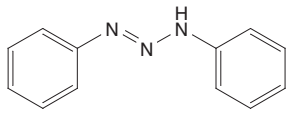
Diazoaminobenzene

CAS No. 136-35-6

Reasonably anticipated to be a human carcinogen

First listed in the *Eleventh Report on Carcinogens* (2004)

Also known as 1,3-diphenyltriazene



Carcinogenicity

Diazoaminobenzene is *reasonably anticipated to be a human carcinogen* based on (1) evidence from studies in experimental animals and with human tissue demonstrating that diazoaminobenzene is metabolized to benzene, a known human carcinogen, and (2) evidence that diazoaminobenzene causes genetic damage. Studies in rats and mice have shown that the metabolism of diazoaminobenzene to benzene is quantitative. Benzene was listed in the First Annual Report on Carcinogens in 1980 based on human epidemiological studies demonstrating that exposure to benzene causes leukemia. Benzene also causes cancer at numerous tissue sites in rodents.

Studies on Mechanisms of Carcinogenesis

Diazoaminobenzene is metabolized to benzene and to the known rodent carcinogen aniline; it also shares similar genotoxic and toxicological properties with these two carcinogens (Bordelon *et al.* 2005). In studies on the absorption, distribution, metabolism, and excretion of diazoaminobenzene orally administered to rats and mice, benzene and aniline were detected in blood, benzene was detected in exhaled breath, and metabolites of benzene and aniline were excreted in urine. Exhalation of benzene implies systemic exposure to this metabolite (Mathews and De Costa 1999; NTP 2002). Metabolites of diazoaminobenzene in the blood of rats and the urine of rats and mice included hydroquinone, muconic acid, and phenylmercapturic acid, which share benzene oxide as a common intermediate, demonstrating that the metabolic pathway of diazoaminobenzene is similar to that of benzene. In studies with human liver slices, diazoaminobenzene was reduced to benzene and aniline (Mathews and De Costa 1999). The proposed metabolic pathway for diazoaminobenzene is reductive cleavage by liver enzymes or by bacteria in the digestive tract to form benzene, aniline, and nitrogen. Benzene and aniline then are metabolized by cytochrome P450 and conjugating enzymes. Electron spin resonance studies have shown that in rats, phenyl radicals also are produced as intermediates in metabolism of diazoaminobenzene to benzene (Kadiiska *et al.* 2000).

In 16-day toxicity studies of rats and mice exposed to diazoaminobenzene (dermally, but without protection of the application site, to allow oral exposure through grooming), the symptoms observed were similar to those characteristic of benzene or aniline toxicity. Diazoaminobenzene also appeared to induce toxic effects not observed with aniline or benzene, including skin lesions at the application site (NTP 2002).

Diazoaminobenzene caused mutations in bacteria with mammalian microsomal metabolic activation (Zeiger *et al.* 1987). It also caused chromosomal aberrations in plants and micronucleus formation in the bone marrow of rodents (Ress *et al.* 2002). Benzene and aniline do not cause mutations in bacteria, but they do induce micronucleus formation in rodents. However, diazoaminobenzene orally administered to mice induced more micronuclei than did equimolar doses of benzene or a mixture of benzene and aniline. The greater genotoxicity of diazoaminobenzene than of its metabolites benzene and aniline may be due to the effects of phenyl radicals formed during its metabolism.

Cancer Studies in Experimental Animals

No studies were identified that evaluated whether exposure to diazoaminobenzene caused cancer in experimental animals.

Cancer Studies in Humans

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

Properties

Diazoaminobenzene is an aromatic amine that exists as small golden-yellow crystals at room temperature. It is insoluble in water but freely soluble in benzene, ether, and hot alcohol. It is stable under normal temperatures and pressures (Akron 2009). Physical and chemical properties of diazoaminobenzene are listed in the following table.

Property	Information
Molecular weight	197.1[a]
Melting point	98°C[a]
Boiling point	305°C[b]
Log K_{ow}	3.99[c]
Water solubility	0.500 g/L[c]
Vapor pressure	1.91×10^{-5} mm Hg at 25°C[c]
Vapor density relative to air	6.8[b]
Dissociation constant (pK_b)	13.00[b]

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

Use

Diazoaminobenzene is used as a chemical intermediate, complexing agent, and polymer additive (Mathews and De Costa 1999). It has uses associated with organic synthesis and dye and insecticide manufacture (Lewis 1997), and it is an effective dopant for laser ablation (micro-machining) of polymethylmethacrylate (Bolle *et al.* 1990). Diazoaminobenzene has been identified as a low-level contaminant in the dyes D&C red no. 33, FD&C yellow no. 5 (tartrazine), and FD&C yellow no. 6; all three are permitted for use in drugs and cosmetics, and the latter two are permitted in food (FDA 2010).

Production

Diazoaminobenzene is produced by reaction of aniline with isoamyl nitrate (Smith and Ho 1990) or by diazotization of aniline dissolved in hydrochloric acid with sodium nitrite, followed by addition of sodium acetate (HSDB 2009). No information was found on levels of diazoaminobenzene production in the United States. Diazoaminobenzene was available from five U.S. suppliers in 2009 (ChemSources 2009). U.S. imports of diazoaminobenzene and *p*-aminoazobenzenedisulfonic acid (combined category) totaled 34,877 lb in 2008 (USITC 2009).

Exposure

The general population may be exposed to diazoaminobenzene through ingestion of products containing dyes or colorants or dermal exposure to such products. A 1977 study by the National Academy of Sciences reported average daily intakes of 43 mg for yellow no. 5 and 37 mg for yellow no. 6 (Feingold 2002). Thus, theoretical maximum average daily exposures to diazoaminobenzene are approximately 1.7 ng for yellow no. 5 and 1.5 ng for yellow no. 6, based on its maximum allowable levels in colorants under U.S. Food and Drug

Administration regulations. Occupational exposure to diazoaminobenzene could occur from its use as a chemical intermediate and polymer additive.

Regulations

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.

Food and Drug Administration (FDA)

The maximum level of diazoaminobenzene in color additives is 40 ppb for FD&C yellow no. 5 and no. 6 and 125 ppb for D&C red no. 33.

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