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SRC TR 81-635

SECOND DRAFT

Information Profiles on Potential Occupational Hazards: Organic Anhydrides

Center for Chemical Hazard Assessment
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15. Supplementary Notes

16. Abstract (Limit: 200 words) Information profiles were presented on the following organic anhydrides by virtue of their importance in the industrial community: acetic-anhydride (108247), butyric-anhydride (106310), citraconic-anhydride (616024), dodecenylsuccinic-anhydride (25377735), isobutyric-anhydride (97723), maleic-anhydride (108316), phthalic-anhydride (85449), propionic-anhydride (123626), pyromellitic-dianhydride (89327), succinic-anhydride (108305), tetrahydrophthalic-anhydride (85438), and trimellitic-anhydride (552307). The organic anhydrides appeared to be moderately toxic with median lethal dose levels for rats ranging from 697 to 2600mg/kg. The maleic, phthalic, acetic and trimellitic anhydrides appeared to be the most acutely toxic of the group discussed. All were irritants to the skin, eyes, and respiratory tract. Injection site tumors have occurred following administration of succinic and maleic anhydrides. Limited evidence suggested teratogenic potentials for acetic, maleic, phthalic, and succinic anhydrides.

17. Document Analysis a. Descriptors

b. Identifiers/Open-Ended Terms NIOSH-Publication, NIOSH-Contract, Contract-210-79-0030, Metal-finishing, Resins, Plasticizers, Agricultural-chemicals, Toxic-effects, Teratogens, Carcinogens

c. COSATI Field/Group

18. Availability Statement	19. Security Class (This Report)	21. No. of Pages 130
	22. Security Class (This Page)	22. Price

(See ANSI-Z39.18) *See Instructions on Reverse* OPTIONAL FORM 272(4-77) (Formerly NTIS-35) Department of Commerce

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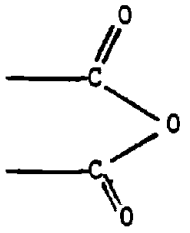
I. SCOPE OF DOCUMENT AND SUMMARY OF MAJOR FINDINGS

A. CLASS IDENTIFICATION

Organic anhydrides contain the following chemical structure:



Hawley (1977) defines an anhydride as a chemical compound derived from an acid by elimination of a molecule of water. For example, phthalic acid minus water gives phthalic anhydride, acetic acid minus water gives acetic anhydride, and maleic acid minus water gives maleic anhydride.

B. CHEMICALS TO BE ADDRESSED

Individual profiles have been prepared for the following organic anhydrides:

Acetic anhydride	Phthalic anhydride
Butyric anhydride	Propionic anhydride
Citraconic anhydride	Pyromellitic dianhydride
Dodecenylsuccinic anhydride	Succinic anhydride
Isobutyric anhydride	Tetrahydrophthalic anhydride
Maleic anhydride	Trimellitic anhydride

The total list of all anhydrides considered for individual treatment is given in the Appendix. The above compounds were selected for individual treatment because their annual production is known to be in excess of one million pounds. Halogenated anhydrides have not been addressed individually although several haloanhydrides are produced in million pound volumes. Haloanhydrides would best be considered as a separate chemical class; however, data on the haloanhydrides has been included in Tables 1-4, Section II for reference.

C. SUMMARY OF BIOLOGICAL ACTIVITY

Limited information is available on the biological effects of commercially important organic anhydrides. Data was not found on the biological effects of butyric, isobutyric, pyromellitic and tetrahydrophthalic anhydride.

The organic anhydrides are moderately toxic with rat oral LD50 values ranging from 697 to 2600 mg/kg; maleic phthalic, acetic and trimellitic anhydrides appear to be the most acutely toxic of the group considered. All of the organic anhydrides are irritants to the skin, eyes, and respiratory tract of animals and humans, and repeated exposure to phthaleic anhydride has been shown to sensitize the skin of guinea pigs. Other than studies of the general irritant effects of organic anhydrides, health effects investigations have not been performed in humans. Both phthalic and trimellitic anhydrides have been observed to elicit immune reactions in humans, with subsequent symptoms of asthma.

Subchronic dietary exposure to phthalic and trimellitic anhydrides has not resulted in compound related pathologic effects, and phthalic anhydride was negative in an NTP carcinogenesis bioassay when incorporated into the diet. Succinic and maleic anhydrides have produced injection site tumors following subcutaneous administration, but carcinogenesis evaluation on the other organic anhydrides have not been performed. Succinic anhydride has been investigated for mutagenic potential in a variety of *in vitro* systems (bacteria, yeast and mammalian cells) and was shown to be negative. Limited evidence also suggests that acetic, maleic, phthalic, and succinic anhydrides are teratogenic.

II. DATA FOR COMMERCIALLY IMPORTANT CHEMICALS NOT INDIVIDUALLY PROFILED

Other organic anhydrides that have or may have some commercial importance are presented in Tables 1, 2, and 3; these anhydrides were not treated in individual profiles. Table 1 lists synonyms, CAS numbers, RTECS numbers, and chemical structures; Table 2 presents chemical and physical properties; Table 3 lists production volumes and uses, and summarizes manufacturing processes, and Table 4 lists the manufacturers of these anhydride compounds.

All organic anhydrides considered for selection, regardless of their commercial importance, are listed in the Appendix.

Table 1. Organic Anhydrides

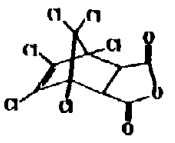
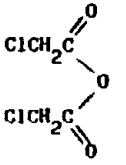
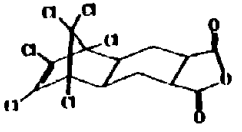
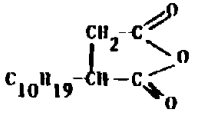
Compound and Synonyms	CAS Number	RTECS Number	Chemical Structure
Chlorendic anhydride 1,4,5,6,7,7-Hexachloro-endo-5-nonbornene-2,3-dicarboxylic anhydride Hexachloroendomethylenetetrahydrophthalic anhydride 1,4,5,6,7,7-Hexachloro-endobicyclo[2.2.1]hept-5-ene-2,3-dicarboxylic anhydride 4,7-Methanoisobenzofuran-1,3-dione, 4,5,6,7,8,8-hexachloro-3=a,4,7,7,7a-tetrahydro	115-27-5	---	
Chloroacetic anhydride Acetic acid, chloro-, anhydride	541-88-8	---	
Chloran 2,3-Dicarboxy-5,8-endo-methylene-5,6,7,8,9,9-hexachloro-1,2,3,4,4a,5,8,8a-octahydronaphthalene anhydride	1782-06-5	---	
Decenyl succinic anhydride 2,5-Furandione, 3-(decenyl)dihydro-	25447-83-0	---	

Table 1. Organic Anhydrides (Cont'd)

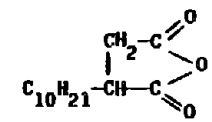
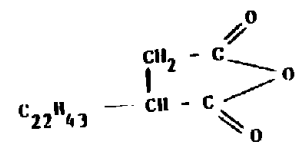
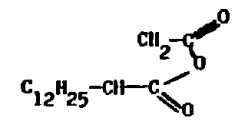
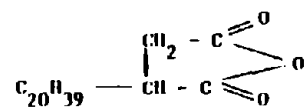
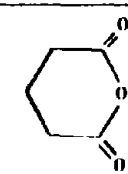
Compound and Synonyms	CAS Number	RTECS Number	Chemical Structure
Decylsuccinic anhydride	---	---	
n-Docosenylsuccinic anhydride 2,5-Furandione,3-(docosenyl)dihydro-	58598-42-8	---	
Dodecylsuccinic anhydride 2,5-Furandione, 3-dodecyldihydro	2561-85-5	---	
n-Eicosenylsuccinic anhydride 2,5-Furandione, 3-(eicosenyl)dihydro-	53520-67-5	---	
Glutaric anhydride 2H-Pyran-2,6(3H)-dione, dihydro- Pentanedioic acid anhydride	108-55-4	MA3850000	

Table 1. Organic Anhydrides (Cont'd)

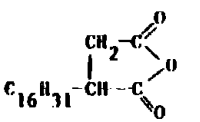
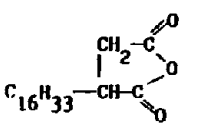
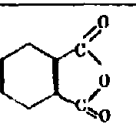
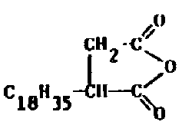
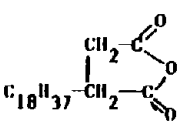
Compound and Synonyms	CAS Number	RTECS Number	Chemical Structure
Hexadecenylsuccinic anhydride 2,5-Furandione, 3-(hexadecenyl)dihydro-	32072-96-1	---	
n-Hexadecylsuccinic anhydride	---	---	
Hexahydrophthalic anhydride 1,2-Cyclohexanedicarboxylic anhydride 1,3-Isobenzofurandione, hexahydro-	85-42-7	---	
Isooctadecenylsuccinic anhydride 2,5-Furandione, dihydro- 3-(isooctadecenyl)-	58239-72-8	---	
n-Isooctadecylsuccinic anhydride 2,5-Furandione, octadecyldihydro-	---	---	

Table 1. Organic Anhydrides (Cont'd)

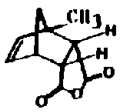
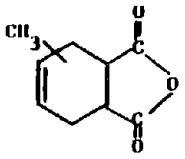
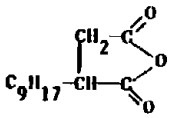
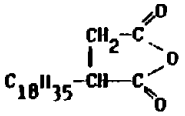
Compound and Synonyms	CAS Number	RTECS Number	Chemical Structure
Methyl-5-norbornene-2,3-dicarboxylic anhydride 4,7-Methanoisobenzofuran-1,3-dione, 3a,4,7,7a-tetra-hydrometh=yl	25134-21-8	---	
Methyltetrahydrophthalic anhydride 1,3-Isobenzofurandione, 3a,4,7,7a-tetrahydromethyl	26590-20-5 1694-82-2 3425-89-6 5333-84-6 11070-44-3	TI3325000	
Nonenylsuccinic anhydride 2,5-Furandione, dihydro-3-(nonenyl)-	28928-97-4	---	
Octadecenylsuccinic anhydride 2,5-Furandione, dihydro-3-(2-octadecenyl)	67066-88-0	---	

Table 1. Organic Anhydrides (Cont'd)

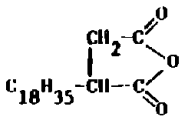
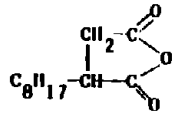
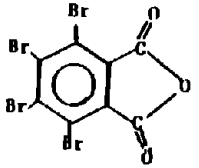
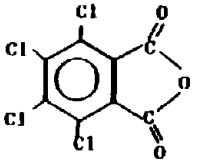
Compound and Synonyms	CAS Number	RTECS Number	Chemical Structure
Octenylsuccinic anhydride 2,5-Furandione, dihydro-3-(octenyl)-	26680-54-6	---	
n-Octylsuccinic anhydride 2,5-Furandione, dihydro-3-(octyl)-	---	---	
Tetrabromophthalic anhydride 1,3-Isobenzofurandione, 4,5,6,7-tetrabromo-	632-79-1	---	
Tetrachlorophthalic anhydride 1,3-Isobenzofurandione, 4,5,6,7-tetrachloro-	117-08-8	---	

Table 1. Organic Anhydrides (Cont'd)

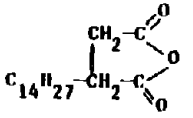
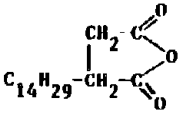
Compound and Synonyms	CAS Number	RTECS Number	Chemical Structure
Tetradecenylsuccinic anhydride 2,5-Furandione, dihydro-3-(2-tetradecenyl)-	54805-64-0	---	
n-Tetradecylsuccinic anhydride 2,5-Furandione, dihydro(tetradecyl)-	---	---	

Table 2. Organic Anhydrides: Chemical and Physical Properties

Compound	Description	Boiling Point (°C)	Melting Point (°C)	Vapor Pressure	Water Solubility	Specific Gravity	Molecular Weight
Chlorendic anhydride	Fine white, free-flowing crystals	---	231-240	---	sl. sol.	1.73	370.86
Chloroacetic anhydride	Crystals	203	46	---	---	1.5494	170.98
Chloran	---	---	---	---	---	---	424.90
3-Chloromaleic anhydride	Yellow liquid	192	10-15	---	---	1.5	132.50
Decenylsuccinic anhydride	---	---	---	---	---	---	238.32
Decylsuccinic anhydride	---	---	---	---	---	---	240.33
3,4-Dichloromaleic anhydride	---	---	---	---	---	---	166.94
Docosenylsuccinic anhydride	---	---	---	---	---	---	406.64
Dodecylsuccinic anhydride	---	---	---	---	---	---	268.39
Dotetracontenylsuccinic anhydride	---	---	---	---	---	---	689.20
Eicosenylsuccinic anhydride	---	---	---	---	---	---	378.59
Glutaric anhydride	Solid	303	56.5	1 mm Hg (100 g °C)	complete on hydrolysis	---	114.11
Hexadecenylsuccinic anhydride	---	---	---	---	---	---	322.48
n-Hexadecylsuccinic anhydride	---	---	---	---	---	---	324.50
Hexahydro-5-methylphthalic anhydride	---	---	---	---	---	---	168.18
Hexahydromethylphthalic anhydride	---	---	---	---	---	---	168.18
Hexahydrophthalic anhydride	Clear, colorless, viscous liquid	158 (17 mm Hg)	35-36			1.19 (40°C)	154.2
Hexatriacontenylsuccinic anhydride	---	---	---	---	---	---	603.02
Isooctadecenylsuccinic anhydride	---	---	---	---	---	---	350.53
n-Isooctadecylsuccinic anhydride	---	---	---	---	---	---	352.55
Methyl-5-norbornene-2,3-dicarboxylic anhydride	---	---	---	---	---	---	178.18
Methyltetrahydrophthalic anydride	---	---	---	---	---	---	166.17
Nonenylsuccinic anhydride	---	---	---	---	---	---	212.28

Table 2. Organic Anhydrides: Chemical and Physical Properties

Compound	Description	Boiling Point (°C)	Melting Point (°C)	Vapor Pressure	Water Solubility	Specific Gravity	Molecular Weight
Octadecenylsuccinic anhydride	---	---	---	---	---	---	350.53
Octatriacontenylsuccinic anhydride	---	---	---	---	---	---	631.07
Octenylsuccinic anhydride	---	---	---	---	---	---	210.26
n-Octylsuccinic anhydride	---	---	---	---	---	--	212.28
Tetrabromophthalic anhydride	Solid needles, pale yellow	---	280	---	insol.	---	463.75
Tetrachlorophthalic anhydride	Solid prisms or needles	sublimes (371°C)	255-265.5	---	decomposes	---	289.92
Tetracontenylsuccinic anhydride	---	---	---	---	---	---	659.13
Tetracosenylsuccinic anhydride	---	---	---	---	---	---	434.70
Tetradecenylsuccinic anhydride	---	---	---	---	---	---	294.43
n-Tetradecylsuccinic anhydride	---	---	---	---	---	---	296.45

Table 3. Production Volumes, Uses, and Manufacturing Processes of Various Anhydrides

Compound	Production	Uses	Manufacturing Processes
Chlorendic anhydride	1974: 10 million lb (Blackford, 1976)	Production of chlorendic acid and fire-retardant resins and polyesters. Also, epoxy hardeners and paints for military applications (Blackford, 1976; Lanson, 1978; Whetstone, 1964).	Diels-Alder reaction of maleic anhydride and hexachlorocyclopentadiene. See Figure 1.
Chloroacetic anhydride	Production not available 1977: 100 to 500 million lb (import) (U.S. EPA, 1980).	Production of cellulose chloroacetates (Bogan et al., 1979). N-Acetylation of amino acids (The Merck Index, 1976).	Treatment of chloroacetic acid (Lurie, 1964; The Merck Index, 1976).
Chloran	Not available	Reactive flame-retardant (Pattison and Hindersinn, 1971).	Reaction of butadiene and maleic anhydride to form tetrahydrophthalic anhydride, which is reacted with hexachlorocyclopentadiene to form cloran (Pattison and Hindersinn, 1971).
3-Chloromaleic anhydride	Not available; <100 thousand lb annually	Catalyst for epoxy resins; intermediate (Hawley, 1977)	Not available
Decenylsuccinic anhydride	1977: 0-1000 lb (U.S. EPA, 1980)	Alkenylsuccinic anhydrides are useful as additives for marine diesel engines lubricants (Turi, 1968; Esso, 1965). Other uses include production of resin, plasticizers, anticorrosion agents, and wetting agents.	Alkenylsuccinic anhydrides are produced by the reaction of maleic anhydride with the appropriate olefin (Irwin and Selwitz, 1968).
Decylsuccinic anhydride	Not available	According to patent literature, alkylsuccinic anhydrides are useful in the production of polyester resins, adhesives, laminates, and coatings. Also useful as lubricant additives.	Commercial process not available; however, alkylsuccinic anhydrides can be prepared by hydrogenation of alkenylsuccinic anhydrides (Bailey and Klein, 1957).

Table 3. Production Volumes, Uses, and Manufacturing Processes of Various Anhydrides (Cont'd)

Compound	Production	Uses	Manufacturing Processes
3,4-Dichloromaleic anhydride	not available: <100 thousand lb annually	Curing epoxy resins (various patent literature)	not available
n-Docosenylsuccinic anhydride	1977: under 1000 lb (U.S. EPA, 1980)	See Decenylsuccinic Anhydride.	See Decenylsuccinic Anhydride.
Dodecylsuccinic anhydride	Not available	See Decylsuccinic Anhydride.	See Decylsuccinic Anhydride.
Dotetracontenylsuccinic anhydride	1977: 0.1-1 million lb (U.S. EPA, 1980)	See Decenylsuccinic Anhydride	See Decenylsuccinic Anhydride
Eicosenylsuccinic anhydride	1977: under 1000 lb (U.S. EPA, 1980)	See Decenylsuccinic Anhydride	See Decenylsuccinic Anhydride
Glutaric anhydride	Production not available 1977: 1-10 thousand lb (import) (U.S. EPA, 1980)	Plasticizers; resin; lubricants; adhesive synthesis; dyes and pharmaceuticals (Hawley, 1977).	Prepared by dehydrating glutaric acid via distillation and fractionating to purify (Gibbsy et al.,1961).
Hexadecenylsuccinic anhydride	1977: 1-10 thousand lb (U.S. EPA, 1980)	See Decenylsuccinic Anhydride	See Decenylsuccinic Anhydride
n-Hexadecylsuccinic anhydride	Not available	See Decylsuccinic Anhydride	See Decylsuccinic Anhydride
Hexahydro-5-methyl phthalic anhydride	1977 (import): 1-10 thousand lb (U.S. EPA, 1980)	See Hexahydrophthalic Anhydride	Not available
Hexahydromethyl phthalic anhydride	1977: 1-10 thousand lb (U.S. EPA, 1980)	See Hexahydrophthalic Anhydride	Not available

Table 3. Production Volumes, Uses, and Manufacturing Processes of Various Anhydrides (Cont'd)

Compound	Production	Uses	Manufacturing Processes
Hexahydrophthalic anhydride	1977: 0.1-1 million lb (U.S. EPA, 1980) 1977: import: 0.1-1 million lb	Intermediate for alkyds, plasticizers, insect repellents and rust inhibitors; hardener in epoxy resins (Hawley, 1977)	Not available
Hexatriacontenylsuccinic anhydride	1977: 0.1-1 million lb (U.S. EPA, 1980)	See Decenylsuccinic Anhydride	See Decenylsuccinic Anhydride
Isooctadecenylsuccinic anhydride	1977: 10-100 thousand lb (U.S. EPA, 1980)	See Decenylsuccinic Anhydride	See Decenylsuccinic Anhydride
n-Isooctadecylsuccinic	Not available	See Decylsuccinic Anhydride	See Decylsuccinic Anhydride
Methyl-5-norbornene-2,3-dicarboxylic anhydride	1977: >0.1-1.0 million lb 1977: 20-200 thousand lb (import) (U.S. EPA, 1980)	Not available.	Not available.
Methyltetrahydrophthalic maleic anhydride	1977: >1 thousand lb 1977: import: 22-120 thousand lb (U.S. EPA, 1980)	Epoxy hardeners (Blackford, 1976). anhydride and isoprene (Blackford, 1976).	Made by the condensation of
Nonenylsuccinic anhydride	1977: 10-100 thousand lb (U.S. EPA, 1980)	See Decenylsuccinic Anhydride	See Decenylsuccinic Anhydride
Octadecenylsuccinic anhydride	1977: under 1000 lb (U.S. EPA, 1980)	See Decenylsuccinic Anhydride	See Decenylsuccinic Anhydride
Octatriacontenylsuccinic anhydride	1977: 0.1-1 million lb (U.S. EPA, 1980)	See Decenylsuccinic Anhydride	See Decenylsuccinic Anhydride
Octenylsuccinic anhydride	1977: >0.1-1.0 million lb 0-1000 lb (import) (U.S. EPA, 1980)	See Decenylsuccinic Anhydride	See Decenylsuccinic Anhydride

Table 3. Production Volumes, Uses, and Manufacturing Processes of Various Anhydrides (Cont'd)

Compound	Production	Uses	Manufacturing Processes
n-Octylsuccinic anhydride	Not available	See Decylsuccinic Anhydride	See Decylsuccinic Anhydride
Tetrabromophthalic anhydride	1973: 10-15 million lb total of tetrabromo and tetrachlorophthalic anhydrides combined (Blackford, 1975).	Fire-retardant monomer used in thermoset polyesters and epoxy resins (Pattison and Hindersinn, 1971).	Direct bromination of phthalic anhydride. See Figure 2.
Tetrachlorophthalic anhydride	1973: 10-15 million lb total of tetrachloro and tetrabromophthalic anhydrides combined (Blackford, 1975) 1977: 1-10 million lb (U.S. EPA, 1980)	Fire-retardant monomer used in plastics (Blackford, 1975). Largest market is in unsaturated polyester resins (Pattison and Hindersinn, 1971).	Direct chlorination of phthalic anhydride. See Figure 3.
Tetracosenylsuccinic	1977: <1000 lb (U.S. EPA, 1980)	See Decenylsuccinic Anydride	See Decenylsuccinic anhydride
Tetracontenylsuccinic anhydride	1977: 0.1-1 million lb (U.S. EPA, 1980)	See Decenylsuccinic Anhydride	See Decenylsuccinic Anhydride
Tetradecenylsuccinic anhydride	1977: under 1000 lb (U.S. EPA, 1980)	See Decenylsuccinic Anhydride	See Decenylsuccinic Anhydride
Tetradecylsuccinic anhydride	Not available	See Decylsuccinic Anhydride	See Decylsuccinic Anhydride

Table 4. Anydride Manufacturers (U.S. EPA, 1980; SRI International, 1980; USITC, 1980a)

Chlorendic anhydride	Hooker Chemical (Niagara Falls, NY) Haven Chemical (Philadelphia, PA) Velsical Chem. (Memphis, TN) Archem. Co. (Houston, TX)
Chloroacetic anhydride	Eastman Kodak (Rochester, NY) Haven Chem. (Philadelphia, PA)
Chloran	Universal Oil Products
3-Chloromaleic anhydride	Fike Chem. (Nitro, WV)
Decenylsuccinic anhydride	The Humphrey Chem. Co. (North Haven, CT)
Decylsuccinic anhydride	The Humphrey Chem. Co. (North Haven, CT)
3,4-Dichloromaleic anhydride	Fike Chem. (Nitro, WV)
Docosenylsuccinic anhydride	Mobil Chem. (Edison, NJ)
Dodecylsuccinic anhydride	Buffalo Color Corp. (Buffalo, NY) The Humphrey Chem. Co. (North Haven, CT) Mobil Chem. (Edison, NJ)
Dotetracontenylsuccinic anhydride	Mobil Chem. (Edison, NJ)
Eicosenylsuccinic anhydride	Mobil Chem. (Edison, NJ)
Glutaric anhydride	Aldrich Chem. (Milwaukee, WI) Union Carbide (Fustitute, WV)
Hexadecenylsuccinic anhydride	The Humphrey Chem. Co. (North Haven, CT)
n-Hexadecylsuccinic anhydride	The Humphrey Chem. Co. (North Haven, CT)
Hexahydro-5-methylphthalic anhydride	Mobay chem. (importer) (Pittsburg, PA)
Hexahydromethylphthalic anhydride	Vega Ind. (Chembeaufort, SC)
Hexahydrophthalic anhydride	Buffalo Color Corp. (Buffalo, NY) Milliken Chem. (Inman, SC)
Hexatriacontenylsuccinic anhydride	Mobil Chem. (Edison, NJ)
Isooctadecenylsuccinic anhydride	The Humphrey Chem. Co. (North Haven, CT)
n-Isooctadecylsuccinic anhydride	The Humphrey Chem. Co. (North Haven, CT)
Methyl-5-norbornene-2,3-dicarboxylic anhydride	Buffalo Color Chem. (Buffalo, NY) Velsicol Chem. (Chattanooga, TN)
Methyltetrahydrophthalic anhydride	AZS (Lancaster Chem.) (Newark, NJ) Milliken Chem. (Inman, SC) 3M Co. (St. Paul, MN) Lindau Chem. (Columbia, SC)
Nonenylsuccinic anhydride	The Humphrey Chem. Co. (North Haven, CT)

Table 4. Anydride Manufacturers (U.S. EPA, 1980; SRI International, 1980; USITC, 1980a) (Cont'd)

Octadecenylsuccinic anhydride	The Humphrey Chem. Co. (North Haven, CT) Milliken Chem. (Inman, SC)
Octadecenylsuccinic anhydride	The Humphrey Chem. Co. (North Haven, CT) Milliken Chem. (Inman, SC)
Octatriacontenylsuccinic anhydride	Mobil Chem. (Edison, NJ)
Octenylsuccinic anhydride	The Humphrey Chem. Co. (North Haven, CT) Rohm and Haas Co. (Philadelphia, PA)
n-Octenylsuccinic anhydride	The Humphrey Chem. Co. (North Haven, CT)
Tetrabromophthalic anhydride	Velsicol Chem. (El Dorado, AK) Saytech Inc. (Sayreville, NJ)
Tetrachlorophthalic anhydride	Monsanto (Bridgeport, NJ)
Tetracontenylsuccinic anhydride	Mobil Chem. (Edison, NJ)
Tetradecenylsuccinic anhydride	The Humphrey Chem. Co. (North Haven, CT)
n-Tetradecenylsuccinic anhydride	The Humphrey Chem. Co. (North Haven, CT)

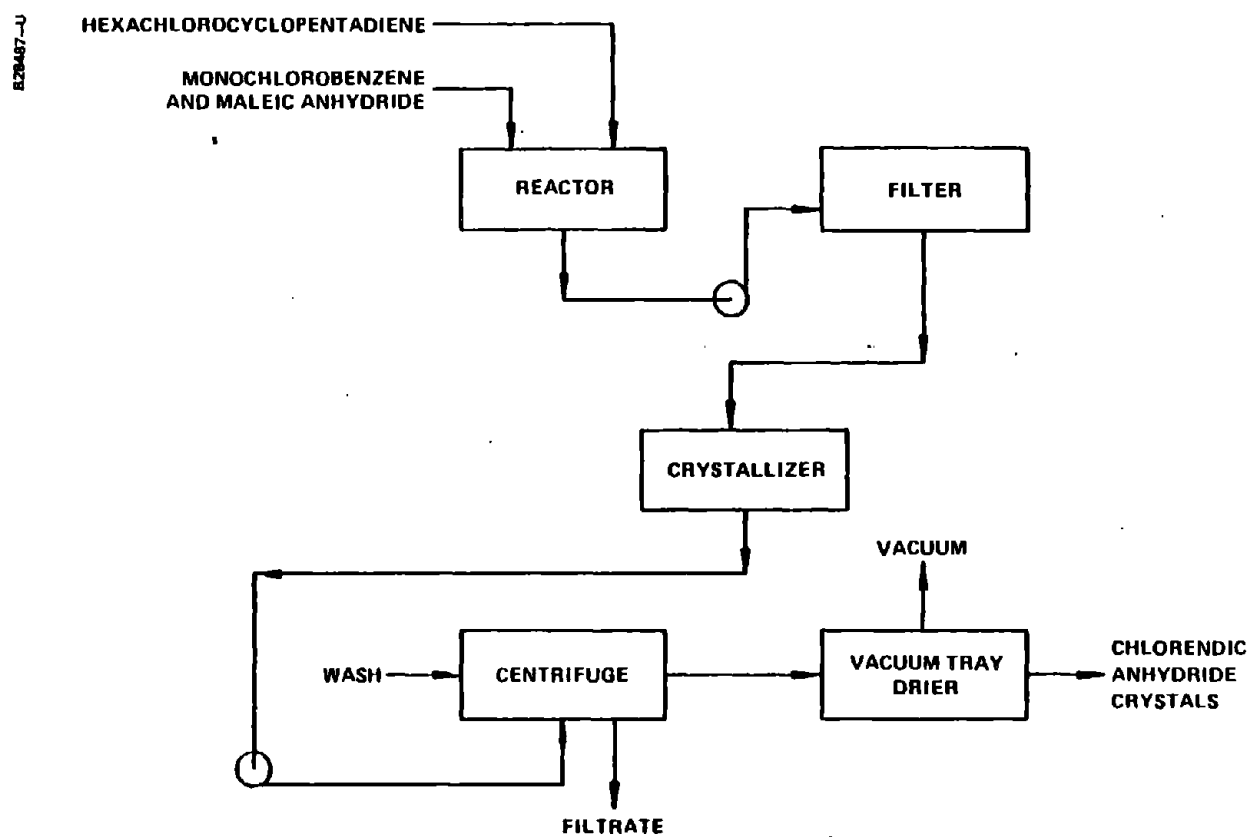


Figure 1. Chlorendic Anhydride Manufacture (Sittig, 1967; adapted from Barnauckas et al., 1959)

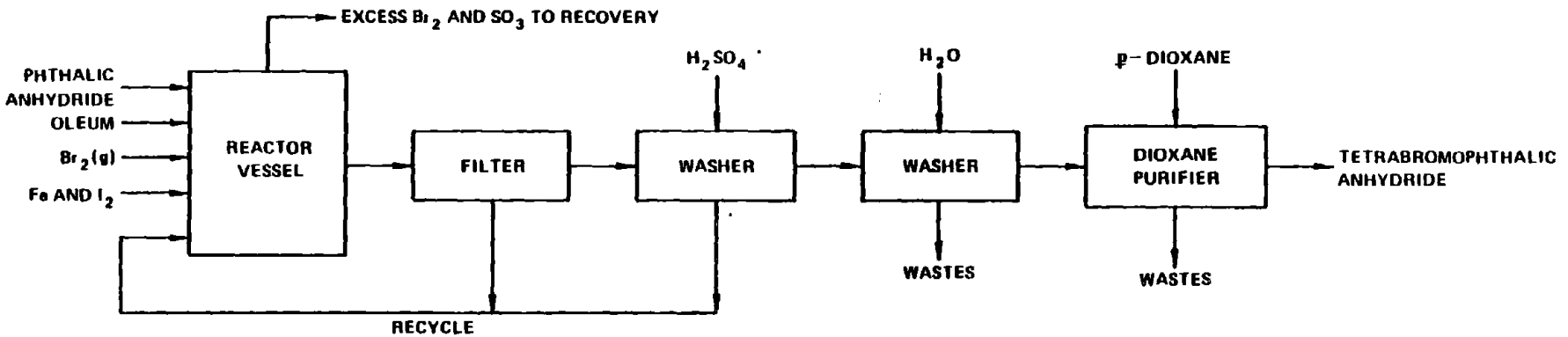


Figure 2. Manufacture of Tetrabromophthalic Anhydride (adapted from Chemische, 1967; Sanger, 1971)

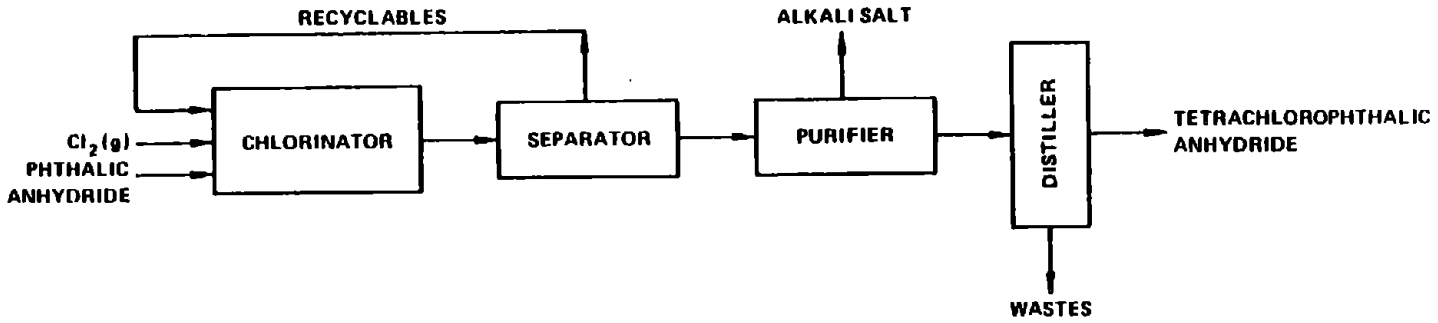


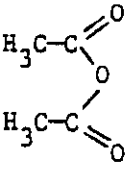
Figure 3. Manufacture of Tetrachlorophthalic Anhydride (adapted from Steahly, 1951; Pattison and Hindersinn, 1971)

III. INFORMATION PROFILES

A. ACETIC ANHYDRIDE

1. Chemical Name: Acetic Anhydride

2. Chemical Structure:



3. Synonyms:

Acetic acid, anhydride
Acetic oxide
Acetyl anhydride
Acetyl ether
Acetyl oxide
Ethanoic anhydrate
Ethanoic anhydride

4. Chemical Abstracts Service (CAS) Number: 108-24-7

5. Registry of Toxic Effects of Chemical Substances (RTECS) Number: AK1925000

6. Chemical and Physical Properties:

Description:	colorless, very mobile, strongly refractive liquid with a strong acetic odor
Molecular Weight:	102.09
Boiling Point:	140°C
Melting Point:	-73.1°C
Vapor Pressure:	4 mm Hg (20°C)
Solubility:	soluble in water (decomposes forming acetic acid) soluble in alcohol, chloroform, benzene, and ethe
Specific Gravity:	1.082 (20°C)
Stability:	combustible, potentially explosive autoignition temp. 750°F; flashpoint 121°F (CC); explosive limits, mg/l: lower 96.2

7. Production

Recent production figures for acetic anhydride are as follows (Storck, 1980; USITC, 1977a, 1977b, 1976):

Year	Millions of Pounds
1979	1510
1978	1500
1976	1506
1975	1458
1974	1633

The historical growth rate for acetic anhydride (1969-1979) has been a negative 0.7% per year; future growth is projected at a positive 1% per year through 1984 (CMR, 1980a). The growth rate is tied directly to the cellulose acetate market for which it is used.

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

In 1978, 4.2 million pounds of acetic anhydride were exported (Bureau of the Census, 1979). Imports during the early 1970's ranged from several million to several tens of million pounds per year. In 1977, in excess of 110 million pounds were imported (U.S. EPA, 1980).

8. Use

The following tabulation presents the percentage of the total amount of acetic anhydride produced that is used in each of the applications listed (CMR, 1978):

	Percentage of Total
Cellulose acetate	90.0
Aspirin	1.4
Other (including cellulose esters)	8.6

The miscellaneous applications of acetic anhydride include starch acetylation to make textile sizing agents, electrolytic metal polishing,

Table 5. Producers of Acetic Anhydride and Production Ranges (U.S. EPA, 1980)

Producer	Type of Production	1977 Production Range
Avtex Fibers Meadville, PA	Manufacturer/ NOT DISTRIBUTED	confidential
Dow Chemical Midland, MI	Manufacturer	1-10 million lb
Union Carbide Corp. Brownsville, TX	Manufacturer	confidential
Tennessee Eastman Kingsport, TN	Manufacturer	500-1000 million lb
American Bio-Synthetics Milwaukee, WI	Manufacturer	none
Holston Army Ammunition Plant Kingsport, TN	Manufacturer	10-50 million lb
Celanese Chemical Pampa, TX	Manufacturer	100-500 million lb
Rock Hill, SC	Manufacturer/ NOT DISTRIBUTED	100-500 million lb
Narrows, VA	Manufacturer/ NOT DISTRIBUTED	100-500 million lb
New York, NY	Importer	10-50 million lb
Nissho-Iwai American Corp. New York, NY	Importer	100-500 million lb
Henley and Co. New York, NY	Importer	confidential
Kanematsu-Gosho (USA) New York, NY	Importer	none
Toms River Chemical Toms River, NJ	Importer	confidential
Montedison USA New York, NY	Importer	none
Holtrachem Natick, NY	Importer	none
Rhone-Poulenc Freeport, TX	Importer	none

synthesis of sulfa drugs and vitamins, an acetylating agent for animal and vegetable oils, intermediate for plasticizers and perfumes, manufacture of acetyl peroxide, explosives, weed killers, chemical treatment of paper and textiles, and a variety of other organic syntheses (Wagner, 1978; LeMonnier, 1965).

A large fraction of the production volume is captively consumed by the manufacturers, particularly for making cellulose acetate, films, and fibers. In 1979, sales of acetic anhydride were 124 million pounds (USITC, 1980a) compared to a production of 1510 million pounds.

9. Manufacturers and Distributors

The manufacturers of acetic anhydride are (CMR, 1980a):

Producer	Location	Annual Capacity in 10^6 pounds
Celanese	Narrows, WV	250
	Pampa, TX	300
	Rock Hill, SC	250
Eastman Kodak	Kingsport, TN	1000
Union Carbide	Brownsville, TX	200
		2000[a]

[a]Avtex Fibers (Meadville, PA) has 60 million lb/yr on stand-by.

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

Alfa Products
Aldrich Chem.
Amer. Sci.
Anachemia Chem.
Ashland Chem.
Atomergic Chemetals
J.T. Baker Chem.
Bio-Clinical Lab.
Bentley Chem.
Chem. Dynamics
Chem. Services
Chemsampo
Collaborative Res.
Columbia Organics
General Plastics Corp.
J.F. Henry Chem.
Holtrachem
Jimmler Inc.
Lachat Chem.
LaPine Sci.
Lux Chem.
Mallinchrodt
MC/B Reagents
McKesson Chem.
Montedisan USA
Pfaltz and Bauer
Phillips Bros. Chem.
Pioneer Salt and Chem.

CPS Chem.
Delamar Inc.
Eastern Chem.
EM Lab.
Fehr Bros.
Fisher Scientific
Gallard-Schelsinger
Suburban Chem.
Toyomenka (Amer)
Tridom Chem.
Union Chem.
Universal Preservachem.
Worth Chem.

10. Manufacturing Processes

Acetic anhydride is manufactured in industry from either acetic acid or acetaldehyde. At least two-thirds of the industrial capacity is based on the acetic acid route (Pervier et al., 1974a).

Figure 4 shows the flow diagram of acetic anhydride from acetic acid. The reactions for this route can be described as follows:

(1) Pyrolysis of acetic acid to ketene

$$CH_3COOH \xrightarrow{\text{catalyst}} CH_2=C=O + H_2O$$

(2) Reaction of ketene with acetic acid to acetic anhydride

$$CH_2=C=O + CH_3COOH \longrightarrow CH_3CO-O-COCH_3$$

Side reactions cause the formation of methane, carbon dioxide, carbon monoxide, hydrogen, and ethylene (Pervier et al., 1974a). The following passages from Survey Reports on Atmospheric Emissions From the Petrochemical Industry, Vol. I, (Pervier et al., 1974a) describe the manufacturing process:

> Glacial acetic acid is vaporized and superheated to 1100°F under 200 mm absolute pressure. Catalyst such as triethyl phosphate is added to the system and the acetic acid vapors are fed to a cracking furnace at 1300°F where they pyrolize to ketene and water (90% per pass conversion) plus minor amounts of hydrocarbons, CO_2, CO and H_2. Cracked gases emerging from the furnace are quickly condensed and cooled to 32°F to remove weak unreacted acetic acid (35%) and to prevent reaction of the ketene formed with the weak acid.
>
> Uncondensed concentrated ketene gas plus small quantities of hydrocarbons, CO, CO_2 and H_2 are directed to the second stage of the process where they are absorbed and scrubbed by concentrated acetic acid to form acetic anhydride in stages from 100°F down to 32°F.

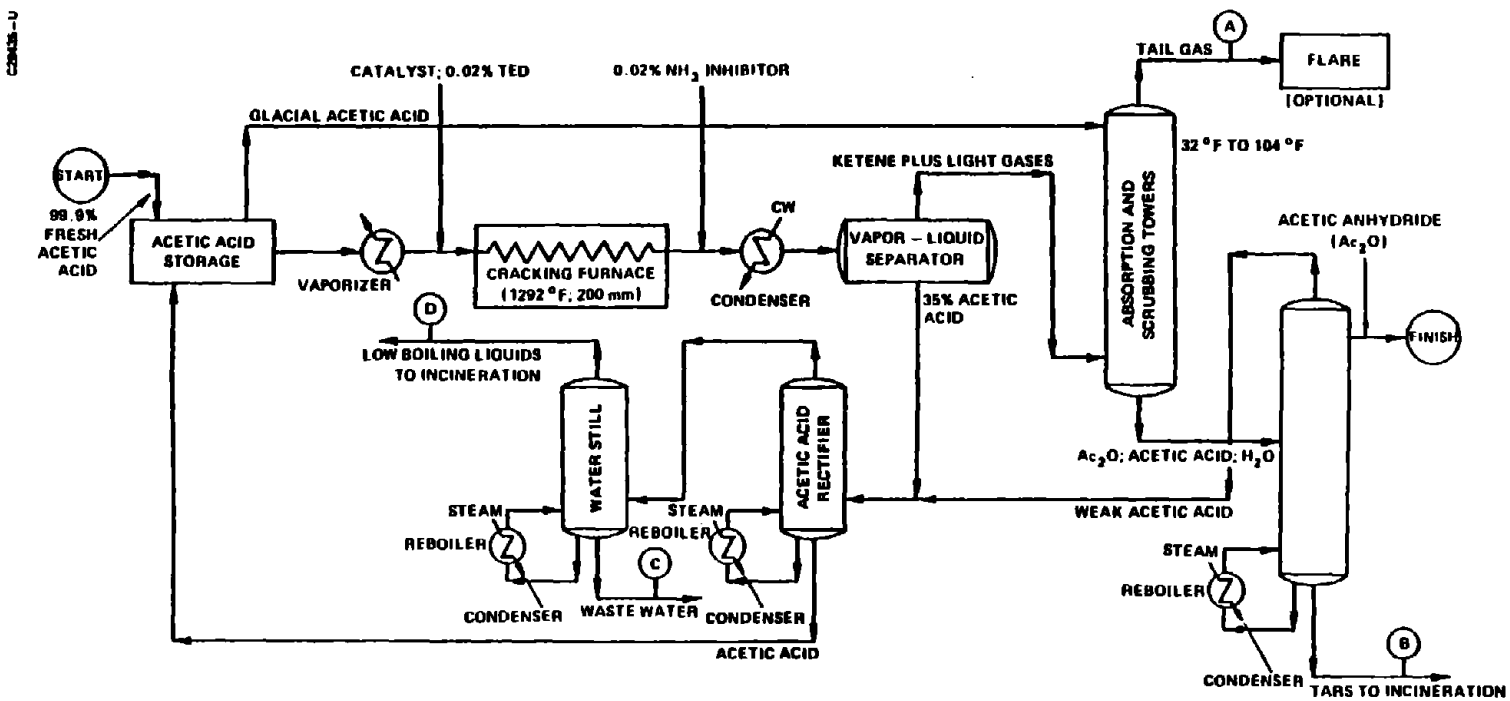


Figure 4. Manufacture of Acetic Anhydride from Acetic Acid

Tail gas from the absorption/scrubbing towers can be incinerated to CO_2 and water but one respondent vents this gas directly to the air. Acetic anhydride is concentrated and purified by distillation. Bottoms from this process consists of small quantities of "tar" which is normally burned [but can also be land-filled]. Weak acetic acid is concentrated in a still and recycled back to the process as feed stock or absorbant. Water produced in the process and removed from the acetic acid is treated in plant before discharge to sewage. So-called low boiling liquids removed from the acetic acid are usually incinerated (Pervier et al., 1974a).

Figure 5 shows the flow diagram for acetic anhydride manufacturing from acetaldehyde. The following passages from Faith, Keyes, and Clark's Industrial Chemicals (Lowenheim and Moran, 1975) describe this process:

Air is bubbled through liquid acetaldehyde in a reactor in the presence of 2% (based on the weight of acetaldehyde) catalyst, such as a mixture of copper and cobalt acetates or manganese acetate, which prevents the formation of explosive amounts of peracetic acid. Approximately 1.4 parts of acetic acid per 1 part of acetaldehyde is present as a diluent to promote acetic anhydride formation. Methyl or ethyl acetate, triactin, or benzene may also be used as a diluent, and the last is generally utilized in conjunction with acetic acid as a withdrawing agent in subsequent vacuum distillation to allow separation of the reaction mixture from water at lower temperatures.

The reactor is maintained at a temperature of 50 to 70°C, and the pressure is approximately 60 psi. The overheat from the crude vacuum column is fractionated in an aldehyde column, yielding acetaldehyde for recycle as the overhead and water and diluent as bottoms. The diluent is returned to the reactor after the water is separated.

The dehydrated mixture of acetic anhydride and acetic acid from the bottom of the crude vacuum column is separated by distillation. Acetic acid is removed as overhead, and the acetic anhydride is withdrawn from a bottom plate. The catalyst is taken from the bottom to be reused. The acetic anhydride may be further purified by vacuum distillation.

Variations of this process involve type and amount of diluent, and several stages in the reactor (with oxygen injection into each stage) under milder reaction conditions.

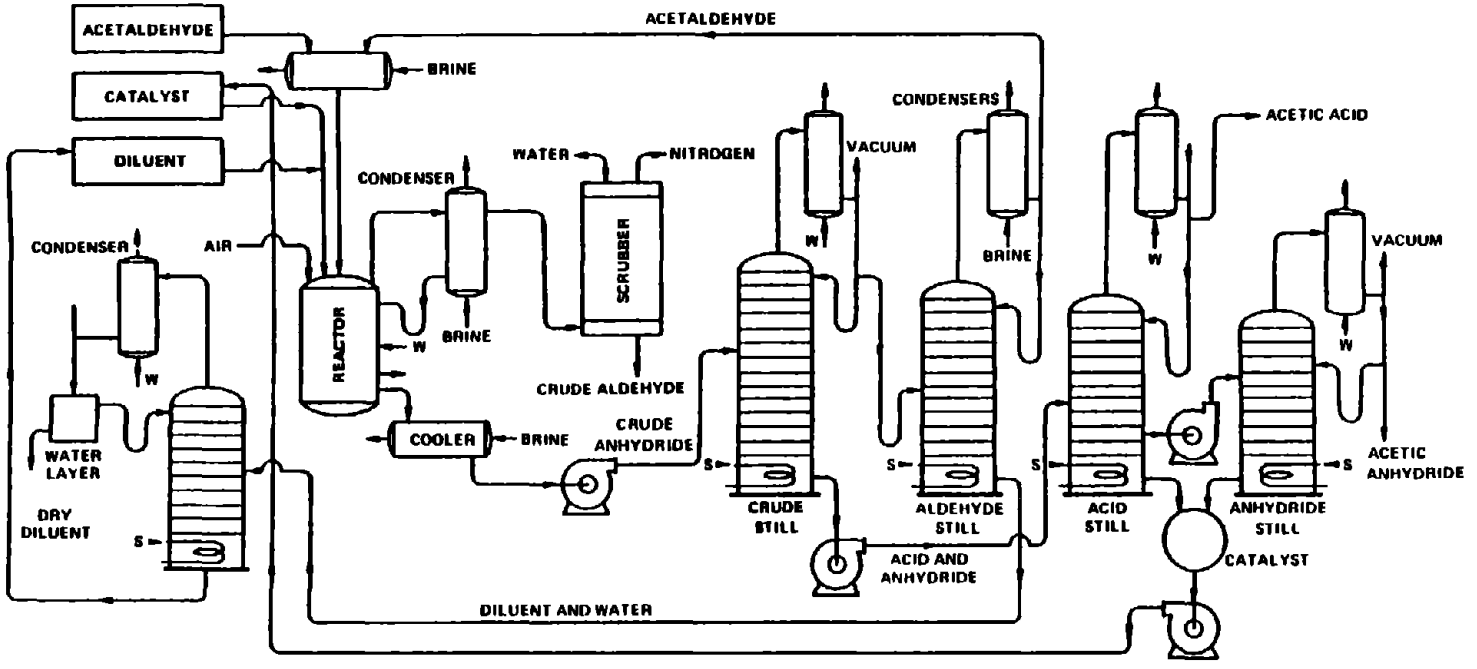


Figure 5. Manufacture of Acetic Anhydride from Acetaldehyde

The manufacture of acetic anhydride occurs in a closed-system. Worker exposure is most likely to occur from fugitive emission, leaks, spills, and waste streams containing the anhydride.

11. Impurities or Additives

The usual specifications for commercial acetic anhydride are a 99 weight percent purity (or better); trace ions present at less than 1 ppm are as follows: Al, Cl, PO_4, SO_4, and Fe. A technical grade is sometimes marketed; it has a lower assay, ordinarily about 97% maximum (Wagner, 1978).

12. Occupational Exposure

The National Occupational Hazard Survey indicates that 19,368 workers are potentially exposed to acetic anhydride.

13. Control Technology and Work Practices

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

14. Biological Effects

a. Animal Studies

(1) Acute Exposures

The results of acute exposure to acetic anhydride in animal studies are presented in Table 6.

Acetic anhydride has been shown to be an irritant; 10 mg produce mild irritation to the skin of rabbits in 24 hours using the Draize procedure (Smyth et al., 1951). When the chemical was not maintained in contact with the skin by an impervious barrier, mild skin irritation in the rabbit was obtained with 540 mg (Union Carbide, 1963). Severe eye irritation in the rabbit occurred with 250 µg of acetic anhydride (Smyth et al., 1951).

Table 6. Acute Toxicity of Acetic Anhydride

Route	Species	Dose[c] (mg/kg)	Response	Reference
oral	rat	1780	LD50[a]	Smyth et al., 1951
inhalation	rat	1000	LCLo	Carpenter et al., 1949
inhalation	rat	1000 ppm x 4 h	0/6 deaths[a]	Smyth et al., 1951
inhalation	rat	2000 ppm x 4 h	6/6 deaths[a]	Smyth et al., 1951
inhalation	rat	saturated vapor[b] x 5 min.	exposure maximum for no death	Smyth et al., 1951
dermal	rabbit	10 mg x 24 h	mild irritation	Smyth et al., 1951
dermal	rabbit	540 mg (open)	mild irritation	Union Carbide, 1963
dermal	rabbit	4000 mg/kg	LD50	Union Carbide, 1963
ocular	rabbit	250 µg	corneal necrosis	Smyth et al., 1951

[a]Mortality in 14 days.

[b]Assuming 20°C, saturation concentration is approximately 4500 ppm.

[c]h = hours

(2) Subchronic Exposures

No information was found in the literature searched.

(3) Chronic Exposures

No information was found in the literature searched.

(4) Carcinogenicity

No information was found in the literature searched.

(5) Mutagenicity

No information was found in the literature searched.

(6) Teratogenicity

Brown et al. (1978) reported in an abstract that acetic anhydride was a teratogen in CD-1 mice. A significant increase in fetal abnormalities (the abnormalities were not specified) occurred following exposure of the mice on days 8 to 10 or 11 of gestation to 0.188 mmol/kg of acetic anhydride.

(7) Reproductive Effects

No information was found in the literature searched.

(8) Other Relevant Information

No information was found in the literature searched.

b. Human Studies

(1) Pharmacokinetics

No information was found in the literature searched.

(2) Health Effects

Acetic anhydride vapors at high concentrations cause severe irritation of the nose and throat, with the possibility of associated lung injury (Hendersen and Haggard, 1943; Tabershaw et al., 1977). Acetic anhydride was reported to be a lachrymater (Fairhall, 1949) and can cause photophobia, conjunctivitis, and severe corneal burns (McLaughlin, 1946; Tabershaw et al., 1977). Corneal injury may result in interstitial keratitis and corneal opacity (Tabershaw et al., 1977).

Delayed severe burns may result from skin contact with liquid acetic anhydride (Tabershaw et al., 1977).

(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 current toxicological or environmental studies of acetic anhydride were found.

16. Exposure Standards

A Threshold Limit Value-Time Weighted Average (TLV-TWA) of 5 ppm has been recommended by the ACGIH (1980) and adopted by OSHA (1976).

17. Sources of Additional Relevant Information

No sources of additional relevant information were identified.

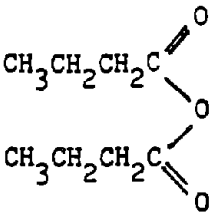
18. Other Pertinent Data

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

B. BUTYRIC ANHYDRIDE

1. Chemical Name: Butyric Anhydride

2. Chemical Structure:



3. Synonyms: Butyric acid anhydride
Butanoic anhydride
n-Butyric anhydride
Butyryl oxide
Butanoic acid, anhydride

4. Chemical Abstracts Service (CAS) Number: 106-31-0

5. Registry of Toxic Effects of Chemical Substances (RTECS) Number:
Not listed

6. Chemical and Physical Properties:

Description:	water-white liquid
Molecular Weight:	158.19
Boiling Point:	199.5°C
Melting Point:	-75°C
Vapor Pressure:	0.20 mm Hg (20°C); 10 mm Hg (140°F)
Solubility:	decomposes in H_2O
Specific Gravity:	0.9946_4^{20}
Stability:	combustible, autoignition temp. 535°F; flash point 180°F(CC); explosive limit, mg/l: lower 54.4

7. Production

U.S. EPA (1980) lists Kodak's production in 1977 as 100 to 500 million pounds.

8. Use

The major use of butyric anhydride is most likely the production of cellulose acetate butyrate (CAB) resins (Eastman Kodak, 1977). CAB is made

from cellulose, acetic anhydride, and butyric anhydride (Whistler and Zysk, 1978). For this use, butyric anhydride is captively used by Kodak, which makes the CAB resins that are formed into high-shock resistant plastics. These resins are used to make films, rods, and sheets for a variety of products from toys to industrial piping. Large quantities are made into film base for further processing into photographic film (Eastman Kodak, 1977). Pryde (1978) indicates that markets for CAB resins are declining as other types of thermoplastics are replacing CAB resins.

Another important use of butyric anhydride is in the preparation of esters for use as flavoring agents such as methyl, ethyl, and isoamyl butyrates (Lurie, 1964). It is also used in a variety of processes for introducing the butyryl group into chemical compounds. In the pharmaceutical field, butyric anhydride is used in the synthesis of bronchial antispasmodics and in the perfume industry, to produce odorants such as linalyl butyrate and geranyl butyrate (Eastman Kodak, 1977).

9. Manufacturers and Distributors

The only commercial manufacturer of butyric anhydride is Eastman Kodak (Tennessee Eastman) in Kingsport, TN (SRI International, 1980; U.S. EPA, 1980; USITC, 1980a).

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

Aldrich Chem.	Chem. Services	Pfaltz and Bauer
Anachemia Chem.	Eastern Chem.	Polysciences
Atomergic Chemetals	Em Lab.	Toyomenka (Amer.)
J.T. Baker Chem.	Fisher Sci.	Tridom Chem.
Bio-Clinical Lab.	ICN/K and K	
Columbia Organics	Lachat Chem.	

10. Manufacturing Processes

The raw material for the manufacture of butyric anhydride is butyraldehyde (Sherman, 1978; Lurie, 1964). Air or oxygen is passed into the

butyraldehyde in the presence of a catalyst. Butyric acid and water, which are formed along with the anhydride, are separated by distillation.

11. Impurities or Additives

Commercial grade n-butyric anhydride assays 98% (Eastman Kodak, 1977).

12. Occupational Exposure

The National Occupational Hazard Survey does not provide an estimate of the numbers of workers who are potentially exposed to butyric anhydride.

13. Control Technology and Work Practices

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

14. Biological Effects

No information was found in the literature searched regarding the biological effects of butyric anhydride.

15. Ongoing Studies

No current toxicological or environmental studies of butyric anhydride were found.

16. Exposure Standards

No recommended or promulgated occupational exposure standards for butyric anhydride were found.

17. Sources of Additional Relevant Information

No sources of additional relevant information were identified.

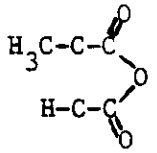
18. Other Pertinent Data

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

C. CITRACONIC ANHYDRIDE

1. Chemical Name: Citraconic Anhydride

2. Chemical Structure:



3. Synonyms: Citraconic acid anhydride
2,5-Furandione, 3-methyl-
2-Methylmaleic anhydride
3-Methylmaleic anhydride
Methylmaleic acid anhydride

4. Chemical Abstract Service (CAS) Number: 616-02-4

5. Registry of Toxic Effects of Chemical Substances (RTECS) Number: GE6825000

6. Chemical and Physical Properties:

Description:	colorless liquid
Molecular Weight:	112.09
Boiling Point:	213-214°C
Melting Point:	7-8°C
Vapor Pressure:	1 mm Hg (47.1°C)
Solubility:	soluble in ether
Specific Gravity:	1.25_4^{15}
Stability:	combustible

7. Production

Data available from the U.S. EPA (1980) regarding procedures of citraconic anhydride and production volumes are presented in Table 7.

8. Use

Citraconic anhydride is used as a reagent for alkalies, alcohols, and amines (Hawley, 1977). It is also useful as a curing agent for epoxy resins (Humprey, 1960) which may be its primary use. Patent literature indicates that it is useful in a variety of chemical syntheses.

Table 7. Producers of Citraconic Anhydride and Production Ranges (U.S. EPA, 1980)

Producer	Type of Production	1977 Production Range
Eastman Kodak Rochester, NY	Manufacturer	none
Chevron USA Richmond, CA	Manufacturer	1-10 million lb
Fritzsche Dodge and Olcott East Hanover, NJ	Manufacturer	none

9. Manufacturers and Distributors

The manufacturers are listed in Table 7.

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

Aldrich Chem.	ICN/K and K
Atomergic Chemetals	ICN Nutritional
Bio-Clinical Lab.	Lachat Chem.
Chem. Dynamics	MCB Reagents
Chem. Procurement Lab.	Monomer-Polymerand Dajac Lab.
Chem. Services	Pierce Chem.
Columbia Organics	Pfaltz and Bauer
Eastern Chem.	Polysciences
EM Lab.	Tridom Chem.
Fisher Sci.	U.S. Biochemical

10. Manufacturing Processes

The exact commercial method is not available; however, citraconic anhydride is prepared in high, reproducible yield by heating itaconic acid in the presence of an alkali metal sulfate or phosphate at a temperature sufficient to liquify the itaconic acid. Distillation of the reaction product yields a high purity product (Humprey, 1960).

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 citraconic anhydride.

13. Control Technology and Work Practices

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

14. Biological Effects

a. Animal Studies

(1) Acute Exposures

The acute toxic effects of citraconic anhydride are summarized in Table 8.

Table 8. Acute Toxicity of Citraconic Anhydride

Route	Species	Dose (mg/kg)	Response	Reference
oral	rat	2600	LD50	Smyth and Carpenter, 1944
inhalation	rat	saturated vapor x 4 hours	maximum exposure for no deaths	Smyth and Carpenter, 1944
dermal	guinea pig	1000	LD50	Smyth and Carpenter, 1944
dermal	rabbit	218	LD50	Shell Chemical Co., n.d.
dermal	rabbit	12.5 mg	mild irritation after 24 hours	Smyth and Carpenter, 1944
ocular	rabbit	not stated	corneal necrosis	Smyth and Carpenter, 1944

Citraconic anhydride has been reported to be mildly irritating to the skin and severely irritating to the eyes of rabbits following single exposures (Smyth and Carpenter, 1944).

Citraconic anhydride was shown to sensitize guinea pigs following twice weekly intracutaneous injections (flank skin) with 0.05 ml of a 0.1% solution (Jacobs, 1940). Treatments were continued for 2 to 2 1/2 weeks, and the animals tested not more than 2 weeks after the last treatment. A type of immediate wheal-and-erythema reaction, similar to that observed in human atopic hypersensitiveness, was induced. Application of citraconic anhydride to the nipples of sensitized guinea pigs has been reported to elicit an eczema after 14 hours (Hunziker, 1968). Fat details of the sensitization schedule were not published.

(2) Subchronic Exposures

No information was found in the literature searched.

(3) Chronic Exposures

No information was found in the literature searched.

(4) Carcinogenicity

No information was found in the literature searched.

(5) Mutagenicity

No information was found in the literature searched.

(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

No information was found in the literature searched.

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 current toxicological or environmental studies of citraconic anhydride were found.

16. Exposure Standards

No recommended or promulgated occupational exposure standards for citraconic anhydride were found.

17. Sources of Additional Relevant Information

No sources of additional relevant information were identified.

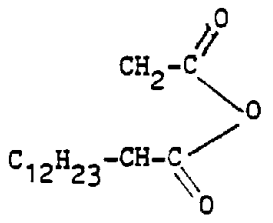
18. Other Pertinent Data

No other information that would aid in the assessment of citraconic anhydride as an occupational hazard were found in the literature searched.

D. DODECENYLSUCCINIC ANHYDRIDE

1. Chemical Name: Dodecenylsuccinic Anhydride

2. Chemical Structure:



3. Synonyms: DDSA
Dicarboxylic anhydride
2,5-Furandione, 3-(dodecenyl)dihydro-
Succinic anhydride, dodecenyl-

4. Chemical Abstract Service (CAS) Number: 25377-73-5

5. Registry of Toxic Effects of Chemical Substances (RTECS) Number: WN122500

6. Chemical and Physical Properties:

Description:	light yellow to clear, viscous oil
Molecular Weight:	281.44
Boiling Point:	180-182°C (5 mm Hg)
Melting Point:	---
Vapor Pressure:	---
Solubility:	practically insoluble in water; completely soluble in oil
Specific Gravity:	1.002 (25°C)
Stability:	combustible

7. Production

Production in recent years is as follows (USITC, 1980a, 1979a, 1978a):

Year	Production in million lb
1979	1.934
1978	1.207
1977	1.342

Data available from the U.S. EPA (1980) regarding producers of dodecenylsuccinic anhydride and production volumes are presented in Table 9.

8. Use

Dodecenylsuccinic anhydride is used to make alkyd, epoxy and other resins, anticorrosion agents, plasticizers, wetting agents for bituminous compounds, and vulcanizable products (Hawley, 1977).

Alkenylsuccinic anhydrides are also useful as additives for marine diesel engine lubricants (Turi, 1968; Esso, 1965).

9. Manufacturers and Distributors

Manufacturers include (SRI International, 1980; USITC, 1980a):

Buffalo Color Corp.	Buffalo, NY
Dixie Chemical Co.	Bayport, TX
Millikem Chem.	Inman, SC
Tenneco	Garfield, NJ
The Humphrey Chem. Co.	North Haven, CT

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

Accurate Chem.
Aceto Chem.
Alfa Prod.
Alpha International
Anhydrides and Chem.
Atomergic Chemetals
Columbia Organics
Electronic Microscopy
EM Lab.
Fisher Sci.
Gallard-Schelsinger
ICN/K and K
MCB Reagents
Miller-Stephenson Chem.
Monomer-Polymer and Dajac
Polysciences
Rhone-Poulens
Trans World Chem.
Tridom Chem.

Table 9. Producers of Dodecenylsuccinic Anhydride and Production Ranges (U.S. EPA, 1980)

Producer	Type of Production	1977 Production Range
Buffalo Color Corp. Buffalo, NY	Manufacturer	0.1-1.0 million lb
Milliken Chemical Co. Inman, SC	Manufacturer	confidential
Allied Chemical Corp. Buffalo, NY	Manufacturer	0.1-1.0 million lb
Tenneco Chemical Garfield, NJ	Manufacturer	none
Tretolite St. Louis, MO	Manufacturer	confidential
The Humprey Chemical Co. North Haven, CT	Manufacturer	under 1000 lb
Rhone-Poulenc Freeport, TX	Importer	none
Ciba-Geigy Corp. Andsley, NY	Importer	none

10. Manufacturing Processes

Alkenylsuccinic anhydrides are produced by the reaction of maleic anhydride with the appropriate olefin (Irwin and Selwitz, 1968).

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 dodecenylsuccinic anhydride.

13. Control Technology and Work Practices

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

14. Biological Effects

a. Animal Studies

(1) Acute Exposures

An intraperitoneal LD50 of 320 mg/kg has been reported for mice (Longley et al., 1964). Injections (corn oil was used as a diluent) were made at dose levels ranging from 10 to 1000 mg/kg; mice subjected to high dosages exhibited slowed voluntary activity, eventual cessation of voluntary activity, profuse lacrimation and augmented startle response. Mid-range exposures showed injected ear vessels, staggering gait, weakened grip reflex and some decline in spontaneous activity. Histopathological examination of an animal that expired 138 hours after interperitoneal injection of 422 mg/kg indicated that death resulted from a low-grade acute peritonitis; the lungs and liver showed congestion and the liver, spleen, intestine and colon were inflamed.

When 400 mg dodecenylsuccinic anhydride was maintained in contact with guinea pig skin for 24 hours, mild irritation occurred (slight edema

for 3 days which healed after 14 days); 40 mg produced no effects (Longley et al., 1964). Instillation of 50 mg into the eyes of guinea pigs was also mildly irritating; slight swelling, very slight corneal opacity, and a moderate discharge was observed which lasted for 1 day.

(2) Subchronic Exposures

No information was found in the literature searched.

(3) Chronic Exposures

No information was found in the literature searched.

(4) Carcinogenicity

No information was found in the literature searched.

(5) Mutagenicity

No information was found in the literature searched.

(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

No information was found in the literature searched.

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 current toxicological or environmental studies of dodecenylsuccinic anhydride were found.

16. Exposure Standards

No recommended or promulgated occupational exposure standards for dodecenylsuccinic anhydride were found.

17. Sources of Additional Relevant Information

A NIOSH Health Hazard Evaluation (HHE) relating to dodecenylsuccinic anhydride has been conducted at the Essex Wire Corp., Kenton, OH (HHE No. 73-151-141).

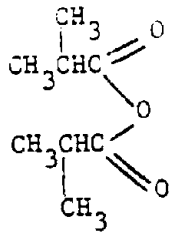
18. Other Pertinent Data

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

E. ISOBUTYRIC ANHYDRIDE

1. Chemical Name: Isobutyric Anhydride

2. Chemical Structure:



3. Synonyms: Isobutyric acid anhydride
Isobutyryl oxide
Propanoic acid, 2-methyl-, anhydride

4. Chemical Abstracts Service (CAS) Number: 97-72-3

5. Registry of Toxic Effects of Chemical Substances (RTECS) Number:
NQ5550000

6 Chemical and Physical Properties:

Description:	liquid
Molecular Weight:	158.19
Boiling Point:	181.5°C (at 734 mm Hg); 182.5°C (760 mm Hg)
Melting Point:	-53.5°C
Vapor Pressure:	0.50 mm Hg (20°C)
Solubility:	decomposes in H_2O and alcohol; soluble in ether
Stability:	combustible; autoignition temperature 625°F, flash point 153°F (CC); explosive limit, mg/l: lower 57.1
Specific Gravity:	$0.951\text{-}0.956^{20}_{20}$

7. Production

The U.S. EPA (1980) lists Kodak's 1977 production as 1 to 10 million pounds.

8. Use

Isobutyric anhydride is employed in the esterification of cellulose to produce cellulose triisobutyrate and cellulose acetate isobutyrate. In combination with acetic anhydride, isobutyric anhydride has been used for esterifying

sucrose to produce a modifying extender for film-formers and extrudable plastics. Isobutyric anhydride also finds application in the manufacture of odorants and peroxide catalysts (Eastman Kodak, 1974).

Isobutyric anhydride and its acid are used to synthesize flavors and perfumes such as apricot, pineapple, banana, and strawberry odors and flavors (Lurie, 1964). They are also useful for introducing the isobutyryl group into chemical compounds and as gasoline sweetening agents.

9. Manufacturers and Distributors

The only commercial manufacturer of isobutyric anhydride is Eastman Kodak (Tennessee Eastman) in Kingsport, TN (SRI International, 1980; U.S. EPA, 1980; USITC, 1980a).

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

Atomergic Chemetals	Fisher Sci.
BASF Wyandotle	Lachat Chem.
Chem. Services	MCB Reagents
EM Lab.	Tridom Chem.

10. Manufacturing Processes

Isobutyric anhydride is most likely made from isobutyraldehyde as the raw material. Kodak produces isobutyraldehyde in Kingsport, TN (SRI International, 1980). Air oxidation of the aldehyde can yield the acid or the anhydride. Purification is most likely accomplished via azeotropic distillation and fractionation (Lurie, 1964).

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 isobutyric anhydride.

13. Control Technology and Work Practices

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

14. Biological Effects

No information was found in the literature searched regarding the biological effects of isobutyric anhydride.

15. Ongoing Studies

No current toxicological or environmental studies of isobutyric anhydride were found.

16. Exposure Standards

No recommended or promulgated occupational exposure standards for isobutyric anhydride were found.

17. Sources of Additional Relevant Information

No sources of additional relevant information were identified.

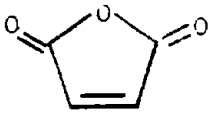
18. Other Pertinent Data

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

F. MALEIC ANHYDRIDE

1. Chemical Name: Maleic Anhydride

2. Chemical Structure



3. Synonyms: cis-Butenedioic anhydride
Dihydro-2,5-dioxofuran
2,5-Furandione
Lytron 810
Lytron 820
Maleic acid anhydride
NCI-C54660
Toxilic anhydride

4. Chemical Abstracts Service (CAS) Number: 108-31-6

5. Registry of Toxic Effects of Chemical Substances (RTECS) Number:
ON36750

6. Chemical and Physical Properties:

Description:	colorless to white needles or flakes
Molecular Weight:	98.06
Boiling Point:	197-202°C
Melting Point:	53°C
Vapor Pressure:	0.0005 mm Hg (20°C)
Solubility:	227g/100g acetone (25°C) 112g/100g ethyl acetate (25°C) 52.5g/100g chloroform (25°C) 50g/100g benzene (25°C) 23.4g/100g toluene (25°C) 19.4g/100g o-xylene (25°C) 0.60g/100g carbon tetrachloride (25°C) 0.25g/100g ligroin (25°C) soluble in dioxane soluble in water forming maleic acid soluble in alcohol with ester formation
Specific Gravity:	0.934_4^{20}

Stability:	combustible; autoignition temperature 80°F; flash point 218°F. Decomposes exothermically in the presence of the alkali metals or amines at temperatures above 150°C; the concentration of these impurities necessary to trigger the decomposition is as low as 200 ppm

7. Production

Recent production figures for maleic anhydride are listed below (USITC, 1980a, 1979a, 1978a, 1977a, 1977b, 1976):

Year	Production in Millions of Pounds
1979	323.2
1978	341.1
1977	294.0
1976	264.0
1975	215.8
1974	289.9

Data available from the U.S. EPA (1980) regarding producers of maleic anhydride and production volumes are presented in Table 10.

The maleic anhydride market is expected to grow at a rate of 3.8% per year through 1984 (CMR, 1980b).

In 1978, 2.88 million pounds of maleic anhydride were exported as compared to 0.92 million pounds in 1975 (Bureau of the Census, 1979, 1976). Separate statistics are not available for imports; however, in 1974 and 1975, about 12 million pounds and about 5 million pounds, respectively, were estimated to have been imported (Blackford, 1976). In 1977, in excess of 13 million pounds were imported (U.S. EPA, 1980).

8. Use

The following tabulation presents the percentage of the total amount of maleic anhydride produced that is used in each of the applications listed:

Table 10. Producers of Maleic Anhydride and Production Ranges (U.S. EPA, 1980)

Producer	Type of Production	1977 Production Range
Odenka Chemical Houston, TX	Manufacturer	10-50 million lb
Chevron USA Richmond, VA	Manufacturer	1-10 million lb
Koppers Co. Bridgeville, PA Chicago, IL	Manufacturer Manufacturer	10-50 million lb 0.1-1.0 million lb
Haven Chemical Philadelphia, PA	Manufacturer	confidential
Monsanto Co. St. Louis, MO	Manufacturer	50-100 million lb
U.S. Steel Chemical Pittsburg, PA	Manufacturer	10-50 million lb
Amoco Chemicals Joliet, IL	Manufacturer	confidential
Ashland Chemical Neal, WV	Manufacturer	10-50 million lb
Tenneco Chem. Fords, NJ	Manufacturer	10-50 million lb
Reichhold Chemical Morris, IL	Manufacturer	none
Marubeni American New York, NY	Importer	0.1-1.0 million lb
Nissho-Iwai American New York, NY	Importer	10-50 million lb
Lonza Inc. Fairlawn, NJ	Importer	confidential
Browning Chemical New York, NY	Importer	none
Withington Co. Pelham Manor, NY	Importer	none
Ishihara Corp. San Francisco, CA	Importer	confidential
Filo Chemical New York, NY	Importer	none
Glidden (SCM Corp.) Cleveland, OH	Importer	10-100 thousand lb

Table 10. Producers of Maleic Anhydride and Production Ranges (U.S. EPA, 1980) (Cont'd.)

Producer	Type of Production	1977 Production Range
Fallek Chemical New York, NY	Importer	none
Arturo F. Flores Eagle Pass, TX	Importer	1-10 million lb
Cemco Inc. New Canaan, CT	Importer	none
Owens-Corning Fiberglas Toledo, OH	Importer	10-100 thousand lb
Milijac Inc. New Canaan, CT	Importer	none
Thorson Chemical New York, NY	Importer	10-100 thousand lb
Sakai Trading NY New York, NY	Importer	none
Steuber Co. New York, NY	Importer	0.1-1.0 million lb
Solchem Inc. New York, NY	Importer	confidential
Mitsubishi International New York, NY	Importer	1-10 million lb
Neville Chemical Santa Fe Springs, CA	Importer	10-100 thousand lb
Rohm and Haas Co. Philadelphia, PA	Importer	10-100 thousand lb
Itoh and Co., Inc. New York, NY	Importer	0.1-1.0 million lb
Tennant and Sons and Co. New York, NY	Importer	1-10 million lb
ICC Industries New York, NY	Importer	confidential
Americhem New Cannan, CT	Importer	none
Plant Site Not on File	Importer	0.1-1.0 million lb
Plant Site Not on File	Importer	0.1-1.0 million lb
Plant Site Not on File	Importer	0.1-1.0 million lb
Plant Site Not on File	Importer	1-10 million lb

	Percentage of Total	
	(CMR, 1980b)	(Lawler, 1977)
Unsaturated polyester resins	52	45
Agricultural chemicals	9	10
Fumaric acid	8	9
Lubricating additives	12	7
Copolymers	6	6
Reactive plasticizers	--	4
Maleic acid	4	4
Surface-active agents	--	3
Alkyd resins	--	2
Chlorendic anhydride and acid	--	1
Miscellaneous	9	9

The agricultural chemicals (herbicides and growth regulators) made from maleic anhydride include malathion, maleic hydrazide, captan, endothall, Difolatan®, and Alar® (Blackford, 1976). Examples of reactive or internal plasticizers are dibutyl maleate and dioctyl maleate.

Maleic anhydride has a variety of miscellaneous uses (Blackford, 1976). On the order of 0.5-1.0 million pounds per year are consumed to make succinic acid anhydride. Less than 0.25 million pounds per year are consumed to make dibutyltin maleate, a stabilizer for copolymers. Four to 5 million pounds per year are consumed to make paper sizing resins. On the order of 2 million pounds per year are used to make tetrahydrophthalic anhydride, a fire retardant. Methyl tetrahydrophthalic anhydride, also made from maleic anhydride, is believed to have a larger market than tetrahydrophthalic anhydride.

9. Manufacturers and Distributors

The commerical manufacturers of maleic anhydride are listed in Table 11.

Table 11. Manufacturers of Maleic Anhydride (SRI International, 1980; CMR, 1980b)

Manufacturer	Location	Annual Capacity Million of lb	Remarks and Raw Materials
Ashland Oil Co.	Neal, WV*	60	Benzene
Denka Chem. Corp.	Houston, TX	50	Benzene - partial switch to butane raw material
Koppers Co.	Cicero, IL	10	Phthalic anhydride by-product
Monsanto Co.**	St. Louis, MO	115	n-Butane (20%); benzene (80%); plant will be converted to 100% butane raw material
Reichhold Chem.	Morris, IL	50	Benzene
	Elizabeth, NJ	40	Shut-down
Standard Oil (Amoco)	Joliet, IL	60	n-Butane
Tenneco Chem.	Fords, NJ	26	Benzene
U.S. Steel Chem.	Neville Island, PA	80	Benzene

* Closed by explosion and fire on Oct. 16, 1980; scheduled restart in 2nd quarter, 1981.
**Monsanto is building a 130 million lb/yr plant in Pensacola, FL scheduled to start-up in 1983.

The many distributors of maleic anhydride include 1980-81 OPD Chemical Buyers Directory, 1980; Chemical Week: 1981 Buyers Guide Issue, 1980; Chemical Sources-USA, 1980):

Advent Chem.
Aldrich Chem.
Alpha Intern.
Anachemia Chem.
Atomergic Chemetals
J.T. Baker Chem.
Bentley Chem.
Biochemical Lab.
Bio-Clinical Lab.
Browning Chem.
Carbonit Houston
Cemco
Chem. Dynamics
Chem. Procurement Lab.
Chemsampo
Chem. Services
Conray Chem.
Continental Trading
Eastern Color and Chem.
Eastman Kodak
EM Lab.
Fallek Chem.
Fisher Sci.
Gallard-Schelsinger
General Plastics
Gill and Duffus Chem.
M.W. Hardy and Co.
HCI Chem.
Helm Houston
Holtrachem
ICD Group
International Commodities
Intsel Corp.
Ishihara Corp.
Lachat Chem.
LUX Chem.
MCB Reagents
Milijac
Milton M. Star Chem.
Monomer-Polymer and Dajac
Montedison
Ore and Chem.
P.A.T. Products
Pierce Chem.
Prior Chem.
Prochimie International
Research Plus Lab.
Sigma Chem.
Signo Trading Internat.
Solchem.
Stinnes Oil and Chem.
Thorson Chem.
Toyomenka (Amer.)
Tridom Chem.
Velco Enterprises
White Cross Labs.

10. Manufacturing Processes

Maleic anhydride is manufactured in the United States by the oxidation of benzene, the oxidation of n-butane, or the recovery of by-product from phthalic anhydride production. Currently, 81.5% of industry capacity is based on benzene oxidation, 16.5% on n-butane oxidation, and 2% on by-product recovery (SRI International, 1980). Koppers Corp. is the only manufacturer using the by-product recovery process; Standard Oil (Amoco) and, in part, Monsanto use n-butane oxidation.

The primary reaction for the production of maleic anhydride from benzene by catalytic vapor-phase oxidation to produce 50-60% of the theoretical yield can be represented as follows:

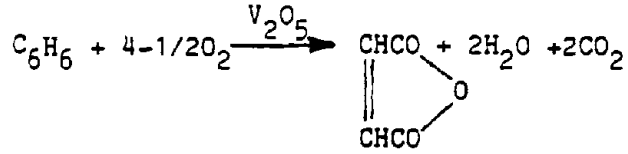
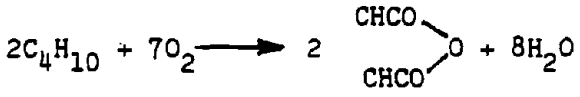


Figure 6 is a flow diagram of the process; while it is typical of the methods used by domestic producers, there are a variety of product recovery and purification techniques used in industry. The following passages from Survey Reports on Atmospheric Emissions From the Petrochemical Industry, Vol. III, (Pervier et al., 1974b) describe the manufacturing process:

> Benzene is either carbureted with air and preheated or vaporized and then mixed with an excess of preheated air prior to being admitted to a multi-tubular catalytic reactor. The vapors pass downward (or upward in some cases) through the tubes, which contain a pelleted V205 catalyst, and exit the reactor at a temperature in the range of 750 to 850°F. The very large heat of reaction (up to 2,600 BTU/lb of MAN [maleic anhydride]) is removed by the heat of transfer fluid--molten salt or boiling mercury--that circulates around the outside of the tubes, and by air preheat.
>
> The effluent vapors, consisting of maleic anhydride, maleic acid, carbon oxides, water and benzene, are cooled and then passed through a partial condenser and separator, where the bulk of the maleic anhydride is separated from the non-condensibles. The overhead material from the separator still contains some maleic anhydride, this material is recovered thru (sic) absorption in aqueous (or non-aqueous) solvents and recovered as maleic acid.
>
> The crude maleic acid is converted to the anhydride by dehydration, usually by azeotropic distillation. This material is combined with the maleic anhydride recovered from the partial condenser and purified by vacuum and/or azeotropic distillation. The product is then either tableted or flaked and packaged or marketed in bulk (Pervier et al., 1974b).

The reaction for the production of maleic anhydride by the vapor-phase oxidation of n-butane may be represented by (Blackford, 1976):



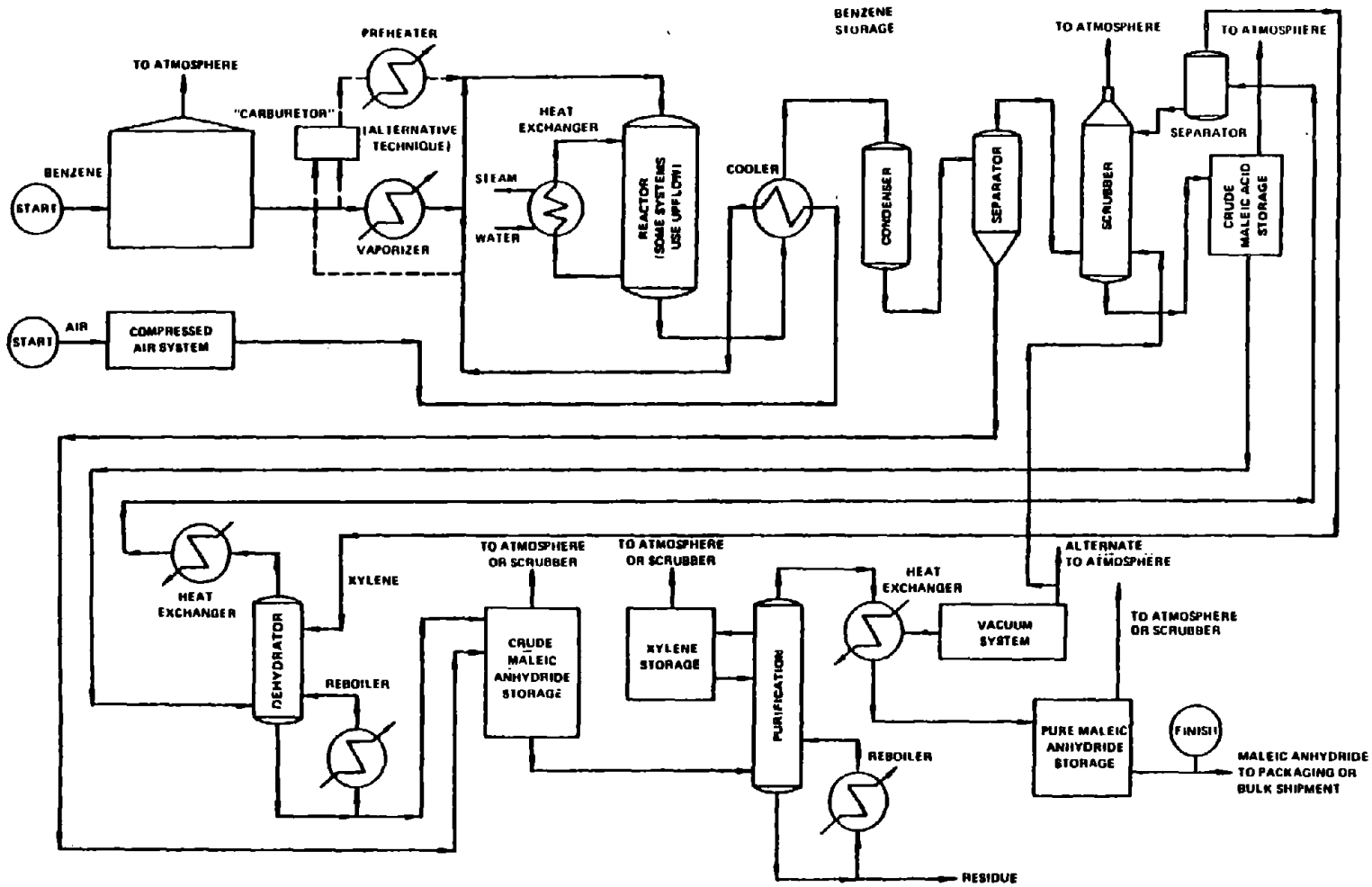


Figure 6. Manufacture of Maleic Anhydride Via Benzene Oxidation

Process operations are similar to that of the previously discussed benzene oxidation; however, a different catalyst system is required. It is believed that a complex phosphorus vanadium catalyst is used and that yields 65-71% of the theoretical yield that are obtained (Blackford, 1976).

Figure 7 diagrams the process by which maleic anhydride is recovered from phthalic anhydride waste gas scrubber water. The following passages from Hydrocarbon Processing (1977) describe this process:

> The scrubber water from the off gases of the PA [phthalic anhydride] process contains in solution about 20% of maleic acid and approximately 5% of other acids e.g. phthalic acid, benzoic acid and citraconic acid. The acid concentration of the waste water is increased under slight vacuum to about 95% in a system of evaporators which guarantee short residence time. All vapors are condensed, collected and recycled to the PA scrubbing section.
>
> The obtained concentrated melt of acids is immediately sent to a special dehydrator where the molten dicarboxylic acids are mainly dehydrated to the corresponding anhydrides and evaporated. The vapors are partially condensed. Crude MA [maleic anhydride] is obtained from the first condenser, while the second condenser yields a melt of MA and maleic acid which is recycled to the dehydrator.
>
> The remaining water vapors are retained in an injection condenser whose recycle water is fed back to the PA scrubber.
>
> Further MA is evaporated in an agitated vessel from the melt leaving the dehydrator. High boiling material is removed as residue, which is collected in an intermediate storage vessel. This residue can be burned.
>
> The crude MA obtained in the first condenser is continuously distilled in a single column under vacuum. The pure MA is withdrawn at the top of the column.
>
> The bottoms contain higher boiling acids and anhydrides which are removed and incinerated.

11. Impurities or Additives

Commercial maleic anhydride has a minimum assay of 99% and maximum values of 0.25% for moisture, 3 ppm for iron, and 20 ppm for heavy metals (Dmuchovsky and Frantz, 1967).

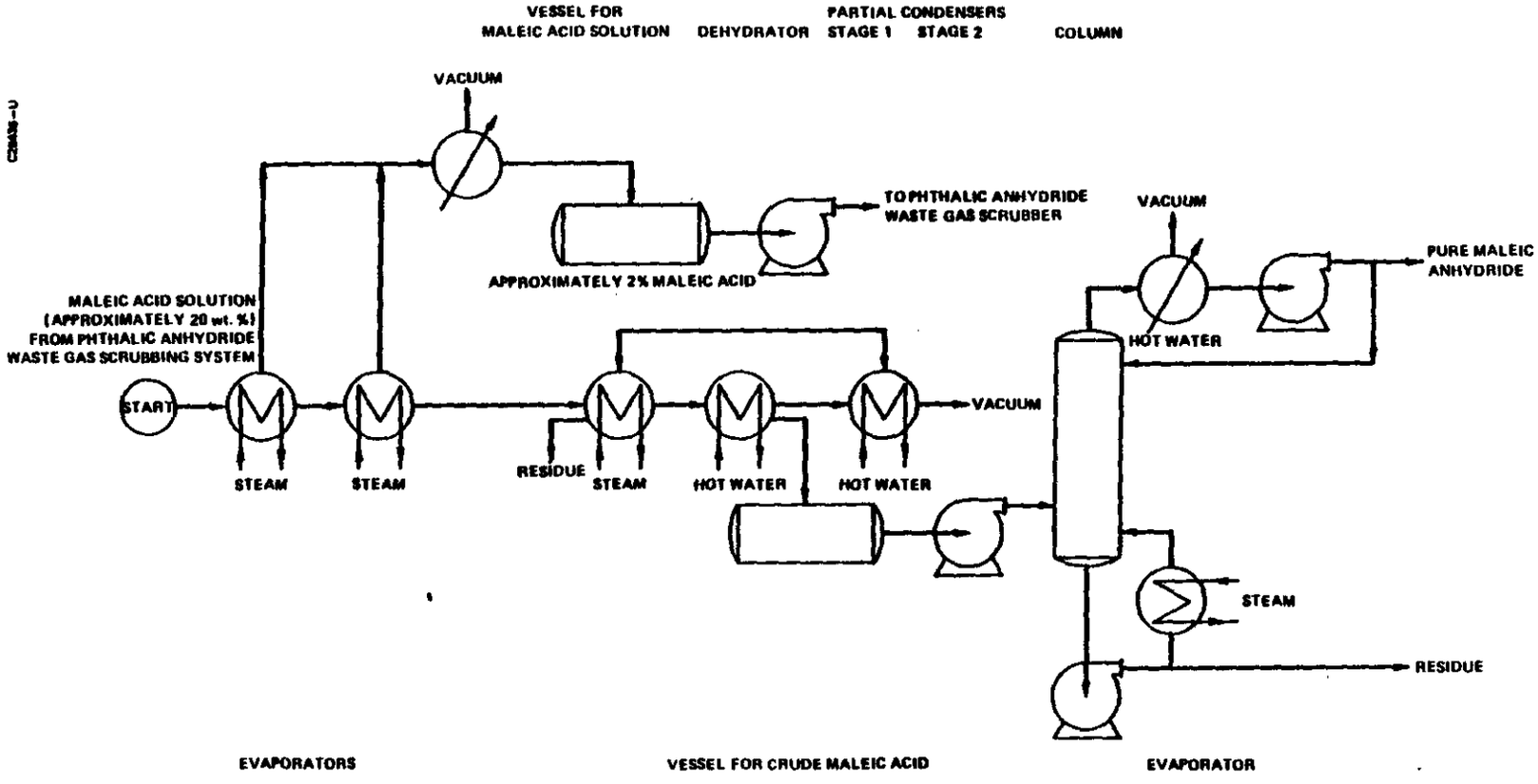


Figure 7. Manufacture of Maleic Anhydride from Phthalic Anhydride

Pervier et al. (1974b) reports that up to 0.6 pounds/hour of maleic anhydride are lost during product flaking, pelleting, packaging, and storage. This loss may be a source of worker exposure.

12. Occupational Exposure

The National Occupational Hazard Survey indicates that 71,397 workers are potentially exposed to maleic anhydride.

13. Control Technology and Work Practices

Care must be exercised in handling and storage to keep maleic anhydride away from flame or sparks, because dust and vapors from the molten product are flammable (MCA, 1974). Heating with amines, alkali and alkaline earth compounds should be avoided due to the likelihood of exothermic reaction; decomposition will take place rapidly and the gas which is evolved may cause equipment to rupture unless relief mechanisms are provided. The use of sodium or potassium carbonate or hydroxide in aqueous ammonia is not recommended for washing equipment which may later contain hot maleic anhydride because of possible explosions. The presence of alkalis in fire extinguishing media should also be avoided.

The following engineering controls have been recommended by the Manufacturing Chemist's Assocation (MCA, 1974):

BUILDING DESIGN

a. The building and partitions should be of fire resistant construction.

b. Ample emergency exits from buildings should be provided (see NFPA No. 101 "Code for Safety to Life"). Fire doors should open in the direction of travel and be of an approved type.

c. All rooms in which maleic anhydride is stored or handled should be provided with adequate ventilation. Explosion venting should be provided in the general construction of equipment and buildings in which flammable vapors or dusts are liable to concentrate.

d. Since the required area of explosion vents depends upon such factors as the intensity of an explosion, vapor temperature, type of structure, the type of vent closure, etc., the determination of vent ratios should be made by experienced engineers and safety and fire protection specialists.

EQUIPMENT DESIGN

a. The design of maleic anhydride installation is specialized. Because of the fume, fire and explosion hazards of the process materials used in the production of maleic anhydride, all operations should be handled in closed systems whenever possible.

b. Maleic anhydride flakes can develop static charges during passage through conveyors, elevators, etc. Such materials-handling equipment should be electrically grounded.

c. All tanks intended for the storage of molten maleic anhydride should be electrically grounded to safely dissipate electric charges.

AIR ANALYSIS

a. Qualitative analysis of the atmosphere may be performed to detect leakage of hazardous vapors from equipment. Due to the high crystallizing point of this compound, all portions of the sampling system, including analysis apparatus, must be maintained at a sufficiently high temperature to keep the maleic anhydride in the vapor state.

ELECTRICAL EQUIPMENT

a. To avoid fires and explosions, all wiring should be installed as given in Article 500 of the National Electrical Code, and no heating apparatus capable of reaching the autoignition temperature of maleic anhydride should be located in the work area.

Unloading procedures for tank cars and tank trucks containing maleic anhydride are detailed by MCA (1974) and Monsanto (n.d.). The chemical is molten when loaded and solidifies during transport, requiring melting in the tank prior to unloading.

14. Biological Effects

a. Animal Studies

(1) Acute Exposures

The acute toxicity of maleic anhydride is summarized in Table 12.

Maleic anhydride caused necrosis in the eyes of rabbits when applied as a 1% solution (Carpenter and Smyth, 1946). Monsanto (1977) reported that when finely ground maleic anhydride was introduced to the conjunctival sac or intact or abraded skin of rabbits, irreversible damage resulted.

(2) Subchronic Exposures

Following exposure (route not mentioned) to 12 and 50 mg/kg, 6 times weekly for 7 weeks, rats showed lower weight gains and renal, hepatic, and pulmonary tissue damage (Kowalski et al., 1967).

(3) Chronic Exposures

No information was found in the literature searched.

(4) Carcinogenicity

Male rats that received 1 mg of maleic anhydride in oil subcutaneously twice a week for 61 weeks developed (2 of 3 animals) local sarcomas at the site of injection (Dickens and Jones, 1963). The tumors that developed were capable of being transplanted into young female rats.

(5) Mutagenicity

No information was found in the literature searched.

(6) Teratogenicity and Reproductive Effects

Brown et al. (1978) observed a significant increase in fetal malformations in the offspring of CD-1 mice that received 0.375 mmol/kg maleic anhydride on days 8 to 10 or 11 of gestation. The types of abnormalities observed were not described in this abstract.

Table 12. Acute Toxicity of Maleic Anhydride

Route[a]	Species	Dose (mg/kg)	Response	Reference
oral	rats	850	LD50	Berzins, 1967, 1969
oral	rats	760	LD50	Kowalski et al., 1967
oral	rats	900[b]	LD50	Monsanto, 1977
oral	rat	1050[c]	LD50	Monsanto, 1977
oral	mice	465	LD50	Berzins, 1967, 1969
oral	guinea pigs	390	LD50	Berzins, 1967
oral	rabbits	875	LD50	Berzins, 1967
i.p.	rats	338	LD50	Kowalski et al., 1967
s.c.	rats	507	LD50	Kowalski et al., 1967
ocular	rabbits	1%	necrosis	Carpenter and Smyth, 1946
ocular	rabbits	0.1 ml (≈93 mg)	irreversible damage after 1 minute	Monsanto, 1977
dermal	rabbits	2620	LD50	Vernot et al., 1977
dermal	rabbits	>398[e]	LD50	Monsanto, 1977
		<631[e]	LD50	Monsanto, 1977
dermal	rabbit	>631[f]	LD50	Monsanto, 1977
		<1000[f]	LD50	Monsanto, 1977
dermal	rabbit	0.5g[d] x 24 hrs	irreversible damage to intact or abraded skin	Monsanto, 1977

[a] i.p. = intraperitoneal; s.c. = subcutaneous

[b] administered as a 20% aqueous solution.

[c] administered as a 20% suspension in corn oil

[d] finely ground maleic anhydride, moistened with water

[e] applied as a 40% aqueous solution and held in continuous 24 hr contact

[f] applied as a 40% suspension in corn oil and held in continuous 24 hr contact

(7) Reproductive Effects

No information was found in the literature searched.

(8) Other Relevant Information

No information was found in the literature searched.

b. Human Effects

(1) Pharmacokinetics

No information was found in the literature searched.

(2) Health Effects

Maleic anhydride acts as a strong local irritant to body tissues; this is particulary noticeable on moist skin or on mucous membranes due to the formation of maleic anhydride (Dmuchovsky and Franz, 1978; Lefaux, 1968; MCA, 1974). Severe acute exposures to dust and vapors are not voluntarily tolerated, and inhalation may result in coughing and sneezing with burning and irritation of the throat. The eyes are particulary sensitive to the dust and vapors, but reported effects such as conjunctival and corneal swelling, photophobia, double vision, and the sensation of seeing rings around lights usually are reported as temporary. McLaughlin (1946) has reported on 14 cases of corneal burns cause by maleic anhydride. All burns promptly healed within 48 hours.

Contact dermatitis may result from repeated exposure to maleic anhydride in the dry or vapor state (LeFaux, 1968; MCA, 1974); this is usually a chronic irritative type, although skin sensitivity can occur. Congestion and ulceration of the nasal mucous membranes and eye irritation may also result from chronic exposure. Repeated inhalation exposure may result in a chronic asthmatic-type bronchitis. Workers have also complained of severe headaches, nose bleeds, nausea and temporary impairment of vision following repeated exposure to maleic anhydride (Dmuchovsky and Franz, 1978).

(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

The toxicology of maleic anhydride is currently being studied at IIT Research Institute (Chicago, Illinois; Sponsored by the Chemical Industry Institute of Toxicology) (SSIE, 1980). The carcinogenic and toxic properties of maleic anhydride are being investigated in rats receiving the compound at 10, 32, and 100 mg/kg/day in the diet.

16. Exposure Standards

The ACGIH (1977) has recommended a Time Weighted Average-Threshold Limit Value (TWA-TLV) of 0.25 ppm for maleic anhydride. This level is recommended on the basis of analogy with the toxic action of phthalic anhydride. Maleic anhydride is regarded by the ACGIH as more severely toxic than phthalic anhydride, and it was noted that the recommended TLV may not be sufficiently low to prevent occasional respiratory sensitization in highly susceptible workers.

17. Sources of Additional Relevant Information

The Environmental Protection Agency has published a Chemical Hazard Information Profile (CHIP) on maleic anhydride (EPA, 1980).

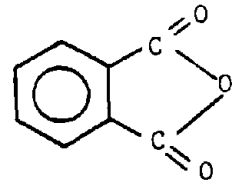
18. Other Pertinent Data

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

G. PHTHALIC ANHYDRIDE

1. Chemical Name: Phthalic Anhydride

2. Chemical Structure:



3. Synonyms: 1,2-Benzenedicarboxylic anhydride
1,3-Dioxophthalan
ESEN
Isobenzofuran, 1,3-dihydron, 1,3-dioxo-
1,3-Isobenzofurandione
NCI-C03601
PAN
PA Phthalandione
Phthalic acid anhydride
Retarder AK; ESEN; PD

4. Chemical Abstracts Service (CAS) Number: 85-44-9

5. Registry of Toxic Effects of Chemical Substances (RTECS) Number:
TI3150000

6. Chemical and Physical Properties:

Description:	white crystalline flakes or needles
Molecular Weight:	148.11
Boiling Point:	285°C (sublimes)
Melting Point:	130.8°C
Vapor Pressure:	0.0002 mm Hg (20°C)
Solubility:	soluble in 162 parts water, more in hot water with conversion to phthalic acid; soluble in 125 parts carbon disulfide; soluble in alcohol; sparingly soluble in ether
Specific Gravity:	1.527
Stability:	combustible; autoignition temp. 1083°F; flash point 305°F (CC)

7. Production

Recent production figures along with import and export figures for phthalic anhydride are listed in Table 13. Chemical Marketing Reporter (CMR, 1979) estimates the future growth of phthalic anhydride to be 3.8% per year through 1983.

Data available from the U.S. EPA (1980) regarding producers of phthalic anhydride and production volumes are presented in Table 14.

8. Use

The following tabulation presents the percentage of the total amount of phthalic anhydride produced that is used in each of the applications listed:

	Percentage of Total	
	(CMR, 1979)	(Lawler, 1977)
Plasticizers	53	50
Polyester resins	22	21
Alkyd resins	19	20
Export		4
Miscellaneous	6	5

The plasticizers made from phthalic anhydride are the phthalate esters such as dioctyl phthalate. The phthalates are discussed in a separate dossier.

Because of the large volume of phthalic anhydride consumed, the amounts used in miscellaneous applications are sizeable. In excess of 10 million pounds annually are consumed in the manufacture of dyes and dye intermediates (Blackford, 1975). The most important of these are anthraquinone dyes, xanthene dyes, fluorescein, rhodamines, and the phthalocyanine dyes, which are derived from phthalonitrile or phthalimide.

In 1973, on the order of 10-15 million pounds of tetrachloro-and tetrabromophthalic anhydride were produced from phthalic anhydride for fire-retardance in plastics (Blackford, 1975). Roughly 3 million pounds of phthalic

Table 13. Phthalic Anhydride Production, Import, and Export Figures[a] (USITC, 1980a,b, 1979a,b, 1978a,b, 1977a,b,c,d, 1976a,b, 1975, 1974; Blackford, 1975; Bureau of the Census, 1979, 1977, 1976)

Year	Production	Imports	Exports
1979	1012.86	19.85	--
1978	978.04	--	0.923
1977	925.95	53.12	--
1976	902.38	31.46	12.217
1975	702.19	21.13	4.004
1974	977.15	1.06	34.37
1973	1022.56	0.08	23.23
1972	932.98	0.69	13.79

[a]All figures in millions of pounds.

Table 14. Producers of Phthalic Anhydride and Production Ranges (U.S. EPA, 1980)

Producer	Type of Production	1977 Production Range
Chevron USA		
Richmond, CA	Manufacturer	10-50 million lb
Koppers Co.		
Chicago, IL	Manufacturer	100-500 million lb
Bridgeville, PA	Manufacturer	50-100 million lb
Exxon Corp.		
Baton Rouge, LA	Manufacturer	100-500 million lb
Allied Chemical		
El Segundo, CA	Manufacturer	10-50 million lb
Monsanto Co.		
Bridgeport, NJ	Manufacturer	50-100 million lb
Texas City, TX	Manufacturer	100-500 million lb
U.S. Steel Corp.		
Pittsburg, PA	Manufacturer	100-500 million lb
BASF Wyandotte		
Kearny, NJ	Manufacturer	100-500 million lb
Stepan Chemical		
Elwood, IL	Manufacturer	50-100 million lb
Hooker Chemical		
Aercibs, PR	Manufacturer	10-50 million lb
Lonza Inc.		
Fairlawn, NJ	Importer	confidential
Browning Chemical		
New York, NY	Importer	1-10 million lb
Withington Co.		
Pelham Manor, NY	Importer	none
Ishihara USA		
San Francisco, CA	Importer	confidential
Pfizer Inc.		
Greensboro, NC	Importer	0.1-1.0 million lb
Glidden (SCM Corp.)		
Cleveland, OH	Importer	10-100 thousand lb
Fallek Chemical		
New York, NY	Importer	1-10 million lb
Graymon Chemical		
Pine Brook, NJ	Importer	10-100 thousand lb
Sattra Trading Co.		
Stamford, CT	Importer	1-10 million lb

Table 14. Producers of Phthalic Anhydride and Production Ranges (U.S. EPA, 1980) (Cont'd.)

Producer	Type of Production	1977 Production Range
Cemco Inc. New Canaan, CT	Importer	none
Owens-Corning Fiberglas Toledo, OH	Importer	0.1-1.0 million lb
Milijac Co. New Canaan, CT	Importer	none
Uniroyal Chemical Naugatuck, CT	Importer	0.1-1.0 million lb
DuPont Wilmington, DE	Importer	none
Thorson Chemical New York, NY	Importer	1-10 million lb
Sakai Trading New York, NY	Importer	none
Steuber Co. New York, NY	Importer	1-10 million lb
Solchem Inc. New York, NY	Importer	confidential
Mitsubishi International New York, NY Houston, TX	Importer Importer	10-100 thousand lb 1-10 million lb
NAPP Chemicals Lodi, NJ	Importer	1-10 thousand lb
Mitsui and Co. San Francisco, LA	Importer	1-10 million lb
Holtrachem. Natick, MA	Importer	none
Reichold Chemicals White Plains, NY	Importer	1-10 million lb
Degussa Corp. Teterboro, NJ	Importer	under 1000 lb
Conray Chemical Rockville Center, NY	Importer	none
Tennant and Sons and Co. New York, NY	Importer	10-100 thousand lb
ICC Industries New York, NY	Importer	confidential

Table 14. Producers of Phthalic Anhydride and Production Ranges (U.S. EPA, 1980) (Cont'd.)

Producer	Type of Production	1977 Production Range
ICI Americas Wilmington, DE	Importer	none
Ruhrohole Trading New York, NY	Importer	confidential
Americhem New Canaan, CT	Importer	none
Plant Site Not on File	Importer	0.1-1.0 million lb
Plant Site Not on File	Importer	0.1-1.0 million lb
Plant Site Not on File	Importer	1-10 million lb
Plant Site Not on File	Importer	1-10 million lb

anhydride are used annually to make the polyester monomer dialkyl phthalate (Blackford, 1975).

On the order of 2 million pounds of phthalic anhydride are used annually to make the herbicide naptalam (Meylan et al., 1976). Phthalic anhydride is also used to make polyester polyols for coatings and elastomers, medicinals such as phenolphthalein, perfume agents such as methyl anthranilate, and metallic phthalates such as lead phthalate, which is used as a stabilizer in wire insulation (Blackford, 1975).

9. Manufacturers and Distributors

The manufacturers of phthalic anhydride are the following (CMR, 1979):

Producer	Location	Annual Capacity in Millions of Pounds
Allied Chem.	El Segundo, CA	36
BASF Wyandotte	Kearney, NJ	150
Chevron	Richmond, CA	45
Exxon	Baton Rouge, LA	130
Koppers	Bridgeville, PA	90
	Cicero, IL	235
Monsanto	Bridgeport, NJ	90
	Texas City, TX	165
Stepan	Millsdale, IL	170
U.S. Steel	Neville Island, PA	205
		1316

Because of the large production volumes and the sizeable recent import volumes of phthalic anhydride, there are many distributors of the compound. The major distributors include (1980-81 OPD Chemical Buyers Directory , 1980; Chemical Week: 1981 Buyers Guide Issue, 1980; Chem. Sources-USA, 1980):

Advent Chem.
Aldrich Chem.
Alpha International
Anachemia Chem.
Atomergic Chemetals
J.T. Baker Chem.
Bentley Chem.
Browning Chem.
Carbonit Houston
Cemco
Chem. Procurement
Chem. Services
Conray Chem.
Eastern Color and Chem.
Eastman Kodak
EM Lab.
Fallek Chem.
Fisher Sci.
G. Frederick Smith Chem.
Gallard-Schelsinger
General Plastics
Gill and Duffus Chem.
Graymor Chem.
M.W. Hardy and Co.
HCI Chem.
Helm Houston
Holtrachem
Hooker Chem.
ICC Indust.
ICD Group
Intsel Corp.
Ishihara Corp.
Jonas Chem.
Kemstar Corp.
Kingsley and Keith Chem.
Kraft Chem.
Kum Yang Co.
Lachat Chem.
LaPine Sci.
Laporte Ltd.
Mallinkradt
MCB Reagents
Metron, Inc.
Milijac
Millmaster Onyx
Mitsubishi Chem.
Monomer-Polymer and Dajac Lab.
Morgan Chem.
Mutchler Chem.
Ore and Chem. Corp.
P.A.T. Products
Parlin Chem.
Pfaltz and Bauer
Prochimie Int.
Rhone-Poulenc
Rit-Chem
Sigma Chem.
Signo Trading
Sobin Chem.
Solchem.
Stinnes Oil and Chem.
Tenneco Chem.
Thorson Chem.
Tobey Chem.
T.R. America
Tridon Chem.
Uhe and Co.
Uniroyal
Velco Enterp.
Westco Chem.
White Cross Labs
Wilson Dye and Chem.

10. Manufacturing Processes

Phthalic anhydride is manufactured from two raw materials, naphthalene and ortho-xylene. As of 1975, 64% of industries' capacity to make phthalic anhydride was based on o-xylene, 21% on naphthalene made by petroleum operators, and 15% on naphthalene made by tar distillers and coke-oven operators (Blackford, 1975).

Figure 8 represents the flow diagram for process of the reaction of phthalic anhydride from naphthalene to produce 70-80% of the theoretical yield.

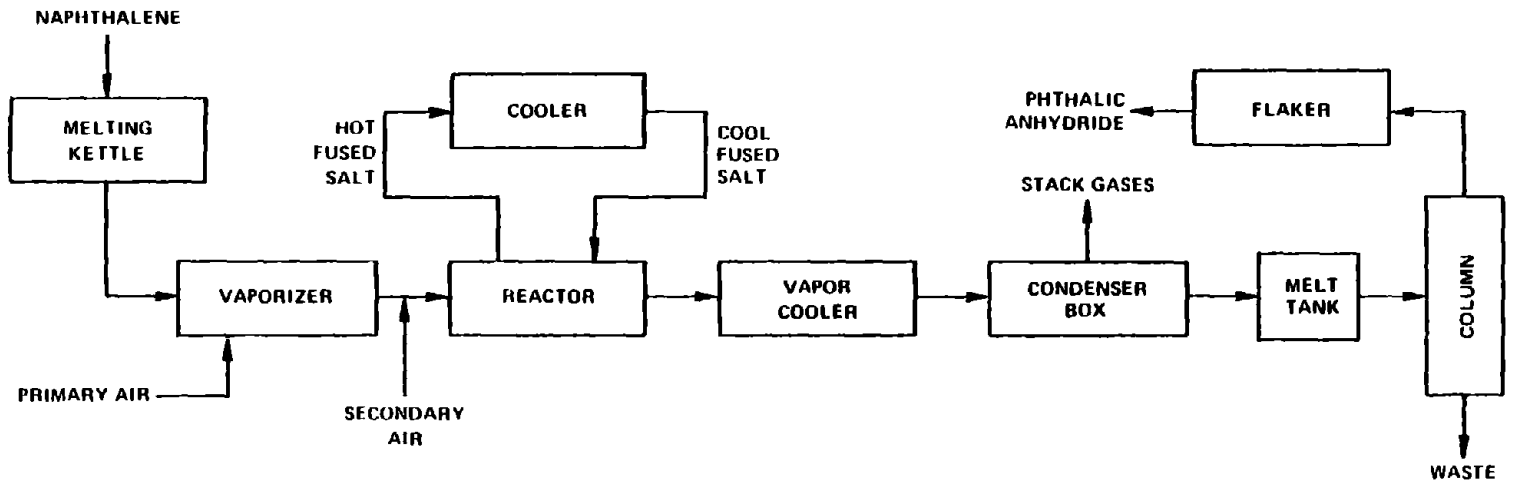


Figure 8. Manufacture of Phthalic Anhydride from Naphthalene

The following passages from Faith, Keyes, and Clark's Industrial Chemicals (Lowenheim and Moran, 1975) describe the manufacturing process:

> Naphthalene is melted and pumped to a vaporizer, where it is vaporized by bubbling primary preheated air through the molten material. Additional (secondary) air is added to the primary air-naphthalene vapor stream in a mixing section in the exit pipe from the vaporizer to bring the air-naphthalene ratio to 18 to 22:1 by weight. This vapor mixture is then led to a converter, consisting of multiple tubes filled with supported vanadium pentoxide catalyst. Heat (4500 to 5600 kcal/kg of naphthalene) is removed from the outside of the fixed catalyst, either by boiling mercury under suitable pressure or by pumping molten salt across the tube bank. In the converter the naphthalene is oxidized to phthalic anhydride, carbon dioxide, and water (temperature, 350 to 450°C; contact time, 0.1 to 0.6 sec).
>
> Exit gases pass through a vapor cooler which reduces the gas temperature to just above the dew point (ca. 126°C) and then enter the recovery system. Formerly, these were large air-cooled condensers, called "hay barns," where the crude phthalic anhydride crystallized on the walls. Modern plants use fin-tube condensers, cyclones, or water scrubbers. In any case the crude product or solution is purified by distillation in a stainless-steel vacuum still. The purified phthalic anhydride is usually melted and flaked for storage and packaging. Maleic anhydride, formed as a by-product, may be removed by working up the crystals in the last compartment of the condenser box system, or by scrubbing the tail gases from the condenser boxes. Most commercial phthalic anhydride contains 0.25 to 0.40% maleic anhydride.
>
> The vanadium pentoxide catalyst possesses a long life, acting satisfactorily for several years of continuous operation. The amount of phthalic anhydride produced is at least 20,000 times the weight of the catalyst present before reactivation is necessitated.
>
> A German-developed process now in use in the United States makes use of a vanadia on silica gel catalyst containing 20 to 30% potassium sulfate. The process operates at a lower temperature (340 to 385°C) and higher contact time (4 to 5 sec) than the conventional vanadia on alundum catalyst. However, higher yields are claimed (104 kg phthalic anhydride/kg naphthalene versus 80 kg for conventional process).
>
> Phthalic anhydride is also produced using a fluidized catalyst (10% V_2O_5 on an inert support). Preheated air at 45 to 60 psi enters the base of the reactor through a distribution plate. Molten naphthalene (1 kg/10 to 12 kg air) is introduced into the reactor and is vaporized by direct contact with the catalyst charge (370°C). The vapors become admixed immediately with the air-catalyst mixture, owing to the severely agitated nature of the catalyst bed. The air-naphthalene vapor mixture passes upward through the bed, and the naphthalene is converted to phthalic anhydride, carbon dioxide,

carbon monoxide, and water vapor. The reaction gases, after leaving the dense catalyst phase, pass through a settling zone and into an internal cyclone system for removal of most of the catalyst. The vapors containing a small amount of catalyst dust are cooled and then passed through a catalyst-recovery system consisting of a series of specially designed filters. There is reported a 100% recovery of catalyst with no poisoning, so that it is unnecessary to replenish the catalyst at any time. About 25 kg catalyst is required in the reactor per kilogram of naphthalene fed per hour. Any carbon formed is burned off the catalyst in situ. A separate regenerator of the type used in fluid petroleum cracking operations is not required.

The product gases containing phthalic anhydride are sent to a waste-heat boiler where the gases are cooled to 150°C, still above the phthalic anhydride dew point (130°C). Phthalic anhydride is recovered in switch condensers, that is, product is being removed from one condenser by melting while the other is on stream.

Contact time in the reactor is 19 to 20 sec, the air/naphthalene ratio is 10:1 to 12:1 by weight, and the yield of 98% phthalic anhydride is 80 kg/100 kg naphthalene charged. The product is said to be purer than that obtained in the fixed-bed process, but usually higher-grade naphthalene feed is required.

The potassium-modified vanadia catalyst mentioned previously is also used in the fluid-bed process. Yields with this catalyst are claimed to be 100 kg phthalic anhydride/100 kg naphthalene charged (Lowenheim and Moran, 1975).

The reaction of phthalic anhydride from o-xylene to produce 70-80% of the theoretical yield may be represented as follows:

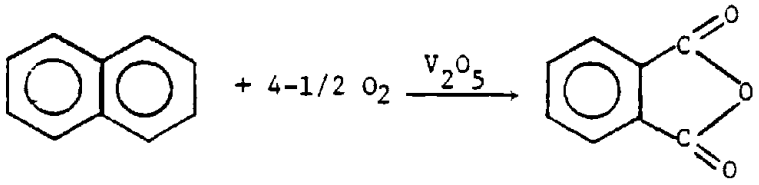


Figure 9 shows the flow diagram for this process.

The following description of the manufacturing process is taken from Faith, Keyes, and Clark's Industrial Chemicals (Lowenheim and Moran, 1975);

o-Xylene is vaporized and mixed with preheated air. About 10 times the theoretical requirement of air is used in order to avoid operating within the explosive limits. The mixture is then fed into the reactor, which is similar to the one described previously for the oxidation of naphthalene. A vanadium pentoxide base catalyst is

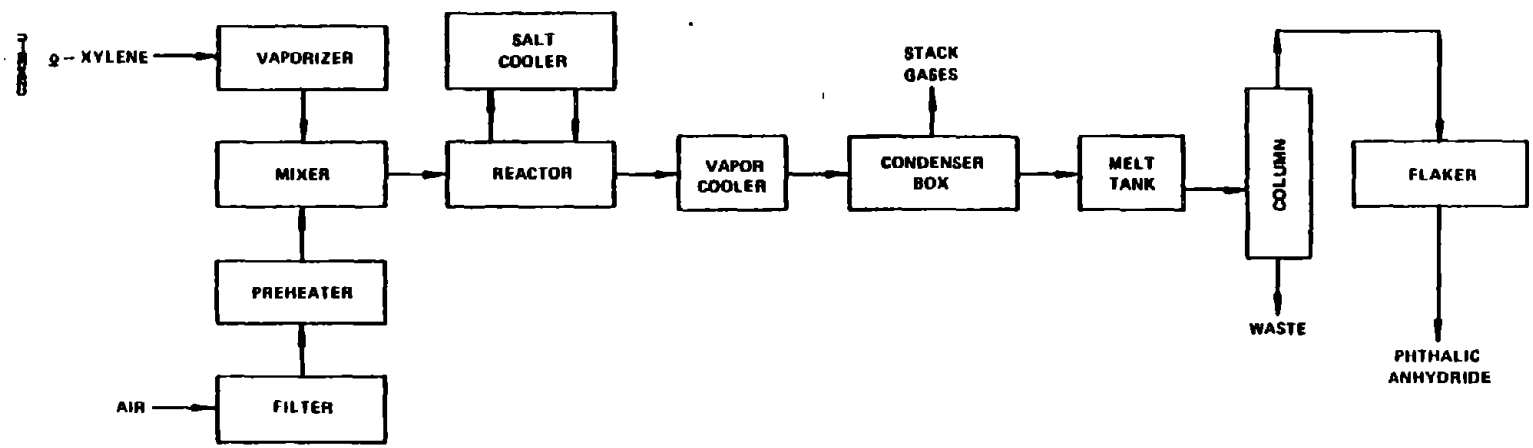


Figure 9. Manufacture of Phthalic Anhydride from o-Xylene

used, and the heat of reaction is removed by circulating molten salt outside the catalyst tubes. The conversion temperature is greater than 540°C and the contact time is of the order of 0.1 to 0.15 sec.

The reaction gases, consisting of phthalic anhydride, carbon dioxide, and water, are cooled in heat exchangers, condensed, distilled, flaked, and packaged, in a manner similar to the purification of the naphthalene oxidation reaction product. The finished material is of high purity, analyzing about 99.7% phthalic anhydride.

A phthalic anhydride yield equivalent to that for conventional naphthalene-oxidation plants (85 to 95 kg product/100 kg raw material) has been claimed (Lowenheim and Moran, 1975).

Because the manufacturing operations are closed-system, worker exposure is most likely a result of fugitive emissions from equipment, or leaks and spills.

11. Impurities or Additives

No information was found in the literature searched.

12. Occupational Exposure

The National Occupational Hazard Survey indicates that 142,657 workers are potentially exposed to phthalic anhydride.

13. Control Technology and Work Practices

The following engineering controls have been recommended by the Manufacturing Chemists' Association (MCA, 1956).

BUILDING DESIGN

a. The building and partitions should be of fire resistant construction.

b. Ample emergency exits from buildings should be provided. Fire doors should open outward and be of the approved type with heavy hinges so that the doors will not be blown off in the event of an explosion.

c. Explosion Venting. All rooms in which phthalic anhydride is stored should be fire resistant and be provided with adequate ventilation. Explosion venting should be provided in the general construction of buildings in which the material is handled or stored. The ratio of venting to building volume should be checked by a competent engineer to determine the required venting area.

EQUIPMENT DESIGN

a. The design of phthalic anhydride installations is specialized. The technical problems of designing such equipment, devising standard operating procedures, and providing such features as are necessary for safe and economical operation should be handled by qualified engineering, technical and safety personnel.

Subsequent maintenance work and changes in equipment or procedures should conform with the requirements of the process as regards safe and economical operation.

b. System Types. Because of the fume, fire and explosion hazards of phthalic anhydride all operations should be handled in closed systems where possible.

VENTILATION

a. For indoor operations, special equipment ventilation and general building or area ventilation should be provided as necessary to remove any and all escaping vapor. Local ordinances must be consulted as well as other authoritative guides which are designed to eliminate fire and explosion hazards and to afford maximum protection to both workers and property.

AIR ANALYSIS

a. Oxygen Content of Tanks and Other Equipment. The vapor spaces of subject vessel should be sampled regularly and analyzed for the oxygen content. A choice of analytical equipment is available. The oxygen content should not exceed 10% by volume to prevent burning of the phthalic anhydride vapors.

ELECTRICAL EQUIPMENT

a. Vaporproof of Explosionproof Equipment. All electrical wiring, motors and other equipment installed or used where phthalic anhydride is stored should be as prescribed by the National Electrical Code.

GROUNDING

a. Phthalic anhydride flakes can develop static charges during passage through conveyors, elevators, etc. Such materials handling equipment should be electrically grounded (See National Fire Codes "Combustible Solids, Dusts, Chemicals and Explosives").

b. All tanks intended for the storage of phthalic anhydride should be electrically grounded to safely dissipate electrical charges due to lightning or static.

Lefaux (1968) has noted that protection is particularly necessary against the irritative effects of phthalic anhydride dust, but that recent practice has been to handle this chemical as a liquid (molten anhydride). Although the vapors of phthalic anhydride are as irritating as the dust, in liquid form it is carried in tank cars and pumped directly to reaction vessels, minimizing worker contact with the anhydride.

Unloading procedures for tank cars and tank trucks containing phthalate anhydride have been detailed by MCA (1956). The chemical is loaded in a molten state and fuses during transport, requiring melting in the tank for unloading.

14. Biological Effects

a. Animal Studies

(1) Acute Exposures

The acute toxic effects of phthalic anhydride are summarized in Table 15.

Following administration of lethal oral doses, Industrial Bio-Test (1970) noted symptoms of hypothermia, lethargy, ruffled fur, diaresis and diarrhea in rats. Inflammation of the gastrointestinal tract and hyperemia of the liver and lungs was found in the decedents, but no significant gross autopsy findings were detected in the survivors.

Table 15. Acute Toxicity of Phthalic Anhydride

Route	Species	Dose	Response	Reference
oral	rats	4020 mg/kg	LD50	Industrial Bio-Test, 1970
oral	rats	800-1600 mg/kg	LD50	Fassett, 1963
inhalation	rats	≈35 ppm	0/6 deaths	Industrial Bio-Test, 1970
i.p.[a]	guinea pigs	<100 mg/kg	LD50	Fassett, 1963
dermal	rabbit	500 mg x 24 h[b]	mild irritation	Industrial Bio-Test, 1970
dermal	rabbit	10,000 mg/kg	0/5 deaths, mild irritation	Industrial Bio-Test, 1970
ocular	rabbit	100 mg	severe irritation	Industrial Bio-Test, 1970

[a] i.p. = intraperitoneal.

[b] h = hour.

Mild skin irritation (erythema and edema) was observed in rabbits following application of 500 mg of phthalic anhydride for 24 hours intact or abraded skin and 4-hour exposures to 10,000 mg/kg (Industrial Bio-Test, 1970). Phthalic anhydride was shown to sensitize guinea pigs following twice weekly intracutaneous injections with 0.05 ml of a 0.1% solution (Jacobs, 1940). Severe eye irritation occurred in rabbits following application of 100 mg phthalic anhydride as a dry powder, and lacrimation was noted following exposure to LC50 concentrations of phthalic anhydride vapor (Industrial Bio-Test, 1970).

(2) Subchronic Exposures

No effect on survival, feed consumption, organ/body weight ratios, or terminal body weight was observed in rats following dietary exposure to 250, 1000, or 3800 ppm phthalic anhydride for 4 weeks (Industrial Bio-Test, 1970). At autopsy, no significant gross lesions were noted among any of the test rats.

Male and female rats and mice were exposed to four dose levels (6200; 12,500; 25,000; and 50,000 ppm) of phthalic anhydride in the diet for 7 weeks (NCI, 1979). At the end of the 8th week in the study, the animals were sacrificed. All tissues examined appeared essentially normal. The only adverse effect was a 25% decrease in body weight in both male and female rats at the 50,000 ppm exposure level.

(3) Chronic Exposures

Chronic ingestion for 32 weeks of 25,000 and 50,000 ppm phthalic anhydride in the diet caused marked weight loss in B6C3F1 mice (NCI, 1979). No other nonneoplastic abnormalities were noted.

(4) Carcinogenicity

A bioassay to assess the oncogenetic potential of phthalic anhydride was conducted using male and female F344 rats and B6C3F1 mice (NCI,

1979). Two dose levels of phthalic anhydride were used. The rats were exposed to 7,500 and 15,000 ppm phthalic anhydride in the diet, and the mice were exposed to a time-weighted average dose of 16,346 and 32,692 ppm for males and 12,019 and 24,038 ppm for females. The initial doses for mice were 25,000 and 50,000 ppm. Because of extreme weight loss in the animals, however, these doses were adjusted downward after 32 weeks of exposure. The length of treatment was 105 weeks for rats and 109 weeks for mice. There was no statistical increase in either the number or the types of neoplasms detected on histological examination of animals that died during the experiment or animals that were sacrificed at the termination of the study.

(5) Mutagenicity

No information was found in the literature searched.

(6) Teratogenicity

Two abstracts of work performed in the same laboratory reported that phthalic anhydride was a teratogen (Fabro et al., 1976; Dixon et al., 1978). Phthalic anhydride was given to pregnant CD-1 mice at a dose level of 80 mg/kg on days 8, 9, and 10 of gestation. Of the viable offspring, 14.4% were malformed with branched ribs, fused vertebrae, and cleft palate. Brown et al. (1978) has also reported that phthalic anhydride was a teratogen in CD-1 mice. The animals received 0.188 mmol/kg on days 8 to 10 or 11 of gestation; however, few details of the types of abnormalities observed were presented in this abstract.

(7) Reproductive Effects

Protsenko (1970) reported that phthalic anhydride at concentrations of 0.17 ppm and 0.03 ppm impaired the fertilization ability of male rats in a chronic inhalation study. Experimental details were not given in this abstract.

(8) Other Relevant Information

No information was found in the literature searched.

b. Human Studies

(1) Pharmacokinetics

No information was found in the literature searched.

(2) Health Effects

The symptoms of occupational exposure to phthalic anhydride have been reviewed (Lefaux, 1968; Autian, 1973; ACGIH, 1977; Tabershaw et al., 1977). Phthalic anhydride (dust, fumes or vapor) acts as a strong local irritant to body tissues. This is particularly noticeable on moist skin or on mucous membranes (eyes, respiratory tract) due to the formation of phthalic acid. Respiratory irritation is indicated by coughing, sneezing, and, in some cases, a bloody nasal discharge. Lefaux (1968) has noted, however, that there is no lung attack, dyspnea, or hemoptysis. Contact dermatitis may occur, with prolonged contact causing severe burns. Repeated inhalation of phthalic anhydride has resulted in bronchitis, emphysema, urticaria, and chronic eye irritation.

Fawcett et al. (1977) have reported on three case histories of asthma produced by long-term exposure to phthalic anhydride. Kern (1939) reported on a chemist who suffered from asthma as a result of exposure to phthalic anhydride. A skin test for sensitivity to phthalic anhydride was strongly positive. Maccia et al. (1976) described similar symptoms in a foreman of a chemical plant. Skin tests for phthalic anhydride were positive and a high titer of serum IgE, specific for phthalic anhydride-protein conjugates, was measured.

(3) Target Organ Toxicity

No information was found in the literature searched.

(4) Epidemiology

Menschick (1955) reported that 18 of 71 workers at a phthalic anhydride factory exhibited irritation of the mucous membranes, particularly the conjuctiva. The throat, trachea and bronchi were also affected. Four cases of bronchial asthma due to workmen becoming sensitized to phthalic anhydride were also noted. Menschick (1955) considered the chemical to be an antigen which can cause true asthma and urticaria.

15. Ongoing Studies

Phthalic anhydride is currently scheduled for mutagenicity testing in Salmonella by the National Toxicology Program (NTP, 1980).

16. Exposure Standards

The ACGIH (1980) currently recommends a Time Weighted Average-Threshold Limit Value (TWA-TLV) of 1 ppm for phthalic anhydride; a short-term (15-minute) continual exposure limit (STEL)- TLV of 4 ppm is also recommended. The OSHA (1976) TWA standard for phthalic anhydride is 2 ppm.

17. Sources of Additional Relevant Information

A NIOSH Health Hazard Evaluation (HHE) relating to phthalic anhydride has been conducted at Uncle Bill's Pick-N-Pay Market, No. 10, Middleburg Heights, OH (HHE No. 74-24-246).

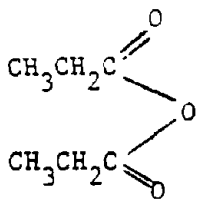
18. Other Pertinent Data

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

H. PROPIONIC ANHYDRIDE

1. Chemical Name: Propionic Anhydride

2. Chemical Structure:



3. Synonyms: Methylacetic anhydride
Propanoic acid, anhydride
Propanoic anhydride
Propionic acid anhydride
Propionyl oxide

4. Chemical Abstracts Service (CAS) Number: 123-62-6

5. Registry of Toxic Effects of Chemical Substances (RTECS) Number:
UF9100000

6. Chemical and Physical Properties:

Description:	colorless liquid with pungent odor
Molecular Weight:	130.14
Boiling Point:	167°C
Melting Point:	-45°C
Vapor Pressure:	1 mm Hg (20°C)
Solubility:	decomposes in water to acid; soluble in ether, methanol, ethanol, chloroform
Specific Gravity:	1.0125
Stability:	combustible, autoignition temp. 545°F; flash point 145°F (cc); explosive limits, mg/l: lower at 166°F = 66.2

7. Production

The U.S. EPA (1980) lists Kodak's 1977 propionic anhydride production volume at 50-100 million pounds.

8. Use

The major use of propionic anhydride is in the production of cellulose tripropionate and cellulose acetate propionate for plastics and fibers (Wocasek,

1968; Eastman Kodak, 1980). For this major use, it is captively used by the manufacturer, Eastman Kodak.

Other uses include an esterifying agent for fats and oils, dehydrating medium for nitrations and sulfonations, and syntheses of alkyd resins, dyestuffs, and pharmaceuticals (Hawley, 1977). Esters of propionic anhydride are used in the flavoring and perfume industries as taste and odor components (Eastman Kodak, 1980).

9. Manufacturers and Distributors

Propionic anhydride is manufactured by Eastman Kodak (Tennessee Eastman) in Kingsport, TN (SRI International, 1980; U.S. EPA, 1980; USITC, 1980a).

10. Manufacturing Processes

Propionic anhydride can be prepared by dehydrating propionic acid or by oxidation of propionaldehyde (The Merck Index, 1976). Eastman Kodak has the capacity in Kingsport, TN, to make 70 million pounds annually of propionic acid (SRI International, 1980); therefore, the anhydride is most likely made by dehydrating the acid.

11. Impurities or Additives

No information was found in the literature searched.

12. Occupational Exposure

The National Occupational Hazard Survey indicates that 66 workers are potentially exposed to propionic anhydride.

13. Control Technology and Work Practices

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

14. Biological Effects

a. Animal Studies

(1) Acute Exposures

The acute toxic effects of propionic anhydride are summarized in Table 16.

Propionic anhydride has been shown to be an irritant when 10 mg produced mild irritation to the skin of rabbits in 24 hours using the Draize procedure (Smyth et al., 1954). When the chemical was not maintained in contact with the skin by an impervious barrier, moderate skin irritation in the rabbit was obtained with 510 mg (Union Carbide, 1970). Severe eye irritation in the rabbit occurred with 750 µg of propionic anhydride.

A single application of 25% propionic anhydride in dioxane to the flank skin of sensitized guinea pigs elicited an eczema characterized by epidermal necrosis after 14 hours (Hunziker, 1968). Application to the nipple of sensitized guinea pigs caused spongiosis, but did not show a necrosis. During the course of sensitization, blood basophilia was observed.

(2) Subchronic Exposure

No information was found in the literature searched.

(3) Chronic Exposures

No information was found in the literature searched.

(4) Carcinogenicity

No information was found in the literature searched.

(5) Mutagenicity

No information was found in the literature searched.

(6) Teratogenicity

No information was found in the literature searched.

Table 16. Acute Toxicity of Propionic Anhydride

Route	Species	Dose	Response	Reference
oral	rat	2360 mg/kg	LD50	Smyth et al., 1954
inhalation	rat	saturated vapor[a] x 1 h[c]	maximum exposure for no death	Smyth et al., 1954
dermal	rabbit	10 g/kg[b]	LD50	Smyth et al., 1954
dermal	rabbit	10 mg x 24 h[c]	mild irritation	Smyth et al., 1954
dermal	rabbit	510 mg (open)	moderate irritation	Union Carbide, 1970
ocular	rabbit	750 µg	necrosis	Smyth et al., 1954

[a] Saturation concentration is approximately 3500 ppm at 20°C.

[b] 24 hr occluded contact; mortality recorded over 14 days.

[c] h = hour.

(7) Reproductive Effects

No information was found in the literature searched.

(8) Other Relevant Information

No information was found in the literature searched.

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 current toxicological or environmental studies of propionic anhydride were found.

16. Exposure Standards

No recommended or promulgated occupational exposure standards for propionic anhydride were found.

17. Sources of Additional Relevant Information

No sources of additional relevant information were identified.

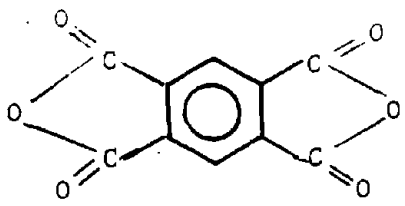
18. Other Pertinent Data

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

I. PYROMELLITIC DIANHYDRIDE

1. Chemical Name: Pyromellitic Dianhydride

2. Chemical Structure:



3. Synonyms: 1,2,4,5-Benzenetetracarboxylic acid dianhydride
1H,3H-Benzo[1,2-C:4, 5-C']difuran-1,3,5,7-tetrone
PMDA
Pyromellitic anhydride

4. Chemical Abstracts Service (CAS) Number: 89-32-7

5. Registry of Toxic Effects of Chemical Substances (RTECS) Number:
Not listed

6. Chemical and Physical Properties:

Description:	white crystalline solid
Molecular Weight:	218.12
Boiling Point:	397-400°C
Melting Point:	287°C
Vapor Pressure:	---
Solubility:	decomposes to acid in water
Specific Gravity:	1.68
Stability:	hydrolyzes to acid when exposed to moisture; combustible

7. Production

Data available from the U.S. EPA (1980) regarding producers of pyromellitic dianhydride and production volumes are presented in Table 17.

8. Use

Pyromellitic dianhydride is used to produce high temperature-resistant polymers for applications in molded parts, films, fibers, and insulating

Table 17. Producers of Pyromellitic Dianhydride and Production Ranges (U.S. EPA, 1980)

Producer and Location	Type of Production	1977 Production Range
DuPont Gibbstown, NJ	Manufacturer	no manufacture or importation in 1977
Haven Chemical Philadelphia, PA	Small Manufacturer	no production range
Thorson Chemical New York, NY	Importer	0-1000 lb
3M Company St. Paul, MN	Importer	0-1000 lb

varnishes. It is also used as a crosslinking agent for epoxy and other resins (Towle et al., 1968; Connolly, 1976).

9. Manufacturers and Distributors

According to SRI International (1979), the only current producer of pyromellitic dianhydride is Princeton Chemical Research in Princeton, NJ. SRI International (1980) has no listing for pyromellitic dianhydride.

Pyromellitic dianhydride has been manufactured by DuPont, in Gibbstown, NJ, and by Princeton Chem. Research, Inc., in Princetown, NJ (Connolly, 1976). DuPont produced a polyimide-grade pyromellitic dianhydride that was used captively to make various polyimide resins; the capacity at the DuPont plant was estimated to be 3-4 million pounds annually, but production never reached those levels (Connolly, 1976). Princeton Chemical produces an epoxy-grade pyromellitic dianhydride.

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

Bio-Clinical Lab.
Chem. Procurement Lab.
Chem. Services
Eastern Chem.
Eastman Kodak
EM Lab.
Fisher Sci.
Frinton Lab.
ICN/K and K
MCB Reagents
Monomer-Polymer and Dajac
Tridom Chem.
George Uhe and Co.
Stinnes Oil and Chem.
Thorson Chem.

10. Manufacturing Processes

DuPont made pyromellitic dianhydride by the nitric acid oxidation of durene (1,2,4,5-tetramethylbenzene) (Towle et al., 1968; Connolly, 1976). Princeton Research produces pyromellitic dianhydride by the vapor-phase oxidation of durene with a technology similar to phthalic anhydride manufacture (Towle et al., 1968). In this process, liquid durene is vaporized and allowed to flow into a reactor tube (700-1200°F) with heated air where the reaction takes place.

The vapors from the reactor tube are condensed to yield a pyromellitic dianhydride of 98.2% purity (Miller, 1951); a VnO and/or SiC catalyst is required for the reaction.

11. Impurities or Additives

Pyromellitic dianhydride is available as a 98+% grade purity (Hawley, 1977).

12. Occupational Exposure

The National Occupational Hazard Survey indicates that 722 workers are potentially exposed to pyromellitic dianhydride.

13. Control Technology and Work Practices

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

14. Biological Effects

No information was found in the literature searched regarding the biological effects of pyromellitic dianhydride.

15. Ongoing Studies

No current toxicological or environmental studies of pyromellitic dianhydride were found.

16. Exposure Standards

No recommended or promulgated occupational exposure standards for pryomellitic dianhydride were found.

17. Sources of Additional Relevant Information

No sources of additional relevant information were identified.

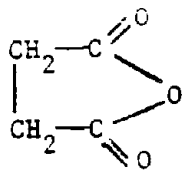
18. Other Pertinent Data

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

J. SUCCINIC ANHYDRIDE

1. Chemical Name: Succinic Anhydride

2. Chemical Structure:



3. Synonyms: Butanedioic anhydride
2,5-Diketotetrahydrofuran
2,5-Furandione, dihydro-
Succinic acid anhydride
Succinyl oxide

4. Chemical Abstracts Service (CAS) Number: 108-30-5

5. Registry of Toxic Effects of Chemical Substances (RTECS) Number:
WN0875000

6. Chemical and Physical Properties:

Description:	colorless to lightly colored needles or flakes
Molecular Weight:	100.07
Boiling Point:	261°C
Melting Point:	119.6°C
Vapor Pressure:	1 mm Hg (92°C)
Solubility:	very slightly soluble in water; soluble in ethanol 2.56 g/100 ml (25°C); soluble in ether 0.64 g/100 ml (25°C); soluble in chloroform 0.87 g/100 ml (25°C); soluble in carbon tetrachloride
Specific Gravity:	1.234_4^{20}
Stability:	combustible

7. Production

In 1971 and 1974, about 0.5-1.0 million pounds of maleic anhydride were used to make succinic anhydride (Blackford, 1976); therefore, succinic anhydride production would have been about the same. In 1977, 772 pounds of succinic

anhydride were imported, while in 1974, 5954 pounds were imported (USITC, 1978 1976b). In 1979, 224.87 thousand pounds were imported (USITC, 1980b).

Data available from the U.S. EPA (1980) regarding producers of succinic anhydride and production volumes are presented in Table 18.

8. Use

Succinic anhydride is used for conversion to succinic acid, which finds use in pharmaceuticals, cosmetics, dyestuffs, and a variety of other organic syntheses (Turi, 1969; Lawler, 1977). The anhydride itself is used to produce adhesive, alkyd, and polyester resins for a variety of coatings, laminates, and moldings (Turi, 1969). Succinic anhydride can also be used as a starch-modifying agent in foods (Chapman and Kertesz, 1966).

9. Manufacturers and Distributors

SRI International (1980) lists the following manufacturer:

Buffalo Color Corp.	Buffalo, NY

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

Armageddon Chem.
Alfa Prod.
Aldrich Chem.
Anachemin Chem.
Atomergic Chemetals
Biddle-Sawyer
Bio-Clinical Lab.
J.T. Baker Chem.
Biochemical Lab.
Browning Chem.
Centerchem.
Chem. Dynamics
Collaborative Res.
Chem. Procurement
Chem. Services
Chemtech Res.
Davos Chem.
Eastern Chem.
Fairfield Chem.
Gallard-Schelsinger
M.W. Hardy and Co.
ICN/K and K
ICN Nutritional
Jonas Chem.
Lachat Chem.
LaPine Sci.
Mallinkrodt
MCB Reagents
Monomer-Polymar Dajac
Pierce Chem.
Pfaltz and Bauer
Research Plus Lab.
Rhone-Poulenc
Ritchem
Sattva Trading Co.
Sigma Chem.

Table 18. Producers of Succinic Anhydride and Production Ranges (U.S. EPA, 1980)

Producer and Location	Type of Production	1977 Production Range
Buffalo Color Corp.[a]		
Buffalo, NY	Manufacturer	0.1-1.0 million lb
Allied Chemical Corp.[a]		
Buffalo, NY	Manufacturer	0.1-1.0 million lb
Plant Site Not on File	Small Manufacturer	confidential
Marubeni America Corp.		
New York, NY	Importer	10-100 thousand lb
Chicago, IL	Importer	zero
Rit-chem Co., Inc.		
Pleasantville, NY	Importer	0.1-1.0 million lb

[a]Same plant

Eastman Kodak
EM Lab.
Filo Chem.
Fisher Sci.
Tridom Chem.
George Uhe and Co.
U.S. Biochemical

10. Manufacturing Processes

Succinic anhydride is usually produced by the hydrogenation of maleic anhydride (Blackford, 1976). In a typical hydrogenation (Turi, 1969), molten maleic anhydride is charged to a hydrogenator. The vessel is purged and filled with hydrogen. The catalyst (nickel or a noble metal) is added as a slurry, agitation is started, and the temperature is raised to 130-140°C. Moderate hydrogen pressure is maintained until the reaction is complete (4-6 hours). The catalyst is then removed and the product is distilled under conditions practically identical to those used for phthalic anhydride (see profile on Phthalic Anhydride). A 99.5% pure product is obtained.

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 succinic anhydride.

13. Control Technology and Work Practices

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

14. Biological Effects

a. Animal Studies

(1) Acute Exposures

Succinic anhydride has produced severe eye injury following application of 50 µl of a 15% solution (750 µg) to the eyes of rabbits (Carpenter and Smyth, 1946).

(2) Subchronic Exposures

No information was found in the literature searched.

(3) Chronic Exposures

No information was found in the literature searched.

(4) Carcinogenicity

Subcutaneous tumors at the site of injection developed in 3 of 6 male rats administered 2 mg succinic anhydride per animal twice weekly for 65 weeks. The 24 control animals did not develop tumors (Dickens and Jones, 1965; IARC, 1977).

(5) Mutagenicity

Succinic anhydride has been tested for mutagenicity in the Ames assay (Simmon, 1979a; Rosenkranz and Poirer, 1979), the yeast assay with S. cerevisiae D3 (Simmon, 1979b), the E. coli pol A^- assay (Rosenkranz and Poirier, 1979) and the L5178Y/$TK^{\pm}$ mouse lymphoma assay (Clive et al., 1979). In all cases, no mutagenic activity was observed. Paes and Thompson (1979) reported in an abstract that succinic anhydride was mutagenic in a forward mutagenicity assay using a strain of S. typhimurium.

(6) Teratogenicity

Fabro et al. (1976) reported in an abstract that succinic anhydride given at 50 mg/kg on days 8, 9, and 10 of gestation caused malformation in 23.3% of the viable offspring. Commonly observed defects were branched ribs, fused vertebrae, and cleft palate.

(7) Reproductive Effects

No information was found in the literature searched.

(8) Other Relevant Information

No information was found in the literature searched.

b. Human Studies

(1) Pharmacokinetics

No information was found in the literature searched.

(2) Health Effects

Succinic anhydride is a moderate irritant (Sax, 1957).

(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

Carcinogenesis bioassay testing of succinic anhydride is currently in progress in rats and mice treated by gavage (NTP, 1980).

16. Exposure Standards

No recommended or promulgated occupational exposure standards for succinic anhydride were found.

17. Sources of Additional Relevant Information

No sources of additional relevant information were identified.

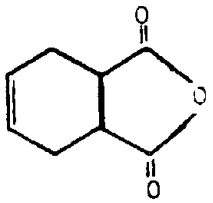
18. Other Pertinent Data

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

K. TETRAHYDROPHTHALIC ANHYDRIDE

1. Chemical Name: Tetrahydrophthalic Anhydride

2. Chemical Structure:



3. Synonyms: 4-Cyclohexene-1,2-dicarboxylic anhydride
1,3-Isobenzofurandione, 3a,4,7,7a-tetrahydro-
Maleic anhydride adduct of butadiene
Memetetrahydrophthalic anhydride
Phthalic anhydride, 1,2,3,6-tetrahydro-
THPA

4. Chemical Abstracts Service (CAS) Number: 85-43-8

5. Registry of Toxic Effects of Chemical Substances (RTECS) Number: GW5775000

6. Chemical and Physical Properties:

Description:	white crystalline flakes
Molecular Weight:	152.15
Boiling Point:	195°C (at 50 mm Hg)
Melting Point:	99-101°C (solidification point)
Vapor Pressure:	<0.01 mm Hg (20°C); 50 mm Hg (195°C)
Solubility:	insoluble in water; soluble in benzene; slightly soluble in petroleum ether and ethyl ether
Specific Gravity:	1.375_{20}^{25}
Stability:	combustible; flash point 157°C(OC)

7. Production

Production of tetrahydrophthalic anhydride as an end product was estimated to have amounted to less than 2 million pounds in 1971 (Carlson and Erskine, 1974) and less than 3.1 million pounds in 1974 (Blackford, 1976). In addition to being produced as an end product, tetrahydrophthalic anhydride is

also produced as an on-site intermediate in the production of the fungicide Captan; based upon consumption estimates of Captan in 1975, roughly 5-6 million pounds of tetrahydrophthalic anhydride intermediate were necessary for Captan synthesis.

Data available from the U.S. EPA (1980) regarding producers of tetrahydrophthalic anhydride and production volumes are presented in Table 19.

8. Use

As a final product, tetrahydrophthalic anhydride is used to produce unsaturated polyester resins and alkyd resins with increased resistance to water and solvents (Blackford, 1976). It is also used (epoxidized) by Union Carbide Corp. to make a combined plasticizer and stabilizer for polyvinyl chloride (Carlson and Erskine, 1974).

Synthesis of tetrahydrophthalic anhydride is the first step in the synthesis of the important fungicide Captan (Kirshenbaum and Cahn, 1964). In 1975, about 10 million pounds of Captan were consumed domestically (Ayers and Johnson, 1976). In 1977, between 10 and 50 million pounds were manufactured (U.S. EPA, 1980).

Roughly 75% of the total amount of tetrahydrophthalic anhydride produced is used to make Captan and 25% is used to make resins and the plasticizer-stabilizer.

9. Manufacturers and Distributors

Tetrahydrophthalic anhydride is manufactured as a final product by Denka Chem. Corp. in Houston, TX and by Exxon in Bayway, NJ (SRI International, 1980). It is also produced as an intermediate during the production of the pesticide Captan by a plant jointly owned by Stauffer Chem. and Chevron in Perry, OH.

Table 19. Producers of Tetrahydrophthalic Anhydride and Production Ranges (U.S. EPA, 1980)

Producer and Location	Type of Production	1977 Production Range
Denka Chemical Corp. Houston, TX	Manufacturer	1-10 million lb
Stauffer Chemical Co. Perry, OH	Manufacturer/ Produced Site Limited	1-10 million lb
Archem Co. Houston, TX	Manufacturer	0.1-1.0 million lb
Marubeni America Corp. NYC, NY	Importer	0-1000 lb
Lonza, Inc. Fairlawn, NJ	Importer	confidential
Ashland Chemical Co. Dublin, OH	Importer	20-200 thousand lb
Thorson Chemical Co. NYC, NY	Importer	0-2000 lb
Solchem Inc. NYC, NY	Importer	confidential

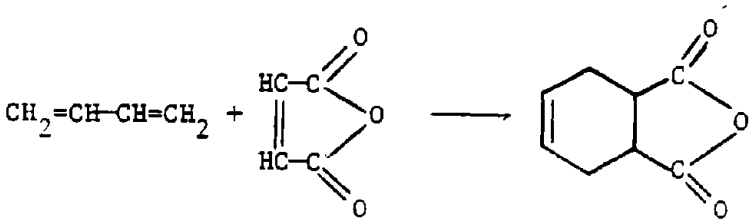
Data available from the U.S. EPA (1980) regarding producers of tetrahydrophthalic anhydride and production volumes are presented in Table 19.

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

Anhydrides and Chemicals, Inc.	Helm, NY
Archem. Co.	Koch Chem.
Bio-Clinical Lab.	Miki Sangyo (USA) Inc.
Chem. Procurement Lab.	Prior Chem.
Chemsampo	Solchem.
Davos Chem.	Stinnes Oil and Chemical
Eastern Chem.	Thorson Chem.

10. Manufacturing Processes

Tetrahydrophthalic anhydride is made by the Diels-Alder reaction of butadiene with maleic anhydride (Carlson and Erskine, 1974; Kirshenbaum and Cahn, 1964; Kirshenbaum, 1978); the reaction may be represented as:



The usual conditions for the Diels-Alder reaction with 1,3-butadiene involve temperatures of about 100-170°C and antogenous pressure (Kirshenbaum and Cahn, 1964). Yields are generally high and catalysts are not usually required (Kirshenbaum and Cahn, 1964); however, aluminum silicates can be used as catalysts (Kirshenbaum, 1978).

11. Impurities or Additives

Tetrahydrophthalic anhydride has the following specifications and typical analysis (Denka Chemical, undated):

Specifications:	Assay	99.0%
	Melting Point	99.0°C
	Hazen Color	80 max

Typical Analysis:	Assay	99.5%
	Melting Point	100.5°C
	Hazen Color	40
	Maleic anhydride	100 ppm

12. Occupational Exposure

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

13. Control Technology and Work Practices

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

14. Biological Effects

No information was found in the literature searched regarding the biological effects of tetrahydrophthalic anhydride.

15. Ongoing Studies

No current toxicological or environmental studies of tetrahydrophthalic anhydride were found.

16. Exposure Standards

No recommended or promulgated occupational exposure standards for tetrahydrophthalic anhydride were found.

17. Sources of Additional Relevant Information

No sources of additional relevant information were identified.

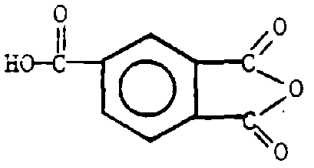
18. Other Pertinent Data

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

L. TRIMELLITIC ANHYDRIDE

1. Chemical Name: Trimellitic Anhydride

2. Chemical Structure:



3. Synonyms: Anhydro trimellic acid
Diphenylmethane-4,4'-diisocyanate-trimellic anhydride-ethonid HT polymer
1,3-Dioxo-5-phthalancarboxylic acid
5-Isobenzofuran carboxylic acid, 1,3-dihydro-1,3-dioxo-
5-Phthalanacarboxylic acid, 1,3-dioxo-
TMAN
Trimellic acid anhydride

4. Chemical Abstracts Service (CAS) Number: 552-30-7

5. Registry of Toxic Effects of Chemical Substances (RTECS) Number:
DC2050000

6. Chemical and Physical Properties:

Description:	white, solid crystals
Molecular Weight:	192.12
Boiling Point:	240-245°C (at 14 mm Hg); 390°C
Melting Point:	165°C
Vapor Pressure:	0.000004 mm Hg (20°C)
Solubility:	hydrolyzes to acid in water (moderately soluble)
Specific Gravity:	1.54
Stability:	combustible

7. Production

The major outlet for trimellitic anhydride is the manufacture of trimellitate plasticizers (Connolly, 1976). In 1978, 32.76 million pounds of these plasticizers were produced (USITC, 1979a); trioctyl trimellitate accounted

for nearly half of this total. The amount of trimellitic anhydride needed to make the plasticizers would have been roughly 12-18 million pounds.

8. Use

As implied in the preceeding section, the major use of trimellitic anhydride is in the manufacture of trimellitate plasticizers (Connolly, 1976). The other main use of trimellitic anhydride is in the production of poly(amide-imide) polymers for use in wire enamels and electrical-insulating varnishes (Towle et al., 1968). A third use is in water-based alkyd finishes in the coating industry.

9. Manufacturers and Distributors

Trimellitic anhydride is manufactured by Standard Oil of Indiana (Amoco) in Joliet, IL (SRI International, 1980). The capacity of the plant is 50 million pounds per year (Connolly, 1976).

In addition to Amoco, Haven Chemical, in Philadelphia, PA, is listed as a small manufacturer by the U.S. EPA (1980). Production ranges are not available.

The U.S. EPA (1980) also lists Ciban Geigy as an importer with zero importation in 1977.

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

Aldrich Chem.
Alfa Prod.
Chem. Dyanmics
Chem. Procurement Lab.
Chem. Services
Columbia Organics
Eastman Kodak
Fisher Sci.
ICN/K and K
Jonas Chem.
Lachat Chem.
MCB Reagents
Monomer-Polymer Dajac
Pfaltz and Bauer
Toyomenka (USA)
Tridom Chem.
George Uhe and Co.

10. Manufacturing Processes

Manufacture of trimellitic anhydride is based upon the liquid-phase air oxidation of pseudocumene to form trimellitic acid, which is subsequently dehydrated to trimellitic anhydride (Towle et al., 1968).

11. Impurities or Additives

No information was found in the literature searched.

12. Occupational Exposure

The National Occupational Hazard Survey indicates that 11,309 workers are potentially exposed to trimellitic anhydride.

13. Control Technology and Work Practices

As detailed in a Current Intelligence Bulletin (Millar, 1978), NIOSH recommends that trimellitic anhydride be handled in the workplace as an extremely toxic substance, because it can cause noncardiac pulmonary edema, immunological sensitization, and severe respiratory irritation. Exposures should be monitored regularly, engineering and work practice controls should be used to minimize exposure, and respiratory protection employed as indicated. Appropriate protective clothing and equipment necessary to prevent repeated or prolonged skin contact or eye contact with trimellitic anhydride should also be provided.

14. Biological Effects

a. Animal Studies

(1) Acute Exposures

The acute toxic effects of trimellitic anhydride are summarized in Table 20.

Amoco (1980) has noted that the compound caused severe irritation to the eyes of rabbits.

Table 20. The Acute Effects of Trimellitic Anhydride

Route	Species	Dose (mg/kg)	Response	Reference
oral	rats	5600	LD50	Amoco, 1980
oral	mice	1250	approximate LD50	Batyrova and Uzhdavini, 1970
oral	rats	1900	approximate LD50	Batyrova and Uzhdavini, 1970
inhalation	rats	≈940 ppm x 4 h[a]	no deaths	Amoco, 1980
dermal	rabbit	>2300	LD50	Amoco, 1980

[a] h = hours.

(2) Subchronic Exposures

Amoco (1980) reported that dietary exposure to trimellitic anhydride for 13 weeks (at concentrations of up to 1% of the diet) did not result in any compound related effects or gross or microscopic pathology in albino rats or dogs.

Subacute inhalation studies in rats (duration of exposure not stated) indicated intra-alveolar hemorrhages at varying concentrations, some "apparently" as low as 0.054 mg/m^3 (≈ 7 ppb).

(3) Chronic Exposures

No information was found in the literature searched.

(4) Carcinogenicity

No information was found in the literature searched.

(5) Mutagenicity

No information was found in the literature searched.

(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

Monkeys exposed to trimellitic anhydride by intratracheal instillation developed both pulmonary and systemic immune responses to challenges by trimellitic anhydride-protein conjugates (Patterson et al., 1980). This has been proposed as a model system for the study of human airway disease caused by trimellitic anhydride.

b. Human Studies

(1) Pharmacokinetics

No information was found in the literature searched.

(2) Health Effects

Interviews with 13 employees exposed to trimellitic anhydride in an epoxy paint manufacturing plant revealed complaints of eye irritation, nasal irritation, shortness of breath, wheezing, cough, throat irritation, heartburn, nausea, headache, and skin irritation (Millar, 1978a; Thomas et al., 1978).

(3) Target Organ Toxicity

Pulmonary edema was observed in 2 workers who were exposed to powdered epoxy material for 3 and 6 weeks, respectively (Rice et al., 1977). The major irritant in the epoxy material was trimellitic anhydride and it was suspected that this was the causative agent, but the concentration of exposure was unknown. The authors speculated that a hypersensitivity reaction may have been the cause of the pulmonary edema. Fawcett et al. (1977) described a single case of asthma caused by inhalation of fumes of epoxy resin and trimellitic anhydride. Trimellitic anhydride was indicated as the causative agent since test exposures of the individuals to resin alone had no effect, while exposure to the resin containing trimellitic anhydride caused an immediate asthmatic response.

Zeiss et al. (1977) described sensitization in 14 workers who were exposed to trimellitic anhydride during its synthesis; respiratory syndromes resulting from inhalation of the chemical included asthma and rhinitis of the immediate type, late onset asthma with systemic symptoms, and airway irritation. It was demonstrated that trimellitic anhydride coupled rapidly to human serum albumin in vitro, and that the asthma-rhinitis syndrome and the syndrome of late onset asthma with systemic symptoms were mediated by antibodies specific for trimellitic anhydride (IgE and Igb, respectively). Patterson et al. (1978) used radioimmunoassay techniques to detect IgE antibodies to trimellitic anhydride-protein conjugates in 3 of 5 workers who were exposed to

trimellitic anhydride and had asthma. IgG and IgA antibodies were detected in most workers, but higher levels of antibody were found in those with respiratory symptoms.

(4) Epidemiology

No information was found in the literature searched.

15. Ongoing Studies

Trimellitic anhydride has been selected for mutagenicity evaluation in Salmonella and reproductive/developmental testing by the National Toxicology Program (NTP, 1980). The compound has also been selected by the NTP for carcinogenesis bioassay (NTP, 1981).

16. Exposure Standards

A Threshold Limit Value-Time Weighted Average (TLV-TWA) of 0.005 ppm (0.04 mg/m^3) has been proposed by the ACGIH (1980).

17. Sources of Additional Relevant Information

The National Institute for Occupational Safety and Health has published a Current Intelligence Bulletin (No. 21) on trimellitic anhydride (Millar, 1978).

18. Other Pertinent Data

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

APPENDIX - ORGANIC ANHYDRIDES

The following list includes all of the organic anhydrides considered under the class definition. The compounds in the list were identified primarily from the following sources: U.S. EPA TSCA list and U.S. EPA (1980), USITC (1980a,b), SRI International (1980), Chem. Sources - USA (1980), and Kirk-Othmer's Encyclopedia of Chemical Technology.

CAS Numbers are given, where available, to aid in identification as these types of compounds can be named by a variety of synonyms.

Acetic anhydride	108-24-7
4-Bromophthalic anhydride	82-73-5
5-Bromophthalic anhydride	86-90-8
Butyric anhydride	106-31-0
Chloran	1782-06-5
Chlorendic anhydride	115-27-5
Chloroacetic anhydride	541-88-8
3-Chloromaleic anhydride	96-02-6
Chlorophthalic anhydride	30205-85-7
4-Chlorophthalic anhydride	117-21-5
5-Chlorophthalic anhydride	118-45-6
Decenylsuccinic anhydride	25447-83-0
Decylsuccinic anhydride	---
3,4-Dibromomaleic anhydride	1122-12-9
3,4-Dichloromaleic anhydride	1122-17-4
4,5-Dichlorophthalic anhydride	56962-07-3
4,6-Dichlorophthalic anhydride	51971-64-3
5,6-Dichlorophthalic anhydride	942-06-3
4,7-Dichlorophthalic anhydride	4466-59-5
Dimethyl maleic anhydride	766-39-2
Docosenylsuccinic anhydride	58598-42-8
Dodecenylsuccinic anhydride	25377-73-5
Dodecylsuccinic anhydride	2561-85-5
Dotetracontenylsuccinic anhydride	64051-58-7
Eicosenylsuccinic anhydride	53520-67-5
Glutaric anhydride	108-55-4
Heptanoic anhydride	626-27-7
Hexadecenylsuccinic anhydride	32072-96-1
Hexadecylsuccinic anhydride	---
Hexahydromethylphthalic anhydride	25550-51-0
Hexahydro-4-methylphthalic anhydride	57110-29-9
Hexahydro-5-methylphthalic anhydride	19438-60-9
Hexahydrophthalic anhydride	85-42-7
Hexatriacontenylsuccinic anhydride	64051-60-1
Isobutyric anhydride	97-72-3
Isooctadecenylsuccinic anhydride	58239-72-8
Isooctadecylsuccinic anhydride	---
Isooctenylsuccinic anhydride	28454-79-7
Itaconic anhydride	---

Maleic anhydride	108-31-6
Methylene maleic anhydride	2170-03-8
3-Methylmaleic anhydride	616-02-4
5-Methyl-norbornene-2,3-dicarboxylic anhydride	25134-21-8
4-Methylphthalic anhydride	4792-30-7
5-Methylphthalic anhydride	19438-61-0
Methyltetrahydrophthalic anhydride	1694-82-2
Methyltetrahydrophthalic anhydride	3425-89-6
Methyltetrahydrophthalic anhydride	5333-84-6
Methyltetrahydrophthalic anhydride	11070-44-3
Methyltetrahydrophthalic anhydride	26590-20-5
Methyltetrahydrophthalic anhydride	34090-76-1
4-Nitrophthalic anhydride	641-70-3
5-Nitrophthalic anhydride	5466-84-2
Nonenylsuccinic anhydride	28928-97-4
5-Norbornene-2,3-dicarboxylic anhydride	129-64-6
Octadecenylsuccinic anhydride	28777-98-2
2-Octadecenylsuccinic anhydride	67066-88-0
Octadecylsuccinic anhydride	47458-32-2
Octatriacontenylsuccinic anhydride	64347-17-7
Octenylsuccinic anhydride	26680-54-6
Octylsuccinic anhydride	---
Phthalic anhydride	85-44-9
2-Propenylsuccinic anhydride	7539-12-0
Propionic anhydride	123-62-6
Pyromellitic di-anhydride	89-32-7
Succinic anhydride	108-30-5
Tetrabromophthalic anhydride	632-79-1
Tetrachlorophthalic anhydride	117-08-8
Tetracontenylsuccinic anhydride	64347-19-9
Tetracosenylsuccinic anhydride	64347-15-5
Tetradecenylsuccinic anhydride	54405-64-0
Tetradecylsuccinic anhydride	---
Tetrafluorosuccinic anhydride	699-30-9
Tetrahydrophthalic anhydride	85-43-8
Tetrahydrophthalic anhydride	4717-58-2
Tetrahydrophthalic anhydride	26266-63-7
Trimellitic anhydride	522-30-7

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