Trimethoxysilane

Document History
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I. IDENTIFICATION

Chemical Name: Trimethoxysilane
Synonyms: None
CAS Number: 2487-90-3
Molecular Formula: $C_3H_{10}O_3Si$
Structural Formula: $HSi(OCH_3)_3$

II. CHEMICAL AND PHYSICAL PROPERTIES[1–3]

Physical State and Appearance: Colorless liquid
Odor Description: Ester odor
Molecular Weight: 122
Conversion Factors 1 ppm = 5 mg/m^3;
1 mg/m^3 = 0.2 ppm
Melting Point: -113.6°C (-236.5°F)
Boiling Point: 84°C (183°F) at 760 mmHg
Specific Gravity: 0.95 at 20°C (68°F)
Vapor Density (Air =1) 4.2
Vapor Pressure: 57 mmHg (7.6 kPa) at 20°C (68°F)
Saturated Vapor Concentration: 75,000 ppm
Flammability Limits in Air (by volume):
Lower explosive limit – 4.3% at 34°C (93°F);
Upper explosive limit – 40.1% at 62°C (144°F)
Flash Point: 7.2°C (45°F) (closed cup)
Autoignition Temperature: No data available Solubility in Water: Reacts slowly
Stability and Reactivity: Reacts with water, liberating methanol.

III. USES

Trimethoxysilane is used as an intermediate in the production of organofunctional silanes.

IV. ANIMAL TOXICITY DATA

A. Acute Toxicity and Irritancy

1. Oral Toxicity

Rats (unfasted males): LD_{50} = 8.9 g/kg[4]

Rats (fasted males): LD_{50} = 2.34 g/kg[5]

Rats (fasted females): LD_{50} = 1.48 g/kg[5]

Rats (fasted males): LD_{50} = 6.41 g/kg[6]

In a range-finding test, a dose of 2 g/kg as a 10% solution in corn oil did not kill either of 2 rats.[7]

2. Eye Toxicity

Instillation of 0.005 mL caused minor corneal injury in rabbits; 0.02 mL caused moderately severe corneal necrosis.[4]

Instillation of 0.005 mL caused iritis and minor to severe conjunctival irritation in 4/6 rabbits, but no corneal injury and complete healing in 7 days: 0.01 mL caused minor to moderate corneal injury, iritis, moderate to severe conjunctival irritation with necrosis in 3/6 rabbits and healing was complete in 6 days; 0.1 mL caused iritis in 6/6 rabbits, moderate to severe conjunctival irritation in 6/6 rabbits with necrosis in 5, and mild corneal injury in 3/6. Healing was essentially complete in 7 days.[5]

Instillation of 0.1 mL caused conjunctivitis and blepharitis after 5 min in rabbits; purulent keratitis and closed eyelids occurred after 2 days; healing was complete in 8–10 days.[6]

Ocular damage in rabbits has been attributed to the formation of $(CH_3O)_3SiOH$ in the mucous fluid of the eyes.[8]

3. Skin Absorption

Rabbits: LD_{50} = 6 g/kg (marked erythema observed)[4]

Rabbits (male): LD_{50} = 7.09 g/kg[5]

Rabbits (female): LD_{50} = 6.39 g/kg[5]

4. Skin Irritation

Application of 0.5 mL for 4 hr on occluded skin caused moderate to severe erythema and severe edema and necrosis hi rabbits. Ecchymoses were observed in 3/6 rabbits. Severe irritation was present for 2 weeks, with desquamation, ulceration, scabs, and alopecia.[5]

Trimethoxysilane applied 8 times to intact or abraded skin caused slight hyperemia and exfoliation hi rabbits. There was some indication that toxic amounts may be absorbed through skin.[7]

5. Skin Sensitization

No data available

6. Inhalation Toxicity

Approximately 71,000 ppm killed 6/6 female rats within 90 mm after a 15-min exposure. At 62.5 ppm, 5/6 rats died 10–13 days after a 4-hr exposure. At 31.25 ppm, 1/6 rats died. At sacrifice, consolidation was found in the lungs in 10%-80% of the animals.[4] From these data, the 4-hr LC_{50} was calculated to be 47 ppm.[9]

Rats (male): LC_{50} (1 hr) - 161 ppm[10]

Rats (female): LC_{50} (1 hr) = 146 ppm[10]

Rats (male): LC_{50} (4 hr) = 81 ppm[10]

Rats (female): LC_{50} (4 hr) = 42 ppm[10]

In addition to these values determined in dynamic exposures, static tests were performed. At 56,000 ppm for 10 min and 60,000 ppm for 1 hr, groups of 5 male and 5 female rats all died during or within 2 hr postexposure. Reaction of trimethoxysilane with water vapor in the air caused rapid decrease in the concentration of the silane with concomitant rise in methanol concentration. In both static and dynamic trials, red discoloration of lungs, purple discoloration of liver, and clear fluid hi the trachea and mouth were found on gross examination. Microscopically, the necrotizing action of the silane was evident in the lungs.[10]

In a range-finding test, 4/4 rats died after a 30-min exposure to the saturated vapor.[7]

Rats (male): LC_{50} (4 hr) = 53 ppm (nose-only exposure).[11]

In a range-finding test, rats withstood a 15-min exposure to the nearly saturated vapor without deaths. A 4-hr exposure to 62.5 ppm killed 5/6 rats.[13]

Two different cuts of trimethoxysilane, identified as TX1747 and TX1748, were examined in 4-hr inhalation studies in rats. The LC_{50}s were 114 ppm and 140 ppm, respectively, for combined male and female rats.[14,15]

One rabbit each was exposed to 5452 ppm and 15,080 ppm for 15 min. Both died within 1 hr.[12]

7. Other Toxicity

a. Intravenous

Rats: LD_{50} = > 50 mg/kg

Animals appeared normal with no lung or other organ pathology. No sign of the injected chemical was found.[16]

b. Intraperitoneal

Rats: LD_{50} = > 1000 mg/kg

Animals appeared normal with no lung or other organ pathology. A hard, whitish, crystalline material was found at the site of injection.[16]

B. Subacute Toxicity

Four species were exposed 7 hr/day for 5 days to trimethoxysilane vapor at concentrations of 0 (control), 10, 25, and 50 ppm. The following values were calculated:

Rats: LC_{50} = 13 ppm

Mice: LC_{50} = 14 ppm

Hamsters: LC_{50} = 72 ppm

Rabbits: LC_{50} = 1 ppm

In all species, severe lung congestion, atelectasis and hemorrhage were found in those that died during exposure and those sacrificed after surviving 14 days. No other adverse internal effects were noted.[17]

Rats were exposed to the vapor of trimethoxysilane 6 hr/day 5 days/week for 9 days at concentrations of 0.2, 1, and 5 ppm. Nearly all of the 5 ppm group died between the 8th and 12th day of the study. Severe and extensive inflammation, degeneration/necrosis of epithelia, squamous metaplasia, and bronchiolar fibrosis were found at necropsy. In the 1 ppm group, lung discoloration, increased lung weight, and body weight loss were among the detectable effects. There were no deaths in the 0.2 ppm group and no significant

changes in clinical observations, ophthalmic examinations, pathology, body and organ weights, or hi the necropsy and histopathological findings. Thus, the no observable effect level (NOEL) was 0.2 ppm.[18]

C. Subchronic Toxicity

Rats were exposed to the vapors of trimethoxysilane 7 hr/day 5 days/week for 4 weeks to concentrations of 0, 0.5, 5, and 10 ppm. Pulmonary atelectasis, subacute and acute bronchitis and bronchiolitis, epithelial desquamation, and bronchial metaplasia were prominent in the 5 ppm and 10 ppm groups. At 0.5 ppm, only a reduced food intake and reduced weight gain were noted. The LC_{50} was calculated to be 5.5 ppm.[19]

Rats were exposed 6 hr/day 5 days/week for 13 weeks to the vapor of trimethoxysilane at concentrations of 0.02, 0.1, and 0.5 ppm. There were no deaths or exposure-related clinical signs. No differences in ophthalmic observations, body weight, body weight gain, food and water consumption, hematology, clinical chemistry, serum protein fractions, urine chemistry, and urinalysis evaluations were observed. Gross examination and microscopic evaluation revealed no lesions attributable to trimethoxysilane exposure, or changes in absolute and relative organ weights. Thus, the NOEL was at least 0.5 ppm.[20]

D. Chronic Toxicity/Carcinogenicity

No data available.

E. Reproductive/Developmental Toxicity

No data available.

F. Genotoxicity

No chromosome breakage or spindle cell poisoning was found in bone marrow analyses of rats exposed 4 hr to 100 ppm trimethoxysilane vapor.[21]

Dilutions of trimethoxysilane in dimethyl sulfoxide were tested for genetic activity in the *Salmonella typhimurium* and *Escherichia coli* reverse mutation assay, with and without S-9 activation. No evidence of mutagenic potential was observed.[22]

G. Metabolism/Pharmacokinetics

Trimethoxysilane was administered orally in a single dose of 2540 mg/kg to rats, and blood samples were taken at 1,2, 4, 8, and 24 hr for methanol and silicon analyses. Another group of rats received 2000 mg/kg of methanol, equivalent to the methanol derivable from the silane. In rats treated with the silane, the methanol level was high 1 hr after treatment, indicating rapid absorption. The level was still elevated at 24 hr, indicating sustained release of methanol. Animals treated with methanol exhibited a much lower methanol level at 24 hr, showing that methanol alone is metabolized fairly rapidly. Silicon levels after trimethoxysilane administration were elevated at 1 hr and even higher at 24 hr, indicating continuous release of this element.[23]

Groups of rabbits received a single oral dose of either 2000 mg/kg methanol or 2800 mg/kg trimethoxysilane. Six hours after dosing, blood from the aorta was analyzed for methanol concentration. No significant difference in methanol level was detected, indicating that the rate or degree of hydrolysis and absorption is the same for both compounds.[24]

V. HUMAN USE AND EXPERIENCE

Eye irritation following exposure to trimethoxysilane vapor has been described in the following reports:

- Six workers engaged in purification of the compound experienced irritation, pain, lacrimation, and disturbance of vision 8–12 hours after work. Eye examinations revealed conjunctival hyperemia, chemosis, and desquamation of corneal epithelium. Healing took 20–90 days, attesting to the latency, severity, and persistence of the eye damage.[8]
- In another incident, 2 workers suffered eye irritation a few hours after exposure from a trimethoxysilane leak, again showing the latency of the effects.[9]
- An epidemiologic study in a plant where trimethoxysilane was handled revealed 6 cases of acute exposure following a leak or spill. Severe eye irritation was noted, sometimes delayed for hours after exposure.[9]
- Adverse effects on the respiratory system have also been reported in the patients who had been engaged in the purification of trimethoxysilane cited above. Two of the 6 workers developed soreness of the throat, and 4 suffered bronchitis or bronchopneumonia.[8]
- Respiratory distress also was experienced by those identified in the epidemiologic study who suffered eye irritation.[9]
- No change in the incidence of cancer or liver, kidney, or urinary disease was detected in employees in a plant where trimethoxysilane was handled.[9]

VI. RATIONALE

Trimethoxysilane has proved to be of exceptionally

high toxicity. The vapors are extremely irritating to the mucous membranes of the eye and respiratory tract. In contact with water, 1 mole of trimethoxysilane yields 3 moles of methanol; however, the high toxicity of trimethoxysilane cannot be attributed, either qualitatively or quantitatively, to methanol release. It has been proposed that hydrolysis produces some form of silicate or other oxygen-containing silicon reaction product to which the high toxicity might be ascribed.[8,25] Human exposure experience does not provide any guide to an appropriate environmental exposure limit for trimethoxysilane since no measures of vapor concentration are recorded in the incidents that have occurred.[8,9]

To develop an exposure limit for trimethoxysilane, emphasis must be placed on experimental data, particularly the longer term inhalation studies. In the 9-day study in rats at concentrations of 0.2, 1, and 5 ppm, it was concluded that the NOEL was 0.2 ppm.[18] In a 4-week study, concentrations of 0.5, 5, and 10 ppm were examined. At 0.5 ppm, some reduction in food intake and weight gain were observed.[19] However, in the most definitive study available, in which rats were exposed to 0.02, 0.1, and 0.5 ppm for 13 weeks, no such reductions were noted.[20] It was concluded that the NOEL was at least 0.5 ppm.

An OEL of 0.05 ppm as an 8-hr time-weighted average (TWA) has been adopted.

VII. RECOMMENDED OEL

8-hr TWA: 0.05 ppm (025 mg/m^3)

VIII. REFERENCES

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NOTE(1): The following databases were searched in developing the 1997 WEEL:

MEDLINE
RTECS
TOXLINE
TOXLIT

NOTE(2): The following databases were searched for the 2009 WEEL Revision:

MEDLINE (1989 – 2008)
IPA (1970 – 2008)
CURRENT CONTENTS (1990 – 2008)
CAB (Global Health)(1973 – 2008)
CINAHL (1982 – 2008)
TOXNET (2006 – January 2010)