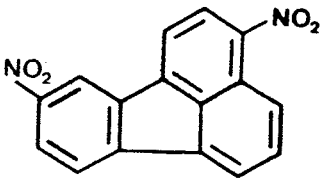
3,9-DINITROFLUORANTHENE

1. Chemical and Physical Data

1.1 Synonyms

Chem. Abstr. Services Reg. No.: 22506-53-2
Chem. Abstr. Name: Fluoranthene, 3,9-dinitro-
IUPAC Systematic Name: 3,9-Dinitrofluoranthene

1.2 Structural and molecular formulae and molecular weight



$C_{16}H_8N_2O_4$ Mol. wt: 292.3

1.3 Chemical and physical properties of the pure substance

(*a*) *Description*: Yellow-orange crystals (Charlesworth & Lithown, 1969); yellow needles (Nakagawa *et al.*, 1987)

(*b*) *Melting-point*: 275–276°C (Charlesworth & Lithown, 1969); 222–224°C (Nakagawa *et al.*, 1987)

(*c*) *Spectroscopy data*: Nuclear magnetic resonance and ultra-violet spectral data have been reported (Nakagawa *et al.*, 1987).

1.4 Technical products and impurities

No data were available to the Working Group.

2. Production, Use, Occurrence and Analysis

2.1 Production and use

No evidence was found that 3,9-dinitrofluoranthene has been produced in commercial quantities or used for other than laboratory applications.

2.2 Occurrence

3,9-Dinitrofluoranthene was detected at a concentration of 0.013 mg/kg in particles emitted from a diesel engine (Tokiwa *et al.*, 1986). Dinitrofluoranthenes have been found in incomplete combustion products of liquefied petroleum gas (Horikawa *et al.*, 1987).

Toners for use in photocopy machines have been produced in quantity since the late 1950s and have seen widespread use. 'Long-flow' furnace black was first used in photocopy toners in 1967; its manufacture involved an oxidation whereby some nitration also occurred. Subsequent changes in the production technique reduced the total extractable nitropyrene content from an uncontrolled level of 5–100 mg/kg to below 0.3 mg/kg (Rosenkranz *et al.*, 1980; Sanders, 1981; Butler *et al.*, 1983), and toners produced from that carbon black since 1980 have not been found to contain detectable levels of mutagenicity or, hence, nitropyrenes (Rosenkranz *et al.*, 1980; Butler *et al.*, 1983).

2.3 Analysis

See the monograph on 1-nitropyrene.

3. Biological Data Relevant to the Evaluation of Carcinogenic Risk to Humans

3.1 Carcinogenicity studies in animals[1]

Subcutaneous administration

Rat: A group of 11 male Fischer 344/DuCrj rats, six weeks old, received subcutaneous injections of 0.05 mg 3,9-dinitrofluoranthene (purity, 99.9%) dissolved in 0.2 ml dimethyl sulfoxide twice a week for ten weeks (total dose, 1 mg; Tokiwa *et al.*, 1987). A group of 21 males was injected similarly with 0.2 ml of the solvent. Animals were observed for 50 weeks; those with tumours at the site of injection were observed until moribund. The first subcutaneous tumour was observed in the treated group on day 88, and 10/11 treated rats had developed tumours at the site of injection by 48 weeks after the beginning of treatment.

[1]The Working Group was aware of a study in progress in rats by single injection into the lung (IARC, 1988).

Seven were described as malignant fibrous histiocytomas [a term used as a specific diagnosis for some subcutaneous and intraperitoneal sarcomas] and three as rhabdomyosarcomas. No metastasis was found, and no subcutaneous tumour developed among the vehicle controls.

3.2 Other relevant data

(*a*) *Experimental systems*

(i) *Absorption, distribution, excretion and metabolism*

No data were available to the Working Group.

(ii) *Toxic effects*

No data were available to the Working Group.

(iii) *Genetic and related effects*

The genetic and related effects of nitroarenes and of their metabolites have been reviewed (Rosenkranz & Mermelstein, 1983; Beland *et al.*, 1985; Rosenkranz & Mermelstein, 1985; Tokiwa & Ohnishi, 1986).

3,9-Dinitrofluoranthene was mutagenic to *Salmonella typhimurium* TA1537, TA1538, TA97, TA98 and TA100 and preferentially inhibited the growth of DNA repair-deficient *Bacillus subtilis* (0.005–0.02 μg/disc; Tokiwa *et al.*, 1986; Nakagawa *et al.*, 1987).

As reported in an abstract, 3,9-dinitrofluoranthene induced mutations to 6-thioguanine resistance of Chinese hamster V79 cells and induced micronuclei in mouse erythrocytes (Horikawa *et al.*, 1987).

(*b*) *Humans*

No data were available to the Working Group.

3.3 Epidemiological studies and case reports of carcinogenicity in humans

No data were available to the Working Group.

4. Summary of Data Reported and Evaluation

4.1 Exposure data

3,9-Dinitrofluoranthene has been detected in the particulate fraction of the exhaust of a diesel engine.

4.2 Experimental data

3,9-Dinitrofluoranthene was tested for carcinogenicity in one experiment in rats by subcutaneous injection, producing sarcomas at the injection site.

4.3 Human data

No data were available to the Working Group.

4.4 Other relevant data

3,9-Dinitrofluoranthene induced DNA damage and mutation in bacteria.

4.5 Evaluation[1]

There is *limited evidence* for the carcinogenicity in experimental animals of 3,9-dinitrofluoranthene.

No data were available from studies in humans on the carcinogenicity of 3,9-dinitrofluoranthene.

Overall evaluation

3,9-Dinitrofluoranthene *is not classifiable as to its carcinogenicity to humans (Group 3).*

5. References

Beland, F.A., Heflich, R.H., Howard, P.C. & Fu, P.P. (1985) The in vitro metabolic activation of nitro polycyclic aromatic hydrocarbons. In: Harvey, R.G., ed., *Polycyclic Hydrocarbons and Carcinogenesis (ACS Symposium Series No. 283)*, Washington DC, American Chemical Society, pp. 371–396

Butler, M.A., Evans, D.L., Giammarise, A.T., Kiriazides, D.K., Marsh, D., McCoy, E.C., Mermelstein, R., Murphy, C.B. & Rosenkranz, H.S. (1983) Application of Salmonella assay to carbon blacks and toners. In: Cooke, M. & Dennis, A.J., eds, *Polynuclear Aromatic Hydrocarbons, 7th International Symposium, Formation, Metabolism and Measurement*, Columbus, OH, Battelle, pp. 225–241

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Horikawa, K., Otofuji, T., Nakagawa, R., Sera, N., Kuroda, Y., Otsuka, H. & Tokiwa, H. (1987) Mutagenicity of dinitrofluoranthenes (DNFs) and their carcinogenicity in F344 rats (Abstract No. 11). *Mutat. Res., 182*, 360–361

[1]For definitions of the italicized terms, see Preamble, pp. 25–28.

Summary table of genetic and related effects of 3,9-dinitrofluoranthene

Nonmammalian systems												Mammalian systems																							
Prokaryotes		Lower eukaryotes				Plants			Insects				*In vitro*													*In vivo*									
													Animal cells								Human cells								Animals						Humans			
D	G	D	R	G	A	D	G	C	R	G	C	A	D	G	S	M	C	A	T	I	D	G	S	M	C	A	T	I	D	G	S	M	C	DL	A	D	S	M	C	A
+	+[1]																																		

A, aneuploidy; C, chromosomal aberrations; D, DNA damage; DL, dominant lethal mutation; G, gene mutation; I, inhibition of intercellular communication; M, micronuclei; R, mitotic recombination and gene conversion; S, sister chromatid exchange; T, cell transformation

In completing the table, the following symbols indicate the consensus of the Working Group with regard to the results for each endpoint:

\+ considered to be positive for the specific endpoint and level of biological complexity

+[1] considered to be positive, but only one valid study was available to the Working Group

IARC (1988) *Information Bulletin on the Survey of Chemicals Being Tested for Carcinogenicity*, No. 13, Lyon, p. 103

Nakagawa, R., Horikawa, K., Sera, N., Kodera, Y. & Tokiwa, H. (1987) Dinitrofluoranthene: induction, identification and gene mutation. *Mutat. Res.*, *191*, 85–91

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