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SRC TR 81-536

SECOND DRAFT

Information Profiles on Potential Occupational Hazards: Nitrophenols

Center for Chemical Hazard Assessment
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15. Supplementary Notes

16. Abstract (Limit: 200 words) Information profiles were presented for the following nitrophenols deemed important in the industrial community: 2-nitrophenol (88755), 3-nitrophenol (554847), 4-nitrophenol (100027), 2,4-dinitrophenol (51285), and 2,4,6-trinitrophenol (88891). The mononitrophenols were moderately toxic to animals, causing initial stimulation and subsequent depression of the respiratory and central nervous systems. Positive results were obtained in several mutagenicity assays for 3-nitrophenol and 4-nitrophenol. 2,4-Dinitrophenol was far more acutely toxic than other important nitrophenol derivatives. It was able to uncouple oxidative phosphorylation by suppressing the coupling of electron flow to synthesis of adenosine-triphosphatase. It caused weakness, intense thirst and sweating, increased body temperature and respiration rate, neuritis, convulsions, and the rapid onset of rigor mortis after death. It has also caused cataracts in humans when used as a weight reducing aid. Inhalation of 2,4,6-trinitrophenol has caused considerable irritation to the eyes and to the mucous membrane of the respiratory tract. Dermal exposure has produced severe skin irritation and sensitization.

17. Document Analysis a. Descriptors

b. Identifiers/Open-Ended Terms NIOSH-Publication, NIOSH-Contract, Contract-210-79-0030, Fungicides, Preservatives, Explosives, Toxic-effects, Nitro-compounds, Mutagens, Skin-exposure, Eye-irritants

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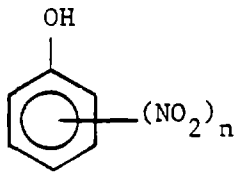
I. SCOPE OF DOCUMENT AND SUMMARY OF MAJOR FINDINGS

A. CLASS IDENTIFICATION

Nitrophenols are identified by the following general chemical structure:



where n, the number of nitro functions attached to the aromatic ring, can vary from 1 to 5.

Although nitrophenols may contain heteroatoms or functions, such as bromine, chloro, methyl, or amino groups, the nitrophenols discussed in these profiles are limited to those defined by the general chemical structure shown above. As defined, there are nineteen possible nitrophenol isomers; they are listed in Appendix A.

B. CHEMICALS TO BE ADDRESSED

Individual profiles have been prepared for the following nitrophenols:

2-Nitrophenol
3-Nitrophenol
4-Nitrophenol
2,4-Dinitrophenol
2,4,6-Trinitrophenol

These nitrophenols were selected for individual profiles because they were identified to have commercial or industrial significance in terms of production or use. The nitrophenols not profiled are primarily produced or used as laboratory or research reagents.

C. SUMMARY OF BIOLOGICAL ACTIVITY

2-, 3-, 4-Mononitrophenols

The mononitrophenols are moderately toxic to animals (rat oral LD50s range from approximately 350-2800 mg/kg, depending upon the isomer), but

no human toxicity information was encountered. Limited animal data indicate that the mononitrophenols initially stimulate and, particularly with fatal doses, subsequently depress respiration and depress the central nervous system. Unlike 2,4-dinitrophenol, the mononitrophenols have little or no effect on body temperature, oxygen consumption, or bile secretion, and do not cause cataracts. Skin painting studies with 2- and 4-nitrophenol failed to produce tumors in mice. Mutagenicity assays were for the most part negative for the mononitrophenols, but positive results in several assays were reported for 3- and 4-nitrophenol.

2,4-Dinitrophenol

In general, 2,4-dinitrophenol is far more acutely toxic than the other commercially important nitrophenol derivatives (rat oral LD50s of <75 mg/kg) and the danger from single exposures may be very great. More specifically, 2,4-dinitrophenol is unique in its ability to "uncouple" oxidative phosphorylation by suppressing the coupling of electron flow to synthesis of ATP. This uncoupling effect produces a profound disturbance of metabolic function in both animals and humans; effects in humans include weakness, intense thirst and sweating, increases in body temperature and respiration rate, neuritis, convulsions, and rapid onset of rigor mortis after death. Another highly specific toxic effect of 2,4-dinitrophenol is cataract development; in humans, it is well documented that ingestion of 2,4-dinitrophenol as a weight reducing aid resulted in cataracts that (1) occurred in young women, (2) were bilateral, (3) appeared rapidly at any time up to a year after ingestion was discontinued, and (4) were not reversible. Cutaneous lesions were the most frequent toxic effect associated with the use of 2,4-dinitrophenol for weight reduction. 2,4-Dinitrophenol did not promote the development of skin tumors in mice, and does not appear to be mutagenic. Developmental abnormalities have been produced by 2,4-dinitrophenol in chick embryos, but teratogenicity testing in mice and rats was negative.

2,4,6-Trinitrophenol (Picric Acid)

The inhalation of picric acid dust causes considerable irritation of the mucous membranes of the eyes and respiratory tract, and dermal exposure results in severe skin irritation and sensitization. Picric acid may cause injury to the kidneys and impairment of liver function in humans, but the effects on the skin appear to be elicited at concentrations far below those associated with systemic poisoning; this fact has led to the recommendation of an ACGIH Threshold Limit Value of 0.1 mg/m^3 for dermal exposures.

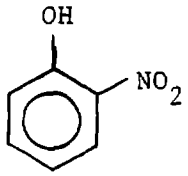
Symptoms of acute poisoning from ingestion or industrial exposure include headache, nausea, vomiting, diarrhea, neuritis, moderate fever, perspiration, anuria, dynuria, weakness, and collapse; in animals, fatal doses typically cause convulsions and death by respiratory paralysis. Picric acid has been reported to be mutagenic in bacteria.

II. INFORMATION PROFILES

A. 2-NITROPHENOL

1. Chemical Name: 2-Nitrophenol

2. Chemical Structure:



3. Synonyms: o-Nitrophenol
2-Hydroxynitrobenzene
Phenol, 2-nitro-

4. Chemical Abstracts Service (CAS) Number: 88-75-5

5. Registry of Toxic Effects of Chemical Substances (RTECS) Number:

SM2100000

6. Chemical and Physical Properties

Description:	sulfur-yellow needles or prisms with an aromatic odor
Molecular Weight:	139.11
Boiling Point:	214-216°C
Melting Point:	44-45°C
Vapor Pressure:	1 mm Hg (49.3°C)
Solubility:	0.21 g/100 ml water (20°C) 1.08 g/100 ml water (100°C) very soluble in alcohol, benzene, ether, carbon disulfide, alkali hydroxides, acetone, chloroform
Specific Gravity:	1.485[14]
Stability:	combustible

7. Production

Data available from the U.S. EPA (1980) regarding producers of 2-nitrophenol and production volumes are presented in Table 1.

2-Nitrophenol is produced in the amount of 10 to 15 million pounds annually (Howard et al., 1976).

Table 1. Producers of 2-Nitrophenol and Production Ranges (U.S. EPA, 1980)

Producer and Location	Type of Production	1977 Production Range
Monsanto Co. Sauget, IL	Manufacturer	10-50 million lb
Alpine Laboratories Bay Minette, AL	Manufacturer	under 1000 lb
DuPont de Nemours and Co. Deepwater, NJ	Manufacturer	confidential
FMC Corp. Baltimore, MD	Importer	1-10 million lb
American Hoechst Bridgewater, NJ	Importer	confidential

Importation in recent years has been reported as follows (USITC, 1980a, 1979, 1978, 1977):

Year	Imports (in millions of pounds)
1979	3.775
1978	4.204
1977	0.694
1976	1.348

8. Use

The chief use of 2-nitrophenol is in the synthesis of 2-aminophenol, 2-nitroanisole, and other dyestuffs (Matsugma, 1967). 2-Aminophenol is apparently the major single derivative; it is a principal intermediate in a variety of industrial dye syntheses and is used as a commercial developer in photography (Farris, 1978). In 1977, between 0.1 and 1.0 million pounds of 2-nitroanisole were manufactured (U.S. EPA, 1980).

2-Nitrophenol is also used in a variety of other organic syntheses, as an analytical indicator, and as a reagent for glucose (Hawley, 1977; The Merck Index, 1976).

9. Manufacturers and Distributors

2-Nitrophenol is manufactured by Monsanto Co. in Sauget, IL (SRI International, 1980; USITC, 1980b). The U.S. EPA (1980) also lists DuPont and Alpine Lab. as manufacturers.

Other distributors include (1980-81 OPD Chemical Buyers Directory, 1980; Chem Sources--USA, 1980):

Accurate Chem.	Fisher Sci.
Aldrich Chem.	Gallard-Schlesinger
American Hoechst	ICN/K and K
Anachemia Chem.	Lachat Chem.
J.T. Baker Chem.	LaPine Sci.
Bio-Clinical Lab.	Mallinckrodt
Chem. Dyanamics	MCB Reagents
Chem Services	Pfaltz and Bauer
Conray Chem.	Rhone-Poulenc
Eastern Chem.	Sigma Chem.
Eastman Kodak	Tridom Chem.

10. Manufacturing Processes

Production of 2-nitrophenol is accomplished by hydrolysis of o-nitrochlorobenzene (Matsugma, 1967). The chemical hydrolysis may be represented as follows:

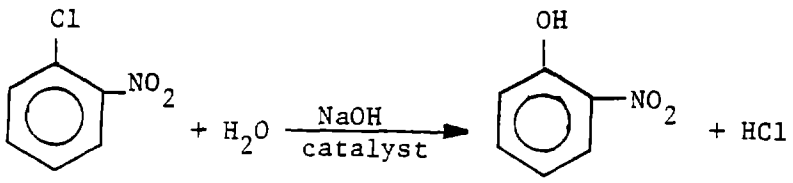


Figure 1 outlines a scheme by which 2-nitrophenol can be industrially prepared. A sodium hydroxide solution is charged into a batch reactor with o-nitrochlorobenzene and a copper catalyst and heated to yield 2-nitrophenol. 4-Nitrophenol is formed as a side-product and is separated from the 2-nitrophenol by steam distillation, as 4-nitrophenol will not steam distill. This process is virtually the same as the industrial process for making 4-nitrophenol which uses p-nitrochlorobenzene as the raw material for hydrolysis.

2-Nitrophenol can also be prepared by nitration of phenol with dilute nitric acid, $NaNO_3$, and sulfuric acid in petroleum ether or benzene (Matsugma, 1967).

11. Impurities or Additives

No data are available from the literature searched; however, a technical grade is likely to contain small percentages of 4-nitrophenol, dinitrophenols, and perhaps, 3-nitrophenol.

12. Occupational Exposure

The National Occupational Hazard Survey indicates that 132 workers are potentially exposed to 2-nitrophenol.

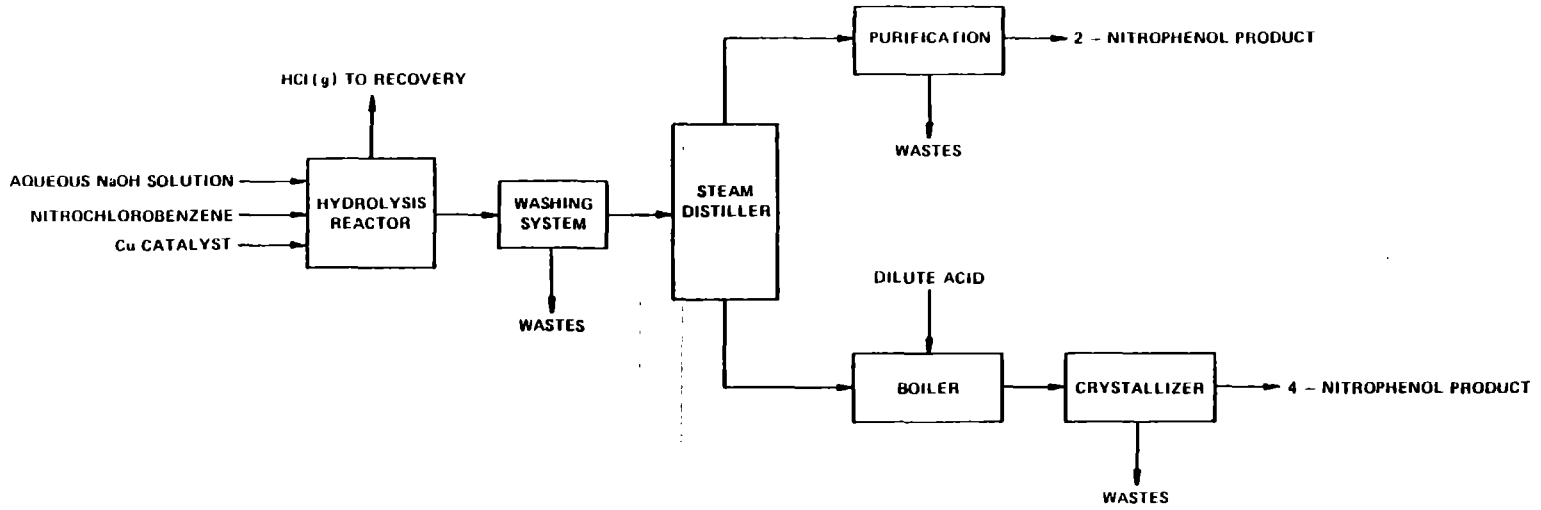


Figure 1. Manufacture of Mononitrophenols via Hydrolysis

13. Control Technology and Work Practices

Specific factors that may contribute to or prevent employee exposure to 2-nitrophenol were not found in the literature searched.

14. Biological Effects

a. Animal Studies

(1) Acute Exposures

The acute toxic effects of 2-nitrophenol are summarized in Table 2. 2-Nitrophenol appears to initially stimulate and, particularly with fatal doses, subsequently depress respiration and depress the central nervous system (Von Oettingen, 1941). Death may also result from cardiac paralysis, and indications of central and peripheral vagus stimulation have been reported.

Cameron (1958) reported that the intraperitoneal administration of approximately 600 mg/kg 2-nitrophenol depressed rectal temperatures in rats, although no change in the rate of oxygen consumption or carbon dioxide output was effected. When approximately 400 mg/kg 2-nitrophenol was injected intraperitoneally in rats, Grant (1959) observed an increased minute volume of ventilation and respiratory rate, but a decreased tidal volume.

2-Nitrophenol has been reported to have no effect on body temperature or bile secretion in dogs following intravenous injection of 5-6 mg/kg (Pugh and Stone, 1968).

In an early review of the literature, Von Oettingen (1941) noted that 2-nitrophenol caused methemoglobinemia in cats. More recently, Grant (1959) detected small, inconstant amounts of methemoglobin in rats following the intraperitoneal administration of approximately 400 mg/kg 2-nitrophenol.

When administered intraperitoneally to rats at 100 mg/kg body weight, 2-nitrophenol significantly increased the blood platelet

Table 2. Acute Effects of 2-Nitrophenol

Route	Species	Dose (mg/kg)	Response	Reference
oral	rats	2828	LD50	Vernot et al., 1977
oral	mice	1300	LD50	Vernot et al., 1977
i.p.	rats	ca. 600	Maximum nonfatal dose; body temperature decreased, no effect on oxygen consumption	Cameron, 1958
i.m.	mice	600	LDLo	Spector, 1956
s.c.	rabbits	1700	LDLo	Spector, 1956
s.c.	cats	600	LDLo	Spector, 1956
i.v.	dogs	100	LDLo	Von Oettingen, 1941
dermal	rabbits	?	not corrosive to skin	Hanavau, 1975

Abbreviations: i.p. = intraperitoneal; i.m. = intramuscular; s.c. = subcutaneous; i.v. = intravenous.

count; this effect was detectable at doses as low as 10 mg/kg (Gabor et al., 1962).

The acute oral administration of approximately 100 mg/kg 2-nitrophenol failed to produce cataracts in chickens (Buschke, 1947).

(2) Subchronic Exposures

Daily intraperitoneal injections of 2.5 mg of 2-nitrophenol (equivalent to 8.3 to 12.5 mg/kg) into three vitamin C-deficient guinea pigs for 20 days did not produce cataracts (Ogino and Yasukvra, 1957).

(3) Chronic Exposures

An abstract from the USSR reports that chronic administration of 2-nitrophenol (dose and duration not detailed) to warmblooded animals (species not indicated) altered neurohumoral regulation. Pathological effects included gastritis, enteritis, colitis, hepatitis, neuritis, and hyperplasia of the spleen (Makhinya, 1969).

(4) Carcinogenicity

2-Nitrophenol failed to produce skin tumors in mice following the repeated dermal application of 20% solutions in dioxane (Boutwell and Bosch, 1959). One drop (approximately 25 µl) of the solution was applied to the backs of each of 31 mice twice weekly for 12 weeks.

(5) Mutagenicity

2-Nitrophenol was not mutagenic in Salmonella typhimurium strains TA98, TA100, TA1535, and TA1537 both with (Taylor, written communication, 1979a) or without (Chiu et al., 1978; Taylor, written communication, 1979a) microsomal activation.

2-Nitrophenol failed to induce streptomycin independence in a strep-dependent strain of Escherichia coli (Szybalski, 1958).

(6) Teratogenicity

No information was found in the literature searched.

(7) Reproductive Effects

No information was found in the literature searched.

(8) Other Relevant Information

2-Nitrophenol is metabolized primarily to glucuronide and sulfate conjugates in the rabbit (Robinson et al., 1951). Reduction to 2-aminophenol, subsequent conjugation, and oxidation to nitroquinol occurs to a slight extent. The major route for 2-nitrophenol excretion is urinary; in rabbits, excretion is virtually complete within 1 day after dosing (Robinson et al., 1951).

2-Nitrophenol inhibits chloride transport in erythrocytes, an energy-independent process (Motais et al., 1978).

b. Human Studies

(1) Pharmacokinetics

No information was found in the literature searched.

(2) Health Effects

No information was found in the literature searched.

(3) Target Organ Toxicity

No information was found in the literature searched.

(4) Epidemiology

No information was found in the literature searched.

15. Ongoing Studies

No references to current toxicological or environmental studies of 2-nitrophenol were found.

16. Exposure Standards

No recommended or promulgated occupational exposure standards for 2-nitrophenol were found.

17. Sources of Additional Relevant Information

No sources of additional relevant information were identified.

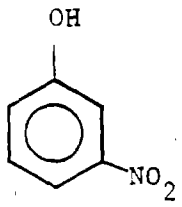
18. Other Pertinent Data

No other information that would aid in the assessment of 2-nitrophenol as an occupational hazard was found in the literature searched.

B. 3-NITROPHENOL

1. Chemical Name: 3-Nitrophenol

2. Chemical Structure:



3. Synonyms: m-Nitrophenol
3-Hydroxynitrobenzene
Phenol, 3-nitro-

4. Chemical Abstracts Service (CAS) Number: 554-84-7

5. Registry of Toxic Effects of Chemical Substances (RTECS) Number:

SM1925000

6. Chemical and Physical Properties:

Description:	colorless to pale yellow crystals
Molecular Weight:	139.11
Boiling Point:	194°C (70 mm Hg)
Melting Point:	97°C
Vapor Pressure:	---
Solubility:	1.35 g/100 ml water (25°C) very soluble in alcohol, ether, acetone, hot benzene soluble in hot and dilute acids, caustic solutions
Specific Gravity:	1.2797_{4}^{10}
Stability:	combustible

7. Production

Data available from the U.S. EPA (1980) regarding producers of 3-nitrophenol and production volumes are presented in Table 3.

Current commercial production of 3-nitrophenol is judged to be less than 10 thousand pounds annually (SRC estimate).

Table 3. Producers of 3-Nitrophenol and Production Ranges (U.S. EPA, 1980)

Producer and Location	Type of Production	1977 Production Range
Eastman Kodak Rochester, NY	Manufacturer	under 1000 lb
Carroll Products Wood River Junction, RI	Produced Site Limited	none

USITC (1980a) reports that 1.164 million pounds were imported in 1979.

8. Use

3-Nitrophenol has been used in the synthesis of m-aminophenol, but this use has dwindled (Matsugma, 1967); m-aminophenol is now usually made commercially by other routes. 3-Nitrophenol is used as an analytical indicator (The Merck Index, 1976) and is used in dye intermediate syntheses. It is also useful in a variety of organic syntheses.

9. Manufacturers and Distributors

SRC International (1980) lists the R.S.A. Corp. in Ardsley, NY, as a manufacturer; the U.S. EPA (1980) lists Eastman Kodak as a manufacturer.

Distributors include (1980-81 OPD Chemical Buyers Directory, 1980; Chem Sources--USA, 1980):

Accurate Chem.	Gallard-Schelsinger
Aldrich Chem.	Hach Chem.
American Hoechst	ICN/K and K
Atomergic Chemetals	Lachat Chem.
Bio-Clinical Lab.	LaPine Sci.
J.T. Baker Chem.	MCB Reagents
Carroll Products	Pfaltz and Bauer
Chem. Procurement Lab.	Reliable Chem.
Chem. Services	Sigma Chem.
Eastern Chem.	Tridom Chem.
Fisher Sci.	George Uhe and Co.

10. Manufacturing Processes

Because of the small annual production, 3-nitrophenol is probably made in small batch amounts when specifically ordered by the dye manufacturers. A convenient route for the synthesis of 3-nitrophenol is the diazotization of m-nitroaniline followed by hydrolysis (Matsugma, 1967). This may be accomplished commercially by the method diagrammed in Figure 2. The diazotization of m-nitroaniline is done by dissolving m-nitroaniline in a warm mixture of hydrochloric acid and water. The mixture is cooled rapidly by adding ice and

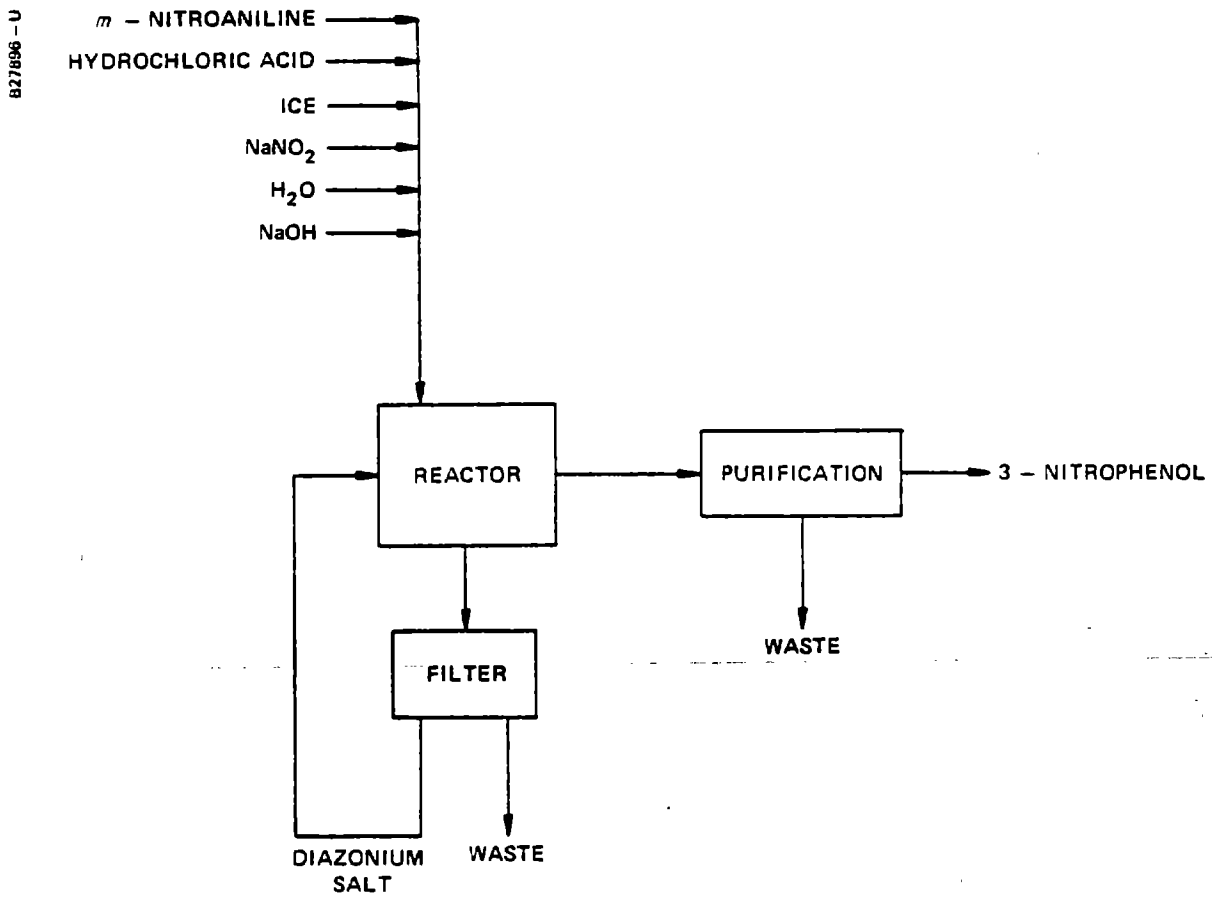


Figure 2. Manufacture of 3-Nitrophenol via Diazotiazation and Hydrolysis

mechanically stirring until a temperature of 0 to 5°C is reached; m-nitroaniline hydrochloride will begin precipitating in crystalline form. A cold solution of sodium nitrite is added quickly to form the diazonium salt in solution. The diazonium salt is precipitated by adding sodium chloride to the reaction liquor. The reaction liquor could then be drained through a filter so that the diazonium salt remains in the reactor. Water and, possibly, a dilute amount of sodium hydroxide are added to the diazonium salt. Increasing the temperature will begin hydrolysis of the diazonium salt to form the product 3-nitrophenol. After hydrolysis completion, the 3-nitrophenol can be separated and purified via filtering, washing, crystallization, and, perhaps, distillation.

With the small estimated production volumes, the production area and number of workers required to accomplish the above procedure would be small. In industry, it is not uncommon for diazotization reactions to be accomplished in open vessels.

11. Impurities or Additives

No information was found in the literature searched.

12. Occupational Exposure

The National Occupational Hazard Survey does not provide an estimate of the number of workers who are potentially exposed to 3-nitrophenol.

13. Control Technology and Work Practices

Specific factors that may contribute to or prevent employee exposure to 3-nitrophenol were not found in the literature searched.

14. Biological Effects

a. Animal Studies

(1) Acute Exposures

The acute toxic effects of 3-nitrophenol are summarized in Table 4. According to Von Oettingen (1941), 3-nitrophenol causes central and peripheral stimulation of the vagus and depression of the central nervous system.

Table 4. Acute Effects of 3-Nitrophenol

Route	Species	Dose (mg/kg)	Response	Reference
oral	rats	930	LD50	Vernot et al., 1977
oral	mice	1410	LD50	Vernot et al., 1977
i.p.	rats	ca. 230	Maximum nonfatal dose; body temperature decreased, oxygen consumption decreased	Cameron, 1958
i.v.	dogs	83	LDLo	Von Oettingen, 1941

Abbreviations: i.p. intraperitoneal; i.v. = intravenous.

Cameron (1958) reported that an intraperitoneal dose of approximately 230 mg/kg 3-nitrophenol had no effect on carbon dioxide output in rats, although it did cause a decrease in oxygen consumption and rectal temperature. When approximately 130 mg/kg was injected intrapertioneally in rats, Grant (1959) observed an increased minute volume of ventilation and respiratory rate, but a decreased tidal volume.

3-Nitrophenol has been reported to have no effect on body temperatures in dogs following intravenous injection of 5 mg/kg, but bile secretion was slightly increased (Pugh and Stone, 1968).

Methemoglobin was not detected following the intraperitoneal administration of approximately 130 mg/kg 3-nitrophenol in rats (Grant, 1959). When 3-nitrophenol was administered intraperitoneally to rats at 100 mg/kg body weight, blood platelet count was unaffected (Gabor et al., 1962).

The acute administration of approximately 184 mg/kg 3-nitrophenol failed to produce cataracts in chickens (Buschke, 1947).

(2) Subchronic Exposures

Daily intraperitoneal injection of 2.5 mg 3-nitrophenol (equivalent to 8.3 to 12.5 mg/kg) into three vitamin C-deficient guinea pigs for 20 days did not produce cataracts (Ogino and Yasukura, 1957).

(3) Chronic Exposures

An abstract from the USSR reports that chronic administration of 3-nitrophenol (dose and duration not detailed) to warmblooded animals (species not indicated) altered neurohumoral regulation. Pathological effects included gastritis, enteritis, colitis, hepatitis, neuritis, and hyperplasia of the spleen (Makhinya, 1969).

(4) Carcinogenicity

No information was found in the literature searched.

(5) Mutagenicity

3-Nitrophenol was mutagenic for Salmonella typhimurium strain TA98 without microsomal activation and for strains TA100 and TA1535 with activation (Taylor, written communication, 1979b). 3-Nitrophenol was not mutagenic in S. typhimurium strain TA1537 both with and without microsomal activation.

3-Nitrophenol failed to induce streptomycin independence in a strep-dependent strain of Escherichia coli (Szybalski, 1958).

(6) Teratogenicity

No information was found in the literature searched.

(7) Reproductive Effects

No information was found in the literature searched.

(8) Other Relevant Information

3-Nitrophenol is metabolized primarily to glucuronide and sulfate conjugates in the rabbit (Robinson et al., 1951). Reduction to 3-aminophenol, subsequent conjugation, and oxidation to nitroquinol and 4-nitrocatechol occurs to a slight extent. The major route for 3-nitrophenol excretion is urinary; in rabbits, excretion is virtually complete within 1 day after dosing (Robinson et al., 1951).

3-Nitrophenol binds to erythrocyte membranes, causing expansion and resistance to hemolysis (Machleidt et al., 1972).

b. Human Studies

(1) Pharmacokinetics

No information was found in the literature searched.

(2) Health Effects

No information was found in the literature searched.

(3) Target Organ Toxicity

No information was found in the literature searched.

(4) Epidemiology

No information was found in the literature searched.

15. Ongoing Studies

No references to current toxicological or environmental studies of 3-nitrophenol were found.

16. Exposure Standards

No recommended or promulgated occupational exposure standards for 3-nitrophenol were found.

17. Sources of Additional Relevant Information

No sources of additional relevant information were identified.

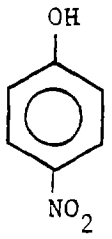
18. Other Pertinent Data

No other information that would aid in the assessment of 3-nitrophenol as an occupational hazard was found in the literature searched.

C. 4-NITROPHENOL

1. Chemical Name: 4-Nitrophenol

2. Chemical Structure:



3. Synonyms: p-Nitrophenol
4-Hydroxynitrobenzene
Phenol, 4-nitro

4. Chemical Abstracts Service (CAS) Number: 100-02-7

5. Registry of Toxic Effects of Chemical Substances (RTECS) Number:

SM2275000

6. Chemical and Physical Properties

Description:	colorless to slightly yellow needles or crystals
Molecular Weight:	139.11
Boiling Point:	279°C (decomposes)
Melting Point:	113-114°C
Vapor Pressure:	2.2 mm Hg at 146°C
Solubility:	0.804 g/100 ml water (15°C) 1.6 g/100 ml water (25°C) very soluble in alcohol, ether, and acetone soluble in hot benzene, chloroform, and toluene slightly soluble in CS_2
Specific Gravity:	1.479 (20°C)
Stability:	combustible

7. Production

Data available from the U.S. EPA (1980) regarding producers of 4-nitrophenol and production volumes are presented in Table 5.

Demand for 4-nitrophenol in 1978 was 36 million pounds (CMR, 1979); this is fairly close to the production figure. The market is expected to grow at only 0 to 2% per year through 1983.

Table 5. Producers of 4-Nitrophenol and Production Ranges (U.S. EPA, 1980)

Producer and Location	Type of Production	1977 Production Range
Monsanto Co. Anniston, AL	Manufacturer	10-50 million lb
Alpine Laboratories Bay Minette, AL	Manufacturer	under 1000 lb
Process Division of UOP Inc. Shreveport, LA	Manufacturer	confidential
E.I. DuPont de Nemours Deepwater, NJ	Manufacturer	confidential
American Hoechst Bridgewater, NJ	Importer	confidential
Rhone-Poulenc Freeport, TX	Importer	none
Conray Chemicals Rockville Centre, NY	Importer	none

USITC (1980a, 1979, 1978, 1977) has reported the following recent importation figures:

Year	Imports (in millions of pounds)
1979	0.016
1978	0.022
1977	0.532
1976	2.907

8. Use

The following tabulation presents the percentage of the total amount of 4-nitrophenol produced that is used in each of the applications listed (CMR, 1979):

	Percentage of Total
Ethyl and methyl parathions	85%
n-Acetyl-p-aminophenol (APAP)	7%
Other	8%

Other uses would include intermediate applications in dye production, fungicides, photochemicals, pharmaceuticals, and leather preservatives (CMR, 1979; Matsugma, 1967). It is also used as an analytical indicator (The Merck Index, 1976).

9. Manufacturers and Distributors

4-Nitrophenol is manufactured by the following companies (CMR, 1979; USITC, 1980b):

	Capacity (in millions of pounds)
DuPont Deepwater, NJ	10
Monsanto Anniston, AL	30

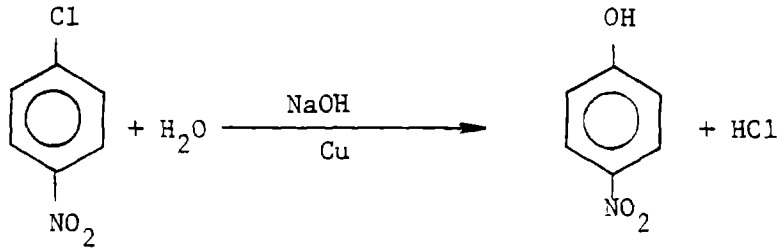
In addition, Martin Marietta in Sodyeco, NC, is believed to make about 1 million pounds per year (CMR, 1979); Alpine Labs and UOP, Inc. are also listed as manufacturers by the U.S. EPA (1980).

Distributors include (1980-81 OPD Chemical Buyers Directory, 1980; Chemical Week: 1981 Buyers' Guide Issue, 1980; Chem Sources--USA, 1980):

Accurate Chem.	Fisher Sci.
Aldrich Chem.	Gallard-Schlesinger
American Hoechst	ICN/K and K
Americal Research Prod.	ICN Nutritional
Anachemia Chem.	LaChat Chem.
Atomergic Chemetals	LaPine Sci.
J.T. Baker Chem.	Mallinckrodt
Biochemical Lab.	MCR Reagents
Bio-Clinical Lab.	Pfaltz and Bauer
Calbiochem-Behring.	Reliable Chem.
Chemical Dynamics	Research Organics
Chem. Procurement Lab.	Research Plus Lab.
Chem Services	Rhone-Poulenc
Conray Chem.	Sigma Chem.
Eastern Chem.	Tridom Chem.
Eastman Kodak	Uniroyal
EM Lab.	U.S. Biochemical
	Vega Biochemical

10. Manufacturing Processes

4-Nitrophenol is commercially prepared by the catalytic (copper) hydrolysis of p-nitrochlorobenzene with sodium hydroxide at 160°C (Matsugma, 1967). Figure 3 outlines a scheme by which 4-nitrophenol may be industrially prepared. A 15% solution of sodium hydroxide is charged into a batch reactor with p-nitrochlorobenzene and the copper catalyst and heated for 4 hours at 160°C to give a good yield of 4-nitrophenol. The chemical hydrolysis may be represented as follows:



The volatile impurities formed by side reactions, such as 2-nitrophenol, are normally removed by steam distillation; the residue is boiled and recrystallized in dilute acid to obtain the p-isomer (Matsugma, 1967). 2-Nitrophenol will be

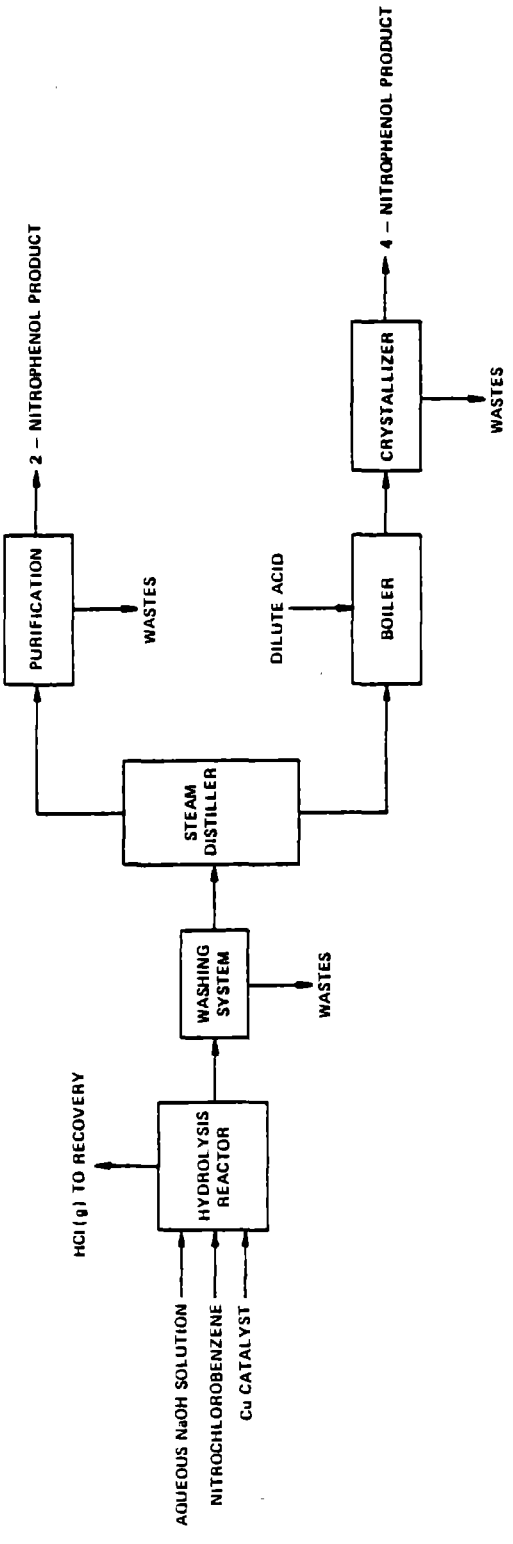


Figure 3. Manufacture of Mononitrophenols via Hydrolysis

the main reaction product if o-nitrochlorobenzene is used as the starting material in place of the p-isomer. Separation of the o-nitrophenol from the p-nitrophenol is again accomplished by steam distillation because p-nitrophenol will not steam distill.

11. Impurities or Additives

No data were available from the literature searched; however, a technical grade 4-nitrophenol is likely to contain small percentages of 2-nitrophenol, dinitrophenols, and, perhaps, 3-nitrophenol.

12. Occupational Exposure

The National Occupational Hazard Survey indicates that 636 workers are potentially exposed to 4-nitrophenol.

13. Control Technology and Work Practices

Specific factors that may contribute to or prevent employee exposure to 4-nitrophenol were not found in the literature searched.

14. Biological Effects

a. Animal Studies

(1) Acute Exposures

The acute toxic effects of 4-nitrophenol are summarized in Table 6. Von Oettingen (1941) noted that small doses of 4-nitrophenol stimulate and large doses depress the central and peripheral vagus mechanism. In nonfatal poisoning, respiration increases and deepens, but fatal doses cause dyspnea and, subsequently, convulsions and death by respiratory paralysis (Von Oettingen, 1941).

Cameron (1958) reported that an intraperitoneal dose of approximately 66 mg/kg 4-nitrophenol increased carbon dioxide output without affecting oxygen uptake in rats, and depressed rectal temperatures. When approximately 44 mg/kg was injected intraperitoneally in rats, Grant (1959)

Table 6. Acute Effects of 4-Nitrophenol

Route	Species	Dose (mg/kg)	Response	Reference
oral	rats	620	LD50	Vernot et al., 1977
oral	mice	470	LD50	Vernot et al., 1977
i.p.	mice	107.6	LDLo	Von Oettingen, 1941
i.p.	rats	97	LD50	Lawford et al., 1954
i.p.	rats	ca. 66	Maximum nonfatal dose; body temperature decreased, no effect on oxygen consumption	Lawford et al., 1954
dermal	rabbits	?	Not corrosive to skin	Hanavan, 1975

Abbreviations: i.p. = intraperitoneal; i.v. = intravenous.

observed increases in minute volume of ventilation, respiratory rate, and tidal volume. 4-Nitrophenol can directly stimulate both the aortic and carotid chemoreceptors of the dog, producing a marked elevation of respiration (Shen, 1962).

4-Nitrophenol has been reported to have no effect on body temperature or bile secretion in dogs following intravenous administration of 5-6 mg/kg (Pugh and Stone, 1968). On the other hand, Von Oettingen (1941) noted that the intraperitoneal injection of 500 mg/kg 4-nitrophenol caused fatal hyperthermia in dogs. This would indicate that 4-nitrophenol may be an uncoupler of oxidative phosphorylation, similar to 2,4-dinitrophenol, which is a well-known uncoupler.

According to Von Oettingen (1941), 4-nitrophenol causes methemoglobinemia in cats. In rats, however, intraperitoneal injection of approximately 44 mg/kg had no effect on methemoglobin formation (Grant, 1959).

The acute oral exposure up to approximately 900 mg/kg 4-nitrophenol failed to produce cataracts in chickens (Buschke, 1947).

(2) Subchronic Exposures

Daily intraperitoneal injection of 2.5 mg of 4-nitrophenol (equivalent to 8.3 to 12.5 mg/kg) into vitamin C-deficient guinea pigs produced cataracts in 2 out of 3 animals on days 7 and 11 of administration (Ogino and Yasukura, 1957); however, no controls were reported.

(3) Chronic Exposures

An abstract from the USSR reports that chronic administration of 4-nitrophenol (dose and duration not detailed) to warmblooded animals (species not indicated) altered neurohumoral regulation. Pathological effects included gastritis, enteritis, colitis, hepatitis, neuritis, and hyperplasia of the spleen (Makhinya, 1969).

(4) Carcinogenicity

4-Nitrophenol failed to produce skin tumors in mice following the repeated dermal application of 20% solutions in dioxane (Boutwell and Bosch, 1959). One drop (approximately 25 µl) of the solution was applied to the backs of each of 31 mice twice weekly for 12 weeks.

(5) Mutagenicity

4-Nitrophenol was weakly mutagenic when tested for mitotic gene conversion in Saccharomyces cerevisiae (Fahrig, 1974). 4-Nitrophenol gave some evidence of DNA damage in a repair-deficient strain of Proteus mirabilis, as measured by a comparison of growth inhibition in the repair-deficient strain with that in the wild type (Adler et al., 1976).

4-Nitrophenol was not mutagenic for Salmonella typhimurium G46 His^- or Serratia marcescens a21 leu^- and a31 His^- in the host-mediated assay with mice or in spot tests in vitro (Buselmaier et al., 1973). 4-Nitrophenol failed to induce mutations in Salmonella typhimurium strains TA98, TA100, TA1535, and TA1537 both with and without microsomal activation (McCann et al., 1975; Bracha , 1979; Taylor, written communication, 1979a).

4-Nitrophenol failed to induce streptomycin independence in a strep-dependent strain of Escherichia coli (Szybalski, 1958).

(6) Teratogenicity

No information was found in the literature searched.

(7) Reproductive Effects

No information was found in the literature searched.

(8) Other Relevant Information

4-Nitrophenol is metabolized primarily to glucuronide and sulfate conjugates (Robinson et al., 1951). The major site for conjugation is the liver (Litterst et al., 1975). Reduction to 4-aminiphenol, subsequent

conjugation, and oxidation to 4-nitrocatechol occurs to a slight extent (Robinson et al., 1951).

In mice, rabbits, guinea pigs, and rats, elimination of 4-nitrophenol from the blood is usually complete within 2 hours after intraperitoneal administration; in monkeys, elimination occurred at a comparable rate following oral and intraperitoneal administration. The major route for excretion is urinary; in rabbits, excretion is virtually complete within 1 day after dosing (Robinson et al., 1951).

4-Nitrophenol inhibits chloride transport in erythrocytes, an energy-independent process (Motais et al., 1978).

b. Human Studies

(1) Pharmacokinetics

No information was found in the literature searched.

(2) Health Effects

No information was found in the literature searched.

(3) Target Organ Toxicity

No information was found in the literature searched.

(4) Epidemiology

No information was found in the literature searched.

15. Ongoing Studies

4-Nitrophenol has been tentatively selected for testing under the Carcinogenesis Bioassay Program (NTP, 1980).

Microbial mutagenesis testing of 4-nitrophenol is scheduled to be completed by Case Western Reserve in 1980 (NIEHS, 1980). The testing is supported by the National Institute of Environmental Health Sciences under contract number N01-ES-9-2136.

16. Exposure Standards

No recommended or promulgated occupational exposure standards for 4-nitrophenol were found.

17. Sources of Additional Relevant Information

No sources of additional relevant information were identified.

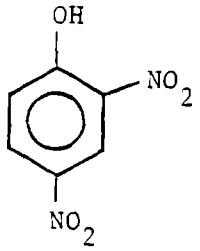
18. Other Pertinent Data

No other information that would aid in the assessment of 4-nitrophenol as an occupational hazard was found in the literature searched.

D. 2,4-DINITROPHENOL

1. Chemical Name: 2,4-Dinitrophenol

2. Chemical Structure:



3. Synonyms:
Aldifen
Chemox PE
alpha-Dinitrophenol
2,4-DNP
Fenoxylcarbon N
1-Hydroxy-2,4-dinitrobenzene
Nitro Kleenup
NSC 1532
Phenol, 2,4-dinitro
Solfo Black B
Solfo Black BB
Solfo Black 2B Supra
Solfo Black G
Solfo Black 5B
Tertrosulphur Black PB
Tertrosulphur PBR

4. Chemical Abstracts Service (CAS) Number: 51-28-5

5. Registry of Toxic Effects of Chemical Substances (RTECS) Number:

SL2800000

6. Chemical and Physical Properties:

Description:	light yellow needles or crystals
Molecular Weight:	184.11
Boiling Point:	sublimes
Melting Point:	111-114°C
Vapor Pressure:	---
Solubility:	0.56 g/100 ml water (18°C)
Specific Gravity:	1.683 (24°C)
Stability:	combustible

7. Production

The most recent production figure for 2,4-dinitrophenol is 863,000 pounds in 1968 (USTC, 1970). Approximate consumption per year is estimated at 1 million pounds (Howard et al., 1976).

Data available from the U.S. EPA (1980) regarding producers of 2,4-dinitrophenol and production volumes are presented in Table 7.

USITC (1980a) reported that 0.121 million pounds were imported in 1979.

8. Use

The major uses of 2,4-dinitrophenol are in the manufacture of chemical intermediates used for making dyes, photochemicals, pest control agents, wood preservatives, and explosives (Matsugma, 1967). The largest single use of 2,4-dinitrophenol as an intermediate is probably in the synthesis of the dye Sulfur Black 1. Sulfur Black 1 is used commercially and is a most important sulfur dye (Orton, 1969). 2,4-Diaminophenol is another industrially important compound made from dinitrophenol; it is sold under the trade names Amidol and Diamol and is used in photographic developing and in dyes (Farris, 1978). Tanalith, a wood preservative sold under the name of "Wolman," is a commercially used product composed of 25% sodium fluoride, 25% disodium arsenate, 37.5% sodium chromate, and 12.5% dinitrophenol (Turner, 1966). 2,4-Dinitrophenol is also used to make 2-amino-4-nitrophenol, a compound used in dye manufacturing; historically, on the order of 10% of the dinitrophenol production is used to make 2-amino-4-nitrophenol (SRC estimate). Picric acid can also be made commercially from dinitrophenol.

9. Manufacturers and Distributors

2,4-Dinitrophenol is commercially manufactured by (SRI International, 1980; USITC, 1980):

Table 7. Producers of 2,4-Dinitrophenol and Production Ranges (U.S. EPA, 1980)

Producer and Location	Type of Production	1977 Production Range
Mobay Chemical Corp. Charleston, SC	Manufacturer	confidential
Alpine Laboratories Bay Minette, AL	Manufacture	under 1000 lb
Martin Marietta Corp. Sodyeco, NC	Manufacturer	confidential
Plant Site Not Listed	Manufacturer	none

Martin Marietta Corp.	Sodyeco, NC
Mobay Chem. Corp.	Bushy Park, SC

Distributors include (1980-81 Chemical Buyers Directory, 1980; Chemical Week: 1981 Buyers Guide Issue, 1980; Chem Sources--USA, 1980):

Accurate Chem.	Fisher Sci.
Aldrich Chem.	Gallard-Schlesinger
American Hoechst	Hach Chem.
Anachemia Chem.	ICN Nutritional
Atomergic Chemetals	LaChat Chem.
J.T. Baker Chem.	LaPine Sci.
Bio-Clinical Lab.	MCB Reagents
Chem. Services	Pfaltz and Bauer
Chem. Procurement Lab.	Sigma Chem.
Continental Trading Co.	Tridom Chem.
Eastern Chem.	U.S. Biochemical
Eastman Kodak	Vertac Chem.
EM Lab.	Wall Chem.

10. Manufacturing Process

Technically, 2,4-dinitrophenol is prepared by the hydrolysis of 2,4-dinitro-1-chlorobenzene with sodium hydroxide at 95 to 110°C. The product is washed after neutralization to remove traces of the more soluble 2,6-dinitrophenol by-product. The yield of this reaction is normally 97% (Matsugma, 1967). A flow diagram of this process is presented in Figure 4.

11. Impurities or Additives

Commercial 2,4-dinitrophenol contains 2,3-dinitrophenol and 2,6-dinitrophenol isomers (Hawley, 1977).

12. Occupational Exposure

The National Occupational Hazard Survey indicates that 8798 workers are potentially exposed to 2,4-dinitrophenol.

13. Control Technology and Work Practices

Specific factors that may contribute to or prevent employee exposure to 2,4-dinitrophenol were not found in the literature searched.

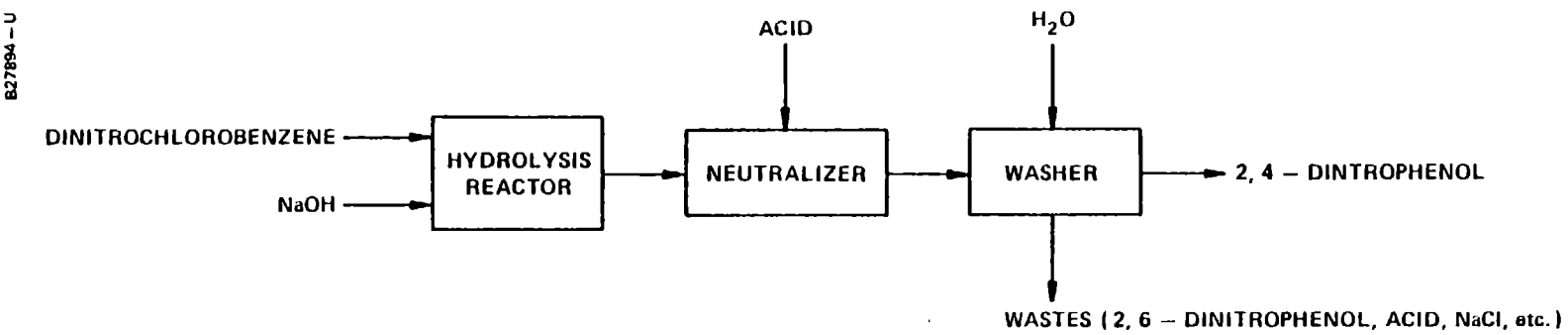


Figure 4. Manufacture of 2,4 -Dinitrophenol via Hydrolysis

14. Biological Effects

a. Animal Studies

(1) Acute Exposures

The acute toxic effects of 2,4-dinitrophenol are summarized in Table 8. 2,4-Dinitrophenol increases body temperature, oxygen consumption, respiration rate, blood pressure, heart rate, glycogenolysis, thyroxin secretion and bile secretion, and affects neuromuscular transmission (Tainter and Cutting, 1933; Cameron, 1958; Harvey, 1959; Kaiser, 1964; Pugh and Stone, 1968; Howard et al., 1976). The elevation of body temperature and oxygen consumption is dose dependent. 2,4-Dinitrophenol can directly stimulate both the aortic and carotid chemoreceptors of the dog, producing a marked elevation of respiration (Shen, 1962).

Fatal doses of 2,4-dinitrophenol produce dyspnea, vomiting, extreme thirst, tremors, convulsions, respiratory paralysis, and early onset of rigor mortis (Tainter and Cutting, 1933; Von Oettingen, 1941; Kaiser, 1964). The toxicity of 2,4-dinitrophenol, as measured by mortality at a given dose, increases when the ambient temperature is raised (Harvey, 1959), and decreases with cooling of the animal by evaporation of water applied to the skin and fur (Tainter and Cutting, 1933).

2,4-Dinitrophenol binds to serum proteins (Gehring and Buerge, 1969b). A study of dogs given fatal doses of 2,4-dinitrophenol demonstrated the presence of dinitrophenol and aminonitrophenol in liver, kidney, brain, blood, and cerebrospinal fluid (Guebert and Mayer, 1932). 2,4-Dinitrophenol has caused mild cortical tubular necrosis in 5 of 16 kidneys from rats given an oral dose of 2 mg/kg (Arnold et al., 1976).

2,4-Dinitrophenol causes the reversible, dose-related formation of cataracts in chickens, ducklings, and immature rabbits following

Table 8. Acute Effects of 2,4-Dinitrophenol

Route	Species	Dose (mg/kg)	Response	Reference
oral	rats	30	LD50	Schafer, 1972
oral	rats	71	LD50; tremors, prostration, increased respiratory rate, tonic convulsions, rigor mortis prior to or immediately after death	Kaiser, 1964
oral	mice	72	LD50; tremors, prostration, increased respiratory rate, tonic convulsions, rigor mortis prior to or immediately after death	Kaiser, 1964
oral	dogs	30	LDLo	Tainter and Cutting, 1933
i.p.	rats	60	LD50; tremors, prostration, increased respiratory rate, tonic convulsions, rigor mortis prior to or immediately after death	Kaiser, 1964
i.p.	rats	32.7	LD50	Lawford et al., 1954
i.p.	rats	36	LD50	Harvey, 1959
i.p.	rats	10-20	Oxygen consumption increased 7-21%	Harvey, 1959
i.p.	rats	50	100% mortality	Obbink and Dalderup, 1964
i.p.	rats	25	25% mortality; average time to death was 94 min. Dose-dependent increase in body temperature	Gatz and Jones, 1970

Table 8. Acute Effects of 2,4-Dinitrophenol (Cont'd)

Route	Species	Dose (mg/kg)	Response	Reference
i.p.	rats	31	100% mortality; average time to death was 77 min.	Gatz and Jones, 1970
i.p.	rats	39	100% mortality; average time to death was 12 min.	Gatz and Jones, 1970
i.p.	mice	52	LD50; tremors, prostration, increased respiratory rate, tonic convulsions, rigor mortis prior to or immediately after death	Kaiser, 1964
i.p.	mice	25.9	LD50	Illivicky and Casida, 1969
i.p.	mice	26	LD50	Lawford et al., 1954
i.p.	mice	36	LD50 at 18-21°C environmental temperature	Harvey, 1959
i.p.	mice	5	100% mortality at 39-41°C environmental temperature	Harvey, 1959
i.m.	dogs	15	LDLo	Tainter and Cutting, 1933
s.c.	rats	44	LD50; tremors, prostration, increased respiratory rate, tonic convulsions, rigor mortis prior to or immediately after death	Kaiser, 1964
s.c.	rats	25	LD50; 10 mg/kg caused no deaths while 50 mg/kg produced 100% mortality	Tainter and Cutting, 1933

Table 8. Acute Effects of 2,4-Dinitrophenol (Cont'd)

Route	Species	Dose (mg/kg)	Response	Reference
s.c.	mice	58	LD50; tremors, prostration, increased respiratory rate, tonic convulsions, rigor mortis prior to or immediately after death	Kaiser, 1964
s.c.	rabbits	30	LD50	Tainter and Cutting, 1933
s.c.	dogs	30	LDLo	Mayer, 1919
s.c.	dogs	22	LD50; no deaths were caused by doses up to 20 mg/kg, which produced 20% mortality; 25 mg/kg produced 100% mortality	Tainter and Cutting, 1933
i.v.	rats	72	LD50; tremors, prostration, increased respiratory rate, tonic convulsions, rigor mortis prior to or immediately after death	Kaiser, 1964
i.v.	mice	56	LD50; tremors, prostration, increased respiratory rate, tonic convulsions, rigor mortis prior to or immediately after death	Kaiser, 1964
dermal	guinea pigs	300	LDLo	Spencer et al., 1948

Abbreviations: i.p = intraperitoneal; s.c. = subcutaneous; i.v. = intravenous; min. = minute.

acute exposure (Robbins, 1944; Buschke, 1947; Gehring and Buerge, 1969a). In chickens, these cataracts disappeared in spite of the continued administration of the chemical in the diet (Buschke, 1947). In rabbits, the disappearance of cataracts was slower and not always complete (Gehring and Buerge, 1969a). Time of cataract development in ducks is related to the route of administration as follows: oral (1 to 3 hours); intraperitoneal (30 minutes); intraocular (less than 10 minutes). In rabbits, cataract susceptibility decreases with the animal's age (Gehring and Buerge, 1969a).

(2) Subchronic Exposures

2,4-Dinitrophenol, given daily in oral doses of 10 mg (equivalent to 33-50 mg/kg) to vitamin C-deficient guinea pigs, produced cataracts in 3 out of 4 animals within 12 to 18 days (Ogino and Yasukura, 1957). Several reduced metabolites of 2,4-dinitrophenol also caused cataracts, but no cataracts were produced when a vitamin C supplement as well as dinitrophenol were administered. Because of a lack of adequate controls (no animals on vitamin C-deficient diets were left untreated) and the small sizes of the experimental groups, however, definitive conclusions cannot be drawn from the results of this study.

As summarized in Table 9, the subchronic administration of 2,4-dinitrophenol has produced slight damage to kidney, liver, and spleen and mild skin irritation (Spencer et al., 1948; Eisenbach et al., 1967).

(3) Chronic Exposures

Rats fed 0.10% 2,4-dinitrophenol for 6 months suffered a reduction in body weight gain of 10-15%, a slight depletion of body fat, a very slight increase in the average weight of the kidneys, and a very slight decrease in the weight of the heart. No significant histopathological changes were found in the tissues. Blood urea-nitrogen levels were elevated in 2 out of 14 animals.

Table 9. Subchronic Effects of 2,4-Dinitrophenol

Route	Species	Dose (mg/kg)	Response	Reference
oral	guinea pigs	33-50 daily x 12-18 days	Cataracts in animals in 12-18 days fed vitamin C-deficient diet; vitamin C-supplemented diet prevented cataracts	Ogino and Yasukura, 1957
oral	dogs	5-125, daily x 1 or 14 days	Electrocarciograms indicated an effect on the myocardium	Kaiser, 1964
dietary	rats	0.2% x 24 days	Animals ate sparingly; 40% mortality; emaciation, enlarged spleen, slight renal degeneration, liver congestion, testicular atrophy, cloudy swelling of liver	Spencer et al., 1948
dietary	ducks	0.25% x 35 days	100% incidence of bilateral cataracts within 24 hours; 40% mortality after 35 days	Spencer et al., 1948
i.v., i.p.	rats	20, twice daily x 3-4 days	Urine volume increased up to 3.5 times within 12 hours for 5-7 days; renal damage including dilation of proximal tubules with some dehydration and necrotic cells; tubular reabsorption depressed	Eisenbach et al., 1967

Abbreviations: i.v. = intravenous; i.p. = intraperitoneal.

[a]Total dose.

Erythrocyte counts, hemoglobin concentrations, leukocyte counts, and differential counts were similar to controls (Spencer et al., 1948).

(4) Carcinogenicity

2,4-Dinitrophenol failed to promote tumor development when repeatedly painted as 20% solutions in acetone on the skin of mice after initiation with 0.3% dimethylbenzanthracene (DMBA) (Boutwell and Bosch, 1959); one drop of the promoter solution (approximately 25 µl) was applied to the backs of each of 36 mice twice weekly for 12 weeks. Similarly, initiation with 100 µg DMBA followed by the administration of (a) 2,4-dinitrophenol and croton oil and (b) 2,4-dinitrophenol and acetone, concentrations not specified, twice a week for 50 weeks, did not produce skin tumors in mice (Stenback and Garcia, 1975). The administration of 0.02 ml 2,4-dinitrophenol for 2 days prior to DMBA initiation, at the time of initiation, and for 2 days after initiation, followed by twice weekly treatment with of 0.02 ml croton oil for 50 weeks, also did not produce skin tumors in mice (Stenback and Garcia, 1975).

No tumors were reported in rats fed 2,4-dinitrophenol at levels of 0.01 to 0.20% in the diet for 6 months (Spencer et al., 1948). This study was of relatively short duration, however, and was not specifically designed to investigate tumorigenesis.

(5) Mutagenicity

2,4-Dinitrophenol increased back mutations from streptomycin dependence to independence in Escherichia coli by several-fold over control values (Demerec et al., 1951).

Chromatid breaks appeared in bone marrow cells of mice injected intraperitoneally 24 hours previously with 2,4-dinitrophenol (Mitra and Manna, 1971). The relationship between frequency of breaks and dose of dinitrophenol was not linear, however, and no control values were reported. Rough

estimates of the doses were calculated by the U.S. Environmental Protection Agency (U.S. EPA, 1979) to be 18.8, 37.6, and 75.3 mg dinitrophenol/kg body weight.

2,4-Dinitrophenol was not mutagenic for Salmonella typhimurium strains TA98, TA100, TA1530, TA1535, and TA1538 both with and without microsomal activation (Kleinhofs and Smith, 1976; Garner and Nutman, 1977; Anderson and Styles, 1978; Chui et al., 1978).

Negative results were also obtained for 2,4-dinitrophenol in a mutagenicity screening assay involving inhibition of DNA synthesis in mice testes (Friedman and Staub, 1976). 2,4-Dinitrophenol also failed to induce DNA damage in Chinese hamster V79 cells in vitro (with or without microsomal activation) as measured in an alkaline elution assay (Swenberg et al., 1976).

(6) Teratogenicity

Gibson (1973) reported that neither intraperitoneal (7.7 and 13.6 mg/kg/day) nor oral administration of 2,4-dinitrophenol to pregnant mice during early organogenesis (days 12 to 15 of gestation) produced morphological defects, although high doses were embryotoxic and produced overt signs of toxicity (hyperexcitability and hyperthermia) in the dams. 2,4-Dinitrophenol administered intragastrically twice daily at 20 mg/kg to female rats prior to mating and throughout pregnancy did not produce neonatal malformations or affect the average litter size or the body weight gains of dams; however, 25% of the offspring born to treated mothers were stillborn while only 6.8% of the offspring of controls were stillborn (Wulff et al., 1935).

2,4-Dinitrophenol has been shown to produce developmental abnormalities involving the nervous system and the beak in the chick embryo (Bowman, 1967; Messier, 1972; Miyamoto et al., 1975).

2,4-Dinitrophenol produced a synergistic teratogenic effect when administered with insulin into yolk sacs of chicken eggs. Insulin alone is a known teratogen; with 2,4-dinitrophenol, the effects were even greater, resulting in increased embryo mortality and shortened upper beaks (Landauer and Clark, 1964).

Hagstrom and Lonning (1966) showed that sea urchin larvae treated with 2,4-dinitrophenol developed several marked irregularities.

(7) Reproductive Effects

No information was found in the literature searched.

(8) Other Relevant Information

The absorption of 2,4-dinitrophenol following intraperitoneal or oral administration is very rapid (Lawford et al., 1954; Harvey, 1959; Kaiser, 1964; Gehring and Buerge, 1969b). 2,4-Dinitrophenol is reported to be metabolized to glucuronide conjugates, aminonitrophenols, and, to a very slight extent, diaminophenol (Parker, 1952; Williams, 1959; Eiseman, 1974). The reduction products are also conjugated with glucuronic acid (Williams, 1959). Elimination of 2,4-dinitrophenol and its metabolites from the blood is complete 30 hours after intraperitoneal or oral administration (Lawford et al., 1954).

2,4-Dinitrophenol is an uncoupler of oxidative phosphorylation (Pinchot, 1967; Ilivicky and Casida, 1969; Weinbach and Garbus, 1969). It prevents the transfer of energy provided by glycolysis and respiration into the high energy phosphate bond of ATP, thus short-circuiting metabolism. The result is the waste of energy as heat, which accounts for the high body temperatures of poisoned organisms (Gatz and Jones, 1970). The uncoupling of oxidative phosphorylation is thought to account for many of the toxic effects of dinitrophenol (U.S. EPA, 1979; Howard et al., 1976).

2,4-Dinitrophenol inhibits chloride transport in erythrocytes, an energy-independent process (Motais et al., 1978).

b. Human Studies

(1) Pharmacokinetics

No information dealing directly with the absorption and tissue distribution of 2,4-dinitrophenol in humans was found. Data on health effects and target organ toxicities indicate that 2,4-dinitrophenol is readily absorbed. 2,4-Dinitrophenol and its metabolites may not be stored in significant amounts in human tissues, as these compounds could not be extracted from tissues of 2 victims of dinitrophenol poisoning (Gisclard and Woodward, 1946).

Metabolites of 2,4-dinitrophenol detected in human urine are, in addition to the unchanged compound, 2-amino-4-nitrophenol, 4-amino-2-nitrophenol, diaminophenol, and glucuronic acid conjugates of these compounds, plus a number of compounds composed of two molecules of aminonitrophenol or diaminophenol (Perkins, 1919; Horner, 1942; Williams, 1959).

No information on the elimination of 2,4-dinitrophenol in humans was encountered.

(2) Health Effects

Subacute toxic reactions in persons exposed to dinitrophenol in the munitions industry or by ingestion of the drug for weight reduction include gastrointestinal symptoms (nausea, vomiting, loss of appetite, sometimes diarrhea and colic), sweating, loss of weight, and occasionally jaundice (Perkins, 1919; Horner, 1942). Many workers in the munitions industry complained of general weakness with headache and dizziness (Perkins, 1919). Some patients using 2,4-dinitrophenol as a drug for weight reduction had symptoms of neuritis (loss of taste for salt and sweet, multiple regional involvement particularly involving the feet and legs) (Horner, 1942).

Workers most susceptible to the toxic effects of 2,4-dinitrophenol were those with a history of alcoholism, those with lesions of the kidneys and liver, and those in poor physical condition (Perkins, 1919).

Acute poisoning, either by ingestion or industrial exposure, has resulted in the sudden onset of weakness, pallor, intense thirst, profuse sweating, anuria sometimes followed by dysuria, agitation, anxiety, difficult breathing, fever as high as 43°C, convulsions, and intense and rapid onset of rigor mortis after death (Perkins, 1919; Gisclard and Woodward, 1946; Horner, 1942).

(3) Target Organ Toxicity

Perkins (1919) stated that the post-mortem examination of victims of dinitrophenol poisoning revealed no characteristic lesions except for acute edema of the lungs. Microscopic lesions in the liver and kidney were inconsistent according to Perkins (1919), and no other typical changes were found.

Ingestion of 2,4-dinitrophenol as a weight reducing aid resulted in over 164 cases of cataract formation in women (Horner, 1942). The cataracts were bilateral and occurred in women who were physically normal (except for various degrees of obesity) and in an age group in which senile cataracts do not occur. Cataracts occurred with recommended doses, often in the absence of other demonstrable toxic effects. The cataracts were all of one type. They developed rapidly with accompanying visual loss and occurred at any time up to 1 year after the drug was discontinued. Unlike the reversible cataracts which were subsequently induced by 2,4-dinitrophenol in experimental animals, cataracts in humans were not reversible, nor did they respond to treatment or withdrawal of the causative agent.

According to Horner (1942), cutaneous lesions were the most frequent toxic effect due to the use of 2,4-dinitrophenol for weight reduction. These lesions included macropapular dermititis, uticaria and swelling, accompanied by itching and burning (Horner, 1942). Although many of these skin problems were mild, some were severe (Hitch and Schwartz, 1936).

A few cases of agranulocytosis, otitis media, and kidney damage associated with 2,4-dinitrophenol usage in weight control are mentioned by Horner (1942). A few cases of neutropenia, eosinophilia, and hemolytic anemia were reported among workers exposed to a parasiticide powder of dinitrophenol (Saita, 1949).

Horner (1942) also noted a few reports of electrocardiographic evidence of functional damage to the heart, and one case of fragmentation of the heart muscle discovered at autopsy as a consequence of ingestion of dinitrophenol.

(4) Epidemiology

The use of 2,4-dinitrophenol as a drug for weight reduction provides some information on the incidence of effects from chronic exposure of humans to this compound.

Horner (1942) reviewed three published clinical studies which indicated that the incidence of cataracts in patients who had taken 2,4-dinitrophenol at recommended doses (50-300 mg/day) for weight reduction was 0.8% (3 out of 397 patients). This estimate is likely to be a minimum, according to Horner (1942), as some of the persons in these studies may have acquired cataracts at a later time. The incidence of cutaneous lesions was 8 to 23% in patients ingesting dinitrophenol for weight reduction (Horner, 1942). Peripheral neutritis was observed in 18 of 170 patients treated by Tainter et al. (1935), an incidence of 11%.

15. Ongoing Studies

No references to current toxicological or environmental studies of 2,4-dinitrophenol were found.

16. Exposure Standards

No recommended or promulgated occupational exposure standards for 2,4-dinitrophenol were found.

17. Sources of Additional Relevant Information

No sources of additional relevant information were identified.

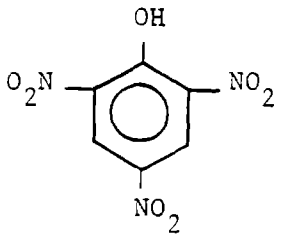
18. Other Pertinent Data

No other information that would aid in the assessment of 2,4-dinitrophenol as an occupational hazard was found in the literature searched.

E. 2,4,6-TRINITROPHENOL

1. Chemical Name: 2,4,6-Trinitrophenol

2. Chemical Structure:



3. Synonyms: Carbazotic acid
CI 10305
2-Hydroxy, 1,3,5-trinitrobenzene
Melinite
Nitroxanthic acid
Phenol, 2,4,6-trinitro-
Phenol trinitrate
Picric acid
Picronitric acid

4. Chemical Abstracts Service (CAS) Number: 88-89-1

5. Registry of Toxic Effects of Chemical Substances (RTECS) Number:

TJ7875000

6. Chemical and Physical Properties:

Description:	pale yellow, odorless, intensely bitter crystals
Molecular Weight:	229.11
Boiling Point:	explodes >300°C
Melting Point:	122-123°C
Vapor Pressure:	---
Solubility:	1.4 g/100 ml water (20°C) soluble in alcohol, ether, acetone, benzene, acetic acid, methanol, chloroform
Specific Gravity:	1.763
Stability:	explodes >300°C; flash point: 302°F

7. Production

Data available from the U.S. EPA (1980) regarding producers of 2,4,6-trinitrophenol and production volumes are presented in Table 10.

Table 10. Producers of 2,4,6-Trinitrophenol and Production Ranges (U.S. EPA, 1980)

Producer and Location	Type of Production	1977 Production Range
Martin Marietta Corp.		
Sodyeco, NC	Manufacturer	confidential
American Research Products		
South Euclid, OH	Small Manufacturer/	confidential
	Importer	confidential
Henley and Co.		
New York City, NC	Importer	confidential

Current production of 2,4,6-trinitrophenol (picric acid) is judged, on the basis of current uses, to be on the order of 100 thousand pounds per year (SRC estimate).

8. Use

Currently, the major commercial use of picric acid is in the synthesis of dye intermediates, especially the sodium salt picramic acid (2-amino-4,6-dinitrophenol). Picramic acid is an important intermediate in the dyestuff industry, particularly for making mordant dyes (Farris, 1978). Before the development of TNT, picric acid was the chief high explosive used by military powers, but it has now been displaced by superior explosives; currently specialty uses of picric acid in explosives are small. Picric acid has been used as a germicide, as a funigicide, in tanning agents, as an analytical reagent, in photochemicals, as a pharmaceutical burn antiseptic, as an intermediate for making specialty medicinals, as a process material for etching metals, in matches, in fireworks and pyrotechnics, and in electric batteries (Matsugma, 1967; Hawley, 1977); these applications are currently judged to be minor uses.

Picric acid is also used to manufacture picrates; ammonium picrate, sodium picrate, and potassium picrate are made on a small commercial scale, up to 1000 pounds annually. Ammonium picrate is used as a specialty explosive in situations where a high explosive is required to be particularly insensitive to shock (Lindner, 1980). On the order of several hundred pounds of potassium picrate are made each year for the purpose of making whistles in fireworks.

9. Manufacturers and Distributors

2,4,6-Trinitrophenol is commercially manufactured by Martin Marietta Corp. in Sodyeco, NC (SRI International, 1980; USITC, 1980).

Distributors include (Chem Sources--USA, 1980):

Aldrich Chem.	Fisher Sci.
Anachemia Chem.	Henley and Co.
Apache Chem.	LaChat Chem.
Atomergic Chemetals	LaPine Sci.
J.T. Baker Chem.	Mallinckrodt
Biochemical Lab.	MCB Reagents
Bio-Clinical Lab.	Medical Chem. Corp.
Chemical Dynamics	Mide Chem.
Chem Services	Monomer-Polymer and Dajac Lab.
Eastern Chem.	Pfaltz and Bauer
Eastman Kodak	Reliable Chem.
EM Lab.	Riches-Nelson
	Tridom Chem.

10. Manufacturing Process

Picric acid can be made commercially by treating phenol with sulfuric acid to form phenosulfonic acids and then subsequently nitrating to picric acid (Rinkenbach, 1965). The picric acid formed is crystallized out, separated by centrifuging, and then washed and dried (Lindner, 1980). The wash water can be reused to decrease losses owing to the water solubility of the picric acid.

Picric acid can also be made commercially by nitration of dinitrophenol (Rinkenbach, 1965). Since the only commercial producer of picric acid, Martin Marietta Corporation, also produces dinitrophenol, it is possible that their picric acid synthesis involves nitration of dinitrophenol. Due to the explosive nature of picric acid and the current low production volumes, it is probably made in a relatively small batch operation. Figure 5 outlines a general scheme by which picric acid may be made commercially. 2,4-Dinitrophenol, produced by the hydrolysis of dinitrochlorobenzene, and 2,6-dinitrophenol, formed as the hydrolysis side product, are charged into a nitrator along with mixed nitric and sulfuric acid. The sulfuric acid aids in the absorption of the reaction water. When nitration is complete, the reaction mixture is sent to a separating decanter where the crude picric acid forms an upper layer on top of

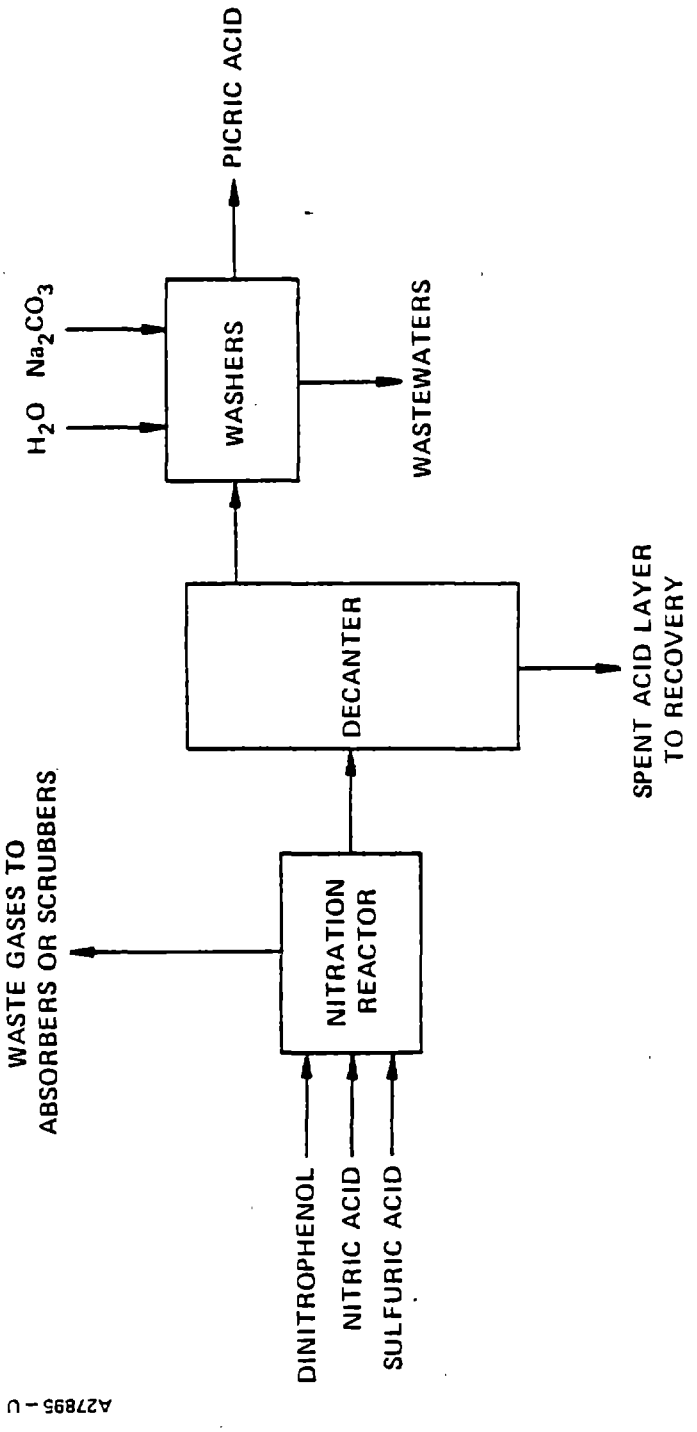


Figure 5. Manufacture of Picric Acid from Dinitrophenol

the spent acid. The spent acid is sent to recovery for recycle or wasting. The crude picric acid is washed with water and sodium carbonate (neutralizer).

11. Impurities or Additives

Picric acid is sold commercially, in drums up to 300 pounds in weight, as a paste that contains water to reduce sensitivity. Water content is commonly 10-12%.

12. Occupational Exposure

The National Occupational Hazard Survey indicates that 29,632 workers are potentially exposed to 2,4,6-trinitrophenol.

13. Control Technology and Work Practices

Specific factors that may contribute to or prevent employee exposure to picric acid were not found in the literature searched.

14. Biological Effects

a. Animal Studies

(1) Acute Exposures

The acute toxic effects of picric acid are summarized in Table 11. In fatal doses, picric acid typically slows respiration and heart beat, causes convulsions, and finally causes death by respiratory paralysis (Von Oettingen, 1941). The inhalation of picric acid dust has caused severe irritation of the mucous membranes of the eyes and respiratory tract and labored respiration in cats (Von Oettingen, 1941).

Yellow staining of tissues following subcutaneous injections in dogs indicated the presence of picric acid in subcutaneous fat, lung, intestines, and blood vessels at autopsy (Dennie et al., 1929).

Kidney damage and "cloudy swelling" of the liver has been reported in dogs and rabbits (Dennie et al., 1929; Von Oettingen, 1941). Picric acid did not stimulate the aortic and carotid chemoreceptors of the dog

Table 11. Acute Effects of Picric Acid

Route	Species	Dose (mg/kg)	Response	Reference
oral	rabbits	350-1000 mg[a]	Severe damage to the kidneys	Von Oettingen, 1941
oral	cats	500 mg[a]	Nausea, vomiting, fatigue, pain, increased reflex excitability within 45 min., tonic and clonic convulsions, ascending paralysis causing death by respiratory failure	Von Oettingen, 1941
s.c.	rabbits	150-200 mg[a]	Lowered body temperature, slowing of heart rate, rise and subsequent fall in blood pressure	Von Oettingen, 1941
?	rabbits	400 mg[a]	Convulsions and death in 3 hours	Von Oettingen, 1941
s.c.	dogs	100	LDLo	Mayer, 1919
s.c.	dogs	60	LDLo; slowing of respiration and heart beat; death by respiratory paralysis	Von Oettingen, 1941; Spector, 1956
i.v.	dogs	6-11	Slight increase in body temperature	Pugh and Stone, 1968

[a]Total dose.

(Shen, 1962), failed to produce acute cataracts in chickens (Buschke, 1947), and does not appear to induce methemoglobinemia (Von Oettingen, 1941).

Guinea pigs can be sensitized to contact with picric acid. The reaction is a slowly developing allergic dermatitis that can be of great intensity and can extend beyond the area of application to the skin. Weaker solutions of picric acid sometimes produce stronger reactions. In addition, when applied to the skin of control animals, weaker concentrations of picric acid are more likely to produce minor irritation than are stronger concentrations (Maguire and Chase, 1972).

(2) Subchronic Exposures

As summarized in Table 12, picric acid administered subchronically has caused jaundice, diarrhea, and weight loss in rabbits and kidney damage in dogs (Von Oettingen, 1941).

(3) Chronic Exposures

No information was found in the literature searched.

(4) Carcinogenicity

The incidence of mammary tumors in female rats treated with picric acid or picramide (both of which are degradation products of hexanitrodiphenylamine) for about 2-1/2 years did not differ from tumor incidence in controls (van Esch et al., 1957). As shown in Table 13, every female rat treated with hexanitrodiphenylamine developed mammary tumors (usually multiple tumors). Neither incidence nor type of tumors observed in treated male rats in this same experiment was different from that of controls. The evidence from this experiment is not conclusive, because the incidence of mammary tumors in controls was higher than usually observed (Table 13), and the number of animals per group was small.

Table 12. Subchronic Effects of Picric Acid

Species	Route	Dose (mg/kg)	Response	Reference
Picric Acid				
Rabbits	Oral	60 mg[a] daily	Jaundice, diarrhea, loss of weight; daily dose of 180 mg caused severe emaciation and death within 2 weeks	Von Oettingen, 1941
Dogs	?	1.8 repeated	Unspecified kidney damage and increased nitrogen retention	Von Oettingen, 1941

[a]Total dose

Table 13. Incidence of Mammary Tumors in Female Rats Treated with Hexanitrodiphenylamine (Van Esch et al., 1957)

Group	No. of Rats	No. Alive After 2 Years	No. With Mammary Tumors	Average Age of Appearance of Tumors
Controls	19 (83)[b]	12 (63)	8 (18)	25 months (26)
Hexanitrodiphenylamine[a]	10	1	10	19 months
Picric acid[a]	10	7	4	22 months
Picramide[a]	8	7	4	29 months

[a]Dosage, 500 ppm mixed in dry food.

[b]The numbers in parentheses are for untreated rats from other experiments during the same period.

(5) Mutagenicity

Picric acid induced a 10-fold increase in mutations to streptomycin independence in a streptomycin-dependent strain of Escherichia coli (Demerec et al., 1951). Picric acid has also been reported to cause mutations in Salmonella typhimurium strain TA98 when tested in a system that included microsomal activation (Yoshikawa et al., 1976).

Treatment of Drosophila eggs with picric acid failed to induce sex-linked lethal mutations (Auerbach and Robson, 1947).

(6) Teratogenicity

No information was found in the literature searched.

(7) Reproductive Effects

No information was found in the literature searched.

(8) Other Relevant Effects

Perfusion experiments with liver, kidney, and spleen showed that liver was the most active in reducing picric acid (2,4,6-trinitrophenol) to picramic acid (2-amino-4,6-dinitrophenol) (Giorgi, 1924). Picric acid appears to be excreted in the urine, because it has been detected in the urine of dogs within 1.5 hours of administration of a fatal dose (Dennie et al., 1929).

Picric acid caused crenation of erythrocytes, an indication of expansion of the cell membranes (Sheetz and Singer, 1976).

b. Human Studies

(1) Pharmacokinetics

No information dealing directly with the absorption and tissue distribution of picric acid in humans was found. Data on health effects and target organ toxicities indicate that picric acid is readily absorbed.

The only metabolite of picric acid (2,4,6-trinitrophenol) identified as being excreted by humans (aside from the unchanged compound) is picramic acid (2-amino-4,6-dinitrophenol). Other products, including a red pigment, are formed but have not been identified (Burrows and Dacre, 1974; Williams, 1959).

No information on the elimination of picric acid from humans was found in the literature searched.

(2) Health Effects

Exposure in industry is typically by skin contact or by inhalation of the dust of picric acid or its salts (e.g., ammonium picrate). Perkins (1919) stated that with the exception of yellow staining of the skin, there were no serious results or illnesses due to exposure to picric acid in the munitions industry in France. According to Von Oettingen (1941), symptoms of acute poisoning from ingestion or industrial exposure to picric acid include headache, nausea, vomiting, diarrhea, neuritis, moderate fever, perspiration, anuria, dysuria, weakness, and collapse. The inhalation of picric acid dust causes considerable irritation of the mucous membranes of the respiratory tract and eyes which may result in sneezing, rhinitis, bronchitis, and ulcerations of the cornea. Toxic doses may cause destruction of erythrocytes and produce gastroenteritis, hemorrhagic nephritis and acute hepatitis, but as far as systemic poisoning in industry is concerned, picric acid has not been considered a severe industrial poison (ACGIH, 1979).

(3) Target Organ Toxicity

Picric acid has caused injury to the kidneys and impairment of liver function as reflected in urinary parameters (Von Oettingen, 1941). In addition, destruction of erythrocytes and leukocytosis have been noted (Von Oettingen, 1941). Ingestion of picric acid in water distilled from sea water resulted in microscopic hematuria (Harris et al., 1946).

Therapeutic (as an antiseptic) and industrial exposures to picric acid have resulted in severe skin irritation and sensitization evidenced by edema, papulae and vesicles, and subsequent desquamation. Reactions sometimes occur distant from the site of contact (Dennie et al., 1929; Von Oettingen, 1941; Schwartz, 1944), and desensitization or adaptation can occur (Schwartz, 1944; Sunderman et al., 1945). In skin sensitization tests, 4 of 100 subjects had positive reactions to picric acid (Dennie et al., 1929).

(4) Epidemiology

Sunderman and coworkers (1945) observed, over a period of 15 months, the development of a dermatitis in 7 of 71 workers who were exposed to ammonium picrate dust in an explosives plant (Table 14). At the sites of milling and performing operations, where the heaviest exposures occurred, atmospheric concentrations ranged from 0.0088 to 0.1942 mg/m^3. It should be noted, however, that the individuals who developed dermatitis were working in groups least exposed to ammonium picrate dust. This lends support to the opinion that desensitization or adaptation may occur following exposure. Upper respiratory disease was negligible among the workers, and systemic toxicity was not recognized.

An outbreak of microscopic hematuria among persons on board ships in the naval anchorage near Wakayama, Japan, was traced to picric acid contamination of drinking water distilled from sea water (Harris et al., 1946). When the urine of nearly all the men on one ship was tested, all specimens revealed microscopic hematuria. A subsequent survey of personnel of 28 ships (15 persons per ship) revealed an incidence of microscopic hematuria of 36%. Hematuria was not detected among military personnel ashore. Evidence indicated that picric acid from ammunition dumped in large quantities near the anchorage was distilled with the harbor water, thus contaminating the drinking water supply.

Table 14. Persons Working with Ammonium Picrate (Sunderman et al., 1945)

Group	Number of Individuals	Average Length of Exposure	Number of Individuals Developing Dermatitis
		Months	
Milling	4	12	
Pressing (a)	5	13	
Pressing (b)	4	4	
Preforming	14	8	
Examining	4	18	
Coating	13	11	3
Firing	11	9	1
Pack House	8	11	
Laundry	2	2	1
Experimental	6	24	2
Total	71		7

15. Ongoing Studies

Microbial mutagenesis testing of 2,4,6-trinitrophenol by Case Western Reserve is scheduled to be completed in 1980 (NIEHS, 1980). The testing, under contract number NO1-ES-9-2136, is supported by the National Institute of Environmental Health Sciences.

16. Exposure Standards

The Time Weighted Average-Threshold Limit Value (TLV-TWA) for 2,4,6-trinitrophenol, recommended by ACGIH (1979) and adopted by OSHA (1976), is 0.1 mg/m^3. ACGIH (1979) has recommended a Short Term Exposure Limit (STEL) of 0.3 mg/m^3 for 2,4,6-trinitrophenol. Both sources have noted that there may be a significant potential contribution to the overall exposure by the cutaneous routes.

17. Sources of Additional Relevant Information

No sources of additional relevant information were identified.

18. Other Pertinent Data

No other information that would aid in the assessment of picric acid as an occupational hazard was found in the literature searched.

APPENDIX A

NITROPHENOLS

The following alphabetical list of chemicals comprises all nitrophenols considered for inclusion in this information profile, regardless of their commercial importance or biological activity.

	CAS Number
2-Nitrophenol	88-75-5
3-Nitrophenol	554-87-7
4-Nitrophenol	100-102-7
2,3-Dinitrophenol	66-56-8
2,4-Dinitrophenol	51-28-5
2,5-Dinitrophenol	329-71-5
2,6-Dinitrophenol	573-56-8
3,4-Dinitrophenol	577-71-9
3,5-Dinitrophenol	586-11-8
2,3,4-Trinitrophenol	NA
2,3,5-Trinitrophenol	NA
2,3,6-Trinitrophenol	NA
2,4,5-Trinitrophenol	NA
2,4,6-Trinitrophenol	88-89-1
3,4,5-Trinitrophenol	NA
2,3,4,5-Tetranitrophenol	NA
2,3,4,6-Tetranitrophenol	641-16-7
2,3,5,6-Tetranitrophenol	NA
Pentanitrophenol	NA

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