

Toluene Diisocyanates

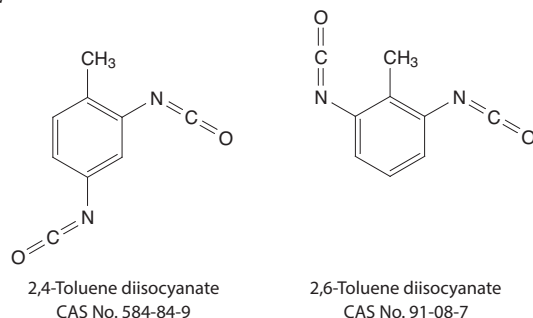
CAS No. 26471-62-5

Reasonably anticipated to be human carcinogens

First listed in the *Fourth Annual Report on Carcinogens* (1985)

Also known as TDI; 1,3-diisocyanatomethyl benzene; isocyanic acid, methyl-*m*-phenylene ester; or tolylene diisocyanate

Isomers also known as toluene-2,4-diisocyanate and toluene-2,6-diisocyanate



Carcinogenicity

Toluene diisocyanates are *reasonably anticipated to be human carcinogens* based on sufficient evidence of carcinogenicity from studies in experimental animals.

Cancer Studies in Experimental Animals

Oral exposure to toluene diisocyanates caused tumors at several different tissue sites in rats and mice. Administration of commercial-grade toluene diisocyanate (analyzed as 85% 2,4 isomer and 15% 2,6 isomer) by stomach tube caused liver tumors (hepatocellular adenoma) in female rats and mice, benign tumors of the mammary gland (fibroadenoma) and pancreas (islet-cell adenoma) in female rats, and benign tumors of the pancreas (acinar-cell adenoma) in male rats. It also increased the combined incidences of benign and malignant tumors of subcutaneous tissue (fibroma and fibrosarcoma) in rats of both sexes and of the blood vessels (hemangioma and hemangiosarcoma) in female mice (NTP 1986).

Cancer Studies in Humans

No epidemiological studies were identified that evaluated the relationship between human cancer and exposure specifically to toluene diisocyanates.

Properties

Toluene diisocyanates exist at room temperature as a clear, colorless to pale-yellow liquid with a pungent odor. They decompose in water, but are very soluble in acetone and benzene, and are miscible with ether, diglycol monomethyl ether, carbon tetrachloride, chlorobenzene, kerosene, and olive oil. They are combustible when exposed to heat or flame and darken when exposed to sunlight (IARC 1999, HSDB 2009). 2,4-Toluene diisocyanate is available as a commercial product with purity of at least 99.5%, but most commonly as an 80:20 mixture of 2,4-toluene diisocyanate and 2,6-toluene diisocyanate (IARC 1986). Physical and chemical properties of toluene diisocyanates are listed in the following table.

Use

Toluene diisocyanates are used primarily to manufacture flexible polyurethane foams for use in furniture, bedding, and automotive and airline seats. Other, smaller uses are for polyurethane elastomers

Property	Toluene diisocyanates mixed	2,4-Toluene diisocyanate	2,6-Toluene diisocyanate
Molecular weight ^a	174.2	174.2	174.2
Specific gravity at 25°C ^a (g/mL)	1.22 or 0.01	1.22 or 0.01	1.22 or 0.01
Melting point ^a	11°C to 14°C (FP)	19.5°C to 21.5°C	18.3°C
Boiling point ^a	251°C	251°C	129°C to 133°C at 18 mm Hg
Log <i>K</i> _{ow} ^b	3.74	3.74	3.74
Water solubility at 25°C ^b	0.0376 g/L	0.0376 g/L	decomposes
Vapor pressure ^a	2.30 × 10 ⁻² mm Hg at 25°C	8.0 × 10 ⁻³ mm Hg at 20°C	2.1 × 10 ⁻² mm Hg at 25°C
Vapor density relative to air ^c	6	6	6

Sources: ^aHSDB 2009, ^bChemIDplus 2009, ^cAkron 2009. FP = freezing point.

(for automobile bumper covers, industrial rollers, sport soles and boots, and mechanical goods) and coatings (for automotive refinishing, wood finishes, and high-performance anti-corrosion coatings) (ICIS 2009). Toluene diisocyanate-based rigid polyurethane foam is used in household refrigerators and for residential sheathing or commercial roofing in board or laminate form (IARC 1986). "Pour-in-place" or "spray-in" rigid foam is used as insulation for truck trailers, railroad freight cars, and cargo containers. Polyurethane-modified alkyds contain approximately 6% to 7% isocyanate, mostly toluene diisocyanates, and are used as coating materials, such as floor finishes, wood finishes, and paints. Moisture-curing coatings are used as wood and concrete sealants and floor finishes. Aircraft, truck, and passenger-car coatings often are composed of toluene diisocyanate prepolymer systems. Castable urethane elastomers are used in applications requiring strength, flexibility, and shock absorption, and are resistant to oil, solvents, and ultraviolet radiation. They are used in adhesive and sealant compounds and in automobile parts, shoe soles, rollerskate wheels, pond liners, and blood bags. They are also used in oil fields and mines. Certain elastomer products are produced from the pure 2,4 isomer rather than the 80:20 mixture.

Production

Toluene diisocyanates have been produced commercially since the late 1930s (IARC 1986). In 1993, the production capacity for toluene diisocyanates in North America was estimated at more than 1 billion pounds (IARC 1999). In 2009, the United States had one supplier of mixed toluene diisocyanates, three suppliers of 2,6-toluene diisocyanate, and fourteen suppliers of 2,4-toluene diisocyanate (Chem-Sources 2009). Combined U.S. production and imports of an 80:20 mixture of 2,4- and 2,6-toluene diisocyanate ranged from 100 million to over a billion pounds between 1986 and 2006 (EPA 2004, 2009); in 2015, the total volume was in the range of 500 million to 750 million pounds (as shown in the table below). U.S. imports of mixed isomers of toluene diisocyanate increased from 2,200 lb in 1996 to 32 million pounds in 2006; the volume has since fluctuated, but reached nearly 100 million pounds in 2017 (USITC 2009, 2018). U.S. exports of mixed isomers of toluene diisocyanate increased from 125 million pounds in 1989 to 609 million pounds in 2003, but have since trended lower; the volume for 2017 was below 50 million pounds (USITC 2009, 2018).

Category	Year	Quantity (million lb)
Production + imports ^a	2015	500 to 750
U.S. imports ^b	2017	98.4
U.S. exports ^b	2017	48.1

Sources: ^aEPA 2016 (reported as "2,4/2,6-toluene diisocyanate"), ^bUSITC 2018 (reported as "mixtures of 2,4- and 2,6-toluene diisocyanates," proportions unknown).

Exposure

The primary routes of potential human exposure to toluene diisocyanates are inhalation and dermal contact. Exposure to toluene diisocyanates is primarily occupational; however, several commercially available household products may pose a risk of exposure to toluene diisocyanates to the general population if used indiscriminately. For example, consumers may be exposed to toluene diisocyanates volatilized from polyurethane varnishes during the application of such coatings (IPCS 1987). A model developed to predict the background concentration of toluene diisocyanate in Western Europe estimated that if annual toluene diisocyanate usage were 100,000 tons, the background air concentration would be approximately $0.0001 \mu\text{g}/\text{m}^3$ (Tury *et al.* 2003).

According to EPA's Toxics Release Inventory, environmental releases of mixed toluene diisocyanates were highest in 2001 and 2004, at over 125,000 lb; 45,642 lb was released in 2003. The same trend held for the individual isomers; however, releases were lowest in 1995 for 2,4-toluene diisocyanate and in 2002 for 2,6-toluene diisocyanate. In 2006, releases of toluene diisocyanates (mixed isomers), 2,4-toluene diisocyanate, and 2,6-toluene diisocyanate from 139 facilities totaled 73,778 lb (TRI 2009).

Because of the high volatility of toluene diisocyanates, exposure can occur in all phases of its manufacture and use (IPCS 1987). Toluene diisocyanate occurs in the work environment, primarily in air, during its commercial production, handling, and processing and during the production of polyurethane foam and coated fabrics. However, manual handlers of uncured polyurethane foam were significantly more likely to have detectable urinary adducts of toluene diisocyanates than non-handlers working in areas with similar air concentrations of toluene diisocyanate (Austin 2007). The National Occupational Exposure Survey (conducted from 1981 to 1983) estimated that nearly 40,000 workers potentially were exposed to toluene diisocyanates (NIOSH 1990). Workers potentially exposed to toluene diisocyanates include adhesive workers, insulation workers, diisocyanate-resin workers, lacquer workers, organic-chemical synthesizers, paint sprayers, polyurethane makers, rubber workers, ship builders, textile processors, and wire-coating workers (IPCS 1987). Worker exposure to toluene diisocyanates is most likely to occur during sample collection, residue removal, spill clean-up, and equipment maintenance; employees are required to use air-line respirators during these operations. The highest exposure levels have occurred during the spray application of polyurethane foam. The construction industry uses polyurethane formulations in thermal insulation, adhesives, lacquers, and paints. In most cases, the foam is applied through air-spraying in confined spaces; exposure to concentrations above safe limits are a particular concern for the sprayers and their helpers. In the United States, a typical modern housing unit of 1,800 ft² floor space, including furniture, carpet underlay, and bedding, contains 306 lb of flexible polyurethane foam. The transportation industry uses approximately 21% of flexible polyurethane foam for automobile seating and padding, resulting in the use of 24 to 31 lb of polyurethane per automobile (IARC 1986).

Studies summarized by the International Agency for Research on Cancer (IARC 1986, 1999) reported workplace air concentrations of toluene diisocyanates ranging from less than 1 to more than $1,000 \mu\text{g}/\text{m}^3$; the current Occupational Safety and Health Administration ceiling concentration is 0.02 ppm ($\sim 140 \mu\text{g}/\text{m}^3$). Workplace air concentrations measured in 2005 close to the mixer in a polyurethane factory were up to $12.1 \mu\text{g}/\text{m}^3$ for 2,4-toluene diisocyanate, $8.1 \mu\text{g}/\text{m}^3$ for 2,6-toluene diisocyanate, and $20.2 \mu\text{g}/\text{m}^3$ for total toluene diisocyanates (Tinnerberg and Mattsson 2008). Analysis of the isomeric composition of atmospheric toluene diisocyanates in a plant pro-

ducing polyurethane foam found a higher concentration of the 2,6 isomer than of the 2,4 isomer, particularly at the finishing end of the production process. Median air concentrations of 2,4-toluene diisocyanate were $5.0 \mu\text{g}/\text{m}^3$ for initial mixing and $2.3 \mu\text{g}/\text{m}^3$ for finishing. The respective median concentrations for the 2,6 isomer were 6.4 and $7.8 \mu\text{g}/\text{m}^3$, with a maximum exceeding $450 \mu\text{g}/\text{m}^3$ at the finishing end. These findings were attributed to enhanced emission of the less chemically active 2,6 isomer from the cured foam bats and retention of the 2,4 isomer as a polymer. Aniline and the 2,4 and 2,6 isomers of toluene diisocyanate were detected under controlled experimental conditions in the thermodegradation fumes of polyurethane varnish used in the insulation of copper wire. Consistent with these findings, the compounds were also detected in the workplace atmosphere during the industrial production of polyurethane-coated wire (IARC 1986, 1999).

Since 2001, exposure has been confirmed by measuring toluene diisocyanate adducts in the plasma and urine of exposed workers. Toluenediamine, a metabolite of toluene diisocyanate, has been measured in the plasma at levels up to 27.2 ng/mL for 2,4-toluenediamine and 62.1 ng/mL for 2,6-toluenediamine (Tinnerberg and Mattsson 2008). Swedish workers manufacturing polyurethane products excreted 53.2 to 259.6 nmol of toluenediamine per gram of creatinine (Bolognesi *et al.* 2001). Concentrations of toluene diisocyanate in urine of occupationally exposed workers ranged from 0 to 76 $\mu\text{g}/\text{L}$ for the 2,4 isomer and from 0 to 31 $\mu\text{g}/\text{L}$ for the 2,6 isomer.

Regulations

Coast Guard (Dept. of Homeland Security)

Minimum requirements have been established for the safe transport of toluene diisocyanate on ships and barges.

Department of Transportation (DOT)

Toluene diisocyanate is considered a hazardous material, and special requirements have been set for marking, labeling, and transporting this material.

Environmental Protection Agency (EPA)

Clean Air Act

National Emission Standards for Hazardous Air Pollutants: 2,4-Toluene diisocyanate is listed as a hazardous air pollutant.

New Source Performance Standards: Manufacture of diisocyanates is subject to certain provisions for the control of volatile organic compound emissions.

Prevention of Accidental Release: Threshold quantity (TQ) = 10,000 lb.

Comprehensive Environmental Response, Compensation, and Liability Act

Reportable quantity (RQ) = 100 lb.

Emergency Planning and Community Right-To-Know Act

Toxics Release Inventory: 2,4-Toluene diisocyanate is subject to reporting requirements.

Resource Conservation and Recovery Act

Listed Hazardous Waste: Waste codes for which the listing is based wholly or partly on the presence of toluene diisocyanates = U223, K027.

Listed as a hazardous constituent of waste.

Occupational Safety and Health Administration (OSHA, Dept. of Labor)

While this section accurately identifies OSHA's legally enforceable PELs for this substance in 2018, specific PELs may not reflect the more current studies and may not adequately protect workers. Ceiling concentration = 0.02 ppm ($0.14 \text{ mg}/\text{m}^3$) for toluene-2,4-diisocyanate.

Guidelines

American Conference of Governmental Industrial Hygienists (ACGIH)

Threshold limit value – time-weighted average (TLV-TWA) = 0.005 ppm.

Threshold limit value – short-term exposure limit (TLV-STEL) = 0.02 ppm.

National Institute for Occupational Safety and Health (NIOSH, CDC, HHS)

Immediately dangerous to life and health (IDLH) limit = 2.5 ppm for toluene-2,4-diisocyanate.

Toluene-2,4-diisocyanate is listed as a potential occupational carcinogen.

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