aromatic compounds

Occupational exposure

FR-VLE 1 ppm (3 mg m^{-3})
JP-OEL 0.3 ppm (0.83 mg m^{-3})
SE-LEVL 2 mg m^{-3} (as F) **UK-STEL** 1 ppm (2.8 mg m^{-3}) **US-STEL** ceiling limit 1 ppm (2.8 mg m^{-3})

UN No. 1008 **Conveyance classification** toxic gas, corrosive
Supply classification very toxic, corrosive
Risk phrases Reacts violently with water – Very toxic by inhalation – Causes severe burns (R14, R26, R35)
Safety phrases Keep locked up and out of the reach of children (if sold to general public) – Keep container in a well ventilated place – In case of contact with eyes, rinse immediately with plenty of water and seek medical advice – 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)

Environmental fate

Adsorption and retention
Some boron is adsorbed by iron and aluminium hydroxy compounds and clay minerals, maximum range pH 7-9 (1).

Mammalian & avian toxicity

Acute data
LC_{50} (4 hr) inhalation rat 1180 mg m^{-3} (2).
LC_{50} (2 hr) inhalation mouse 3460 mg m^{-3} (2).
LC_{50} (4 hr) inhalation guinea pig 109 mg m^{-3} (3).

Sub-acute and sub-chronic data
Kidney necrosis, rales, lachrymation, reversible depression of serum total protein and globulin, and increased urinary, serum and bone fluoride reported in rats exposed to 17 mg m^{-3}, 6 hr day^{-1}, 5 day wk^{-1} for 13 wk (4). Inhalation rats, rabbits and guinea pigs (up to 6 months) 35, 21 or 8.2 mg min^{-3} 7 hr day^{-1}, 5 days $week^{-1}$ caused respiratory irritation at the lowest concentration, and mortality at the highest exposure (5).

Metabolism and toxicokinetics
During inhalation exposure of rats for up to 6 months at 12.8 ppm, 3-4 ppm and 1.5 ppm, the average fluorine contents of teeth and bone were elevated at all exposure levels but not in soft tissues, lung, liver and blood (6). Fluoride exchanged with hydroxy groups of hydroxyapatite in bone, to form fluorohydroxyapatite. Unretained fluoride was excreted rapidly in urine (7).

Irritancy
Inhalation rat 17 mg m^{-3} showed irritation of mucous membranes and eyes (4).

Other effects

Other adverse effects (human)
A study of 78 workers exposed for 10-15 yr to boron trifluoride in the former Soviet Union showed workers suffered from dryness and bleeding of nasal mucosa, bleeding gums, dry and scaly skin, and pain in joints. Exposure levels were not reported (8).
In the USA 13 workers exposed to boron trifluoride concentration range 0.1-1.8 ppm showed reduced pulmonary function (5).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Boron: guide level 1000 μg l^{-1}. Fluoride: maximum admissible concentration 1500 μg l^{-1} at 8-12°C, 700 μg l^{-1} at 25-30°C (9).
Included in Schedule 6 (Release into Land: Prescribed Substances) of Statutory Instrument No. 472, 1991 (10).

Other comments

Toxicity and hazards reviewed (4).
Reviews on physico-chemical properties, experimental toxicology, human health effects, epidemiology and workplace experience listed (11).
Incompatible with alkali metals, alkaline earth metals (except magnesium), alkyl nitrates and lime (CaO), hydrofluoric and hydrofluoroboric acids.

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B148 boron trifluoride diethyl etherate

$$(CH_3CH_2)_2O.BF_3$$

$C_4H_{10}BF_3O$ **Mol. Wt.** 141.93 **CAS Registry No.** 109-63-7

Synonyms boron trifluoride etherate; boron trifluoride diethyl ether

EINECS No. 203-689-8

Uses In co-polymer initiation reactions.

Physical properties

M. Pt. –60.4°C **B. Pt.** 125.7°C **Flash point** 64°C (open cup) **Specific gravity** 1.125 at 25°C with respect to water at 4°C

Occupational exposure

DE-MAK 2.5 mg m^{-3} (as F) (total dust)

UN No. 2604 **HAZCHEM Code** 4WE **Conveyance classification** corrosive substance, danger of fire (flammable liquid)

Mammalian & avian toxicity

Metabolism and toxicokinetics

Borates are rapidly absorbed from mucous membranes and abraded skin, but not from intact or unbroken skin. Borate excretion occurs mainly through kidneys, ~50% is excreted in first 12 hr and remainder is eliminated over 5-7 days (1).

Irritancy

Contact with skin caused burning and redness. Exposure to vapour caused pain, redness, watering and blurred vision in eyes (2).

Other effects

Other adverse effects (human)

Systemic effects include vomiting, abdominal pain and diarrhoea (2).

Destructive to tissues of mucous membranes and upper respiratory tract, eyes and skin. Inhalation can be fatal due to spasm, inflammation and oedema of the larnyx and bronchi, chemical pneumonitis and pulmonary oedema. Symptoms of exposure may include burning sensation, coughing, shortness of breath, wheezing, laryngitis, headache, nausea and vomiting (3).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Boron: guide level 1000 μg l^{-1}, maximum admissible concentration 2000 μg l^{-1}. Fluoride: maximum admissible concentration 1500 μg l^{-1} at 8-12°C, 700 μg l^{-1} at 25-30°C (4).

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

Other comments

Toxicity and hazards reviewed (6).

Corrosive. Moisture sensitive. Incompatible with oxidising materials. Can form peroxides. Fire hazard.

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B149 boron trifluoride dimethyl etherate

$(H_3C)_2CO.BF_3$

$C_2H_6BF_3O$ **Mol. Wt.** 113.88 **CAS Registry No.** 353-42-4

EINECS No. 206-532-1 **RTECS No.** ED 8400000

Uses Used to produce ^{10}B isotope.

Physical properties

M. Pt. –15°C **B. Pt.** 26-127°C **Flash point** 35°C **Specific gravity** 1.239

Occupational exposure

DE-MAK 2.5 mg m^{-3} (as F) (total dust)

UN No. 2965 **HAZCHEM Code** 4WE **Conveyance classification** substance which in contact with water emits flammable gas, danger of fire (flammable liquid), corrosive

Mammalian & avian toxicity

Acute data

LC_{Lo} (4 hr) inhalation guinea pig 50 ppm (1).

Other effects

Other adverse effects (human)

Destructive to tissues of mucous membranes and upper respiratory tract, eyes and skin. Inhalation may be fatal as a result of spasm, inflammation and oedema of larynx and bronchi, chemical pneumonitis and pulmonary oedema. Symptoms of exposure include burning sensation, coughing, wheezing, laryngitis, shortness of breath, headache, nausea and vomiting (2).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Boron: guide level 1000 μg l^{-1}. Fluoride: maximum admissible concentration 1500 μg l^{-1} at 8-12°C, 700 μg l^{-1} at 25-30°C (3).

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

Other comments

Toxicity and hazards reviewed (5).

Flammable liquid. Corrosive. Reacts violently with water. Incompatible with acids, bases, alcohols and alkali metals. Decomposes to produce toxic fumes of carbon monoxide, carbon dioxide and hydrogen fluoride.

References

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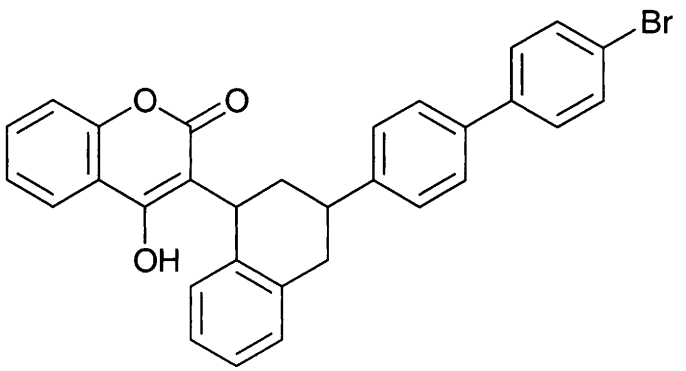
B150 brodifacoum



$C_{31}H_{23}BrO_3$ **Mol. Wt.** 523.43 **CAS Registry No.** 56073-10-0

Synonyms Talon; Brocum; De-Mice; Folgorat; Haoc; Klerat; Matikus; Mouser; Ratak; 3-(3-(4'-bromobiphenyl-4-yl)-1,2,3,4-tetrahydronaphth-1-yl)-4-hydroxycoumarin; 3-[3-(4'-bromo[1,1'-biphenyl]-4-yl)-1,2,3,4-tetrahydro-1-naphthalenyl]-4-hydroxy-2*H*-1-benzopyran-2-one

EINECS No. 259-980-5 **RTECS No.** GN 4934750

Uses Anticoagulant rodenticide which inhibits prothrombin synthesis.

Physical properties

M. Pt. 228-230°C **Specific gravity** 1.39 **Volatility** v.p. $<9.776 \times 10^{-7}$ mmHg at 25°C
Solubility Water: <10 mg l^{-1} at 20°C pH 7. Organic solvents: acetone, benzene, chloroform, ethanol

Occupational exposure

Supply classification very toxic
Risk phrases Very toxic in contact with skin and if swallowed – Toxic: danger of serious damage to health by prolonged exposure in contact with skin and if swallowed (R27/28, R48/24/25)
Safety phrases Keep locked up and out of the reach of children (if sold to general public) – Wear suitable protective clothing and gloves – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S36/37, S45)

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) rainbow trout, bluegill sunfish 91-165 μg l^{-1} (1).
LC_{50} (3-7 days) carp, Crucian carp, tench 0.1->1 mg l^{-1} (2).

Environmental fate

Degradation studies
Degraded in soils, pH 5.5-8, under aerobic and flooded conditions (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral mallard duck 5.0 mg kg^{-1} (1).
LD_{50} oral rat, rabbit, mouse 160-400 μg kg^{-1} (3,4).

LD_{50} oral gerbil 1 mg kg^{-1} (5).
LD_{50} dermal rat 50 µg kg^{-1} (6).
LD_{50} percutaneous rat 50 mg kg^{-1} (technical grade compound) (1).
In one-day feeding trials 0.005% brodifacoum caused 100% mortality in rats (7).

Sub-acute and sub-chronic data
Oral ♂ Leghorn (3 day) 0.005% brodifacoum in feed; 6/8 birds died after 3 days (8).
Oral barn owl (15 day) via brodifacoum-fed mice to simulate exposure in the wild. No fatalities up to a cumulative dose of ≥1.9 mg kg^{-1} (equivalent to two 25 g mice with 1 mg kg^{-1} brodifacoum residue day^{-1} for 15 days). Analysis showed that the majority of rodenticide residue is retained in the liver (9).

Metabolism and toxicokinetics
Gavage horse 0.125 mg kg^{-1}. 2/6 horses had detectable levels of brodifacoum 9 days after exposure; $t_{1/2}$ 1.22 days (10).

Irritancy
Dust non-irritating in Vermac tests (11).

Other effects

Any other adverse effects
1 µg brodifacoum caused complete inhibition of vitamin K formation in warfarin-resistant rats (12).
In rabbits treated with brodifacoum no direct effect was observed on the clearance of vitamin K from either plasma or liver (13).
Administration of the LD_{50} to rats increased bleeding time, coagulation time, white blood cells and prothrombin. Decreases were recorded in red blood cell count, haemoglobin content and haemocrit values (14).
Gavage horse 0.125 mg kg^{-1} caused weight loss, severe hypocoagulability and haemogram disturbances. 4/6 horses became anoretic and depressed. Increases in clotting times were observed, and the mean haematocrit was decreased. The haemoglobin and erythrocyte numbers and platelet counts were decreased. The data suggest that a single exposure to brodifacoum may cause clinical illness and possibly death in horses (10).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides and related products: maximum admissible concentration 0.1 µg l^{-1} (15).
Included in Schedule 6 (Release into Land: Prescribed Substances) of Statutory Instrument No. 472, 1991 (16).

Other comments

Baits containing >100 mg kg^{-1} are hazardous to humans and availability should be restricted (17).
A review with references on the rodenticide brodifacoum (18).
Water is a suitable vehicle for brodifacoum (19).

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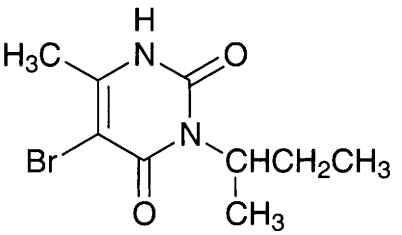
B151 bromacil



$C_9H_{13}BrN_2O_2$ **Mol. Wt.** 261.12 **CAS Registry No.** 314-40-9

Synonyms 5-bromo-3-*sec*-butyl-6-methyluracil; 5-bromo-6-methyl-3-(1-methylpropyl)-2,4(1*H*,3*H*)-pyrimidinedione; Borocil; Bromax; Hyvar X; Rokar X L; Staa-Free; Uragan; Urox B

EINECS No. 206-245-1 **RTECS No.** YQ 9100000

Uses Herbicide.

Physical properties

M. Pt. 158-159°C **Specific gravity** 1.55 at 25°C **Volatility** v.p. 2.0×10^{-5} mmHg at 25°C
Solubility Water: 815 mg l^{-1} at 25°C. Organic solvents: acetone, acetonitrile, ethanol, xylene

Occupational exposure

FR-VME 1 ppm (10 mg m^{-3})
UK-LTEL 1 ppm (11 mg m^{-3}) **UK-STEL** 2 ppm (22 mg m^{-3})
US-TWA 10 mg m^{-3}

Ecotoxicity

Fish toxicity
LC_{50} (48 hr) bluegill sunfish, rainbow trout 71-75 mg l^{-1}.
LC_{50} (48 hr) carp 164 mg l^{-1} (1).
Fathead minnows 30 days old were exposed to bromacil. LC_{50} values were 185, 183, 182 and 167 mg l^{-1} at 25, 48, 96 and 168 hr, respectively. Eggs, newly hatched fry and juvenile fish were continuously exposed to lower concentrations for 64 days. Growth was significantly reduced at 1 mg l^{-1} (2).

Invertebrate toxicity
Non-toxic to bees (1).
LD_{50} (24 hr) *Artemia salina* larvae 71 mg l^{-1} (3).
EC_{50} (5 min) *Photobacterium phosphoreum* 6.71 mg l^{-1} Microtox test (4).

Environmental fate

Degradation studies

Residual activity in soil ~7 months (1).

Of 55 fungal and 73 bacterial cultures isolated from soil, only 4 fungi were capable of degrading 5-bromo-3-*sec*-butyl-6-methyluracil; one culture was identified as *Penicillium paraherquei* Abe (5).

Abiotic removal

Photolytic and hydrolytic removal of bromacil occurs via the formation of intermediates 5-bromo-6-methyluracil and 6-methyluracil (6).

Loss from soil due to volatilisation is negligible (7).

Adsorption and retention

Weakly adsorbed by soils and uniformly distributed in the soil, but exhibits slight retardation in heavier soils. After several cycles of wetting and drying, it was completely leached from around the emitter in soils and was concentrated at the outer edges of the wetted zone (8).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, mouse 5200, 3040 mg kg^{-1}, respectively (1,9).

LC_{50} (4 hr) inhalation rat >4.8 mg l^{-1} (1).

LD_{50} percutaneous rabbit >5000 mg kg^{-1} (1).

LC_{50} (8 day) mallard duck >10,000 mg kg^{-1} in diet (1).

LC_{50} (8 day) bobwhite quail >10,000 mg kg^{-1} in diet (1).

Sub-acute and sub-chronic data

Oral intubation ♂ Sprague-Dawley rats 25, 50 or 250 mg kg^{-1}. The neurotoxic effects of exposure to bromacil were studied in an open-field model of animal behaviour. Behavioural assessment was carried out 20-24 hr after the last administered dose following single exposure, repeated administration (1 and 2 wk) and following termination of drug administration (1 and 2 wk post-exposure). Dose-dependent effects were evident after acute exposure; the highest dose caused a significant decrease in locomotor activity. Repeated administration of 25 mg kg^{-1} produced an increased in locomotor activity which persisted for 2 wk after drug administration (10).

Carcinogenicity and chronic effects

In a 2-yr feeding study the no-effect level in rats and dogs was 250 mg kg^{-1} (1).

Teratogenicity and reproductive effects

TC_{Lo} Inhalation rat (7-14 day gestation, 2 hr) 165 mg m^{-3}, no prenatal or teratogenic effects observed (11).

Not teratogenic in New Zealand white rabbits when fed in the diet at 0, 50 or 250 ppm on days 8-16 of pregnancy. Dietary level of 250 ppm had no adverse effects on reproduction or lactation in a 3-generation 6 litter study (12).

Metabolism and toxicokinetics

In humans, bromacil is excreted unchanged in the urine or as the 5-bromo-3-*sec*-butyl-6-hydroxymethyluracil metabolite primarily as the glucuronide and/or sulfonate conjugate (11).

Concentration in cow feed of 5 and 30 ppm, secretion of intact compound in milk reached 0.019 and 0.13 ppm, respectively. Absent in urine and faeces (5).

Irritancy

50% aqueous suspension applied to intact and abraded skin of albino ♂ guinea pigs. Reaction after 24 hr indicated mild irritation in young animals and slightly greater irritation in older animals. 10 mg (as dry powder) sprinkled onto eyes of ♂ rabbits caused mild conjunctivitis with no corneal injury (12).

Sensitisation

50% aqueous suspension applied to abraded skin of albino ♂ guinea pigs, 3 × wk^{-1} for 3 wk. Animals were re-exposed after 2- and 3-wk rest periods. No evidence of sensitisation (12).

Genotoxicity

Salmonella typhimurium TA100, TA1535, TA1537, TA1538 with and without metabolic activation negative (11).
Saccharomyces cerevisiae D3, D7 with and without metabolic activation negative (13).
Drosophila melanogaster sex chromosome loss and non-disjunction negative (14).
Oral B6C3/FI mice 50, 150 and 500 mg kg^{-1}, acute and sub-chronic exposure trials. Bone marrow cells were removed for chromosome analysis 15 hr after treatment, and spleen lymphocytes were cultured for chromosome analysis. Results show that bromacil does not cause chromosomal aberrations (15).

Other effects

Any other adverse effects
In vitro rat hepatocytes, highly toxic (dose unspecified) but less toxic in rat bone marrow cell cultures (16).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides and related products: maximum admissible concentration 0.1 $\mu g\ l^{-1}$ (17).
Included in Schedule 6 (Release into Land: Prescribed Substances of Statutory Instrument No. 472, 1991 (18).

Other comments

Metabolic pathways reviewed (19).

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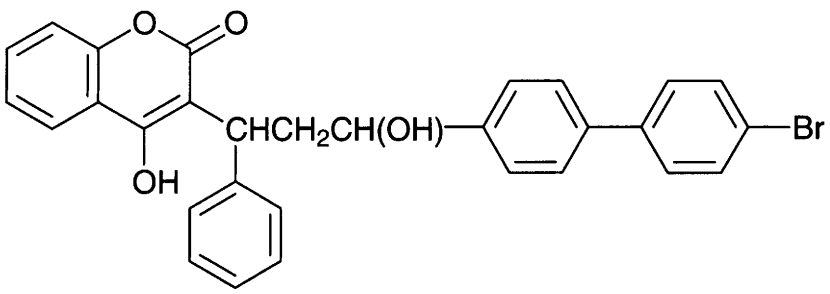
B152 bromadiolone



$C_{30}H_{23}BrO_4$ **Mol. Wt.** 527.41 **CAS Registry No.** 28772-56-7

Synonyms 3-(α-(*p*-(*p*-bromophenyl)-β-hydroxyphenethyl)benzyl)-4-hydroxycoumarin; 3-[3-(4'-bromo-[1,1'-biphenyl]-4-yl)-3-hydroxy-1-phenylpropyl]-4-hydroxy-2*H*-1-benzopyran-2-one; Apobas; Arvicolex; Boot Hill; Bromodialone; Bromorat; Deadline

EINECS No. 249-205-9 **RTECS No.** GN 4934700

Uses An anticoagulant rodenticide which inhibits prothrombin synthesis.

Physical properties

M. Pt. 200-210°C

Solubility Water: 19 mg l^{-1} at 20°C. Organic solvents: acetone, dimethylformamide, ethanol

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) rainbow trout 1.4 mg l^{-1} (1).

Invertebrate toxicity

Non-toxic to bees (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral rabbit, rat, mouse, 1125, 1000, 1750 μg kg^{-1}, respectively (1,2).

LD_{50} oral ♀ rat 0.59 mg kg^{-1} (3).

LD_{50} dermal rat 4.66 mg kg^{-1} (4).

LD_{100} dermal rat 5.62 mg kg^{-1} (4).

LD_{50} percutaneous rabbit 2100 μg kg^{-1} (5).

In 1-day feeding trials 0.1% bromadiolone solution caused 100% mortality in rats (3).

Sub-acute and sub-chronic data

Oral ♂ leghorn (3 day) 0.005% bromadiolone in feed caused no fatalities after 2 days; 2/8 birds died after 3 days (6).

Dermal rat, four non-LD applications. Significant increases in serum aspartate aminotransferase, alanine aminotransferase and total lactate dehydrogenase activities, but no consistent changes in serum creatine kinase activity were observed. A decrease in urine osmolality and an increase in serum creatinine concentration were noted, but no changes in urinary *N*-acetylglucosamidase activity took place. These results suggest that topical application of bromadiolone affects liver cell integrity and impairs glomerular functions (4).

Gastric intubation rats given a single lethal dose of 1.25 mg kg^{-1} or a higher dose of 2.51 mg kg^{-1} in propylene glycol were autopsied at 1, 3 and 5 days after administration. Severe and irreversible hepatic damage was caused at both doses, and changes were visible after 1 day, becoming more pronounced with time. The high dose caused a greater degree of damage. The changes observed included margination of nuclei, dilation of sinusoids, swelling

of hepatocytes, fatty degeneration with vacuolisation, and lymphocytic infiltration in and around the portal and central veins and in sinusoids. Mild to moderate portal fibrosis, hyperplasia, cytoplasmolysis and karyolysis were also observed. Deformity of cellular architecture of the liver was found in the later autopsies (7).
Oral rodent *Meriones hurrianae* 1.36, 1.75 and 3.20 mg kg^{-1} caused 75% mortality in 9-21 days, 100% mortality in 7-19 days and 100% mortality in 5-16 days, respectively (8).

Metabolism and toxicokinetics
Oral rat 0.8 and 3 mg kg^{-1} elimination only from liver; 30% of administered dose is excreted in bile as a glucuronide conjugate during first 8 hr after dosing (9).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides and related products: maximum admissible concentration 0.1 µg l^{-1} (10).
Included in Schedule 6 (Release into Land: Prescribed substances of Statutory Instrument No. 472, 1991 (11).

Other comments

Baits containing >100 mg kg^{-1} are hazardous to humans and their availability should be restricted (12).
Bittrex, the taste-deterrent for humans and non-target animals, increased the palatability of baits to rats and mice (13).

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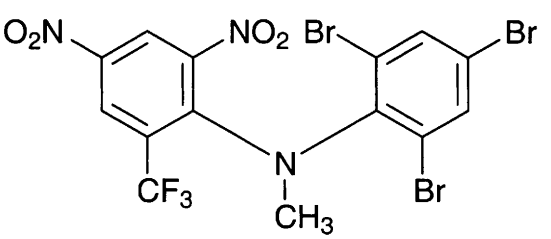
B153 bromethalin



$C_{14}H_7Br_3F_3N_3O_4$ **Mol. Wt.** 577.93 **CAS Registry No.** 63333-35-7

Synonyms *N*-methyl-2,4-dinitro-*N*-(2,4,6-tribromophenyl)-6-(trifluoromethyl)benzenamine; α,α,α-trifluoro-*N*-methyl-4,6-dinitro-*N*-(2,4,6-tribromophenyl)-*o*-toluidine; Doratid; Vengeance

RTECS No. CY 0383000

Uses Rodenticide effective against warfarin-resistant mice and rats.

Physical properties

M. Pt. 150-151°C **Volatility** v.p. 0.776×10^{-8} mmHg at 25°C
Solubility Water: <0.01 mg l^{-1}. Organic solvents: chloroform, dichloromethane, methanol

Mammalian & avian toxicity

Acute data
LD_{50} oral rat, mouse 2-5 mg kg^{-1} (technical grade in propane-1,2-diol).
LC_{50} (1 hr) inhalation rat 0.024 mg l^{-1} (in air) (1).
LD_{50} percutaneous ♂ rabbit 1000 mg kg^{-1} (2).
Doses in excess of the LD_{50} 2 mg kg^{-1} in rats caused death within 8-12 hr and was preceded by 1-3 episodes of clonic convulsions, with death usually due to respiratory arrest. Guinea pigs could tolerate ≥1000 mg kg^{-1} without effect (3).

Sub-acute and sub-chronic data
In 90-day feeding trials the no-observed-effect level for rats and dogs was 0.025 mg kg^{-1} day^{-1} (2).

Metabolism and toxicokinetics
Metabolised to the desmethyl analogue in rats (3).

Other effects

Any other adverse effects
Multiple low doses of sublethal intoxications yields hind leg weakness and loss of tactile sensation in rodents. Spongy degeneration of the white matter (intramycleric oedema) occurred in the brain and spinal cord of these animals. No inflammation or cellular destruction of neuronal tissue was noted (3).
In rats a potent uncoupler of oxidative phosphorylation (3).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides and related products: maximum admissible concentration 0.1 μg l^{-1} (4).
Included in Schedule 6 (Release into Land: Prescribed substances of Statutory Instrument No. 472, 1991 (5).

Other comments

The toxicity, mechanism of action and rodenticidal efficiency of bromethalin is reviewed (6).
Mode of action, toxicity, clinical effects and treatment efficacy in rats, dogs and cats reviewed (7).

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B154 bromine

Br_2

Br_2 **Mol. Wt.** 159.81 **CAS Registry No.** 7726-95-6

EINECS No. 231-778-1 **RTECS No.** EF 9100000

Uses Water disinfectant. Bleaching fibres and silk. Manufacture of medicinal bromine compounds and dyestuffs. Manufacture of ethylene dibromide (anti-knock gasoline). Used in form of adduct with a quaternary ammonium compound in the treatment of plantar warts (1).
Occurrence Occurs in igneous rock and in seawater.

Physical properties

M. Pt. –7.25°C **B. Pt.** 58.73°C **Volatility** v.p. 175 mmHg at 21°C ; v.den. 55
Solubility Water: 17.11 g l^{-1} at 25°C. Organic solvents: carbon disulfide, chloroform, diethyl ether, ethanol, tetrachloromethane

Occupational exposure

DE-MAK 0.1 ppm (0.66 mg m^{-3})
FR-VLE 0.1 ppm (0.7 mg m^{-3})
JP-OEL 0.1 ppm (0.65 mg m^{-3})
SE-LEVL 0.1 ppm (0.7 mg m^{-3})
SE-STEL 0.3 ppm (2 mg m^{-3})
UK-LTEL 0.1 ppm (0.66 mg m^{-3})
UK-STEL 0.3 ppm (2.0 mg m^{-3})
US-TWA 0.1 ppm (0.66 mg m^{-3})
US-STEL 0.2 ppm (1.3 mg m^{-3})

UN No. 1744 **HAZCHEM Code** 2XE **Conveyance classification** corrosive substance, toxic
Supply classification corrosive, very toxic
Risk phrases Very toxic by inhalation – Causes severe burns (R26, R35)
Safety phrases Keep locked up and out of the reach of children (if sold to general public) – Keep container tightly closed and in a well ventilated place – In case of contact with eyes, rinse immediately with plenty of water and seek medical advice – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S7/9, S26, S45)

Mammalian & avian toxicity

Acute data
LD_{Lo} oral human 14 mg kg^{-1} (2).
LC_{50} (9 min) inhalation mouse 750 ppm (3).
LC_{Lo} (6.5 hr) inhalation rabbit 180 ppm (4).

Teratogenicity and reproductive effects
Spermatogenisis and reproductive performance were assessed in eight men and their spouses after accidental exposure to bromine vapour. Two cases of mild oligo-teratoasthenozoospermia (OTA) were diagnosed, with unaffected reproductive performance. Plasma FSH and LH levels were normal in all men. Of five pregnancies conceived soon after exposure, one first-trimester absorption and one late abortion (due to chorioammionitis) occurred (5).

Metabolism and toxicokinetics
Bromine vapours enter body by respiratory system, skin and digestive system; deposited in tissues as bromides (6).

Irritancy
Destructive and painful burns to skin and eyes from contact with liquid or vapour (7).

Other effects

Other adverse effects (human)

Ingestion may cause severe gastroenteritis and death (1).

Chronic bronchitis was the most common disorder of workers in the manufacture of bromine and bromine-containing materials in the former Soviet Union. Pathological changes in the respiratory tract, contact and allergic dermatitis and arterial hypertension were observed and related to exposure levels (8).

Accidental acute exposure of six people to bromine vapours caused respiratory symptoms and first to second degree skin burns over small areas. Six to eight weeks after exposure, some still had symptoms such as cough, chest tightness, shortness of breath, eye irritation, headache, dizziness, fatigue, and memory, sleep and sexual disturbances, but no clinical evidence of adverse effects could be found (9).

Any other adverse effects

Severe exposure may result in pulmonary oedema (7).

Inhalation of vapours may cause chemical pneumonitis (7).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Substances extractable in chloroform: guide level 0.1 mg l^{-1} dry residue (10).

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

Other comments

Three applications of a chemical solution simulating swimming pool run-off water to Kentucky blue grass (*Poa pratensis*) had no phytotoxic effects, even at the highest concentration solutions containing ~100 × the recommended amount of 1.0 to 1.5 μg ml^{-1} bromine (12).

Free bromine average effective Henry's Law constant 0.0293 atm (13).

Levels of bromide in excess of 50 mg kg^{-1} have been detected in herbs imported into Switzerland, although plants were not treated with any bromide-containing pesticide (14).

Bromine toxicity and environmental hazards reviewed (15).

Reviews on physico-chemical properties, human health effects, experimental toxicology, epidemiology, workplace experience and environmental effects listed (16).

Corrosive. Explosion risk.

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B155 bromine chloride

BrCl

BrCl **Mol. Wt.** 115.36 **CAS Registry No.** 13863-41-7

Synonyms bromine monochloride; bromochloride

EINECS No. 237-601-4

Uses In organic addition and substitution reactions. Disinfectant in wastewater treatment.

Physical properties

M. Pt. –66°C **B. Pt.** 10°C (decomp.)
Solubility Organic solvents: carbon disulfide, diethyl ether

Occupational exposure

UN No. 2901 **Conveyance classification** toxic gas, fire intensifying hazard, corrosive

Ecotoxicity

Fish toxicity

Brominated compounds were detected in fathead minnows from bromine/chloride disinfected sewage; concentrations of bromine 5-200 ng g^{-1} for various compounds (1).

Fathead minnows and lake trout with >2 hr exposure to chlorobrominated effluent were capable of tolerating high levels of total residual bromine chloride for longer periods than for fish not previously exposed to the wastewater disinfectant (2).

LC_{50} (96 hr) Atlantic menhaden, Atlantic silverside 0.21-0.23 mg l^{-1} (3).

Invertebrate toxicity

LC_{50} (24, 48, 96 hr) grass shrimp 1.1, 0.8, 0.6 mg l^{-1}, respectively.

LC_{50} (48-96 hr) blue crab 1.2, 0.8 mg l^{-1} (4).

LC_{50} (48 hr) oyster, copepods 0.10-0.21 mg l^{-1}.

LC_{50} (96 hr) shrimp 0.70 mg l^{-1} (5).

Environmental fate

Degradation studies

In water, interacts with ammonia to form bromoamines which are less toxic to fish than chloramines formed when chlorine is used (6).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Chlorides: guide level 25 mg l^{-1} (7).

Included in Schedule 6 (Release Into Land: Prescribed Substances) of Statutory Instrument No. 472, 1991 (8).

Other comments

Readily hydrolyses to HOBr over wide pH range (4).

Oxidising agent.

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B156 bromine pentafluoride

BrF_5

BrF_5 **Mol. Wt.** 174.90 **CAS Registry No.** 7789-30-2

EINECS No. 232-157-8 **RTECS No.** EF 9350000

Uses Fluorinating agent in organic synthesis. Formation of uranium fluorides for isotope enrichment and for fuel element reprocessing.

Physical properties

M. Pt. –61.3°C **B. Pt.** 40.5°C **Specific gravity** 2.466 at 25°C **Volatility** v.den. 6.05

Occupational exposure

DE-MAK 2.5 mg m^{-3} (as F) (total dust)
FR-VME 0.1 ppm (0.7 mg m^{-3})
SE-LEVL 2 mg m^{-3} (as F)
UK-LTEL 0.1 ppm (0.73 mg m^{-3}) **UK-STEL** 0.3 ppm (2.2 mg m^{-3})
US-TWA 0.1 ppm (0.72 mg m^{-3})

UN No. 1745 **HAZCHEM Code** 4WE **Conveyance classification** oxidising substance, toxic, corrosive

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Fluoride: maximum admissible concentration 1500 μg l^{-1} at 8-12°C, 700 μg l^{-1} at 25-30°C (1).
Included in Schedule 6 (Release Into Land: Prescribed Substances) of Statutory Instrument No. 472, 1991 (2).

Other comments

Fire risk. Corrosive. Very reactive, therefore must be handled in resistant materials like nickel, Monel metal or Teflon plastics. Reacts with every known element except inert gases, nitrogen and oxygen (3).
Reviews on human health effects, experimental toxicology and environmental effects listed (4).

References

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B157 bromine trifluoride

BrF_3

BrF_3 **Mol. Wt.** 136.90 **CAS Registry No.** 7787-71-5

EINECS No. 232-132-1

Uses As a fluorinating agent in organic synthesis. Electrolyte solvent. Rocket propellant.

Physical properties

M. Pt. 9°C (decomp.) **B. Pt.** 125°C **Specific gravity** 2.803 at 25°C

Occupational exposure

DE-MAK 2.5 mg m^{-3} (as F) (total dust)
SE-LEVL 2 mg m^{-3} (as F)
UK-LTEL 2.5 mg m^{-3} (as F)

UN No. 1746 **HAZCHEM Code** 4WE **Conveyance classification** oxidising substance, toxic, corrosive

Other effects

Other adverse effects (human)
Corrosive, irritating to skin, eyes, mucous membranes and respiratory tract (1,2).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Fluoride: maximum admissible concentration 1500 μg l^{-1} at 8-12°C, 700 μg l^{-1} at 25-30°C (3).
Included in Schedule 6 (Release Into Land: Prescribed Substances) of Statutory Instrument No. 472, 1991 (4).

Other comments

Very reactive, must be handled in resistant materials such as nickel, Monel metal, Teflon plastics (5).
Numerous violent explosive reactions can occur with organic and inorganic materials.

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B158 bromoacetic acid

$$BrCH_2CO_2H$$

$C_2H_3BrO_2$ **Mol. Wt.** 138.95 **CAS Registry No.** 79-08-3

Synonyms bromoethanoic acid; α-bromoethanoic acid; monobromoacetic acid

EINECS No. 201-175-8 **RTECS No.** AF 5950000

Physical properties

M. Pt. 49-51°C **B. Pt.** 208°C **Flash point** >110°C **Specific gravity** 1.93 at 20°C

Solubility Water: highly soluble. Organic solvents: ethanol

Occupational exposure

UN No. 1938 **HAZCHEM Code** 2X **Conveyance classification** corrosive substance

Supply classification toxic, corrosive

Risk phrases Toxic by inhalation, in contact with skin and if swallowed – Causes severe burns – Very toxic to aquatic organisms (R23/24/25, R35, R50)

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)

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 177 mg kg^{-1} (1).

LD_{50} oral mouse 100 mg kg^{-1} (as 5% solution) (2).

LD_{50} intraperitoneal rat, mouse 50, 66 mg kg^{-1}, respectively (3,4).

LD_{Lo} intravenous mouse 45 mg kg^{-1} (5).

Sub-acute and sub-chronic data

Oral rat 100 mg kg^{-1} single dose or 25 mg kg^{-1} day^{-1} for 14 days produced no adverse spermatogenic effects (1).

Carcinogenicity and chronic effects

Inhalation rat (30 month) total exposure 114 g m^{-3} caused irritation effects to respiratory system (4).

Genotoxicity

In vitro mouse L-1210 leukocytes induced DNA damage (6).

Salmonella typhimurium TA100 Ames fluctuation test positive (7).

Escherichia coli PQ 37 SOS chromotest negative (7).

Other effects

Any other adverse effects

Corrosive to the skin, although the effects are not necessarily immediate, blisters may not appear for 12 hr or more. Application of a 10% aqueous solution to rabbit skin caused death within 16 hr (8).

Legislation

Included in Schedule 6 (Release Into Land: Prescribed Substances) of Statutory Instrument No. 472, 1991 (9).

Other comments

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

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B159 bromoacetonitrile

$BrCH_2CN$

C_2H_2BrN **Mol. Wt.** 119.95 **CAS Registry No.** 590-17-0

Synonyms bromomethyl cyanide

EINECS No. 209-672-1 **RTECS No.** AL 7970000

Physical properties

B. Pt. 60-62°C at 24 mmHg **Flash point** 110°C **Specific gravity** 1.722

Genotoxicity

Salmonella typhimurium TA98, TA100 with metabolic activation negative (1).

The *in vitro* reaction of bromoacetonitrile with calf thymus DNA produced a fluorescent alkylation product, a 7-(cyanomethyl)guanine adduct (2).

Legislation

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

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

Other comments

Corrosive. Lachrymatory.

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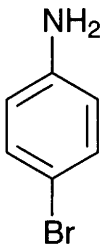
B160 4-bromoaniline



C_6H_6BrN **Mol. Wt.** 172.02 **CAS Registry No.** 106-40-1

Synonyms *p*-bromoaniline; 4-bromobenzenamine; *p*-bromophenylamine

EINECS No. 203-393-9 **RTECS No.** BW 9280000

Uses Synthesis of azo dyestuffs and dihydroquinazolines.

Physical properties

M. Pt. 62-64°C **Specific gravity** 1.497 at 99.6°C with respect to water at 4°C
Solubility Organic solvents: diethyl ether, ethanol

Ecotoxicity

Bioaccumulation
Calculated bioconcentration factor 4.4 (1).

Environmental fate

Degradation studies
Purified enzymes of the soil fungus *Geotrichum candidum* biotransformed 4-bromoaniline to 4,4'-dibromoazobenzene (2).
A strain of *Moraxella* sp. used 4-bromoaniline as sole source of carbon and nitrogen (3).

Abiotic removal
Significantly absorbs UV light above 290 nm in alcohol solution indicating a potential for direct photolysis in the environment (4).
Estimated $t_{1/2}$ with sunlight-produced hydroxyl radicals in a typical ambient atmosphere 2 days (5).

Adsorption and retention
Soil adsorption studies using four silt loam soils and a 2-hr adsorption period measured a soil adsorption coefficient of 7 (6).
Undergoes rapid and reversible covalent bonding with humic materials in aqueous solution (7).

Mammalian & avian toxicity

Acute data
LD_{50} oral mouse, rat 289, 456 mg kg^{-1}, respectively (8,9).
LD_{50} intraperitoneal mouse 248 mg kg^{-1} (9).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA1535, TA1537 with and without metabolic activation negative (10).
In vitro rat liver cells induced unscheduled DNA synthesis (11).

Legislation

Included in Schedule 6 (Release into Land: Prescribed Substances) of Statutory Instrument No. 472, 1991 (12).

Other comments

Toxicity and hazards reviewed (13).

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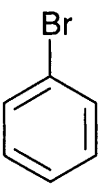
B161 bromobenzene



C_6H_5Br **Mol. Wt.** 157.01 **CAS Registry No.** 108-86-1

Synonyms phenyl bromide

EINECS No. 203-623-8 **RTECS No.** CY 9000000

Uses Intermediate in organic synthesis. Solvent. Motor oil and fuel additive.

Physical properties

M. Pt. –31°C **B. Pt.** 156°C **Flash point** 51°C **Specific gravity** 1.4952 at 20°C with respect to water at 4°C
Partition coefficient log P_{ow} 2.99 **Volatility** v.p. 3.3 mmHg at 20°C ; v.den. 5.4
Solubility Water: 450 mg l^{-1} at 30°C. Organic solvents: benzene; miscible with chloroform, diethyl ether, ethanol, petroleum spirit

Occupational exposure

UN No. 2514 **HAZCHEM Code** 2Y **Conveyance classification** flammable liquid
Supply classification irritant
Supply classification dangerous for the environment

Risk phrases Flammable – Irritating to the skin – Toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment (R10, R38, 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_{50} (96 hr) fathead minnow 35.7 mg l^{-1} (1).
Invertebrate toxicity
LD_{50} (24 hr) *Ceriodaphnia dubia* 5.8 mg l^{-1} (1).
EC_{50} (30 min) *Photobacterium phosphoreum* 9.46 mg l^{-1} Microtox test (2).

Mammalian & avian toxicity

Acute data
LC_{50} oral guinea pig, rabbit 1700, 3300 mg kg^{-1}, respectively (3).
LD_{50} oral mouse, rat 2700, 2699 mg kg^{-1}, respectively (4,5).
LC_{50} (2 hr) inhalation mouse 21 g m^{-3} (4).
LD_{50} intraperitoneal rat 3880 mg kg^{-1} (6).
Mice given a single intraperitoneal dose of ≥754 mg l^{-1} revealed degeneration and necrosis of the glands of Bowman and degenerative changes in the olfactory epithelium. Focal degeneration and necrosis were found in the lateral nasal glands and cyst-like dilation of acini in the lateral nasal glands (7).

Sub-acute and sub-chronic data
Inhalation mice, rats, rabbit (4 hr) 250-3400 ppm. 48 hr after termination of exposure revealed injury to Clara cells and adjacent epithelium in mouse bronchioli at a concentration of 250 and 1000 ppm and to Clara cells of rat bronchi and bronchioli (1000 ppm) and rabbit bronchi (2500 ppm and 3400 ppm). Kidney toxicity was observed in mice (20% showed tubular necrosis and elevated concentration of plasma area) and rats (all had elevated plasma concentrations of creatinine) exposed to 1000 ppm (8).
Experiments in mice suggest that hexosaminidase activity and the isoenzyme pattern in urine can be used to indicate kidney damage by bromobenzene intoxication (9).

Metabolism and toxicokinetics
Absorbed through lungs, gastrointestinal tract and intact skin. Excreted as catechol derivatives, both free and conjugated with sulfate or mercapturic acid (10).
4 hr after intraperitoneal administration to rats, bromobenzene was found in adipose tissue ≥300-fold than in other tissues. 85% was excreted in urine in 24 hr (11).
May be metabolised to an epoxide and then excreted in bile, re-absorbed through enterohepatic circulation and metabolised in several steps to *S-p*-bromophenyl mercapturic acid which is then excreted in urine (12).
Intraperitoneal phenobarbitol-induced rats 0.5-1.5 mmol kg^{-1}. Three dimethoxythioanisoles and eight bromodimethoxythioanisoles were formed by alkaline permethylation of rat urine 0-24 hr after treatment with bromobenzene. The major thioanisole was 2,5-dimethoxythioanisole, which arises from 2,5-dihydroxyphenylmercapturic acid, also present in the rat urine. The yield of quinone-derived mercapturic acids was <1% of the administered dose; that of epoxide-derived mercapturic acids was 40% of the dose (13).
Intragastric administration mice (unspecified dose) caused liver necrosis, increased lipid peroxidation, decreased protein thiols, GSH content and calcium uptake (14).

Genotoxicity

Salmonella typhimurium TA1535/pSK1002 *umu* test negative (15).
Escherichia coli polA+/A- DNA modifying activity weakly positive (16).
Micronucleus test intraperitoneal mouse (24 hr) 125 mg kg^{-1} positive (17).
Increased formation of micronucleated polychromatic erythrocytes in bone marrow of mice after intraperitoneal injection of up to 70% of LD_{50} (18).

Other effects

Any other adverse effects

The concentration of α-1-acid glycoprotein in the blood of rats with bromobenzene-induced liver injury increased 2-3.5 × the normal level at 24 hr after intoxication; the plasma albumin concentration was unaffected (19).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Substances extractable in chloroform: guide level 0.1 mg l^{-1} dry residue (20).

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

Other comments

Physico-chemical properties, human health effects and experimental toxicology reviewed (22,23).

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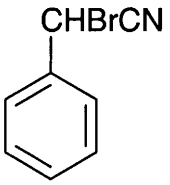
B162 α-bromobenzyl cyanide



C_8H_6BrN **Mol. Wt.** 196.05 **CAS Registry No.** 5798-79-8

Synonyms α-bromophenylacetonitrile; α-bromo-α-tolunitrile; α-bromobenzylnitrile

EINECS No. 227-348-8 **RTECS No.** AL 8050000

Uses Chemical weapon.

Physical properties

M. Pt. 29°C **B. Pt.** 242° (decomp.) **Specific gravity** 1.539 at 29°C with respect to water at 4°C **Volatility** v.p. 0.012 mmHg at 20°C ; v.den. 6.8

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

Occupational exposure

FR-VME 5 mg m^{-3} (as HCN) **SE-CEIL** 5 mg m^{-3} (as CN)

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

UN No. 1694 **HAZCHEM Code** 2XE **Conveyance classification** toxic substance

Mammalian & avian toxicity

Acute data

LD_{Lo} oral rat 100 mg kg^{-1} (1).

LC_{50} (duration unspecified) inhalation human 3500 mg m^{-3} (2).

Legislation

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

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

Other comments

Strong lachrymator (5).

References

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B163 2-bromo-2-(bromomethyl)pentanedinitrile

$BrCH_2C(Br)(CN)CH_2CH_2CN$

$C_6H_6Br_2N_2$ **Mol. Wt.** 265.94 **CAS Registry No.** 35691-65-7

Synonyms 1,2-dibromo-2,4-dicyanobutane; Tektamer 38

EINECS No. 252-681-0 **RTECS No.** MA 5599000

Uses Biocide in liquid soaps and cosmetic formulations. Paper coatings for food products. Adhesives. Latex paints.

Physical properties

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

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) bluegill sunfish, rainbow trout 9-12 mg l^{-1} (1).

Environmental fate

Degradation studies

Using ^{14}C compound in activated sludge, no significant impact on the microbial population in a 10-day period. Complete degradation occurred in 24 hr at exposure of ≤99 ppm (2).

Abiotic removal

Undergoes rapid alkaline catalysed hydrolysis (3).

Adsorption and retention

Expected to be very mobile and non-persistent in aquatic and soil environments (3).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 1800 mg kg^{-1} (1).

Irritancy

Severe eye irritant (3).

Sensitisation

Human skin sensitiser (3).

Genotoxicity

Positive in one mutagenicity assay, but this positive finding was not confirmed in other mutagenicity studies (3).

Legislation

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

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

EPA Toxicity Class III (3).

Other comments

Effective antimicrobial compared to other cosmetic preservatives. Activity decreased with heat treatment (6).

Evaluation of fungitoxicity *in vitro* to 26 species of phytopathogenic fungi (1).

Can cause plasmid-mediated bacterial resistance to *Pseudomonas* spp. (2).

References

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B164 1-bromobutane

$$CH_3(CH_2)_3Br$$

C_4H_9Br **Mol. Wt.** 137.02 **CAS Registry No.** 109-65-9

Synonyms butyl bromide

EINECS No. 203-691-9 **RTECS No.** EJ 6225000

Uses In preparation of drugs.

Physical properties

M. Pt. –112.4°C **B. Pt.** 101.4°C **Flash point** 18.3°C (open cup) **Specific gravity** 1.258 at 20°C with respect to water at 4°C **Partition coefficient** log P_{ow} 2.75 **Volatility** v.den. 4.72
Solubility Organic solvents: acetone, chloroform, diethyl ether, ethanol

Occupational exposure

UN No. 1126 **HAZCHEM Code** 2[illegible]E **Conveyance classification** flammable liquid

Mammalian & avian toxicity

Acute data
LC_{50} (30 min) inhalation rat 237 g m^3 (1).
LD_{50} intraperitoneal rat, mouse 4450-6680 mg kg^{-1} (2).

Carcinogenicity and chronic effects
The effect on lung tumour frequency in laboratory mice at low doses was investigated. The toxicity of butyl bromide was too great to allow testing at dosages used for other halides (3).

Legislation

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

Other comments

Review of toxic effects in laboratory animals (5).
Toxicity of brominated hydrocarbons given (6).
Flammable.

References

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B165 2-bromobutane

$$CH_3CH_2CHBrCH_3$$

C_4H_9Br **Mol. Wt.** 137.02 **CAS Registry No.** 78-76-2

Synonyms *sec*-butyl bromide; methylethylbromomethane

EINECS No. 201-140-7 **RTECS No.** EJ 6228000

Physical properties

M. Pt. –112°C **B. Pt.** 91°C **Flash point** 21°C **Specific gravity** 1.2530 at 25°C with respect to water at 4°C
Solubility Organic solvents: diethyl ether, ethanol

Occupational exposure

UN No. 2339 **HAZCHEM Code** 2[illegible]E **Conveyance classification** flammable liquid

Mammalian & avian toxicity

Carcinogenicity and chronic effects
Intraperitoneal injection of 3000 mg kg^{-1} (total dose given in 24 injections over 24 wk) to 8-wk-old mice caused a slight but significant increase in lung tumours (1).

Legislation

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

Other comments

Narcotic (3).

References

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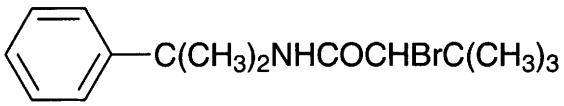
B166 bromobutide



$C_{15}H_{22}BrNO$ **Mol. Wt.** 312.25 **CAS Registry No.** 74712-19-9

Synonyms butanamide, 2-bromo-3,3-dimethyl-*N*-(1-methyl-1-phenylethyl)-; 2-bromo-*N*-(α,α-dimethylbenzyl)-3,3-dimethylbutyramide; S-47; Sumiherb

RTECS No. EJ 3500750

Uses Selective herbicide.

Physical properties

M. Pt. 180°C

Solubility Water: 3.54 mg l^{-1}

Ecotoxicity

Fish toxicity

LC_{50} (48 hr) carp >10 mg l^{-1} (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat >5000 mg kg^{-1} (1).

LD_{50} percutaneous rat >5000 mg kg^{-1} (1).

Legislation

Limited Under EC Directive on Drinking Water Quality 80/777/EEC. Pesticides and related products: maximum admissible concentration 0.1 μg l^{-1} (2).

Included in Schedule 6 (Release into Land: Prescribed Substances) of Statutory Instrument No. 472, 1991 (3).

Other comments

EPA Toxicity Class IV.

References

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B167 bromochloroacetonitrile

BrCHCl(CN)

$C_2HBrClN$ **Mol. Wt.** 154.39 **CAS Registry No.** 83463-62-1

RTECS No. AL 8010000

Environmental fate

Abiotic removal

Hydrolytic $t_{1/2}$ 55 hr at pH 8.3 (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).

Oral ♀ A/J mice 10 mg kg^{-1} in 10% Emulphor 3 × wk^{-1} for 8 wk, 32/40 survived for 9 months, compared with 31/40 of controls; 10/32 developed lung adenomas compared with 3/31 of controls, and the average number of adenomas per mouse was 0.34 compared with 0.10 in the control group (3).

Dermal ♀ Sencor mice (2 wk) 200, 400 and 800 mg kg^{-1} 3 × $week^{-1}$; 1/35, 7/37 and 6/37 mice developed carcinoma, respectively. At the highest dose, 3/37 also developed papilloma (4).

Teratogenicity and reproductive effects

In vivo teratology screening rat (route/dose unspecified) reduced postnatal growth (5).

Metabolism and toxicokinetics

Rats given 116 mg kg^{-1} in tricaprylin by gavage excreted 12.8% of the dose in urine as thiocyanate within 24 hr (6).

Genotoxicity

Salmonella typhimurium reverse mutation assay TA98, TA1537, TA1538 with and without metabolic activation negative; TA100 without metabolic activation negative with metabolic activation positive; TA1535 with and without metabolic activation positive (4).

Chinese hamster ovary cells *in vitro* sister chromatid exchange positive (4).

Human lymphoblast cell line, DNA strand breaks without metabolic activation positive (7).

CD-1 mice *in vivo* micronucleus test negative (4).

$B6C3F_1$ mice *in vivo* sperm morphology assay negative (8).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Organochlorine compounds: guide level 1 μg l^{-1} (9).

Included in Schedule 6 (Release into Land: Prescribed Substances) of Statutory Instrument No. 472, 1991 (10).

Other comments

Contaminant in water samples, caused by interaction of chlorine on humic substances (11,12).

Human health effects and experimental toxicology reviewed (13,14).

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B168 bromochlorodifluoromethane

$CBrClF_2$

$CBrClF_2$ **Mol. Wt.** 165.36 **CAS Registry No.** 353-59-3

Synonyms chlorodifluorobromomethane; chlorodifluoromonobromomethane

EINECS No. 206-537-9 **RTECS No.** PA 5270000

Uses Blowing agents. Foaming agents. Fire extinguishers.

Physical properties

M. Pt. –159.5°C **B. Pt.** –4.01 to –3.3°C **Volatility** v.p. 1260 mmHg at 10°C

Occupational exposure

UN No. 1974 **HAZCHEM Code** 2RE **Conveyance classification** non-flammable non-toxic gas

Mammalian & avian toxicity

Acute data

LC_{50} (4 hr) inhalation rat 211 mg l^{-1} (1).

EC_{50} (5 min) inhalation dog 1.9% v/v cardiac sensitisation to epinephrine-induced arrhythmias (2).

Single inhalation exposure (2 hr) rats, guinea pigs concentrations of 5-10% were the highest non-effective dose (3).

LC_{Lo} (3-5 hr) repeated dose inhalation dogs, cats, guinea pigs 2-7% caused reversible heart muscle lesion and fatty livers (3).

Inhalation human (1 min) highest no-effect dose 4-5%. Prolonged exposure at this concentration caused dizziness, paresthesia of the fingers and toes. After 2 min, central nervous system stimulation and spontaneous transient heartbeat disorder occurred. Recovery rapid in fresh air with no after effects. Inhalation rats, mice exposure >10% caused tremors within 10 min. Inhalation rats, mice, guinea pigs, dogs, monkeys concentrations of 5-30% caused central nervous system stimulation, decreased systolic blood pressure and cardiac contractile force in rats (4).

Sub-acute and sub-chronic data

Inhalation rats (3 wk) 3300 ppm 6 hr day^{-1}, 5 days wk^{-1} no adverse effects (4).

Inhalation dog (4 wk) 3300 ppm 6 hr day^{-1} 5 days wk^{-1}, cardiac sensitivity when blood concentration reached 21-24 $\mu g\ l^{-1}$ (4).
Inhalation rats (2, 4 or 12 wk) (concentration unspecified) reduced haemoglobin concentration, decreased haematocrit value, leukocyte, erythrocyte and thrombocyte counts. No organ damage apparent (5).
Repeated inhalation (dose and duration unspecified) rats increased cholesterol and phospholipids, decreased blood serum sodium, potassium and calcium counts (6).

Genotoxicity

Salmonella typhimurium TA1535 with or without metabolic activation positive; TA98, TA100, TA1537, TA1538, with or without metabolic activation negative (7).
L-5178Y tk^+/tk^- mouse lymphoma micronuclei assay negative (7).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Organochlorine compounds: guide level 1 $\mu g\ l^{-1}$. Haloform concentrations must be as low as possible (8).
Included in Schedules 4 and 6 (Release into Air/Land: Prescribed Substances) of Statutory Instrument No. 472, 1991 (9).

Other comments

Atmospheric pollutant. Atmospheric abundance increasing by 12% yr^{-1} (10).
Spruce trees *Picea abies* L. Karst were fumigated for 41 days with 10 ppb bromochlorodifluoromethane, resulting in non-specific reactions to a pollutant climate (changes in needle fresh weight, protein content, and pigment pattern) and a specific reaction to bromochlorodifluoromethane, namely, an up to four-fold increase in the activity of glutathione-S-transferase, a constitutive detoxification enzyme in spruce trees (11).
General review of health and safety (12).
Review of toxicology (13).
Reviews on physico-chemical properties, human health effects, exposure levels, workplace experience and environmental effects listed (14).

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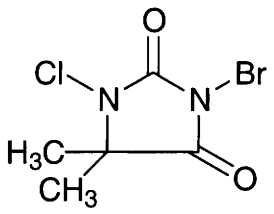
B169 3-bromo-1-chloro-5,5-dimethylhydantoin



$C_5H_6BrClN_2O_2$ **Mol. Wt.** 241.47 **CAS Registry No.** 126-06-7

Synonyms 3-bromo-1-chloro-5,5-dimethyl-2,4-imidazolidinedione

EINECS No. 204-766-9 **RTECS No.** MT 9195500

Uses Disinfecting agent for swimming pool and water cooling systems.

Physical properties

M. Pt. 160-164°C

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) adult fathead minnow 0.46-0.57 mg l^{-1} and juvenile fathead minnow 0.28-0.41 mg l^{-1} (1).
LC_{50} (96 hr) bluegill sunfish 0.56-0.71 mg l^{-1} (1).
LC_{50} (96 hr) rainbow trout 0.87 mg l^{-1} (2).
LC_{50} (24 hr) sheepshead minnow 20 mg l^{-1} (2).

Invertebrate toxicity

EC_{50} (48 hr) *Daphnia magna* 0.47 mg l^{-1} (2).
LC_{50} (48 hr) grass shrimp 13 mg l^{-1} (2).
LC_{50} (48 hr) American oyster >640 mg l^{-1} (2).

Environmental fate

Degradation studies

During a ^{14}C biodegradation study with activated sludge it was observed that dehalogenation to 5,5-dimethylhydantoin (RN 77-77-4) occurred, which in turn decreased to <1 ppm in 3 days, and by day-19, 94% of the ^{14}C had been recovered as carbon dioxide (2).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 200 mg kg^{-1} (2).

Sub-acute and sub-chronic data

Three 5-month-old ♀ rats receiving 10 and 60 mg kg^{-1} day^{-1} (duration and route of exposure unspecified) showed no gross pathological changes, no significant changes to haemoglobin, erythrocytes, leucocytes, no internal disturbances and no treatment-related lesions on autopsy to heart, lungs, gastrointestinal tract and kidneys (2).

Teratogenicity and reproductive effects

Oral ♀ rat 5, 7.5 and 10 mg kg^{-1} uterine examination values were unaffected, however embryo lethality was noted in the high-dose groups. No malformations or increased developmental variants were observed in the range 500-4500 mg kg^{-1} (2).

Metabolism and toxicokinetics

Using ^{14}C in rats at 20 and 100 mg kg^{-1} doses, an average of 91% was found in the urine, with 88% elimination

during the first 24 hr. No measurable ^{14}C was observed in tissues from the 20 mg kg^{-1} dose, but some ^{14}C was found in kidney and bone of rats receiving the higher dose (2).

Genotoxicity

Salmonella typhimurium TA98, TA100 with and without metabolic activation negative.
Saccharomyces cerevisiae with and without metabolic activation negative (2).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Organochlorine compounds: guide level 1 $\mu g\ l^{-1}$ (3).
Included in Schedule 6 (Release into Land: Prescribed Substances) of Statutory Instrument No. 472, 1991 (4).

Other comments

Maximum permissible concentration of dimethylhydantoin in water reservoir 1 mg l^{-1} (5).

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B170 1-bromo-2-chloroethane

$$BrCH_2CH_2Cl$$

C_2H_4BrCl **Mol. Wt.** 143.41 **CAS Registry No.** 107-04-0

Synonyms ethylene chlorobromide; *syn*-chlorobromoethane

EINECS No. 203-456-0 **RTECS No.** KH 6500000

Physical properties

M. Pt. –16.6°C **B. Pt.** 106-107°C **Specific gravity** 1.7392 at 20°C with respect to water at 4°C

Ecotoxicity

Bioaccumulation
Calculated bioconcentration factor 9.6 suggesting accumulation in aqueous organisms is unlikely (1).

Environmental fate

Abiotic removal
Estimated photochemical $t_{1/2}$ with hydroxyl radicals 49.4 days (2).
Volatilisation $t_{1/2}$ is 4.7 hr from a model river 1 m deep with a 1 m sec^{-1} current and a 3 m sec^{-1} wind speed (1).

Adsorption and retention
Using the water solubility of 6.83 g l^{-1} at 30°C, estimated soil adsorption coefficient is 34 which suggests adsorption to soil and sediment is unlikely (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 64 mg kg^{-1} (3).

Genotoxicity

Salmonella typhimurium TA100 with metabolic activation positive (4).

In vitro Chinese hamster ovary cells sister chromatid exchange positive (5).

Genetic activity evaluation in *Drosophila melanogaster* germ cells and somatic tissue suggests that the genotoxicity of 1-bromo-2-chloroethane is caused by the glutathione mediated pathway (6).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Organochlorine compounds: guide level 1 $\mu g\ l^{-1}$ (7).

Included in Schedule 6 (Release into Land: Prescribed Substances) of Statutory Instrument No. 472, 1991 (8).

Other comments

Reviews on human health effects, experimental toxicology and environmental effects listed (9).

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B171 bromochloromethane

$BrCH_2Cl$

CH_2BrCl **Mol. Wt.** 129.38 **CAS Registry No.** 74-97-5

Synonyms chlorobromomethane; methylene chlorobromide

EINECS No. 200-826-3 **RTECS No.** PA 5250000

Uses Solvent. Component in fire extinguishers. Diesel fuel additive. Nail varnish remover.

Physical properties

M. Pt. –88°C **B. Pt.** 68°C **Specific gravity** 1.9344 at 20°C with respect to water at 4°C

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

Occupational exposure

DE-MAK 200 ppm (1100 mg m^{-3})
FR-VME 200 ppm (1050 mg m^{-3})
UK-LTEL 200 ppm (1080 mg m^{-3}) **UK-STEL** 250 ppm (1340 mg m^{-3})
US-TWA 200 ppm (1060 mg m^{-3})

UN No. 1887 **HAZCHEM Code** 2Z **Conveyance classification** toxic substance

Ecotoxicity

Bioaccumulation

Based on the water solubility of 16.7 g l^{-1} at 25°C and log P_{ow} 1.41, bioconcentration factors have been calculated as 3 and 7, respectively, which suggests accumulation in fish and aquatic organisms will not occur to any significant extent (1,2).

Environmental fate

Degradation studies

In a screening test, bromochloromethane at 5 or 10 mg l^{-1} underwent 100% degradation within seven days using a settled domestic wastewater inoculum under aerobic conditions. Complete degradation followed with three successive subcultures (3,4).

Reported to undergo microbial degradation under anoxic conditions when cultured with soil bacteria (5).

Abiotic removal

Does not absorb ultraviolet light at >290 nm which suggests direct photochemical degradation in the atmosphere or water is unlikely (6).

Estimated photochemical $t_{1/2}$ with hydroxyl radicals 160 days suggesting it will not be a significant removal process (7).

Hydrolysis in environmental waters is not expected to be a significant method of removal estimated $t_{1/2}$ is 44 yr (8).

Volatilisation $t_{1/2}$ ~1 hr, significant removal process from either moist or dry soil (9).

Adsorption and retention

Soil adsorption coefficients of 21 and 139 have been calculated based on water solubility and log P_{ow}, respectively, indicating high to very high mobility in soil (10).

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse, rat 4300, 5000 mg kg^{-1}, respectively (11,12).

LC_{50} (7 hr) inhalation mouse 3000 ppm (13).

Metabolism and toxicokinetics

Dogs exposed to 1000 ppm bromochloromethane in air 7 hr day^{-1} 5 day wk^{-1}, inorganic bromide detected in blood serum and urine. During the 3rd wk, serum inorganic bromide had increased from 5-10 mg 100 ml^{-1} to >200 mg. By the 13th and 14th wk, the concentration of inorganic bromide in blood was >300 mg 100 ml^{-1} of inorganic bromide in blood (14).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537, TA1538 without metabolic activation negative (15).

Other effects

Any other adverse effects

Affects myocardial energy metabolism. Anaesthetised dogs 45 min exposure to 0.3-1.0% in oxygen resulted in elevation of venous blood PO_2 and O_2 content (16,17).

In rats metabolic products included carboxyhaemoglobin (18).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Organochlorine compounds: guide level 1 $\mu g\ l^{-1}$ (19).
Included in Schedule 6 (Release into Land: Prescribed Substances) of Statutory Instrument No. 472, 1991 (20).

Other comments

Contaminant of water samples in most industrial countries.
Reviews on human health effects, epidemiology, workplace experience, experimental toxicology and environmental effects listed (21).
Moderate narcotic action.

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B172 1-bromo-3-chloropropane

$$Br(CH_2)_3Cl$$

C_3H_6BrCl **Mol. Wt.** 157.44 **CAS Registry No.** 109-70-6

Synonyms 3-bromopropyl chloride; 1,3-CHBP; o-chlorobromopropane; trimethylene bromochloride

EINECS No. 203-697-1 **RTECS No.** TX 4113000

Physical properties

M. Pt. –59°C **B. Pt.** 144-145°C **Specific gravity** 1.5969 at 20°C with respect to water at 4°C
Solubility Organic solvents: chloroform, diethyl ether, ethanol

Ecotoxicity

Fish toxicity
LC_{50} (24 hr) goldfish 75 mg l^{-1} (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat, mouse 930, 1290 mg kg^{-1}, respectively (2,3).
LC_{Lo} (2 hr) inhalation mouse 7270 mg kg^{-1} (3).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Organochlorine compounds: guide level 1 μg l^{-1} (4).
Included in schedule 6 (Release into Land: Prescribed Substances) of Statutory Instrument No. 472, 1991 (5).

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B173 bromodichloromethane

$CHBrCl_2$

$CHBrCl_2$ **Mol. Wt.** 163.83 **CAS Registry No.** 75-27-4
Synonyms dichlorobromomethane
EINECS No. 200-856-7 **RTECS No.** PA 5310000
Uses Fire extinguisher fluid. Solvent. Intermediate in organic synthesis.

Physical properties

M. Pt. –55°C **B. Pt.** 90°C **Specific gravity** 1.97 **Volatility** v.p. 50 mmHg at 20°C

Occupational exposure

UN No. 2810

Environmental fate

Anaerobic effects
IC_{50} 1.6 mg l^{-1} at 35°C, anaerobic toxicity assay with methanogenic bacteria (1).

Degradation studies

>50% degradation in bacterial cultures after 8 wk under anaerobic conditions. No degradation in sterile controls (2).

Total degradation within 2 wk in anaerobic tests using mixed methanogenic bacterial cultures from sewage effluents. No degradation in aerobic tests in sterile or seeded conditions (3).

Degradation 28-day incubation bromodichloromethane in static flask screening test removed 51-59% (4).

Abiotic removal

Aqueous hydrolysis at 25°C and pH 7, estimated $t_{1/2}$ 137 yr (5).

50% of applied amount volatilised from soil columns in laboratory studies of transport and fate mechanisms (6).

Adsorption and retention

Water infiltration study in the Rhine river, the Netherlands, detected high soil mobility (7).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 450 mg kg^{-1} (8).

Carcinogenicity and chronic effects

Inadequate evidence for carcinogenicity to humans, sufficient evidence for carcinogenicity to animals, IARC classification group 2B (9).

National Toxicology Program evaluation of bromodichloromethane in rats and mice by gavage, clear evidence of carcinogenicity (10).

In a 2-yr study, ♂ F344/N rats given 0, 50 and 100 mg kg^{-1} day^{-1} by oral gavage in corn oil, 0/50, 1/50 and 13/50, respectively, developed kidney tubular cell neoplasms; 0/53, 13/50 and 45/50, respectively, developed cancer of the large intestine. In ♀ rats, 0/50, 1/50 and 15/50, respectively, developed kidney tubular cell neoplasms; 0/46, 0/50 and 12/47, respectively, developed cancer of the large intestine. In ♂ $B6C3F_1$ mice given 0, 25 and 50 mg kg^{-1} day^{-1} by corn oil gavage, 1/49, 2/50 and 9/50 developed kidney tubular cell neoplasms. In ♀ mice given 0, 75 and 150 mg kg^{-1} day^{-1}, 3/50, 18/48 and 29/50 developed hepatocellular neoplasms (11).

Oral F344 rats (52 wk) 22 and 39 mg kg^{-1} in drinking water did not produce any systemic toxicity, nor any lesions in the reproductive organs and no tumours were detected in any tissues. The high concentration dose caused a significant decrease in the mean straight-line, average path and curvilinear velocities of sperm from the cauda epididymis (12).

Teratogenicity and reproductive effects

Gavage Sprague-Dawley rats (6-15 day gestation) 0, 50, 100, 200 mg kg^{-1} decreased maternal weight gain and kidney weight at 200 mg kg^{-1}. No increase in incidence of resorptions, litter size, foetal weight, external or visceral malformations. Increased incidence of sternum aberrations at 100 or 200 mg kg^{-1} (13).

Metabolism and toxicokinetics

Oral ♂ rats single doses of 1 or 100 mg kg^{-1} and 10 day repeat doses of 10 or 100 mg kg^{-1} radiolabelled bromodichloromethane. 80-90% metabolised within 24 hr. Urinary and faecal elimination 4-5% and 1-3% of dose, respectively. Persistence in tissues was 3-4% 24 hr after single dose, mainly in liver (14).

Oral rat single dose 20 mg kg^{-1} ^{14}C-bromodichloromethane was cleared rapidly. 32% recovered from gut and carcass after 3 hr and 41% after 6 hr. Most recovered from stomach. Fat contained more than other tissue. <1% eliminated via urine (15).

Genotoxicity

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

Salmonella typhimurium TA100 with metabolic activation positive, provided the bacteria are exposed in closed container to the vapour (17).

Escherichia coli PQ37 SOS chromotest with metabolic activation induced primary DNA damage (18).

Pleurodeles waltl larvae newt micronucleus assay detected clastogenic effect on peripheral blood erythrocytes (18).

In vitro Chinese hamster ovary cells with metabolic activation chromosome aberrations positive (19).

In vitro human lymphocyte sister chromatid exchange positive (20).
In vivo mice without metabolic activation micronucleus test negative (21).
Rat liver unscheduled DNA synthesis test negative (22).

Other effects

Any other adverse effects

Intraperitoneal ♂ Sprague-Dawley rats single non-lethal dose of 3 mmol kg^{-1} caused increased blood urea nitrogen, reduced renal concentrating ability (measured by H_2O intake/output ratios, urinary total osmolality and electrolyte levels), and reduced glomerular filtration rate. The largest effects on blood urea nitrogen and glomerular filtration rate were observed at 24 hr and 21-24 hr post-administration, respectively (23).
Intraperitoneal ♂ Sprague-Dawley rats single non-lethal dose of 3 mmol kg^{-1} caused impaired proximal tubular function, which appears to be the primary event leading to further signs of renal dysfunction (24).
Gastric gavage rat, evidence of fatty liver infiltration and haemorrhaging in the adrenal glands, lungs and brain (8).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Organochlorine compounds: guide level 1 $\mu g\ l^{-1}$. Haloform concentrations must be as low as possible (25).
Included in Schedule 6 (Release into Land: Prescribed Substances) of Statutory Instrument No. 472, 1991 (26).

Other comments

From chlorination of water. Contaminant in drinking, surface, groundwater and seawater (27-30).
In effluent from industrial wastewater discharges and wastewater treatment facilities (31,32).
Review and discussion of toxicity of brominated trihalomethanes (33).
Human health effects, environmental effects, exposure levels and experimental toxicology reviewed (34,35).
Mean levels of bromodichloromethane of 7-22 ng g^{-1} (dry wt.) detected in marine algae (36).

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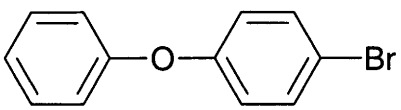
B174 4-bromodiphenyl ether



$C_{12}H_9BrO$ **Mol. Wt.** 249.11 **CAS Registry No.** 101-55-3

Synonyms 4-bromophenyl phenyl ether; 1-bromo-4-phenoxybenzene

EINECS No. 202-952-4

Physical properties

M. Pt. 18°C **B. Pt.** 305°C **Flash point** >110°C **Specific gravity** 1.423

Ecotoxicity

Invertebrate toxicity

EC_{50} (48 hr) *Daphnia magna* 0.36 mg l^{-1} (1).

Environmental fate

Anaerobic effects

Does not inhibit anaerobic digestion in laboratory trials at 100 mg l^{-1} (2).

Degradation studies

Biodegradable (3).

Metabolised in soil by *Pseudomonas* sp. to phenol and 2-phenoxymuconic acid derivatives (4).

Sphingomonas sp. strain 553, enriched from soil samples of an industrial waste deposit, utilises 4-bromodiphenyl ether as sole carbon and energy source. The first step in metabolism is 1,2-dioxygenation to form unstable phenolic hemiacetals. Phenol and catechol are formed as intermediates, which then follow the 3-oxoadipate pathway. The formation of phenol, catechol, halophenol and halocatechol implies non-specific action of the dioxygenating enzyme (5).

Other effects

Any other adverse effects

Oral mice (14-day and 90-day studies), central nervous system depression and behavioural changes were observed. The liver and immune system were sensitive target areas, ♂ more sensitive than ♀ mice (6).

Legislation

Included in Schedule 6 (Release into Land: Prescribed Substances) of Statutory Instrument No. 472, 1991 (7).

Other comments

Contaminant in water samples. Occurs in effluent from sewage sludge (8,9).
Toxicity reviewed (10).
Removal from drinking water discussed (11).
Reviews on human health effects, experimental toxicology and environmental effects listed (12).

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B175 bromoethane

$$CH_3CH_2Br$$

C_2H_5Br **Mol. Wt.** 108.97 **CAS Registry No.** 74-96-4

Synonyms ethyl bromide; bromic ether; hydrobromic ether

EINECS No. 200-825-8 **RTECS No.** KH 6475000

Uses Ethylating agent in organic synthesis. Refrigerant and extraction solvent. Investigated as a possible substitute for chlorofluorocarbons in compression heat pumps.

Physical properties

M. Pt. –114°C **B. Pt.** 37-40°C **Flash point** –23°C **Specific gravity** 1.460 at 20°C with respect to water at 4°C
Partition coefficient log P_{ow} 1.61 **Volatility** v.p. 400 mmHg at 21°C ; v.den. 3.75
Solubility Water: 10.67 g l^{-1} at 0°C. Organic solvents: miscible with chloroform, diethyl ether, ethanol

Occupational exposure

FR-VME 200 ppm (890 mg m^{-3})
UK-LTEL 200 ppm (906 mg m^{-3}) **UK-STEL** 250 ppm (1130 mg m^{-3})
US-TWA 5 ppm (22 mg m^{-3})

UN No. 1891 **HAZCHEM Code** 3Z **Conveyance classification** toxic substance
Supply classification harmful
Risk phrases Harmful by inhalation, in contact with skin and if swallowed (R20/21/22)

Safety phrases Keep out of reach of children (if sold to general public) – After contact with skin, wash immediately with plenty of water (S2, S28)

Environmental fate

Degradation studies
Biodegraded by *Acinetobacter* sp. strain GJ70 (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 1350 mg kg^{-1} (2).
LC_{50} (1 hr) inhalation mouse 16,230 ppm (3).
LD_{50} intraperitoneal mouse, rat 1750, 2850 mg kg^{-1}, respectively (4).

Sub-acute and sub-chronic data
All ♂ and ♀ Fischer 344/N rats and B6C3F1 mice exposed by inhalation (2 wk) to 4000 ppm and 2000 ppm for 6 hr day^{-1} 5 day wk^{-1} died. Signs of toxicity were prostration, dyspnoea, lachrymation, haemorrhage and congestion in the respiratory tract (5).

Carcinogenicity and chronic effects
No adequate evidence for carcinogenicity to humans, limited evidence for carcinogenicity to animals, IARC classification group 3 (6).
Rats and mice inhalation (0, 100, 200 or 400 ppm) 6 hr day^{-1} 5 day wk^{-1} for 103 or 104 wk. Induced pheochromocytomas of the adrenal gland, neoplasms of brain and lung in ♂ F344/N rats; equivocal evidence in ♀ rats indicated by marginally increased incidences of brain and lung neoplasms. Equivocal evidence in ♂ B6C3F1 mice based on marginally increased lung neoplasm evidence; neoplasms of uterus in ♀ mice (5).
National Toxicology Program tested rats and mice via inhalation. Some evidence of carcinogenicity in ♂ rats, equivocal evidence of carcinogenicity in ♀ rats and ♂ mice, clear evidence of carcinogenicity in ♀ mice (7).

Teratogenicity and reproductive effects
In a 14-wk inhalation study with B6C3F1 mice and Fischer 344 rats exposed to 100-1600 ppm for 6 hr day^{-1} 5 day wk^{-1}, severe testicular atrophy was observed in all rats but not in mice at 1600 ppm. Four of ten ♂ rats in the 1600 ppm group died. In ♀ mice the size and number of corpora lutea in the ovary decreased at 1600 ppm and at 800 ppm (4).

Genotoxicity

Salmonella typhimurium TA100, TA1535 with and without metabolic activation positive (8).
Mutations were not induced in *Drosophila melanogaster* and chromosomal aberrations were not induced in cultured mammalian cells (6).
Increased incidence of sister chromatid exchange in Chinese hamster ovary cells (9).

Other effects

Other adverse effects (human)
Reported to be narcotic at high concentrations (10).

Legislation

Included in Schedule 4 and 6 (Release into Air and Release into Land Prescribed Substances) of Statutory Instrument No. 472, 1991 (11).
Limited under EC Directive on Drinking Water Quality 80/778/EEC. Substances extractable in chloroform: guide level 0.1 μg l^{-1} (12).

Other comments

Toxicity reviewed (13).

Reviews on physico-chemical properties, human health effects, experimental toxicology, epidemiology and workplace experience listed (14).

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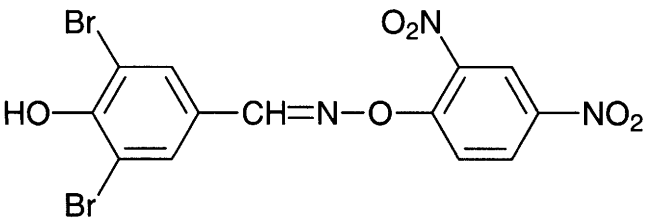
B176 bromofenoxim



$C_{13}H_7Br_2N_3O_6$ **Mol. Wt.** 461.02 **CAS Registry No.** 13181-17-4

Synonyms benzaldehyde, 3,5-dibromo-4-hydroxy-, *O*-(2,4-dinitrophenyl)oxime; bromophenoxim

EINECS No. 236-129-6 **RTECS No.** EG 7000000

Uses Herbicide.

Physical properties

M. Pt. 196-197°C **Specific gravity** 2.15 at 20°C **Partition coefficient** log P_{ow} 3.2 (pH 7.0) **Volatility** v.p. 9.8×10^{-8} mmHg at 20°C

Solubility Water: 0.6 mg l^{-1} (pH 3.8) at 20°C. Organic solvents: benzene, hexane, isopropanol

Occupational exposure

Supply classification harmful

Risk phrases Harmful if swallowed (R22)

Safety phrases Keep out of reach of children (if sold to general public) – Avoid contact with the eyes (S2, S25)

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) carp, rainbow trout, 0.088, 0.18 mg l^{-1}, respectively (1).

Environmental fate

Degradation studies

Little or no persistence in soil (1).

Abiotic removal

At 70°C, 50% hydrolysis in 41.4 hr at pH 1, in 9.6 hr at pH 5, and 0.76 hr at pH 9 (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral dog >1000 mg kg^{-1} (1).
LD_{50} oral rat 1217 mg kg^{-1} (1).
LC_{50} (6 hr) inhalation rat >0.24 mg l^{-1} (1).
LC_{50} percutaneous rat >3000 mg kg^{-1} (1).

Sub-acute and sub-chronic data

In a 90-day feeding trial, no-effect level in rats was 300 mg kg^{-1} diet and in dogs 100 mg kg^{-1} (1).

Metabolism and toxicokinetics

Following oral administration to rats metabolised to dinitrophenol and hydroxdibromobenzonitrile (1).

Irritancy

Mild eye and skin irritant in rabbits (1).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides and related products: maximum admissible concentration 0.1 µg l^{-1} (2).
Included in Schedule 6 (Release Land Prescribed Substances) of Statutory Instrument No. 472, 1991 (3).
WHO Toxicity Class III (4).
EPA Toxicity Class III (1).

Other comments

Non-toxic to birds and bees (1).
In plants metabolised to 3,5-dibromo-4-hydroxybenzoic acid (1).
Metabolic pathways reviewed (5).

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B177 bromoform

$HCBr_3$

$CHBr_3$ **Mol. Wt.** 252.73 **CAS Registry No.** 75-25-2

Synonyms tribromomethane

EINECS No. 200-854-6 **RTECS No.** PB 5600000

Uses Solvent. Sedative. Antitussive.

Physical properties

M. Pt. 8.3°C **B. Pt.** 150-151°C **Flash point** none **Specific gravity** 2.894 at 20°C with respect to water at 20°C
Volatility v.p. 5.6 mmHg at 25°C ; v.den. 8.7
Solubility Water: 0.8 g l^{-1}. Organic solvents: acetone, benzene, chloroform, diethyl ether, ethanol

Occupational exposure

FR-VME 0.5 ppm (5 mg m^{-3})
UK-LTEL 0.5 ppm (5.3 mg m^{-3})
US-TWA 0.5 ppm (5.2 mg m^{-3})

UN No. 2515 **HAZCHEM Code** 2X **Conveyance classification** toxic substance
Supply classification toxic
Supply classification dangerous for the environment
Risk phrases Toxic by inhalation – Irritating to eyes and skin – Toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment (R23, R36/38, 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 – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) – Avoid release to the environment. Refer to special instructions/safety data sheet (S1/2, S28, S45, S61)

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) bluegill sunfish 29 mg l^{-1} static bioassay (1).
LC_{50} (96 hr) sheepshead minnow 17 mg l^{-1} static bioassay (1).
LC_{50} (96 hr) bluegill sunfish 29 mg l^{-1} (2).

Invertebrate toxicity
EC_{50} (48 hr) *Daphnia magna* 46 mg l^{-1} (3).
LC_{50} (48 hr) eastern oyster larvae 1 mg l^{-1} static bioassay (4).
LC_{50} (96 hr) mysid shrimp 24 mg l^{-1} (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat, mouse 1150, 1400 mg kg^{-1}, respectively (5,6).
LD_{50} subcutaneous mouse 1820 mg kg^{-1} (7).

Sub-acute and sub-chronic data
Intravenous guinea pig (10 day) 100-200 mg kg^{-1} day^{-1} resulted in pathological changes in liver and kidney (8).

Carcinogenicity and chronic effects
Inadequate evidence for carcinogenicity to humans, limited evidence for carcinogenicity to animals, IARC classification group 3 (9).

National Toxicology Program tested in rats and mice via gavage. Clear evidence of carcinogenicity in ♀ rats, no evidence in ♂ or ♀ mice, some evidence in ♂ rats (10).

Teratogenicity and reproductive effects

Gavage Swiss CD-1 mice (18 wk) 0, 50, 100, 200 mg kg^{-1} continuous breeding protocol. No adverse effects on fertility. Reduced body and kidney weight, increased liver weight at 200 mg kg^{-1} and 100 mg kg^{-1}. Reduced neonatal survival at 200 mg kg^{-1} (11).

Gavage Sprague-Dawley rats (day 6-15 of gestation) 0, 50, 100, 200 mg kg^{-1} no maternal toxicity, no increased incidence of resorptions, litter size or foetal weight observed. Dose-related increase in incidence of skeletal variations (12).

Metabolism and toxicokinetics

Rectal or inhalation administration to rabbits. Biotransformed in the liver to inorganic bromides, which were later found in tissues and urine (13).

Rectal anaesthesia with bromoform, 0.3-1.2% recovered in urine as sodium bromide (14).

Intragastric administration of radiolabelled compound to Sprague-Dawley rats and B6C3F1 mice. Total radioactivity of bladder, brain, kidneys, liver, lungs, pancreas and thymus 3-6% of total dose in rats and 5-14% in mice. Urine contained <5% at 8 hr after administration, and <10% of total radiolabel at 36-48 hr (15).

Irritancy

Absorbed through rabbit skin causing moderate irritation, lethargy and weight loss. Moderately irritating to eyes (16).

Genotoxicity

Salmonella typhimurium TA98, TA100 with and without metabolic activation positive when tested in a desiccator and in vapour phase (not using Agar) (17,18).

Salmonella thypimurium TA97, TA98 without metabolic activation positive, with metabolic activation negative (19).

In vitro Chinese hamster ovary cells without metabolic activation sister chromatid exchange and chromosomal aberrations positive, with metabolic activation negative (20).

Mouse bone marrow micronucleus test negative; rat liver unscheduled DNA synthesis test negative (21).

In vitro human lymphocytes without metabolic activation sister chromatid exchange positive (22).

In vivo mouse bone marrow cells sister chromatid exchange positive, chromosome aberrations negative.

In vivo B6C3F mice micronucleus test positive (20).

In vitro mouse lymphoma L5178Y tk+/– cell forward mutation assay without metabolic activation positive, with metabolic activation negative (23).

Sister chromatid exchange (marine fish) did not increase the rate of dividing leucocytes (24).

Other effects

Other adverse effects (human)

Epidemiology studies indicated higher oesophagus and stomach cancer mortality where there are high levels of all haloalkanes in drinking water (25).

Legislation

US Drinking Water recommendation 2 μg l^{-1} (26).

Included in Schedule 4 and 6 (Release into Air and Release into Land Prescribed Substances) of Statutory Instrument No. 472, 1991 (27).

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Substances extractable in chloroform: guide level 0.1 mg l^{-1} (28).

Other comments

Human health effects, experimental toxicology, ecotoxicology, physico-chemical properties, workplace experience, environmental effects and exposure levels reviewed (29,30).

Contaminant in water samples, concentration range <0.8-92 μg l^{-1} (1).

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B178 bromomethane

CH_3Br

CH_3Br **Mol. Wt.** 94.94 **CAS Registry No.** 74-83-9

Synonyms methyl bromide; Dowfume; Halon 1001

EINECS No. 200-813-2 **RTECS No.** PA 4900000

Uses Ionisation chambers. Degreasing wool. Extracts oils from nuts, seeds and flowers. Insect fumigant.

Physical properties

M. Pt. –94°C **B. Pt.** 4°C **Flash point** not available **Specific gravity** 1.730 at 0°C with respect to water at 4°C
Volatility v.p. 1420 mm Hg at 20°C ; v.den. 3.27
Solubility Water: 17.5 g l^{-1} at 20°C, 748 mmHg. Organic solvents: benzene, carbon disulfide, chloroform, diethyl ether, ethanol

Occupational exposure

FR-VME 5 ppm (20 mg m^{-3})
SE-LEVL 5 ppm (19 mg m^{-3})
SE-STEL 10 ppm (40 mg m^{-3})
UK-LTEL 5 ppm (20 mg m^{-3})
UK-STEL 15 ppm (59 mg m^{-3})
US-TWA 1 ppm (3.9 mg m^{-3})

UN No. 1062 **HAZCHEM Code** 2XE **Conveyance classification** toxic gas
Supply classification toxic, dangerous for the environment
Risk phrases Toxic by inhalation – Irritating to eyes, respiratory system and skin – Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment – Dangerous for the ozone layer (R23, R36/37/38, R50/53, R59)
Safety phrases Keep locked up and out of the reach of children (if sold to general public) – Keep away from heat – Take off immediately all contaminated clothing – Wear suitable protective clothing, gloves and eye/face protection – In case of insufficient ventilation, wear suitable respiratory equipment – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) – Refer to manufacturer/supplier for information on recovery/recycling – Avoid release to the environment. Refer to special instructions/safety data sheet (S1/2, S15, S27, S36/37/39, S38, S45, S59, S61)

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) inland silverside, bluegill sunfish 11, 12 ppm, respectively (1).

Invertebrate toxicity
Non-toxic to bees (2).
LC_{50} (24 hr) Coleoptera 4.505 mg l^{-1} (3).

Environmental fate

Abiotic removal
Primarily removed from the atmosphere by reaction with hydroxyl radicals. Residence time in urban atmosphere was estimated to be 289 days, with a daily rate of loss (12 sunlit hr) of 0.4% (1).
240 kg ha^{-1} was applied, at a depth of 0.25 m, to a field and covered with a polyethylene sheet. 61% of applied bromomethane was lost via volatilisation (4).
Degradation decreases with soil depth due to the reduction of organic matter. In sandy loams degradation in moist conditions is limited and varies with soil depth (5).

Mammalian & avian toxicity

Acute data
LC_{100} (6 hr) inhalation rat 0.63 mg l^{-1} (2).
LC_{50} (2 hr) inhalation mouse 1540 mg m^{-3} (6).
LC_{Lo} (2 hr) inhalation child 1 mg m^{-3} (7).

Sub-acute and sub-chronic data
Inhalation rat (6 hr day^{-1} for 5 days) 150 ppm. No histological evidence of brain lesions, but inhibition of glutathione-*S*-transferase activity and depletion of glutathione, monoamines and amino acid levels was noted (8).

Carcinogenicity and chronic effects
Inadequate evidence for carcinogenicity to humans, limited evidence for carcinogenicity to animals, IARC classification group 3 (9).
National Toxicology Program tested mice via inhalation. No evidence of carcinogenicity in ♂ or ♀ mice (10).
♂ and ♀ Wistar rats inhalation (29 month) 0, 3, 30 or 90 ppm 6 hr day^{-1}, 5 day wk^{-1}, and 10 rats sex^{-1} $group^{-1}$ were killed after 13, 52 and 104 wk. Mortality was increased by wk 114 in 90 ppm and body weights were lower. Increased incidences of degenerative and hyperplastic changes of the nasal olfactory epithelium were observed in all groups. Exposure to 90 ppm induced lesions in the heart and hyperkeratosis in the oesophagus and forestomach (11).

Teratogenicity and reproductive effects

Oral ♀ rat and rabbit (days 6-15 and 6-18 of gestation, respectively) 0, 3, 10 and 30 or 0, 1, 3 and 10 mg kg^{-1} day^{-1} respectively. Rats and rabbits were euthanised at days 20 and 27 of gestation, respectively. Maternal toxicity was observed in the high-dose ♀s of both species. Significant decreases in body weight and food consumption were observed. Erosive lesions of the stomach and surrounding organs was observed; foetuses, however, were unaffected (12).

Metabolism and toxicokinetics

Readily absorbed through lungs (13).

Serum bromide levels achieved in serious cases of bromomethane poisoning are considerably lower than those required for poisoning by inorganic bromides, suggested as being due to greater lipid solubility of bromomethane and hence greater penetration into the brain (14).

Following absorption in rat blood, levels of residual non-volatile bromide increased. Bromomethane rapidly distributed to various tissues and broken down to inorganic bromide. Storage, only as bromides, occurred mainly in lipid-rich tissues (15).

Elimination was initially rapid, largely through the lung as bromomethane and the remainder was eliminated in urine as bromomethane/bromide. In rats fed bromomethane-fumigated diets with residual bromide levels, higher tissue bromide levels were found in their eyes, lung, blood, spleen and testes, while the lowest tissue levels were in the fat, skeletal muscle, bone and liver (15).

♂ Fischer-344 rats were exposed (nose only) to a vapour concentration of 9 ppm at 25°C for 6 hr and urine, faeces, expired air and tissues were collected for up to 65 hr after exposure. Carbon dioxide was the major route of excretion (47% of total absorbed). Distribution of the compound was in lung, adrenal, kidney, liver and nasal turbinates in decreasing order of concentration (16).

Irritancy

Unintentional exposure of the skin of six persons to 40 g m^{-3} for 40 min led to redness and blistering. Plasma bromide levels were highest immediately following exposure averaging 9 ± 1.4 mg l^{-1} and decreased to average 6.8 ± 2.3 mg l^{-1} 12 hr after exposure (17).

Thirty adult ♂ Long-Evans rats (2 wk) 200 ppm 4 hr day^{-1}, 4 day wk^{-1} extensive damage to olfactory epithelium and impaired function on first day of exposure; even with continuous exposure, function was essentially normal after 4 days of exposure. Repair of the epithelium was in progress thereafter (18).

Genotoxicity

Mutagenic to plants and bacteria. *In vitro* human lymphocytes induced sister chromatid exchange. *In vitro* mouse lymphoma cells positive mutagen. Inhalation rat induced micronuclei in bone marrow and peripheral blood cells. DNA methylation of liver and spleen observed in mouse. *Drosophila melanogaster* induced sex-linked recessive lethal mutations (19).

Other effects

Other adverse effects (human)

Nine greenhouse workers were accidentally exposed to >200 ppm of bromomethane. Seven workers were discharged from hospital after uneventful overnight observation. Two patients required intensive-care treatment for several weeks due to severe reactive myoclonus and tonic-clonic convulsions. Prior sub-chronic exposure may have been a contributing factor (20).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides and related products: maximum admissible concentration 0.1 μg l^{-1} (21).

Included in Schedule 6 (Release into Land Prescribed Substances) of Statutory Instrument No. 472, 1991 (22).

Other comments

Found in seawater collected off Dorset, UK, in 1975 ranging from 1.5-3.9 μg l^{-1} (23).

Man-made and natural sources contribute to the concentration of bromomethene in ambient air (24).
Residues have been reported in some foodstuffs after fumigation with bromomethane (15).
Reviews on physico-chemical properties, human health effects, experimental toxicology, environmental effects, ecotoxicology, exposure levels, epidemiology and workplace experience listed (25).
Hazardous properties reviewed (26).
Industrial poisoning, its diagnosis and therapy reviewed (27).
The inclusion of bromomethane in the Montreal protocol and the effect of this on the treatment of plant disorders is discussed (28).

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24. Dennis, N. M. et al *J. Econ. Entomol.* 1972, **65**, 1753.
25. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium.
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27. Inoue, N. et al *Sangyo Igaky Janaruy* 1987, **10**(4), 38-43 (Jap.) (*Chem. Abstr.* 1987, **107**, 182391m).
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B179 1-bromo-3-methylbutane

$$(CH_3)_2CHCH_2CH_2Br$$

$C_5H_{11}Br$ **Mol. Wt.** 151.05 **CAS Registry No.** 107-82-4

Synonyms isoamyl bromide; isopentyl bromide; 3-methylbutyl bromide

EINECS No. 203-522-9 **RTECS No.** EJ 6230000

Uses Organic synthesis.

Physical properties

M. Pt. –112°C **B. Pt.** 120-121°C **Flash point** 32°C **Specific gravity** 1.210 at 15°C with respect to water at 4°C
Solubility Organic solvents: miscible with diethyl ether, ethanol

Occupational exposure

UN No. 2341 **HAZCHEM Code** 2YE **Conveyance classification** flammable liquid

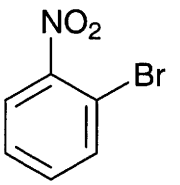
Mammalian & avian toxicity

Acute data
LD_{50} intraperitoneal rat 6150 mg kg^{-1} (1).
LD_{50} intraperitoneal mouse 13,750 mg kg^{-1} (1).

References

1. Izmerov, N. F. et al *Toxicometric Parameters of Industrial Toxic Chemicals under Single Exposure* 1982, 76, Moscow, USSR

B180 2-bromonitrobenzene



$C_6H_4BrNO_2$ **Mol. Wt.** 202.01 **CAS Registry No.** 577-19-5
Synonyms benzene, 1-bromo-2-nitro-; *o*-nitrophenyl bromide; nitrobenzene, 2-bromo-
EINECS No. 209-409-0 **RTECS No.** CY 9040450

Physical properties

M. Pt. 40-42°C **B. Pt.** 261°C **Flash point** >110°C

Occupational exposure

UN No. 2732 **HAZCHEM Code** 2X **Conveyance classification** toxic substance

Ecotoxicity

Fish toxicity
LC_{50} (24 hr) goldfish 46 mg l^{-1} (1).

Invertebrate toxicity
EC_{50} (30 min) *Photobacterium phosphoreum* 1.6 mg l^{-1}; Microtox test (2).

Genotoxicity

Salmonella typhimurium TA98, TA100 with metabolic activation positive, without metabolic activation negative (3).

Legislation

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

References

1. Bridie, A. L. et al *Water Res.* 1979, **13**, 623.
2. Kaiser, K. L. E. et al *Water Pollut. Res. J. Can.* 1991, **26**(3), 361-431.
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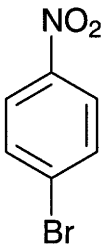
B181 4-bromonitrobenzene



$C_6H_4BrNO_2$ **Mol. Wt.** 202.01 **CAS Registry No.** 586-78-7

Synonyms benzene, 1-bromo-4-nitro-; *p*-nitrophenyl bromide; nitrobenzene, 4-bromo-

EINECS No. 209-583-8 **RTECS No.** CY 9040550

Physical properties

M. Pt. 125-127°C **B. Pt.** 255-256°C

Occupational exposure

UN No. 2732 **HAZCHEM Code** 2X **Conveyance classification** toxic substance

Ecotoxicity

Invertebrate toxicity

EC_{50} (30 min) *Photobacterium phosphoreum* 16.8 mg l^{-1}; Microtox test (1).

Genotoxicity

Salmonella typhimurium TA98 with and without metabolic activation negative; TA100 with metabolic activation positive, without metabolic activation negative (2).

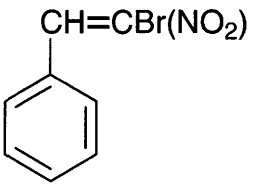
Legislation

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

References

1. Kaiser, K. L. E. et al *Water Pollut. Res. J. Can.* 1991, **26**(3), 361-431.
2. Kawai, A. et al *Sangyo Igaku* 1987, **29**, 34-35.
3. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK

B182 β-bromo-β-nitrostyrene



$C_8H_6BrNO_2$ **Mol. Wt.** 228.05 **CAS Registry No.** 7166-19-0

Synonyms 2-bromo-2-nitroethenylbenzene; Slimetrol RX-39

EINECS No. 230-515-8 **RTECS No.** WL 4040000

Uses Biocide in paper making.

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) bluegill sunfish, fathead minnow, rainbow trout 0.32-1.2 mg l^{-1} (1).

Environmental fate

Degradation studies

Biodegrades to form bromonitromethane (1).

Abiotic removal

Usually treated with sodium sulfide for detoxification (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 966 mg kg^{-1} (1).

Sub-acute and sub-chronic data

In a 30-day oral study, rat 110 mg kg^{-1} caused no ill-effects and 300 mg kg^{-1} was of minimal toxicity (1).

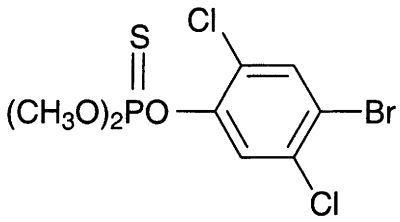
Carcinogenicity and chronic effects

National Toxicology Program study in progress in rats and mice via gavage (2).

References

1. *Material Safety Data Sheets* 1981, Betz Chemical Company.
2. *National Toxicology Program, Research and Testing Division* 1998, Report No. Tox-40 NTIS PB95-144531, NIEHS, Research Triangle Park, NC, USA

B183 bromophos



$C_8H_8BrCl_2O_3PS$ **Mol. Wt.** 366.00 **CAS Registry No.** 2104-96-3

Synonyms phosphorothioic acid, *O*-(4-bromo-2,5-dichlorophenyl)- ,*O*,*O*-dimethyl ester; bromophos-methyl

EINECS No. 218-277-3 **RTECS No.** TE 7175000

Uses Insecticide (superseded).

Physical properties

M. Pt. 53-54°C **B. Pt.** 140-142°C at 0.01 mmHg **Volatility** v.p. 1.2×10^{-4} mmHg at 20°C
Solubility Water: 40 mg l^{-1} at 20°C. Organic solvents: acetone, dichloromethane, xylene 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) – Wear suitable protective clothing (S2, S36)

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) guppy, rainbow trout 0.05-0.5 mg l^{-1} (1).

Invertebrate toxicity
EC_{50} (48 hr) *Daphnia pulex* 0.0064 mg l^{-1} (2).
Toxic to bees (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral mouse, rat 3311-5850, 3750-8000 mg kg^{-1}, respectively (1).
LD_{50} oral guinea pig 1500 mg kg^{-1} (1).
LD_{50} percutaneous rabbit 2190 mg kg^{-1} (1).

Carcinogenicity and chronic effects
In 2-yr feeding trials the no-effect level in rats was 0.63 mg kg^{-1} day^{-1} and in dogs 1.5 mg kg^{-1} day^{-1} (1).

Metabolism and toxicokinetics
Following oral administration in mammals, >90% excreted in urine in 24 hr. The principal metabolite is 4-bromo-2,5-dichlorophenol (1).

Legislation

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

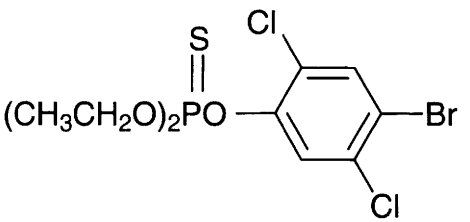
Other comments

Toxicity and hazards reviewed (5,6).

References

1. *The Agrochemicals Handbook* 3rd ed., 1991, The Royal Society of Chemistry, London, UK.
2. Frear, D. E. H. et al *Int. J. Econ. Entomol.* 1967, **60**, 1228-1238.
3. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
4. *S.I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
5. Izmerov, N. F. *Scientific Reviews of Soviet Literature on Toxicity & Hazards of Chemicals* 1992-1993, **96**, Eng. Trans., Richardson, M. L. (Ed.), UNEP/IRPTC, Geneva, Switzerland.
6. Pachaly, P. *Dtsch. Apoth. Ztg.* 1989, **129**(27), 1447 (Ger.) (*Chem. Abstr.* **111** 148686j)

B184 bromophos-ethyl



$C_{10}H_{12}BrCl_2O_3PS$ **Mol. Wt.** 394.05 **CAS Registry No.** 4824-78-6

Synonyms phosphorothioic acid, *O*-(4-bromo-2,5-dichlorophenyl)-,*O*,*O*-diethyl ester

EINECS No. 225-399-0 **RTECS No.** TE 7000000

Uses Insecticide (superseded).

Physical properties

B. Pt. 122-123°C at 0.001 mmHg **Specific gravity** 1.52 at 20°C **Volatility** v.p. 4.5×10^{-5} mmHg at 30°C
Solubility Water: 2 mg l^{-1}. Organic solvents: miscible with acetone, benzene, ethanol

Occupational exposure

Supply classification toxic, dangerous for the environment
Risk phrases Harmful in contact with skin – Toxic if swallowed – Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment (R21, R25, R50/53)
Safety phrases Keep locked up and out of the reach of children (if sold to general public) – After contact with skin, wash immediately with plenty of water – Wear suitable protective clothing and gloves – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) – This material and/or its container must be disposed of as hazardous waste – Avoid release to the environment. Refer to special instructions/safety data sheet (S1/2, S28, S36/37, S45, S60, S61)

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) rainbow trout, guppy 0.14-0.4 mg l^{-1} (1).

Invertebrate toxicity
Toxic to bees (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral quail 200 mg kg^{-1} (1).
LD_{50} oral ♂ rat, mouse 52-170, 210-550 mg kg^{-1}, respectively (1).
LD_{50} percutaneous rabbit 100-600 mg kg^{-1} (1).

Carcinogenicity and chronic effects
In 2-yr feeding trials no-effect level rats 78 mg kg^{-1} day^{-1} and dogs 0.26 mg kg^{-1} day^{-1} (1).

Metabolism and toxicokinetics
Following oral administration in mammals, 85-90% excreted in urine and faeces in 4 days. The principal metabolite is 4-bromo-2,5-dichlorophenol (1).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides and related products: maximum admissible concentration 0.1 μg l^{-1} (2).
Included in Schedule 6 (Release into Land Prescribed Substances) of Statutory Instrument No. 472, 1991 (3).

References

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

B185 1-bromopropane

$$CH_3CH_2CH_2Br$$

C_3H_7Br **Mol. Wt.** 122.99 **CAS Registry No.** 106-94-5
Synonyms propyl bromide
EINECS No. 203-445-0 **RTECS No.** TX 4110000
Uses Organic synthesis.

Physical properties

M. Pt. –110°C **B. Pt.** 71°C **Flash point** 25°C **Specific gravity** 1.354 at 20°C with respect to water at 20°C
Solubility Water: 2.5 g l^{-1}. Organic solvents: ethanol

Occupational exposure

UN No. 2344 **HAZCHEM Code** 2[redacted]E **Conveyance classification** flammable liquid
Supply classification harmful
Risk phrases Flammable – Harmful by inhalation (R10, R20)
Safety phrases Keep out of reach of children (if sold to general public) – Keep container in a well ventilated place – Avoid contact with the skin (S2, S9, S24)

Mammalian & avian toxicity

Acute data

LD_{Lo} oral rat 4000 mg kg^{-1} (1).

LC_{50} (30 min) inhalation rat 253 g m^{-3} (2).

LD_{50} intraperitoneal mouse, rat 2530, 2950 mg kg^{-1}, respectively (3).

Metabolism and toxicokinetics

Parent compound and metabolites excreted in urine as mercapturic acid in rats (4).

Genotoxicity

Salmonella typhimurium TA1535 with and without metabolic activation negative (5).

Other effects

Other adverse effects (human)

Narcotic (3).

Other comments

Reviews on human health effects, experimental toxicology, ecotoxicology and physico-chemical properties listed (6).

References

1. *Mutat. Res.* 1982, **101**, 321.
2. *Fiziologiekeshi Aktivnye Veshihestva (Physiologically Active Substances)* 1975, **7**, 35.
3. Izmerov, N. F. et al *Toxicometric Parameters of Industrial Toxic Substances under Single Exposure* 1982, 102, Moscow, USSR.
4. Jones, A. R. et al *Xenobiotica* 1980, **9**(12), 763-772.
5. Barker, E. V. et al *Environ. Sci. Rev.* 1982, **25**, 3-18.
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

B186 2-bromopropane

$CH_3CHBrCH_3$

C_3H_7Br **Mol. Wt.** 122.99 **CAS Registry No.** 75-26-3

Synonyms isopropyl bromide

EINECS No. 200-855-1 **RTECS No.** TX 4111000

Uses Intermediate in organic synthesis. Freon substitute.

Physical properties

M. Pt. –89°C **B. Pt.** 59°C **Flash point** 19°C **Specific gravity** 1.310

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

Occupational exposure

UN No. 2344 **HAZCHEM Code** 2[redacted]E **Conveyance classification** flammable liquid

Genotoxicity

Salmonella typhimurium TA1535 with and without metabolic activation negative (1).
Salmonella typhimurium TA100 with metabolic activation, TA 1535 with or without activation induced chromosome adberrations in a dose-dependent manner (2).
In vitro Chinese hamster lung cells (6 hr) with or (24 hr) without metabolic activation chromosomal aberration negative up to 2.46 mg ml^{-1} (2).
In vivo rat bone marrow cells (28 days) negative in micronucleus frequency tests; decrease in % polychromatic erythrocytes (2).

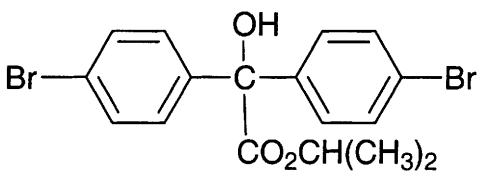
Other comments

Modelling risk assessment for nursing infants exposed to volatile organics including 2-bromopropane via mother's occupational inhalation exposure is discussed (3).

References

1. Barker, E. V. et al *Environ. Sci. Rev.* 1982, **257**, 3-18.
2. Maeng, S. H. et al *Ind. Health* 1997, **35**(1), 87-95.
3. Shelly, M. L. et al *Appl. Ind. Hyg.* 1989, **4**(1), 21-26

B187 bromopropylate



$C_{17}H_{16}Br_2O_3$ **Mol. Wt.** 428.12 **CAS Registry No.** 18181-80-1

Synonyms 4-bromo-α-(4-bromophenyl)-α-hydroxybenzeneacetic acid 1-methylethyl ester; 4,4'-dibromobenzelic acid isopropyl ester; 4,4'-dibromobenzilate; phenisobromolate; Acanal; Acaril; Acarol; Folbex VA; Lorix; Nuvan; Neoron

EINECS No. 242-070-7 **RTECS No.** DD 2100000

Uses Acaricide.

Physical properties

M. Pt. 77°C **Specific gravity** 1.59 at 20°C **Volatility** v.p. 5.1×10^{-8} mmHg at 20°C
Solubility Water: <5 mg l^{-1} at 20°C. Organic solvents: acetone, benzene, dichloromethane, dioxane, methanol, isopropanol, xylene

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) rainbow trout, bluegill sunfish, carp 0.35, 0.5 and 2.4 mg l^{-1}, respectively (1).

Invertebrate toxicity
Not toxic to bees (1).
Causes immediate mortality when applied to the parasitoid adult ♀ *Eretmocerus debachi* (2).

Environmental fate

Adsorption and retention
Low mobility in soil (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral Japanese quail >2000 mg kg^{-1} (1).
LD_{50} oral rat >5000 mg kg^{-1} (1).
LD_{50} percutaneous rat >4000 mg kg^{-1} (1).

Sub-acute and sub-chronic data
LC_{50} (8 day) oral duck 600 mg kg^{-1} in diet (1).
LC_{50} (8 day) oral Japanese quail 1000 mg kg^{-1} in diet (1).

Carcinogenicity and chronic effects
In 2-yr feeding trials the no-effect level for rats was 500 mg kg^{-1} (1).

Metabolism and toxicokinetics
Rapidly eliminated in animals by cleavage of isopropyl ester (1).

Irritancy
Dermal rabbit (duration unspecified) 600 μg moderate irritation effects, while 600 μg instilled into rabbit eye caused mild irritation (3).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides and related products: maximum admissible concentration 0.1 μg l^{-1} (4).
Included in Schedule 6 (Release into Land Prescribed Substances) of Statutory Instrument No. 472, 1991 (5).
Admissible daily intake human 8 μg kg^{-1} (total intake from all sources) (1).

References

1. *The Pesticide Manual* 11th ed., 1997, The British Crop Protection Council, Farnham, UK.
2. Uygun, N. et al *Bull. Entomol. Res.* 1994, **84** (1), 119-122.
3. *Ciba-Geigy Toxicology Data* 1977.
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

B188 bromotrifluoromethane

$CBrF_3$

$CBrF_3$ **Mol. Wt.** 148.91 **CAS Registry No.** 75-63-8
Synonyms trifluorobromomethane; trifluoromonobromomethane
EINECS No. 200-887-6 **RTECS No.** PA 5425000

Physical properties

M. Pt. –168°C **B. Pt.** –58 to –57°C **Volatility** v.p. 9774 mmHg at 21°C ; v.den. 5.3 at 21°C
Solubility Organic solvents: chloroform

Occupational exposure

DE-MAK 1000 ppm (6200 mg m^{-3})
FR-VME 1000 ppm (6100 mg m^{-3})
UK-LTEL 1000 ppm (6190 mg m^{-3}) **UK-STEL** 1200 ppm (7430 mg m^{-3})
US-TWA 1000 ppm (6090 mg m^{-3})

UN No. 1009 **HAZCHEM Code** 2RE **Conveyance classification** non-flammable non-toxic gas

Mammalian & avian toxicity

Acute data
LC_{50} inhalation rat 416 g m^{-3} (1).
LC_{50} inhalation mouse 381 g m^{-3} (1).

Other effects

Other adverse effects (human)
Mildly toxic by inhalation (2).

Legislation

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

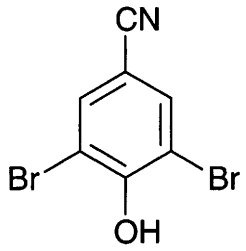
Other comments

Colourless gas. Incompatible with aluminium. When heated to decomposition it emits toxic fumes of F^- and Br^-.

References

1. *Gig. Tr. Prof. Zabol.* 1982, **26**(8), 53.
2. *Sax's Dangerous Properties of Industrial Materials* 8th ed., 1992, Van Nostrand Reinhold, New York, NY, USA.
3. *S.I. No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK

B189 bromoxynil



$C_7H_3Br_2NO$ **Mol. Wt.** 276.91 **CAS Registry No.** 1689-84-5

Synonyms 3,5-dibromo-4-hydroxybenzonitrile; 3,5-dibromo-4-hydroxyphenyl cyanide; 2,6-dibromo-4-cyanophenol; Brominil; Buctril

EINECS No. 216-882-7 **RTECS No.** DI 3150000

Uses Herbicide.

Physical properties

M. Pt. 194-195°C **Volatility** v.p. 7.6×10^{-6} mmHg at 20°C
Solubility Water: 130 mg l^{-1} at 25°C. Organic solvents: acetone, cyclohexanone, ethanol, methanol, tetrahydrofuran

Occupational exposure

Supply classification toxic
Risk phrases Toxic if swallowed – Possible risk of harm to the unborn child (R25, R63)
Safety phrases Keep locked up and out of the reach of children (if sold to general public) – Wear suitable protective clothing and gloves – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S36/37, S45)

Ecotoxicity

Fish toxicity
LC_{50} (48 hr) goldfish 0.46 mg l^{-1} (1).
LC_{50} (48 hr) catfish 0.063 mg l^{-1} (1).

Invertebrate toxicity
Non-toxic to bees (1).

Environmental fate

Nitrification inhibition
Inhibits nitrification in soil at 50 ppm (2).

Degradation studies
In soil $t_{1/2}$ ~10 days. Degraded by hydrolysis and debromination to less toxic substances such as hydroxybenzoic acid. In plants, the ester and nitrile groups are hydrolysed, and debromination also occurs (1).
Flexibacter BR4 rapidly degraded bromoxynil. After 5 wk only 5% remained. Benzamide and benzoic acid metabolites were identified (3).

Mammalian & avian toxicity

Acute data
LD_{50} oral mouse, rat 110, 190 mg kg^{-1}, respectively (1).
LD_{50} oral rabbit 260 mg kg^{-1} (1).
LD_{50} oral dog 100 mg kg^{-1} (1).
LD_{50} percutaneous rat >2000 mg kg^{-1} (1).
LD_{50} percutaneous rabbit 3660 mg kg^{-1} (1).

Sub-acute and sub-chronic data
In 90-day feeding trials, the no-effect level for rats was 16.6 mg kg^{-1} (K salt) (1).

Teratogenicity and reproductive effects
Gavage pregnant rats and mice 15 and 96.4 mg kg^{-1} day^{-1}, respectively, on days 6-15 of gestation. Frequency of supernumerary ribs was determined in foetuses at term and in offspring on postnatal days 6, 20 and 40. In rats supernumerary ribs occurred in 62% of treated foetuses and in mice 45%. In mice the elevated incidence persisted through day 40 (42.3%), but no significant difference was observed in rats (4).

Metabolism and toxicokinetics
Studies on fate of bromoxynil in cows have shown that no residual bromoxynil was present in either milk or faeces. Nine days after feeding, <20% was excreted in urine as parent compound (5).

Legislation

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

Other comments

Metabolised in plants via hydrolysis of ester and nitrile groups, and debromination (1).
Reviews on physico-chemical properties, human health effects, ecotoxicology and experimental toxicology listed (8).
Metabolic pathways reviewed (9).

References

1. *The Pesticide Manual* 11th ed., 1997, British Crop Protection Council.
2. Parr, J. F. *Pesti. Soil Water* 1974, 321-340.
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B190 bronopol

$$HOCH_2CBr(NO_2)CH_2OH$$

$C_3H_6BrNO_4$ **Mol. Wt.** 199.99 **CAS Registry No.** 52-51-7

Synonyms 2-bromo-2-nitro-1,3-propanediol; β-bromo-β-nitrotrimethylene glycol; Bronosal; Bronotak; Canguard 409

EINECS No. 200-143-0 **RTECS No.** TY 3385000

Uses Disinfectant. Bacteriostat. Bactericide especially effective against *Pseudomonas aeruginosa*.

Physical properties

M. Pt. 130-133°C **Volatility** v.p. 1.3×10^{-5} mmHg at 20°C
Solubility Water: 250 $g\ l^{-1}$ at 22°C. Organic solvents: acetone, ethanol, ethyl acetate, isopropanol

Occupational exposure

UN No. 3241 **Conveyance classification** toxic substance
Supply classification harmful, dangerous for the environment
Risk phrases Harmful in contact with skin and if swallowed – Irritating to respiratory system and skin – Risk of serious damage to eyes – Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment (R21/22, R37/38, R41, R50/53)

Safety phrases Keep out of reach of children (if sold to general public) – In case of contact with eyes, rinse immediately with plenty of water and seek medical advice – Wear suitable gloves and eye/face protection – This material and/or its container must be disposed of as hazardous waste – Avoid release to the environment. Refer to special instructions/safety data sheet (S2, S26, S37/39, S60, S61)

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 180-400 mg kg^{-1} (1).
LD_{50} oral mouse 250-500 mg kg^{-1} (1).
LC_{50} (6 hr) inhalation rat 5 mg l^{-1} (1).
LD_{50} percutaneous rat >1600 mg kg^{-1} (1).

Sub-acute and sub-chronic data

In 72-day feeding trials, rats receiving up to 1000 mg kg^{-1} diet showed no ill-effects (1).

Irritancy

Contact dermatitis from bronopol (milk preservative) identified in a milk recorder with hand eczema (2).
A study of 149 eczematous patients determined that 0.25% in soft yellow paraffin caused mild irritation. No evidence of sensitisation or cross-sensitisation (3).
Acute allergic contact dermatitis reported in seven patients using Eucerin cream preserved with bronopol. Patients patch-tested positive to bronopol (4).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides and related products: maximum admissible concentration 0.1 μg l^{-1} (5).
WHO Toxicity Class II (6).
EPA Toxicity Class (formulation) II (1).

Other comments

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

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6. *The WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification 1998-1999* WHO/PCS/98.21.
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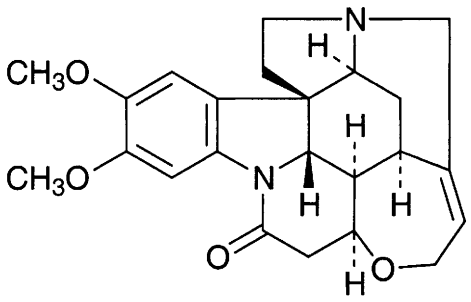
B191 brucine



$C_{23}H_{26}N_2O_4$ **Mol. Wt.** 394.47 **CAS Registry No.** 357-57-3

Synonyms 2,3-dimethoxystrychnidin-10-one; dimethoxystrychine; (–)-brucine; anhydrous brucine

EINECS No. 206-614-7 **RTECS No.** EH 8925000

Uses Denaturing ethanol, lubricant additive, treatment of digestive disorders.

Occurrence Isolated from the flower of *Strychnos nux-vomica* (1).

Physical properties

M. Pt. 178°C **Partition coefficient** log P_{ow} 0.98 (2) **Volatility** v.p. 1.5×10^{-8} mmHg at 25°C

Solubility Water: 760 mg l^{-1}. Organic solvents: acetone, benzene, chloroform, diethyl ether, ethanol, ethyl acetate, methanol

Occupational exposure

UN No. 1570 **HAZCHEM Code** 2X **Conveyance classification** toxic substance

Supply classification very toxic

Risk phrases Very toxic by inhalation and if swallowed (R26/28)

Safety phrases Keep locked up and out of the reach of children (if sold to general public) – 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) (S1/2, S13, S45)

Ecotoxicity

Fish toxicity

LC_{50} (24 hr static) bluegill sunfish and inland silverside 20-36 mg l^{-1} (2).

Environmental fate

Nitrification inhibition

Nitrosomonas sp. no inhibition of ammonia oxidation at 100 mg l^{-1} (3).

Adsorption and retention

Estimated K_{oc} of 81 indicates a high mobility in soil (4).

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse 150 mg kg^{-1} (5).

LD_{50} subcutaneous mouse 60 mg kg^{-1} (6).

LD_{50} intraperitoneal rat and mouse 62-91 mg kg^{-1} (5,7).

Genotoxicity

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

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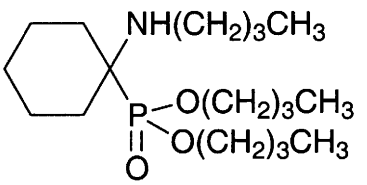
B192 buminafos



$C_{18}H_{38}NO_3P$ **Mol. Wt.** 347.48 **CAS Registry No.** 51249-05-9

Synonyms dibutyl 1-(butylamino)cyclohexylphosphonate; 1-butylaminocyclohexanephosphonic acid, butyl ester

EINECS No. 257-085-4 **RTECS No.** SZ 6900000

Uses Herbicide (superseded).

Physical properties

M. Pt. –25°C **B. Pt.** 95-99°C at 1 mmHg **Specific gravity** 0.969 at 20°C **Volatility** v.p. 7.5×10^{-4} mmHg at 20°C

Solubility Water: 170 mg l^{-1}. Organic solvents: acetone, methanol, xylene

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) guppy 7 mg l^{-1} (1).

Environmental fate

Degradation studies

$t_{1/2}$ in soil 8-11 days (1).

Abiotic removal

Hydrolysis 50% at pH 6 in 3 days (1).

In aqueous medium 50% hydrolysis occurs in 13 days at pH 6, 20 hr at pH 8 and 2.75 hr at pH 11 (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse, rat 3475, 7000 mg kg^{-1}, respectively (1,2).
LD_{50} percutaneous rat 12-15 g kg^{-1} (1).
LD_{50} percutaneous rabbit 5000-8000 mg kg^{-1} (1).

Sub-acute and sub-chronic data

In 130-day feeding trials, the no-effect level for rats was 140 mg kg^{-1} day^{-1} (1).

Metabolism and toxicokinetics

Oral administration (species unspecified), rapidly metabolised by dealkylation at the oxygen and nitrogen atoms, followed by deamination (1).

Legislation

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

References

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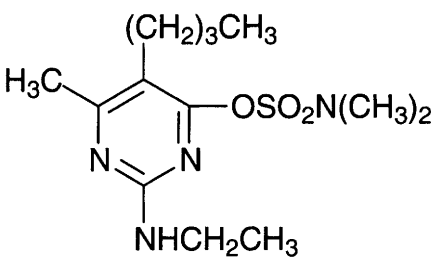
B193 bupirimate



$C_{13}H_{24}N_4O_3S$ **Mol. Wt.** 316.42 **CAS Registry No.** 41483-43-6

Synonyms sulfamic acid, dimethyl-, 5-butyl-2-(ethylamino)-6-methyl-4-pyrimidinyl ester; 5-butyl-2-ethylamino-6-methylpyrimidin-4-yldimethyl sulfamate; Nimrod

EINECS No. 255-391-2 **RTECS No.** WO 5970000

Uses Fungicide.

Physical properties

M. Pt. 50-51°C **Flash point** >50° **Volatility** v.p. 4.1×10^{-7} mmHg at 20°C
Solubility Water: 22 mg l^{-1} at 20°C. Organic solvents: acetone, diethyl ether, ethanol

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) rainbow trout 1.0 mg l^{-1} (1).

Invertebrate toxicity

No-effect oral bees 0.20 mg bee^{-1} (1).

Environmental fate

Abiotic removal

The $t_{1/2}$ in soil was ~6-7 wk. Major degradation product is ethirimol (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral pigeon >2700 mg kg^{-1} (1).
LD_{50} oral quail >5200 mg kg^{-1} (1).
LD_{50} oral rat, mouse, rabbit, guinea pig >5000 mg kg^{-1} (1,2).
LD_{50} percutaneous rat 4800 mg kg^{-1} (1).

Carcinogenicity and chronic effects

In 2-yr feeding trials, the no-effect level for rats was 100 mg kg^{-1} diet (1).

Metabolism and toxicokinetics

Oral administration (species unspecified), 68% of dose eliminated in urine within 24 hr. 77% eliminated in urine and 21% in faeces within 10 days (1).

Irritancy

Mild irritant to rabbit skin (1).

Sensitisation

Moderate skin sensitiser in guinea pigs (1).

Legislation

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

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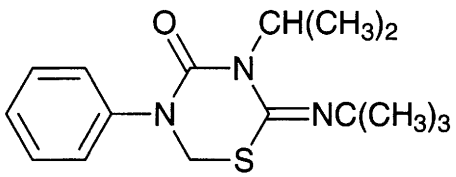
B194 buprofezin



$C_{16}H_{23}N_3OS$ **Mol. Wt.** 305.44 **CAS Registry No.** 69327-76-0

Synonyms 4*H*-1,3,5-thiadiazin-4-one, 2-[(1,1-dimethylethyl)imino]tetrahydro-3-(1-methylethyl)-5-phenyl-; 2-*tert*-butylimino-3-isopropyl-5-phenyl-3,4,5,6-tetrahydro-2*H*-1,3,5-thiadiazin-4-one; Applaud

RTECS No. XI 2865000

Uses Insecticide. Acaricide.

Physical properties

M. Pt. 104.5-105.5°C **Volatility** v.p. 9.3×10^{-6} mmHg at 23°C

Solubility Water: 0.9 mg l^{-1} at 25°C. Organic solvents: acetone, chloroform, ethanol, *n*-hexane, toluene

Occupational exposure

JP-OEL 2 mg m^{-3}

Ecotoxicity

Fish toxicity

LC_{50} (48 hr) carp 2.7 mg l^{-1} (1).

Invertebrate toxicity

EC_{50} (3 hr) *Daphnia* 50.6 mg l^{-1} (1).

No direct effects on honey bees at 2000 mg l^{-1} (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral ♂, ♀ rats 2198, 2355 mg kg^{-1}, respectively (1).

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

LC_{50} (4 hr) inhalation rat >4.57 mg l^{-1} (2).

LD_{50} dermal rat >5000 mg kg^{-1} (1).

Sub-acute and sub-chronic data

Oral Sprague-Dawley rats (90 day) 0, 40, 200, 1000 or 5000 ppm. No effects on mortality or clinical appearance were observed. Body weight gains were suppressed in ♂ and ♀ at 5000 ppm and in ♀ at 1000 ppm. Haematocrit, haemoglobin red cell count, serum glucose and triglyceride levels were decreased in high-dose animals, while levels of total cholesterol and phospholipids were increased. Liver and thyroid were identified as target organs (2).

Oral beagle dog (13 wk) 0, 2, 10, 50 or 300 mg kg^{-1} day^{-1}. No mortalities observed throughout study. Slight ataxia and abdominal distension observed in high dose animals. At necropsy no treatment-related lesions were noted. The no-observed-adverse-effect level was determined as 10 mg kg^{-1} day^{-1} based on changes in liver (2).

Carcinogenicity and chronic effects

Oral mice (2 yr) 0, 20, 200, 2000 or 5000 ppm in diet. High-dose animals exhibited retarded growth, decreased Specific gravity of urine, reduced levels of protein in the urine, elevation in platelet and lymphocyte count, increased absolute and relative liver weight and an increased incidence of hepatocellular swelling (centrilobular

and diffuse) and hepatocellular hyperplasia were seen in both sexes. The incidence of hepatocellular adenoma was increased in high-dose ♀, but the combined incidence of hepatocellular adenomas and carcinomas was not significant. However, the overall incidence of lung adenoma and carcinoma in high-dose ♂ animals was significantly higher than controls. The no-observed-adverse-effect level for ♂ animals was determined to be 1.82 mg kg^{-1} buprofezin day^{-1} (2).
Oral rat (2 yr) 0, 5, 20, 200, 2000 ppm in feed. No effect of treatment on clinical observations was observed, survival in all groups was >40%. In high-dose ♀ increased incidence of cystitis, chronic nephrosis and interstitial oedema in the heart observed (2).

Teratogenicity and reproductive effects
Oral rat (13 wk) 0, 10, 100 or 1000 ppm in diet. F_0, F_1 and F_2 animals were studied. Litter data revealed decrease in survival for F_0 pups during 0-4 day lactation from high-dose animals. Lower mean live pup weight observed in all dose groups. The authors conclude at doses ≤1000 ppm buprofezin has no influence on reproductive performance (2).
Gavage Sprague-Dawley rat (6-15 day gestation) 0, 50, 200 or 800 mg kg^{-1} day^{-1}. Maternal toxicity in high-dose animals evidenced by reduced food intake, decreased body weight, loose faeces, urogenital staining, lethargy, hunched posture, thin appearance and piloerection. At 800 mg kg^{-1} day^{-1} 4 ♀ showed total resorption and increased early post-implantation loss, reduced litter size and foetal weight were recorded. Foetuses in highest dose group showed significant increased incidence of subcutaneous oedema and signs of slight foetal immaturity including reduced mean foetal weight. The no-observed-adverse-effect level was 50 mg kg^{-1} day^{-1} for maternal toxicity and ≤166-188 mg kg^{-1} day^{-1} for embryotoxicity (2).

Metabolism and toxicokinetics
♂ Sprague-Dawley rats 10 or 100 mg kg^{-1} ^{14}C buprofezin in olive oil. Rats were sacrificed 2, 5, 9, 24 or 96 hr after dosing. Following administration of 10 mg kg^{-1}, the highest radioactivity was detected in the urinary bladder 9 hr after dosing. Maximum dose detected in liver 5 hr after dosing. Radioactivity was also detected in adipose tissue, kidney, adrenal gland, pancreas and blood. Following administration of 100 mg kg^{-1} highest radioactivity was detected in adipose tissue after 9 hr. Distribution pattern to other organs and tissues was similar to lower dose animals. The $t_{1/2}$ in all tissues and organs examined was 3.5-15 hr (between 9 and 24 hr) after dosing and 15-72 hr (between 24 and 96 hr) (2).
Oral rat single 10 mg kg^{-1} dose excreted in urine, faeces and bile within 24 hr. Main route of metabolism was via hydroxylation of phenyl ring and oxidation of sulfur. Hydroxylation of phenyl ring gave 4-hydroxy, 3,4-dihydroxy and 3-hydroxy-4-methoxy buprofezin and some of these were conjugated with glucuronic acid or sulfate. The oxidation products of sulfur were thought to form isopropyl phenyl urea through cleavage of the thiadiazine ring. 12% of dose excreted into faeces as parent compounds. In urine and bile only, more polar metabolites were detected (2).
Oral rat single dose 10 or 100 mg kg^{-1}, polar metabolites in faeces and urine included 1-(4-hydroxyphenyl)-3-isopropylurea, 4-aminophenol and 4-acetamidophenol. The sulfuric acid conjugate of 4-acetamidophenol was the major metabolite in urine, accounting for 3.9% of the dose (2).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537, TA1538 with and without metabolic activation negative. *Escherichia coli* WP2 uvrA with and without metabolic activation negative. *In vitro* mouse lymphoma L5178Y tk+/tk– with and without metabolic activation negative. *In vivo* mouse bone marrow micronucleus test negative (2).
Syrian hamster embryo cells induction of DNA repair negative, but morphological transformation and kinetochore-positive micronuclei are induced (3).

Other effects

Other adverse effects (human)
Medical surveillance of workers who routinely handled buprofezin in a factory in Japan has been undertaken. The survey revealed no effects which could be attributed to exposure to buprofezin (2).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides and related products: maximum admissible concentration 0.1 $\mu g\ l^{-1}$ (4).
Included in Schedule 6 (Release into Land: Prescribed Substances) of Statutory Instrument No. 472, 1991 (5).
EPA Toxicity Class III (1).
WHO Toxicity Class Table 5 (6).

Other comments

The toxicity of buprofezin has been extensively reviewed (2).

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B195 busulfan

$$CH_3SO_2O(CH_2)_4OSO_2CH_3$$

$C_6H_{14}O_6S_2$ **Mol. Wt.** 246.31 **CAS Registry No.** 55-98-1

Synonyms 1,4-butanediol dimethanesulfonate; Myleran; 1,4-bis(methanesulfonoxy)butane; bisulfane; 1,4-dimesyloxybutane

EINECS No. 200-250-2 **RTECS No.** EK 1750000

Uses Treatment for chronic myeloid leukaemia.

Physical properties

M. Pt. 116-117°C
Solubility Organic solvents: acetone, ethanol

Mammalian & avian toxicity

Acute data
LD_{50} oral redwing blackbird 56 mg kg^{-1} (1).
LD_{50} oral rat 1860 $\mu g\ kg^{-1}$ (2).
LD_{50} intraperitoneal rat 18 mg kg^{-1} (3).
LD_{Lo} intravenous dog, monkey 8 mg kg^{-1} (4).

Carcinogenicity and chronic effects
Sufficient evidence for carcinogenicity to humans, limited evidence for carcinogenicity to animals, IARC classification group 1 (5).
Leukaemia patients who had been treated with Myleran developed cytological abnormalities and some developed carcinomas; effects were not dose-related, although the cases were confirmed to be those patients who had received no radiation and no other cytotoxic agent (6,7).

Teratogenicity and reproductive effects

Extreme intra-uterine arrest of growth, congenital anomalies of the eyes, palate, thyroid and ovaries, and disseminated cytomegaly reported in an infant whose mother received chemotherapy (4-6 mg day^{-1}) during pregnancy. The infant died at 10 wk (8).

Atypical cervical cytology reported after prolonged therapy (9).

In mice, non-teratogenic low doses (5 or 10 mg kg^{-1}) given orally on day-13 of pregnancy reduced testis and ovary weight, and reduced fertility and reproductive performance of offspring (10).

Metabolism and toxicokinetics

In humans, largely excreted in the urine as sulfur-containing metabolites (11).

It is readily absorbed from the gastrointestinal tract and rapidly disappears from the blood with a $t_{1/2}$ of 2 to 3 hr (11,12).

Genotoxicity

Salmonella typhimurium TA100, TA1535 with and without metabolic activation positive (13).

Salmonella typhimurium TA98 with metabolic activation positive; without metabolic activation negative (14,15).

Human peripheral blood lymphocytes increased frequencies of sister chromatid exchange and chromosomal aberrations (5,14).

Drosophila melanogaster induced sex-linked recessive lethal mutations (14).

In vivo mouse induced dominant lethal mutations and increased frequency of chromosomal aberrations and micronuclei in bone-marrow cells (16).

Induced DNA damage but not mutation; covalent binding to DNA, RNA and protein in mice treated *in vivo* (17).

Other effects

Any other adverse effects

Side-effects at high dosage include leucopenia, thrombocytopenia and haemorrhagic symptoms, bone marrow depression which may not become apparent until several months after the start of treatment (11).

Other comments

Reviews on experimental toxicology and human health effects listed (18).

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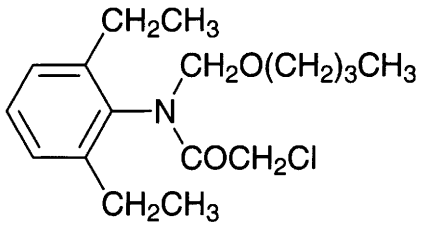
B196 butachlor



$C_{17}H_{26}ClNO_2$ **Mol. Wt.** 311.85 **CAS Registry No.** 23184-66-9

Synonyms acetamide, *N*-(butoxymethyl)-2-chloro-*N*-(2,6-diethylphenyl); *N*-butoxymethyl-2-chloro-2',6'-diethyltacetanilide; Aimchlor; Butanex; Butanox; Hiltaklor; Machete; Pillarsete; Yeer; Trapp

EINECS No. 245-477-8 **RTECS No.** AE 1200000

Uses Herbicide.

Physical properties

M. Pt. <5°C **B. Pt.** 156°C at 0.5 mmHg **Specific gravity** 1.070 at –25°C
Volatility v.p. 4.2×10^{-6} mmHg at 25°C
Solubility Water: 20 mg l^{-1} at 20°C. Organic solvents: acetone, benzene, diethyl ether, ethanol, ethyl acetate, *n*-hexane

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) carp, bluegill sunfish, rainbow trout 0.32, 0.44, 0.52 mg l^{-1}, respectively (1).

Invertebrate toxicity
LC_{50} (24 hr) silkworm larvae 60 g l^{-1} (2).
LC_{50} (24 hr) earthworm 30 mg l^{-1}, significantly inhibits ATP-ase (3).
EC_{50} (48 hr) *Daphnia* 2.4 mg l^{-1} (4).

Bioaccumulation
Macrobranch shrimp 10 and 100 μg l^{-1} showed a bioconcentration factor of 0.01-0.03 (5).

Environmental fate

Degradation studies
Cultures of the soil fungi *Fusarium solani* and *Chaetomium globosum* metabolised butachlor in mineral salt solution. The metabolism involved dechlorination, hydrolysis, dehydrogenation, *N*-dealkylation, *O*-dealkylation, *C*-dealkylation, and cyclisation (6).

Mammalian & avian toxicity

Acute data
LD_{50} oral mallard duck, bobwhite quail >4640, >10,000 mg kg^{-1}, respectively (1).
LD_{50} oral rat 2000 mg kg^{-1} (1).
LD_{50} dermal rabbit 4080 mg kg^{-1} (4).

Sub-acute and sub-chronic data
LC_{50} (8 day) oral mallard duck, bobwhite quail 6597, >10,000 mg kg^{-1} diet, respectively (1).
One-year no-effect level for dogs 5 mg kg^{-1} day^{-1} (4).

Carcinogenicity and chronic effects

In 2-yr feeding trials rats and dogs receiving 1000 mg kg^{-1} diet exhibited no ill-effects (7).

Metabolism and toxicokinetics

In vitro incubation with rat liver S9, microsome and cytosolic fractions produced butachlor glutathione conjugate (BGSC); this process was inefficient in rat kidney S9 fraction. More enzyme activity was detected in the ♀ liver fraction, which appears to contain more glutathione S-transferase than the ♂ liver fraction. BGSC was transformed to butachlor acetyl cysteine conjugate in the presence of acetyl CoA, and to butachlor cysteine conjugate without acetyl CoA. Biotransformation of BGSC to the mercapturate was not observed in the liver S9 fraction. The conjugation of butachlor with GSH is carried out by glutathione S-transferase in the liver; GBSC then appears to be transported to the kidneys, where is it transformed to the mercapturate (8).

In vitro human skin (24 hr) 1.01 μg, ~5% was absorbed, on average. The mean peak absorption rate was 0.7% of the applied dose hr^{-1}, and 1.4 to 8.1% was retained. 0.9% of the dose recovered from the skin had been metabolised to 4-hydroxybutachlor. 1.8% of the dose in receptor fluid consisted of polar conjugates: cysteine 0.29%, glutathione 0.1%, unidentified metabolites 1.4%. Skin cytosolic fractions formed butachlor glutathione and butachlor cysteine conjugates at 12.0±1.5 and 48.0±3.6 pmol min^{-1} mg^{-1} protein, respectively. Human skin microsomes incubated with butachlor formed 4-hydroxybutachlor in the presence of NADPH at 55.0±15.0 pmol min^{-1} mg^{-1} protein (9).

Genotoxicity

Chinese hamster ovary cells induced chromosome aberrations with and without metabolic activation (10).

In vitro human peripheral blood lymphocytes showed a dose-dependent increase in the frequency of chromosomal aberrations. No sister chromatid exchanges were induced (11).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides and related products: maximum admissible concentration 0.1 μg l^{-1} (12).

Included in Schedule 6 (Release into Land: Prescribed Substances) of Statutory Instrument No. 472, 1991 (13).

EPA Toxicity Class III (1).

WHO Toxicity Class Table 5 (14).

Other comments

Metabolic pathways reviewed (15).

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B197 1,3-butadiene

$$H_2C{=}CHCH{=}CH_2$$

C_4H_6 **Mol. Wt.** 54.09 **CAS Registry No.** 106-99-0

Synonyms buta-1,3-diene; bivinyl; divinyl; vinylethylene; pyrrolylene

EINECS No. 203-450-8 **RTECS No.** EI 9275000

Uses In the manufacture of polymers and synthetic rubbers.

Physical properties

M. Pt. –109°C **B. Pt.** –4.5°C **Flash point** –70°C **Specific gravity** 0.6211 (liquified) at –20°C
Volatility v.p. 2.5 mmHg at 20°C ; v.den. 1.9

Occupational exposure

SE-LEVL 0.5 ppm (1 mg m^{-3}) **SE-STEL** 5 ppm (10 mg m^{-3})
UK-LTEL MEL 10 ppm (22 mg m^{-3})
US-TWA 2 ppm (4.4 mg m^{-3})

UN No. 1010 **HAZCHEM Code** 2WE **Conveyance classification** flammable gas
Supply classification extremely flammable, toxic
Risk phrases May cause cancer – Extremely flammable (R45, R12)
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) pinperch 71.5 mg l^{-1} (1).

Bioaccumulation
Calculated bioconcentration factor of 19.1 indicates that environmental accumulation is unlikely (2).

Environmental fate

Degradation studies
Nocardia sp. 249 degraded butadiene by catabolic mechanisms using butadiene as sole carbon energy source (3). Oxidised by methylotrophic bacteria and utilised by a *Nocardia* sp. as sole carbon source (4).

Abiotic removal
Estimated $t_{1/2}$ due to reactions with hydroxyl radicals and ozone is 4.9 hr (2).
Stable reaction products of photo-oxidation are acetaldehyde and acrolein. Due to its low boiling point (–4.5°C), it would be expected to evaporate rapidly from soils (5-7).

Adsorption and retention
Estimated adsorption coefficients in soils and sediments are 72-228 indicating that appreciable adsorption is unlikely (2).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 5.48 g kg^{-1} (8).
LC_{50} (23 min) inhalation rabbit 250,000 ppm (in air) (9).
LC_{50} (2 hr) inhalation mouse 270,000 mg m^{-3} (10).
LC_{50} (4 hr) inhalation rat 285,000 mg m^{-3} (10).

Carcinogenicity and chronic effects

Inadequate evidence for carcinogenicity to humans, sufficient evidence for carcinogenicity to animals, IARC classification group 2B (11).

Carcinogenic to ♂ and ♀ rats producing haemangiosarcomas of the heart, malignant lymphomas, alveolar/bronchiolar adenomas and carcinomas, papillomas and carcinomas of the stomach, hepatocellular adenomas and carcinomas, mammary gland carcinomas and ovarian granulomas (12).

National Toxicology Program inhalation study on mice shows clear evidence of carcinogenic activity (13).

♂ and ♀ B6C3F1 mice (65 wk) exposed to 625 ppm. Anaemia occurred at >62.5 – 625 ppm, testicular atrophy was induced at 625 ppm and ovarian atrophy was observed ≥20 ppm. During the first 50 wk, lymphocytic lymphoma was the major cause of death at 625 ppm. Heart, forestomach, lung, Harderian gland, mammary gland, ovary and liver neoplasms were observed in mice that died between 40 and 65 wk (14).

In inhalation studies on rats and mice conducted by the National Toxicology Program, high rates of early lethal lymphomas occurring at exposure levels of 625 ppm or higher reduced the development and expression of later developing tumours at other sites. An increase in lung tumours in ♀ mice was observed at exposure concentrations as low as 6.25 ppm, the lowest concentration ever used in a long-term carcinogenicity study of this gas. Human exposure to 1,3-butadiene by workers employed at facilities that produce this chemical and at facilities that produce styrene-butadiene rubber have been measured at levels higher than those that cause cancer in animals. Epidemiology studies have consistently revealed associations between occupational exposure to 1,3-butadiene and excess mortality due to lymphatic and haematopoietic cancers. In response to the carcinogenicity findings for 1,3-butadiene in animals and humans, the Occupational Safety and Health Administration has proposed lowering the occupational exposure standard for this chemical from 1000 ppm to 2 ppm (15).

Inhalation studies show that mice have high blood levels of butadiene monoxide and butadiene diepoxide compared with levels in rats. This may have relevance for the greater incidence of butadiene-induced carcinogenicity in mice (16).

Teratogenicity and reproductive effects

Pregnant Sprague-Dawley rats and Swiss (CD-1) mice (0, 40, 200 or 1000 ppm) 6 hr day^{-1} on days 6-15 of gestation and killed on day 18 (mice) or 20 (rats). In rats, maternal toxicity, in the form of reduced extra gestational weight gain, was observed in animals dosed with 1000 ppm. No evidence of developmental toxicity recorded. In mice, the foetuses were more susceptible than the dam; maternal toxicity was observed at 200 and 1000 ppm and mean body weights of ♀ foetuses were reduced (17).

Metabolism and toxicokinetics

♀ Sprague-Dawley rats exposed to 62.5 ppm 1,3-butadiene 6 hr day^{-1} for 10 days had levels of butadiene monoepoxide 5 × higher in mammary tissue and 2 × higher in fat tissue compared with the levels found in rats exposed only once for 6 hr to 62.5 ppm 1,3-butadiene. Butadiene diepoxide levels also increased in fat tissue following multiple exposures to 1,3-butadiene (18).

Rats exposed for 2 hr to an airborne concentration of 130,000 ppm revealed highest accumulation in the perirenal fat (152 mg%). Lower concentrations (36-51 mg%) were found in the liver, brain, spleen and kidney (19).

Intraperitoneal administration to ♂ B6C3F1 mice, most of the dose was exhaled unchanged, carbon dioxide was the next largest pool, lesser amounts in urine and faeces; little remained in the carcass 65 hr later (20).

♂ Sprague Dawley rats and B6C3F1 mice exposed by inhalation (nose only) for 3.4 hr to 1220 and 121 μg l^{-1} in air, respectively. 1,3-Butadiene was distributed in lung, trachea, nasal turbinates, small and large intestine, liver, kidneys, bladder and pancreas within 1 hr after exposure in both species. Reported $t_{1/2}$ of 2-10 hr (21).

1,3-Butadiene is an indirect-acting mutagen that is bioactivated in laboratory animals to at least two mutagenic metabolites, 1,2-epoxy-3-butene and 1,2,3,4-diepoxybutene (22).

In mice, 1,3-butadiene is metabolised to 1,2-epoxybut-3-ene at <1000 ppm and 2000 ppm at twice the metabolic rate of rats (23).

In vitro peak rates for 1,3-butadiene (BD) oxidation to butadiene monoepoxide (V_{max}) were higher for B6C3F1 mouse liver microsomes than for human or Sprague-Dawley rat microsomes (2.6, 1.2 and 0.6 nmol mg^{-1} protein min^{-1}, respectively). The V_{max} for oxidation by mouse lung microsomes was similar to that for mouse liver microsomes, and more than 10 × the rate for human or rat lung microsomes. Analysis showed that cytochrome P450 2E1 was the enzyme responsible for oxidation to butadiene monoepoxide (BMO). Only mouse liver microsomes metabolised BMO to butadiene diepoxide, a known rodent carcinogen, at a quantifiable rate. V_{max} for

the conjugation of BMO with glutathione, catalysed by glutathione S-transferase, was higher in mouse liver cytosol than in human or rat liver cytosol (500, 45 and 241 nmol mg^{-1} protein min^{-1}, respectively). Human liver microsomes had the highest rate of BMO hydrolysis by epoxide hydrolases (V_{max} 9 to 58 nmol mg^{-1} protein min^{-1}), at least 2 × higher than that in mouse and rat liver microsomes. In general, the K_m (Michaelis constant) for detoxication reactions was 1000 × greater than that for oxidation reactions. The V_{max}/K_m ratio is likely tobe important for BD and BMO metabolism *in vivo*, as BD has a low solubility and a high K_m for oxidation. *In vitro* data were used to calculate *in vivo* clearance constants. The overall activation/detoxication ratios for mice, rats and humans were 72, 5.8 and 5.9 respectively; the difference between these for mice and rats correlate with the higher carcinogenicity of BD in mice (24).

Inhalation ♂ Sprague-Dawley rats and B6C3F1 mice (6 hr) nose-only exposure to 62.5, 625 and 1250 ppm. Blood samples were collected at 2, 3, 4, and 6 hr of exposure to measure 1,3-butadiene and butadiene monoxide levels, and at 3 and 6 hr of exposure to measure butadiene diepoxide. After exposure, samples were taken at 2-10 min intervals for 30 min. In both rats and mice, 1,3-butadiene and butadiene monoxide levels in the blood were at steady-state at 2, 3, 4 and 6 hr of exposure, and rapidly decreased after exposure. Steady-state concentrations of 1,3-butadiene were 2.4, 37 and 58μM in mice and 1.3, 18 and 37 μM in rats exposed to 62.5, 625 and 1250 ppm, respectively. The steady-state concentrations of butadiene monoxide were 0.6, 3.7 and 8.6 μM in mice and 0.07, 0.94 and 1.3 μM in rats, respectively. The peak concentrations of butadiene diepoxide in mice at 6 hr were 0.65, 1.9 and 2.5 μM, respectively. Rats did not have quantifiable levels of butadiene diepoxide in the blood (16).

1,3-butadiene was metabolised to butadiene monoxide by B6C3F1 mouse and human bone marrow cells, and by purified human myeloperoxidase, an abundant enzyme in bone marrow. Metabolism was stimulated in all cell types by hydrogen peroxide, suggesting a peroxidase-mediated process. Hydrogen peroxide but not NADPH stimulated metabolism in mouse bone marrow cell lysates, suggesting that cytochrome P450 does not play a part in butadiene monoxide formation; this hydrogen peroxide-stimulated metabolism is, however, more than two orders of magnitude lower than in NADPH-stimulated mouse or rat hepatic microsomes (25).

Irritancy

Inhalation human (1 min) 100,000 ppm caused irritation to respiratory system (26).

Conjunctivitis was reported in mice exposed to 90,000-140,000 ppm and rabbits exposed to 150,000-250,000 ppm. No eye injury was observed in rabbits exposed to 6700 ppm for 7.5 hr day^{-1} 6 day wk^{-1} for 8 month. It has been suggested that the conjunctivitis is due to the presence of the dimer 4-vinyl-1-cyclohexane (27).

Genotoxicity

Salmonella typhimurium TA1530 with metabolic activation positive (28).

Human lymphocytes (2 hr) induced sister chromatid exchange with and without metabolic activation (29).

Potent *in vivo* genotoxin but weak genotoxin *in vitro*: *Salmonella typhimurium* TA1535 with metabolic activation weakly positive; did not induce sister chromatid exchanges in human whole blood lymphocytes with or without metabolic activation; induced sister chromatid exchanges and micronuclei in bone marrow cells of mice but not rats after inhalation exposure to 10-10,000 ppm, 6 hr day^{-1} for 2 days; failed to induce unscheduled DNA synthesis in rat or mouse hepatocytes *in vivo* (30).

In vivo mice (5 days, 6 hr day^{-1}) 50, 200, 500 or 1300 ppm caused non-linear formation of micronuclei in bone marrow and peripheral blood erythrocytes. Male mice exposed to 1300 ppm developed dominant lethal mutations in spermatozoa and late spermatids. Female mice exposedto 500 ppm on days 8-12 of pregnancy exhibited coat colour spots in the mouse spot test (31).

Induced micronuclei and sister chromatid exchanges in bone marrow of mice but not rats *in vivo* (28).

In vivo mouse bone marrow induced micronuclei and sister chromatid exchange (32).

Weakly clastogenic in premeiotic germ cells of inhalation mice 130, 250, and 500 ppm (33).

Clastogenic in splenocytes and peripheral blood reticulocytes of inhalation mice 130, 250, and 500 ppm. Weakly aneugenic in splenocytes at a short time-interval after exposure (34).

Micronucleus assays were used to study the genotoxic effects of 1,3-butadiene and its metabolites in germ cells and somatic cells of rats and mice. Inhalation exposure of mice to 200, 500 or 1300 ppm of 1,3-butadiene for 6 hr day^{-1} 7 days wk^{-1} induced chromosome damage in spermatocytes. 1,2-Epoxybutene (40 and 80 mg kg^{-1}) and 1,2,3,4-diepoxybutane (15-40 mg kg^{-1}), both metabolites of 1,3-butadiene, induced clastogenic damage in splenocytes and spermatocytes of rats and mice. Different concentrations of the metabolites produced species

differences in their effects. Diepoxybutane was the stronger clastogen in both rats and mice. The higher exposure levels showed some toxic effects (35).

♂ mice, exposed to 1300 ppm of 1,3-butadiene on 5 days for 6 hr day^{-1} were mated to ♀s 8 to 14 days after the end of exposure. Heritable translocations were noted in the F1 hybrids at a frequency of 2.7% compared with 0.05% in the untreated control group. Dose-response data are required to quantify the genetic risk after 1,3-butadiene exposure (36).

Other effects

Other adverse effects (human)

Several studies have shown elevated standardised mortality ratios for cancers in various organs in rubber industry workers. The results could, however, be complicated by exposure to other chemicals (37).

Legislation

Included in Schedule 4 (Release into Air: Prescribed Substances) of Statutory Instrument No. 472, 1991 (38).

Other comments

Detected but not quantified in drinking water (39).

Fugitive emission from petrochemical processes (40).

Toxicity and hazards reviewed (41).

1,3-Butadiene rubber-based plastic containers can contaminate foodstuffs (42).

Reviews on physico-chemical properties, human health effects, experimental toxicology, epidemiology, workplace experience, exposure and environmental effects are listed (43).

Future directions in toxicology studies reviewed (44).

Worldwide regulatory activity for occupational exposure with reference to control technology and economics reviewed (45).

Toxicity and carcinogenicity reviewed (46).

Genotoxicity reviewed (47).

Carcinogenicity, mutagenicity and developmental toxicity reviewed (48).

Epidemiological and mechanistic carcinogenicity data reviewed and discussed (49).

Health effects and metabolic differences between species reviewed (50).

In vivo metabolism, adduct formation and genotoxicity data from rodent and human exposure reviewed (51).

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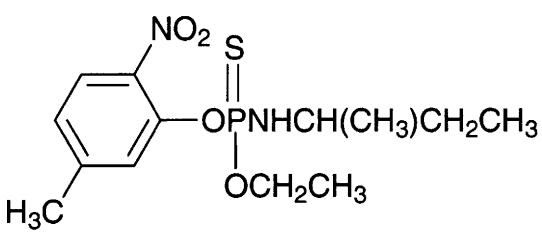
B198 butamifos



$C_{13}H_{21}N_2O_4PS$ **Mol. Wt.** 332.36 **CAS Registry No.** 36335-67-8

Synonyms Phosphoromidothiroic acid, (1-methylpropyl), *O*-ethyl-*O*-(5-methyl-2-nitrophenyl)ester; *O*-ethyl, *O*-6-nitro-*m*-tolyl*sec*-butylphosphoramidothioate; Cremart

RTECS No. TB 4920000

Uses Herbicide.

Physical properties

Specific gravity 1.188 at -25°C **Partition coefficient** log P_{ow} 4.62 at 25°C (1) **Volatility** v.p. 5.5×10^{-4} mmHg at 27°C
Solubility Water: 6.19 mg l^{-1} at 25°C. Organic solvents: acetone, methanol, xylene

Ecotoxicity

Fish toxicity
LC_{50} (48 hr) carp 2.4 mg l^{-1} (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral ♂, ♀ rat 1030, 1975 mg kg^{-1}, respectively (1).
LD_{50} percutaneous rat >2000 mg kg^{-1} (1).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides and related products: maximum admissible concentration 0.1 μg l^{-1} (2).
Included in Schedule 6 (Release into Land: Prescribed Substances) of Statutory Instrument No. 472, 1991 (3).

Other comments

Metabolic pathways reviewed (4).

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3. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
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B199 butane

$$CH_3CH_2CH_2CH_3$$

C_4H_{10} **Mol. Wt.** 58.12 **CAS Registry No.** 106-97-8
Synonyms *n*-Butane
EINECS No. 203-448-7 **RTECS No.** EJ 4200000
Uses Fuel. Aerosol propellant.
Occurrence Natural gas.

Physical properties

M. Pt. –135°C **B. Pt.** –0.5°C **Flash point** –138°C **Specific gravity** 0.5788 at 20°C with respect to water at 4°C
Partition coefficient log P_{ow} 2.89 **Volatility** v.p. 2 mm Hg at 18.8°C ; v.den. 2.0
Solubility Water: 61 μg g^{-1} at 20°C. Organic solvents: diethyl ether, ethanol

Occupational exposure

DE-MAK 1000 ppm (2400 mg m^{-3})
FR-VME 800 ppm (1900 mg m^{-3})
JP-OEL 500 ppm (1200 mg m^{-3})
UK-LTEL 600 ppm (1450 mg m^{-3}) **UK-STEL** 750 ppm (1810 mg m^{-3})
US-TWA 800 ppm (1900 mg m^{-3})

UN No. 1011 **HAZCHEM Code** 2WE **Conveyance classification** flammable gas
Supply classification extremely flammable
Risk phrases Extremely flammable (R12)
Safety phrases Keep out of reach of children (if sold to general public) – Keep container in a well ventilated place – Keep away from sources of ignition – No smoking (S2, S9, S16)

Ecotoxicity

Bioaccumulation
Calculated bioconcentration factor of 1.9 indicates that environmental accumulation is unlikely (1).

Environmental fate

Nitrification inhibition
Butane degradation proceeded more rapidly in unsaturated sandy soil with added nitrogen than in soil with added phosphate or trace minerals, or without added nutrients. As the initially available inorganic nitrogen was utilised, the rate of butane degradation decreased. After three months, butane degradation rates began to increase as the soil bacteria apparently overcame this nitrogen limitation, indicating that nitrogen fixation had occurred (2).

Degradation studies
With oxygen, butane supports the growth of *Neurospora crassa* as well as the germination of *N. ascrospores* and growth of *Escherichia coli* B and Sd4, thus rendering butane potentially biodegradable (3).
Incubation with natural flora in groundwater in the presence of the other components of high octane gasoline (100 $\mu g\ l^{-1}$) biodegradable 0% after 192 hr at 13°C (initial concentration 0.63 $\mu l\ l^{-1}$) (4,5).
Within 24 hr, butane was oxidised to 2-butanone and 2-butanol by cell suspensions of over 20 methyltrophic organisms isolated from lake water and soil samples (6).
Degradation by microorganisms occurs via the beta-oxidation pathway (7).
Butane is not consumed by the pogonophore *Siboglinum poseidoni* (8).
Non-biodegradable/qualified (9).

Abiotic removal
A model for the reaction of butane and nitrous oxides in air determined products of the photo-oxidation as 2-butyl nitrate, butyraldehyde, 1-butyl nitrate, methyl nitrate, peroxyacetyl nitrate, propene oxide, propionaldehyde, formaldehyde and acetaldehyde (10).
Estimated lifetime under photochemical smog conditions in south-east England 15 hr (4).

Adsorption and retention
Calculated soil adsorption coefficient range from 450-900 which indicates a medium to low soil mobility (11,12).

Mammalian & avian toxicity

Acute data
LC_{50} inhalation (4 hr) rat, (2 hr) mouse 658, 680 g m^{-3}, respectively (13).

Metabolism and toxicokinetics
Inhalation (4 hr) rats and mice exposed to lethal concentration (27.8-29%) revealed highest concentrations in perinephric fat (2086 ppm), then brain (750 ppm), spleen (522 ppm), liver (492 ppm) and kidney (441 ppm) (14).

Irritancy

Direct contact of eye and skin with liquefied butane may cause burns or frostbite. Repeated exposure may cause dermatitis in humans (15).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537, TA1538 with and without metabolic activation negative (16).

Other effects

Other adverse effects (human)

An autopsy of a 25-yr-old man who had been abusing lighter refill gas for 10 yr revealed butane in blood, gastric content, brain, lung, heart, liver, kidney, spleen and pancreas. Bronchi and alveolar abnormalities were present. It was concluded that death was caused by asphyxia due to respiratory obstruction (17).

Legislation

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

Other comments

Contaminant in drinking, surface and ground water. Released into air from waste incinerators and landfill sites. Product of gasoline combustion (19-25).

Reviews on physico-chemical properties, human health effects, experimental toxicology, epidemiology, workplace experience and exposure listed (26).

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B200 1,3-butanediamine

$$CH_3CH(NH_2)CH_2CH_2NH_2$$

$C_4H_{12}N_2$ **Mol. Wt.** 88.15 **CAS Registry No.** 590-88-5

Synonyms 1,3-diaminobutane

EINECS No. 209-692-0 **RTECS No.** EJ 6700000

Uses Intermediate in organic synthesis.

Physical properties

B. Pt. 142-150°C **Flash point** 52°C (open cup) **Volatility** v.den. 3.0
Solubility Organic solvents: ethanol

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 1350 mg kg^{-1} (1).
LD_{50} dermal rat 430 mg kg^{-1} (1).

Irritancy
Dermal rabbit (24 hr) 10 mg and 250 µg instilled into rabbit eye caused severe irritation (1).

Genotoxicity

Salmonella typhimurium TA98 and TA100 with and without metabolic activation negative (2).

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B201 1,4-butanediamine

$$H_2N(CH_2)_4NH_2$$

$C_4H_{12}N_2$ **Mol. Wt.** 88.15 **CAS Registry No.** 110-60-1

Synonyms 1,4-diaminobutane; putrescine; tetramethylenediamine

EINECS No. 203-782-3 **RTECS No.** EJ 6800000

Uses Organic synthesis. Biochemical research.
Occurrence Product of decomposition of animal matter and sewage sludge.

Physical properties

M. Pt. 27-28°C **B. Pt.** 158-160°C **Flash point** 51°C **Specific gravity** 0.877 at -25°C
Solubility Water: very soluble in water

Environmental fate

Anaerobic effects
Biodegradable (1).

Mammalian & avian toxicity

Acute data
LD_{Lo} oral mouse, rabbit 1600 mg kg^{-1} (2,3).
LD_{Lo} intravenous rabbit 80 mg kg^{-1} (3).
LD_{Lo} rectal rabbit 400 mg kg^{-1} (3).
LD_{Lo} subcutaneous rabbit, rat 200, 300 mg kg^{-1}, respectively (4).
Acute oral toxicity Wistar rat 2000 mg kg^{-1} (5).

Sub-acute and sub-chronic data
Oral Wistar rat (6 wk) 0, 200, 2000, or 5000 ppm in diet. No-observed-effect level 2000 ppm (180 mg kg^{-1} day^{-1}). In the top dose group decreased body weights associated with diminished food intake were generally seen (5).

Teratogenicity and reproductive effects
Intraperitoneal injection of 78.5 mg kg^{-1}, 4 × at 3 hr intervals, on days 10-14 pregnancy. Reduced foetal weight but no gross malformations, maternal or foetal death reported (6).

Metabolism and toxicokinetics
Deaminated by rat liver monoamine oxidase A and B (7).

Genotoxicity

Stimulates chromatin transcription (8).
HeLa cells cytotoxicity 170 mg l^{-1} (9).
Mouse liver unscheduled DNA synthesis at 170 mg l^{-1} (10).
Mouse ascites tumour DNA inhibition 880 mg l^{-1} (10).
Mouse liver DNA inhibition 1700 mg l^{-1} (10).

Other effects

Any other adverse effects
Intraperitoneal ♂ rats 200 mg kg^{-1} resulted in behaviour including wet dog shakes and motor incoordination. The severity of clinical signs was paralleled by the concentration of 1,4-butanediamine in the brain. Two hours after treatment, histological examination showed perivascular oedema and moderate spongiosis. After 24 hr, levels in the frontal cortex decreased, but the histology of the brain tissue was unchanged (11).
Trace amounts found in normal erythrocytes and significantly increased amounts in erythrocytes parasitised by *Plasmodium knowlesi*, a simian malaria parasite (12).

Other comments

Added to the culture medium of *Dunaliella primolecta* stimulates growth and causes increased photosynthesis (+107% at 3 days, and 241% at 15 days), increased chlorophyll *a* content (+276% at 13 days, 140% at 21 days and 94% at 36 days old) and increased ATP content (126% measured in the stationary phase) (13).

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B202 1,2-butanediol

$$CH_3CH_2CH(OH)CH_2OH$$

$C_4H_{10}O_2$ **Mol. Wt.** 90.12 **CAS Registry No.** 584-03-2

Synonyms 1,2-butylene glycol

EINECS No. 209-527-2 **RTECS No.** EK 0380000

Uses Polymerisation agent. Antimicrobiol. Pharmaceutical preparations.

Physical properties

M. Pt. 48-55°C **B. Pt.** 193.5-195°C **Flash point** 90°C **Specific gravity** 1.0024 at 20°C with respect to water at 4°C **Volatility** v.den. 3.1

Solubility Organic solvents: acetone, ethanol

Environmental fate

Degradation studies

Non-biodegradable/qualified (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse 3720 mg kg^{-1} (2).

LD_{50} oral rat 16 g kg^{-1} (3).

Other comments

Toxicity reviewed (4).

Reviews on human health effects and experimental toxicology listed (5).

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B203 1,3-butanediol

$$CH_3CH_2OHCH_2CH_2OH$$

$C_4H_{10}O_2$ **Mol. Wt.** 90.12 **CAS Registry No.** 107-88-0

Synonyms 1,3-butylene glycol; 1,3-dihydroxybutane; β-butylene glycol; methylmethylene glycol

EINECS No. 203-529-7 **RTECS No.** EK 0440000

Uses Intermediate in the manufacture of polyester. Plasticiser. Humectant for cellophane, tobacco. In the preparation of some cosmetics and pharmaceuticals.

Physical properties

B. Pt. 203-204°C **Flash point** 121°C **Specific gravity** 1.004-1.006 at 20°C with respect to water at 20°C
Volatility v.p. 0.6 mmHg at 20°C ; v.den. 3.1
Solubility Water: soluble. Organic solvents: acetone, castor oil, dibutyl phthalate, ethanol, methyl ethyl ketone

Environmental fate

Degradation studies
Non-biodegradable/qualified (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral guinea pig, mouse, rat 11, 12.98, 18.61 g kg^{-1}, respectively (2-4).
LD_{50} subcutaneous rat 20 g kg^{-1} (5).

Carcinogenicity and chronic effects
In 2-yr study test, 1-10% exposure to rats via food, and 0.5-3% exposure to dogs via food caused no discernible toxic efects (6).

Teratogenicity and reproductive effects
Gavage ♀ rat during organogenesis 0, 4236 and 7060 mg kg^{-1} day^{-1}. Maternal sedation observed at 4236 and 7060 mg kg^{-1}. Food consumption and maternal body weights were unaffected. A dose-dependent decrease in offspring birth weights was observed (7).

Irritancy
Dermal rabbit, guinea pig, miniature pig, human (48 hr) (dose unspecified) open and closed patch tests, no irritation in any species except humans and only in closed patch test (8).

Other effects

Other adverse effects (human)
Systemic effects include coughing, headache, pharyngitis, dizziness, nausea, and dyspnoea. Gastrointestinal irritation and diarrhoea may occur after exposure to high concentrations. Toxicity characterised by central nervous system depression (9).

Other comments

Very hygroscopic; absorbs 38.5 wt% water within 144 hr at 81% relative humidity (10).
Experimental toxicology and human health effects reviewed (9,11-13).
Physiological effects, chronic and acute toxicity and metabolism reviewed (14).

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B204 1,4-butanediol

$$HO(CH_2)_4OH$$

$C_4H_{10}O_2$ **Mol. Wt.** 90.12 **CAS Registry No.** 110-63-4

Synonyms 1,4-dihydroxybutane; tetramethylene glycol; 1,4-butylene glycol; 1,4-tetramethylene glycol

EINECS No. 203-786-5 **RTECS No.** EK 0525000

Uses Solvent. Chemical intermediate. Wood preservative.

Physical properties

M. Pt. 16°C **B. Pt.** 230°C **Flash point** >110°C **Specific gravity** 1.017

Ecotoxicity

Toxicity to other species

LC_{50} (duration unspecified) Salientia sp. tadpole <10,000 mg l^{-1} (1).

Environmental fate

Degradation studies

98.7% COD, 40 mg COD g dry inoculum^{-1} hr^{-1} with substance as sole carbon source (2).

Biodegradable (3).

Mammalian & avian toxicity

Acute data

LD_{50} oral guinea pig, rat, mouse, rabbit 1200-2500 mg kg^{-1} (4).

LD_{50} intraperitoneal rat 1370 mg kg^{-1} (5).

LD_{Lo} intraperitoneal mouse 500 mg kg^{-1} (6).

Sub-acute and sub-chronic data

Ten ♂ Crl:CD rats (6 hr day^{-1}, 5 days wk^{-1} for 2 wk) aerosol concentrations of 0, 0.2, 1.1 or 5.2 mg l^{-1}. Pathological, urinalysis and clinical chemical examinations after the last dose and after a 2-week recovery period showed no adverse effects in rats exposed to either 0.2 or 1.1 mg l^{-1}; rats exposed to 5.2 mg l^{-1} showed non-specific reversible

systemic effects. These high-dose rats had decreased body weight after the third exposure; at the end of treatment, they had increased erythrocyte counts and haematocrits, and decreased serum cholesterol concentrations. Pathological examination showed slight atrophy of lymphoid cells in the thymus and lowered mean heart weights. No adverse effects were seen after a 2 wk recovery period (7).

Carcinogenicity and chronic effects

National Toxicology Program post peer review technical report in progress (8).

Other comments

Toxic to fish (9).

Reviews on experimental toxicology and human health effects listed (10).

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B205 2,3-butanediol

$$CH_3CH(OH)CH(OH)CH_3$$

$C_4H_{10}O_2$ **Mol. Wt.** 90.12 **CAS Registry No.** 513-85-9

Synonyms 2,3-butylene glycol; 2,3-dihydroxybutane; dimethylene glycol

EINECS No. 208-173-6 **RTECS No.** EK 0532000

Uses Solvent. Intermediate in organic synthesis.

Physical properties

M. Pt. 25°C **B. Pt.** 183-184°C **Flash point** 85°C **Specific gravity** 0.995

Environmental fate

Degradation studies

Non-biodegradable/qualified (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse 5460 mg kg^{-1} (2).

Teratogenicity and reproductive effects

In vitro 10-day Albino Wistar rat embryo 2-day incubation, effects on embryonic protein, DNA, somite development, gross morphology and viability negative (3).

Metabolism and toxicokinetics

In vivo ♂ Wistar rats (1 hr) 5 mmol kg^{-1}. 2,3-Butanediol was present in the liver, kidney and brain; a small amount was oxidised to acetoin and diacetyl in the liver. Rat liver was perfused for 1 hr with a 1 mM solution; the liver and the perfusate contained small amounts of the oxidation products. Approximately 33% of the compound was estimated to have been metabolised or conjugated (4).

Other effects

Any other adverse effects

In vitro isolated perfused rat liver 0, 5, 10, 20 and 30% (v/v) 2,3-butanediol in University of Wisconsin solution or Leibovitz L15 culture medium. No effects on intrahepatic resistance, bile production or enzymatic release were observed at the low concentration solutions of 5 and 10%. At the higher concentrations of 20 and 30% major liver damage was observed, i.e. oedema, Glisson's capsule rupture, large scale destruction of the portal system and hepatocytes, and necrosis of endothelial cells (5).

Cultured porcine aortic endothelial cells 0, 5, 10, 20 and 30% (v/v) 2,3-butanediol in University of Wisconsin solution or Leibovitz (L15) culture medium. The trypan blue exclusion test showed that 5 or 10% solutions had no adverse effect on cell viability, but 20 or 30% solutions were toxic to cells (6).

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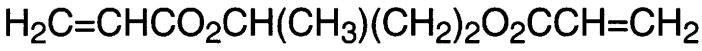
B206 1,3-butanediol diacrylate



$H_2C=CHCO_2CH(CH_3)(CH_2)_2O_2CCH=CH_2$

$C_{10}H_{14}O_4$ **Mol. Wt.** 198.22 **CAS Registry No.** 19485-03-1

Synonyms 1,3-butylene glycol diacrylate; acrylic acid, 1-methyltrimethylene ester; 1,3-butylene diacrylate; 1-methyltrimethylene diacrylate; 2-propenoic acid, 1-methyl-1,3-propanediyl ester

EINECS No. 243-105-9 **RTECS No.** AS 5250000

Uses Polymer cross-linking agent. Coating agents.

Occupational exposure

Supply classification corrosive

Risk phrases Harmful in contact with skin – Causes burns – May cause sensitisation by skin contact (R21, R34, R43)

Safety phrases Keep locked up and out of the reach of children (if sold to general public) – In case of contact with eyes, rinse immediately with plenty of water and seek medical advice – Wear suitable protective clothing, gloves and eye/face protection – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S26, S36/37/39, S45)

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 3540 mg kg^{-1} (1).

LD_{50} dermal rabbit 450 mg kg^{-1} (1).

Other comments

Reviews on experimental toxicology and human health effects listed (2).

References

1. *Toxicol. Appl. Pharmacol.* 1974, **28**, 313.
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B207 1,4-butanediol diacrylate

$$H_2C{=}CHCO_2(CH_2)_4O_2CCH{=}CH_2$$

$C_{10}H_{14}O_4$ **Mol. Wt.** 198.22 **CAS Registry No.** 1070-70-8

Synonyms acrylic acid, tetramethylene ester; 1,4-butylene glycol diacrylate; butylene diacrylate; 2-propenoic acid, 1,4-butanediyl ester; tetramethylene diacrylate

EINECS No. 213-979-6 **RTECS No.** UD 3130000

Uses Cross-linking agent for polymers.

Occupational exposure

Supply classification corrosive

Risk phrases Harmful in contact with skin – Causes burns – May cause sensitisation by skin contact (R21, R34, R43)

Safety phrases Keep locked up and out of the reach of children (if sold to general public) – In case of contact with eyes, rinse immediately with plenty of water and seek medical advice – Wear suitable protective clothing, gloves and eye/face protection – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S26, S36/37/39, S45)

Mammalian & avian toxicity

Sensitisation

Guinea pig maximisation test moderate to strong sensitiser. Cross-reactivity is possible (1).

Genotoxicity

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

Other effects

Other adverse effects (human)

In a study of twenty electron beam welding workers exposure to 1,4-butylene glycol diacrylate caused delayed contact irritancy. Within 12-14 hr skin lesions developed with aching or itching. Healing was straightforward when contact removed (3).

Data on allergic contact dermatitis from acrylates and four patients sensitised during routine patch testing are reported (4).

Other comments

Sensitisation potential of diacrylates and dimethylacrylates reviewed (5,6).

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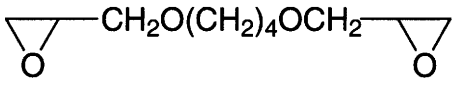
B208 1,4-butanediol diglycidyl ether



$C_{10}H_{18}O_4$ **Mol. Wt.** 202.25 **CAS Registry No.** 2425-79-8

Synonyms 1,4-bis(2,3-epoxypropoxy)butane; 2,2'-[1,4-butanediylbis(oxymethylene)bisoxirane]

EINECS No. 219-371-7 **RTECS No.** EJ 5100000

Uses Binding and transfer agent for fibres. Cross-linking agent for epoxy resins. Used in the manufacture of adhesives and protective coatings.

Physical properties

B. Pt. 260°C **Flash point** >112°C **Specific gravity** 1.100 at 20°C with respect to water at 4°C

Occupational exposure

Supply classification harmful

Risk phrases Harmful by inhalation and in contact with skin – Irritating to eyes and skin – May cause sensitisation by skin contact (R20/21, R36/38, R43)

Safety phrases Keep out of reach of children (if sold to general public) – In case of contact with eyes, rinse immediately with plenty of water and seek medical advice – After contact with skin, wash immediately with plenty of water – Wear suitable gloves and eye/face protection (S2, S26, S28, S37/39)

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 2980 mg kg^{-1} (1).

LD_{50} dermal rat 1130 mg kg^{-1} (1).

Sensitisation

Skin sensitiser guinea pigs, concentrations ≥0.5% cause cross-reaction in 95% of animals tested (2).

Guinea pig skin sensitivity maximisation test positive (3).

Sensitiser to skin patch tests for allergens in humans (4).

Genotoxicity

Salmonella typhimurium TA1535, TA98, TA100 with and without metabolic activation positive (5).
Escherichia coli PQ37 SOS chromotest with and without metabolic activation positive (6).

Other comments

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

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B209 2,3-butanedione

$$CH_3COCOCH_3$$

$C_4H_6O_2$ **Mol. Wt.** 86.09 **CAS Registry No.** 431-03-8

Synonyms diacetyl; biacetyl; 2,3-diketobutane; dimethyl diketone; dimethylglyoxal; 2,3-butadione

EINECS No. 207-069-8 **RTECS No.** EK 2625000

Uses Aroma agent for coffee and other foods.
Occurrence Found in essential oils and butter.

Physical properties

B. Pt. 88°C **Flash point** 26°C **Specific gravity** 0.981

Ecotoxicity

Toxicity to other species

The specific growth rate of *Leuconostoc mesenteroides* subsp. *cremaris* was increased in the presence of 2,3-butadione, but the biomass was not affected. Acetate production was increased, ethanol production was slightly decreased and an inhibitory effect was observed on phosphotransacetylase, alcohol dehydrogenase and NADH oxidase activity (1).

Environmental fate

Degradation studies

2,3-Butanedione has been identified as an intermediate in microbial oxidation. Since 2-butanol is biodegradable using river water or sewage inoculums with extensive mineralisation, it can be predicted that 2,3-butanedione would be biodegradable (2).

Abiotic removal

Absorbs visible radiation <460 nm and is subject to loss by photolysis as well as reaction with reactive atmospheric species. Photolytic $t_{1/2}$ is 0.7 hr compared with $t_{1/2}$ estimated for reaction with hydroxyl radicals of 621 hr (3).

Mammalian & avian toxicity

Acute data

LD_{50} oral guinea pig 990 mg kg^{-1} (4).
LD_{50} oral rat 3.0-3.4 g kg^{-1} (5).
LD_{50} intraperitoneal rat 400 mg kg^{-1} (5).

Irritancy

Dermal rat (24 hr) 500 mg caused moderate irritation (6).

Genotoxicity

Salmonella typhimurium TA98, TA100 with and without metabolic activation positive (7).
In vitro human embryo test equivocal (8).

Other comments

Reviews on human health effects and experimental toxicology listed (9).

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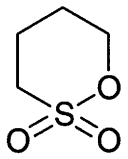
B210 1,4-butane sultone



$C_4H_8O_3S$ **Mol. Wt.** 136.17 **CAS Registry No.** 1633-83-6

Synonyms 4-hydroxy-1-butanesulfonic acid δ-sultone; 1,4-butylene sulfone; δ-valerosultone; 1,2-oxathiane-2,2-dioxide

EINECS No. 216-647-9 **RTECS No.** RP 4300000

Uses Alkylating agent.

Physical properties

M. Pt. 12.5-14.5°C **B. Pt.** 134-136°C at 4 mmHg **Flash point** >110°C **Specific gravity** 1.331

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 500 mg kg^{-1} (1).
LD_{50} subcutaneous rat 350 mg kg^{-1} (1).
LD_{50} intravenous rat 270 mg kg^{-1} (1).
LD_{50} intraperitoneal mouse 138 mg kg^{-1} (2).

Carcinogenicity and chronic effects

Subcutaneous rat (26 wk) 10, 15 or 30 mg kg^{-1} weak incidence of sarcomas at injection site (2).
Subcutaneous ICR/Ha Swiss mice (42 wk) 1680 mg kg^{-1} intermittently induced sarcomas at injection site (3).

Genotoxicity

Salmonella typhimurium TA98, TA100 with and without metabolic activation positive (4).
Escherichia coli DNA repair positive (4).
Saccharomyces cerevisiae D3 gene conversion and mitotic recombination positive (5).
Salmonella typhimurium TA1530, TA1535, TA1538 with and without metabolic activation positive (5).
Hamster kidney and hamster embryo oncogenic transformation positive (6).

Other comments

Contaminant in water samples (India) (1).
Reviews on experimental toxicology and human health effects listed (7).

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B211 1-butanethiol

$$CH_3(CH_2)_3SH$$

$C_4H_{10}S$ **Mol. Wt.** 90.19 **CAS Registry No.** 109-79-5

Synonyms butyl mercaptan; *n*-butanethiol; *n*-butyl thioalcohol; thiobutyl alcohol

EINECS No. 203-705-3 **RTECS No.** EK 6300000

Uses Solvent. Intermediate in organic synthesis. Guided missile propellant and oxidiser. Odour agent.

Physical properties

M. Pt. –116°C **B. Pt.** 98°C **Flash point** 2°C (closed cup) **Specific gravity** 0.8365 at 25°C with respect to water at 4°C **Partition coefficient** log P_{ow} 2.28 **Volatility** v.den. 3.1
Solubility Water: 590 mg l^{-1} at 22°C. Organic solvents: diethyl ether, ethanol

Occupational exposure

DE-MAK 0.5 ppm (1.9 mg m^{-3})
FR-VME 0.5 ppm (1.5 mg m^{-3})
US-TWA 0.5 ppm (1.8 mg m^{-3})

UN No. 2347 **HAZCHEM Code** 3WE **Conveyance classification** flammable liquid

Ecotoxicity

Fish toxicity

LC_{50} (24-48 hr) bluegill sunfish 7.4-5.5 mg l^{-1} (1).

Exposure of catfish to 500 mg l^{-1} 1-butanethiol increased percentage of methaemoglobin to 16.5% of total haemoglobin (2).

Environmental fate

Degradation studies

Alcaligenes faecalis, a microorganism in activated sludge flora, oxidised 1-butanethiol (3).

Abiotic removal

Reacts with oxygen atoms and hydrogen radicals in the troposphere, estimated $t_{1/2}$ 38 hr (4-6).

Mammalian & avian toxicity

Acute data

LC_{50} oral rat 1500 mg kg^{-1} (7).

LC_{50} (4 hr) inhalation mouse, rat 2500, 4020 ppm, respectively (7).

LC_{50} (30 min) inhalation dog 770 ppm (8).

LD_{50} intraperitoneal rat 399 mg kg^{-1} (7).

Teratogenicity and reproductive effects

TC_{Lo} inhalation mouse (6-16 day gestation) 10, 68 or 152 ppm 6 hr day^{-1} embryotoxic, increased post-implantation loss and increased early resorption. Non-significant increases in cleft palate. Maternal lethality ≥68 ppm (9).

Irritancy

83 mg instilled into rabbit eye caused irritation (10).

Other effects

Other adverse effects (human)

Seven workers suffered acute poisoning from 1-butanethiol in a laboratory producing acrylic resins. Chemical and toxicological properties and industrial applications are discussed (11).

Any other adverse effects

Oral hen >80 mg kg^{-1} severe cholinergic effects (10).

Other comments

Potential occupational hazards reviewed (12,13).

Reviews on experimental toxicology and human health effects listed (13).

Residues detected in the environment after commercial spraying with the defoliant DEF (14).

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B212 1-butanol

$$CH_3(CH_2)_3OH$$

$C_4H_{10}O$ **Mol. Wt.** 74.12 **CAS Registry No.** 71-36-3

Synonyms *n*-butyl alcohol; butyric alcohol; propylcarbinol; propylmethanol; 1-hydroxybutane; butylhydroxide

EINECS No. 200-751-6 **RTECS No.** EO 1400000

Uses Solvent for fats, waxes, resins, gums and varnishes. Solvent in urea formaldehyde foams. Used in the manufacture of butyl acetate, butyl acrylate, detergents, rayon, and lacquers. Diluent for brake fluids. Extractant in pharmaceutical synthesis of antibiotics, vitamins and hormones.

Physical properties

M. Pt. –88.9°C **B. Pt.** 117.5°C **Flash point** 29°C (open cup) **Specific gravity** 0.810 at 20°C with respect to water at 4°C **Partition coefficient** log P_{ow} 0.84 **Volatility** v.p. 7.02 mmHg at 25°C ; v.den. 2.55 at 25°C **Solubility** Water: 77 g l^{-1}. Organic solvents: acetone, benzene, diethyl ether, ethanol

Occupational exposure

DE-MAK 100 ppm (310 mg m^{-3})
FR-VLE 50 ppm (150 mg m^{-3})
JP-OEL ceiling limit 50 ppm (150 mg m^{-3})
SE-LEVL 15 ppm (45 mg m^{-3}) **SE-CEIL** 30 ppm (90 mg m^{-3})
UK-STEL 50 ppm (154 mg m^{-3})
US-STEL ceiling limit 50 ppm (152 mg m^{-3})

UN No. 1120 **HAZCHEM Code** 3[illegible]E **Conveyance classification** flammable liquid
Supply classification harmful
Risk phrases Flammable – Harmful by inhalation (R10, R20)
Safety phrases Keep out of reach of children (if sold to general public) – Keep away from sources of ignition – No smoking (S2, S16)

Ecotoxicity

Fish toxicity
LC_{100} (24 hr) creek chub 1400 mg l^{-1} in Detroit River water (1).
LC_{50} (96 hr) fathead minnow 1910 mg l^{-1} 18-22°C in fresh water (2).
EC_{50} (96 hr) fathead minnow 1510 mg l^{-1} (33-day-old) water hardness 47.7 mg l^{-1} calcium carbonate, temperature 24.7°C, pH 7.64, dissolved oxygen 6.3 mg l^{-1} (3).

Invertebrate toxicity

Cell multiplication inhibition test, *Pseudomonas putida* 650 mg l^{-1}, *Scenedesmus quadricauda* 875 mg l^{-1}, *Entosiphon sulcatum* 55 mg l^{-1} (4).

EC_{50} (30 min) *Photobacterium phosphoreum* 2187 mg l^{-1} Microtox test (5).

EC_{50} (48 hr) *Daphnia magna* 1980 mg l^{-1} (6).

Environmental fate

Nitrification inhibition

Inhibition of NH_3 oxidation, pure culture, 50% at 8200 mg l^{-1} (7).

Degradation studies

Biodegradable (8).

38 process wastewaters and 37 organic substances identified in the effluent from a petrochemical complex were subjected to the activated sludge degradability test; sludge was acclimated to the wastewater and organic substances. Water in the test container was sampled during aeration at 0 hr and 24 hr. After 1 day of acclimation, 100 mg l^{-1} 1-butanol resulted in chemical oxygen demand of 82% and 93% total organic carbon (9).

Abiotic removal

Volatilisation from river water, $t_{1/2}$ estimated at 3-9 hr (10).

Sunlit urban atmosphere, $t_{1/2}$ estimated at 5 hr (11).

Activated carbon absorbs 0.0107 g g^{-1} carbon, 53.4% reduction; influent 1000 mg l^{-1}, effluent 466 mg l^{-1} (12).

Mammalian & avian toxicity

Acute data

LD_{50} oral redwing blackbird 2500 mg kg^{-1} (13).

LD_{50} oral rat 4360 mg kg^{-1} (14).

LD_{50} oral rabbit 4250 mg kg^{-1} (15).

LC_{50} (4 hr) inhalation rat 8000 ppm (15).

LD_{50} intraperitoneal rat 1122 mg kg^{-1} (16).

LD_{50} intravenous rat 310 mg kg^{-1} (16).

Inhalation mouse (7 hr) 1650 ppm, no adverse effects reported (17).

Teratogenicity and reproductive effects

Inhalation rat (7 day) 0-8000 ppm, teratology assessment during gestation 1-19 days. Highest concentration produced maternal toxicity. Slight increase in skeletal malformations observed at 8000 ppm (18).

Metabolism and toxicokinetics

Metabolised via butyraldehyde to butanoic acid which is eliminated mainly as carbon dioxide (19).

The metabolism of 1-butanol by rat hepatic and pulmonary cytosolic preparations was measured with regard to ADH activity as influenced by pH and substrate concentration. Compared to lung, hepatic ADH activity showed little pH dependence. The optimum conditions for pulmonary ADH activity require an alkaline pH and high substrate concentrations (20).

Volunteers exposed to concentrations of 100 and 200 ppm for 2 hr developed blood concentrations that were below 1 mg l^{-1}, whether at rest or during exercise. Exposure to an air concentration of 50 ppm for 2 hr resulted in blood levels < 0.08 mg l^{-1} (21).

Single oral dose rats (24 hr) 83% converted into carbon dioxide, 4% excreted in the urine and 13% was retained in tissues (22).

Irritancy

Dermal rabbit (24 hr) 500 mg caused moderate irritation and 750 µg instilled in rabbit eye caused severe irritation (23).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537 with metabolic activation negative (24).

In vitro Chinese hamster ovary cells sister chromatid exchange negative (25).
In vitro micronuclei assay V79 cell line (1 hr) chromosomal aberrations negative (26).

Other effects

Other adverse effects (human)
Alcoholic intoxicant and narcotic. Can cause central nervous system depression, with headache, dizziness and drowsiness (11).

Any other adverse effects
Following repeated inhalation exposure to animals, observed effects have included pathological changes in the lungs, degenerative lesions in the liver and kidneys, and narcosis (27).

Legislation

Included in Schedule 6 (Release Into Land: Prescribed Substances) of Statutory Instrument No. 472, 1991 (28).

Other comments

Detected in industrial effluents, surface water (1,2).
Experimental toxicology and human health effects reviewed (12,29-31).
Biological studies of human exposure to organic solvents reported (32). Poses an indirect hazard for the aquatic environment because it is readily biodegradable which may lead to oxygen depletion (27).
Rhodococcus rhodochrous metabolises 1-butanol *via* butyric acid (33).

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B213 2-butanol

$$CH_3CH_2CH(OH)CH_3$$

$C_4H_{10}O$ **Mol. Wt.** 74.12 **CAS Registry No.** 78-92-2

Synonyms *sec*-butyl alcohol; butylene hydrate; 2-hydroxybutane; methyl ethyl carbinol

EINECS No. 201-158-5 **RTECS No.** EO 1750000

Uses Used in flavours and perfumes. Dyestuff synthesis. Paint removers and industrial cleaners.

Physical properties

M. Pt. –114°C (±-form) **B. Pt.** 99.5°C (±-form) **Flash point** 31°C (open cup) (±-form)
Specific gravity 0.808 (±-form) at 20°C with respect to water at 4°C **Volatility** v.p. 12 mmHg at 20°C (±-form)
Solubility Water: 125 g l^{-1}. Organic solvents: acetone, benzene, ethanol, diethyl ether

Occupational exposure

DE-MAK 100 ppm (310 mg m^{-3})
FR-VME 100 ppm (300 mg m^{-3})
JP-OEL 100 ppm (300 mg m^{-3})
SE-LEVL 50 ppm (150 mg m^{-3}) **SE-STEL** 75 ppm (250 mg m^{-3})
UK-LTEL 100 ppm (308 mg m^{-3}) **UK-STEL** 150 ppm (462 mg m^{-3})
US-TWA 100 ppm (303 mg m^{-3})

UN No. 1120 **HAZCHEM Code** 3[redacted]E **Conveyance classification** flammable liquid
Supply classification harmful
Risk phrases Flammable – Harmful by inhalation (R10, R20)
Safety phrases Keep out of reach of children (if sold to general public) – Keep away from sources of ignition – No smoking (S2, S16)

Ecotoxicity

Fish toxicity
LC_{50} (24 hr) goldfish 4300 mg l^{-1} (1).

Invertebrate toxicity
Cell multiplication inhibition, *Pseudomonas putida* 500 mg l^{-1}, *Scenedesmus quadricauda* 95 mg l^{-1}, *Entosiphon sulcatum* 1280 mg l^{-1}, *Microcystis aeruginosa* 312 mg l^{-1} (2,3).

Environmental fate

Degradation studies
100% degradation obtained after 14 days lag by acetate-acclimated cultures (4).
Long-term study using anaerobic upflow filters and acetate enriched cultures, 93% utilisation rate obtained after 52 days of operation (5).
Adapted activated sludge with 2-butanol as sole carbon source: 98.5% COD, 55 mg COD g^{-1} dry inoculum^{-1} hr^{-1} (6).

Biodegradable (7).
$ThOD_5$ sewage seed or activated sludge 82-98% (8-10).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 6480 mg kg^{-1} (11).
LC_{Lo} (4 hr) inhalation rat 16,000 ppm (11).
LD_{50} intraperitoneal guinea pig, hamster, rat 1060-1200 mg kg^{-1} (12).
LD_{50} intravenous rat 138 mg kg^{-1} (12).
LD_{50} intraperitoneal rabbit 277 mg kg^{-1} (12).

Metabolism and toxicokinetics

Ethanol (1-33mM) and phenobarbital (5-33mM) induced rat hepatic microsomes to produce enzymes capable of 2-butanol oxidation (13).
Acute pyridine treatment (200 mg kg^{-1}, i.p.) increased hepatic metabolism of 2-butanol in the rat twofold and in the rabbit threefold (14).

Irritancy

16 mg instilled into rabbit eye caused irritation (15). Sensory irritation due to inhalation was determined from the reflexively induced decrease in respiratory rate in CF-1 mice. An (extrapolated) threshold concentration of 640 ppm for the first 2-min exposure period was obtained (16).

Genotoxicity

Saccharomyces cerevisiae cytotoxic at concentrations of 750 mg $tube^{-1}$ (17).
In vivo rat bone marrow chromosomal aberrations and polyploidy positive (18).

Legislation

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

Other comments

Contaminant in drinking and surface waters. Discharged from industrial effluent. Industries include mechanical products, petroleum refining and paint and inks (20-22).
Found as a volatile component in a diverse array of foodstuffs (23).
Reviews on experimental toxicology and human health effects listed (24).
Environmental health criteria reviewed (25).

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B214 *tert*-butanol

$(CH_3)_3COH$

$C_4H_{10}O$ **Mol. Wt.** 74.12 **CAS Registry No.** 75-65-0

Synonyms *tert*-butyl alcohol; *tert*-butyl hydroxide; 1,1-dimethylethanol; 2-methylpropan-2-ol; trimethylcarbinol

EINECS No. 200-889-7 **RTECS No.** EO 1925000

Uses Denaturant for ethanol. Manufacture of flotation agents. Agent in flavourings and perfumes. Used as a solvent in paint removers. Octane booster in gasoline.

Physical properties

M. Pt. 25.3°C **B. Pt.** 82.8°C **Flash point** 10°C (closed cup) **Specific gravity** 0.7887 at 20°C with respect to water at 4°C **Partition coefficient** log P_{ow} 0.35 **Volatility** v.p. 40 mmHg at 24.5°C ; v.den. 2.55
Solubility Water: miscible. Organic solvents: acetone, benzene, diethyl ether, ethanol

Occupational exposure

DE-MAK 100 ppm (310 mg m^{-3})
FR-VME 100 ppm (300 mg m^{-3})
JP-OEL 50 ppm (150 mg m^{-3})
SE-LEVL 50 ppm (150 mg m^{-3}) **SE-STEL** 75 ppm (250 mg m^{-3})
UK-LTEL 100 ppm (308 mg m^{-3}) **UK-STEL** 150 ppm (462 mg m^{-3})
US-TWA 100 ppm (303 mg m^{-3})

UN No. 1120 **HAZCHEM Code** 3[redacted]E **Conveyance classification** flammable liquid
Supply classification highly flammable, harmful
Risk phrases Highly flammable – Harmful by inhalation (R11, R20)
Safety phrases Keep out of reach of children (if sold to general public) – Keep container in a well ventilated place – Keep away from sources of ignition – No smoking (S2, S9, S16)

Ecotoxicity

Fish toxicity
LC_{50} (7 day) guppy 3500 ppm (1).
LD_{100} (24 hr) creek chub 6000 mg l^{-1} Detroit river water (2).

Invertebrate toxicity
Chlorella pyrenoidosa toxic effects at 24 g l^{-1} (3).

Toxicity to other species
LD_{Lo} parenteral frog 12 g kg^{-1} peripheral nerve and sensitisation effects (4).

Bioaccumulation
Non-accumulative or low accumulative (5).

Environmental fate

Nitrification inhibition
Nitrification inhibition limit concentration 39 g l^{-1} (6).

Degradation studies
Degradation rates for subsurface soils with *tert*-butanol were in the range 0.1-0.3 mg l^{-1} day^{-1} (7).
Degradation in anoxic groundwater systems was enhanced by presence of nitrate at pH ≥7 (8).
Anaerobic degradation in soil was enhanced by nutrient addition in nutrient-poor soils but hindered by the presence of other easily degraded organic compounds (9).

Abiotic removal
Adsorbability 0.059 g g^{-1} carbon; 29.5% reduction in influent sludge (10).

Mammalian & avian toxicity

Acute data
LD_{50} oral rabbit, rat 3500 mg kg^{-1} (11,12).
LD_{50} intraperitoneal, intravenous mouse 930, 1530 mg kg^{-1}, respectively (13,14).

Sub-acute and sub-chronic data
Oral young ♂ Wistar rats (10 weeks) *ad libitum* in drinking water containing *tert*-butanol (TBA) 0.5% v/v, or 25 ppm trichloroacetic acid (TCA), or a combined dose 0.5% v/v TBA plus 25 ppm TCA. The animals were fed a normal diet. A remarkable loss in body weight, increased liver weight and decrease in liver triglycerides were observed in the treated groups in the order TBA + TCA >TCA >TBA. Changes in biochemical parameters occurred in the TBA + TCA treated rats which may play a pivotal role in toxic responses on long-term exposure (15).

Carcinogenicity and chronic effects
Oral F344/N rats and B6C3F1 mice (2 yr) in drinking water ♂ rats, 0, 1.25, 2.5 or 5 mg ml^{-1} (average daily doses of ~ 85, 195 or 420 mg kg^{-1}), ♀ rats 0, 2.5, 5 or 10 mg ml^{-1} (~ 175, 330, or 650 mg kg^{-1}), ♂ and ♀ mice 0, 5, 10 or 20 mg ml^{-1} (♂ ~ 535, 1035, or 2065 mg kg^{-1}, ♀ 510, 1015, or 2105 mg kg^{-1}). Survival significantly reduced in ♂ rats receiving 5 mg ml^{-1}, ♀ rats receiving 10 mg ml^{-1}, and ♂ mice receiving 20 mg ml^{-1}. Long-term exposure caused increased incidences of renal tubule adenoma and carcinoma in ♂ rats, transitional epithelial hyperplasia of the kidney in ♂ and ♀ rats, follicular cell adenoma of the thyroid in ♀ mice, and follicular cell hyperplasia of the thyroid and inflammation and hyperplasia of the urinary bladder in ♂ and ♀ mice. A slight increase in follicular cell adenoma or carcinoma of the thyroid (combined) in ♂ mice may have been caused by the administration of *tert*-butanol (16).

Teratogenicity and reproductive effects
Oral mouse (6-20 day gestation) 0.5, 0.75 and 1% w/v produced developmental delay in postparturition physiological and psychomotor performance scores. Significant postnatal maternal nutritional and behavioural factors affecting lactation or nesting behaviour were also evident (17).
TC_{Lo} (1-19 day gestation) inhalation rat 2000 ppm 7 hr day^{-1} observed foetotoxicity. TC_{Lo} (1-19 day pregnant) inhalation rat 3500 ppm 7 hr day^{-1} specific developmental abnormalities in musculoskeletal system (18).
Oral CBA/J and C57BL/6J mice (6-18 day gestation) 0.8 g kg^{-1} induced a significant increase in resorptions per litter. No significant abnormalities reported (19).

Metabolism and toxicokinetics
Oral rat single dose 2 g kg^{-1} rapid absorption into blood, <1% excreted via urine (20).
Intraperitoneal rat 0.84 g kg^{-1}, blood $t_{1/2}$ 13 hr (20).

Irritancy

Exposure via inhalation or contact (species unspecified). Conjunctivitis and dermatitis reported (19).

Genotoxicity

Saccharomyces cerevisiae cytotoxic at concentrations of 3.7 μg tube^{-1} (21).

In vitro mouse lymphoma L5178Y tk+/tk– without metabolic activation equivocal (22).

L5178Y tk+/tk– mouse lymphoma cell forward mutation assay with and without metabolic activation negative (23).

Other effects

Other adverse effects (human)

Central nervous system depressant, can cause liver and kidney damage. Ingestion effects include headache, vomiting, fatigue, ataxia and unconsciousness. Aspiration may cause respiratory failure and death (18).

Legislation

Included in Schedule 6 (Release into Land: Prescribed Substances) of Statutory Instrument No. 472, 1991 (24).

Other comments

Contaminant in drinking water (25).

Crystalline form hygroscopic. Physical properties, fire and health hazards, toxicology and safe handling recommendations reviewed (26-28).

Experimental toxicology and human health effects reviewed (29).

Environmental health criteria reviewed (30).

Crystalline form hygroscopic.

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30. *Environmental Health Criteria No. 65: Butanols* 1987, World Health Organisation, Geneva, Switzerland

B215 1-butene

$$CH_3CH_2CH{=}CH_2$$

C_4H_8 **Mol. Wt.** 56.11 **CAS Registry No.** 106-98-9

Synonyms butylene; α-butylene; butylene-1; ethylethylene

EINECS No. 203-449-2 **RTECS No.** EM 2896000

Uses Butenes are weak anaesthetics. Used in petroleum and chemical industry for polymer synthesis.
Occurrence In diesel engine exhaust gas and refinery gases.

Physical properties

M. Pt. –185.35°C **B. Pt.** –6.3°C **Flash point** –80°C (closed cup) **Specific gravity** 0.6255 at –6.47°C with respect to water at 4°C **Volatility** v.p. 3480 mmHg at 21°C ; v.den. 1.94
Solubility Organic solvents: benzene, diethyl ether, ethanol

Occupational exposure

UN No. 1012 **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
Exposure to 20% concentration in mice resulted in respiratory failure within 2 hr and mice exposed to 40% concentration died within 10 min (1).

Metabolism and toxicokinetics
Metabolised slowly to 1-hydroxy metabolite (1).

Genotoxicity

Butene (isomer unspecified) in the vapour phase, tested with *Salmonella typhimurium* TA97, TA98, TA100 with and without metabolic activation negative (2).

Other effects

Other adverse effects (human)
Six workers assigned to removal of paraffinic oil residue including butylene had systemic effects of narcosis including generalised convulsions, nystagmus, finger tremors and gastritis (3).

Any other adverse effects

♂ Swiss Webster mice (5 min) 0.4 to 18 ppm exposure to photochemical oxidant mixture of 1-butene at 0, 1, 2, 3 and 4 hr of reaction period. Severe irritation of upper respiratory tract reported (4).

Narcotic, asphyxiant at high concentrations can cause respiratory failure (5).

Other comments

Found in diesel engine exhaust gas and refinery gases.

Toxicology and anaesthetic potency of butylene discussed (5).

Working conditions and health status of workers involved in butylene production are reviewed (6,7).

Liquid form can cause burns and frostbite (1).

Fire hazard. Explodes in mixtures with oxygen.

References

1. Browning, E. *Toxicity and Metabolism of Industrial Solvents* 2nd ed., 1987, **1**, 362-367, Elsevier, Amsterdam, Netherlands.
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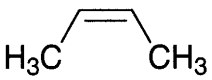
B216 *cis*-2-butene



C_4H_8 **Mol. Wt.** 56.11 **CAS Registry No.** 590-18-1

Synonyms butene-2; β-butylene; butylene-2; dimethylethylene; pseudobutylene

EINECS No. 209-673-7

Uses In the production of gasolines, butadiene and other chemicals.

Physical properties

M. Pt. –139.3°C **B. Pt.** 3.7°C **Flash point** –12°C **Specific gravity** 0.6213 at 20°C with respect to water at 4°C

Partition coefficient log P_{ow} 2.33 **Volatility** v.p. 760 mmHg at 37°C ; v.den. 1.9

Solubility Organic solvents: benzene, diethyl ether, ethanol

Occupational exposure

UN No. 1012 **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

Exposure of mice to 13% concentration (duration unspecified) resulted in deep narcosis, exposure to 19% concentration was fatal (1).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100 butene (isomer unspecified) in vapour phase with and without metabolic activation negative (2).

Other effects

Any other adverse effects

Inhalation ♂ Swiss Webster mice (5 min) 0.4-18 ppm at 0, 1, 2, 3 and 4 hr of reaction with nitrogen dioxide caused severe irritation to upper respiratory tract (3).

Cardiac sensitiser (4).

Other comments

Low environmental contaminant which occurs in diesel exhaust. Recovered from refining gases or by petroleum cracking.

Eye irritation of a range of hydrocarbons including *cis*-2-butene reviewed (5).

Butenes are weak anaesthetics and asphyxiants at high concentrations. 2-Butene is more narcotic than the corresponding 1-isomer.

References

1. Van Oettingen, W. R. *Toxicity and Potential Dangers of Aliphatic and Aromatic Hydrocarbons* 1940, **256S**, Public Health Bulletin.
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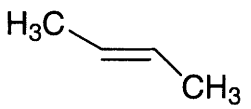
B217 *trans*-2-butene



C_4H_8 **Mol. Wt.** 56.11 **CAS Registry No.** 624-64-6

Synonyms β-butylene; *sym*-dimethylethylene

EINECS No. 210-855-3

Uses In the production of gasolines. Intermediate in the synthesis of butadiene and other chemicals.

Physical properties

M. Pt. –105.5°C **B. Pt.** 0.9°C **Flash point** –6°C **Specific gravity** 0.6042 at 20°C with respect to water at 4°C
Partition coefficient log P_{ow} 2.31 **Volatility** v.p. 760 mmHg at 0.9°C ; v.den. 1.90
Solubility Organic solvents: benzene, diethyl ether, ethanol

Occupational exposure

UN No. 1012 **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)

Environmental fate

Degradation studies
Nocardia sp. are capable of growth using *trans*-2-butene as carbon source. Degradation occurs via crotonic acid (1).

Mammalian & avian toxicity

Acute data
Mice exposed to 13% concentrations (duration unspecified) suffered deep narcosis, while 19% was fatal (2).

Metabolism and toxicokinetics
In vitro conversion of simple prochiral and chiral alkenes into oxiranes occurs in liver microsomes of treated rats, mice and humans (3).

Irritancy
Low mucous membrane irritant (2).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100 butene (isomer unspecified) in the vapour phase with and without metabolic activation negative (4).

Other effects

Any other adverse effects
Cardiac sensitiser (5)

Legislation

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

Other comments

In exhaust of diesel engines. Low environmental contaminant.
Eye irritation of hydrocarbons including *trans*-2-butene reviewed (7).
The more highly reactive *trans*-2-butene occurs at a much lower concentration in atmosphere than other comparable hydrocarbons (8).
Butenes are weak anaesthetics, 2-butene is an asphyxiant and narcotic at high concentrations.

References

1. Van Ginkel, C. G. et al *J. Gen. Microbiol.* 1987, **133**(7), 1713-1720.
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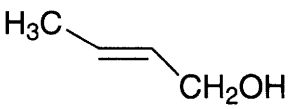
B218 *trans*-2-buten-1-ol



C_4H_8O **Mol. Wt.** 72.11 **CAS Registry No.** 504-61-0

Synonyms *trans*-but-2-en-1-ol; *E*-but-2-en-1-ol; *trans*-crotyl alcohol

EINECS No. 207-996-8

Uses Manufacture of epoxy resins. Electrochromic display solvents.
Occurrence Natural substance in cabbage *Brassica oleraceae* leaf (1,2).
In raspberry flavour (3).

Physical properties

B. Pt. 120-122°C **Specific gravity** 0.8454 at 20°C with respect to water at 4°C

Mammalian & avian toxicity

Metabolism and toxicokinetics
Subcutaneous rat 54 mg kg^{-1}, 24-hr urine metabolites (via crotonaldehyde) included 3-hydroxy-1-methylpropylmercapturic acid and 2-carboxy-1-methylethylmercapturic acid (4).

References

1. Greenhalgh, J. R. et al *New Phytol.* 1976, **77**(2), 391-398.
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B219 3-buten-1-ol

$$CH_2{=}CHCH_2CH_2OH$$

C_4H_8O **Mol. Wt.** 72.11 **CAS Registry No.** 627-27-0

Synonyms but-3-en-1-ol; allylcarbinol; Δ^3-1-butenol

EINECS No. 210-991-3

Uses Ethylene polymerisation catalyst.
Occurrence Occurs in *Aspalathus linearis* Rooibos tea (1).
Beef fat distillates (2).
Colza oil (3).

Physical properties

B. Pt. 112-114°C **Flash point** 32°C **Specific gravity** 0.8424 at 20°C with respect to water at 4°C
Solubility Water: miscible. Organic solvents: miscible with diethyl ether

Environmental fate

Abiotic removal

Wastewater treatment, reverse osmosis, 40°C, 600 psi. From a 0.72 g l^{-1} aqueous solution, 28.3% of solute is rejected (4).

Other comments

IC_{50} *Lactuca sativa* germination, 30°C 0.111 g l^{-1} (5).
Induction of ethylene response in *Tabacum* spp. (6,7).

References

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B220 3-buten-2-ol

$$CH_3C(OH)CH{=}CH_2$$

C_4H_8O **Mol. Wt.** 72.11 **CAS Registry No.** 598-32-3

Synonyms methyl vinyl carbinol; 1-methylpropenol; but-3-en-2-ol; 3-hydroxy-1-butene; 1-methylallyl alcohol; Δ^3-2-butenol

EINECS No. 209-929-8 **RTECS No.** EM 9275050

Uses Vulcanising agent. Stabiliser for methylchloroform.
Occurrence Possible constituent of mushroom aroma [(±)isomer] (1).
Wood-spirit oil (2).

Physical properties

M. Pt. <-80°C (–100°C) **B. Pt.** 96-98°C **Flash point** 16°C **Specific gravity** 0.8318 at 20°C with respect to water at 4°C

Mammalian & avian toxicity

Irritancy

Humans exposed to 50 ppm for 15 min suffered eye irritation. Exposure for 8 hr to 50 ppm caused irritation to both eyes and nose (3).

Genotoxicity

Salmonella typhimurium TA100 with and without metabolic activation weakly positive (4).

References

1. Ney, K. H. et al *Gordian* 1978, **78**(5), 144, 146, (Ger.) (*Chem. Abstr.* **89**, 174437a).
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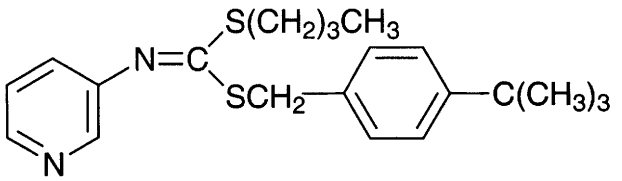
B221 buthiobate



$C_{21}H_{28}N_2S_2$ **Mol. Wt.** 372.60 **CAS Registry No.** 51308-54-4

Synonyms butyl 4-*tert*-butylbenzyl-*N*-(3-pyridyl)dithiocarbonimidate; butyl 4-(1,1-dimethylethyl)phenyl]-methyl-3-pyridinylcarbonimidodithioate; carbonimidodithioic acid, 3-pyridinyl-, butyl[4-(1,1-dimethylethyl)phenyl]methyl ester

EINECS No. 257-128-7 **RTECS No.** FG 3414500

Uses Fungicide.

Physical properties

M. Pt. 31-33°C **Specific gravity** 1.0865 at 25°C with respect to water at 25°C **Volatility** v.p. 4.52×10^{-7} mmHg at 20°C

Solubility Water: 1 mg l^{-1} at 25°C. Organic solvents: methanol, xylene

Ecotoxicity

Fish toxicity

LC_{50} (48 hr) carp 6.4 mg l^{-1} (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral mallard duck >10,000 mg kg^{-1} (1).

LD_{50} oral rat 2700 mg kg^{-1} (2).

LD_{50} percutaneous rat >5000 mg kg^{-1} (1).

Metabolism and toxicokinetics

Degradation by rat liver enzymes systems yielded *S*-*n*-butyl-*S'*-*p*-(1, 1-dimethyl-2-hydroxyethyl)benzyl-*N*-3-pyridyldithiocarbonimidate and 2-(3'-pyridylimino)-4-carboxylthiazolidine. It is suggested the intermediates could decompose to 3-aminopyridine (3).

Genotoxicity

Allium cepa (4, 24 hr) 4, 20, 100 and 500 ppm inhibited mitosis and induced chromosomal aberrations (4).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides and related products: maximum admissible concentration 0.1 μg l^{-1} (5).

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

Other comments

Believed to be no longer manufactured or marketed for crop protection use (1).

References

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2. *The Merck Index* 12th ed., 1996, Merck & Co., Inc., Whitehouse Station, NJ, USA.
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4. Badr, A. *Cytologia* 1988, **53**(4), 635-640.
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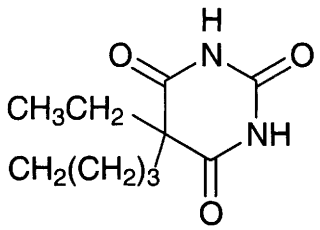
B222 butobarbitone



$C_{10}H_{16}N_2O_3$ **Mol. Wt.** 212.25 **CAS Registry No.** 77-28-1

Synonyms 5-butyl-5-ethylbarbituric acid; 5-butyl-5-ethyl-2,4,6(1*H*,3*H*,5*H*)pyrimidinetrione; 5-ethyl-5-*N*-butylbarbituric acid; 2,4,6-(1*H*,3*H*,5*H*)-pyrimidinetrione, 5-butyl-5-methyl

EINECS No. 201-019-9 **RTECS No.** CQ 1575000

Uses Central nervous system depressant. Sedative. Hypnotic.

Physical properties

M. Pt. 124-127°C

Solubility Organic solvents: chloroform, diethyl ether, ethanol

Ecotoxicity

Toxicity to other species

Frog heart *Rana pipiens* exposed to 4.25 mg l^{-1} recorded mild depressive effects (1).

Mammalian & avian toxicity

Acute data

LD_{Lo} oral mouse, rabbit 100 mg kg^{-1} (2,3).

LD_{Lo} intraperitoneal rat, rabbit 135, 115 mg kg^{-1}, respectively (4).

LD_{Lo} subcutaneous rat, rabbit 100, 190 mg kg^{-1}, respectively (5,6).

LD_{Lo} intravenous rabbit 90 mg kg^{-1} (7).

LD_{50} intraperitoneal mouse 320 mg kg^{-1} (8).

TD_{Lo} oral woman 166 mg kg^{-1} central nervous system effects observed (9).

Teratogenicity and reproductive effects

TD_{Lo} (7-19 day gestation) subcutaneous rat 1300 mg kg^{-1} total dose decreased rat litter size and foetal weight. No foetal malformations reported (10).

Metabolism and toxicokinetics

In humans inactivated in liver by hydroxylation, small amounts excreted in urine as unchanged drug. Reported $t_{1/2}$ 40-55 hr (11).

Following single dose in human volunteers, butobarbitone was metabolised to 4'-hydroxybutobarbitone and 4'-hydroxypentobarbitone (12).

Other effects

Other adverse effects (human)

A woman who took 6 g butobarbitone over three days had vertical gaze paralysis suggestive of brain lesions (13).

Any other adverse effects

TD_{Lo} intramuscular ♂ rat 28 mg kg^{-1} altered testis and caput and cauda epididymis metabolism. The changes were transient and reversible by administration of ascorbic acid (14).

Legislation

Controlled substance in the US (15).

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Substances extractable in chloroform: guide level 0.1 mg l^{-1} dry residue (16).

Other comments

Adult hypnotic dose orally 100-200 mg (17).

Toxicity reviewed (18).

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B223 butocarboxim

$$CH_3SCH(CH_3)C(CH_3)=NOCONHCH_3$$

$C_7H_{14}N_2O_2S$ **Mol. Wt.** 190.27 **CAS Registry No.** 34681-10-2

Synonyms 3-(methylthio)-*O*-[(methylamino)carbonyl]oxime-2-butanone; 3-(methylthio)-2-butanone-*O*-[(methylamino)carbonyl]oxime; 3-(methylthio)butanone-*O*-methylcarbamoyloxime; 2-butanone, 3-(methylthio)-*O*-[(methylamino)carbonyl]oxime; Afilene; Blattlausfrei; Drawin; Hydrosekt

EINECS No. 252-139-3 **RTECS No.** EL 9215000

Uses Systemic insecticide.

Physical properties

M. Pt. 32-37°C **Specific gravity** 1.12 at 20°C **Partition coefficient** log P_{ow} 1.11 **Volatility** v.p. 7.97×10^{-5} mmHg at 20°C

Solubility Water: 35 g l^{-1} at 20°C. Organic solvents: miscible with aromatic hydrocarbons, esters and ketones

Occupational exposure

Supply classification toxic, dangerous for the environment

Risk phrases Flammable – Toxic by inhalation, in contact with skin and if swallowed – Irritating to the eyes – Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment (R10, R23/24/25, R36, R50/53)

Safety phases Keep locked up and out of reach of children (if sold to general public) – Wear suitable protective clothing and gloves – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) – This material and/or its container must be disposed of as hazardous waste – Avoid release to the environment. Refer to special instructions/safety data sheet (S1/2, S36/37, S45, S60, S61)

Ecotoxicity

Fish toxicity

LC_{50} (96, 24 hr) rainbow trout 29, 35 mg l^{-1}, respectively (1).

Invertebrate toxicity

Toxic to bees LD_{50} 1 μg bee^{-1} (1).

Environmental fate

Degradation studies

Degrades in soil by losing the methylamine group, and sulfur oxidises to sulfoxide and sulfone; $t_{1/2}$ soil 1-8 days for unchanged compound 16-44 days for metabolites (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 153 mg kg^{-1} (2).

LD_{50} oral rabbit 275 mg kg^{-1} (1).

LD_{50} percutaneous rabbit 360 mg kg^{-1} (3).

Sub-acute and sub-chronic data

LC_{50} (8 day) Japanese quail 1180 mg kg^{-1} in diet (1).

In 90-day feeding trials, no-effect level for dogs was 100 mg kg^{-1} (1).

Day-old chicks were given 500, 1000 or 1500 ppm in feed for 75 days. Blood samples taken at fortnightly intervals showed a dose-dependent and progressive reduction in blood cholinesterase activity. Glutamic pyruvate transaminase activity and urea nitrogen levels in the blood were significantly raised (4).

Carcinogenicity and chronic effects
In 2-yr feeding trials the no-effect level for rats was 100 mg kg^{-1} (1).

Metabolism and toxicokinetics
Metabolised in mammals to butoxycarboxim and excreted in the urine (1).

Genotoxicity

Administration of 100 mg kg^{-1} (24 hr) to rat gave positive chromosomal aberrations, 10 mg kg^{-1} dose negative (5).

Legislation

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

Other comments

Cholinesterase inhibitor (8).

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B224 butonate

$$H_3C(CH_2)_2CO_2CH(CCl_3)P(O)(OCH_3)_2$$

$C_8H_{14}Cl_3O_5P$ **Mol. Wt.** 327.53 **CAS Registry No.** 126-22-7

Synonyms butanoic acid, 2,2,2-trichloro-1-dimethoxyphosphinyl)ethyl ether; dimethyl-1-butyryloxy-2,2,2-trichloroethylphosphonate

EINECS No. 204-778-4 **RTECS No.** ET 0175000

Uses Superseded insecticide

Physical properties

B. Pt. 129°C at 0.5 mmHg

Environmental fate

Degradation studies
Eutrophic carp ponds were treated with 400-1000 μg butonate. $t_{1/2}$ 46-108 hr (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral chicken 210 mg kg^{-1} (1).
LD_{50} oral mouse, guinea pig, rat 760-1100 mg kg^{-1} (2,3).
LD_{50} dermal dog 3080 mg kg^{-1} (2).

Metabolism and toxicokinetics

Intraperitoneal ♂ mouse 200 and 400 mg kg^{-1} labelled with ^{14}C. Radioactivity detected in lung, kidney, testes and liver. $t_{1/2}$ liver 2 hr (4).

Genotoxicity

In vivo intraperitoneal mouse 200 and 400 mg kg^{-1} DNA methylation positive (4).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticide: maximum admissible concentration 0.1 μg l^{-1} (5).

Other comments

Toxicity reviewed (6).

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B225 butoxycarboxim

$$CH_3S(O)_2CH(CH_3)C(CH_3)=NOCONHCH_3$$

$C_7H_{14}N_2O_4S$ **Mol. Wt.** 222.27 **CAS Registry No.** 34681-23-7

Synonyms 3-(methylsulfonyl)-*O*-((methylamino)carbonyl)oxime-2-butanone; 2-methylsulfonyl-*O*-(*N*-methyl-carbamoyl)-butanon-(3)-oxime; 3-mesylbutanone-*O*-methylcarbamoyloxime; 3-(methylsulfonyl)-2-butanone-*O*-[(methylamino)carbonyl]oxime; 2-butanone, 3-(methylsulfonyl)-*O*-[(methylamino)carbonyl]oxime; Bellasol; Plant Pin

EINECS No. 252-140-9 **RTECS No.** EL 9210000

Uses Systemic insecticide. Acaracide.

Physical properties

M. Pt. 85-89°C **Partition coefficient** log P_{ow} 1.11 (pH 6-7) **Volatility** v.p. 2×10^{-6} mmHg at 20°C
Solubility Water: 209 g l^{-1} at 20°C. Organic solvents: acetone, chloroform, heptane, isopropanol, toluene

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) rainbow trout 170 mg l^{-1} (1).

Invertebrate toxicity
Non-toxic to bees (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral hen 367 mg kg^{-1} (1).
LD_{50} oral rabbit, rat 275, 458 mg kg^{-1}, respectively (1).
LD_{50} subcutaneous rat 288 mg kg^{-1} (2).

Sub-acute and sub-chronic data
In 90-day feeding trials, no-effect level for rats 300 mg kg^{-1} (1).

Genotoxicity

Salmonella typhimurium TA100, TA98, TA1535, TA1537 and TA1538 with and without metabolic activation negative. *Escherichia coli* WP2 hcr with and without metabolic activation negative (3).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticide: maximum admissible concentration 0.1 μg l^{-1} (4).
Included in Schedule 6 (Release Into Land: Prescribed Substances) of Statutory Instrument No. 472, 1991 (5).

Other comments

Cholinesterase inhibitor (1).

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B226 2-butoxyethanol

$$CH_3(CH_2)_3O(CH_2)_2OH$$

$C_6H_{14}O_2$ **Mol. Wt.** 118.18 **CAS Registry No.** 111-76-2

Synonyms ethylene glycol monobutyl ether; butyl cellosolve; glycol monobutyl ether; butyglycol; 2-butoxy-1-ethanol; ethylene glycol monobutyl ether; butyl cellosolve; glycol monobutyl ether; butylglycol; 2-butoxy-1-ethanol

EINECS No. 203-905-0 **RTECS No.** KJ 8575000

Uses Solvent for nitrocellulose, resins, grease, oil and albumin. Dry cleaning solvent.

Physical properties

M. Pt. –70°C **B. Pt.** 168-170°C **Flash point** 62°C (closed cup) **Specific gravity** 0.9030 at 20°C with respect to water at 4°C **Volatility** v.p. 0.6 mmHg at 20°C ; v.den. 4.07
Solubility Water: ≥100 mg l^{-1} at 22°C. Organic solvents: acetone, DMSO, ethanol

Occupational exposure

DE-MAK 20 ppm (98 mg m^{-3})
FR-VME 25 ppm (120 mg m^{-3})
SE-LEVL 10 ppm (50 mg m^{-3}) **SE-STEL** 20 ppm (100 mg m^{-3})
UK-LTEL 25 ppm (123 mg m^{-3})
US-TWA 20 ppm (121 mg m^{-3})

UN No. 2369 **HAZCHEM Code** 2X **Conveyance classification** toxic substance
Supply classification harmful
Risk phrases Harmful by inhalation, in contact with skin and if swallowed – Irritating to the respiratory system (R20/21/22, 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 1650 mg l^{-1} (1).
LC_{50} (7 day) guppy 983 ppm (1).
LC_{50} (96 hr) bluegill sunfish 1490 mg l^{-1} static bioassay in fresh water at 23°C, mild aeration applied after 24 hr (2).
LC_{50} (96 hr) Atlantic silverside 1250 mg l^{-1} static bioassay in synthetic seawater at 23°C , mild aeration applied after 24 hr (2).

Invertebrate toxicity
LC_{50} (48 hr) brown shrimp 600-1000 mg l^{-1} (3).
LC_{50} (96 hr) *Artemia* sp. 100 mg l^{-1} (3).
Cell multiplication inhibition test, *Pseudomonas putida* 700 mg l^{-1}, *Scenedesmus quadricauda* 900 mg l^{-1}, *Entosiphon sulcatum* 91 mg l^{-1}, *Uronema parduczi* 465 mg l^{-1}, *Microcystis aeruginosa* 35 mg l^{-1} (4-6).

Environmental fate

Degradation studies
Wastewater treatment: activated sludge adsorbability 0.112 g g^{-1} carbon; 55.9% reduction; influent 1000 mg l^{-1}; effluent 441 mg l^{-1} (7).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 1480 mg kg^{-1} (8).
LD_{50} oral rabbit 300 mg kg^{-1} (9).
LC_{50} (4 hr) inhalation rat 450 ppm (10).
LD_{50} dermal rabbit 490 mg kg^{-1} (11).
LD_{50} intravenous rat 340 mg kg^{-1} (12).
LD_{50} intraperitoneal rat 220 mg kg^{-1} (13).
TC_{Lo} (8 hr) inhalation human 195 ppm gastrointestinal tract effects (12).
The lethal oral dose in humans is ~1.4 ml kg^{-1}, equivalent to ~100 ml for a 70 kg person (14).

Carcinogenicity and chronic effects
The National Toxicology Program tested rats and mice via inhalation. No evidence of carcinogenicity in ♂ rats, equivocal evidence of carcinogenicity in ♀ rats, some evidence of carcinogenicity in ♂ and ♀ mice (15).

Teratogenicity and reproductive effects

TC_{Lo} (6-15 day gestation) inhalation rat 100 or 200 ppm 6 hr day^{-1} caused maternal toxicity (decreased body weight and weight gain; decreased organ weight, decreased food and water consumption and anaemia) embryotoxicity (increased resorptions and decreased implantation rate) and foetoxicity (reductions in skeletal ossification). No increase in foetal malformations. Inhalation rabbit (day 6-18 of gestation) 200 ppm 6 hr day^{-1} caused maternal toxicity and embryotoxicity. No treatment-related foetotoxicity or foetal malformations observed (16).
Development of F-344 rat was not uniquely sensitive at oral dose 30-100 mg kg^{-1} day^{-1}, but reduced prenatal viability was noted at 200 mg kg^{-1} day^{-1}. 2-Butoxyethanol was administered on days 9-11 of gestation (17).
In the rat whole-embryo culture assay 2-butoxyethanol showed adverse effects on embryonic morphology at 0.3 mg ml^{-1} and on growth and development at 0.5 mg ml^{-1}. In the hydra regeneration assay, concentrations up to 0.37 mg ml^{-1} had little effect on polyps, some shortening of tentacles and body were seen at 0.74 mg ml^{-1} and 0.92 mg ml^{-1} caused polyps to be totally contracted (18).

Metabolism and toxicokinetics

^{14}C 2-Butoxyethanol was administered for 24 hr to ♂ F344/N rats in drinking water, absorbed doses were 12 to 171 mg kg^{-1}. Elimination of radioactivity was monitored for 72 hr: 50-60% was eliminated in the urine as butoxyacetic acid, 8-10% as carbon dioxide and approximately 10% was excreted in the urine as ethylene glycol (19,20).
Inhalation (6 hr) F344 rats, uptake and metabolism were linearly linked to the exposure concentration up to 438 ppm. >80% of the inhaled dose present in blood was in the plasma: butoxyacetic acid (BAA) was the major blood metabolite, with ethylene glycol present in lesser amounts. 2-Butoxyethanol glucuronide was also detected, as a minor urinary metabolite. The results suggest that formation of BAA, the haemolytic product, is linearly related to exposure concentrations up to concentrations causing mortality (21).
Gavage ♂ rats (unspecified dose) rapidly absorbed; 48 hr after administration 2-butoxyethanol was detected in the forestomach, liver, kidney, spleen and the glandular stomach. Major routes of elimination were via the urine and as carbon dioxide (22).
Skin penetration was investigated in 12 exposure experiments with 5 men. Presence of 2-butoxyethanol was detected in the blood and urine confirming its entry into the systemic circulation in man *in vivo* during dermal exposure. Epicutaneous administration of 5-100% of 2-butoxyethanol for 2 hr compared to administration of the undiluted compound showed that water facilitates the absorption of the chemical (23).
Following dermal exposure (unspecified dose) in five human volunteers, 2-butoxyethanol was detected in the blood and butoxyacetic acid in the urine. Calculated dermal uptake rates ranged from 0.8-11 μg min^{-1} cm^{-2}.
The authors state that persons exposing large portions of their skin to butoxyethanol are at risk of absorbing acutely toxic doses (24).
Species differences in pharmacokinetics indicate that human blood is significantly less susceptible than rat blood to the haemolytic effects of 2-butoxyethanol (25).

Irritancy

Dermal rabbit (duration unspecified) 500 mg caused mild irritation (26).
100 μl instilled into rabbit eye (duration unspecified) was classified as non-irritating (27).
Irritation to eye and upper respiratory tract, dyspnoea and dermatitis reported in humans (28).

Genotoxicity

Not mutagenic in any of the short-term *in vivo* or *in vitro* tests performed by the National Toxicology Program (15).
Salmonella typhimurium TA98, TA100 and TA102 with and without metabolic activation negative; TA97a with and without metabolic activation positive (29).
Not mutagenic at HGPRT locus of Chinese hamster ovary cells *in vitro* with or without metabolic activation.
Equivocal results for unscheduled DNA synthesis in rat primary hepatocyte test *in vitro* (30,31).
In vitro CHO-AS52 cells negative (32).
All available data indicate that 2-butoxyethanol is not genotoxic (33).

Other effects

Other adverse effects (human)

Inhalation humans systemic effects include nausea, vomiting, headache, and eye injury. 2-Butoxyethanol is nephrotoxic, a haemolytic agent, and can cause central nervous system depression and liver and kidney damage (28).

Toxicity is associated with changes to blood and secondary effects on liver, kidney and spleen. Narcotic at high concentrations (12).

The haemolytic effect of 2-butoxyethanol can be attributed primarily to its metabolite butoxyacetic acid (34,35).

A study of 9365 individuals employed in two US leather tanneries between 1940-1982 was undertaken. Mortality from all causes was lower than expected (36).

PBPK modelling of the blood and urine levels of 2-butoxyethanol (BE) and its metabolites in six human volunteers exposed via one arm to 50 ppm BE for 2 hr led the author to conclude that humans are unlikely to reach haemolytic concentrations of the metabolite butoxyacetic acid in the blood following worst-case exposure scenarios to BE vapour (37).

Legislation

Included in Schedule 6 (Release Into Land: Prescribed Substances) of Statutory Instrument No. 472, 1991 (38).

Other comments

Contaminant in drinking water, surface water and groundwater (39-41).

Reviews on experimental toxicology and human health effects listed (42).

Genotoxicity of 2-butoxyethanol reviewed (33).

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B227 2-(2-butoxyethoxy)ethanol

$$HO(CH_2)_2O(CH_2)_2O(CH_2)_3CH_3$$

$C_8H_{18}O_3$ **Mol. Wt.** 162.23 **CAS Registry No.** 112-34-5

Synonyms diethylene glycol monobutyl ether; butoxydiglycol; butylcarbitol; butyl carbitol; butyl digol

EINECS No. 203-961-6 **RTECS No.** KJ 9100000

Uses Industrial solvent. Mosquito repellent.

Physical properties

M. Pt. –68.1°C **B. Pt.** 230.6°C **Flash point** 66.7°C **Specific gravity** 0.9553 at 20°C with respect to water at 4°C **Partition coefficient** log P_{ow} 0.82 (1) **Volatility** v.p. 0.02 mmHg at 20°C ; v.den. 5.58
Solubility Water: miscible. Organic solvents: miscible

Occupational exposure

DE-MAK 100 mg m^{-3}
SE-LEVL 15 ppm (100 mg m^{-3}) **SE-STEL** 30 ppm (200 mg m^{-3})
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

Fish toxicity
LC_{50} (96 hr) bluegill sunfish, inland silverside 1300, 2000 ppm, respectively, static bioassay in fresh water at 23°C mild aeration applied after 24 hr (2).
LC_{50} (24 hr) goldfish 2700 mg l^{-1} (3).

Invertebrate toxicity
EC_{50} *Saccharomyces cerevisiae* (24 hr) 17000 mg l^{-1} (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral guinea pig, rat 2000, 6560 mg kg^{-1}, respectively (4,5).
LD_{50} dermal rabbit 4120 mg kg^{-1} (5).
LD_{50} intraperitoneal mouse 850 mg kg^{-1} (6).
Lethal single oral dose to humans of diethylene glycols estimated as 1 ml kg^{-1} (7).

Sub-acute and sub-chronic data
Gavage ♂ rat (6 wk) no-observed-effect level was 891 mg kg^{-1} day^{-1}. At doses higher than this, food consumption was reduced, body weight decreased, and liver, kidney and haematological effects were observed (8).

Teratogenicity and reproductive effects

Oral ♂ rat (2 month) 0, 250, 500 or 1000 mg kg^{-1} day^{-1}. Oral ♀ rat (14 day) 0, 250, 500 1000 mg kg^{-1} day^{-1} no adverse effect on fertility in either sex (9,10).

Dermal Sprague-Dawley rats (13 wk) 2 ml kg^{-1} under occlusion 6 hr day^{-1}, 5 day wk^{-1}. The rats were mated, and the females treated until day-20 of gestation. They were allowed to deliver and nurse their offspring to day-21 of lactation. Dermal irritation was observed, which was more severe in females than in males; no histopathological changes were observed in the testes, and oestrus cycling in females was unaffected. No changes in reproductive performance were seen (11).

Metabolism and toxicokinetics

Dermal Sprague-Dawley rats (24 hr) 0.2 or 2.0 g kg^{-1} ^{14}C-labelled compound under occlusion. Washing with soap and water after 5 min removed >89% of dose from the skin at both exposure levels. At the end of exposure, 83 to 89% of radio-labelled compound from the applied dose was recovered, mostly from the urine. 5.2 to 8.2% of the urinary ^{14}C-compound was present as the glucuronide. The dermal absorption rates were estimated to be 0.73 and 1.46 mg cm^{-2} hr^{-1} for males and females, respectively (12).

Irritancy

5 mg instilled into rabbit eye caused severe irritation (13).

Dermal rabbit 0, 100, 300, or 1000 mg kg^{-1} day^{-1} mild skin irritation observed (9).

A 0.1 ml solution of diethylene glycol monobutyl ether instilled into rabbit eye caused moderately severe conjunctivitis, with mild blepharitis and mild diffuse keratitis. Symptoms subsided within 14 days of cessation of exposure (14).

Genotoxicity

In vitro mouse lymphoma L5178Y without metabolic activation positive, with metabolic activation negative. Little activity seen in other systems such as the Ames test, CHO cytogenetics, UDS in rat hepatocytes or the *Drosophila* sex-linked recessive lethality assay (15).

Saccharomyces cerevisiae diploid strain RX11; 152 mg l^{-1} causes 20% inhibition of RNA synthesis (16).

Chinese hamster ovary cells forward mutation assay at the HGPRT locus with and without metabolic activation negative (17).

In vivo mouse bone marrow micronucleus test negative (17).

Other effects

Other adverse effects (human)

Can be absorbed through human skin, but only in toxic amounts if exposure is prolonged and continuous (18).

Any other adverse effects

LD_{50} intraperitoneal mice 850 mg kg^{-1} systemic effects included pulmonary congestion, atelectasis and oedema. Toxic reaction occurred in spleen and lymph tissue. Congestion of viscera, marked renal tubular damage (19).

Inhalation rat (5 wk) 18 ppm, no observed effects (20).

EC_{50} Chinese Hamster Ovary cells (24 hr) 3280 mg l^{-1} (1).

Legislation

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

Other comments

Contaminant in drinking and surface water. Discharged in industrial effluent, industries include paint and ink, print and publishing, foundries and electronics (22-24).

Toxic effects of glycol ethers reviewed (25).

Reviews on experimental toxicology and human health effects listed (26).

Flammable.

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B228 2-(2-butoxyethoxy)ethanol acetate

$$CH_3CO_2[(CH_2)_2O]_2(CH_2)_3CH_3$$

$C_{10}H_{20}O_4$ **Mol. Wt.** 204.27 **CAS Registry No.** 124-17-4

Synonyms butyl carbitol acetate; diethylene glycol butyl ether acetate; DGBA; diglycol monobutyl ether acetate

EINECS No. 204-685-9 **RTECS No.** KJ 9275000

Uses Insect repellant synergist. Used in plastics and cosmetics. Solvent.

Physical properties

M. Pt. –32.2°C **B. Pt.** 247°C **Flash point** 115.6°C (open cup) **Specific gravity** 0.981 at 20°C with respect to water at 4°C **Volatility** v.p. 0.01 mmHg at 20°C

Solubility Water: miscible. Organic solvents: miscible with most solvents

Occupational exposure

SE-LEVL 15 ppm (130 mg m^{-3}) **SE-STEL** 30 ppm (250 mg m^{-3})

Mammalian & avian toxicity

Acute data

LD_{50} oral chicken 5000 mg kg^{-1} (1).

LD_{50} oral rat, mouse 6500, 6600 mg kg^{-1}, respectively (2,3).

LD_{50} oral guinea pig, rabbit 2340, 2600 mg kg^{-1}, respectively (4,3).

Metabolism and toxicokinetics

In vitro studies on ♂ Sprague Dawley rats (0-14 min) 0-1 g l^{-1} hydrolysed to diethylene glycol monobutyl ether by rat blood (5).

In vivo gavage ♂ Sprague-Dawley rats 200 or 2000 mg kg^{-1} [^{14}C]2-(2-butoxyethoxy)ethanol acetate. Urine, faeces and expired air were collected for 72 hr. After 24 hr, 82% radiolabelled compound excreted in urine, 2-3% in faeces, 5% as expired air. Major metabolite detected 2-(2-butoxyethoxy)acetic acid (5).

Irritancy

Dermal rabbit (duration unspecified) 500 mg caused mild irritation (6).

500 mg instilled into rabbit eye caused irritation (7).

Other comments

Light sensitive (8).

Reviews on experimental toxicology and human health effects listed (9).

Designated unsafe for military use in US (10).

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B229 2-butoxyethyl acetate

$$CH_3(CH_2)_3O(CH_2)_2O_2CCH_3$$

$C_8H_{16}O_3$ **Mol. Wt.** 160.21 **CAS Registry No.** 112-07-2

Synonyms 2-butoxyethanol acetate; butyl cellusolve acetate; ethanol, 2-butoxy acetate; glycolmonobutylether acetate; butylglycol acetate

EINECS No. 203-933-3 **RTECS No.** KJ 8925000

Uses High boiling solvent for nitrocellulose lacquers.

Occurrence Epoxy resins.

Physical properties

M. Pt. –63.5°C **B. Pt.** 192.3°C **Flash point** 87.8°C

Specific gravity 0.9424 at 20°C with respect to water at 20°C

Solubility Water: 11 g l^{-1}. Organic solvents: hydrocarbons

Occupational exposure

DE-MAK 20 ppm (130 mg m^{-3})

SE-LEVL 10 ppm (70 mg m^{-3}) **SE-STEL** 20 ppm (140 mg m^{-3})

Supply classification harmful
Risk phrases Harmful by inhalation and in contact with skin (R20/21)
Safety phrases Keep out of reach of children (if sold to general public) – Avoid contact with the skin (S2, S24)

Environmental fate

Degradation studies
Degradation >90% using Zahr-Wellen screening method, measured rate 12% day^{-1}, no observable lag period required (1).

Abiotic removal
Reacts in the atmosphere with photochemically produced hydroxyl radicals. At hydroxyl radical concentration of 5×10^5 molecules cm^{-3} estimated $t_{1/2}$ 18 hr (2).

Adsorption and retention
The high water solubility of butyl glycol acetate predicts that the compound will be very mobile in soil (3).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat, mouse 2400, 3200 mg kg^{-1}, respectively (4,5).
LD_{50} dermal rabbit 1500 mg kg^{-1} (4).
Inhalation rat, rabbit (4 hr) 400 ppm non-toxic to either species (6).

Metabolism and toxicokinetics
Glycol ether acetates are dehydrogenated to alkoxyacetic acid congeners in occupationally exposed humans (7).

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

Other effects

Any other adverse effects
Inhalation exposure of rabbits to butyl glycol acetate for one month caused haemoglobinuria and haematuria (9).

Other comments

Air pollutant. Industrial sources include painting and inks and automotive industry (10,11).
Reviews on experimental toxicology and human health effects listed (12).
Mean NR_{50} (concentration that produces a 50% reduction in neutral red uptake compared with controls) and mean $AP_{(peak)}$ (concentration at which peak acid phosphatase activity occurs) values for human keratinocyte cultures 57.1±6.1 mg ml^{-1} and 200 mg ml^{-1}, respectively (13).

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B230 butoxypropanol

$$CH_3(CH_2)_3O(CH_2)_3OH$$

$C_7H_{16}O_2$ **Mol. Wt.** 132.20 **CAS Registry No.** 29387-86-8

Synonyms propylene glycol monobutyl ether; propylene glycol butoxy ether

EINECS No. 249-598-7 **RTECS No.** TZ 0630000

Uses Antifreeze agent. Foam stabiliser. Detergent base.

Occupational exposure

Supply classification irritant
Risk phrases Irritating to eyes and skin (R36/38)
Safety phrases Keep out of reach of children (if sold to general public) (S2)

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 1900 mg kg^{-1} (1).

Other comments

Reviews on physical, chemical properties, experimental toxicology and human health effects listed (2).

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B231 1-butoxy-2-propanol

$$CH_3(CH_2)_3OCH_2CH(OH)CH_3$$

$C_7H_6O_2$ **Mol. Wt.** 122.12 **CAS Registry No.** 5131-66-8

Synonyms 1,2-propylene glycol 1-monobutyl ether; 2-hydroxy-3-butoxypropane

EINECS No. 225-878-4 **RTECS No.** UA 7700000

Uses Used in plasticisers, detergents. Solvent for coatings and surfactants. In water desalination. Termite attractant. Solvent for nitrocellulose and acetylcellulose.

Physical properties

M. Pt. –100°C **B. Pt.** 168°C **Flash point** 59°C (closed cup) **Specific gravity** 0.8789 at 20°C with respect to water at 4°C **Volatility** v.p. <0.978 mmHg at 20°C
Solubility Water: 64 g l^{-1} at 20°C

Occupational exposure

Supply classification irritant

Risk phrases Irritating to eyes and skin (R36/38)
Safety phrases Keep out of reach of children (if sold to general public) (S2)

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 2200 mg kg^{-1} (1).
LD_{50} dermal rabbit 3100 mg kg^{-1} (2).

Legislation

Included in Schedule 6 (Release Into Land: Prescribed Substances) of Statutory Instrument No. 472, 1991 (3).

Other comments

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

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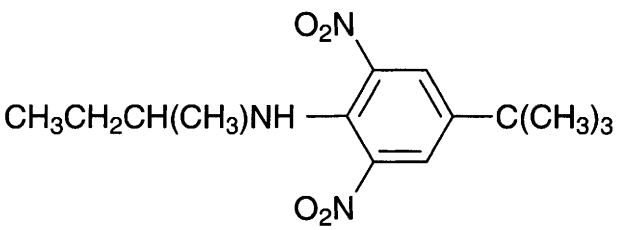
B232 butralin



$C_{14}H_{21}N_3O_4$ **Mol. Wt.** 295.34 **CAS Registry No.** 33629-47-9

Synonyms benzenamine, 4-(1,1-dimethylethyl)-*N*-(1-methylpropyl)-2,6-dinitro-; *N-sec*-butyl-4-*tert*-butyl-2,6-dinitroaniline; dibutalin; 4-(1,1-dimethylethyl)-*N*-(1-methylpropyl)-2,6-dinitrobenzamine; Amex; Amexine; Tabamex; Tamex; Tobago

EINECS No. 251-607-4 **RTECS No.** BW 9500000

Uses Pre-emergence herbicide. Plant growth regulator.

Physical properties

M. Pt. 60-61°C **B. Pt.** 134-136°C at 0.5 mmHg **Flash point** 36°C **Volatility** v.p. 1.278×10^{-5} mmHg at 25°C
Solubility Water: 1 mg l^{-1} at 25°C. Organic solvents: acetone, benzene, butanone, carbon tetrachloride, methanol, xylene

Ecotoxicity

Fish toxicity
LC_{50} (48 hr) rainbow trout, bluegill sunfish 3.4, 4.2 mg l^{-1}, respectively (1).

Environmental fate

Degradation studies

Microbial degradation occurs to evolve carbon dioxide (1).

Major metabolite isolated from soil 4-*tert*-butyl-2,6-dinitroaniline. In microbial studies using *Aspergillus fumigatus* and *Fusarium oxysporum* major metabolite isolated was an oxygenated analogue of butralin, 3-(4-*tert*-butyl-2,6-dinitroaniline)-2-butanol (2).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 12.6 g kg^{-1} (1).

LD_{50} dermal rabbit 10.2 g kg^{-1} (1).

Sub-acute and sub-chronic data

LC_{50} (8 day) Japanese quail, mallard duck >10 g kg^{-1} in diet (1).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides and related products: maximum admissible concentration 0.1 μg l^{-1} (3).

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

EPA Toxicity Class IV (1).

WHO Toxicity Class Table 5 (5).

Other comments

Non-corrosive to metals but permeates or can distort plastic and rubbers (6).

Metabolic pathways reviewed (7).

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B233 butyl acetate

$$CH_3CO_2(CH_2)_3CH_3$$

$C_6H_{12}O_2$ **Mol. Wt.** 116.16 **CAS Registry No.** 123-86-4

Synonyms butyl ethanoate

EINECS No. 204-658-1 **RTECS No.** AF 7350000

Uses Used in lacquers, artificial leathers, photographic films, plastics and safety glass.

Physical properties

M. Pt. –77°C **B. Pt.** 125-126°C **Flash point** 38°C **Specific gravity** 0.88 at 20°C with respect to water at 20°C
Volatility v.p. 15 mmHg at 25°C ; v.den. 4.0
Solubility Water: 8 ml l^{-1} at 25°C. Organic solvents: diethyl ether, miscible in ethanol, hydrocarbons

Occupational exposure

DE-MAK 100 ppm (480 mg m^{-3})
FR-VME 150 ppm (710 mg m^{-3}) **FR-VLE** 200 ppm (940 mg m^{-3})
JP-OEL 100 ppm (475 mg m^{-3})
SE-LEVL 100 ppm (500 mg m^{-3}) **SE-STEL** 150 ppm (700 mg m^{-3})
UK-LTEL 150 ppm (724 mg m^{-3}) **UK-STEL** 200 ppm (966 mg m^{-3})
US-TWA 150 ppm **US-STEL** 200 ppm

UN No. 1123 **HAZCHEM Code** 3[redacted]E **Conveyance classification** flammable liquid
Supply classification flammable
Risk phrases Flammable (R10)
Safety phrases Keep out of reach of children (if sold to general public) (S2)

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) fathead minnow 18 mg l^{-1} (1).
LC_{50} (96 hr) bluegill sunfish 100 ppm, freshwater static bioassay at 23°C (2).
LC_{50} (96 hr) inland silverside 185 ppm, seawater static bioassay at 23°C (2).
In fish, butyl acetate is metabolised by *in vivo* hydrolysis of the carboxylic acid esters. Lethality properties of this class of compounds cannot be compared unless relative carboxylase esterase activities for the species are known (3).

Invertebrate toxicity
EC_{50} (48 hr) *Daphnia magna* 44 ppm at 23°C conditions of bioassay unspecified (3).
Cell multiplication inhibition test *Pseudomonas putida* 78 mg l^{-1}, *Microcystis aeruginosa* 420 mg l^{-1}, *Scenedesmus quadricauda* 3700 mg^{-1}, *Entosiphon sulcatum* 970 mg l^{-1} (4,5).

Bioaccumulation
Calculated bioconcentration factors range 4-14, indicated that environmental accumulation is unlikely (6).

Environmental fate

Degradation studies
BOD value: 0.444 using a BOD biosensor (7).

Abiotic removal
Hydrolytic calculated $t_{1/2}$ 3 yr at pH 7 (8).
Estimated evaporation rate from solid surfaces, $t_{1/2}$ 50 min (9).

Mammalian & avian toxicity

Acute data
LD_{50} oral mouse, rabbit 7100-7400 mg kg^{-1} (10).
Acute oral rat 8-16 g kg^{-1} affected kidney and liver, caused granular dystrophy of the cytoplasm of hepatocytes and dystrophy of ganglion cells in the brain (11).
♂ CFW albino mice were exposed to 0-8000 ppm acetate vapour for 20 min. Decrease in locomotor activity at the highest level only; LOEC 8000 ppm. High concentrations also affected observed functional behaviour. Recovery was rapid (12).
TC_{Lo} (exposure unspecified) inhalation human 200 ppm – effects to nose, eye and pulmonary system (13).

Sub-acute and sub-chronic data

Sub-chronic intoxication of rats (route unspecified) with 0.8-1.6 g kg^{-1} day^{-1} for 1 month caused glomerulonephritis. Administration of 0.5 mg kg^{-1} for 6 months caused no change in organs (11).

Irritancy

Reported to cause irritation and conjunctivitis (species unspecified) (14).

A pharmaceutical worker developed dermatitis from butyl acetate through its attack on PVC gloves (15).

Shows mild *in vitro* activity in the bovine corneal opacity assay for ocular irritancy (16).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA1535, TA1537 with and without metabolic activation negative (17).

Other effects

Other adverse effects (human)

Increased levels of serum bile acids, indicative of early signs of liver failure, were found in a group of workers exposed to a mixture of organic solvents including butyl acetate (18).

Any other adverse effects

Reported to have mild irritant and central nervous system depressant effects (species unspecified) (19).

Other comments

Narcotic in high concentrations (20).

Considered safe for use as a cosmetic ingredient (21).

Reviews on experimental toxicology, epidemiology and human health effects are listed (22,23).

Acute toxicity data presented (24).

Acute inhalation toxicity studies are reviewed (25).

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B234 *sec*-butyl acetate

$$CH_3CO_2CH(CH_3)CH_2CH_3$$

$C_6H_{12}O_2$ **Mol. Wt.** 116.16 **CAS Registry No.** 105-46-4

Synonyms acetic acid, 1-methylpropyl ester; acetic acid, *sec*-butyl ester; 2-acetoxybutane; 1-methylpropyl acetate; 2-butyl acetate; *sec*-butyl alcohol acetate

EINECS No. 203-300-1 **RTECS No.** AF 7380000

Physical properties

M. Pt. –99°C **B. Pt.** 112-113°C (*dl*-form) 116-117°C (*d*-form) **Flash point** 31°C (open cup) (*dl*-form) **Specific gravity** 0.865 (*dl*-form) at 25°C with respect to water at 4°C
Solubility Organic solvents: diethyl ether, ethanol

Occupational exposure

DE-MAK 100 ppm (480 mg m^{-3})
FR-VME 200 ppm (950 mg m^{-3})
SE-LEVL 100 ppm (500 mg m^{-3}) **SE-STEL** 150 ppm (700 mg m^{-3})
UK-LTEL 200 ppm (966 mg m^{-3}) **UK-STEL** 250 ppm (1210 mg m^{-3})
US-TWA 200 ppm (950 mg m^{-3})
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)

Mammalian & avian toxicity

Acute data
Exposure to 10,000 ppm for 5 hr caused irritation and death in guinea pigs (1).

Legislation

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

Other comments

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

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1. Tagaki, K. et al *J. Pharm. Pharmacol.* 1966, **18**(12), 795-800.
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. VanNieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

B235 *tert*-butyl acetate

$$CH_3CO_2C(CH_3)_3$$

$C_6H_{12}O_2$ **Mol. Wt.** 116.16 **CAS Registry No.** 540-88-5

Synonyms acetic acid, *tert*-butyl ester; acetic acid, 1,1-dimethylethyl ester

EINECS No. 208-760-7 **RTECS No.** AF 7400000

Uses Gasoline additive. Used in the synthesis of *tert*-butyl esters and N- protected amino acids.

Physical properties

B. Pt. 97.8°C **Flash point** 15°C (closed cup) **Specific gravity** 0.8665 at 20°C with respect to water at 4°C
Solubility Organic solvents: diethyl ether, ethanol

Occupational exposure

DE-MAK 100 ppm (480 mg m^{-3})
SE-LEVL 100 ppm (500 mg m^{-3}) **SE-STEL** 150 ppm (700 mg m^{-3})
UK-LTEL 200 ppm (966 mg m^{-3}) **UK-STEL** 250 ppm (1210 mg m^{-3})
US-TWA 200 ppm (950 mg m^{-3})

UN No. 1123 **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
Cell multiplication inhibition test *Pseudomonas putida* 78 mg l^{-1}, *Scenedesmus quadricauda* 3700 mg l^{-1}, *Entosiphon sulcatum* 970 mg l^{-1} (1).

Environmental fate

Abiotic removal
Reacts with photochemically produced hydroxyl radicals in the atmosphere. Assuming atmospheric hydroxyl radical concentration of 8×10^5 molecules cm^{-3}, estimated $t_{1/2}$ is 26 days (2).

Other comments

Pollutant in air samples, source emissions from printing ink, paints and varnishes and automobile industry (3). Reviews on experimental toxicology and human health effects listed (4).

References

1. Bringmann, G. et al *Water Res.* 1980, **14**, 231-241.
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B236 butyl acetoacetate

$$CH_3COCH_2CO_2(CH_2)_3CH_3$$

$C_8H_{14}O_3$ **Mol. Wt.** 158.20 **CAS Registry No.** 591-60-6

Synonyms acetoacetic acid butyl ester; 3-oxo-butanoic acid butyl ester

EINECS No. 209-722-2 **RTECS No.** AK 5100000

Uses Intermediate in organic synthesis. Manufacture of metal derivatives. Dyestuffs. Pharmaceuticals and flavourings.

Physical properties

B. Pt. 214°C **Flash point** 85°C **Specific gravity** 0.96 **Volatility** v.p. 0.19 mmHg at 20°C ; v.den. 5.55
Solubility Organic solvents: diethyl ether, ethanol

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 11 g kg^{-1} (1).

Irritancy
Dermal rabbit (24 hr) 500 mg caused mild irritation and 500 mg instilled into rabbit eye caused mild irritation (2).

Other comments

Flammable.

References

1. *AMA Arch. Ind. Hyg. Occup. Med.* 1954, **10**, 61.
2. *Prehled Prumysluve Toxicol. Org. Latky* 1986

B237 butyl acid phosphate

$$CH_3(CH_2)_3H_2PO_4$$

$C_4H_{11}PO_4$ **Mol. Wt.** 154.10 **CAS Registry No.** 12788-93-1

Synonyms acid butyl phosphate; butyl phosphoric acid; phosphoric acid, butyl ester

EINECS No. 235-826-2 **RTECS No.** TB 8490000

Uses Antifoaming agent for drilling muds. Catalyst. Flame retardant.

Physical properties

Flash point 110°C (open cup) **Specific gravity** 1.120-1.125 at 25°C with respect to water at 40°C
Partition coefficient log P_{ow} 0.28
Solubility Water: insoluble in water. Organic solvents: acetone, ethanol, toluene

Occupational exposure

UN No. 1718 **HAZCHEM Code** 2X **Conveyance classification** corrosive substance

Ecotoxicity

Invertebrate toxicity

Cell multiplication inhibition test, *Pseudomonas putida* >100 mg l^{-1} *Microcystis aeruginosa* 4.1 mg l^{-1} (1).

Other comments

Contaminant in natural and drinking water supplies from River Po at Turin, Ferrara and Como in Northern Italy (1).

References

1. Bringmann, G. et al *Gwf. Wasser Abwasser.* 1976, **117**(9), 119

B238 butyl acrylate

$$CH_2=CHCO_2(CH_2)_3CH_3$$

$C_7H_{12}O_2$ **Mol. Wt.** 128.17 **CAS Registry No.** 141-32-2

Synonyms acrylic acid, butyl ester; butyl 2-propenoate

EINECS No. 205-480-7 **RTECS No.** UD 3150000

Uses Used in manufacture of polymers and resins for textile and leather finishes, paints, etc.

Physical properties

M. Pt. –64.6°C **B. Pt.** 145°C **Flash point** 49°C (open cup) **Specific gravity** 0.8986 at 20°C with respect to water at 4°C **Partition coefficient** log P_{ow} 2.36 **Volatility** v.p. 4 mmHg at 20°C ; v.den. 4.42
Solubility Water: 1.4 g l^{-1} at 20°C. Organic solvents: acetone, diethyl ether, ethanol

Occupational exposure

DE-MAK 2 ppm (11 mg m^{-3})
FR-VME 10 ppm (55 mg m^{-3})
SE-LEVL 10 ppm (50 mg m^{-3}) **SE-STEL** 15 ppm (80 mg m^{-3})
UK-LTEL 10 ppm (53 mg m^{-3})
US-TWA 2 ppm

UN No. 2348 **HAZCHEM Code** 3Y **Conveyance classification** flammable liquid
Supply classification irritant
Risk phrases Flammable – Irritating to eyes, respiratory system and skin – May cause sensitisation by skin contact (R10, R36/37/38, R43)
Safety phrases Keep out of reach of children (if sold to general public) – Keep container in a well ventilated place (S2, S9)

Ecotoxicity

Invertebrate toxicity

Threshold concentration of cell multiplication inhibition of *Uronema parduczi* 21 mg l^{-1} (1).
EC_{50} *Photobacterium phosphoreum* 30.8 ppm Microtox test (2).

Environmental fate

Degradation studies

Biodegradable (3).

Mammalian & avian toxicity

Acute data

LD_{50} oral redwing blackbird >103 mg kg^{-1} (4).

LD_{50} oral rat 3.7-8.1 g kg^{-1} (5).

LD_{50} oral rat 3730 mg kg^{-1}; inhalation (duration unspecified) approximate lethal concentration 10,000 ppm (6).

LC_{50} inhalation mouse (2 hr) 7800 mg m^{-3} (7).

LC_{50} inhalation rat (4 hr) 2730 ppm (8).

LD_{50} dermal rabbit 1.8-3.0 g kg^{-1} (5).

LD_{50} intraperitoneal mouse, rat 1.6 g kg^{-1} (5).

Carcinogenicity and chronic effects

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

Dermal mouse 6.6 mg kg^{-1} for life. No treatment-related tumours observed compared with tumours found in 39/40 mice treated with 3-methylcholanthrene (positive control) (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 (5).

Inhalation ♂, ♀ rats (24 months) 0, 15, 45 and 135 ppm 6 hr day^{-1}, 5 × wk^{-1}. No exposure-related signs of lesions or systemic toxicity and no oncogenic responses were observed. Dose-related atrophy of the neurogenic epithelial cells and hyperplasia of reserve cells were seen in the nasal mucosa of all exposed rats. Opacity and neovascularisation of the cornea were seen in rats exposed to 135 ppm. Reconstructive effects such as replacement of altered olfactory epithelium with respiratory epithelium and partial regression of corneal neovascularisation were observed in rats studied for 6 months after exposure (10).

Teratogenicity and reproductive effects

Inhalation rat (7-16 day gestation) 0, 130, 700 or 1310 mg m^{-3}. Maternal body-weight gain was reduced at 700 and 1310 mg m^{-3} with both groups showing signs of irritation. A concentration-related reduction in the number of live foetuses per litter was seen, but the differences were not statistically significant. Post-implantation deaths were increased at the two highest concentrations but no teratogenic response was seen (5).

Metabolism and toxicokinetics

Wistar rats administered 90 mg kg^{-1} by intraperitoneal injection excreted 6% of the dose as mercapturic acids in urine within 24 hr; this increased to 38% if the rats were pre-treated with an esterase inhibitor tri-*o*-tolyl phosphate (5).

Butyl acrylate disappeared rapidly from rat blood *in vitro* and from rat liver homogenates via hydrolysis mediated by non-specific esterases; binding to erythrocytes may also account for the disappearance from the blood (5).

Irritancy

Dermal rabbit (24 hr) 10 mg caused mild irritation (11).

Dermal rabbit 500 mg caused mild irritation (duration unspecified) (12).

50 mg instilled into the eye of a rabbit caused mild irritation (duration unspecified) (12).

Sensitisation

Shown to be a sensitising agent. Guinea-pigs sensitised to butyl acrylate showed cross-reactions to other monoacrylates (5).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537, TA1538 with and without metabolic activation negative (5).

In vivo hamster and rat bone marrow cells no chromosomal damage seen after exposure to 4300 mg m^{-3} 5-6 hr day^{-1} for 4 days (5).

Did not induce micronuclei or unscheduled DNA synthesis in Syrian hamster embryo fibroblasts and no morphological transformations were observed (13).

Other effects

Other adverse effects (human)

14/33 workers exposed to 50 mg m^{-3} over 5 yr complained of autonomic and neurotic symptoms but electroencephalographic examination showed no organic dysfunction (5).

Any other adverse effects

Gastric oedema produced in ♂ F344 rats administered 520 mg kg^{-1} by gavage in water but not when given in corn oil (5).

Other comments

Human health effects, experimental toxicology, physico-chemical properties reviewed (14,15).
The hazards associated with the compound have been reviewed (16).
Autoignition temperature 292°C.

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6. Kennedy, G. L. et al *Toxicol. Lett.* 1991, **56**(3), 317-326.
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16. *Dangerous Prop. Ind. Mater. Rep.* 1987, **7**(3), 61-65

B239 butylamine

$$CH_3(CH_2)_3NH_2$$

$C_4H_{11}N$ **Mol. Wt.** 73.14 **CAS Registry No.** 109-73-9

Synonyms *n*-butylamine; 1-aminobutane; mono-*n*-butylamine; 1-butanamine

EINECS No. 203-699-2 **RTECS No.** EO 2975000

Uses Chemical intermediate for organic synthesis. Used in the manufacture of pharmaceuticals, dyestuffs, rubber chemicals, emulsifying agents, insecticides and synthetic tanning agents.

Physical properties

M. Pt. –50°C **B. Pt.** 78°C **Flash point** –12.2°C **Specific gravity** 0.741 at 20°C with respect to water at 4°C
Partition coefficient log P_{ow} 0.86 **Volatility** v.p. 72 mmHg at 20°C ; v.den. 2.52
Solubility Water: miscible. Organic solvents: miscible with diethyl ether, ethanol

Occupational exposure

DE-MAK 5 ppm (15 mg m^{-3})
FR-VLE 5 ppm (15 mg m^{-3})
JP-OEL ceiling limit 5 ppm (15 mg m^{-3})
SE-CEIL 5 ppm (15 mg m^{-3})
UK-STEL 5 ppm (15 mg m^{-3})
US-STEL ceiling limit 5 ppm (15 mg m^{-3})

UN No. 1125 **HAZCHEM Code** 2WE **Conveyance classification** flammable liquid, corrosive
Supply classification highly flammable
Supply classification corrosive
Risk phrases Highly flammable – Harmful by inhalation, in contact with skin and if swallowed – Causes severe burns (R11, R20/21/22, R35)
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 30-70 mg l^{-1} (1).
LC_{50} (96 hr) inland silverside, bluegill sunfish 24-32 mg l^{-1} aeration after 24 hr, static bioassay pH 7.6 at pH 7.9 temperature range 20-23°C (2).

Invertebrate toxicity
Cell multiplication inhibition test, *Pseudomonas putida* 800 mg l^{-1}, *Entosiphon sulcatum* 9 mg l^{-1}, *Scenedesmus quadricauda* 0.53 mg l^{-1} (3).
LC_{50} (24 hr) brine shrimp 30-70 mg l^{-1} (4).
EC_{50} (30 min) *Photobacterium phosphoreum* 18.3 g l^{-1} Microtox test (5).

Environmental fate

Carbonaceous inhibition
IC_{50} Polytox culture, activated sludge microorganisms 90, 111 mg l^{-1}, respectively (6).

Degradation studies
Aerobacter sp. degraded 200 mg l^{-1} at 30°C parent strain degraded 100% in 22 hr and mutant strain 100% in 7 hr (7).
COD_2 >90% degradation using the Hoechst Bahl Method (8).
BOD_{12} 67% reduction in dissolved oxygen activated sludge (9).
BOD_6 50% reduction in dissolved oxygen using aniline acclimated activated sludge (10).
BOD (5, 10, 15 and 50 day) incubation settled sewage seed range 26-52% reduction in dissolved oxygen (11).

Abiotic removal
Evaporation is expected to be major removal process, $t_{1/2}$ of 2 days predicted (12).
Activated carbon adsorbability 0.103 g g^{-1} carbon, 52% reduction; influent 1000 mg l^{-1}, effluent 480 mg l^{-1} (13).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat, guinea pig 366, 430 mg kg^{-1}, respectively (14,15).
LC_{50} (2 hr) inhalation mouse 800 mg m^{-3} (15).
LC_{Lo} (4 hr) inhalation rat 4000 ppm (16).

LD_{50} intraperitoneal mouse 629 mg kg^{-1} (17).
LD_{50} intravenous mouse 198 mg kg^{-1} (17).
LD_{50} dermal guinea pig, rabbit 370, 850 mg kg^{-1}, respectively (18,19).

Irritancy
Dermal rabbit (24 hr) 500 mg caused severe irritation (19).
In humans, potent skin, eye, mucous membrane irritant. Direct skin contact causes severe primary irritation and blistering (20).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537 with and without metabolic activation negative (21).

Other effects

Any other adverse effects
Inhalation of *n*-butylamine depressed the respiratory rate in normal and tracheally cannulated mice at concentrations of 121 and 300 ppm, respectively. Sensory and pulmonary irritation reported (22).
Systemic effects include sedation, ataxia, nasal discharge, gasping, salivation and convulsions. Gavage rats 100-600 mg kg^{-1}, pathological examination showed pulmonary oedema (23).

Other comments

Contaminant in River Elbe in one of two sites tested. Concentration determined 1.5 ppb (24).
Contaminant in surface water and advanced water treatment concentrates (24,25).
Experimental toxicology and human health effects reviewed (26-28).

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B240 *sec*-butylamine

$$CH_3CH_2CH(NH_2)CH_3$$

$C_4H_{11}N$ **Mol. Wt.** 73.14 **CAS Registry No.** 13952-84-6

Synonyms 2-aminobutane; Butafume; 2-butanamine; Deccotane; 1-methylpropylamine; Tutane; (*RS*)-*sec*-butylamine; Citramin; Fruitguard AB

EINECS No. 237-732-7 **RTECS No.** EO 3325000

Uses Fungicide.

Physical properties

M. Pt. –104°C (±-form) **B. Pt.** 63°C (±-form) **Flash point** –9.4°C (closed cup) **Specific gravity** 0.724 at 20°C with respect to water at 20°C **Volatility** v.den. 2.52

Solubility Water: miscible. Organic solvents: acetone, diethyl ether, ethanol

Occupational exposure

DE-MAK 5 ppm (15 mg m^{-3})

Supply classification highly flammable, corrosive, dangerous for the environment

Risk phrases Highly flammable – Harmful by inhalation and if swallowed – Causes severe burns – Very toxic to aquatic organisms (R11, R20/22, R35, R50)

Safety phrases Keep locked up and out of the reach of children (if sold to general public) – Keep container in a well ventilated place – Keep away from sources of ignition – No smoking – 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) – Avoid release to the environment. Refer to special instructions/safety data sheet (S1/2, S9, S16, S26, S28, S36/37/39, S45, S61)

Ecotoxicity

Fish toxicity

LC_{50} (24 hr) creek chub 20-60 mg l^{-1} (1).

Environmental fate

Nitrification inhibition

Nitrosomonas sp. no inhibition of ammonia oxidation at 100 mg l^{-1} (2).

Degradation studies

Readily biodegradable (3).

Mammalian & avian toxicity

Acute data

LD_{50} oral redwing blackbird >96.0 mg kg^{-1} (4).

LD_{50} oral rat, dog 152, 225 mg kg^{-1}, respectively (5,6).

LD_{50} dermal rabbit 2500 mg kg^{-1} (6).

Carcinogenicity and chronic effects

In 2-yr study rats and dogs receiving 2500 mg kg^{-1} in diet suffered no ill-effects (7).

Genotoxicity

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

Other effects

Any other adverse effects

Systemic effects in rats which were given 100-600 mg kg^{-1} by gavage included sedation, ataxia, nasal discharge, gasping, salivation convulsions and death at highest doses. Pathological examination showed pulmonary oedema (5).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides and related products: maximum admissible concentration 0.1 $\mu g\ l^{-1}$ (9).

Included in Schedule 6 (Release into Land: Prescribed Substances) of Statutory Instrument No. 472, 1991 (10).

Other comments

Reviews on experimental toxicology and human health effects listed (11).

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B241 *tert*-butylamine

$$(CH_3)_3CNH_2$$

$C_4H_{11}N$ **Mol. Wt.** 73.14 **CAS Registry No.** 75-64-9

Synonyms 2-aminoisobutane; 2-amino-2-methylpropane; trimethylaminomethane; 1,1-dimethylethylamine; TBA

EINECS No. 200-888-1 **RTECS No.** EO 3330000

Uses Intermediate in organic synthesis.

Physical properties

M. Pt. –72°C **B. Pt.** 44-46°C **Specific gravity** 0.69 at 20°C with respect to water at 4°C

Solubility Organic solvents: ethanol

Occupational exposure

DE-MAK 5 ppm (15 mg m^{-3})

Ecotoxicity

Fish toxicity

LC_{50} (96 hr) rainbow trout 28 mg l^{-1} (1).

EC_{50} (96 hr) *Selenastrum capricornutum* 16 mg l^{-1} (2).

Invertebrate toxicity

EC_{50} (24 hr) *Daphnia magna* 136 mg l^{-1} (2).

Environmental fate

Carbonaceous inhibition

IC_{50} Activated sludge microorganisms, Polytox culture 90, 85 mg l^{-1}, respectively (3).

Degradation studies

No biodegradation observed over a 12-day incubation period using Sapromat respiration assays with river mud bacteria inocula, treatment plant sludge inocula and adapted bacteria inocula. Initial concentration 10-100 ppm (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 80 mg kg^{-1} (4).

LD_{50} oral mouse 900 mg kg^{-1} (5).

Other comments

Detected in leachate from a municipal refuse waste disposal site in the Netherlands, at a concentration of 41 ppm (6).
The relationship between biotransformation of aromatic nitrogenous compounds in rabbit liver microsomal preparations and carcinogenicity is discussed (7).
Reviews on experimental toxicology and human health effects listed (8).

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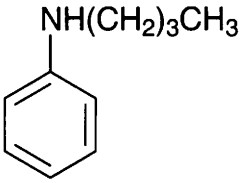
B242 *N*-butylaniline



$C_{10}H_{15}N$ **Mol. Wt.** 149.24 **CAS Registry No.** 1126-78-9

Synonyms benzenamine-*N*-butyl; *N*-(*n*-butyl)aniline; *N*-butylbenzenamine; 4-(phenylamino)butane

EINECS No. 214-425-6 **RTECS No.** BW 9450000

Uses Intermediate in organic synthesis. In dyestuff manufacture.

Physical properties

M. Pt. –14.4°C **B. Pt.** 241.6°C **Flash point** 107°C **Specific gravity** 0.932 at 20°C with respect to water at 4°C
Partition coefficient log P_{ow} 3.10
Solubility Organic solvents: diethyl ether, ethanol

Occupational exposure

UN No. 2738 **HAZCHEM Code** 3X **Conveyance classification** toxic substance

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 1620 mg kg^{-1} (1).
LD_{50} dermal rabbit 5990 mg kg^{-1} (1).

Irritancy
Dermal rabbit (24 hr) 10 mg caused severe irritation (1).

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B243 butylate

$$CH_3CH_2SCON[CH_2CH(CH_3)_2]_2$$

$C_{11}H_{23}NOS$ **Mol. Wt.** 217.38 **CAS Registry No.** 2008-41-5

Synonyms carbamothioic acid, bis(2-methylpropyl)-, *S*-ethyl ester; carbamic acid, diisobutylthio-, *S*-ethyl ester; diisobutylthiocarbamic acid, *S*-ethyl ester; Diisocarb; *S*-ethyl bis(2-methylpropyl)carbamothioate; ethyl *N*,*N*-diisobutylthiocarbamate; Sutan; Anelda; Sutar

EINECS No. 217-916-3 **RTECS No.** EZ 7525000

Uses Herbicide.

Physical properties

B. Pt. 137.5-138°C at 21 mmHg **Specific gravity** 0.9402 at 25°C **Partition coefficient** log P_{ow} 1.146 (1)
Volatility v.p. 1.3×10^{-3} mmHg at 25°C ; v.den. 0.9402 at 25°C
Solubility Water: 45 mg l^{-1} at 25°C. Organic solvents: acetone, ethanol, isobutyl ketone, kerosene, methyl, xylene

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) rainbow trout, bluegill sunfish 4.2, 6.9 mg l^{-1}, respectively (1).

Invertebrate toxicity
LC_{50} (96 hr) scud 11 mg l^{-1} (2).
EC_{50} (30 min) *Photobacterium phosphoreum* 18.1 mg l^{-1} Microtox test (3).

Environmental fate

Degradation studies
Degrades in soil to ethylmercaptan, carbon dioxide and diisobutylamine. Residual activity ~4 months (1). Biodegradation $t_{1/2}$ in soil 1-3 wk (4). Biodegradation in soil with a history of butylate use $t_{1/2}$ 10.9-11.6 days, in soil with no history of butylate use $t_{1/2}$ 20.0-24.9 days (5).

Abiotic removal
Removed by vaporisation when applied to surface of wet soils without incorporation. Little loss occurs after application to dry soil surfaces (4).
In water exposed to sunlight 99% loss within 48 hr (6).

Mammalian & avian toxicity

Acute data
LD_{50} oral guinea pig 1660-4000 mg kg^{-1} (1,3).
LD_{50} percutaneous rabbit >5000 mg kg^{-1} (1).

Sub-acute and sub-chronic data
In 90-day feeding study in rats 32 mg kg^{-1} day^{-1} caused no adverse effects (1).

Metabolism and toxicokinetics
A major metabolic pathway in rats, accounting for 27-45% of the administered dose, was thiocarbamate → thiocarbamate sulfoxide → *S*-(*N*,*N*-dialkylcarbamoyl)glutathione → *S*-(*N*,*N*-dialkylcarbamoyl) cysteine → *S*-(*N*,*N*-dialkylcarbamoyl)mercapturic acid, *S*-(*N*,*N*-dialkylcarbamoyl)mercaptoacetic acid and *N*[(*S*-*N*,*N*-dialkylcarbamoyl)mercaptoacetyl]glycine (7).

Genotoxicity

In vivo mouse bone marrow cells increased frequency of chromosomal aberrations (8).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides and related products: maximum admissible concentration 0.1 μg l^{-1} (9).
Included in Schedule 6 (Release into Land: Prescribed Substances) of Statutory Instrument No. 472, 1991 (10).

Other comments

Physico-chemical properties, metabolic and environmental fate, genotoxicity and toxicology reviewed (11,12).
Metabolic pathways reviewed (13).

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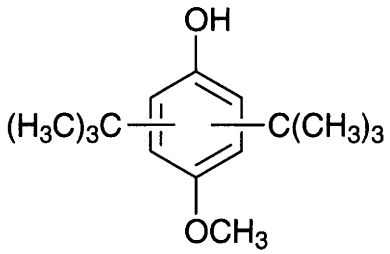
B244 butylated hydroxyanisole



$C_{11}H_{16}O_2$ **Mol. Wt.** 180.25 **CAS Registry No.** 25013-16-5

Synonyms BHA; phenol, (1,1-dimethylethyl)-4-methoxy-; phenol, *tert*-butyl-4-methoxy-*tert*-butyl-4-hydroxyanisole; Antracine 12; Embanox; Nipantiox 1-F; Sustane 1-F; Sustane BHA

EINECS No. 246-563-8 **RTECS No.** SL 1945000

Uses Antioxidant in the polymer and food industries. Used in cosmetics and essential oils. Antimicrobial properties.

Physical properties

M. Pt. 48-55°C **B. Pt.** 264-270°C at 733 mmHg

Solubility Organic solvents: arachis oil, chloroform, diethyl ether, ethanol, propylene glycol

Ecotoxicity

Fish toxicity

Exposure of trout to 0.03-0.3% for 8 wk had no effect on hepatic tumour incidence (1).

Japanese eel (12 wk) 0.02-1.6% in feed resulted in reversible liver enlargement. Lesions observed in hepatocytes indicated hyperplasia, eosinophilia and megalocytic hepatosis. The monitoring of radiolabelled compound showed that it spread quickly through the tissues, and accumulated in the bile to a maximum level on the third day, then decreased gradually (2).

Mammalian & avian toxicity

Acute data

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

LD_{50} oral rabbit 2100 mg kg^{-1} (4). LD_{50} intraperitoneal rat 881 mg kg^{-1} (5).

Sub-acute and sub-chronic data

Groups of 10 (5-wk-old) ♂, ♀ Wistar rats were fed a diet containing 0-2% BHA *ad libitum* for 2 wk, BrdU (bromodeoxyuridine) was injected and incorporated into the DNA of cells during DNA synthesis. Cell kinetic parameters were measured and results showed the oesophagus, glandular stomach, small intestine, large bowel and forestomach were possible target tissues for the proliferation-enhancing effects of BHA (6).

Carcinogenicity and chronic effects

No adequate data for carcinogenicity to humans, sufficient evidence for carcinogenicity to animals, IARC classification group 2B (7).

Administration in diet (80 wk) 0-2% BHA to Japanese house musk shrews, which have no forestomach, caused all high-dose animals to die of gastrointestinal bleeding within 8 wk of commencement of treatment. Other surviving animals exhibited adenomatous hyperplasia of the lung (8).

Lakeview (LVG) Syrian golden hamsters were fed diets containing 2% BHA for 30 wk, no papilloma or severe hyperplasia was found in any of the experimental or control groups. A significant increase in hamsters with mild hyperkeratosis and mild hyperplasia was observed. 90% of Miski hamsters developed moderate to severe hyperplasia and 80% had papilloma in the forestomach (9).

In 2-yr feeding study on F344 rats 2% BHA induced carcinomas, epithelial downgrowths and cellular proliferation. Superficial hyperplasias, inflammatory lesions and many papillomas regressed when treatment was stopped after 12 months (10).

Fed in the diet of rats, hamsters and mice, 2% BHA caused stomach papillomas in 91.5%, 95% and 14.3%, respectively. Squamous cell carcinomas occurred at lower rates (11).

Although humans do not have squamous epithelium in the stomach, possible tumour induction in squamous cell epithelium of the oesophagus is unlikely at food additive levels of use (12).

Teratogenicity and reproductive effects

Fed to rats in diet at 0, 0.125, 0.25 or 5.0% from prior-to-conception to 90-days-old. No changes in maternal weight, reproductive performance, mortality, offspring growth post-weaning or brain weight. Marginal increase in mortality up to 30 days at 0.25%. Delayed startle development at 0.5 and 0.25% (13).

IC_{50} rat embryonic culture 50 mg l^{-1} inhibited production of differential foci in limb bud cells and 84 mg l^{-1} inhibited differentiation in mid-brain cells. Human embryonic platal mesenchymal cell growth assay with microbial activation inhibited cell growth (14).

Metabolism and toxicokinetics

Absorbed from gastrointestinal tract and excreted in urine as glucuronide and sulfate metabolites (15).

Following a single oral dose 0.5 mg kg^{-1} to humans, BHA recovered in urine and faeces was 95%. BHA was excreted mainly as conjugated BHA in the urine and conjugated *tert*-butyl hydroquinone in the faeces. No free BHA was found in urine or faeces. In rats BHA is *O*-demethylated to *tert*-butylhydroquinone (16).

Following oral administration in rat, rabbit and human BHA is absorbed and rapidly excreted with little evidence of long-term tissue storage (17).

Absorbed from gut by passive diffusion. No evidence of tissue storage in rats fed 0.12% in diet for 21 months (18).

Oral dog up to 100 mg kg^{-1} day^{-1} for 1 yr. No storage observed in fat, liver or brain (19).

27 to 77% excreted in urine by humans, mostly in 24 hr. No dealkylation or hydroxylation (20).

Incubation with sodium nitrite at pH 2.0 or pH 5.0 produced eight derivatives: 2-*tert*-butyl-*p*-quinone (BQ), 3,3'-di-*tert*- butyl-(2,5,2',5')-biphenyldiquinone (BBDQ) 2,6-di-*tert*- butyl-8-hydroxydibenzofuran-1,4- quinone (BHDQ), 6-nitro-BHA, 2,2'-dihydroxy-3,3'-di-*tert*-butyl-5,5'-dimethoxy biphenyl (di-BHA), an oxidised product of di-BHA, and two unstable reaction intermediates. At pH 2.0, but not pH 5.0, BQ was a major final product. 6-Nitro-BHA and the oxidation products of di-BHA were also final products (di-BHA formed BBDQ which easily converted to BHDQ) (21).

Low concentrations of BHA and nitrite in physiological saline at pH 2 reacted to form *tert*-butylquinone and an unidentified second compound (22).

Sensitisation

Three positive reactions observed from a total 112 patients with eczematous dermatitis patch-tested with 2% butylated hydroxyanisole (23).

Genotoxicity

Salmonella typhimurium TA97, TA102, TA104, TA100 with and without metabolic activation negative. Doses >100 μg plate^{-1} exhibited toxic effects (24,25).

Saccharomyces cerevisiae D6, D7, with metabolic activation induced epigenic action, gene conversion and reverse mutation (26).

Chinese hamster fibroblast cell line *in vitro* with metabolic activation only weakly induced chromosomal aberrations (24).

BHA induced chromosomal aberrations in Chinese hamster ovary cells with metabolic activation (27).

BHA did not induce micronuclei in mice after single intraperitoneal injection (28).

BHA stimulates superoxide formation in rat liver microsomes up to 10-fold with metabolic activation via the BHA metabolites *tert*-butylhydroquinone and *tert*-butylquinone. No oxygen-activating properties can be attributed to BHA itself (29).

The BHA derivatives 2-*tert*-butyl-*p*-quinone and 3,3'-di-*tert*-butyl-(2,5,2',5')-biphenyldiquinone were found to be base-substitution type mutagens in the *Salmonella typhimurium* mutagenicity test, while 2,6-di-*tert*-butyl-8-hydroxy-dibenzofuran-1,4-quinone was a potent desmutagen against the mutagenicity of Trp-P-2 (21).

Newt larvae negative results in micronucleus test using erythrocytes (30).

Other effects

Other adverse effects (human)

Oral ♂ human 0.5 mg kg^{-1} BHA for ten consecutive days had no effect on clinical, biochemical parameters and Phase I and Phase II biotransformation capacity (31).

An outbreak of toxic methaemoglobinaemia in a paediatric ward was attributed to the preservative in an infant feed formula (32).

BHA inhibits respiratory control by stimulating state-4 respiration, thus acting as a membrane uncoupler (33).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Substances extractable in chloroform: guide level 0.1 mg l^{-1} dry residue (34).

Acceptable daily intake of 300 μg kg^{-1} body weight established (35).

Other comments

The toxicity, physical and metabolic properties, genotoxicity and antitumour activity of BHA reviewed (12,17,36-43).

The toxicology of food additives evaluated (44).

Reviews on human health effects and experimental toxicology listed (45).

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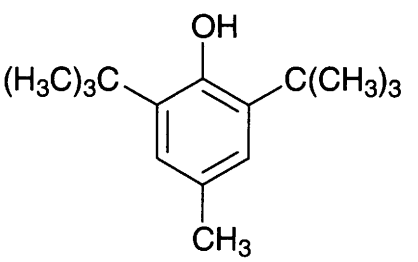
B245 butylated hydroxytoluene



$C_{15}H_{24}O$ **Mol. Wt.** 220.35 **CAS Registry No.** 128-37-0

Synonyms BHT; 2,6-bis(1,1-dimethylethyl)-4-methylphenol; *p*-cresol, 2,6-di-*tert*-butyl-; antioxidant 4; E321; Improval; Tropanol; DBPC; Deenax; Ionol; Ralox BHT food grade; Vanox PCX; Nipanox BHT

EINECS No. 204-881-4 **RTECS No.** GO 7875000

Uses Antioxidant used in food, petroleum products, synthetic rubbers, plastics, animal and vegetable oils and soaps. Antiskinning agent in paints and inks.

Physical properties

M. Pt. 70°C **B. Pt.** 265°C **Flash point** 127°C **Specific gravity** 1.048 at 20°C with respect to water at 4°C
Volatility v.den. 7.6
Solubility Water: <1 mg ml^{-1}. Organic solvents: acetone, benzene, dimethyl sulfoxide, ethanol, isopropanol, methanol, toluene

Occupational exposure

FR-VME 10 mg m^{-3}
UK-LTEL 10 mg m^{-3}
US-TWA 10 mg m^{-3}

Ecotoxicity

Fish toxicity
Non-toxic to goldfish in saturated solution 0.4 mg l^{-1} (1).

Mammalian & avian toxicity

Acute data
TD_{Lo} oral human 80 mg kg^{-1} (2).
LD_{Lo} oral rabbit 2100 mg kg^{-1} (3).
LD_{50} intraperitoneal, intravenous mouse 138, 180 mg kg^{-1}, respectively (4,5).

Sub-acute and sub-chronic data
Slc:ddy ♂ mice (21 day) 1.35-5.0% in feed caused dose-dependent nephrosis. ED_{50} (1 month) 2.3 g kg^{-1} day^{-1} (6).
Intraperitoneal ♂ mice (24hr, 48hr and 7 day) 200, 400 or 800 mg kg^{-1} in olive oil. Collection of bronchoalveolar lavage fluid showed a dose-dependent increase in the number of cells; total protein content and LDH activity also increased significantly. (7).

Carcinogenicity and chronic effects
No adequate data for carcinogenicity to humans, limited evidence for carcinogenicity to animals, IARC classification group 3 (8).
Oral F344 rats (76 wk) 100-6000 ppm in food, no increase in neoplasms at any site (9).
National Toxicology Program tested ♂ and ♀ rats and mice (2 yr) via feed; carcinogenic activity negative (10).
Rats fed diets containing butylated hydroxytoluene over two generations did not develop tumours (11).

Teratogenicity and reproductive effects
Mice (from 5 wk of age to the weaning of the third generation) 0, 0.015, 0.045, 0.135 and 0.405% BHT in feed showed no significant effect on the number of litters, litter size or litter weight at birth in each generation. The body weight of pups of the 0.015% group was increased at birth and during the lactation period for both generations. In the third generation, body weights of the pups of other treatment groups were also increased during the lactation period (12).
BHT in diet of doses of 0.875, 1.75 and 2.5% to mice significant differences in litter size, pup weight and litter weight reported (13).
Developmental toxicity of doses of 0.25, or 0.5%, little effect on adult behaviour and no special toxicity to the central nervous system reported (14).
Metabolism and toxicokinetics
After a single oral dose administered to mice, 80%-90% was excreted in the urine within 120 hr (15).
Cytochrome P450 catalyses oxidation of BHT to form three metabolites: quinone methide, hydroxy-*tert*-butyl analogue of BHT and hydroxy-quinone methide (16).

Irritancy

Dermal human (48 hr) 500 mg caused mild irritation (17).

Dermal rabbit (48 hr) 500 mg caused moderate irritation, and 100 mg instilled into rabbit eye caused moderate irritation (17,18).

Sensitisation

Delayed-type hypersensitivity and non-immunogenic skin reactions have been reported (19).

Of 112 patients with eczematous dermatitis patch-tested with 2% BHT, three had positive reactions (20).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537 with or without metabolic activation negative (21,22).

Mouse lymphoma L5178Ytk+/tk– with metabolic activation cell forward mutation assay positive (23).

Chinese hamster ovary cells with or without metabolic activation induction of chromosome aberrations and sister chromatid exchange negative (24).

Chinese hamster ovary cells induction of chromosome aberrations positive, anaphase-telophase alterations (induction of multipolar mitoses) positive (25).

Human peripheral blood lymphocytes induction of sister chromatid exchange negative (26).

Other effects

Other adverse effects (human)

A woman who ingested 4g BHT experienced epigastric cramping, nausea, vomiting and generalised weakness, dizziness, confusion and brief loss of consciousness (4).

Cutaneous, urticarial, disseminated eruption associated with chewing gum containing BHT reported (26).

Accumulates in human adipose tissue (27).

An outbreak of toxic methaemoglobinaemia in a paediatric ward was attributed to the antioxidant BHA, BHT and propyl gallate used as preservatives in a soybean infant food formula (28).

Any other adverse effects

BHT was tested for guinea pig, rat and human erythrocyte haemolysis. BHT induced complete lysis (29).

Adverse effects to kidneys, lungs, heart and blood reported in rodents (30).

Induced lung injury in mice (31).

Pulmonary toxicity in mice is activated by cytochrome P450 2B isoenzymes (32).

Causes concentration-dependent acute cell death in isolated rat hepatocytes with loss of cellular ATP and GSH (33).

Legislation

Acceptable daily intake of 125 $\mu g\ kg^{-1}$ (34).

Other comments

The German Advisory Board on Existing Chemicals has compiled data on the environmental fate, ecotoxicity and toxicity of BHT (35).

The antioxidant mechanism of BHT, metabolism and pulmonary toxicity, antiviral properties, carcinogenic and anticarcinogenic effects reviewed (13,36-39).

Mutagenicity and genotoxicity reviewed (40).

Reviews on human health effects, experimental toxicology, environmental effects, ecotoxicology, exposure levels, epidemiology and workplace experience are listed (41).

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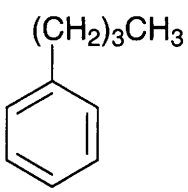
B246 butylbenzene



$C_{10}H_{14}$ **Mol. Wt.** 134.22 **CAS Registry No.** 104-51-8

Synonyms 1-phenylbutane; *n*-butylbenzene

EINECS No. 203-209-7 **RTECS No.** CY 9070000

Uses Intermediate in chemical synthesis. Solvent. Manufacture of pesticides.

Physical properties

M. Pt. –88°C **B. Pt.** 183°C **Flash point** 71°C **Specific gravity** 0.86 at 20°C with respect to water at 4°C
Partition coefficient log P_{ow} 4.27 (1) **Volatility** v.p. 1 mmHg at 22.7°C
Solubility Organic solvents: miscible with benzene, diethyl ether, ethanol

Occupational exposure

UN No. 2709 **HAZCHEM Code** 3Y **Conveyance classification** flammable liquid

Environmental fate

Adsorption and retention
Experimental soil and sediment adsorption coefficient (K_{oc}) of 2454.7 (2).

Mammalian & avian toxicity

Acute data
LD_{50} intraperitoneal mouse 1.99 g kg^{-1} (3).
LD_{Lo} rat 5000 mg kg^{-1} (4).

Irritancy
Eye irritant (5).

Legislation

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

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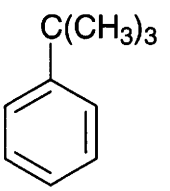
B247 *tert*-butylbenzene



$C_{10}H_{14}$ **Mol. Wt.** 134.22 **CAS Registry No.** 98-06-6

Synonyms 2-methyl-2-phenylpropane; (1,1-dimethylethyl)benzene; trimethylphenylmethane; pseudobutyl benzene

EINECS No. 202-632-4 **RTECS No.** CY 9120000

Uses Solvent. Intermediate in organic synthesis.

Physical properties

M. Pt. –58.1°C **B. Pt.** 168.5°C **Flash point** 60°C **Specific gravity** 0.8669 at 20°C with respect to water at 4°C
Partition coefficient log P_{ow} 4.11 **Volatility** v.p. 1.5 mmHg at 20°C ; v.den. 4.62
Solubility Organic solvents: miscible with benzene, diethyl ether and ethanol

Occupational exposure

UN No. 2709 **HAZCHEM Code** 3Y **Conveyance classification** flammable liquid

Environmental fate

Degradation studies
Non-biodegradable/qualified (1).

Adsorption and retention
Mediterranean red sandy clay soil samples with different moisture contents (0, 0.8, 4 and 12% w/w) were contaminated with vapour or liquid mixtures containing *tert*-butylbenzene. Adsorption on soil was 50 and 15 μg g^{-1} at 7°C; 120 and 47 μg g^{-1} at 17°C; 210 and 60 μg g^{-1} at 27°C and 333 and 100 μg g^{-1} at 34°C for oven dried and air dried samples, respectively. Volatilisation was rapid 92-99% in 2-6 hr period (2).

Mammalian & avian toxicity

Acute data
LD_{Lo} oral rat 5000 mg kg^{-1} (3).

Teratogenicity and reproductive effects
Does not induce morphological transformation of Syrian hamster embryo cells, nor enhance frequency of transformations induced by benzo[*a*] pyrene. Does not reduce intercellular communication in the primary embryo cells (4).

Irritancy
Eye irritant (5).

Legislation

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

References

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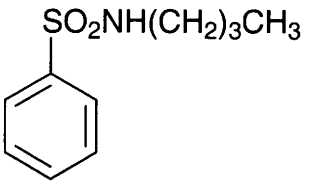
B248 *N*-butylbenzenesulfonamide



$C_{10}H_{15}NO_2S$ **Mol. Wt.** 213.30 **CAS Registry No.** 3622-84-2

Synonyms Cetamoll BMB; Plastomoll BMB; BBSA; Uniplex 24

EINECS No. 222-823-6

Uses Plasticiser for polyamides and other plastics.

Physical properties

M. Pt. –35°C **B. Pt.** 192.5°C **Specific gravity** 1.147

Other effects

Any other adverse effects

Young adult New Zealand white rabbits inoculated repeatedly by intracisternal or intraperitoneal routes developed dose-dependent motor dysfunction characterised by limb splaying, hyperreflexia, hypertomia, gait impairment and abnormal righting reflexes. Histopathological changes consisted of intramedullary thickening of the ventral horn axons, random neuroaxonal spheroids confined to brain stem nuclei and spinal motor neurons and swollen dendritic processes of spinal motor neurons (dose and duration unspecified) (1).

Other comments

Contaminant in ground and surface water.

References

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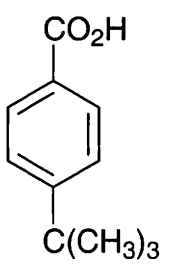
B249 4-*tert*-butylbenzoic acid



$C_{11}H_{14}O_2$ **Mol. Wt.** 178.23 **CAS Registry No.** 98-73-7

Synonyms benzoic acid, 4-(1,1-dimethylethyl); benzoic acid, *p-tert*-butyl; *p-tert*-butylbenzoic acid; TBBA

EINECS No. 202-696-3 **RTECS No.** DG 4708000

Uses Cross-linking agent with epoxy resins. Dispersing agent in pigments.

Physical properties

M. Pt. 166.3°C **Specific gravity** 1.142 at 20°C with respect to water at 4°C
Solubility Organic solvents: benzene, ethanol

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) goldfish 33 mg l^{-1} (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 735 mg kg^{-1} (2).

Sub-acute and sub-chronic data
Dermal rat (13 wk) 70-140 mg kg^{-1} 5 day wk^{-1} caused changes to liver, testis, epididymis and kidneys (3).

Teratogenicity and reproductive effects
Dermal application or dust inhalation rat (7 day) dose unspecified cause reduction in testis weights, sperm counts and lactate dehydrogenase-Y enzyme levels. A reduction or absence of spermatogenic cell types was observed. Recovery following cessation of exposure would be anticipated (4).

Other comments

No association reported between ♂ human occupational exposure to 4-*tert*-butyl benzoic acid and sperm count (5).
Experimental toxicology, human health and reproductive effects, and occupational exposure reviewed (6,7).

References

1. *Shell Industrie Chemicalien Gids* 1975, Shell Chemie, Gravenshagen.
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3. Cagen, S. Z. et al *J. Am. Coll. Toxicol.* 1989, **8**(5), 1027-1038.
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B250 butyl butyrate

$$CH_3(CH_2)_2CO_2(CH_2)_3CH_3$$

$C_8H_{16}O_2$ **Mol. Wt.** 144.21 **CAS Registry No.** 109-21-7
Synonyms butyl butanoate
EINECS No. 203-656-8 **RTECS No.** ES 1200000
Uses Flavouring.

Physical properties

B. Pt. 164-165°C **Flash point** 49°C **Specific gravity** 0.871
Solubility Organic solvents: ethanol, diethyl ether

Occupational exposure

Risk phrases Flammable (R10)
Safety phrases Keep out of reach of children (if sold to general public) (S2)

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) fathead minnow 11.6 mg l^{-1} (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral rabbit 9520 mg kg^{-1} (2).
LD_{50} intraperitoneal rat 2300 mg kg^{-1} (3).
LD_{50} intraperitoneal mouse 8900 mg kg^{-1} (3).

Irritancy
Dermal rabbit (24 hr) 500 mg caused moderate irritation (3).

Other comments

Reviews on experimental toxicology and human health effects listed (4).
Undergoes hydrolysis to *n*-butanol and butanoic acid.

References

1. Curtis, M. W. et al *J. Hydrol.* 1981, **51**, 359.
2. *Ind. Med. Surgery* 1972, **41**, 31.
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B251 butyl chloride

$$CH_3(CH_2)_3Cl$$

C_4H_9Cl **Mol. Wt.** 92.57 **CAS Registry No.** 109-69-3
Synonyms butane, 1-chloro; *n*-butylchloride; 1-chlorobutane; *n*-propylcarbinylchloride
EINECS No. 203-696-6 **RTECS No.** EJ 6300000
Uses Butylating agent in organic synthesis. Veterinary medicine as an anthelmintic.

Physical properties

M. Pt. -123.1°C **B. Pt.** 77-78°C **Flash point** -9.4°C (closed cup) **Specific gravity** 0.8875 at 20°C with respect to water at 20°C **Partition coefficient** log P_{ow} 2.64 **Volatility** v.p. 80.1 mmHg at 20°C ; v.den. 3.21
Solubility Water: 660 mg l^{-1} at 12°C. Organic solvents: miscible with diethyl ether, ethanol

Occupational exposure

UN No. 1127 **HAZCHEM Code** 3[redacted]E **Conveyance classification** flammable liquid
Supply classification highly flammable
Risk phrases Highly flammable (R11)
Safety phrases Keep out of reach of children (if sold to general public) – Keep container in a well ventilated place – Keep away from sources of ignition – No smoking – Do not empty into drains (S2, S9, S16, S29)

Ecotoxicity

Fish toxicity
LC_{50} (7 day) guppy 97 ppm (1).

Invertebrate toxicity
EC_{50} (30 min) *Photobacterium phosphoreum* 735 mg l^{-1} Microtox test (2).

Environmental fate

Degradation studies
Activated sludge (24 hr) 2.6% ThoD (3).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 2200-2670 mg kg^{-1} (4,5).
LD_{50} oral mouse, guinea pig 5600, 8000 mg kg^{-1}, respectively (5,6).
LC_{Lo} (4 hr) inhalation rat 8000 ppm (4).
LD_{Lo} dermal rabbit 20 g kg^{-1} (7).

Sub-acute and sub-chronic data
Oral rat (6 month) 2 mg kg^{-1} day^{-1} raised the level of inorganic phosphate in blood and altered the activity of blood alkaline phosphatase and succinate dehydrogenase activity (6).

Carcinogenicity and chronic effects
No increase in the incidence of lung tumour observed in ♂, ♀ rats and mice (dose and duration unspecified) (8,9).
National Toxicology Program gavage rats, mice (2 yr) no evidence of carcinogenicity (10).

Teratogenicity and reproductive effects
Embryotoxic and teratogenic effects observed in rats at the sublethal dose of 733 mg kg^{-1} (6).

Irritancy
Dermal rabbit (24 hr) 10 mg caused mild irritation and 500 µg instilled into rabbit eye caused mild irritation (4).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA1535, TA1537 with and without metabolic activation negative (11).
DNA polymerase deficient *Escherichia coli* negative (12).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Organochlorine compounds: guide level 1 µg l^{-1} (13).
Included in Schedule 6 (Release into Land: Prescribed Substances) of Statutory Instrument No. 472, 1991 (14).
Former Soviet Union maximum permissible concentration in open water 4 µg l^{-1} (5).

Other comments

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

References

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2. Kaiser, K. L. E. et al *Water Pollut. Rep. J. Canada* 1991, **26**(3), 361-431.
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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

B252 *sec*-butyl chloride

$$CH_3CHClCH_2CH_3$$

C_4H_9Cl **Mol. Wt.** 92.57 **CAS Registry No.** 78-86-4

Synonyms 2-chlorobutane; 2-chloro-3-methylpropane

EINECS No. 201-151-7 **RTECS No.** EJ 6475000

Physical properties

M. Pt. −140°C **B. Pt.** 68°C **Flash point** −15°C **Specific gravity** 0.873 at 20°C with respect to water at 4°C
Partition coefficient log P_{ow} 2.57 (1) **Volatility** v.den. 3.2
Solubility Water: 1 g l^{-1} at 25°C. Organic solvents: miscible diethyl ether, ethanol, soluble in benzene, chloroform

Occupational exposure

UN No. 1127 **HAZCHEM Code** 3[redacted]E **Conveyance classification** flammable liquid

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 17.4 g kg^{-1} (2).
LC_{Lo} (4 hr) inhalation rat 8000 ppm (2).
LD_{50} dermal rabbit 20 g kg^{-1} (2).

Carcinogenicity and chronic effects

A slight but significant increase in lung tumour incidence was observed in ♂ and ♀ strain A mice following 13 intraperitoneal injections over 24 wk (total dose 3.24 g kg^{-1}) (3).

Genotoxicity

Aspergillus nidulans diploid strain P1 mitotic chromosome malsegregation assay negative (1).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Organochlorine compounds: guide level 1 $\mu g\ l^{-1}$ (4).
Included in Schedule 6 (Release into Land: Prescribed Substances) of Statutory Instrument No. 472, 1991 (5).

References

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2. Smyth, H. F. et al *AMA Arch. Ind. Hyg. Occup. Med.* 1969, **30**, 470.
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4. *EC Directive Relating to the Quality of Water Intended for Human Consumption* 1982, 80/778/EEC, Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.
5. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK

B253 *tert*-butyl chloride

$$(CH_3)_3CCl$$

C_4H_9Cl **Mol. Wt.** 92.57 **CAS Registry No.** 507-20-0
Synonyms 2-chloro-2-methylpropane; 2-chloroisobutane; trimethylchloromethane
EINECS No. 208-066-4 **RTECS No.** TX 5040000

Physical properties

M. Pt. –25.4°C **B. Pt.** 52°C **Flash point** 18°C (1) **Specific gravity** 0.8420 at 20°C with respect to water at 4°C
Solubility Organic solvents: benzene, carbon tetrachloride, chloroform, diethyl ether, ethanol

Occupational exposure

UN No. 1127 **HAZCHEM Code** 3[illegible]E **Conveyance classification** flammable liquid

Ecotoxicity

Fish toxicity
Cell multiplication inhibition test (24 hr) sea trout, bluegill sunfish, yellow perch and goldfish 5 $mg\ l^{-1}$, negative (2).

Mammalian & avian toxicity

Carcinogenicity and chronic effects
Intraperitoneal mice (24 wk) 1, 3, 6 $g\ kg^{-1}$ induced lung tumours in 6/8 high dose surviving animals and 6/11 medium/low dose animals (3).

Genotoxicity

Aspergillus nidulans diploid strain P1 mitotic chromosome malsegregation negative (4).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Organochlorine compounds: guide level 1 $\mu g\ l^{-1}$ (5).
Included in Schedule 6 (Release into Land: Prescribed Substances) of Statutory Instrument No. 472, 1991 (6).

Other comments

Quantitative structure activity relationship (QSAR) evaluation of the mutagenic potential of halogenated aliphatic hydrocarbons (4,7-9).

References

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6. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations*1991, HMSO, London, UK.
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9. Eriksson, L. et al *Environ. Toxicol. Chem.* 1990, **9**(11), 1339-1351

B254 butyl chloroformate

$$ClCO_2(CH_2)_3CH_3$$

$C_5H_9ClO_2$ **Mol. Wt.** 136.58 **CAS Registry No.** 592-34-7

Synonyms *n*-butyl chloroformate; butoxycarbonyl chloride; butyl chlorocarbonate; carbonochloridic acid, butyl ester

EINECS No. 209-750-5

Uses Chemical synthesis of mixed or symmetrical carbonates. Cross-linking agent for cellulose textiles.

Physical properties

B. Pt. 142°C **Flash point** 25°C **Specific gravity** 1.074

Occupational exposure

UK-LTEL 1 ppm (5.7 mg m^{-3})

UN No. 2743 **HAZCHEM Code** 3W **Conveyance classification** toxic substance, corrosive
Supply classification toxic
Risk phrases Flammable – Toxic by inhalation – Causes burns (R10, R23, R34)
Safety phrases Keep locked up and out of the reach of children (if sold to general public) – In case of contact with eyes, rinse immediately with plenty of water and seek medical advice – Wear suitable protective clothing – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S26, S36, S45)

Other effects

Other adverse effects (human)
Systemic effects include burning sensation, coughing, wheezing, laryngitis, shortness of breath, headache, nausea and vomiting. Inhalation, ingestion or absorption through skin may be fatal as a result of spasm, inflammation and oedema of the bronchi and larynx, chemical pneumonitis and oedema (1).
Any other adverse effects
Vapours of lower chloroformates caused pneumonia (sometimes fatal) in animal studies (2).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Organochlorine compounds: guide level 1 $\mu g\ l^{-1}$ (3).
Included in Schedule 6 (Release into Land: Prescribed Substances) of Statutory Instrument No. 472, 1991 (4).

Other comments

Butyl chloroformate is flammable and forms explosive mixtures in air. Incompatible with strong oxidising agents, strong reducing agents and amines. May decompose on exposure to moist air or water. Heat sensitive (1). Experimental toxicology and human health effects reviewed (5).

References

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5. *ECETOC Technical Report No. 30(5)* 1994, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium

B255 *tert*-butyl chromate

$$(CH_3)_3COCr(O)_2OC(CH_3)_3$$

$C_8H_{18}CrO_4$ **Mol. Wt.** 230.22 **CAS Registry No.** 1189-85-1

Synonyms *tert*-butyl chromate (VI); chromic acid (H_2CrO_4), bis(1,1-dimethylethyl) ester; chromic acid, di-*tert*-butyl ester

RTECS No. GB 2900000

Uses Oxidising agent. Catalyst for alkene polymerisation. Corrosion inhibitor.

Physical properties

M. Pt. -5-0°C

Occupational exposure

FR-VLE 0.1 mg m^{-3}
SE-LEVL 0.02 mg m^{-3}
UK-LTEL MEL 0.05 mg m^{-3} (as Cr) **US-STEL** ceiling limit 0.1 mg m^{-3} (as CrO_3)
Supply classification toxic
Supply classification dangerous for the environment
Risk phrases May cause cancer by inhalation – May cause sensitisation by skin contact – Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment (R49, R43, R50/53)
Safety phrases Avoid exposure – obtain special instruction before use – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) – This material and/or its container must be disposed of as hazardous waste – Avoid release to the environment. Refer to special instructions/safety data sheet (S53, S45, S60, S61)

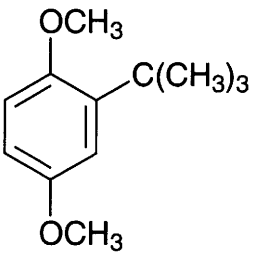
Other comments

Toxicity of chromium compounds reviewed (1).
Reviews on experimental toxicology and human health effects listed (2).

References

1. *IARC Monograph* 1990, **49**, 49-256.
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

B256 2-*tert*-butyl-1,4-dimethoxybenzene



$C_{12}H_{18}O_2$ **Mol. Wt.** 194.27 **CAS Registry No.** 21112-37-8

Synonyms benzene, 2-*tert*-butyl-1,4-dimethoxy-; benzene, 2-(1,1-dimethylethyl)-1,4-dimethoxy-; mono-*tert*-butylhydroquinone dimethyl ether

EINECS No. 244-216-5

Uses Antioxidant in polymer synthesis.

Physical properties

B. Pt. 117-118°C at 12 mmHg **Specific gravity** 1.007 at 20°C with respect to water at 4°C

Other effects

Any other adverse effects

Administered to rats i.p. the compound is 100-fold more toxic than administered orally owing to its depressive effect on the contractility of the gut musculature and the consequent impairment of intestinal transit (1).
Ability to induce glutathione S-transferase (EC 2.5.1.18) and NAD(P)H-quinone reductase (EC 1.6.99.2) in the cytosol of liver, mucosa of small intestine and the forestomach of female mice was tested. 2-*tert*-Butyl-1, 4-dimethoxybenzene was fed to mice (gavage) in five daily doses of 4.8 mg l^{-1}. Increased enzyme activity observed in liver and intestinal mucosa. No induction of enzyme in forestomach (2).

References

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B257 butyl ethyl ether

$$CH_3(CH_2)_3OCH_2CH_3$$

$C_6H_{14}O$ **Mol. Wt.** 102.18 **CAS Registry No.** 628-81-9

Synonyms ethyl butyl ether; 1-ethoxybutane; 3-oxaheptane

EINECS No. 211-055-7 **RTECS No.** KN 4725000

Physical properties

M. Pt. –124°C **B. Pt.** 91-92°C **Flash point** –5°C **Specific gravity** 0.7528 at 20°C with respect to water at 20°C
Partition coefficient log P_{ow} 2.03 **Volatility** v.p. 44.4 mmHg at 20°C ; v.den. 3.52
Solubility Organic solvents: diethyl ether, ethanol

Occupational exposure

UN No. 1179 **HAZCHEM Code** 3YE **Conveyance classification** flammable liquid

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 1870 mg kg^{-1} (1).
LC_{50} (15 min) inhalation mouse 153 mg m^{-3} (2).

Irritancy
Dermal rabbit (24 hr) 10 mg caused mild irritation (1).

References

1. *Arch. Ind. Hyg. Occup. Med.* 1951, **4**, 119.
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B258 butyl formate

$$HCO_2(CH_2)_3CH_3$$

$C_5H_{10}O_2$ **Mol. Wt.** 102.13 **CAS Registry No.** 592-84-7

Synonyms formic acid, butyl ester; *n*-butyl formate

EINECS No. 209-772-5 **RTECS No.** LQ 5500000

Uses Resin hardner. Solvent.

Physical properties

M. Pt. –90°C **B. Pt.** 106-107°C **Flash point** 13°C **Specific gravity** 0.892 at 20°C with respect to water at 4°C
Volatility v.p. 40 mmHg at 31.6°C ; v.den. 3.52

Occupational exposure

UN No. 1128 **HAZCHEM Code** 3YE **Conveyance classification** flammable liquid
Supply classification highly flammable

Risk phrases Highly flammable (R11)
Safety phrases Keep out of reach of children (if sold to general public) – Keep container in a well ventilated place – Keep away from sources of ignition – No smoking – Take precautionary measures against static discharges (S2, S9, S16, S33)

Mammalian & avian toxicity

Acute data
LD_{50} oral rabbit 2700 mg kg^{-1} (1).
LC_{Lo} (70 min) inhalation cat 10,400 ppm (2).
Inhalation dog, cat (1 hr) 41.6 mg l^{-1} caused irritation and narcosis. Dogs recovered, but exposure was fatal to cats (3).

Irritancy
Inhalation exposure caused intolerable irritation to human subjects in <1 min (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).
Autoignition temperature 322°C.

References

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2. *AMA Arch. Ind. Health* 1959, **20**, 517.
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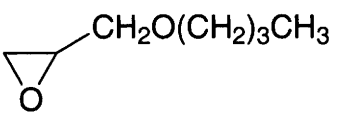
B259 butyl glycidyl ether



$C_7H_{14}O_2$ **Mol. Wt.** 130.19 **CAS Registry No.** 2426-08-6

Synonyms butyl 2,3-epoxypropyl ether; (butoxymethyl)oxirane; 1-butoxy-2,3-epoxypropane; 1-(2,3-epoxypropoxy)butane; glycidyl butyl ether; 2,3-epoxypropyl butyl ether; Ageflex BGE; Epirez 501; Heloxy 61

EINECS No. 219-376-4 **RTECS No.** LQ 1450000

Uses Vicoscity-reducing agent for epoxy resins. Plasticiser. Lubricant antioxidant. In adhesives and cross-linking agents. Solvent for epoxy resins.

Physical properties

B. Pt. 164-166°C **Flash point** 57-59°C **Specific gravity** 0.91 at 25°C with respect to water at 4°C

Volatility v.p. 3.2 mmHg at 25°C ; v.den. 3.78
Solubility Water: 20 g l^{-1} at 20°C. Organic solvents: acetone, benzene, diethyl ether, ethanol

Occupational exposure

FR-VME 25 ppm (135 mg m^{-3})
SE-LEVL 10 ppm (50 mg m^{-3}) **SE-STEL** 15 ppm (80 mg m^{-3})
UK-LTEL 25 ppm (135 mg m^{-3})
US-TWA 25 ppm (133 mg m^{-3})
Supply classification harmful
Risk phrases Harmful by inhalation – May cause sensitisation by skin contact (R20, R43)
Safety phrases Keep out of reach of children (if sold to general public) – Avoid contact with skin and eyes (S2, S24/25)

Mammalian & avian toxicity

Acute data
LD_{50} oral gavage mouse, rat 1520, 2500 mg kg^{-1}, respectively (1,2).
LC_{50} (4 hr) inhalation mouse >3500 ppm (3).
LD_{50} dermal rabbit 2520-4930 mg kg^{-1} (4).
LD_{50} intraperitoneal mouse, rat 700, 1140 mg kg^{-1}, respectively (1).

Sub-acute and sub-chronic data
Inhalation ♂ rats (35 hr) 300 ppm atrophied testes in 5 out of 10 animals. Inhalation ♂ rats (35 hr) 75 ppm patchy atrophy of testes in 1 out of 10 animals (5).
Oral mouse (2 wk) 225 or 405 mg kg^{-1} day^{-1}. The high dose caused a reduction in thymus weight and T-cell count in the peripheral blood (6).
Intramuscular rat (3 day) 400 mg kg^{-1} day^{-1} increased the leucocyte count (7).

Teratogenicity and reproductive effects
♂ mice (8-10 wk) dermal application of 0, 0.375, 0.75 or 1.5 g kg^{-1}, 3 × wk^{-1} for 8 wk, then mated to unexposed ♀. No significant dose-related change in pregnancy rates of number of implants, but foetal deaths significantly higher in high dose group (8).

Metabolism and toxicokinetics
Oral ♂ rats 20 mg kg^{-1} 87% eliminated via urine within 24 hr increased to 91% after 96 hr (9).
Oral ♂ New Zealand White rabbits 20 mg kg^{-1} 78% eliminated via urine within 24 hr, increased to 80% after 96 hr (10).

Irritancy
Dermal rabbit (24 hr) 500 mg caused irritation and 750 μg instilled into rabbit eye (24 hr) caused severe irritation (11).

Sensitisation
Contact sensitiser to human skin (12).
10% of workers tested developed reaction to challenge by patch test (13,14).

Genotoxicity

Salmonella typhimurium TA100, TA1535 with metabolic activation positive (15-18).
Escherichia coli WP2 *uvrA* 48 hr incubation at 37°C induced DNA damage (16).
In vitro human lymphocytes induced DNA damage (19).
In vivo mouse bone marrow increased micronuclei (18).

Other effects

Other adverse effects (human)
The exposure of two men to a spillage of 3.5 litres of butyl 2,3-epoxypropyl ether for 1.5 and 4 hr, respectively,

produced irritation of gastrointestinal tract resulting in anorexia and vomiting. The severity of the symptoms were related to the length of time exposed. Other effects noted were persistent and severe headache and mild respiratory irritation (20,21).

Other comments

Physical properties, use, carcinogenicity, mammalian toxicity, mutagenicity and metabolism of glycidyl ethers reviewed (21,22).

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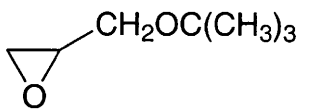
B260 *tert*-butyl glycidyl ether



$C_7H_{14}O_2$ **Mol. Wt.** 130.19 **CAS Registry No.** 7665-72-7

Synonyms glycidyl-*tert*-butyl-ether; ((1,1-dimethylethoxy)methyl)-oxirane; T-BGE

EINECS No. 231-640-0 **RTECS No.** RR 0475000

Uses In epoxy resins for applications in protective coatings, reinforced plastics, bonding materials and adhesives.

Physical properties

B. Pt. 152°C **Flash point** 43°C **Specific gravity** 0.917

Solubility Water: 10-50 g l^{-1} at 23°C. Organic solvents: acetone, dimethyl sulfoxide, ethanol

Mammalian & avian toxicity

Acute data

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

Genotoxicity

Salmonella typhimurium TA100, TA1535 with and without metabolic activation positive (2).
Escherichia coli without metabolic activation positive (3).
In vitro human peripheral blood lymphocytes induced unscheduled DNA damage (4).

References

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B261 *tert*-butyl hydroperoxide

$$(CH_3)_3COOH$$

$C_4H_{10}O_2$ **Mol. Wt.** 90.12 **CAS Registry No.** 75-91-2

Synonyms 1,1-dimethylethyl hydroperoxide; 2-hydroproperoxy-2-methylpropane; Aztec TBHP-70, Aq; Trigonox A-80; T-Hydro; TBHP

EINECS No. 200-915-7 **RTECS No.** EQ 4900000

Uses Polymerisation, oxidation and sulfonation catalyst. Reagent for selective oxygenation of olefins and acetylenes. Used in bleaching and deodorising.

Physical properties

M. Pt. –8°C **B. Pt.** 35°Cn at 20 mmHg **Flash point** 26.7°C **Specific gravity** 0.880 at 25°C with respect to water at 4°C **Volatility** v.den. 2.07
Solubility Organic solvents: chloroform, diethyl ether, ethanol

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, mouse 406, 710 mg kg^{-1}, respectively (1,2).
LC_{50} (4 hr) inhalation mouse, rat 350, 500 ppm, respectively (1).
LD_{50} dermal rat 790 mg kg^{-1} (2).
LD_{50} intraperitoneal rat 90 mg kg^{-1} (1).

Metabolism and toxicokinetics

tert-Butyl hydroperoxide is a substrate for glutathione peroxidase (3).
Metabolism of *tert*-butylhydroperoxide by isolated enterocytes from proximal rat intestine subscribes to regulation by glucose availability, suggesting that nutrient availability would be an important factor in the detoxification of the compound by the small intestine (4).

Irritancy

Dermal rabbit (24 hr) 500 mg caused moderate irritation and 100 mg instilled into rabbit eye caused severe irritation (5).

150 mg instilled into rabbit eye for 1 min then rinsed with water caused severe irritation (6).
Severe irritant and corrosive material to intact and abraded skin (7).

Genotoxicity

In vitro Chinese hamster V79 cells chromosomal aberrations positive (8).

Other effects

Other adverse effects (human)

Human erythrocytes were treated with *tert*-butyl hydroperoxide (10 min); 45 mg l^{-1} inhibited basal calcium and magnesium ATPase activity by 40% and calmodulin-stimulated activity by 54% (9).

Any other adverse effects

Hydroperoxides play an important role in the control of mammalian platelet cyclooxygenase and lipoxygenase activities (10).

The biosynthesis of GSH *de novo* by cultured Chinese hamster V79 cells is enhanced by *tert*-butylhydroperoxide (11).

Effect of *tert*-butyl hydroperoxide on metabolism of liver and hepatoma reported. Induces peroxidation of lipid membranes leading to cell damage (12).

The effects of *tert*-butyl hydroperoxide on the activity of antioxidant enzymes were investigated in cultured Chinese hamster V79 cells. Incubation of cells with *tert*-butyl hydroperoxide for 1 hr significantly increased the activity of Cu-Zn superoxide dismutase up to a level 1.4 times that of control cells (13).

The cell killing mechanism by *tert*-butylhydroperoxide is the same in cultured rat hepatocytes containing physiological or low concentrations of vitamin E (14).

Results from cultured rat hepatocytes indicate the existence of a specific, kinetically defined cellular iron binding site. Such binding is involved in peroxide-mediated toxicity, but independent of lipid peroxidation (15).

In mammalian thymoma cells there are two mechanisms of *tert*-butylhydroperoxide toxicity: the first, involving glutathione peroxidase and nicotinamide nucleotides, leads to cell death by alteration of calcium homeostasis; the second, involving potent oxygen reactive species, affects cell viability by ATP depletion. In normal thymocytes only the second mechanism operates (16).

Results from the perfusion of Langendorff rat hearts (15, 30 or 75 min) with *tert*-butylhydroperoxide (0.25 mmol l^{-1}) suggest that its cardiotoxic effects cannot be explained by the appearance of oxygen radicals alone and that an increased lipid peroxidation is not the mechanism which is primarily responsible for cell death (17).

Biochemical changes in isolated mammalian hepatocytes exposed to *tert*-butylhydroperoxide indicated that GSH depletion and modification in phosphorylation a (Ca^{2+} levels) were the most relevant intracellular events to explain its cytotoxicity (18).

NADH prevents mitochondrial dysfunction and cell death caused by short-term exposure of U937 cells to *tert*-butyl hydroperoxide (19).

Other comments

Escherichia coli exposed to *tert*-butyl-hydroperoxide underwent progressive and irreversible impairment of respiratory function (20).

Industrial toxicity of organic peroxides reported (9).

Metabolised by human carcinoma skin keratinocytes to free radicals. Study provided first direct evidence that human carcinoma skin cells can generate free radicals from organic hydroperoxides. The authors consider this metabolic capacity to be an important determinant of human cancer risk from hydroperoxides (21).

Dermatological and biological effects of organic peroxides reviewed (22,23).

Reviews on experimental toxicology and human health effects listed (24).

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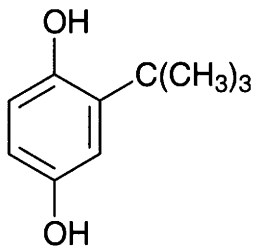
B262 *tert*-butylhydroquinone



$C_{10}H_{14}O_2$ **Mol. Wt.** 166.22 **CAS Registry No.** 1948-33-0

Synonyms 1,4-benzenediol, 2-(1,1-dimethylethyl)-; hydroquinone, *tert*-butyl; mono-tertiarybutylhydroquinone; MTBHQ; TBHQ

EINECS No. 217-752-2 **RTECS No.** MX 4375000

Uses An antioxidant used in foods.

Physical properties

M. Pt. 127-129°C

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, mouse 700, 1000 mg kg^{-1}, respectively (1,2).

LD_{50} intraperitoneal rat, mouse 300, 144 mg kg^{-1}, respectively (1,3).

Sub-acute and sub-chronic data

Oral rat (28 days) 2% *tert*-butylhydroquinone in diet caused mild hyperplasia of the forestomach with increased hyperplasia of basal cells (4).

Carcinogenicity and chronic effects

National Toxicology Program (2 yr) studied rats, mice via food. No evidence of carcinogenic activity (5).
Administration in diet to ♂ Syrian golden hamsters, *tert*-butylhydroquinone was inactive in causing forestomach hyperplasia and lesions (6).

Teratogenicity and reproductive effects

Concentrations of 0.125 to 0.5% in diet of pregnant rats produced no teratogenic effects (7).

Metabolism and toxicokinetics

Following i.p. administration to rats, 2-*tert*- butyl-5-methylthiohydroquinone and 2-*tert*-butyl-6-methylthiohydroquinone were detected in the urine (8).
2-*tert*-Butyl-5-glutathion-*S*-ylhydroquinone, 2-*tert*-butyl-3,6-bisglutathion-*S*-ylhydroquinone, and 2-*tert*-butyl-3,6-bisglutathion-*S*-ylhydroquinone were identified as biliary metabolites of *tert*-butylhydroquinone after i.p. administration (1.0 mmol kg^{-1}) to ♂ F344 rats. These conjugates undergo further metabolism prior to excretion in the urine (9).

Irritancy

10 mg introduced into the lower conjunctival sac of ♀ New Zealand White rabbits caused moderate to severe corneal damage which was resolved by 21 days (10).

Genotoxicity

Salmonella typhimurium TA92, TA100, TA102, TA104 with and without metabolic activation negative. Doses >100 μg $plate^{-1}$ were cytotoxic (11).
Saccharomyces cerevisiae D7 with and without metabolic activation negative (12).
In vitro V79 Chinese hamster lung cells, slight and sporadic response may indicate weak genotoxicity which is sensitive to slight difference in test conditions. Doses >5 μg l^{-1} were cytotoxic (12).
In vivo mouse bone marrow cells sister chromatid exchange positive (13).

Other effects

Any other adverse effects

tert-Butylhydroquinone was toxic to freshly isolated rat hepatocytes. The toxicity was dose-dependent, related to the rate of oxygen consumption, and was accompanied by losses of intracellular GSH, protein thiols and ATP (14).
The toxicity of GSH conjugates of *tert*-butylhydroquinone to rat kidney and bladder may contribute to the carcinogenic promoting effect of *tert*-butylhydroquinone in these tissues (15).

Legislation

Acceptable daily intake of 200 μg established (16).

Other comments

Chemical and physical properties, experimental toxicology and human health effects reviewed (17-20).
May have antimicrobial as well as antioxidant properties (21).

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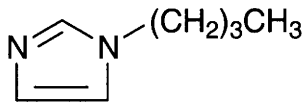
B263 *N*-butylimidazole



$C_7H_{12}N_2$ **Mol. Wt.** 124.19 **CAS Registry No.** 4316-42-1

Synonyms 1-butylimidazole; imidazole, 1-butyl; 1*H*-imidazole, 1-butyl

EINECS No. 224-335-9

Physical properties

B. Pt. 110°C at 11 mmHg **Flash point** 110°C **Specific gravity** 0.945

Occupational exposure

UN No. 2690 **HAZCHEM Code** 2X **Conveyance classification** toxic substance

Ecotoxicity

Fish toxicity

LC_{50} (24 hr) goldfish 30 mg l^{-1} (1).

Other effects

Any other adverse effects

Inhibits platelet aggregation induced by ADP or collagen (2).

Thromboxane synthetase inhibitor (3).

References

1. Bridie, A. L. et al *Water Res.* 1979, **13** 623-630.
2. Avirans, M. et al *Br. J. Clin. Pharmacol.* 1985, **19**(6) 715-719.
3. Crockard, A. et al *J. Cereb. Blood Flow Metals* 1982, **2**(1), 67-62

B264 butyl isocyanate

$$CH_3(CH_2)_3NCO$$

C_5H_9NO **Mol. Wt.** 99.13 **CAS Registry No.** 111-36-4

Synonyms BIC; butane, 1-isocyanato; 1-isocyanatobutane; isocyanic acid, butyl ester

EINECS No. 203-862-8 **RTECS No.** NQ 8250000

Uses An active-site specific reagent for yeast ethanol dehydrogenase. Intermediate in manufacture of pesticides, herbicides and pharmaceuticals.

Physical properties

B. Pt. 115°C **Flash point** 26°C **Specific gravity** 0.880 at 20°C with respect to water at 4°C

Occupational exposure

SE-LEVL 0.005 ppm **SE-CEIL** 0.01 ppm

UK-LTEL MEL 0.02 mg m^{-3} (as NCO) **UK-STEL** MEL 0.07 mg m^{-3} (as NCO)

UN No. 2485 **HAZCHEM Code** 3WE **Conveyance classification** toxic substance, danger of fire (flammable liquid)

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse, guinea pig, rat 150, 250, 600 mg kg^{-1}, respectively (1).

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

Sub-acute and sub-chronic data

Young adult ♂ Wistar rats (5 day, 6h day^{-1}) 0, 1.1, 6.2, 15 or 26 mg m^{-3} air. Most rats exposed to 26 mg m^{-3} died or were sacrificed in a moribund state during wk 2. All other rats survived the exposure regimen but suffered obstructive and progressive lung disease with associated gas trapping and severe disturbance of the ventilation perfusion relationship (3).

Genotoxicity

Pretreatment of H/r30R cells with butyl isocyanate did not alter X-ray induced mutagenesis (4).

Other effects

Other adverse effects (human)

Eighteen persons exposed to *n*-butyl isocyanate developed acute respiratory system distress (5).

Any other adverse effects

HepG2 cells treated with 1.25-20 μg ml^{-1} (24 hr) showed decreased ethoxyresorufin deethylase and ethoxycoumarin dethylase activities (6).

Other comments

Growth of Ehrlich ascites tumours in Swiss ICR/HA mice was inhibited by butyl isocyanate (7).

The toxicity of isocyanates reviewed (8).

References

1. *Labour Hyg. Occup. Dis.* 1976, **20**(3), 53.
2. *US Army Armament Res. Dev. Command* (NX 05701).

3. Pauluhn, J. et al *Arch. Toxicol.* 1992, **66**(2), 118-125.
4. Kawazoe, Y. *Gann* 1982, **73**(2), 255-238.
5. Engelhard, H. Z. *Gesamte Hyg.* 1976, **22**(4), 235-238.
6. Radice, S. et al *Toxicology* 1997, **123**(1,2), 135-142.
7. Moos, G. E. *Cancer Res.* 1971, **31**(7), 937-941.
8. Woolrich, P. F. *Technical Bull.* 1973, **106**, 1-19

B265 butyl isovalerate

$$(CH_3)_2CHCH_2CO_2(CH_2)_3CH_3$$

$C_9H_{18}O_2$ **Mol. Wt.** 158.24 **CAS Registry No.** 109-19-3

Synonyms butanoic acid, 3-methyl-, butyl ester; *n*-butyl isopentanoate; butyl 3-methylbutyrate; isovaleric acid, butyl ester; 3-methylbutanoic acid, butyl ester

EINECS No. 203-654-7 **RTECS No.** NY 1502000

Uses Fragances. Artificial flavourings.

Occurrence Natural substance in *Valerianella locusta*, in the oil from leaves of *Eriostermon coxii* and *Phebaluim dentatum* and in bananas and peas (1,2).

Physical properties

B. Pt. 150°C **Specific gravity** 0.87 **Volatility** v.den. 5.45

Mammalian & avian toxicity

Acute data

LD_{50} oral rat, rabbit 5000, 8200 mg kg^{-1}, respectively (1,2).

Metabolism and toxicokinetics

A solution 1 g in acetone fed through to the rumen of cows was detected unchanged in milk 2 hr after administration (3).

Irritancy

Dermal rabbit (24 hr) 500 mg caused mild irritation (2).

Humans closed patch tested with 1% in petrolatum showed no irritation effects 48 hr after application of the dose (2).

Other effects

Any other adverse effects

Narcotic dose in rabbits 6000 mg kg^{-1} caused stupor and loss of voluntary movement in 50% of animals tested (4).

References

1. Goetz-Schmidt, E. M. et al *Phytochemistry* 1988, **27**(3), 845-848.
2. Opdyke, D. J. L. *Food Cosmet. Toxicol.* 1980, **18**, 659-660.
3. Honkanen, E. et al *Acta Chem. Scand.* 1964, **18**, 612.
4. Munch, J. C. et al *Ind. Med. Surg.* 1972, **41**(4), 31-33

B266 butyl lactate

$$CH_3CH(OH)CO_2CH_2CH_2CH_2CH_3$$

$C_7H_{14}O_3$ **Mol. Wt.** 146.19 **CAS Registry No.** 138-22-7

Synonyms 2-hydroxypropanoic acid, butyl ester; butyl α-hydroxypropionate; *n*-butyl lactate

EINECS No. 205-316-4 **RTECS No.** OD 4025000

Physical properties

M. Pt. -28°C **B. Pt.** 185-187°C **Flash point** 69°C (closed cup) **Specific gravity** 0.984 **Volatility** v.p. 0.4 mmHg at 20°C ; v.den. 5.04

Solubility Organic solvents: miscible in diethyl ether, ethanol

Occupational exposure

FR-VME 5 ppm (25 mg m^{-3})
SE-LEVL 5 ppm (30 mg m^{-3}) **SE-STEL** 10 ppm (60 mg m^{-3})
UK-LTEL 5 ppm (30 mg m^{-3})
US-TWA 5 ppm (30 mg m^{-3})

Mammalian & avian toxicity

Acute data

LD_{50} subcutaneous mouse, rat 11-12 g kg^{-1} (1,2).
LD_{Lo} intraperitoneal mouse 200 mg kg^{-1} (3).

Irritancy

Dermal rabbit (24 hr) 500 mg caused moderate to severe erythema and moderate oedema (1).

Legislation

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

Other comments

Reviews on experimental toxicology, human health effects, workplace experience listed (5).
Affinity in biological systems described using solubility parameter techniques (6).
Autoignition temperature 382°C.

References

1. *Food Cosmet. Toxicol.* 1979, **17**, 727.
2. *Raw Material Data Handbook, Vol.1 Organic Solvents* 1974, National Association of Printing Ink Research Institute, Francis McDonald Sinclair Memorial Laboratory, Lehigh University, Bethlehem, PA, USA.
3. *Summary Tables of Biological Tests* 1955, No.7, National Research Council Chemical – Biological Coordination Center, Washington, DC, USA.
4. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK.
5. *ECETOC Technical Report No. 71* 1996, European Centre for Ecotoxicology and Toxicology of Chemicals, 4 Avenue E. Van Nieuwenhuyse (Bte 6), B-1160 Brussels, Belgium.
6. Hansen, C. M. et al *Am. Ind. Hyg. Assoc. J.* 1988, **49**(6), 301-308

B267 butyl methacrylate

$$CH_2=C(CH_3)CO_2CH_2CH_2CH_2CH_3$$

$C_8H_{14}O_2$ **Mol. Wt.** 142.20 **CAS Registry No.** 97-88-1

Synonyms methacrylic acid, butyl ester; butyl 2-methyl-2-propenoate

EINECS No. 202-615-1 **RTECS No.** OZ 3675000

Physical properties

B. Pt. 163°C **Flash point** 50°C **Specific gravity** 0.895 at 20°C with respect to water at 4°C
Partition Coefficient log P_{ow} 2.88 **Volatility** v.p. 4.9 mmHg at 20°C ; v.den. 4.8

Occupational exposure

SE-LEVL 50 ppm (300 mg m^{-3}) **SE-STEL** 75 ppm (450 mg m^{-3})

UN No. 2227 **HAZCHEM Code** 3Y **Conveyance classification** flammable liquid
Supply classification irritant
Risk phrases Flammable – Irritating to eyes, respiratory system and skin – May cause sensitisation by skin contact (R10, R36/37/38, R43)
Safety phrases Keep out of reach of children (if sold to general public) (S2)

Ecotoxicity

Fish toxicity
LC_{50} (72 hr) goldfish 5.52 mg l^{-1} (1).

Invertebrate toxicity
EC_{50} (30 min) *Photobacterium phosphoreum* 55.3 mg l^{-1} Microtox test (2).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 22,600 mg kg^{-1} (3).
LD_{50} oral mouse 13,500 mg kg^{-1} (4).
LD_{Lo} oral rabbit 6270 mg kg^{-1} (5).
LC_{50} (4 hr) inhalation rat 4910 ppm (6).
LD_{50} dermal rabbit 11,300 mg kg^{-1} (3).
LD_{50} intraperitoneal rat 2304 mg kg^{-1} (7).
LD_{50} intraperitoneal mouse 1490 mg kg^{-1} (8).

Metabolism and toxicokinetics
Intraperitoneal rat (concentration unspecified) quickly absorbed and accumulated in liver, kidney, blood, heart and brain (9).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537, TA1538 with and without metabolic activation negative (10,11).

Legislation

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

References

1. Reinert, K. H. *Regul. Toxicol. Pharmacol.* 1987, **7**, 384-389.
2. Kaiser, K. L. E. et al *Water Pollut. Res. J. Can.* 1991, **26**(3), 361-431.
3. *Am. Ind. Hyg. Assoc. J.* 1969, **30**, 470.
4. *Gig. Tr. Prof. Zabol.* 1975, **19**(9), 57.
5. *J. Ind. Hyg. Toxicol.* 1941, **23**, 343.
6. *J. Toxicol. Environ. Health* 1985, **16**, 811.
7. *J. Dental Res.* 1972, **51**, 1632.
8. *J. Pharm. Sci.* 1973, **62**, 778.
9. Svetlakov, A. V. et al *Gig. Tr. Prof. Zabol.* 1989, (3), 51-52 (Russ.) (*Chem. Abstr.* **111**, 110595r).
10. Waegemakers, T. H. et al *Mutat. Res.* 1984, **137** (2-3), 95-102.
11. Zeiger, E. et al *Environ. Mutagen.* 1987, **9**(Suppl. 9) 1-109.
12. *S. I. 1991 No. 472 The Environmental Protection (Prescribed Processes and Substances) Regulations* 1991, HMSO, London, UK

B268 butyl nitrate

$$CH_3(CH_2)_3ONO_2$$

$C_4H_9NO_3$ **Mol. Wt.** 119.12 **CAS Registry No.** 928-45-0

Synonyms nitric acid, butyl ester

EINECS No. 213-172-9

Physical properties

B. Pt. 135.5°C **Flash point** 36°C **Specific gravity** 1.0228 at 30°C
Solubility Organic solvents: diethyl ether, ethanol

Genotoxicity

Escherichia coli T4B (24-48 hr) low mutagenic activity (1).

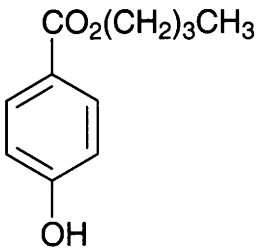
Other comments

Explosion risk.
C3-C5 alkyl nitrates measured on the southeast coast of South Africa were in the low-ppt concentration range, and varied with meteorological conditions (2).

References

1. Kononova, S. D. *Teor. Khim. Mutageneza Mater. Vses, Soveshch. 4th* 1969, 34-36, (Russ.) (*Chem. Abstr.* **76**, 95128d).
2. de Kock, A. C. et al *Chemosphere* 1994, **29**(2), 299-310

B269 butylparaben



$C_{11}H_{14}O_3$ **Mol. Wt.** 194.23 **CAS Registry No.** 94-26-8

Synonyms butyl *p*-hydroxybenzoate; butyl 4-hydroxybenzoate; benzoic acid, 4-hydroxy-, butyl ester; Paridol Butyl; Butyl Parasept NF; Lexguard B; Nipabutyl

EINECS No. 202-318-7 **RTECS No.** DH 1980000

Uses Antifungal pharmaceutical aid. Preservative in foods, creams, lotions, ointments and other cosmetics, drugs and dentifrices.

Physical properties

M. Pt. 68-69°C

Solubility Organic solvents: acetone, chloroform, diethyl ether, ethanol, propylene glycol

Mammalian & avian toxicity

Acute data

LD_{50} intraperitoneal mouse 230 mg kg^{-1} (1).

Sub-acute and sub-chronic data

Oral mice (6 wk) 1.25% butylparaben marked atrophy of lymphoid tissue in organs including the spleen, thymus, lymph nodes, and multifocal degeneration and necrosis in liver parenchyma (2).

Carcinogenicity and chronic effects

Oral mice (2 yr) 0.15, 0.3, 0.6% in diet induced tumours of haematopoietic system and lungs. However there was no significant difference from controls. The authors concluded that there was no evidence of tumorigenic effects at doses up to 0.6% (2).

Irritancy

Dermal guinea pig (48 hr) 5% butylparaben caused mild irritation (1).

Other effects

Other adverse effects (human)

In vitro incubation of butylparaben (30 mins) 1 g l^{-1} caused potent spermicidal activity against human spermatozoa. All spermatozoa were immobolised with no revival after 30 mins (3).

Other comments

Experimental toxicology and human health effects reviewed (4,5).

References

1. *J. Soc. Cosmet. Chem.* 1977, **28**, 357.
2. Inai, K. et al *Food Chem. Toxicol.* 1985, **23**(6), 575-578.
3. Song, B. et al *Contraception* 1989, **39**(3), 331-335.

4. *BIBRA Toxicity Profile* 1989, British Industrial Biological Research Association, Carshalton, 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

B270 *tert*-butyl peracetate

$$(CH_3)_3COOCOCH_3$$

$C_6H_{12}O_3$ **Mol. Wt.** 132.16 **CAS Registry No.** 107-71-1

Synonyms acetyl *tert*-butyl peroxide; *tert*-butyl peroxyacetate; ethaneperoxoic acid, 1,1-dimethyl ester; peroxyacetic acid, *tert*-butyl ester

EINECS No. 203-514-5 **RTECS No.** SD 8925000

Uses Polymerisation initiator for vinyl monomers. Manufacture of polyethylene and polystyrene.

Physical properties

Flash point <26.7°C **Specific gravity** 0.923 **Volatility** v.p. 50 mmHg at 26°C

Occupational exposure

UN No. 2095 (maximum concn. 76% in solution)

UN No. 2096 (maximum concn. 52% in solution)

Mammalian & avian toxicity

Acute data

LD_{50} oral mouse, rat 632, 675 mg kg^{-1}, respectively (1).
LC_{50} (4 hr) inhalation rat 8200 mg m^{-3} (1).
LC_{50} (2 hr) inhalation mouse 6000 mg m^{-3} (1).

Other effects

Any other adverse effects

Inhalation ♂ rats (4 month) 0.001 mg l^{-1} 4 hr day^{-1} had decreased numbers of spermatogonia but motility and fertility were not impaired (2).

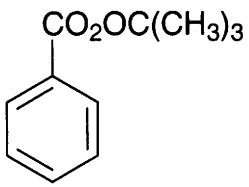
Other comments

Safety guidelines for organic peroxides discussed (3,4).
Reviews on experimental toxicology and human health effects listed (5).

References

1. Izmerov, N. F. et al *Toxicometric Parameters of Industrial Toxic Chemicals under Single Exposure* 1982, 30, Moscow, USSR.
2. Sanotskii, I. V. et al *Toksikol. Nov. Prom. Khim. Veshchestv.* 1968, **10**, 44-55, (Russ.) (*Chem. Abstr.* **71**, 89634w).
3. Martin, J. J. *Ind. Eng. Chem.* 1960, **52**(4), 65A-68A.
4. Walrud, D. H. et al *Plast. Compound* 1979, **2**(1), 52-54.
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

B271 *tert*-butyl peroxybenzoate



$C_{11}H_{14}O_3$ **Mol. Wt.** 194.23 **CAS Registry No.** 614-45-9

Synonyms benzenecarboperoxoic acid, 1,1-dimethylethyl ester; benzoyl *tert*-butylperoxide; *tert*-butyl perbenzoate; Esperox 10; Novox; peroxybenzoic acid, *tert*-butyl ester; Trigonox C

EINECS No. 210-382-2 **RTECS No.** SD 9450000

Uses Polymerisation indicator for polyethylene, polystyrene, polyacrylates and polyesters. Intermediate in organic synthesis.

Physical properties

M. Pt. 8°C **B. Pt.** 112°C (decomp.) **Flash point** 66°C (closed cup) **Specific gravity** 1.04 at 25°C with respect to water at 25°C **Volatility** v.p. 0.33 mmHg at 50°C
Solubility Organic solvents: diethyl ether, esters, ethanol, ketones

Mammalian & avian toxicity

Acute data
LD_{50} oral mouse, rat 914, 1012 mg kg^{-1}, respectively (1).

Carcinogenicity and chronic effects
Dermal application of *tert*-butyl peroxybenzoate to mice treated with an initiator and promoter increased rate of conversion of benign skin papillomas to carcinomas (2).
Application of retinoic acid inhibits the process of malignant conversion induced by free-radical generating compounds (3).

Irritancy
Dermal rabbit (24 hr) 500 mg caused mild irritation and 500 mg instilled into rabbit eye (24 hr) caused mild irritation (4).
100 mg instilled into rabbit eye for (1 min) and then rinsed with water caused mild irritation (5).

Genotoxicity

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

Other effects

Any other adverse effects
Metabolised by human carcinoma skin keratinocytes to free radicals. Study provides first direct evidence that human carcinoma skin cells can generate free radicals from organic hydroperoxides. This metabolic capacity may be an important determinant of human cancer risk from hydroperoxides (7).

Other comments

Safety and hazard classification tests for organic peroxides documented (8).

References

1. Izmerov, N. F. et al *Toxicometric Parameters of Industrial Toxic Chemicals under Single Exposure* 1982, 30, Moscow, USSR.
2. Mohammad, A. et al *Carcinogenesis (London)* 1989, **10**(10), 1841-1845.
3. Mohammad, A. et al *Carcinogenesis (London)* 1991, **12**(12), 2325-2329.
4. *Sbornik Vysledku Toxixologickeho Vysetreni Latek A Pripravku* 1972, -, 52, Prague, Czechoslovakia.
5. *Zentralbl. Arbeitmed. Arbeitsschutz* 1958, **8**, 25.
6. Mortelmans, K. et al *Environ. Mol. Mutagen.* 1986, **8**(Suppl. 7), 1-119.
7. Mohammad, A. et al *Carcinogenesis (London)* 1989, **10**(8), 1499-1503.
8. Noller, D. C. et al *Ind. Eng. Chem.* 1964, **56**(12), 18-27

B272 *tert*-butyl peroxyisobutyrate

$$(CH_3)_3COOC(O)CH(CH_3)_2$$

$C_8H_{16}O_3$ **Mol. Wt.** 160.21 **CAS Registry No.** 109-13-7

Synonyms *tert*-butyl perisobutyrate; peroxyisobutyric acid, *tert*-butyl ester; propaneperoxoic acid, 2-methyl-1,1-dimethyl ester; Aztec TBPIB-75-OMS; Trigonox 41-C75

EINECS No. 203-650-5 **RTECS No.** SE 0560000

Uses Polymerisation catalyst.

Physical properties

Flash point <26.6°C

Occupational exposure

UN No. 2142 (>52% but ≤77% in solution)

UN No. 2562 (≤52% in solution)

Other comments

Hazard classification system discussed (1).
Guidelines for safe storage and handling (2).

References

1. Noller, D. C. et al *Ind. Eng. Chem.* 1964, **56**(1,2), 18-27.
2. Donaldson, C. R. *Safety High Pressure Polyethylene Plants* 1973, 31-34, American Institute of Chemical Engineering, New York, NY, USA

B273 *tert*-butyl peroxypivalate

$$(CH_3)_3CCO_2OC(CH_3)_3$$

$C_9H_{18}O_3$ **Mol. Wt.** 174.24 **CAS Registry No.** 927-07-1

Synonyms Propaneperoxoic acid, 2,2-dimethyl-, 1,1-dimethylethyl ester; Esperox 31M; Trigonoz 25-C75; peroxypivalic acid, *tert*-butyl ester; *tert*-butyl perpivalate; *tert*-butyl trimethylperoxyacetate

EINECS No. 213-147-2

Uses Polymerisation initiator. Catalyst.

Physical properties

M. Pt. 20°C (decomp.) **Flash point** 68-71°C (open cup) **Specific gravity** 0.854 at 25°C with respect to water at 25°C

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 4300 μg kg^{-1} (1).

Other comments

Rapid decomposition occurs at 21°C.

References

1. Society of Plastics *SPI Bull.* 1985, 1/75-19B

B274 *tert*-butyl peroxy-3,5,5-trimethylhexanoate

$$(H_3C)_3CCH_2CH(CH_3)CH_2(O)CO_2C(CH_3)_3$$

$C_{13}H_{26}O_3$ **Mol. Wt.** 230.35 **CAS Registry No.** 13122-18-4

Synonyms *tert*-butyl perisononanoate; 1,1-dimethylethyl 3,5,5-trimethylhexaneperoxoate; *tert*-butyl 3,5,5-trimethylperoxyhexanoate

EINECS No. 236-050-7

Uses Polymerisation catalyst. Light stabilisers for ultraviolet-transparent polymers. Source of free radicals in polymer manufacture.

Physical properties

Solubility Organic solvents: benzene

Occupational exposure

UN No. 2104

Other effects

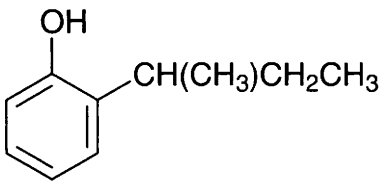
Other adverse effects (human)

Systemic effects of mild exposure (via inhalation and ingestion) are dyspnoea, coughing, sore throat, vomiting and abdominal pain. Severe exposure causes dyspnoea, lung congestion, vomiting blood and unconsciousness (1).

References

1. Nakagawa, S. *Anzen Kogaku (J. Jpn. Soc. Saf. Engineering)* 1979, **18**(1), 14-21

B275 2-*sec*-butylphenol



$C_{10}H_{14}O$ **Mol. Wt.** 150.22 **CAS Registry No.** 89-72-5

Synonyms 2-(1-methylpropyl)phenol; phenol, *o-sec*-butyl; phenol, 2-(1-methylpropyl)

EINECS No. 201-933-8 **RTECS No.** SJ 8920000

Uses Chemical intermediate in the preparation of resins, plasticisers and surface-active agents.

Physical properties

M. Pt. 16°C **B. Pt.** 226-228°C at 25 mmHg **Flash point** 107.2°C **Specific gravity** 0.981 at 25°C with respect to water at 25°C

Solubility Water: <1 mg ml^{-1} at 20°C. Organic solvents: acetone, dimethyl sulfoxide, ethanol

Occupational exposure

FR-VME 5 ppm (30 mg m^{-3})
UK-LTEL 5 ppm (31 mg m^{-3})
US-TWA 5 ppm (31 mg m^{-3})

Ecotoxicity

Invertebrate toxicity

Lethal threshold brown shrimp (96 hr) 0.77 mg l^{-1} (1).
LC_{50} brown shrimp (96 hr) 1.3 mg l^{-1} (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 2700 mg kg^{-1} (2).
LD_{50} dermal guinea pig 600 mg kg^{-1} (3).
LD_{50} intravenous, intraperitoneal mouse 60, 63 mg kg^{-1}, respectively (4,5).

Irritancy

Dermal rabbit (24 hr) 500 mg caused severe irritation and 50 μg instilled into rabbit eye caused severe irritation (2).

Genotoxicity

Salmonella typhimurium TA1535, TA1537, TA97, TA98, TA100 with and without metabolic activation negative (6).

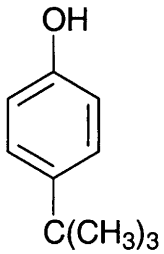
Other comments

Review on experimental toxicology and human health effects listed (7).

References

1. McLeese, D. W. et al *Chemosphere* 1981, **10**(7), 723-730.
2. *Sbornik Vysledku Toxixologickeho Vysetreni Latek A Pripravku* 1972, **-**, 55.
3. *Doc. Threshold Limit Values of Substances in Workroom Air* 1980, **4**, 58.
4. *J. Med. Chem.* 1980, **23**, 1350.
5. *J. Med. Chem.* 1975, **18**, 868.
6. Mortelmans, K. et al *Environ. Mol. Mutagen.* 1986, **8** (Suppl.7), 1-119.
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

B276 4-*tert*-butylphenol



$C_{10}H_{14}O$ **Mol. Wt.** 150.22 **CAS Registry No.** 98-54-4

Synonyms butylphen; 4-(1,1-dimethylethyl)phenol; 1-hydroxy-4-*tert*-butylbenzene; phenol, 4-(1,1-dimethylethyl)-

EINECS No. 202-679-0 **RTECS No.** SJ 8925000

Uses Ingredient in de-emulsifiers for oil-field use. In motor oil additives. Intermediate in the manufacture of varnish and lacquer resins. Soap antioxidant.

Physical properties

M. Pt. 98°C **B. Pt.** 238°C **Specific gravity** 0.9081 at 114°C with respect to water at 4°C
Partition Coefficient log P_{ow} 3.65 **Volatility** v.p. 1 mmHg at 70°C ; v.den. 5.1
Solubility Water: 700 mg l^{-1}. Organic solvents: diethyl ether, ethanol

Occupational exposure

DE-MAK 0.08 ppm (0.5 mg m^{-3})

Ecotoxicity

Fish toxicity

Trout, bluegill sunfish and goldfish exposed to 5 ppm died within 2-6 hr (1).

LC_{50} (96 hr) fathead minnow 5.1 mg l^{-1} (2).
LC_{50} (96 hr) juvenile Atlantic salmon 0.74 mg l^{-1} (3).
Oestrogenically active in cultures of trout hepatocytes as measured by the secretion of vitellogenin. Possible endocrine disruptor *in vivo* (4).

Invertebrate toxicity
EC_{50} (24 hr) *Daphnia magna* 4.2 mg l^{-1} (5).
EC_{50} (5 min) *Photobacterium phosphoreum* 0.21 mg l^{-1} Microtox test (6).

Bioaccumulation
Non-accumulative or low accumulative (3).

Environmental fate

Degradation studies
Non-biodegradable (3).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 2950 mg kg^{-1} (7).
LC_{Lo} (4 hr) inhalation rat 5600 mg m^{-3} (8).
LD_{50} dermal rabbit 2288 mg kg^{-1} (7).
LD_{50} intraperitoneal mouse 78 mg kg^{-1} (9).

Irritancy
Dermal ♂, ♀ rabbit (24 hr) 16 g kg^{-1} caused local toxicity and irritation at site of application, but no mortality.
Dermal application (4 hr) 0.5 g produced a range of effects from no reaction to necrosis (10).
Dermal rabbit (4 hr) 500 mg caused mild irritation (11).
50 μg instilled into rabbit eye for 24 hr caused severe irritation (12).

Sensitisation
Skin sensitiser in humans (13).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1535, TA1537 with and without metabolic activation negative (14).

Other effects

Any other adverse effects
Probable mechanism of action of alkyl phenols is a toxic effect on functional melanocytes. Exposure can cause depigmentation, hepatosplenomegaly and thyroid enlargement. May cause occupational leukoderma (8).
Inhalation rats (6 hr) exposure to respirable dust aerosol 5.6 mg l^{-1} or saturated vapour 6 mg l^{-1}. The vapour had no effect on body weight. Caused no adverse clinical signs, necropsy or mortality. The dust caused mucosal irritation and respiratory distress up to 7 days post-exposure (10).

Other comments

Occupational exposure, experimental toxicology and human health effects reviewed (15,16).

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B277 butyl propionate

$$CH_3CH_2CO_2(CH_2)_3CH_3$$

$C_7H_{14}O_2$ **Mol. Wt.** 130.19 **CAS Registry No.** 590-01-2

Synonyms butyl propanoate; propanoic acid, butyl ester; *n*-butyl propionate

EINECS No. 209-669-5 **RTECS No.** UE 8245000

Uses Solvent for nitrocellulose. Retarder in lacquer thinner. Ingredient of perfumes and flavours.

Physical properties

M. Pt. –89.6°C **B. Pt.** 145.4°C **Flash point** 32.2°C **Specific gravity** 0.875 at 20°C with respect to water at 4°C
Volatility v.den. 4.49
Solubility Organic solvents: diethyl ether, ethanol

Occupational exposure

UN No. 1914 **HAZCHEM Code** 3Y **Conveyance classification** flammable liquid
Risk phrases Flammable (R10)
Safety phrases Keep out of reach of children (if sold to general public) (S2)

Mammalian & avian toxicity

Acute data
LD_{50} oral ♀ Sprague-Dawley rat 11.0 g kg^{-1} (1).
LD_{50} oral ♂ Sprague-Dawley rat 12.34 g kg^{-1} (1).
LD_{50} dermal rabbit >14 g kg^{-1} (1).

Sub-acute and sub-chronic data
Inhalation rat (9 days, 6 hr day^{-1}) 800, 1600, or 3200 ppm. Structural changes in the anterior olfactory mucosa of the nasal cavity were observed (2).

Irritancy
Dermal rabbit (24 hr) 500 mg caused moderate irritation (3).
0.1 ml instilled into rabbit eye caused iritis in 2/6 rabbits, and minor to moderate conjunctivitis which healed in 48-72 hr (1).

Other comments

Experimental toxicology and human health effects reviewed (4,5).

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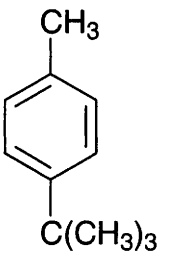
B278 4-*tert*-butyltoluene



$C_{11}H_{16}$ **Mol. Wt.** 148.25 **CAS Registry No.** 98-51-1

Synonyms *p*-methyl-*tert*-butylbenzene; 1-methyl-4-*tert*-butylbenzene; *p*-*tert*-butyltoluene; 8-methylparacymene; PTBT; benzene, 1,-(1,1-dimethylethyl)-4-methyl

EINECS No. 202-675-9 **RTECS No.** XS 8400000

Uses Solvent in preparation of resins. Oil additive. Perfume component. Intermediate in organic synthesis.

Physical properties

M. Pt. –62.5°C **B. Pt.** 192.8°C **Flash point** 68.3°C (closed cup) **Specific gravity** 0.857 at 20°C with respect to water at 20°C **Volatility** v.p. 0.65 mmHg at 25°C ; v.den. 4.6
Solubility Organic solvents: diethyl ether, ethanol

Occupational exposure

FR-VME 10 ppm (60 mg m^{-3})
US-TWA 1 ppm (6.1 mg m^{-3})

UN No. 2667 **HAZCHEM Code** 3Z **Conveyance classification** toxic substance

Ecotoxicity

Fish toxicity
LC_{50} (24 hr) goldfish 3 mg l^{-1} (1).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat, rabbit 1500, 2000 mg kg^{-1}, respectively (2).

LC_{50} (4 hr) inhalation mouse 248 ppm (2).
LD_{50} dermal rat 14-28 mg kg^{-1} (3).
TC_{Lo} (3 min) inhalation human 10 ppm gastrointestinal tract effects (2).
TC_{Lo} (5 min) inhalation human 20 ppm eye, gastrointestinal tract effects (3).

Sub-acute and sub-chronic data
Inhalation rat (25 day) 50 ppm 7 hr day^{-1} no adverse effects reported (4).

Metabolism and toxicokinetics
Metabolites include *p-tert*-butylbenzoic acid; 2-(*p*-carboxyphenyl)-2-methylpropan-1-ol; *p-tert*-butylbenzoylglycine and 2-methyl-2-*p*-tolyl-propan-1-ol in rats exposed by inhalation. Accumulates in mesenteric fat, liver, kidney and the brain, rapidly eliminated via urine (5).

Irritancy
Dermal rabbit (24 hr) 500 mg caused mild irritation (2).
Exposure (5 min) 8 ppm caused moderate eye irritation in humans. Nasal mucosal and throat irritation observed at concentrations of 10 ppm and 60 ppm, respectively (2).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1537 with and without metabolic activation negative (6,7).
Escherichia coli, Saccharomyces cerevisiae with and without metabolic activation mitotic gene conversion and structural chromosome damage negative (7).

Other effects

Other adverse effects (human)
Inhalation human systemic effects include: nausea, vomiting, conjunctival irritation, effects on sense of taste. Inhalation of vapours caused irritation to lungs and depression of central nervous system. Prolonged exposure may result in damage to liver and kidneys (3).

Legislation

Included in Schedule 6 (Release into Land: Prescribed Substances) of Statutory Instrument No. 472, 1991 (8).

Other comments

Hazards associated with *p-tert*-butyltoluene reviewed (9).
Reviews on experimental toxicology and human health effects listed (10).

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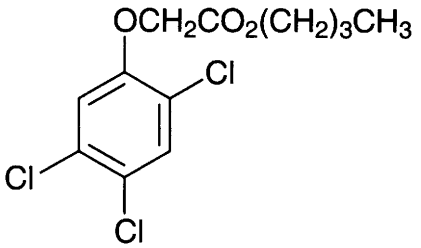
B279 butyl 2,4,5-trichlorophenoxyacetate



$C_{12}H_{13}Cl_3O_3$ **Mol. Wt.** 311.59 **CAS Registry No.** 93-79-8

Synonyms 2,4,5-trichlorophenoxyacetic acid, butyl ester; butylate-2,4,5-T

EINECS No. 202-277-5 **RTECS No.** AJ 8485000

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) – Avoid contact with the skin (S2, S24)

Ecotoxicity

Fish toxicity

It reduced oxygen uptake from 23%-64% (succinate) and from 63%-89% (α-ketoglutarate) in bluegill sunfish liver mitochondria (1).

Environmental fate

Adsorption and retention

Soil residues persisted as 2,4,5-TCP, 12-100 ng g^{-1} after 185 days (2).

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Pesticides: maximum admissible concentration 0.1 μg l^{-1} (3).

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

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B280 butyl vinyl ether

$$CH_3(CH_2)_3OCH{=}CH_2$$

$C_6H_{12}O$ **Mol. Wt.** 100.16 **CAS Registry No.** 111-34-2

Synonyms vinyl butyl ether; butoxyethene; 1-(ethenyloxy)butane; vinyl *n*-butyl ether

RTECS No. KN 5950000

Uses Intermediate in organic synthesis. Co-polymerisation agent.

Physical properties

M. Pt. –92°C **B. Pt.** 94.2°C **Flash point** –9°C **Specific gravity** 0.7803 at 20°C with respect to water at 20°C
Volatility v.den. 3.45
Solubility Organic solvents: acetone, benzene, diethyl ether, ethanol

Occupational exposure

UN No. 2352 **HAZCHEM Code** 3[illegible]E **Conveyance classification** flammable liquid

Environmental fate

Abiotic removal
Reacts with photochemically produced hydroxyl radicals and ozone in the atmosphere, $t_{1/2}$ estimated 9 hr, at an atmospheric concentration of 5×10^5 hydroxyl radicals cm^{-3} and 7×10^{11} ozone molecules cm^{-3}. Direct photolysis is not expected to be an important removal process since aliphatic ethers do not absorb light at wavelengths >290 nm (1). Susceptible to hydrolysis in environmental waters especially at acidic pH. $t_{1/2}$ 9 hr at pH5 and 10 yr at pH9 (2).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 10 g kg^{-1} (3).
LC_{50} (2 hr) inhalation mouse 62 g m^{-3} (4).
LC_{Lo} (4 hr) inhalation rat 8000 ppm (5).
LC_{100} (4 hr) inhalation rat 16,000 ppm (5).
LD_{50} dermal rabbit 4240 mg kg^{-1} (6).

Irritancy
Dermal rabbit (duration unspecified) 500 mg caused mild irritation (7).

Genotoxicity

Salmonella typhimurium TA100 with metabolic activation weakly positive (8).

Other comments

Detected as a contaminant in air and water samples (9-11).
Toxicity and physical properties reviewed (12).
Spontaneous explosion risk.

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B281 1-butyne

$$CH_3CH_2C{\equiv}CH$$

C_4H_6 **Mol. Wt.** 54.09 **CAS Registry No.** 107-00-6

Synonyms ethylacetylene; ethylethyne

EINECS No. 203-451-3

Physical properties

M. Pt. –130°C **B. Pt.** 8.3°C **Flash point** 7°C **Specific gravity** 0.669 at 0°C with respect to water at 0°C
Solubility Organic solvents: diethyl ether, ethanol

Occupational exposure

UN No. 2452 **HAZCHEM Code** 2WE **Conveyance classification** flammable gas

Environmental fate

Nitrification inhibition
At 30°C 90-97% nitrification inhibition in soils at a partial pressure of 7.5×10^{-2} mmHg, 36-80% inhibition at $7.5 \times$
Identified in exhaust gases from motor vehicles (1).
10^{-3} mmHg and 0-6% at 7.5×10^{-4} mmHg (2).

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B282 1,4-butynediol

$$HOCH_2C{\equiv}CCH_2OH$$

$C_4H_6O_2$ **Mol. Wt.** 86.09 **CAS Registry No.** 110-65-6

Synonyms bis(hydroxymethyl)acetylene; 2-butynediol; 2-butyne-1,4-diol

EINECS No. 203-788-6 **RTECS No.** ES 0525000

Uses In the manufacture of polyurethanes and synthetic rubber. Used in synthesis of the blood substitute polyvinylpyrrolidone.

Physical properties

M. Pt. 57.5°C **B. Pt.** 238°C **Flash point** 152°C **Specific gravity** 1.114 at 60°C **Partition Coefficient** log P_{ow} −1.83 (1)
Solubility Organic solvents: acetone, ethanol

Occupational exposure

UN No. 2716 **HAZCHEM Code** 2W **Conveyance classification** toxic substance
Supply classification toxic
Risk phrases Toxic if swallowed – Causes burns (R25, R34)
Safety phrases Keep locked up and out of the reach of children (if sold to general public) – Do not breathe dust – Wear suitable protective clothing – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S22, S36, S45)

Ecotoxicity

Fish toxicity
Exposure of steelhead trout to 6 mg l^{-1} caused loss of equilibrium in 4-6 hr and death within 6-8 hr (1).
LC_{50} (96 hr) fathead minnow 53 mg l^{-3} flow-through bioassay with measured concentrations 25°C, 6.8 mg l^{-1} dissolved oxygen content, hardness 46.5 mg l^{-1} calcium carbonate, pH 7.7. No loss of equilibrium prior to death (2).

Invertebrate toxicity
IGC_{50} (50% growth inhibitory concentration, 2 day) *Tetrahymena pyriformis* 15.6 mM (3).

Environmental fate

Degradation studies
Fusarium merismoides BII can utilise 2-butyne-1,4-diol as the sole carbon source with production of mannitol, 2,4,6-triketosuberic acid, 2,4,6,8-tetraketosuberic acid and phthalic acid using the enzyme 2-alkyne-1-ol dehydrogenase (4).

Mammalian & avian toxicity

Acute data
LD_{50} oral redwing blackbird 75 mg kg^{-1} (5).
LD_{50} oral rat, guinea pig, rabbit 104, 130, 150 mg kg^{-1}, respectively (6).
LC_{Lo} (2 hr) inhalation rat 150 mg m^{-3} (7). Dermal rat (24 hr) 5 g kg^{-1} as 40% aqueous solution caused half the dosed rats to die within 48 hr. Liver and kidney damage including necrosis was observed (8).

Sub-acute and sub-chronic data
Oral rat (14 day) 1, 10 or 100 mg kg^{-1}. Toxic effects at 100 mg kg^{-1} included severe body weight changes, increased liver weight and serum cholesterol in both sexes. Increased serum calcium, and decreased red cell count, haemoglobin content and haematocrit values reported in ♀ at 100 mg kg^{-1} (9).
Oral ♂ and ♀ Wistar Imp:DAK rats (28 day) 1, 10 or 50 mg kg^{-1}. The highest dose caused fatalities and increased liver and/or kidney weights in both ♂s and ♀s, and decreased body weight gain in ♂s. Sorbitol dehydrogenase activity, reticulocyte count and leukocyte count was increased in both sexes, as was total serum protein content in ♀s and glucose concentration in ♂s. Histopathological evidence for hepatotoxicity and nephrotoxicity was found in decedents, and hepatic and splenic changes were found in survivors. Some ♀s given the middle dose showed minor hepatic, splenic and erythrocytic changes. 1 mg kg^{-1} day^{-1} was considered to be the no-observed-effect level (10).
Teratogenicity and reproductive effects
Gavage pregnant Wistar rats (days 6-15 post-conception) 10, 40, and 80 mg kg^{-1} body weight day^{-1}. At the highest dose, food consumption and maternal body weight were reduced. The incidence of affected foetuses per litter with accessory 14th ribs was increased. This was assessed as an embryotoxic effect resulting from non-specific

stress on the dams. No teratogenic effects were caused by the compound. The NOAEL on the dams and developing foetuses was 40 mg kg^{-1} body weight day^{-1} (11).

Irritancy
Dermal rabbit (1, 24, 48, 72 hr) 0.3 g solid (moistened with water), and 40% and 20% aqueous solutions caused slight irritation. 100 mg solid applied to rabbit eyes (72 hr) caused slight irritation (8).

Sensitisation
Did not cause allergic contact dermatitis in guinea pigs (8).

Other comments

Toxicity reviewed (12).
The effect of 1,4-butynediol on animals reported (13).
Reviews on experimental toxicology and human health effects listed (14).

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B283 butyraldehyde

$$CH_3(CH_2)_2CHO$$

C_4H_8O **Mol. Wt.** 72.11 **CAS Registry No.** 123-72-8

Synonyms butanal; butylaldehyde; butyric aldehyde

EINECS No. 204-646-6 **RTECS No.** ES 2275000

Uses Rubber accelerators. Synthetic resins. Solvents. Plasticisers.

Physical properties

M. Pt. –99°C **B. Pt.** 74.8°C **Flash point** –6.6°C (closed cup) **Specific gravity** 0.8016 at 20°C with respect to water at 4°C **Partition Coefficient** log P_{ow} 1.18 **Volatility** v.p. 91.5 mm Hg at 20°C ; v.den. 2.48
Solubility Organic solvents: acetone, diethyl ether, ethanol, ethyl acetate, toluene

Occupational exposure

UN No. 1129 **HAZCHEM Code** 3WE **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 – Do not empty into drains – Take precautionary measures against static discharges (S2, S9, S29, S33)

Ecotoxicity

Fish toxicity
LC_{50} (96 hr) fathead minnow 25.8 mg l^{-1} (1).

Invertebrate toxicity
EC_{50} (5 min) *Photobacterium phosphoreum* 16.5 mg l^{-1} Microtox test (2).
Cell multiplication inhibition test, *Pseudomonas putida* 100 mg l^{-1}, *Scenedesmus quadricauda* 83 mg l^{-1}, *Entosiphon sulcatum* 4.2 mg l^{-1}, *Uronema parduczi* 98 mg l^{-1} (3).

Environmental fate

Degradation studies
Activated sludge, 22.8% removal of ThOD in 24 hr (4).
Biodegradable (2).

Abiotic removal
85% removal by air stripping in 8 hr (5).

Mammalian & avian toxicity

Acute data
LD_{50} oral rat 5890 mg kg^{-1} (6).
LC_{50} (0.5 hr) inhalation rat 60,000 ppm (7).

Carcinogenicity and chronic effects
Butyraldehyde is currently being investigated by the US National Toxicology Program (8).

Irritancy
Dermal rabbit (24 hr) 500 mg caused severe irritation and 20 mg instilled into rabbit eye for 24 hr caused moderate irritation (9).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA1535, TA1537 with and without metabolic activation negative (10).
V79 Chinese hamster lung cells induced a dose-dependent increase in 6-thioguanine- and ouabain-resistant mutants (11).
Cell degeneration and polyploidy during spermatogenesis, chromosome aberrations and altered sperm morphology were reported in mice (12).
The induction of unscheduled DNA synthesis was measured in primary cultures of rat and human hepatocytes. Exposure to 10-100 mM induced a significant and dose-dependent increase in net nuclear grain counts in rat hepatocytes; this effect was not detected in human hepatocytes (13).

Other comments

Evaluation by trypan blue exclusion test shows similar cytotoxicity to primary cultures of rat and human hepatocytes after 20-hr exposure (13).
Reviews on physico-chemical properties, human health effects and experimental toxicology listed (14).

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B284 butyraldoxime

$$CH_3(CH_2)_2CH{=}NOH$$

C_4H_9NO **Mol. Wt.** 87.12 **CAS Registry No.** 110-69-0

Synonyms butanal oxime; butyraldehyde oxime; *n*-butyraldehyde oxime; *N*-butyraldoxime

EINECS No. 203-792-8 **RTECS No.** ES 3500000

Uses Anti-skinning agent.

Physical properties

M. Pt. –29.5°C **B. Pt.** 152°C **Flash point** 57.8°C (closed cup) **Specific gravity** 0.923 at 20°C with respect to water at 4°C **Volatility** v.den. 3.01

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

Occupational exposure

UN No. 2840 **HAZCHEM Code** 3Y **Conveyance classification** flammable liquid

Supply classification toxic

Risk phrases Harmful if swallowed – Toxic in contact with skin – Irritating to the eyes (R22, R24, R36)

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)

Mammalian & avian toxicity

Acute data

LD_{Lo} oral rabbit 100 mg kg^{-1} (1).

LD_{50} intraperitoneal mouse 200 mg kg^{-1} (2).

Carcinogenicity and chronic effects

National Toxicology Program Prechronic Study in progress (3).

Genotoxicity

Salmonella typhimurium TA98, TA100, TA1537, TA1538 with metabolic activation negative (4).
Mouse lymphoma L51787 tk+/tk– with and without metabolic activation negative (4).

Other effects

Other adverse effects (human)
Exposure to butyraldoxime after consumption of alcohol can cause flushing of face, red non-itching blotches, redness of eyes, drowsiness, shortness of breath and heart palpitations (5).

Other comments

Reviews on experimental toxicology and human health effects listed (6).

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B285 butyric acid

$$CH_3(CH_2)_2CO_2H$$

$C_4H_8O_2$ **Mol. Wt.** 88.11 **CAS Registry No.** 107-92-6

Synonyms butanoic acid; ethylacetic acid; 1-propanecarboxylic acid; propylformic acid

EINECS No. 203-532-3 **RTECS No.** ES 5425000

Uses Manufacture of esters. Artificial flavouring ingredient in liqueurs, soda water syrups and confectionery. Varnishes. Decalcifier of hides.

Physical properties

M. Pt. –7.9°C **B. Pt.** 163.5°C **Flash point** 77°C (closed cup) **Specific gravity** 0.9590 at 20°C with respect to water at 20°C **Partition Coefficient** log P_{ow} 0.79 **Volatility** v.p. 0.433 mmHg at 20°C ; v.den. 3.04
Solubility Water: ≥100 mg ml^{-1} at 19°C. Organic solvents: acetone, dimethyl sulfoxide, ethanol

Occupational exposure

UN No. 2820 **HAZCHEM Code** 2X **Conveyance classification** corrosive substance
Supply classification corrosive
Risk phrases Causes burns (R34)
Safety phrases Keep locked up and out of the reach of children (if sold to general public) – In case of contact with eyes, rinse immediately with plenty of water and seek medical advice – Wear suitable protective clothing – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S26, S36, S45)

Ecotoxicity

Fish toxicity

LC_{50} (24 hr) bluegill sunfish 200 mg l^{-1} (1).

Invertebrate toxicity

EC_{50} (48 hr) *Daphnia magna* 61 mg l^{-1} (1).

Cell multiplication inhibition test *Pseudomonas putida* 875 mg l^{-1}, *Microcystis aeruginosa* 318 mg l^{-1}, *Scenedesmus quadricauda* 2600 mg l^{-1}, *Entosiphon sulcatum* 26 mg l^{-1} (2,3).

Environmental fate

Degradation studies

Methanogenic microbes raised on acetate completely removed butyric acid after a 3-day lag period at a rate of 284 mg l^{-1} day^{-1}, initial concentration not provided (4).

BOD_5 initial concentration 5 ppm 76% reduction in dissolved oxygen in fresh water and 72% reduction in sea water (5).

ThOD (6, 12, 18 and 24 hr) 17-27% with activated sludge seed at an initial concentration of 500 ppm (6).

Screening study using sewage seed theoretical BOD_5 72-78% reduction in dissolved oxygen content BOD_{20} 92-99% (7).

BOD_5 0.34 standard dilution; 0.90 standard dilution sewage sludge, 1.16 standard dilution acclimated sewage sludge (8).

Biodegradable (9).

ThOD (5 hr) 72% with activated sludge, initial concentration 100 mg l^{-1} (10).

Abiotic removal

Activated carbon adsorbability 0.119 g kg^{-1} carbon; 60% reduction; influent 1000 mg l^{-1}, effluent 405 mg l^{-1} (11).

Adsorption and retention

Adsorbs to kaolinite or montmorillonite clay. After 48 hr at 22°C 14-20% was adsorbed, after 144 hr adsorption increased to 24-31% (12).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 2940 mg kg^{-1} (13).

LD_{Lo} oral mouse 500 mg kg^{-1} (14).

LD_{50} dermal rabbit 530 mg kg^{-1} (15).

LD_{50} intraperitoneal mouse 3180 mg kg^{-1} (16).

LD_{50} intravenous mouse 800 mg kg^{-1} (17).

Metabolism and toxicokinetics

Butyric acid is a normal substrate of the mammalian fatty acid metabolic pathway. Butyric acid is also produced as a metabolic product by colonic bacteria (18).

Intraperitoneal injection mice butyric acid or arginine salts to investigate possible antitumour therapies. Rapid appearance in blood, longest retention in liver, $t_{1/2}$ <5 min. In humans rapid initial excretion $t_{1/2}$ 30 sec followed by a slower second elimination phase $t_{1/2}$ 13 min (19).

Irritancy

Dermal rabbit (duration unspecified) 500 mg caused moderate irritation (15).

Dermal rabbit (24 hr) 10 mg caused severe irritation and 250 μg instilled into rabbit eye caused severe irritation (20).

Genotoxicity

Low concentrations stopped reversibly the proliferation of chick embryo fibroblasts and human HeLa cells by inhibiting DNA synthesis. Extensive acetylation of histones was also observed (21).

Human lymphocytes P3HR- inhibited DNA synthesis and cell growth (22).

Other effects

Any other adverse effects

Intrarectal butyric acid 1-12% induced consistent and reproducible colitis in mice (18).

Other comments

Present in butter as an ester to the extent of 4-5%.

The gastrointestinal tract is desensitised from food allergies by oral ingestion of butyric acid or its salts (23).

There is evidence that sodium butyrate inhibits tumour colony formation in adapted cell lines (24).

Experimental toxicology and human health effects reviewed (25,26).

Contaminant in surface and groundwater (27,28).

Detected in effluent discharges from sewage treatment and landfill sites (27,29).

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B286 butyric anhydride

$$[CH_3(CH_2)_2CO]_2O$$

$C_8H_{14}O_3$ **Mol. Wt.** 158.20 **CAS Registry No.** 106-31-0

Synonyms butanoic acid anhydride; butanoic anhydride; butyric acid anhydride; *n*-butyric acid anhydride; butyryl oxide

EINECS No. 203-383-4 **RTECS No.** ET 7090000

Uses Vulcanisation retarder. Intermediate in organic synthesis.

Physical properties

M. Pt. –75°C **B. Pt.** 199.4-201.4°C **Flash point** 88°C (open cup) **Specific gravity** 0.9668 at 20°C with respect to water at 4°C

Solubility Organic solvents: diethyl ether, ethanol (decomp.)

Occupational exposure

UN No. 2739 **HAZCHEM Code** 2X **Conveyance classification** corrosive substance

Supply classification corrosive

Mammalian & avian toxicity

Acute data

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

LD_{50} oral rat 8790 mg kg^{-1} (2).

Other comments

Toxicity reviewed (3).

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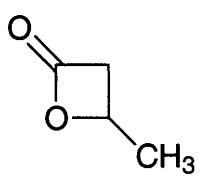
B287 β-butyrolactone



$C_4H_6O_2$ **Mol. Wt.** 86.09 **CAS Registry No.** 3068-88-0; 36536-46-6 (±-form)

Synonyms 3-hydroxybutanoic acid β-lactone; β-hydroxybutyric acid lactone; 3-hydroxybutyric acid lactone; 4-methyl-2-oxetanone; β-methylpropiolactone; 2-oxetanone, 4-methyl-

EINECS No. 221-330-3 **RTECS No.** RQ 8050000

Uses Production of β-oxybutynyl-*para*-phenetidine.

Physical properties

B. Pt. 54-56°C **Specific gravity** 1.0555 at 20°C with respect to water at 20°C

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 17 g kg^{-1} (1).

Carcinogenicity and chronic effects

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

Subcutaneous rat, mouse (30 wk) 0.1-10 mg wk^{-1} and oral rat, mouse 5-100 mg wk^{-1} via food. High dose 100 mg wk^{-1} in food-induced gastric tumours in rats (3).

Subcutaneous ♀ Sprague-Dawley rats (533 days) 800-833 mg kg^{-1} caused sarcomas in 9/20 rats at the injection site (4).

Irritancy

Dermal rabbit (duration unspecified) 500 mg caused moderate irritation (5).

Genotoxicity

Salmonella typhimurium TA1535, pSIC1002, SOS-inducing activity detected by *Umu* gene expression, suppressed by human urine (6).

Mammalian lymphocyte 860mg l^{-1} DNA damage (7).

Investigation of reactivity and adducts formed by lactones. β-Butyrolactone alkylated guanosine, RNA and DNA. Chemical reactivity correlated with carcinogenic potency (8).

Other effects

Any other adverse effects

The reactivity of β-butyrolactone with guanosine, RNA, DNA and 4-(p-nitrobenzyl)pyridine was studied. The rate of alkylation by the lactones was guanosine >RNA, denatured DNA >double stranded DNA (8).

Other comments

Toxicity reviewed (9).

Reviews on experimental toxicology and human health effects listed (10).

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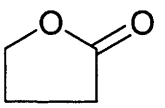
B288 γ-butyrolactone



$C_4H_6O_2$ **Mol. Wt.** 86.09 **CAS Registry No.** 96-48-0

Synonyms butyric acid lactone; γ-hydroxybutyrolactone; dihydro-2-(*3H*)-furanone; 1,4-butanolide; 2,(*3H*)-furanone, dihydro-

EINECS No. 202-509-5 **RTECS No.** LU 3500000

Uses As a constituent of paint removers, textile aids and drilling oils. Intermediate in synthesis of polyvinylpyrrolidine. Solvent.

Physical properties

M. Pt. –44°C **B. Pt.** 206°C **Flash point** 98.3°C (open cup) **Specific gravity** 1.124 at 25°C with respect to water at 4°C **Volatility** v.den. 3.0

Solubility Water: miscible. Organic solvents: acetone, benzene, diethyl ether, ethanol, methanol

Ecotoxicity

Fish toxicity

Listed as negative in tests on trout, bluegill sunfish and goldfish. However the authors state that the high mineral content of the water used in the studies adds an additional source of error. Therefore the compound listed as negative might be toxic in softer water supplies (1).

Mammalian & avian toxicity

Acute data

LD_{50} oral rat 1260-1800 mg kg^{-1} (2,3).
LD_{50} oral mouse 1720 mg kg^{-1} (4).
LD_{50} dermal rabbit >5000 mg kg^{-1} (4).
LD_{50} intraperitoneal rat, mouse 1000, 1100 mg kg^{-1}, respectively (5).
LD_{Lo} intravenous rabbit 500 mg kg^{-1} (5).

Carcinogenicity and chronic effects

No adequate data for carcinogenicity to humans, insufficient evidence for carcinogenicity to animals, IARC classification group 3 (6).

National Toxicology Program study, gavage rats, mice (2 yr) dose unspecified no evidence of carcinogenicity in either ♂ or ♀ rats, or ♀ mice, equivocal evidence in ♂ mice (7).

Dermal Swiss-Millerton ♂ mice 100 mg 3 × wk^{-1} (in 10% benzene solution) two tumours and one cancer reported from 30 mice treated. The authors conclude γ-butyrolactone has a low order of activity and that strained lactone rings may favour carcinogenicity (8).

Teratogenicity and reproductive effects

Gavage Sprague-Dawley rats (days 6-15 gestation) 0, 10, 50, 125, 250 or 500 mg kg^{-1}.

Necropsy showed lung oedema, hyperaemia and emphysema. Foetal weights significantly increased in high dosage groups (9).

Metabolism and toxicokinetics

Intravenous rat (dose unspecified) metabolised to γ-hydroxybutyric acid (10).

86% of unspecified dose inhaled by rats was excreted as carbon dioxide within 18 hr (11).

Irritancy

Shows mild/moderate *in vitro* activity in the bovine corneal opacity and permeability test for ocular irritancy (12).

Sensitisation

Negative results were obtained in guinea pig skin sensitisation tests using doses of 5.6 g kg^{-1} (13).

Genotoxicity

Bacillus subtilis H17, M45 with metabolic activation positive (14).

No chromosome damage in rat liver RL_1 cell line (15).

BHK-21 cell transformation test with metabolic activation positive (16).

Other effects

Any other adverse effects

Metabolite γ-hydroxybutyric acid can cause depression of central nervous system (9).

Legislation

Included in Schedule 6 (Release Into land: Prescribed Substances) of Statutory Instrument No. 472, 1991 (17).

Other comments

Has been detected in a commercial natural liquid wood smoke preparation and in tobacco smoke condensates (18,19).

An eye, skin and mucous membrane irritant (20).

Butyrolactone protected chicken embryos from digitoxin toxicity (21).

The sodium salt has been used as an anaesthetic (22).

When administered orally or intravenously can cause drowsiness (23).

A review with references examined the analgesic action of γ-butyrolactone in humans and laboratory animals (24).

Reviews on experimental toxicology and human health effects listed (25).

Hygroscopic.

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B289 butyronitrile

$$CH_3(CH_2)_2CN$$

C_4H_7N **Mol. Wt.** 69.11 **CAS Registry No.** 109-74-0

Synonyms butanenitrile; *n*-butanenitrile; butyric acid nitrile; 1-cyanopropane; propyl cyanide

EINECS No. 203-700-6 **RTECS No.** ET 8750000

Uses Polymer synthesis. Intermediate in organic synthesis.

Physical properties

M. Pt. –112.6°C **B. Pt.** 117°C **Flash point** 26.1°C (open cup) **Specific gravity** 0.7954 at 15°C with respect to water at 4°C **Partition Coefficient** log P_{ow} 0.60 **Volatility** v.p. 10 mmHg at 15°C ; v.den. 2.4
Solubility Organic solvents: benzene, diethyl ether, dimethylformamide, ethanol

Occupational exposure

UN No. 2411 **HAZCHEM Code** 3WE **Conveyance classification** flammable liquid, toxic
Supply classification toxic
Risk phrases Flammable – Toxic by inhalation, in contact with skin and if swallowed (R10, R23/24/25)
Safety phrases Keep locked up and out of the reach of children (if sold to general public) – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S1/2, S45)

Environmental fate

Degradation studies
Klebsiella pneumoniae adapted to benzonitrile as the sole source of C and N metabolised butyronitrile to butyramide and NH_3 (1).
Can be used as sole nitrogen source by the soil microorganisms *Candida fabianii* (strains UOFS-52 and UOFS-56), *C. guilliermondii* (strains UOFS-53, UOFS-54 and UOFS-57) and *Williopsis saturnus* (strain UOFS-55) (2).

Mammalian & avian toxicity

Acute data
LD_{50} oral mouse, rat 27.7, 140 mg kg^{-1}, respectively (3,4).
LC_{Lo} (4 hr) inhalation rat 1000 ppm (4).
LC_{50} (1 hr) inhalation mouse 250 ppm (5).
LD_{50} dermal rabbit 500 mg kg^{-1} (4).
LD_{Lo} dermal guinea pig 100 mg kg^{-1} (6).
LD_{Lo} intravenous rabbit 980 mg kg^{-1} (7).
LD_{50} intraperitoneal mouse 38 mg kg^{-1} (8).

Teratogenicity and reproductive effects
Inhalation ♀ Sprague-Dawley rats (days 6-20 of gestation) 200 ppm 6 hr day^{-1} caused foetotoxicity (9).

Metabolism and toxicokinetics

Inhaled organonitriles metabolised to cyanide in the nasal cavity (species unspecified) (10).

Intraperitoneal rat (duration unspecified) 150 mg kg^{-1}. Accumulation in liver, stomach, intestine, kidney and testis. Elimination via urine accounted for very small amounts and was slow (11).

Irritancy

Dermal rabbit (duration unspecified) 395 mg caused mild irritation (12).

500 mg instilled into rabbit eye for 24 hr caused mild irritation (13).

Other effects

Other adverse effects (human)

Systemic effects include bronchial tightness, gastric and respiratory distress, hypotension, conjunctivitis, chest pain, skin discoloration, tachypnea, dizziness, vomiting, convulsions, coma, cyanosis, retching, thyroid reaction and duodenal ulcers (14).

Other comments

Highly toxic to birds (15).

Toxicity of butyronitrile reviewed (16-18).

Reviews on experimental toxicology and human health effects listed (19).

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B290 Butyryl chloride

$$CH_3(CH_2)_2COCl$$

C_4H_7ClO **Mol. Wt.** 106.55 **CAS Registry No.** 141-75-3

Synonyms butanoyl chloride; butyric acid chloride; *n*-butyryl chloride

EINECS No. 205-498-5

Uses Acylating agent. Polymerisation catalyst. Intermediate in organic synthesis.

Physical properties

M. Pt. –89°C **B. Pt.** 101-102°C **Flash point** 18°C (closed cup) **Specific gravity** 1.028 at 20°C with respect to water at 20°C **Volatility** v.den. 3.67

Solubility Water: (decomp.). Organic solvents: ethanol (decomp.), diethyl ether

Occupational exposure

UN No. 2353 **HAZCHEM Code** 2WE **Conveyance classification** flammable liquid, corrosive

Supply classification highly flammable, corrosive

Risk phrases Highly flammable – Causes burns (R11, R34)

Safety phrases Keep locked up and out of the reach of children (if sold to general public) – Keep away from sources of ignition – No smoking – 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, S16, S23, S26, S36, S45)

Legislation

Limited under EC Directive on Drinking Water Quality 80/778/EEC. Organochlorine compounds: guide level ` 1 μg l^{-1} (1).

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

Other comments

Experimental toxicology and human health effects reviewed (3,4).

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. Smyth, H. F. et al *Am. Ind. Hyg. Assoc. J.* 1962, **23**, 95.
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

Abbreviations

ACGIH	American Conference of Governmental Industrial Hygienists
ADH	alcohol dehydrogenase
ADI	acceptable daily intake
ADP	adenosine diphosphate
AFNOR	Association Francaise de Normalization
AIDS	acquired immune deficiency syndrome
ala	alanine
AMP	adenosine monophosphate
arg	arginine
atm	atmosphere
ATP	adenosine triphosphate
BCPC	British Crop Protection Council
BOD	biochemical (biological) oxygen demand
Bq	becquerel
BrdU	bromodeoxyuridine
C.I.	colour index
ca.	circa
CAS	Chemical Abstracts Service
CAS RN	Chemical Abstracts Service Registry Number
CFC	chlorofluorocarbon
CHO	Chinese hamster ovary (cells)
Ci	curie
CIP	Centre for International Projects
cm	centimetres
COD	chemical oxygen demand
DDE	2,2-(bis(4-chlorophenyl)-1,1-dichloroethylene
decomp.	decomposition
DE-MAK	maximum permissible concentration (Germany)
DMBA	7,12-dimethylbenz[*a*]anthracene
DMSO	dimethyl sulfoxide
DNA	deoxyribonucleic acid
DO	dissolved oxygen
DoE	Department of the Environment (UK)
DOPA	dihydroxy-l-phenylalanine
DPTA	diethylenetriaminepentaacetic acid
DT_{50}	time for 50% loss; half-life
E_BC_{10}	effective concentration for 10% loss of biomass
EC	European Community
EC_{50}	median effective concentration
ECETOC	European Chemical Industry Ecology and Toxicology Centre
ECG	electrocardiogram
ED	effective dose
Ed	editor
ed	edition
EDTA	(ethylenedinitrilo)tetraacetic acid
EEC	European Economic Community
EEG	electroencephalogram
ELISA	enzyme-linked immunosorbent assay
ENU	*N*-ethyl-*N*-nitrosourea
EPA	Environmental Protection Agency (US)
et al	and others (authors)
FAO	Food and Agriculture Organisation
FDA	Food and Drug Administration (US)
FR-VLE	short-term limit value (France)
FR-VME	long-term limit value (France)
FSH	follicle-stimulating hormone
ft	feet
g	gram
GABA	γ-aminobutyric acid
GC-MS	gas chromatography-mass spectrometry
GLC	gas-liquid chromatography
gly	glycine
GSH	reduced glutathion
GST	glutathione S-transferase
GTP	guanosine triphosphate
ha	hectare
Hb	haemoglobin
HGPRT	hypoxanthine-guanine phosphorisobutyltransferase
HIV	human immunodeficiency virus
HMSO	Her Majesty's Stationery Office
HPLC	high performance liquid chromatography
hr	hour
HSC	Health & Safety Commission
HSE	Health & Safety Executive
5-HT	5-hydroxytryptamine
Hz	hertz
i.u.	international unit
IARC	International Agency for Research on Cancer

IC_{50}	median inhibition of growth concentration
IC_{Lo}	lowest concentration that inhibits growth
ID_{50}	irritant dose in 50% of individuals
IgA	immunoglobulin A
IgG	immunoglobulin G
IgM	macroglobulin
ile	isoleucine
ILO	International Labour Office
IRPTC	International Register of Potentially Toxic Chemicals
IUPAC	International Union of Pure and Applied Chemistry
J	joule
JETOC	Japan Chemical Industry Ecology and Toxicology Information Center
JP-OEL	long-term occupational exposure limit (Japan)
K_{oc}	soil sorption coefficient
K_{ow}	octanol:water dissociation constant
K_a	acid dissociation constant
kg	kilogram
l	litre
LC_{50}	concentration to kill 50% of organisms
LD_{50}	dose to kill 50% of organisms
LD_{Lo}	lowest lethal dose
LDH	lactose dehydrogenase
leu	leucine
LOEC	lowest-observed-effect concentration
log P_{ow}	log_{10} of octanol:water partition coefficient
Ltd	limited
M	molar
MAC	maximum admissible concentration
MEL	maximum exposure limit
MetHb	methaemoglobin
mg	milligram
MIC	median inhibitory concentration
min	minute
MITI	Ministry of International Trade and Industry (Japan)
ml	millilitre
mm	millimetre
mmHg	millimetres of mercury pressure
mmol	millimole
mol	mole
mRNA	messenger RNA
µ	micro
N	newton
N	normal
NAD^+	nicotinamide-adenine dinucleotide (oxidised form)
NADH	nicotinamide-adenine dinucleotide (reduced form)
NADPH	nicotinamide-adenine dinucleotide phosphate (reduced form)
NIEHS	National Institute of Environmental Health Sciences
NIOSH	National Institute of Occupational Safety and Health
nm	nanometre
NMR	nuclear magnetic resonance
NOEC	no-observed-effect concentration
NOEL	no-observed-effect level
NTA	nitrilotriacetic acid
NTIS	National Technical Information Service
NTP	National Toxicology Program
OECD	Organisation for Economic Cooperation and Development
PAH	polycyclic aromatic hydrocarbon
PCB	polychlorinated biphenyl
PEG	polyethylene glycol
pg	picogram
pH	$-log_{10}$ hydrogen ion concentration
pKa	$-log_{10}$ acid dissociation constant
ppb	parts per billion (10^9)
pph	parts per hundred (10^2)
ppm	parts per million (10^6)
ppt	parts per thousand (10^3)
psi	pound force – square inch
PTFE	polytetrafluoroethylene
QSAR	quantitative structure – activity relationships
R_{50}	repellency factor
RD_{50}	50% decrease in respiratory rate
RN	registry number
RNA	ribonucleic acid
RSC	The Royal Society of Chemistry
RTECS	Registry of Toxic Effects of Chemical Substances
sec	second
SE-CEIL	occupational exposure ceiling limit (Sweden)
SE-LEVL	long-term exposure limit (Sweden)
SE-STEL	short-term exposure limit (Sweden)
sp.	species (single)
spp.	species (plural)
STEL	short-term exposure limit

$t_{1/2}$	half-life
TC_{50}	median toxic concentration
TC_{Lo}	lowest toxic concentration
TCA	tricarboxylic acid
TD_{Lo}	lowest toxic dose
ThOD	theoretical oxygen demand
TLV	threshold limit value
TOC	total organic carbon
TPA	12-*o*-tetradecanoylphorbol-13-acetate
trp	tryptophan
TSCA	Toxic Substances Control Act
TWA	time-weighted average
UK	United Kingdom
UK-LTEL	long-term exposure limit (UK)
UK-STEL	short-term exposure limit (UK)
UNEP	United Nations Environment Programme
USA	United States of America
US-STEL	short-term exposure limit (US)
US-TWA	time-weighted average (long-term) exposure limit (US)
UV	ultraviolet
v.den.	vapour density
v.p.	vapour pressure
v/v	volume/volume
vol	volume
W	watt
w/v	weight/volume
w/w	weight/weight
WHO	World Health Organization
wk	week
wt	weight
yr	year

Glossary of Medical and Biological Terms

A

Abomasum The fourth, or true, stomach of a ruminant.

Abscess A circumscribed collection of pus in a cavity.

Acantholysis The loosening and dissolution of the layers of the epidermis.

Acanthosis Proliferation of the prickle-cell layer of the epidermis. A condition seen typically in psoriasis and eczema.

Acaricide An agent capable of destroying acarids or mites.

Acaudia (acaudal) Tail-less.

Achondroplasia A hereditary disease of the skeleton resulting in dwarfism.

Acidosis An increase in the $[H^+]$ in body fluids above the normal range.

Acinar Pertaining to or affecting an acinus.

Acinus One of the minute sac-like secretory portions of an acinous gland.

Acne Skin eruption characterised by red pimples.

Acrocyanosis A circulatory disorder in which the hands, and less commonly the feet, are persistently cold, blue and sweaty.

Acrodynia Inflammation of the peripheral nerves of fingers or toes.

Acrosome The minute organ situated at the head of a mature spermatozoa.

Acute A short and sharp course, as opposed to chronic, of an effect or disease.

Adenocarcinoma A malignant tumour of epithelial cells in glandular or gland-like pattern, frequently with infiltration of adjacent tissue.

Adenofibroma A benign neoplasm of connective tissues, with a relatively large proportion of glandular elements.

Adenoma A simple, benign tumour of glandular epithelium and connective tissue.

Adenomatosis A condition in which excessive glandular growth occurs.

Adenosarcoma A malignant tumour of mesodermal tissue; sarcoma of a gland.

Adipocyte Fat-producing cell.

Adjuvant That which aids or assists.

Adrenal Pertaining to the adrenal glands.

Adrenergic Relating to the sympathetic nerve fibres; stimulated by adrenaline.

Adrenocortical Pertaining to the adrenal cortex.

Adrenocorticotrophic Exerting a hormonal influence upon the growth or action of the cortex of the adrenal gland.

Aetiology Assignment of a cause.

Agonist Denoting a muscle in a state of contraction against its opposing muscle, causing movement.

Agranulocytosis A severe disease marked by a diminution or absence of granular leukocytes from the bone marrow and in the blood.

Albuminuria The presence of serum albumin and globulin in the urine.

Aleukaemia A condition in which there is a low or diminished total white cell count in the blood.

Allele Any one of a series of two or more different genes that may occupy the same position or locus on a specific chromosome.

Allergen A substance that produces an allergic reaction.

Alopecia Baldness; loss of hair.

Alpha-globulin A class of globulin fraction in blood.

Alveolar Relating to an alveolus, a small cell or cavity (generally referred to in the lung).

Alzheimer's disease A form of presenile dementia characterised by memory failure.

Amblyopia Dimness of vision.

Amenorrhea Absence or abnormal cessation of the menses.

Amitosis Simple or direct division of a cell by cleavage of the nucleus only.

Amnesia Loss of memory.

Adynamia Lack of motor activity or strength.

Amelia Congenital absence of limb(s).

Anabolic Relating to, or promoting, anabolism.

Anabolism The process of making new living tissue from nutrient material.

Anaemia Any condition in which the number of red blood cell or the amount of haemoglobin are below normal.

Analeptic An agent which causes arousal; a restorative remedy.

Analgesic A remedy or agent which relieves pain.

Anaphase In mitosis and meiosis, the stage during which chromosomes move away from each other towards the poles of the spindle.

Anaphylaxis A condition of hypersensitivity to certain foreign proteins.

Anaplastic A term applied to cells which are affected by anaplasia, or are imperfect in development.

Anasarca A more or less generalised oedema of subcutaneous tissues.

Androgen The general name given to natural and artificial steroids promoting growth in, and maintaining the function of, the secondary structures in the male.

Anencephalia A developmental anomaly characterised by the complete absence, or reduced mass, of the cranial vault and cerebral hemispheres.

Aneuploid Term describing an abnormal complement of chromosomes in cells.

Angioedema; angioneuroedema Angioneurotic oedema

Angiogenesis Development of blood vessels.

Angioma A simple tumour composed of blood vessels or of lymphatic vessels.

Angiosarcoma A malignant tumour originating from the vascular elements in muscle and other soft tissues.

Anisocytosis Considerable variation in the size of cells (e.g. erythrocytes) which are normally uniform.

Anisokaryosis Variation in the size of nucleus in cells.

Anorexia Condition of being without, or of having lost, the appetite for food.

Anorgasmia; anorgasmy Failure to achieve an orgasm during coitus.

Antagonist That which opposes, or resists, the action of another; denoting certain muscles, drugs, etc.

Anthelmentic A remedy for worm infestation.

Anthracosis Blackening of the lungs due to deposits of carbon particles.

Anuria Complete cessation of urine excretion.

Aplastic Conditions characterised by defective regeneration process.

Apnoea The absence of breathing.

Apraxia A disorder of voluntary movement.

Arrhythmia Loss of rhythm (e.g. irregularity of heart beat).

Arthroplasty The making of an artifical joint; an operation for the restoration of the function of a joint by reconstruction or by prosthetic replacement.

Arthralgia Pain of any kind affecting a joint.

Arthropathy Any disease affecting a joint.

Ascites An abnormal accumulation of fluid in the peritoneal cavity.

Atelectasis Collapse of the lung.

Atherosclerosis Focal deposits or degenerative accumulation of material (plaques) mainly in arteries.

Atopy A constitutional tendency in certain individuals to develop immediate hypersensitivity states such as asthma or hay fever.

Atrophy To waste away; a wasting of tissues, organs or the entire body.

Axon The axis of the body; the long process of a nerve cell.

B

B-lymphocytes A white blood cell formed in lymphoid tissue throughout the body; B-cells are generated from stem cells in the bone marrow.

Baritosis; barytosis A condition produced in the lung by exposure to barytes dust.

Basophilic Capable of being stained by basic dyes.

Beta-blockers Drugs used for the management of hypertension, angina pectoris and related heart conditions.

Beta-cells A type of cell; for example, beta-cells of the pituitary, and of the pancreas.

Blastogenesis Reproduction by budding; inheritance characteristics transmitted by the germ plasm.

Blastoma A tumour composed chiefly of immature cells.

Blastula An early form of embryo found in many animals.

Blepharitis Inflammation of the eyelids.

Bolus A large pill, or potion, intended to be taken at once; mass of masticated food ready to be swallowed.

Bradycardia Slowness of the heart beat.

Bradypnoea Abnormal slowness of breathing.

Bronchiectasis; (bronocho-alveolar) Broncho-vesicular.

Broncho-alveolitis Bronchopneumonia.

Bronchorroea An abnormally copious discharge of mucus from the bronchial tubes.

Bulbo-urethral Relating to the bulb of the penis.

Bulimia nervosa Morbid hunger marked by neurotic symptoms.

Bullous pemphigoid Pertaining to the eruption of bullae (large blisters).

Buphthalmia Congenital glaucoma occurring in infancy, marked by enlargement of the eyeball.

Bursa of Fabricius Gut-associated lymphoid organ in birds which act as a source of cells that mediate humoral immunity.

C

Calculi; calculus A solid pathological concretion formed in any part of the body, especially in reservoir organs.

Cannula A tube inserted into a body cavity for the removal of body fluids, or for the introduction of a fluid.

Candidiasis An acute or chronic infection by species of *Candida.*

Capsula; capsule In anatomy, a sheath or envelope around an organ; any structure in the body resembling an envelope in form; a case made of gelatine or starch used to dispense drugs.

Carcinoma A malignant tumour of the epithelial tissues.

Carcinosarcoma A mixed malignant tumour that contains elements of carcinoma and also sarcoma.

Cardiomegaly Enlargement of the heart.

Cardiomyopathy Disease of the heart muscle.

Cardiovascular Relating to the heart and the blood vessels or the circulation.

Caries A gradual decay or death of bones or teeth due to infection.

Cariogenic Producing caries.

Catabolism The breaking-down in the body of chemical compounds to simpler ones; as opposed to anabolism.

Catalepsy A morbid condition in which there is sudden suspension of sensibility and voluntary movement.

Cataract Opacity in the crystalline lens of eye.

Catatonic Relating to, or characterised by, catatonia, a stuporous state.

Catheter A tube for withdrawing fluid from a body cavity, or for introducing fluid into a body cavity.

Caudal Relating to or resembling a tail.

Celosomia Hernia of the viscera in the foetus.

Centromere The region(s) of the chromosomes which become(s) associated with the spindle fibres in mitosis and meiosis.

Cerebellum The posterior brain mass. It consists of two lateral hemispheres united by a narrow middle portion.

Cerebrospinal Relating to the brain and spinal cord.

Cerebrovascular Relating to the arteries and veins of the brain, or affecting them.

Cerebroventricular Relating to the ventricles in the brain.

Cerebrum The principle portion of the brain.

Ceruloplasmin A blue copper-containing globulin of blood plasma (mol. wt. 150,000; 8 atoms Cu per molecule).

Cholecystitis Inflammation of the gall bladder.

Cholestasis An arrest of bile flow.

Chondrocyte A mature cartilage cell.

Chondrodystrophy Anomalies of bone caused by faulty growth of the cartilage of long bones, resulting in the condition of dwarfism.

Chondrogenesis The process of forming cartilage.

Choreoathetosis Abnormal movement of body.

Chorioamnionitis Inflammation resulting from infection of the amniotic sac.

Chromatid The two halves into which a chromosome is divided at mitosis and meiosis.

Chromodacryorrhoea The act of shedding tears in which there are elements of blood.

Clastogenic Ability to produce chromosome breakage.

Claudication Limping; condition caused by the narrowing of the arteries of the legs.

Cocarcinogen Anything that furthers the action of a carcinogen in producing a malignant tumour.

Corneocyte Cells in the cornea.

Cortical Relating or belonging to, or composed of the cortex (the outer portion of an organ).

Craniorrhachischisis Congenitally unclosed skull and spinal cord.

Craniosynostosis Premature ossification of the skull and obliteration of its sutures.

Cretinism A condition caused by congenital underactive thyroid function.

Cristae Plural or crista, a ridge, crest or elevated line projecting from a level of evenly rounded surface.

Cryptorchidism The failure of descent of a testis.

Cycloplegic Appertaining to cycloplegia, the paralysis of a ciliary muscle of the eye leading to loss of accommodation.

Cytomegaly Enlargement of the cell.

Cytopenia A reduction of the cellular elements in the blood.

Cytoplasmolysis The shrinking or the dissolution of the cytoplasm of a cell.

D

Demodicosis Infestation of hair and skin with *Demodex folliculorum hominis*.

Dermatofibrosarcoma A fibrosarcoma of the skin. A malignant tumour consisting of one or more dermal nodules, usually on the trunk.

Diapedesis The passage of blood, or any of its formed elements through an unruptured blood vessel.

Diaphoresis Sweating, perspiration.

Diploidy Term indicating that the chromosome complement of a cell is formed by two homologous chromosomes.

Diplopia Double vision.

Dopaminergic Relating to nerve fibres releasing dopamine.

Dyscrasia A morbid general state resulting from toxic materials in the blood. (An obsolete term.)

Dysmenorrhea Difficult and painful menstruation.

Dysmorphia Abnormality of shape; deformity.

Dysmorphogenesis The origin or cause of dysmorphia.

Dyspepsis Indigestion.

Dysphagia Difficulty in swallowing.

Dysplasia Abnormal development of tissue.

Dysplastic Relating to abnormal development of tissue.

Dyspnoea Difficulty in breathing.

Dysproteinaemia An abnormality in the composition of plasma proteins.

Dysrhythemia Defect or disturbance of rhythm.

Dystasia; (dysstasia) A condition in which there is difficulty in standing.

Dysthyroidism Abnormality in thyroid function.

Dystonia A state of the abnormal tonicity in any of the tissues.

Dystrophy A disorder of the structure and function of an organ or tissue (e.g. muscle or bone), due to defective nutrition.

Dysuria A condition in which the passing of urine is painful and difficult.

E

Ectrodactyly Congenital absence of one or more fingers or toes.

Ectropion Eversion of the eyelids, usually of the lower ones.

Emmenagogue An agent that induces or increases menstrual flow.

Emphysema A condition in which the alveoli of the lungs are dilated.

Encephalitis Inflammation of the brain.

Encephalocoele The entire cavity enclosed by the skull.

Encepholomylitis A group of conditions caused by various forms of virus which attack the nervous system in particular.

Endocardium The innermost tunic of the heart, which includes endothelium and subendothelial connective tissue.

Endocrine The internal secretion of a gland directly into the blood stream.

Endodontic Pertaining to endodontia, the science and practice of root-canal therapy in a tooth.

Endometrium The mucous membrane which lines the uterus.

Endomyocardial Relating to the endocardium and the myocardium.

Endothelial Relating to or composed of the endothelium, the flat lining cell of various serous cavities, blood vessels and lymphatics.

Endotheliocytes An endothelial phagocyctic cell.

Endotheliomas A malignant tumour originating in the endothelium.

Enteritis Inflammation of the mucous membrane of the intestines.

Enterocytes Intestinal cells.

Eosinophilia-myalgia A painful condition of muscles associated with an abnormal increase of eosinophilic leukocytes.

Eosinophiluria Increased urinary excretion of eosin-staining cells.

Ependymoblastoma A tumour composed of embryonic ependymal cells. (Epithelial cells lining the central canal of the spinal cord and the ventricles of the brain.)

Epididymis Coil of efferent duct behind the testis.

Epigastrium Part of the abdomen immediately over the stomach.

Epispadias A congenital deformity in which the urethra opens on the posterior part of the penis.

Epithelioma A carcinoma arising from the squamous epithelial cells of the skin, oesophagus or external genital organs.

Erethism A state of excessive nervous irritability.

Erythema Redness and inflammation of the skin.

Erythrocyte A mature non-nucleated red blood cell.

Erythroderma Generalised redness and inflammation of the skin.

Erythropoiesis The formation of red blood cells.

Erythropoietic Having relation or belonging to erythropoiesis.

Erythroanisocytosis Considerable variations in the size of red blood cells.

Erythrocytopenia A state in which there are too few red blood cells.

Erythrocytosis A condition in which the red blood cells and haemoglobin are increased above normal values.

Etiopathogenesis Origin of a pathological condition.

Eunochoidism A condition of eunochism in which the external organs are complete but the internal secretions are lacking, so that sexual power is impaired.

Exophthalmia Protrusion or prominence of the eye balls to such an extent that the eyelids will not cover it.

F

Fallopian tube The uterine tube.

Fascioliasis Condition in which there is infection with parasitic flukes of the family Fasciolidae.

Fibroadenoma An adenoma in which there is dense formation of fibrous tissue.

Fibrosarcoma A malignant tumour derived from fibrous connective tissue characterised by immature and imperfectly differentiated elements and cells.

Follicle A small cavity or recess and an excretory or secretory function.

Folliculitis Inflammation of a follicle.

Forestomach Upper part of stomach, characterised in the rodent by being lined with squamous cells as in the skin.

Funiculus One of the bundles of fibres which make up a peripheral nerve trunk.

G

Ganglion 1. A group of nerve cells with a common function.
2. A cystec swelling connected with a tendon sheath.

Gastrophy Nutrition to the stomach.

Gastroschisis Congenital fissure of the abdominal wall, the cavity being open.

Gastrula A hollow vesicular stage in the development of many vertebrate and invertebrate embryos.

Gastrulate The formation of the gastrula by transformation of the blastula.

Germ cell Ovum or spermatozoon; sex cell.

Gestation Pregnancy.

Gliosis A proliferation of astrocytes, often seen as a reparative process following cerebral injury.

Globinuria The urinary excretion of globins, a group of proteins.

Glomerulonephritis Nephritis which is characterised primarily by inflammation of the glomeruli of the kidney.

Glomerulus A tuft formed of capillary loops in the kidney.

Glomerulonephrosis A syndrome caused by a degeneration of the renal tubules.

Glossitis Inflammation of the tongue.

Glycolysis The energy yielding catabolism of glucose and natural hexoses in the body.

Gonads Reproductive sexual glands.

Granulocyte A leukocyte containing granules.

Granulocytopenia A deficiency of granulocytes in the blood.

Granulomatosis A chronic inflammatory process leading to the formation of nodules or tumour-like masses.

Gustatory Relation or belonging to the sense and the organs of taste.

Gynaecomastia A condition in the male characterised by the excessive development of mammary glands.

H

Haemangio-endothelioma A relatively unusual or rare tumour derived from blood vessels.

Haemangio-pericytoma A capillary tumour composed of perivascular cells.

Haemangio-sarcoma A malignant tumour derived from blood vessels and connective tissues.

Haemorrhoids A swelling of the anal region; piles.

Haematemesis Vomiting of blood.

Haematoma A tumour or swelling composed of blood.

Haematopoiesis The formation of blood cells.

Haematuria The presence of blood in the urine.

Haemoglobin The respiratory pigment of vertebrates in the red blood cells.

Haemoglobinaemia A condition in which free haemoglobin is present in blood plasma.

Haemolympho-reticular Relating to the blood and lymphatic system.

Haemolysis The leakage of haemoglobin from red blood cells as result of damage to the cell walls.

Haemophilia A hereditary bleeding disease affecting males only, but transmitted by females.

Haemosiderosis A condition in which haemosiderin, an iron-protein compound, is deposited in the liver, spleen and other organs.

Helminthicidal Having the ability to kill parasitic worms.

Hepatocarcinoma Malignant tumour of the liver.

Hepatoblastoma A malignant tumour of the liver made up of cells of epithelial type.

Hepatocytomegaly Enlargement of liver cells.

Hepatosplenomegaly Enlargement of liver and spleen.

Heterozygous	A hybrid produced from unlike gametes; an organism derived from two different sets of genes.
Hippocampus	An elongated rounded elevation projecting into the temporal horn of the lateral ventricle of the brain.
Homeostasis	The state of equilibrium in a living body with respect to various functions.
Hydropsy	An archaic team for dropsy, an abnormal collection of serous fluid in tissue spaces.
Hydroureter	Distension of the ureter (bladder) with urine or watery fluid.
Hyperactive	Activity beyond normal.
Hyperaemia	An excess of blood in any part of the body.
Hyperammonaemia	An excessive amount of ammonia in the blood.
Hyperbilirubinaemia	An excessive amount of bilirubin, a bile pigment, in the blood.
Hypercalcaemia	An excessive amount of calcium in the blood.
Hypercapnia	A raised carbon dioxide content in the blood.
Hyperchloraemia	An excessive amount of chloride in the blood.
Hypercholesterolaemia	An excessive amount of cholesterol in the blood.
Hypercupraemia	An excessive amount of copper in the blood.
Hyperdiploid	A chromosome complement in diploid cells containing one or more extra chromosomes.
Hypergammaglobinaemia	An excessive amount of gamma-globulin in the blood.
Hyperglucagonaemia	An excessive amount of glucagon in the blood.
Hyperglycaemia	An excessive amount of glucose in the blood.
Hypergonadism	Excessive secretory activity of the ovary or testis.
Hyperkalaemia	An excessive amount of potassium in the blood.
Hyperkeratosis	Overgrowth of the horny layer of the skin.
Hyperkinesis	Excessive movement as in muscle spasm.
Hyperlacticaemia (hyperlacticacidaemia)	An excessive amount of lactic acid in the blood
Hypernoea	Excessive mental activity.
Hyperoxaluria	Excessive excretion of oxalic acid in the urine.
Hyperoxia	The condition in which there is too much oxygen in the blood.
Hyperparthyroidism	Over-activity of the parathyroid gland.
Hyperplasia	Any condition in which there is an increase in the number of cells in a part.
Hyperplastic	Relating to or marked by hyperplasia.
Hyperploidy	A condition marked by an increase in the number of chromosomes.
Hyperpyrexia	Raised body temperature well above normal.
Hypertelorism	A condition marked by an abnormal distance between two paired organs.
Hypertension	High arterial blood pressure.
Hyperthermia	Very high body temperature.
Hyperthyroidism	Over-activity of the thyroid gland.
Hyperthyreosis (hyperthyrea)	Hyperthyroidism.
Hypertonia	Extreme tension of the muscles or arteries.
Hypertrophy	An increase in the size and function of an organ.
Hypnoea	Relating to sleep.
Hypoaemia	A lack of blood in any organ.
Hypocatalasaemia	A deficiency in catalase activity in the blood.
Hypocellular	A condition in which there is a deficiency in cells in a tissue or organ.
Hypochloraemia	A defiency in the amount of chloride in the blood.
Hypocholesterolaemia	A deficiency in the amount of cholesterol in the blood.
Hypochondrium	Either of the lateral regions in the upper zone of the abdomen.
Hypodiploidy	A deficiency in the number of diploid cells.
Hypglossal	Lying beneath the tongue.
Hypoglycaemia	A deficiency in the amount of glucose in the blood.
Hypognathia	A congenital defect in the development of the lower jaw.
Hypogonadism	A deficiency in the secretory activity of the ovary or the testis.

Hypokalaemia A defiency in the amount of potassium in the blood.
Hypphysis The pituitary body, a two-lobed organ, located at the base of the brain.
Hypoplastic A deficiency in the number of cells in an organ or tissue.
Hypothalamus A group of tissues, with specialised hormonal function, found at the base of the brain.
Hypothermia Body temperature that is markedly below normal.
Hypothyroidism Under-activity of the thyroid gland.
Hypotonia Reduced tension in the muscles and arteries.
Hypoxaemia A deficiency in the oxygen content in arterial blood.
Hypoxia An inadequate supply of oxygen to a tissue or organ.

I

Immunoglobulin Proteins endowed with known antibody activity.
Inanition Severe wasting and weakness of the body due to lack of food or non-assimilation of food.
Interferon A small basic protein produced in cells in response to a variety of viral and bacterial agents, affording protection.
Interleukins A class of mediators (cytokines) responsible for maintaining normal immune function.
Interstitial Related or belonging to the interstices of tissues.
Intratracheal Within the trachea.
Intraparenchymal Within the parenchymatous tissue (the functional part, not the structural frame-work).
Intrathecal Within a sheath.
Ischaemic Related or belonging to insufficient blood supply to an organ or tissue.
Ischiatic Relating to the sciatic nerve.

J

Jejunum The middle section of the small intestine between the duodenum and the ileum.

K

Karyolysis The apparent destruction by lysis of the cell nucleus.
Karyomegaly Enlargement of the cell nucleus.
Karyorrhexis Disintegration of the nucleus of a cell.
Karyotype The chromosome characteristics of an individual or a cell.
Keratin A fibrous protein found in hair, nails, horns etc.
Keratinocyte Keratin-producing cell.
Keratitis Inflammation of the cornea.
Keratoacanthoma A subcutaneous nodule usually occurring on the face.
Keratoconjunctivitis Inflammation of the conjunctiva at the border of the cornea.
Keratolytic A substance having the ability to dissolve the epidermis.
Keratopathy Disease of the epidermis.
Keratoplastic Relating to the plastic surgery of the cornea.
Keratosis A skin lesion.
Ketonuria The excretion of acetone and ketone bodies in the urine.
Ketosis The presence of excessive amounts of ketone bodies in tissues.
Kupffer The Munich anatomist who identified certain tissues and cells which are named after him, for example, Kupffer's cells and Kupffer's canals.

L

Lacrimatory Causing the excessive secretion of tears.
Lactation The production and secretion of milk.
Laryngitis Inflammation of the mucous membrane of the larynx.
Laryngospasm Muscular spasm of the larynx.
Lavage The act of washing-out or irrigation of an organ.
Laxative Having the action of loosening the bowels.

Leiomyosarcoma A malignant tumour derived from smooth muscle.
Leprosy A chronic infective disease of man caused by the leprosy bacillus.
Lesion A wound or injury.
Leucocyte (Leukocyte) Any one of the various types of white blood cells.
Leucocytopenia Deficiency of white blood cells.
Leucocytosis An increase in the total number of leucocytes in blood above normal.
Leucopoenia (Leucopenia) Deficiency of white blood cells.
Leukaemia Pertains to any one of a complex group of fatal diseases characterised by the uncontrolled proliferation of one of the types of leucocytes.
Leukaemogen A substance that causes leukaemia.
Leukocyte See Leucocyte.
Leukocytosis See Leucocytosis.
Leydig cell Interstitial cells in the testis, responsible for testosterone production.
Libido Sexual drive.
Lingual Belonging to the tongue.
Lipaemia The presence of abnormal quantities of fats in the blood.
Lipidosis Any disorder in the metabolism of fats.
Lipolysis The hydrolysis of fats and lipids.
Liposome Artificial membranous structures prepared incorporating cholesterol and fatty constituents.
Lumbar Relating to the loins, or the part of the back and sides between the ribs and pelvis.
Lumen The bore of a tube such as the intestine or artery.
Lupus An ulcerating disease of the skin and mucous membrane.
Luteum The yellow endocrine body (as in Corpora Luteum).
Lymph The pale-yellow clear or cloudy liquid that flows in the lymphatic channels.
Lymphoblast A young immature cells that matures to a lymphocyte.
Lymphocyte A white blood cell formed in lymphoid tissue.
Lymphocytopenia; (lymphopenia) Deficiency of lymphocytes in the blood.
Lymphopoiesis The formation of lymphocytes.
Lymphoreticular Lymphatic network system.
Lymphosarcoma A malignant tumour of lymphoid tissue with features of sarcoma.
Lypothymia Obsolete term for melancholia.

M

Macrophage A large phagocytic cell found in the connective connective tissues.
Malignant Threatening life or tending to cause death with special reference to cancerous growth.
Malpighian tubules Tubules found in insects, named after the anatomist, Marcello Malpighi.
Megakaryocyte The mother cell from which blood platelets are derived.
Megakaryocytosis The presence of megakaryocytes in the blood.
Megaloblastic Pertaining to megaloblasts, the large nucleated embryonic type of cells seen exclusively in pernicious anaemia.
Megalocytic Relating to megalocytes, red blood cells of large size.
Meiosis A special process of cell division which results in the product of cells with a single set of chromosomes (haploid cells) from cells with two sets of chromosomes (diploid cells).
Melancholia A depressed and unhappy mental state with abnormal inhibition of mental and physical activity.
Melanocyte Any pigment-containing cell such as that found in the skin and eyes.
Melanoma A tumour consisting of darkly pigmented cells.
Melanosis An abnormal deposition of the dark pigment, melanin, in the skin and other tissues.
Meningitis Inflammation of the membranes of the brain or spinal cord.
Meningocele A hernial protrusion of the meninges covering brain or spinal cord.
Menopause The cessation of spontaneous menstrual periods; the climacteric or change of life.

Menstrual Relating to menstruation.

Mesentery The double layer of the peritoneum connecting the intestine to the posterior abdominal wall.

Mesothelioma A tumour of the mesothelium, pavement epithelial cells lining serous cavities, e.g., peritoneum, pleura etc.

Metabolism The biochemical processes participating in the essential for the phenomena of life. The process by which nutritive material is built up into living matter.

Metacarpus The set of five bones in the hand connecting the carpus to the digits.

Metaphase A stage in cell division. The stage when the chromosomes become aligned on the equatorial plate of the cell.

Metaplasia The transformation of one tissue into another during adult life, as in the case of certain tumours.

Metaplastic Pertaining to metaplasia.

Metastasis The transfer of disease from a primary site to distant parts of the body by way of natural passages, e.g., blood vessels etc.

Methaemoglobin Oxidised form of haemoglobin incapable of transporting oxygen by red blood cells in the body.

Methaemoglobinaemia The presence of abnormal amounts of methaemoglobin in the blood.

Metoestrus The interval between ovulation periods.

Microcephaly Having a small head.

Microcystic Pertaining to a tiny cyst.

Micronuclei Small nuclei in cells.

Microphthalmia A condition in which the eyes are abnormally small in size.

Microsome Refers to the biochemical fraction of a tissue consisting mainly of the endoplasmic reticulum, an organelle rich in the cytochrome P450-dependent mixed-function oxidase system.

Micturate Urinate.

Mitochondria The organelle responsible for cell respiration.

Monocyte The largest unicellular, nucleated white cell seen in blood.

Monocytopenia Abnormal deficiency of monocytes in blood.

Monophthalmia The condition in which there is only one eye.

Morbid Belonging or related to a disease.

Morphology The branch of biology dealing with the structure and form of a living organism.

Mutagen An agent which induces mutation.

Myalgia A painful condition of a muscle or muscles.

Mydriasis Enlargement of the pupil.

Myeloma A locally malignant tumour of the bone.

Myoblastic Pertaining to an embryonic cell which develops into a muscle fibre.

Myocardium The muscular structure of the heart.

Myometrium The general muscular mass of the uterus.

Myopathy Any diseased condition of the muscles.

N

Narcosis Stupor or general anaesthesia produced by drugs.

Narcotic A drug that induces narcosis.

Nausea A feeling of sickness with a desire to vomit

Necropsy Post-mortem examination of a body.

Necrosis Death of a portion of a tissue.

Neonate Referring to the newborn.

Neoplasia The growth of a neoplasm.

Neoplasm Any new and morbid formation of tissue; a tumour.

Neoplastic Relating or belonging to neoplasty.

Neoplasty 1. The replacement by plastic surgery of a part in the body.
2. see Neoplasia.

Nephritis A bilateral disease of the kidneys.
Nephroblastoma A highly malignant complex renal tumour of young children.
Neuropathy The deposition of calcium in the kidneys and the formation of calculi.
Neurulation Processes involved in the formation of the nerulae stage in the developing embryo.
Neutrophil A condition characterised by the presence of gravel or calculi in the kidneys.

O

Obese Very fat; corpulent.
Oedema The presence of excessive amounts of fluid in the intracellular spaces of the body.
Oesophagus The gullet.
Oligomenorrhoea Infrequent occurrence of menstruation.
Oligospermia A condition in which the spermatozoa count in semen is low.
Oliguria Daily output of urine below normal levels.
Omentum The membrane that encloses the bowels.
Oncogene The genes considered to encourage tumour formation.
Ontogeny The origin and evolution of the individual organism.
Onycholysis The separation of the nail from its bed by the accumulation of cellular debris.
Operculum 1. A plug of mucus found in the cervical canal of a pregnant woman.
2. Anything resembling a lid, specifically, in anatomy the frontal, parietal and temporal lobes of the cerebral hemisphere.
Opisthotonus A tetanic spasm in which the spine and extremities are bent backwards.
Osteoarthritis Chronic degenerative inflammation of a joint.
Osteoblast A bone-forming cell.
Osteochondroma A tumour composed of both bone and cartilaginous tissues.
Osteoclast A large multinucleated cell formed in the bone marrow.
Osteodystrophy Defective formation of bone.
Osteomalacia A painful disease characterised by the gradual softening and bending of bones.
Osteomyelitis Inflammation of the bone marrow and adjacent bone and cartilage.
Osteosclerosis The abnormal hardening of bones.
Otitis Inflammation of the ear.
Ova Plural of ovum, the egg or female sexual cell.
Ovary One of the two reproductive glands in females containing the ova or germ cells.

P

P.O. Per os (by the oral route).
Pancytopenia A reduction in all the cellular elements in blood (red blood cells, leucocytes and platelets).
Panleucocytopenia A reduction in all the white cells in blood.
Paraesthesia Numbness and tingling.
Parakeratosis Imperfect formation of the horn cells of the epidermis.
Paranoia A mental disorder characterised by the slow, insidious onset and development of delusional ideas.
Parasympathetic Pertaining to a division of the autonomous nervous system.
Paratuberculosis A morbid condition similar to tuberculosis but in which the causative organism cannot be demonstrated.
Paravenous Beside or situated near a vein.
Paraventricular Relating to a ventricle.
Parenchyma The specific or functional constituent of an organ or tissue.
Parkinsonism A group of nervous conditions resembling and including Parkinson's disease.
Paronychia Suppurative inflammation in the tissues surrounding nails of fingers or toes; whitlow.
Parotid The gland beside the ear; occurring near the ear.
Paroxysmal Having the characteristics of a paroxysm, a sudden attack of a recurrent symptom, or convulsions.

Parturition	The process of childbirth.
Peribronchiolar	Surrounding the bronchioles, the small divisions of the bronchial branches.
Pericapillary	Surrounding a capillary.
Pericapsular	Occurring around a capsule.
Pericardium	A membrane enveloping the heart, and formed of two parts.
Pericholangitis	Inflammation of the structures lying around the bile duct.
Perilymphatic	1. Surrounding a lymphatic vessel. 2. Spaces and tissues in the inner ear.
Perinatal	At about the time of birth; the term includes both pre- and post-natal periods.
Perinephric	Situated around the kidney.
Periocular	Occurring or situated around the eye.
Periodontium	The tissues which surround and support the teeth.
Peristalsis	The contracting and relaxing movement of the intestine by which the contents are propelled forward.
Peritoneum	The serous sac lining the abdominal cavity.
Peritonitis	Inflammation of the peritoneum caused by bacterial infection.
Phallus	The penis.
Pharyngitis	Inflammation of the pharynx.
Phosphaturia	Excessive excretion of phosphates in the urine.
Placenta	The organ separating the mother from the developing foetus, and through which metabolic interchange occurs.
Plasmacytoma	A malignant tumour composed of plasma cells, most often found in lymph nodes and bone marrow.
Pleurisy	Inflammation of the pleura, the serous membrane covering the lungs.
Pneumoconiosis	An industrial disease of the respiratory system caused by the inhalation of particles.
Pneumosclerosis	Pulmonary fibrosis.
Poikilocyte	A red blood cell, usually larger than normal and irregularly shaped, associated with anaemia.
Pollex (pl. pollices)	The thumb.
Polydipsia	An excessive degree of thirst.
Polyneuritis	Inflammation of many nerves.
Polyneuropathy	A disease process involving a number of peripheral nerves.
Popliteal	Relating or belonging to the space behind the knee joint.
Porphyria	A metabolic disorder in which porphyrin is retained in the tissues.
Preneoplastic	Pertaining to the period preceding to the establishment of a tumour in tissues.
Preputial	Belonging to the prepuse, the foreskin of the penis
Pronephros	The primordial kidney; a structure developing in the embryo before the mesonephros.
Prostate	A chestnut-shaped gland in males, which surrounds and is continuous with the neck of the bladder.
Ptyalism	A condition in which there is increased secretion or flow of saliva.
Pyknosis	The process of the condensation of the nuclear material following cell death.
Pyloric	Relating or belonging to the pylorus, the distal end of the stomach.
Pyogenic	Forming or producing pus.
Pyometra	A collection of pus in the uterus.
Pyosis	Suppuration; pus formation.
Pyrenolysis	The disintegration of the nucleolus of a cell.
Pyuria	A condition in which pus is present in the urine.

R

Rachischisis	Spina bifida; a congential defect of the vertebral column and the spinal cord
Radius	The lateral bone of the forearm.
Radius-ulna	The medial and larger of the two bones of the forearm.

Raynaud's disease A condition characterised by intermittent pallor and cyanosis of extremities resulting from coldness or emotion.

Reticulocytopenia Diminution of the number of reticulocytes in the blood.

Reticulocytosis The presence of excessive amounts of reticulocytes in the blood.

Reticulo-endothelium The basic substances which forms the reticulo-endothelial system.

Reticulosarcoma A malignant tumour composed of cells derived from the reticulo-endothelium of lymph glands and spleen chiefly.

Reticulosis An increase in reticulo-endothelial cells in bone marrow and bone.

Retinopathy Any diseased condition of the retina.

Retrocarotid Occurring behind the carotid artery.

Rhabdomyolysis Urinary excretion of myoglobin, derived from the muscle.

Rhabdomyosarcoma A malignant tumour derived from skeletal muscle.

Rhinitis An inflammation of the nasal mucous membrane.

Rhinorrhoea Profuse discharge of thin mucous from the nose.

Rhombencephalic Pertaining to the rhombencephalon, the hind-brain.

Rigor 1. Stiffness, rigidity; 2. A shivering fit.

S

Sacral Relating to or in the neighbourhood of the sacrum, a bone at the back of the pelvic girdle.

Sarcoid A cutaneous lesion.

Sarcoidosis A generalised granulomatous disease whose lesions predominate in the lymphatic system.

Sarcoma A malignant tumour of the connective tissue or its derivatives.

Schistosomiasis A group of diseases caused by parasitic flukes; Bilharziasis.

Schwannoma A tumour derived from the sheaths of Schwann cells.

Sciatic Pertaining to the sciatic nerve, the largest nerve in the body.

Sclerosis The hardening of a tissue due to inflammation.

Scrotum Sac containing the testes.

Seminal Relating or belonging to semen.

Seminoma A tumour of the testis.

Septicaemia A severe type of infection of the blood stream.

Sequela A disease or morbid condition resulting from another disease. Used in the plural to indicate complications arising from a certain disease.

Sialorrhea An excessive flow of saliva.

Siderosis Deposits of fine particles of iron in the lymphoid system in the lungs.

Silicosis A type of lung disease caused by the inhalation of silica particles.

Spermatocele A cystic enlargement of the epididymis containing spermatozoa.

Spermatocyst A seminal vesicle.

Spermatocyte An early stage in the development of a spermatozoon.

Spermatogenesis The formation and development of spematozoa.

Splenocyte A large phagocytic cell found in the spleen.

Splenomegaly Enlargement of the spleen.

Spongiform Having resemblance to a sponge.

Spongiosis Oedema in the epidermis, a characteristic feature in eczema.

Sputum The material expelled from the respiratory passages by coughing or clearing the throat.

Squamous Resembling a scale, plate-like; scaly.

Steatorrhoea A condition in which excessive hydrolysed fats occur in the stools.

Steatosis 1. Fatty degeneration. 2. Excess of fat in any place in the body.

Sternebrae The bone segments which fuse in early life to form the sternum.

Sub-chronic Phase between acute and chronic.

Subclavian Beneath the clavicle, the long bone of the shoulder girdle.

Subcutaneous Beneath the skin.

Sublingual Beneath the tongue.

Supraoccipital Located in the region above the occiput, the back part of the head.
Sympathetic Relating to the automated nervous system.
Syncytical Relating to a syncytium, a protoplasmic mass without apparent divisions into cells.
Syndrome A distinct group of symptoms or signs, which characterise a clinical condition or disease.
Synergist A medication which aids the action of another, and where the combined effect is greater than that of the individual drugs.
Syphilis A contagious venereal disease transmitted through sexual intercourse.

T

T-cells Thymus-derived lymphocytes responsible for cell-mediated immunity.
T-lymphocyte See T-cells.
Tachyarrythmia A rapid abnormal cardiac rhythm.
Tachycardia Rapid action of the heart.
Tachypnoea Unduly rapid breathing.
Teratocarcinoma A malignant teratoma.
Teratogen An agent that produces birth defects and abnormalities.
Teratogenesis The development and birth of monsters [Gk. Teras: monster, Genein: to produce].
Teratoma A group of tumours composed of tissues derived from the germinal layer of the embryo.
Teratospermia Abnormal and malformed spermatozoa.
Testis The male gonad suspended in the scrotum by the spermatic cord.
Thesaurismosis A general term for a group of metabolic disorders in which there is abnormal storage of some substances in reticulo-endothelial cells.
Tetralogy of Fallot A form of congenital heart disease.
Thigotaxis The attraction or repulsion response of a motile cell to contact stimulation.
Thrombin An albumin-like protein with powerful blood clotting activity.
Thrombocyte Blood platelet, a very small cell essential for clotting of blood.
Thrombocytopenia Reduction in the number of platelets present in the blood.
Thrombocytosis An increase above normal of platelets in the blood.
Thrombopenia See Thrombocytopenia
Thrombophlebitis Inflammation of a vein following the formation of an intravascular clot.
Thrombus A blood clot formed in and remaining in a blood vessel or the heart.
Thymocytes Thymus-gland cells.
Thymus A lymphoid organ located in the lower part of the neck.
Thymoma A tumour formed from thymic tissue.
Thyroid Large ductless gland lying between the larynx and trachea responsible for producing growth-regulating hormones.
Thyroiditis Inflammation of the thyroid gland.
Tibia The large shin bone.
Toxoplasma A genus of protozoa.
Trachea The windpipe.
Tracheitis Inflammation of the membrane lining the trachea.
Tracheobronchitis Inflammation of the bronchi, spreading to the trachea.
Trichoepithelioma Small, benign lesion in the skin about the eyes.
Trichomoniasis Acute or sub-acute infection leading to inflammation of the vagina and urethra. It is usually sexually transmitted.
Trophoblastic Pertaining to trophoblasts, the ectodermal cell layer of developing mammalian embryos in contact with the uterine wall.
Trypanosomiasis The diseases caused by infection with the parasites of the genus, *Trypanosoma*.
Tuberculosis The disease caused by infection with *Mycobacterium tuberculosis*.

U

Umbilical Pertaining to the umbilicus, the navel.

Uraemia The condition which results from acute kidney failure leading to an excess of urea and other waste products in the blood.

Ureter The duct conveying urine from the kidney to the bladder.

Urithritis Inflammation of the urethra, the canal through which urine passes from the bladder to the exterior.

Urticaria Hives, nettle rash. An eruption of itching wheals.

Uroporphyria The condition characterised by excessive urinary excretion of uroporphyria.

V

Vacuole A fluid-filled cavity within a cell.

Vagina The genital canal in the female; any sheath-like structure.

Vasculitis Inflammation of a blood vessel.

Vasodilator An agent that induces the dilatation of blood vessels.

Vasoconstrictor An agent that induces the constriction of blood vessels.

Ventricle A small cavity, chamber or compartment, especially one in the brain or the heart.

Vertigo Giddiness, a sense of instability, often with a sense of rotation.

Vitiligo A skin condition characterised by failure to produce melanin; also known as *leukoderma* and *piebald skin*.

Vitrectomy Surgical operation on the vitreous, jelly-like tissue filling the eyeball.

X

Xeroderma pigmentosum A rare genetic disease of the skin which in infancy is characterised by erythema (redness of skin), progressing by stages to malignancy.

Glossary of Organism Names

Abies alba	silver fir tree
Acacia spp.	trees or shrubs
Acanthopax sessiflorus	flowering plant
Acanthoscelides obtectus	brucid beetle
Acartia clausia	saltwater copepod
Acer spp.	maple trees
Acetobacter xylinium	bacterium
Acetobacterium malicum	bacterium
Acheta domesticus	house cricket
Achromobacter spp.	bacteria
Achyla spp.	fungi
Acinetobacter spp.	bacteria
Acinos suaveolens	herb
Acmaea testudinalis	Barents sea limpet
Acokanthera ouabaio	poisonous flowering plant
Acokanthera schimperi	poisonous flowering plant
Aconitum napellus	monk's hood plant
Acroneuria pacifica	stonefly
Acroynchia baueri	shrub
Actinomyces spp.	bacteria
Adonis vernalis	flowering plant
Aedes aegypti	Yellow fever mosquito
Aeolosomas headlyi	aquatic annelid
Aeolosomas hemprichi	aquatic annelid
Aeolus elegans	soil microbe
Aerobacter spp.	bacteria
Aeromonas spp.	bacteria
Agaricus spp.	fungi
Agonis spp.	myrtle trees
Agrobacterium spp.	bacteria
Ailyssum	plants
Alcaligenes spp.	bacteria
Allium spp.	onions
Allolobophora caliginosa	earthworm
Allolobophora tuberculata	earthworm
Allorchestes compressa	amphipod
Aloe spp.	aloe plant
Alternaria aleraceae	fungus
Alternaria radicina	carrot black root rot
Amanita muscaria	fly agaric toadstool
Amblyomma americanum	lone star tick
Ambystoma mexicanum	Mexican axolotl
Ampelisca abdita	estuarine/marine amphipod
Amphimelania holandri	mollusc
Amputlarium canaliculatus	nematode
Amycolata autotrophica	bacterium
Anabaena spp.	cyanobacteria
Anabaenopsis spp.	cyanobacteria
Anabas testudineus	common cockroach
Anagasta kuehniella	Mediterranean flour moth
Anamirta cocculus	plant
Andrena erythronii	bee
Anethum graveolens	dill
Angelica spp.	aromatic umbelliferous plants
Anguilla anguilla	eel
Ankistrodesmus spp.	green algae
Anodonata spp.	mussels
Anodonta woodiana	clam
Anticarsia gematalis	velvet bean caterpillar
Aphanizomenon flos-aquae	cyanobacterium
Aphelenchus avenae	nematode
Apion corchori	jute stem weevil
Apis mellifera	honey bee
Aplexa hypnorum	snail
Aporrectodea caliginosa	earthworm
Arabidopsis thaliana	plant
Arca granosa	ark shell
Argulus spp.	fish ectoparasites
Aristichthys nobilis	bighead fish
Armillaria mellea	honey fungus
Artemia spp.	brine shrimps
Artemisia dracunculus	tarragon
Arthrobacter spp.	bacteria
Arundo donax	giant reed
Asellus spp.	sowbugs
Aspalathus linearis	rooibos tea
Asparagopsis spp.	red algae
Aspergillus spp.	fungi
Asperula spp.	woodruff
Aspidisca spp.	protozoans
Asterias rubens	sea star
Astragalus spp.	wild lentil, alpine milk-vetch, and wild liquorice species
Atropa belladona	deadly nightshade plant
Aulosira spp.	cyanobacteria
Aureobasidium spp.	yeast
Australorbis glabratus	intermediate host of blood fluke
Azobacter spp.	cyanobacteria
Azolla pinnata	semi-aquatic perennial herb
Azomonas agilis	bacterium
Azospirillum spp.	bacteria
Azotobacter spp.	bacteria
Bacillus spp.	bacteria

Bacteroides spp.	bacteria
Baetis rhodani	mayfly
Balanus amphitrite	barnacle
Banisteria caapi	plant
Barbus conchonius	red barb
Barytelphusa guerini	freshwater crab
Beijerinekia mobilis	bacterium
Beta vulgaris	red beetroot
Bifdobacterium spp.	bacteria
Biomphalaria pfeitteri	human schistosomiasis snail host
Biomphalaria spp.	freshwater snails
Blastocladiella pringsheimii	aquatic fungus
Blastocladiella ramosa	aquatic fungus
Blattella germanica	German cockroach
Blepharisma spp.	protozoans
Blumea balsamifera	plant
Bombus terricola	bumble bee
Bordetella pertussis	bacterium
Bortrylio cinerea	fungus
Brachionus calyciflorus	rotifer
Brachionus plicatilis	rotifer
Brachydanio rerio	zebra fish
Bradyrhizobium japonicum	bacterium
Branchiura sowerbyi	tubifex worm
Branhamella catarrhalis	bacterium
Brassica nigra	black mustard
Brassica oleraceae	cabbage
Brevibacterium spp.	bacteria
Bufo americanus	American toad
Bufo arenarum	toad
Bufo bufo japonicus	common toad
Bufo marinus	toad
Bufo regularis	Egyptian toad
Bulinus truncatus	human schistosomiasis snail host
Bullia rhodostoma	mollusc
Butyribacterium - methylotropicum	bacterium
Caenorhabditis elegans	nematode
Calderobacterium-hydrogenophilum	bacterium
Callibaetes spp.	mayflies
Callinectes sapidus	blue crab
Calyptogena spp.	clams
Cambarus spp.	crayfish
Campylobacter pylori	bacterium
Candida spp.	yeasts
Cantharellus cinnabarinus	edible mushroom
Cantharis vesicatoria	herb
Capsicum annuum	Chile pepper
Carcinus maenas	green crab
Carica papaya	tree
Carpinus betulus	european hornbeam tree
Cassia roxburghii	flowering plant
Cassostrea virginea	oyster
Catharanthus spp.	periwinkles (plants)
Cellulomonas spp.	bacteria
Celonella spp.	microcrustaceans
Ceratonia siliqua	carob tree
Ceratophyllum demersum	coontail
Ceriodaphnia dubia	water flea
Chaetomium cupreum	filamentous fungus
Chaetomium globosum	fungus
Channa orientalis	western snakehead fish
Channa punctatus	snakehead fish
Chara spp.	muskgrass
Chilomanas spp.	flagellate protozoans
Chironomus spp.	midges
Chlamydia trachomatis	bacterium
Chlamydomonas spp.	green algae
Chlorella spp.	green algae
Chlorococcum spp.	green algae
Choristoneura occidentalis	western spruce budworm
Chromobacterium spp.	bacteria
Chroococcus spp.	algae
Cinchona officinalis	quinine plant
Cinnamomum camphora	camphor tree
Cinnamomum platyphyllum	tree
Cirrhina mrigala	freshwater carp
Citrobacter freundii	bacterium
Claclosporium lignicola	fungus
Clarias spp.	catfish
Cloeon dipterum	mayfly
Clostridium spp.	bacteria
Coccus cati	cochineal insect
Colchicum antumnale	meadow safron
Coleoptera	beetle and weevil family
Colpidium campylum	ciliate protozoan
Colpoda spp.	soil ciliates
Coriolus versicolor	mushroom
Corylus heterophylla	hazel tree
Corylus mandschurica	hazel tree
Corynebacterium simplex	bacterium
Crangon spp.	sand shrimps
Crangonyx pseudogracilis	crustacean
Crassostrea virginica	eastern oyster
Crepis capillaris	smooth hawk's-beard plant
Crepis tectorum	hawk's beard plant
Crotalaria spp.	plants
Croton tiglium	plant
Crungonyx pseudogracilis	sowbug
Crypthecodinium cohnii	green alga
Cryptochiton stelleri	giant gumboot chiton

Culex spp.	mosquito flies
Culicid spp.	mosquitoes
Cuminum cyminum	tree
Cunninghamella elegans	fungus
Cupressus torulosa	Bhutan cypress tree
Curcuma longa	turmeric plant
Cyamopsis tetragonolobus	leguminous plant
Cycas circinalis	false sagopalm
Cycas revoluta	Japanese cycad
Cycas spp.	palms
Cyclops strennus	water shrimp
Cyclops viridis	water shrimp
Cylindrocarpon destructans	fungus
Cylindrospermum licheniforme	cyanobacterium
Cynodon niemfuensis	giant star grass
Cypria spp.	microcrustaceans
Cypridopsis vidua	seed shrimp
Cyprinus carpio	carp
Daphnia spp.	water fleas
Datura stramonium	thorn apple
Delia antiqua	onion fly
Deroceras reticulatum	slug
Desulfitobacterium anilini	bacterium
Desulfococcus multivorum	bacterium
Desulfovibrio spp.	bacteria
Diaptomus spp.	microcrustaceans
Dicentra spp.	bleeding heart plant
Dichapetalum cymosum	woody plant
Digitalis lanata	foxglove
Dina dubia	leech
Ditylenchus dipsaci	eelworm
Ditylenchus spp.	nematodes
Dorax serra	gastropod mollusc
Drosophila spp.	fruit flies
Dryobalanops aromatica	plant
Dunaliella spp.	green algae
Echinogammarus pirloti	amphipod
Eisenia foetida	kelp
Elminius modestus	barnacle
Elodea canadiensis	freshwater macrophyte
Elodea densa	freshwater macrophyte
Engeria densa	aquatic plant
Entamoeba histolytica	protozoan
Enterobacter cloacae	bacterium
Enterobacter gerogenes	bacterium
Enterococcus faecium	bacterium
Entosiphon sulcatum	flagellate protozoan
Eohaustorius estuarius	estuarine/marine amphipod
Ephedra spp.	branching shrubs
Eretmocerus debachi	parasitic wasp
Eriostermon coxii	herb
Erpobdella punctata	leech
Erwinia spp.	bacteria
Erythroxylum coca	cocoa tree
Escherichia spp.	bacteria
Eucalyptus tereticonus	eucalyptus tree
Eucheuma spinosum	seaweed
Eucryphia cordifolia	flowering shrub
Eucyclops spp.	microcrustaceans
Euglena spp.	flagellate protozoans
Eurytemora affinis	estuarine copepod
Fagus sylvatica	beech tree
Flexibacter spp.	bacteria
Fluorobacter spp.	bacteria
Fusarium spp.	filamentous fungi
Gadus morhua	Atlantic cod
Gadus virens	cod
Gammarus spp.	scud
Gelidum spp.	red algae
Gentiana spp.	gentian plants
Geotrichum candidum	potato rubbery rot fungus
Giardia lamblia	protozoan
Gibberella fujikuroi	black heart, cotton boll rot, maize stalk rot fungus
Glaucium flavum	yellow horned poppy
Gliocladium roseum	fungus
Gliocladium virens	fungus
Glomus mosseae	mycorrhizal fungus
Gossypium barbadense	cotton plant
Gossypium hirsutum	cotton plant
Grandidierella japonica	amphipod
Graphium spp.	deuteromycete fungi
Grassostrea virginica	oyster
Gymnodinium spp.	algae
Gyromitra spp.	fungi
Haematococcus pluvialis	alga
Haematoxylon campechianum	logwood
Halobacterium halobium	bacterium
Hebeloma crustiliniforme	fungus
Helicobacter pylori	bacterium
Heliothis zea	corn earworm
Heliotropium europaeum	european heliotrope plant
Heliotropium lasiocarpum	heliotrope plant
Helisoma trivolvis	aquatic mollusc
Helminthosporium spp.	leaf spot fungi
Helobdella stagnalis	leech
Heracleum giganteum	giant hogweed
Heracleum sphondylium	hogweed
Hermidium alipes	winged four-o'clock plant
Heterobasidion annosum	conifer butt rot fungus
Heteropneustes fossilis	airsac catfish
Hibiscus sabdoriffa	shrub
Homarus americanus	northern lobster
Hordeum leporinum	wild barley

Hordeum sativum	barley
Hordeum vulgare	barley
Hyacinthus orientalis	plant
Hyale plumulosa	amphipod
Hyalella azteca	shrimp
Hydra spp.	protozoans
Hydrilla verticillata	aquatic macrophyte
Ichthyophthirius multifiliis	fish ectoparasite
Ide melanote	fish
Ilyodrilus frantzi	oligochaete
Indoplanorbis exustus	snail
Ischnura spp.	damsel flies
Isochrysis galbana	marine microalga
Jordanella floridae	American flagfish
Juga plicifera	gastropod
Juncus bulbosas	soft-water plant
Juncus roemerianus	soft-water plant
Kitasatosporia setae	bacterium
Klebsiella spp.	bacteria
Kluyveromyces marxianus	yeast
Labeo rohita	carp
Laccaria spp.	fungi
Lactua sativa	lettuce
Lagodon rhomboides	marine pin perch
Lantana indica	sage
Lavandula vera	lavender
Leiostomus xanthurus	teleost fish
Lemna minor	duckweed
Lepomis macrochirus	bluegill sunfish
Leptocoris coimbatorensis	bug
Leptotrichia buccallis	bacterium
Leuciscus idus	ide
Leuciscus idus melanotus	chub
Leuconostoc mesenteroides	fungus
Leuctra moselyi	stonefly
Liderocapsa treabii	bacterium
Ligularia clivorum	plant
Ligustrum lucidum	glossy privet
Lilium lancifolium	tiger lily
Limnaea peregra	snail
Limnephilus spp.	caddis flies
Liriomyza trifolii	leafminer
Listeria spp.	bacteria
Littorella uniflora	soft-water plant
Lonchocarpus	lancepod (flowering plant)
Lumbriculus variegatus	aquatic worm
Lumbricus rubellus	earthworm
Lumbricus terrestris	common earthworm
Lupinus luteus	yellow lupin
Lycopersicon esculentum	tomato
Lycopersicon lycopersicum	tomato
Lymaca stagnalis	snail
Lymnaea acuminata	mollusc
Lymnaea stagnalis	freshwater snail
Lymnea acuminata	freshwater snail
Lysimachia capillipes	loosestrife
Macaca fascicularis	macaque
Macaca mulatta	rhesus monkey
Macoma balthica	mollusc
Macrobrachium lamerrei	shrimp
Macrocystis pyrifera	kelp
Macromia spp.	dragonflies
Macronema radiatum	golden rod
Malabaria paludicola	earthworm
Megachile rotundata	bee
Megascolex mauritii	earthworm
Melanoplus sanguinipes	grasshopper
Melicope leptococca	citrus tree from New Caledonia
Melilotis spp.	sweet clover
Meloidogyne spp.	nematodes
Mensipermum cocculus	plant
Mentha aquatica	bog mint
Mentha arvensis	field mint
Mentha polegium	pennyroyal plant
Mercenaria mercenaria	hard clam
Meretrix casta	clam
Meriones hurrianae	Indian desert gerbil
Merismopedia spp.	algae
Mesocyclops leuckarti	copepod
Metaperaeus moroceros	shrimp
Metarhizium anisopliae	fungus
Methanobacterium spp.	bacteria
Methanobarkeri 227	bacterium
Methanobrevibacter spp.	bacteria
Methanococcus spp.	bacteria
Methanosarcina spp.	bacteria
Methanospirillum spp.	bacteria
Methanothrix spp.	bacteria
Methylococcus spp.	bacteria
Methylosinus trichosporium	bacterium
Microbacterium vaccae	bacterium
Micrococcus spp.	bacteria
Microcystis aeruginosa	cyanobacterium
Minutocellus polymorphus	diatom
Modialus modiolus	mussel
Moina macrocopa	cladoceran
Monarda puctatata	plant (Lamiaceae)
Monodonata turbinata	marine snail
Monodus subterraneus	alga
Monopterus albus	asian swamp eel
Monoraphidium griffithii	diatom
Moraxella spp.	bacteria
Mortierella isabellina	fungus

Moschus moschiferus	musk deer
Mougeotic spp.	filamentous green algae
Mucor spp.	fungi
Mugil cephalus	striped mullet
Munidopsis spp.	hydrothermal crabs
Muntiacus muntjac	Indian deer, Indian muntjac
Mus musculus	house mouse
Musca domestica	House fly
Musculium transversum	bivalve
Mustela vison	mink
Mya arenaria	soft shell clam
Mycobacterium spp.	bacteria
Mycoplasma pulmonis	bacterium
Mysidopsis bahia	mysid shrimp
Mystus vittatus	striped catfish
Mytilus spp.	mussels
Myzus persicae	Peach-potato aphid
Nais communis	oligochaete
Navicula incerta	diatom
Navicula pelliculosa	diatom
Neanthes arenaceodentata	ragworm
Neisseria ovis	bacterium
Nemoria esthamus	freshwater fish
Nereis virens	sandworm
Nereocystis luetkeana	phaeophyte
Neurospora crassa	mould
Neurospora sitophila	fungus
Nicotiana tabacum	tobacco plant
Nigella damascena	love-in-a-mist (flowering plant)
Nigella sativa	love-in-a-mist (flowering plant)
Nippostrongylus brasiliensis	gut parasite of rodents
Nitocra spinipes	shrimp
Nitrobacter spp.	bacteria
Nitrosococcus oceanus	nitrogen-fixing bacterium
Nitrosolobus multiformis	bacterium
Nitrosomonas spp.	nitrogen-fixing bacteria
Nitzschia closterium	diatom
Nocardia spp.	bacteria
Nodularia spp.	cyanobacteria
Normuraea rileyi	fungus
Nostoc spp.	cyanobacteria
Notopterus notopterus	knifefish
Oedogonium spp.	filamenous green algae
Oesophagostomum columbianum	intestinal worm of sheep and goats
Oikomonas termo	cyanobacterium
Oligocottus maculosus	tidepool sculpin
Oncopeltus fasciatus	milkweed bug
Oncorhynchus kisutch	coho salmon
Oocystis parva	green alga
Opercularia spp.	protozoans
Ophiogomphus spp.	dragonflies
Orconectes immunis	crayfish
Orconectes nais	crayfish
Oreochromis niloticus	catfish, hybrid tilapia
Oryzias latipes	rice fish
Oscillatoria terebriformis	cyanobacterium
Ostrea sinuata	oyster
Paecilomyces spp.	fungi
Palaemon elegans	shrimp
Palaemon macrodactylus	grass shrimp
Palaemon serratus	shrimp
Palaemonetes pugio-holthius	crustacean
Palaemonetes spp.	crustaceans
Palicourea maregiavii	flowering plant
Pandalus montagui	shrimp
Paracentrotus lividus	sea urchin
Paracoccus spp.	bacteria
Paralabrax clathratus	site kelp bass
Paralichthys olivaceus	flatfish
Paramecium spp.	ciliate protozoans
Paratanytarsus parthenogeneticus	midge
Paratya compressa improvisa	freshwater shrimp
Paravinella palmiformis	polychaete worm
Paxillus involutus	toadstool
Pectein maximus	scallop
Pediastrum tetras	green alga
Peganum harmala	herb
Pelobacter massiliersis	bacterium
Pelobacter venetianus	bacterium
Penaeus spp.	shrimps
Penicillium spp.	moulds
Peranema gracilis	protozoan
Peridinium spp.	algae
Periplaneta americana	common cockroach
Perna viridis	green mussel
Peromyscus maniculatus	deer mouse
Petroselinum sativum	parsley
Phaeodactylum tricornutum	diatom
Phalaria aquatica	aquatic plant
Phanerochaete chrysosporium	fungus
Phaseolus vulgaris	French bean
Phebalium dentatum	plant
Philodina erythrophthalma	rotifer
Phomopsis sclerotioides	cucumber black root rot fungus
Phormidium fragile	cyanobacterium
Phormidium tenue	cyanobacterium
Photobacterium spp.	bacteria
Phoxinus phoxinus	minnow
Physa spp.	freshwater snails

Physarum polycephalum slime mould
Phytophthora citricola fungus
Phytophthora nicotiana fungus
Phytoseiulus persimilis predatory phytoseiid mite
Picea excelsa Norway spruce tree
Pieris brassicae cabbage white butterfly
Pilocarpus jaborandi jaborandi herb
Pimephales promelas fathead minnow
Pinus spp. pine trees
Pisulithas tinctarius fungus
Pisum sativum green pea
Pityogenes chalcographus bark beetle
Plasmodium spp. protozoans
Platichthys flesus flounder
Platymonas subcordiformis green alga
Pleurodeles waltl sharp-ribbed salamander
Pleurotus ostreatus mushroom
Podocarpus elatus species of yew
Poecilia reticulata guppy
Polycelis tenius flatworm
Polygonum multiflorum Chinese medicinal herb
Polypodium vulgare bracken fern
Porphyridium cruentum red alga
Posidonia oceanica marine phanerogam
Potamogeton natans broad-leaved pondweed
Poteriochromonas malhamensis alga
Procambarus clarkii crayfish
Prorocentrum micans green alga
Proteus spp. bacteria
Protomonas spp. bacteria
Protonemura meyeri stonefly
Prunus domesticus Victoria plum tree
Pseudoacris regilla Pacific bullfrog
Pseudomonas dimunitra bacterium
Pseudomonas spp. bacteria
Pseudorasbora parva fish
Pseudotsuga menziesii Douglas fir tree
Pteronarcys californica stonefly
Pteronarcys dorsata stonefly
Pterotheca falconeri diatom
Pterygophora californica phaeophyte
Puccinia leaf rusts
Puntius conchonius rosy barb
Pycnopsyche spp. aquatic insects
Pyrethrum cinerariaefolium chrysanthemum
Pyricularia oryzae fungus
Pythium ultimatum fungus
Quercus mongolica oak tree
Rana spp. frogs
Raphanus sativus radish
Rasbora trilineata guppy
Rauwolfia spp. tropical African shrubs
Rengia cuneata atlantic rangea clam
Rhabdosargus holubi estuarine fish
Rhepoxynius abronius estuarine/marine amphipod
Rhithropanopeus hamisii Harris mud crab
Rhizobium spp. bacteria
Rhizoctonia bataticola fungus
Rhizoctonia solani fungus
Rhizopus spp. fungi
Rhodobacter sphaeroides purple non-sulfur bacterium
Rhodococcus spp. bacteria
Rhododendron sichtonensis rhododendron
Rhodophyllus icterus fungus
Rhodopseudomonas palustris bacterium
Rhus vernicifera sumac tree
Ricinus communis castor bean
Ridgeia pisceae tube worm
Riftia pachyptila tube worm
Rubina oncotricha plant
Rubus laciniatus evergreen blackberry
Ruminococcus flavefaciens bacterium
Russula foetens mushroom
Russula vesca mushroom
Ruta graveolens rue (herb)
Saccharomyces cerevisiae brewer's yeast
Saccobranchus fossilis airsac catfish
Salientia frogs and toads
Salix matsudana willow tree
Salmo gairdneri rainbow trout
Salmonella spp. bacteria
Salsola goosefoot plants
Saprolegnia terrestrial fungi
Sargassum filipendula seaweed
Sargassum fruitans brown alga
Sarotheredon spp. cichlids
Scaphechinus mirabilis sand dollar
Scedosporium spp. fungi
Scenedesmus spp. green algae
Schinus molle Brazilian pepper tree
Schistosoma mansoni blood fluke
Schizosaccharomyces pombe yeast
Scirpophaga incertulas yellow stem borer (lepidopteran)
Sclerotinia sclerotiorum fungus
Scopulariopsis brevicaule Bain fungus
Scopulariopsis brumptii fungus
Scrobicularia plana marine bivalve
Scylla serrata marine edible crab
Scytonema schmidlei nitrogen-fixing cyanobacterium
Secale cereale winter rye
Selenastrum spp. green algae
Semisulcospira libertina freshwater gastropod

Senecio spp.	groundsel, ragwort
Serratia spp.	bacteria
Shigella spp.	bacteria
Sialis flavilatera	fishfly
Siboglinum poseidoni	marine beard worm
Sickingia rubra	tree
Siderocapsa spp.	bacteria
Simocephalus serrulatus	water flea
Simulium venustum	black flies
Sitophilus oryzae	rice weevil
Skeletonema costatum	alga
Solandra nitida	golden chalice vine
Somateria mollissima	common eider duck
Spathosternum prasiniferum	grasshopper
Sphaerechinus granularis	sea urchin
Sphaerium stratinum	fingernail clam
Sphaerotilus spp.	bacteria
Sphagnum cuspidatum	sphagnum moss
Sphingomonas spp.	bacteria
Spirodela polyrhiza	greater duckweed
Spirulina platensis	cyanobacterium
Spizella pallida	clay-coloured sparrow
Spodoptera frugipeda	fall armyworm moth
Spodoptera litura	tobacco cutworm
Spondyius squamosus	shellfish
Staphylococcus spp.	bacteria
Stemphylium loti	cyanogenic plant
Sterculia urens	tree
Stereum purpureum	filamentous fungus
Stibiobacter senarmontii	bacterium
Stichococcus bacillaris	alga
Stigeoclonium pachydermum	green alga
Streptocephalus proboscideus	shrimp
Streptococcus spp.	bacteria
Streptomyces spp.	bacteria
Streptoverticillium ladakanus	bacterium
Strongylocentrotus purpuratus	purple sea urchin
Strophanthus gratus	cream fruit plant
Strophanthus kombe	latex bearing shrub
Strychnos nux-vomica	poisonous plant
Sympetrum frequens	dragonfly
Symphytum caucasicums	comfrey
Synechococcus spp.	cyanobacteria
Syntrophomonas spp.	bacteria
Tanytarsus dissimilis	midge
Temora longicornis	zooplankton
Tendipedidae	midges
Tephrosia hamiltonii	flowering plant
Terpius zeteki	sponge
Tetrahymena spp.	ciliate protozoans
Tetranychus urticae	glasshouse spider mite
Thalassiosira pseudonana	marine diatom
Thermoactinomycetes spp.	bacteria
Thiara tuberculata	freshwater mussel
Thiobacillus spp.	bacteria
Thiosphaera pantotropha	bacterium
Thymus vulgaris	thyme (herb)
Tilapia mossambica	cichlid
Tilapia nilotica	cichlid
Tineidae spp.	moths
Tinomiscium philippense	plant
Tolypocladium inflatum	fungus imperfectus
Trachelophyllum spp.	protozoans
Tradescentia spp.	flowering plants
Trapa natans	aquatic plant
Tribolium castaneum	flour beetle
Tribonema aequale	yellow-green alga
Trichinella spinalis	nematode
Trichoderma spp.	filamentous fungi
Trichogramma brassicae	parasitic wasp
Trichomonas vaginalis	protozoan
Trichoplusia ni	cabbage looper moth
Trichosporan cutaneum	fungus
Trichosporon spp.	yeasts
Tridacna spp.	clams
Trifolium spp.	clover
Trigriopus brevicornis	copepod
Triticum aestivum	wheat
Triturus helveticus	newt
Tubifex tubifex	tubifex worm
Tussilago farfara	coltsfoot (plant)
Tydeus spp.	mites
Typhula spp.	fungi
Uca pugilator	fiddler crab
Unio pictorium	mollusc
Urginea maritima	sea onion
Uronema parduczi	ciliate protozoan
Valerianella locusta	herb
Vallisneria natans	aquatic plant
Veillonella parvula parvula	bacterium
Verticilliastrum spp.	fungi
Verticillium agaricinum	wilt fungus
Verticillium albo-atrum	fungus
Vibrio spp.	bacteria
Vicia faba	broad bean
Vigna sinensis	cowpea plant
Vinca spp.	periwinkles
Viviporus bergalersis	freshwater snail
Vorticella spp.	protozoans
Westiellopsis prolifica	cyanobacteria
Williopsis saturnus	yeast
Woloszynskia coronata	green alga
Xanthium strumarium	cocklebur plant
Xanthobacter spp.	bacteria

Xanthomonas spp.	bacteria	*Zea mays*	maize
Xenopus spp.	frogs	*Zoogloea ramigera*	bacterium

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