

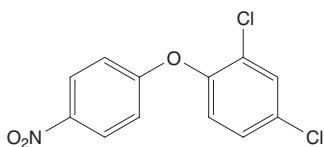
## Nitrofen

### CAS No. 1836-75-5

Reasonably anticipated to be a human carcinogen

First listed in the *Third Annual Report on Carcinogens* (1983)

Also known as 2,4-dichlorophenyl-*p*-nitrophenyl ether or niclofen



### Carcinogenicity

Nitrofen 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 nitrofen caused tumors in two rodent species and at two different tissue sites. Dietary administration of technical-grade nitrofen caused benign and malignant liver tumors in mice (hepatocellular adenoma and carcinoma in both sexes and hemangiosarcoma in males) and cancer of the pancreas (carcinoma) in female rats (NCI 1978, 1979, IARC 1983).

#### Cancer Studies in Humans

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

### Properties

Nitrofen (2,4-dichlorophenyl-*p*-nitrophenyl ether) is a substituted diphenyl ether which at room temperature is a white to yellow to dark brown crystalline solid (NCI 1978, HSDB 2009). It is insoluble in water, soluble in acetone, methanol, xylene, benzene, and *n*-hexane, and slightly soluble in ethanol (HSDB 2009). It darkens on exposure to light (Akron 2009). Physical and chemical properties of nitrofen are listed in the following table.

Property	Information
Molecular weight	284.1 <sup>a</sup>
Specific gravity	1.33 at 90°C <sup>a</sup>
Melting point	70°C to 71°C <sup>a</sup>
Boiling point	180°C to 190°C at 0.25 mm Hg <sup>a</sup>
Log $K_{ow}$	5.534 <sup>a</sup>
Water solubility	0.001 g/L at 22°C <sup>a</sup>
Vapor pressure	$8 \times 10^{-6}$ mm Hg at 40°C <sup>b</sup>

Sources: <sup>a</sup>HSDB 2009, <sup>b</sup>IARC 1983.

### Use

Nitrofen has been used as a contact herbicide on a variety of food and ornamental crops for pre- and post-emergence control of annual grasses and broadleaf weeds (NCI 1979, HSDB 2009). Nitrofen was applied to crops in 25 U.S. states by growers of rice, broccoli, cauliflower, cabbage, Brussels sprouts, onions, garlic, and celery. In 1975, it was estimated that over 800,000 lb of nitrofen was used in the United States; estimated usage on crops was 904,000 lb in 1978 and remained close to that level in 1980 (IARC 1983, HSDB 2009). Nitrofen was also used in nurseries that grew roses and chrysanthemums and on roadsides, but it was not used around homes and gardens (HSDB 2009).

### Production

Nitrofen is no longer manufactured or sold in the United States (HSDB 2009). In 2010, nitrofen was produced by one manufacturer each in China and East Asia (SRI 2010) and was available from 14 suppliers, including 10 U.S. suppliers (ChemSources 2010).

### Exposure

The routes of potential human exposure to nitrofen are inhalation, dermal contact, and incidental ingestion (HSDB 2009). Residues of nitrofen have been found in food crops treated with nitrofen (Yu *et al.* 1979). In 1979, residues were determined in root crops at concentrations of less than 100 ppb in kohlrabi and rutabaga, over 500 ppb in turnips, and over 1 ppm in radishes. In Germany, organic meat products were found to contain nitrofen after a nitrofen storage site was not properly cleaned before its conversion to an organic grain farm (Tuffs 2002). The grain was sold as animal feed to poultry farmers, who sold their animals and animal products to baby-food manufacturers, among others.

When released to air, nitrofen is adsorbed to particulate matter and quickly falls to the ground (HSDB 2009). When released to water, it adsorbs to sediment particles and photolyzes (65% in the first week); its photodecomposition products are 2,4-dichlorophenol and *p*-nitrophenol (Nakagawa and Crosby 1974). When applied to soil, nitrofen adsorbs strongly to soil particles and biodegrades; it is therefore unlikely to leach into groundwater (HSDB 2009).

In China, during screening for endocrine-disrupting pesticides in the Beijing Guanting reservoir, nitrofen was measured in surface water, pore water, and sediment (Xue *et al.* 2005). Nitrofen concentrations were highest in sediment, lower in pore water, and lowest in surface water. The concentrations in water were below Chinese guidelines for surface-water concentrations, and the concentrations in sediment were described as being below the New York State environmental guidance for sediment quality criteria for the protection of human health and the guidelines to protect wildlife (Xue and Xu 2006). A later study confirmed the continuing presence of nitrofen in the reservoir's sediment, pore water, and surface water; concentrations were highest during the times of pesticide application and usually lower during the rest of the year. In sediments measured at seven sites in northern Beijing, the mean concentration of nitrofen was 0.030 ng/g (dry-weight basis) (Xue *et al.* 2008). Nitrofen has been measured in soils very high in organic content (muck soils) in Ontario, Canada, at a peak concentration of 35 ppm in August. The concentration decreased to 18 ppm by October and 14.6 ppm by the following spring; the cold Canadian winter did not promote soil degradation (Murty *et al.* 1982).

Occupational exposure to nitrofen could have occurred mainly through inhalation and dermal contact among workers at production facilities (HSDB 2009). Field handlers of the herbicide also could have been exposed by inhalation and dermal contact during application. Dermal and inhalation exposures were evaluated for applicators using protective garments and handling practices to reduce exposure (Putnam *et al.* 1983). For application of wettable powder formulations, estimated daily exposure was 40,040 µg without protective gear and 535 µg with protective gear. For a pumped emulsifiable concentrate formulation, estimated exposure was 3,916 µg without protection and 225.8 µg with protection.

### Regulations

#### Environmental Protection Agency (EPA)

*Emergency Planning and Community Right-To-Know Act*  
*Toxic Release Inventory*: Listed substance subject to reporting requirements.

## Report on Carcinogens, Fourteenth Edition

### Federal Insecticide, Fungicide, and Rodenticide Act

All product registrations have been voluntarily cancelled.

## References

- Akron. 2009. *The Chemical Database*. The Department of Chemistry at the University of Akron. <http://ull.chemistry.uakron.edu/erd> and search on CAS number. Last accessed: 6/2/09.
- ChemSources. 2010. *Chem Sources - Chemical Search*. Chemical Sources International. <http://www.chemsources.com/chemonline.html> and search on nitrofen. Last accessed: 4/5/10.
- HSDB. 2009. *Hazardous Substances Data Bank*. National Library of Medicine. <http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?HSDB> and search on CAS number. Last accessed: 2/19/09.
- IARC. 1983. Nitrofen. In *Miscellaneous Pesticides*. IARC Monographs on the Evaluation of Carcinogenic Risk of Chemicals to Humans, vol. 30. Lyon, France: International Agency for Research on Cancer. pp. 271-282.
- Murty AS, Miles JRW, Tu CM. 1982. Persistence and mobility of nitrofen (niclofen, TOK) in mineral and organic soils. *J Environ Sci Health—Part B. Pestic, Food Contam Agric Wastes* 17(2): 143-152.
- Nakagawa M, Crosby DG. 1974. Photodecomposition of nitrofen. *J Agric Food Chem* 22(5): 849-853.
- NCI. 1978. *Bioassay of Nitrofen for Possible Carcinogenicity*. Technical Report Series no. 26, DHEW (NIH) Publication no. 78-826. Bethesda, MD: National Institutes of Health. 98 pp.
- NCI. 1979. *Bioassay of Nitrofen for Possible Carcinogenicity*. National Cancer Institute Technical Report Series no. 184, DHEW (NIH) Publication no. 79-1740. Bethesda, MD: National Institutes of Health. 46 pp.
- Putnam AR, Willis MD, Binning LK, Boldt PF. 1983. Exposure of pesticide applicators to nitrofen—influence of formulation, handling systems, and protective garments. *J Agric Food Chem* 31(3): 645-650.
- SRI. 2010. *Directory of Chemical Producers*. Menlo Park, CA: SRI Consulting. Database edition. Last accessed: 4/5/10.
- Tuffs A. 2002. Organic meat products contaminated with carcinogenic herbicide. *Brit Med J* 324(7351): 1416.
- Xue ND, Xu XB. 2006. Composition, distribution, and characterization of suspected endocrine-disrupting pesticides in Beijing GuanTing Reservoir (GTR). *Arch Environ Contam Toxicol* 50(4): 463-473.
- Xue ND, Xu XB, Jin ZL. 2005. Screening 31 endocrine-disrupting pesticides in water and surface sediment samples from Beijing Guanting reservoir. *Chemosphere* 61(11): 1594-1606.
- Xue N, Li F, Hou H, Li B. 2008. Occurrence of endocrine-disrupting pesticide residues in wetland sediments from Beijing, China. *Environ Toxicol Chem* 27(5): 1055-1062.
- Yu TC, Johnson ER, Montgomery ML. 1979. Simultaneous extraction and analysis of trifluralin and nitrofen residues in crucifers. *J Agric Food Chem* 27(6): 1413-1414.