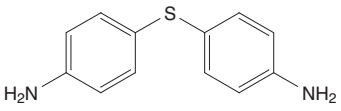
4,4′-Thiodianiline

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

Cancer Studies in Experimental Animals

Oral exposure to 4,4′-thiodianiline caused tumors at several different tissue sites in mice and rats. Dietary admnistration of 4,4′-thiodianiline caused thyroid-gland cancer (follicular-cell carcinoma) in mice and rats of both sexes and liver cancer (hepatocellular carcinoma) in mice of both sexes and in male rats (NCI 1978). In rats, 4,4′-thiodianiline also caused cancer of the uterus (adenocarcinoma) in females and increased the combined incidence of benign and malignant tumors of the ear canal (Zymbal gland) in males. In addition, colon tumors in male rats and Zymbal-gland tumors in female rats were considered to be related to 4,4′-thiodianiline exposure because of the rarity of these types of tumors (NCI 1978, Cueto and Chu 1979). In studies with *ras*H2 transgenic mice (which carry a human gene that increases their susceptibility to cancer), dietary exposure to 4,4′-thiodianiline caused increased proliferation of thyroid follicular cells and benign thyroid-gland tumors (follicular-cell hyperplasia and adenoma) in transgenic mice and their nontransgenic littermates (Yamamoto *et al.* 1998a,b).

Cancer Studies in Humans

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

Studies on Mechanisms of Carcinogenesis

4,4′-Thiodianiline caused mutations in some strains of *Salmonella typhimurium* (TA98 and TA100) but not others (TA1535 and TA1537). 4,4′-Thiodianiline orally administered to mice caused DNA damage in the brain, liver, urinary bladder, and lungs. In rats, 4,4′-thiodianiline binds to hemoglobin as both the diamine and the *N*-acetylamine. Among several bicyclic diamines studied (including 4,4′-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 4,4′-thiodianiline is most likely involved in its carcinogenicity. Three other dianiline compounds listed in the Report on Carcinogens as *reasonably anticipated to be human carcinogens* — 4,4′-oxydianiline, 4,4′-methylenedianiline, and 4,4′-methylenebis(2-chloroaniline) — cause some of the same types of tumors in animals as 4,4′-thiodianiline does.

Properties

4,4′-Thiodianiline is an aromatic amine that exists as brown powder or needles at room temperature. It is very slightly soluble in water and very soluble in alcohol, ether, and hot benzene. 4,4′-Thiodianiline is stable under normal temperatures and pressures (Akron 2009).

Physical and chemical properties of 4,4′-thiodianiline are listed in the following table.

Property	Information
Molecular weight	216.3[a]
Melting point	108°C to 109°C[a]
Boiling point	361°C[b]
Log K_{ow}	2.18[b]
Water solubility	0.310 g/L at 25°C[b]
Vapor pressure	1.11×10^{-5} mm Hg at 25°C[b]

Sources: [a]HSDB 2009, [b]ChemIDplus 2009.

Use

4,4′-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 mordant yellow 16 had any commercial significance in the United States (IARC 1982, HSDB 2009); it was used to dye wool and for printing on wool, silk, and cotton (SDC 1971). Mordant yellow 16 has been used as an indicator in the U.S. government's nerve gas detector program (SOCMA 2002). However, no uses of either 4,4′-thiodianiline or mordant yellow 16 since the early 1990s have been reported.

Production

4,4′-Thiodianiline is prepared by reaction of aniline with sulfur (IARC 1982, HSDB 2009). U.S. production was first reported for 1941 to 1943 (IARC 1982); however, 4,4′-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 speculated in 2002 that only a few hundred pounds of 4,4′-thiodianiline were imported into the United States each year (SOCMA 2002). U.S. production of mordant yellow 16 was last reported for 1991 (USITC 1993). Separate production statistics for mordant yellow 16 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). In 2009, 4,4′-thiodianiline was produced in China (SRI 2009) and was available from 15 U.S. suppliers (ChemSources 2009). One U.S. producer of mordant yellow 16 was identified in 1983 and 1984 (SRI 1983, 1984), but none in 2009 (SRI 2009).

Exposure

Dye workers may have been exposed to 4,4′-thiodianiline through skin contact, accidental ingestion, or inhalation.

Regulations

Environmental Protection Agency (EPA)

Emergency Planning and Community Right-To-Know Act

Toxics Release Inventory: Listed substance subject to reporting requirements.

Department of Transportation (DOT)

Toxic dyes and toxic dye intermediates are considered hazardous materials, and special requirements have been set for marking, labeling, and transporting these materials.

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