

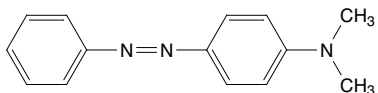
4-Dimethylaminoazobenzene

CAS No. 60-11-7

Reasonably anticipated to be a human carcinogen

First listed in the *Second Annual Report on Carcinogens* (1981)

Also known as *para*-dimethylaminoazobenzene, *N,N*-dimethyl-4-aminoazobenzene, or butter yellow



Carcinogenicity

4-Dimethylaminoazobenzene is *reasonably anticipated to be a human carcinogen* based on sufficient evidence of carcinogenicity from studies in experimental animals.

Cancer Studies in Experimental Animals

4-Dimethylaminoazobenzene caused tumors in several species of experimental animals, at several different tissue sites, and by several different routes of exposure. In rats of unspecified sex, oral administration or subcutaneous injection of 4-dimethylaminoazobenzene caused liver cancer (hepatocellular carcinoma) that metastasized to other organs. Liver tumors also were observed in rats of unspecified sex administered 4-dimethylaminoazobenzene by intraperitoneal injection. Following subcutaneous injection of 4-dimethylaminoazobenzene in newborn mice, males developed liver tumors by 1 year of age. In dogs of unspecified sex, oral exposure to 4-dimethylaminoazobenzene caused benign urinary-bladder tumors (papilloma). Dermal exposure to 4-dimethylaminoazobenzene caused skin cancer (squamous- or basal-cell carcinoma or anaplastic carcinoma) in male rats, but not in mice. (IARC 1975).

Since 4-dimethylaminoazobenzene was listed in the *Second Annual Report on Carcinogens*, additional studies in rodents have been identified. Dietary administration of 4-dimethylaminoazobenzene to male mice for 14 months resulted in development of benign and malignant liver tumors (adenoma after 104 days and carcinoma after 10 months) (Caballero *et al.* 2004). Following intraperitoneal injection with 4-dimethylaminoazobenzene before the age of 22 days, male rats developed liver cancer (hepatocellular carcinoma) by the age of 2 years. Intraperitoneal injection of 12-day-old mice with 4-dimethylaminoazobenzene increased the incidence of liver tumors and number of tumors per animal in males (Delclos *et al.* 1984). Implantation of pellets containing 4-dimethylaminoazobenzene in the livers of male rats increased the incidence of liver cancer (hepatocellular carcinoma); however, implantation in the kidney did not cause kidney tumors (Aterman 1987).

Cancer Studies in Humans

No epidemiological studies were identified that evaluated the relationship between human cancer and exposure specifically to 4-dimethylaminoazobenzene.

Properties

4-Dimethylaminoazobenzene is an azo amine dye that exists at room temperature as yellow crystalline leaflets. It is practically insoluble in water, but is soluble in alcohol, benzene, chloroform, ether, petroleum ether, mineral acids, and oils, and is very soluble in pyridine. It is stable under normal temperatures and pressures (Akron 2009). Physical and chemical properties of 4-dimethylaminoazobenzene are listed in the following table.

Property	Information
Molecular weight	225.3 ^a
Density	1.2 g/cm ^{3b}
Melting point	114°C to 117°C ^a
Boiling point	371°C ^b
Log <i>K</i> _{ow}	4.58 ^a
Water solubility	0.23 mg/L at 25°C ^c
Vapor pressure	3.3 × 10 ⁻⁷ mm Hg ^a
Vapor density relative to air	7.78 ^a
Dissociation constant (p <i>K</i> _a)	2.96 at 25°C ^c

Sources: ^aHSDB 2009, ^bAkron 2009, ^cChemIDplus 2009.

Use

4-Dimethylaminoazobenzene is an industrial chemical that has been used to color polishes and other wax products, polystyrene, gasoline, and soap. It has been used as a pH indicator, especially for gastric juices, and as a spot test for identification of peroxidized fats. It is also used as a positive-control substance to induce liver cancer in experimental animals. Previously, it was used as a colorant (butter yellow) in hair creams (brilliantine) in Scandinavia (IARC 1975, Akron 2009, HSDB 2009). 4-Dimethylaminoazobenzene was approved for use as a food additive in 1918, but was withdrawn six months later because of contact dermatitis from occupational exposure (IARC 1975).

Production

4-Dimethylaminoazobenzene was first made in 1876, and large-scale production in the United States was first reported in 1914 (IARC 1975). In 1972, 4-dimethylaminoazobenzene was one of a group of at least 20 colorants with U.S. production totaling 466,000 kg (1 million pounds); however, no individual production data were available. In 2009, no producers of 4-dimethylaminoazobenzene were identified worldwide (SRI 2009), but it was available from 24 suppliers, including 13 U.S. suppliers (ChemSources 2009). No data on U.S. imports or exports were found specifically for 4-dimethylaminoazobenzene.

Exposure

The routes of potential human exposure to 4-dimethylaminoazobenzene are inhalation, dermal contact, and ingestion. 4-Dimethylaminoazobenzene was a component of brilliantine, which was commonly applied after men's haircuts in some portions of Europe until about 1950 (Skov and Lynge 1994).

According to the U.S. Environmental Protection Agency's Toxics Release Inventory, no environmental releases of 4-dimethylaminoazobenzene occurred in 2000. Releases totaled 750 lb in 2001 and 250 lb in 2002, and have since remained at about the same level. In 2009, one facility released 256 lb of 4-dimethylaminoazobenzene to an off-site hazardous waste landfill (TRI 2009). When released to air, 4-dimethylaminoazobenzene is expected primarily to bind to particulate matter; however, the vapor-phase fraction may be subject to direct photolysis or reaction with photochemically produced hydroxyl radicals, with a half-life of 7 hours. When released to surface water, 4-dimethylaminoazobenzene is expected to bind to sediment or to bioaccumulate in aquatic organisms; it will not hydrolyze and may be subject to biodegradation. When released to soil, it will most likely bind to soil particles and not leach into groundwater; however, its mobility is affected by soil pH (HSDB 2009).

The National Occupational Exposure Survey (conducted from 1981 to 1983) estimated that 1,453 workers in the Health Services industry, including 996 women, and an additional 23 workers in the Textile Mill Products industry potentially were exposed to 4-dimethylaminoazobenzene (NIOSH 1990). Also potentially exposed to 4-dimethylaminoazobenzene are laboratory workers who use it as a positive-control substance in studies of liver cancer or as a

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reagent in determining free hydrochloric acid in gastric juices (IARC 1975, HSDB 2009).

Regulations

Environmental Protection Agency (EPA)

Clean Air Act

National Emissions Standards for Hazardous Air Pollutants: Listed as a hazardous air pollutant.

Comprehensive Environmental Response, Compensation, and Liability Act

Reportable quantity (RQ) = 10 lb.

Emergency Planning and Community Right-To-Know Act

Toxics Release Inventory: Listed substance subject to reporting requirements.

Resource Conservation and Recovery Act

Listed Hazardous Waste: Waste code for which the listing is based wholly or partly on the presence of 4-dimethylaminoazobenzene = U093.

Listed as a hazardous constituent of waste.

Occupational Safety and Health Administration (OSHA)

Potential occupational carcinogen: Engineering controls, work practices, and personal protective equipment are required.

Guidelines

National Institute for Occupational Safety and Health (NIOSH)

Listed as a potential occupational carcinogen.

References

Akron. 2009. *The Chemical Database*. The Department of Chemistry at the University of Akron. <http://ull.chemistry.uakron.edu/erd> and search on CAS number. Last accessed: 5/09.

Aterman K. 1987. Localized hepatocarcinogenesis: the response of the liver and kidney to implanted carcinogens. *J Cancer Res Clin Oncol* 113(6): 507-538.

Caballero F, Meiss R, Gimenez A, Batlle A, Vazquez E. 2004. Immunohistochemical analysis of heme oxygenase-1 in preneoplastic and neoplastic lesions during chemical hepatocarcinogenesis. *Int J Exp Pathol* 85(4): 213-222.

ChemIDplus. 2009. *ChemIDplus Advanced*. National Library of Medicine. <http://chem.sis.nlm.nih.gov/chemidplus/chemidheavy.jsp> and select Registry Number and search on CAS number. Last accessed: 5/12/09.

ChemSources. 2009. *Chemical Sources - Chemical Search*. Chemical Sources International. <http://www.chemsources.com/chemonline.html> and search on dimethylaminoazobenzene. Last accessed: 5/09.

Delclos KB, Tarpley WG, Miller EC, Miller JA. 1984. 4-aminoazobenzene and *N,N*-dimethyl-4-aminoazobenzene as equipotent hepatic carcinogens in male C57BL/6 X C3H/He F₁ mice and characterization of *N*-(deoxyguanosin-8-yl)-4-aminoazobenzene as the major persistent hepatic DNA-bound dye in these mice. *Cancer Res* 44(6): 2540-2550.

HSDB. 2009. *Hazardous Substances Data Bank*. National Library of Medicine. <http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?HSDB> and search on CAS number. Last accessed: 5/09.

IARC. 1975. *para*-Dimethylaminoazobenzene. In *Some Aromatic Azo Compounds*. IARC Monographs on the Evaluation of Carcinogenic Risk of Chemicals to Humans, vol. 8. Lyon, France: International Agency for Research on Cancer. pp. 125-146.

NIOSH. 1990. *National Occupational Exposure Survey (1981-83)*. National Institute for Occupational Safety and Health. Last updated: 7/1/90. <http://www.cdc.gov/noes/noes1/26175sic.html>.

Skov T, Lyngge E. 1994. Cancer risk and exposures to carcinogens in hairdressers. *Skin Pharmacol* 7(1-2): 94-100.

SRI. 2009. *Directory of Chemical Producers*. Menlo Park, CA: SRI Consulting. Database edition. Last accessed: 5/09.

TRI. 2009. *TRI Explorer Chemical Report*. U.S. Environmental Protection Agency. <http://www.epa.gov/triexplorer> and select 4-Dimethylaminoazobenzene. Last accessed: 5/09.