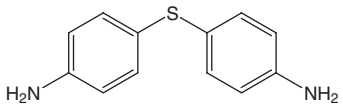
4,4´-Thiodianiline
CAS No. 139-65-1

Reasonably anticipated to be a human carcinogen
First Listed in the *Eleventh Report on Carcinogens* (2004)



Carcinogenicity

4,4´-Thiodianiline (thiodianiline) is *reasonably anticipated to be a human carcinogen* based on sufficient evidence of carcinogenicity in experimental animals. Dietary exposure to thiodianiline significantly increased the incidence of tumors at multiple tissue sites in mice and rats. In mice, thiodianiline caused liver and thyroid tumors (NCI 1978). In rats, thiodianiline caused primarily tumors of the thyroid, liver, and ear canal (Zymbal gland) in males and tumors of the thyroid and uterus in females. Colon tumors in male rats and Zymbal gland tumors in female rats also were observed and were considered to be related to thiodianiline exposure because of the rarity of these types of tumors (NCI 1978, Cueto and Chu 1979). The International Agency for Research on Cancer (1982) also has concluded that there was sufficient evidence for the carcinogenicity of thiodianiline in experimental animals. Further support for the carcinogenicity of thiodianiline was provided by subsequent studies in *ras*H2 transgenic mice (which carry a human gene potentially associated with cancer). Dietary exposure to thiodianiline caused thyroid follicular-cell hyperplasia (increased cell proliferation) and adenoma (benign tumors) in transgenic mice and their nontransgenic littermates (Yamamoto *et al.* 1998a, Yamamoto *et al.* 1998b).

No studies evaluating the carcinogenicity of thiodianiline in humans were found in the published literature.

Additional Information Relevant to Carcinogenicity

Thiodianiline caused mutations in some strains of the bacterium *Salmonella typhimurium* (TA98 and TA100) but not others (TA1535 and TA1537) (IARC 1982). Thiodianiline orally administered to mice caused DNA damage in the brain, liver, urinary bladder, and lungs.

No information on human absorption, metabolism, or excretion of thiodianiline was found in the published literature. In rats, thiodianiline bound to hemoglobin as both the diamine and *N*-acetylamine. Among several bicyclic diamines studied (including thiodianiline), the extent of hemoglobin binding was positively correlated with carcinogenic potency (IARC 1982). Studies of the relationship between chemical structure and carcinogenic activity have suggested that the aryl-amino group of thiodianiline is most likely to be involved in its carcinogenicity. Three other dianiline compounds (4,4´-oxydianiline, 4,4´-methylenedianiline, and 4,4´-methylenebis[2-chloroaniline]) that are listed in the Report on Carcinogens as *reasonably anticipated to be human carcinogens* cause some of the same types of tumors in animals as thiodianiline.

Properties

Thiodianiline is an aromatic amine with a molecular weight of 216.3, occurring as brown to brown-violet powder or needles. It is slightly soluble in water and soluble in ethanol, ether, and hot benzene. Its melting point is 108°C to 111°C. Thiodianiline is noncombustible, but when heated, it may decompose to form irritating and toxic fumes. Hazardous decomposition products include nitrogen oxides, carbon monoxide, carbon dioxide, nitrogen, and sulfur oxides. Thiodianiline is stable under normal laboratory conditions but is incompatible with oxidizing agents and excess heat (IARC 1982, Fisher Scientific 2000, HSDB 2003).

Use

Thiodianiline was used almost exclusively as a chemical intermediate in the production of three dyes: C.I. mordant yellow 16, milling red G, and milling red FR. However, only C.I. mordant yellow had any commercial significance in the United States (IARC 1982, HSDB 2003); it was used to dye wool and for printing on wool, silk, and cotton (SDC 1971). C.I. mordant yellow 16 has been used as an indicator in the United States government's nerve gas detector program (SOCMA 2002). However, no uses of either thiodianiline or C.I. mordant yellow 16 since the early 1990s have been reported.

Production

Thiodianiline is prepared by reaction of aniline with sulfur (IARC 1982, HSDB 2003). U.S. production was first reported for 1941 to 1943 (IARC 1982); however, thiodianiline is no longer produced in the United States. The U.S. Dye Manufacturers Operating Committee of the Ecological and Toxicological Association of Dyes and Organic Pigments Manufacturers speculates that only a few hundred pounds of thiodianiline are imported into the United States each year (SOCMA 2002). U.S. production of C.I. mordant yellow 16 was last reported for 1991 (USITC 1993). Separate statistics for this dye were not available; however, total mordant dye production was 33,100 kg (73,000 lb) in 1987, 29,000 kg (64,000 lb) in 1989, and 9,000 kg (19,800 lb) in 1990 (USITC 1988, 1990, 1991). One U.S. producer was identified in 1983 and 1984 (SRI 1983, 1984), but none was listed in 2003 (SRI 2003). Thiodianiline is produced in China (SRI 2003), and at least 11 U.S. suppliers of thiodianiline were reported in 2003 (ChemSources 2003).

Exposure

Dye workers may have been exposed to thiodianiline through skin contact, accidental ingestion, or inhalation.

Regulations

EPA

Emergency Planning and Community Right-to-Know Act

Toxics Release Inventory: Listed substance subject to reporting requirements

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