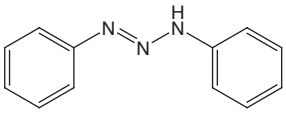
Diazoaminobenzene
CAS No. 136-35-6

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



Carcinogenicity

Diazoaminobenzene (DAAB) is *reasonably anticipated to be a human carcinogen* based on evidence from studies in animals and with human tissue demonstrating that DAAB is metabolized to benzene, a known human carcinogen, and on evidence that DAAB causes genetic damage. Studies in rats and mice have shown the metabolism 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.

In studies on the absorption, distribution, metabolism, and excretion of DAAB orally administered to rats and mice, benzene and aniline (a known animal carcinogen) 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 DAAB 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 DAAB is similar to that of benzene. In studies with human liver slices, DAAB was reduced to benzene and aniline (Mathews and De Costa 1999). The proposed metabolic pathway for DAAB 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 P-450 and conjugating enzymes. Electron spin resonance studies have shown that in rats, phenyl radicals also are produced as intermediates in metabolism of DAAB to benzene (Kadiiska *et al.* 2000).

DAAB causes mutations in bacteria with metabolic activation (addition of rodent liver microsomes to simulate mammalian metabolism) (Zeiger *et al.* 1987). It also causes chromosomal aberrations (changes in chromosome structure or number) in plants and micronucleus formation in the bone marrow of rodents (Ress *et al.* 2002; EPA 1982). Benzene and aniline do not cause mutations in bacteria, but do induce micronuclei in rodents. However, DAAB orally administered to mice induced more micronuclei than did equimolar doses of benzene or a mixture of benzene and aniline. The greater genotoxicity of DAAB than of its metabolites benzene and aniline may be due to the effects of phenyl radicals formed during DAAB metabolism.

Additional Information Relevant to Carcinogenicity

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

No adequate studies in experimental animals were identified in the literature. No human studies were identified that mention exposure specifically to DAAB.

Properties

DAAB is a triazene occurring as small, golden-yellow crystals or an orange solid at room temperature. It melts at 98°C, decomposes at 130°C, and explodes at its boiling point of 150°C. Decomposition products of DAAB include benzene, *o*- and *p*-aminodiphenyl, diphenylamine, and azobenzene. DAAB is soluble in ethyl alcohol, ethyl ether, benzene, pyridine, and hexane, and it is insoluble in water (Mortimore *et al.* 1979, Budavari *et al.* 1996, NTP 2002).

Use

DAAB 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 (micromachining) of polymethylmethacrylate (Bolle *et al.* 1990). DAAB 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 2001).

Production

DAAB 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 2003). No information was found on levels of DAAB production in the United States. DAAB was available from seven U.S. suppliers in 2001. U.S. imports of DAAB and *p*-aminoazobenzenedisulfonic acid (combined category) totaled 94,237 lb (42,746 kg) from January through October 2001 (ITA 2001).

Exposure

The general public may be exposed to DAAB through ingestion of products containing dyes or colorants (e.g., FD&C yellow no. 5) or dermal exposure to such products. A 1977 study by the National Academy of Sciences reported average daily intakes of 43 mg for FD&C yellow no. 5 and 37 mg for FD&C yellow no. 6 (Feingold 2002). Thus, theoretical maximum average daily exposures to DAAB are approximately 1.7 ng for FD&C yellow no. 5 and 1.5 ng for FD&C yellow no. 6, based on the maximum allowable levels of DAAB in colorants under U.S. Food and Drug Administration regulations. Occupational exposure to DAAB could occur from its use as a chemical intermediate and polymer additive.

Regulations

FDA

The maximum level of DAAB in color additives is 40 ppb (FD&C Yellow No. 5 and No. 6), 125 ppb (D&C Red No. 33)

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