Dioctyltin dicarboxylate esters: Human health tier II assessment

02 March 2018

Chemicals in this assessment

Chemical Name in the Inventory	CAS Number
Stannane, dioctylbis[(1-oxododecyl)oxy]-	3648-18-8
Stannane, dioctylbis[(1-oxoneodecyl)oxy]-	68299-15-0
Stannane, dioctylbis[(1-oxooctyl)oxy]-, branched	93686-52-3
Stannane, dioctylbis[(1-oxoisoundecyl)oxy]-	93893-97-1
Stannane, dioctylbis[(1-oxoisononyl)oxy]-	93965-21-0
Stannane, dioctylbis[(1-oxoisodecyl)oxy]-	93965-26-5

Preface

This assessment was carried out by staff of the National Industrial Chemicals Notification and Assessment Scheme (NICNAS) using the Inventory Multi-tiered Assessment and Prioritisation (IMAP) framework.

The IMAP framework addresses the human health and environmental impacts of previously unassessed industrial chemicals listed on the Australian Inventory of Chemical Substances (the Inventory).

The framework was developed with significant input from stakeholders and provides a more rapid, flexible and transparent approach for the assessment of chemicals listed on the Inventory.

Stage One of the implementation of this framework, which lasted four years from 1 July 2012, examined 3000 chemicals meeting characteristics identified by stakeholders as needing priority assessment. This included chemicals for which NICNAS already held exposure information, chemicals identified as a concern or for which regulatory action had been taken overseas, and chemicals detected in international studies analysing chemicals present in babies' umbilical cord blood.

Stage Two of IMAP began in July 2016. We are continuing to assess chemicals on the Inventory, including chemicals identified as a concern for which action has been taken overseas and chemicals that can be rapidly identified and assessed by using Stage One information. We are also continuing to publish information for chemicals on the Inventory that pose a low risk to human health or the environment or both. This work provides efficiencies and enables us to identify higher risk chemicals requiring assessment.

The IMAP framework is a science and risk-based model designed to align the assessment effort with the human health and environmental impacts of chemicals. It has three tiers of assessment, with the assessment effort increasing with each tier. The Tier I assessment is a high throughput approach using tabulated electronic data. The Tier II assessment is an evaluation of risk on a substance-by-substance or chemical category-by-category basis. Tier III assessments are conducted to address specific concerns that could not be resolved during the Tier II assessment.

These assessments are carried out by staff employed by the Australian Government Department of Health and the Australian Government Department of the Environment and Energy. The human health and environment risk assessments are conducted and published separately, using information available at the time, and may be undertaken at different tiers.

This chemical or group of chemicals are being assessed at Tier II because the Tier I assessment indicated that it needed further investigation.

For more detail on this program please visit:**www.nicnas.gov.au**

Disclaimer

ACRONYMS & ABBREVIATIONS

Grouping Rationale

The chemicals in this group are di-substituted organotin compounds, specifically dioctyltin dicarboxylate esters with varying alkyl chain lengths (8–12 carbons). Di-substituted organotin compounds have the general formula R_2SnX_2. The toxicity of organotin compounds depends largely on the organotin moiety (R group), with the anionic ligand (X) mostly influencing physicochemical properties. These chemicals are grouped together for risk assessment due to their similar end uses and expected toxicity profiles (ATSDR, 2005; OECD, 2006; WHO, 2006).

Import, Manufacture and Use

Australian

No specific Australian use, import, or manufacturing information has been identified.

The National Pollutant Inventory (NPI) holds data for all sources of organotin compounds in Australia.

The following site-limited uses were identified for organotin compounds by the NPI in 2015-16:

- glass and glass product manufacturing; and
- polymer product manufacturing.

International

The following international uses have been identified through Galleria Chemica; the European Union (EU) Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) dossiers; and Classification, Labelling and Harmonisation (CLH) Reports (CLHa, 2017; CLHb, 2017).

The chemicals have reported site-limited uses, including in producing:

- adhesives and sealants;
- coatings and paints;
- thinners and paint removers;
- paper and board dyes and finishing products;
- leather care products;
- surface treatment products;
- polishes and waxes;
- polymer preparations and compounds; and
- additives for use in pH regulators, flocculants, precipitants and neutralisation agents.

No evidence of the presence of these chemicals in consumer products was found in available North American databases (Household Products Database and Personal Care Council), indicating that the chemicals are not likely to be widely available for domestic or cosmetic uses. The chemicals have reported domestic use in the Substances and Preparations in Nordic countries (SPIN) database. However, it should be noted that SPIN does not distinguish between direct use of the chemical, or use of the materials that are produced from chemical reactions involving the chemicals.

Restrictions

Australian

Tin and its compounds are listed in the Work Health and Safety Regulations (2016 revision) as restricted hazardous chemicals—the restricted use is 'abrasive blasting at a concentration of greater than 0.1 % as tin' (Galleria Chemica).

International

Dioctyltin compounds are listed on the following (Galleria Chemica):

- Annex XVII to REACH Regulations—dioctyltin compounds shall not be used after 1 January 2012 in several articles for supply to, or use by, the general public, where concentration in the article, or part thereof, is greater than the equivalent of 0.1 % by weight of tin. Organostannic compounds are also restricted for biocide and water treatment uses (European Parliament and Council, 2006); and
- Council of Europe Resolution AP (92) 2 on the control of aids to polymerisation for plastic materials and articles intended to come into contact with foodstuffs—Limits for finished articles; a limit of 0.02 mg/kg (as Sn) applies for di-n-octyltin.

Tin compounds (organic) are listed on the:

- Europe Directive 2009/48/EC of the European Parliament and of the Council on the safety of toys—Maximum Migration Limits; limits of 0.2, 0.9 and 12 mg/kg of organic tin applies in liquid or sticky toy material, dry or brittle or powder like material, and scraped-off toy material, respectively (Galleria Chemica).

Existing Worker Health and Safety Controls

Hazard Classification

The chemicals are not listed on the Hazardous Chemical Information System (HCIS) (Safe Work Australia).

Exposure Standards

Australian

Tin organic compounds (as Sn) have an exposure standard of 0.1 mg/m^3 time weighted average (TWA) and 0.2 mg/m^3 short-term exposure limit (STEL).

International

The following exposure standards are identified for tin organic compounds (as Sn) (Galleria Chemica).

An exposure limit of 0.1 mg/m^3 TWA and 0.2 mg/m^3 STEL in different countries such as Bulgaria, Canada (Alberta, British Columbia, Ontario, Quebec, Saskatchewan, Yukon), Chile, Denmark, Egypt, Estonia, France, Greece, Malaysia, Mexico, Norway, Philippines, Singapore, South Africa, Spain, Sweden, Taiwan, the United Kingdom and the United States of America (California, Hawaii, Minnesota, Tennessee, Vermont).

Health Hazard Information

Only limited toxicological data are available for one of the chemicals in this group—dioctyltin dilaurate (DOTL; CAS No. 3648-18-8). This data is considered to apply to all chemicals in the group because of their similar structure and end uses (see **Grouping Rationale** section).

When data for the chemicals being assessed are not available, health hazard information for dioctyltin dichloride (DOTC, CAS No. 3542-36-7; NICNASa) and dioctyltin oxide (DOTO, CAS No. 870-08-6; NICNASb) has been included in this report for read across for systemic toxicity endpoints. All chemicals are structurally similar as they contain a dioctyltin (Oct_2Sn-) group, and two labile ligands (X). Oral administration is expected to result in a similar hydrolysis pathway and elicit similar toxicological responses (CLHa, 2017; CLHb, 2017).

Toxicokinetics

One of the chemicals in this group—DOTL, is readily absorbed into the body orally, while dermal absorption is not expected to occur as studies in animals indicate that there is minimal tin absorption into the blood (CLHa, 2017; REACH). No information on inhalation absorption is available for DOTL. Once orally absorbed, DOTL is hydrolysed to the distannoxane $ClOct_2SnOSnOct_2Cl$, an oxo-bridged mono-chloride mono-carboxylate species, and a non-assigned tin species under conditions representative of the mammalian stomach (CLHa, 2017).

One of the chemicals in this group—DOTL, is progressively hydrolysed to a dimeric distannoxane ($ClOct_2SnOSnOct_2Cl$) as the only product, similar to DOTC. Target organs affected following oral administration of DOTC include the liver, kidneys, adrenals, spleen, pituitary, lymph, thymus and brain. Approximately 10 % of DOTC remained unchanged at the end of a simulated gastric hydrolysis study. After oral administration, urinary excretion (22%) remained constant for the duration of the study and after 2 days, 80 % of the initial oral dose was excreted in the faeces (NICNAS). It is expected that DOTL and the other chemicals in the group will have a similar toxicokinetics profile.

Acute Toxicity

Oral

Based on the available data for one of the chemicals in this group—DOTL, the chemicals in this group are considered to have low acute oral toxicity. The data for DOTC support this finding (NICNAS).

The following oral median lethal dose (LD50) values were reported (REACH; RTECS):

- >2000 mg/kg bw in female Wistar rats; and
- 6450 mg/kg bw in rats.

No deaths or signs of toxicity were reported.

Dermal

Based on the available data for a commercial preparation of DOTL (TIB KAT® 216), the chemicals in this group are considered to have low acute dermal toxicity.

A dermal LD50 of >2000 mg/kg bw in male and female rats (species unspecified) was reported. This may in part be due to the low dermal absorption of the chemical (see **Toxicokinetics** section). There were no deaths or signs of toxicity reported (REACH).

Inhalation

No data are available.

Corrosion / Irritation

Skin Irritation

Based on the available data in the DOTL REACH dossier for an 'unnamed liquid constituent', the chemicals in this group are not considered to be irritating to skin.

In an ex vivo / in vitro skin irritation study (according to the Organisation for Economic Co-operation and Development (OECD) Test Guidelines (TG) 439), 10 µL of the chemical was topically administered to reconstructed human epidermis for 15 minutes before rinsing. The relative mean viability of the treated epidermis was just over 100 % after the 15 minute exposure period. Based on this finding it was concluded that the chemical was not irritating (REACH).

In an in vitro skin corrosion study (OECD TG 431), reconstructed human epidermis was topically administered 50 µL of the chemical for 3, 60 or 240 minutes. The relative mean viability of the treated epidermis was >80 % for all three time periods. Based on these results it was concluded that the chemical was not corrosive (REACH).

Eye Irritation

Based on the available data in the DOTL REACH dossier for an 'unnamed liquid constituent', the chemicals in this group are not considered to be irritating to the eye.

In an in vivo eye irritation study (OECD TG 405), two male New Zealand White rabbits were exposed to 0.1 mL chemical in one eye each, and then assessed for a period of 72 hours. There were no effects on the cornea or iris. Moderate conjunctival irritation was observed in both treated eyes after one hour, becoming minimal at 24–48 hours and a full recovery was reported 72 hours after administration (REACH).

In an in vitro eye irritation study (non-guideline), 30 µL chemical was administered onto a reconstructed human corneal model (SkinEthic) for 10 minutes and cell viability assessed. The relative mean viability of the treated test material after 10 minute exposure was >80 %. Based on this result it was concluded that the chemical was not irritating to eyes (REACH).

Sensitisation

Skin Sensitisation

No data are available for the chemicals. Based on the available data for DOTC (NICNASa) and DOTO (NICNASb) the chemicals in this group are not considered to cause skin sensitisation reactions.

Repeated Dose Toxicity

Oral

No data are available for the chemicals. Based on the available data for DOTC (NICNASa) and DOTO (NICNASb), the chemicals in this group are expected to cause serious health effects in the thymus following repeated oral exposure, warranting hazard classification (see **Recommendation** section).

Dermal

No data are available.

Inhalation

No data are available.

Genotoxicity

No data are available for the chemicals. Based on the available data for DOTC (NICNASa) and DOTO (NICNASb) the chemicals in this group are not considered to be genotoxic.

Carcinogenicity

No data are available for the chemicals. Limited data available using mixtures containing dioctyltins are insufficient to derive a conclusion on carcinogenicity (NICNASa).

Reproductive and Developmental Toxicity

No data are available for the chemicals. Based on the available data for DOTC (NICNASa) and DOTO (NICNASb), the chemicals are not expected to show specific reproductive toxicity. However, developmental effects were observed with DOTC (skeletal malformations; see NICNASa) and DOTO (pup mortality in rats; see NICNASb), therefore warranting hazard classification for this group of chemicals (see **Recommendation** section).

Risk Characterisation

Critical Health Effects

The critical health effects for risk characterisation include systemic long-term effects from repeated oral exposure (developmental toxicity and thymus effects).

Public Risk Characterisation

Based on the available use information, the chemicals are not likely to be available for domestic or cosmetic uses. Hence, the public risk from direct use of these chemicals is not considered to be unreasonable.

Internationally, a group tolerable daily intake (TDI) of 0.1 µg/kg bw (as Sn) for tributyltins, triphenyltins, dibutyltins and dioctyltins has been established (EFSA, 2004). Based on an impact assessment report conducted in Europe (European Commission, 2009), the chemicals with their identified uses are not considered to significantly contribute to the overall TDI. In addition, the dominant contribution to human intake of organotins (mainly tributyltin compounds) is via the consumption of fish. Hence, the public risk from these chemicals is not considered to be unreasonable.

If data becomes available indicating specific uses in Australia that could significantly contribute to the overall TDI for organotins, further assessment of these chemicals may be required.

Occupational Risk Characterisation

During product formulation, exposure may occur, particularly where manual or open processes are used. These could include transfer and blending activities, quality control analysis, and cleaning and maintaining equipment. Worker exposure to the chemical at lower concentrations could also occur while using formulated products containing the chemical. The level and route of exposure will vary depending on the method of application and work practices employed.

Given the critical systemic long-term health effects, the chemical could pose an unreasonable risk to workers unless adequate control measures to minimise exposure are implemented. The chemical should be appropriately classified and labelled to ensure that a person conducting a business or undertaking (PCBU) at a workplace (such as an employer) has adequate information to determine the appropriate controls.

The data available support an amendment to the hazard classification in the HCIS (Safe Work Australia) (see **Recommendation** section).

NICNAS Recommendation

Assessment of these chemicals is considered to be sufficient, provided that the recommended amendment to the classification is adopted, and labelling and all other requirements are met under workplace health and safety and poisons legislation as adopted by the relevant state or territory.

If data becomes available indicating specific uses in Australia that could significantly contribute to the overall TDI for organotins, further assessment of these chemicals may be required.

Regulatory Control

Work Health and Safety

The chemicals are is recommended for classification and labelling aligned with the Globally Harmonized System of Classification and Labelling of Chemicals (GHS) as below. This does not consider classification of physical hazards and environmental hazards.

From 1 January 2017, under the model Work Health and Safety Regulations, chemicals are no longer to be classified under the Approved Criteria for Classifying Hazardous Substances system.

Hazard	Approved Criteria (HSIS)[a]	GHS Classification (HCIS)[b]
Repeat Dose Toxicity	Not Applicable	Causes damage to the immune system through prolonged or repeated exposure - Cat. 1 (H372)
Reproductive and Developmental Toxicity	Not Applicable	Suspected of damaging the unborn child - Cat. 2 (H361d)

[a] Approved Criteria for Classifying Hazardous Substances [NOHSC:1008(2004)].

[b] Globally Harmonized System of Classification and Labelling of Chemicals (GHS) United Nations, 2009. Third Edition.

[*] Existing Hazard Classification. No change recommended to this classification

Advice for industry

Control measures

Control measures to minimise the risk from oral exposure to the chemical should be implemented in accordance with the hierarchy of controls. Approaches to minimise risk include substitution, isolation and engineering controls. Measures required to eliminate, or minimise risk arising from storing, handling and using a hazardous chemical depend on the physical form and the manner in which the chemicals are used. Examples of control measures that could minimise the risk include, but are not limited to:

- using closed systems or isolating operations;
- air monitoring to ensure control measures in place are working effectively and continue to do so;
- minimising manual processes and work tasks through automating processes;
- work procedures that minimise splashes and spills;
- regularly cleaning equipment and work areas; and
- using protective equipment that is designed, constructed, and operated to ensure that the worker does not come into contact with the chemical.

Guidance on managing risks from hazardous chemicals are provided in the *Managing risks of hazardous chemicals in the workplace—Code of practice* available on the Safe Work Australia website.

Personal protective equipment should not solely be relied upon to control risk and should only be used when all other reasonably practicable control measures do not eliminate or sufficiently minimise risk. Guidance in selecting personal protective

equipment can be obtained from Australian, Australian/New Zealand or other approved standards.

Obligations under workplace health and safety legislation

Information in this report should be taken into account to help meet obligations under workplace health and safety legislation as adopted by the relevant state or territory. This includes, but is not limited to:

- ensuring that hazardous chemicals are correctly classified and labelled;
- ensuring that (material) safety data sheets ((M)SDS) containing accurate information about the hazards (relating to both health hazards and physicochemical (physical) hazards) of the chemical are prepared; and
- managing risks arising from storing, handling and using a hazardous chemical.

Your work health and safety regulator should be contacted for information on the work health and safety laws in your jurisdiction.

Information on how to prepare an (M)SDS and how to label containers of hazardous chemicals are provided in relevant codes of practice such as the *Preparation of safety data sheets for hazardous chemicals—Code of practice* and *Labelling of workplace hazardous chemicals—Code of practice*, respectively. These codes of practice are available from the Safe Work Australia website.

A review of the physical hazards of these chemicals has not been undertaken as part of this assessment.

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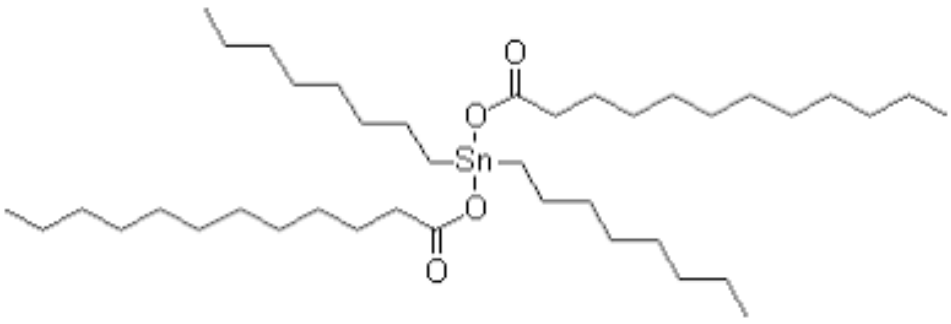
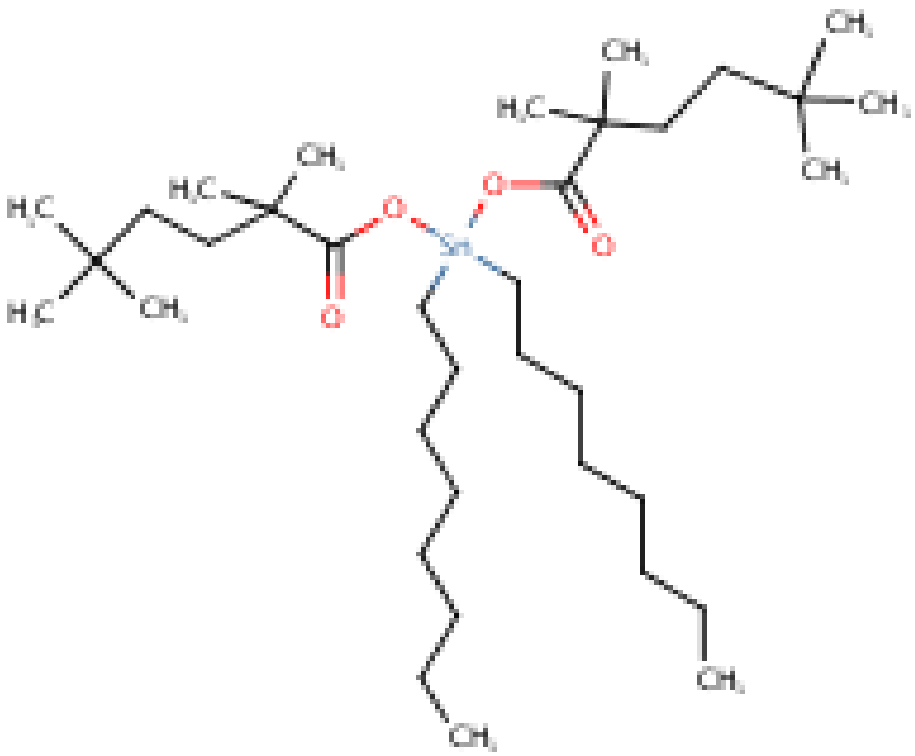
Last Update 02 March 2018

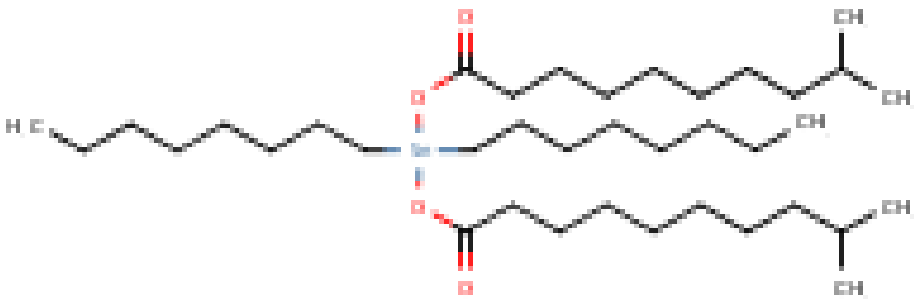
Chemical Identities

Chemical Name in the Inventory and Synonyms	**Stannane, dioctylbis[(1-oxododecyl)oxy]-** bis(lauroyloxy)dioctylstannane dioctyltin dilaurate DOTL
CAS Number	3648-18-8
Structural Formula	
Molecular Formula	C40H80O4Sn
Molecular Weight	743.78

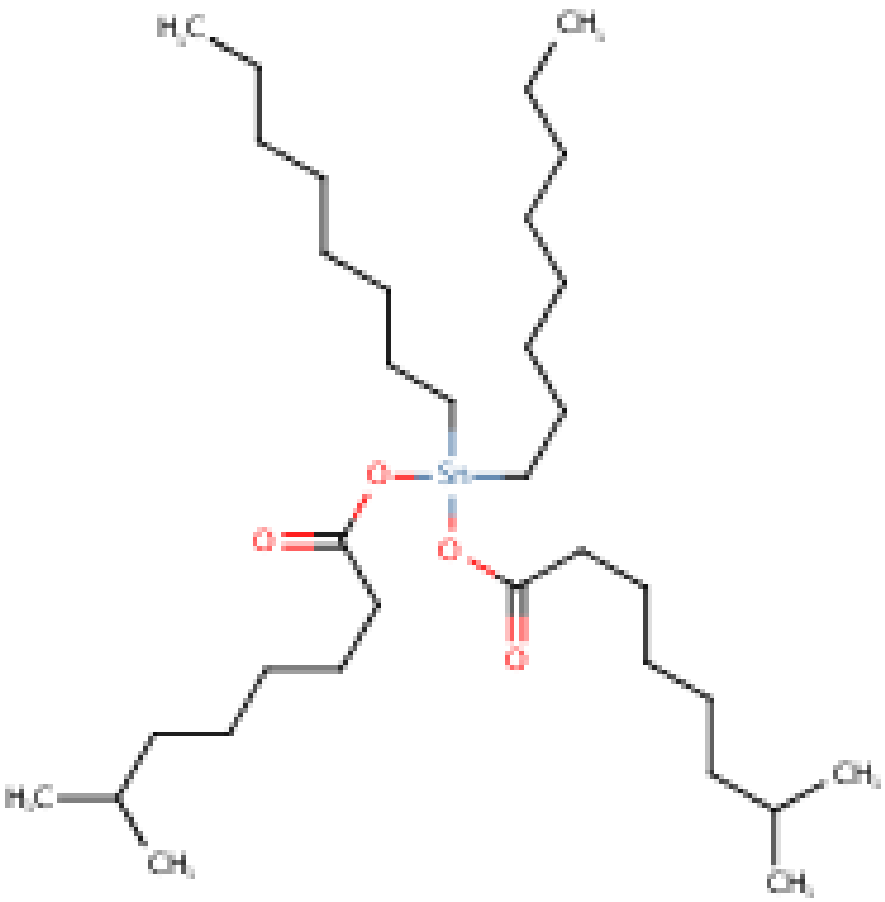
Chemical Name in the Inventory and Synonyms	**Stannane, dioctylbis[(1-oxoneodecyl)oxy]-** dioctyltin dineodecanoate bis(neodecanoyloxy)dioctylstannane
CAS Number	68299-15-0
Structural Formula	
Molecular Formula	C36H72O4Sn
Molecular Weight	687.67

Chemical Name in the Inventory and Synonyms	**Stannane, dioctylbis[(1-oxooctyl)oxy]-, branched**
CAS Number	93686-52-3
Structural Formula	

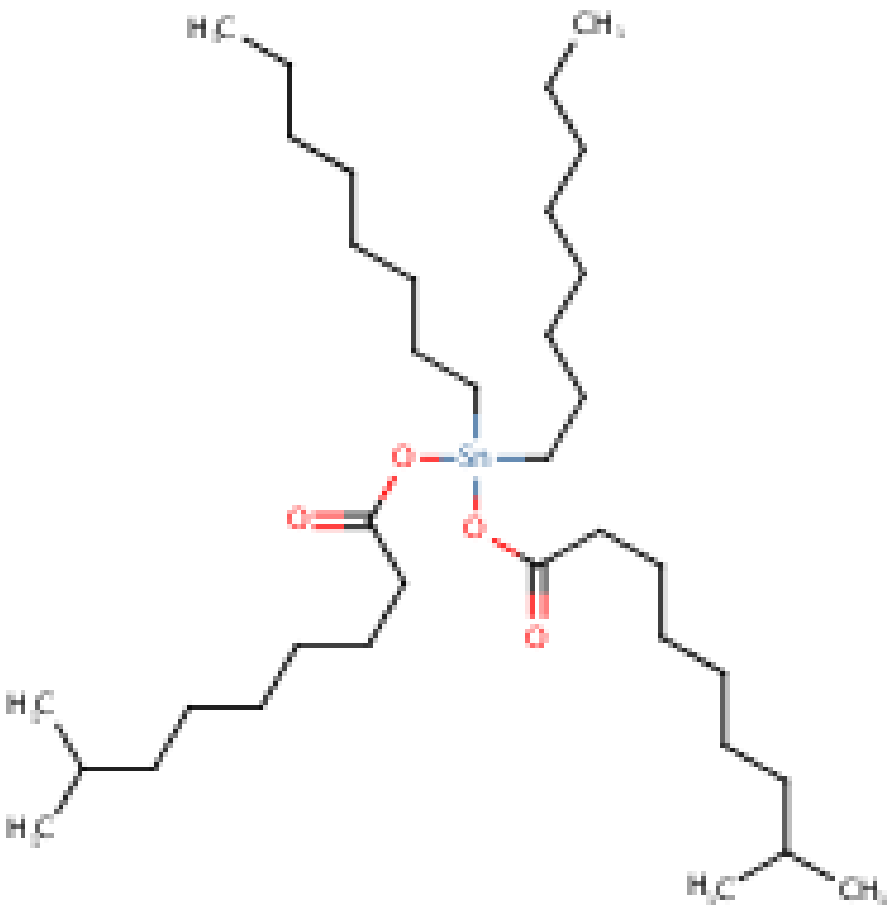
	No Structural Diagram Available
Molecular Formula	Unspecified
Molecular Weight	Unspecified

Chemical Name in the Inventory and Synonyms	**Stannane, dioctylbis[(1-oxoisoundecyl)oxy]-** bis(isoundecanoyloxy)dioctylstannane
CAS Number	93893-97-1
Structural Formula	

Molecular Formula	C38H76O4Sn
Molecular Weight	715.72

Chemical Name in the Inventory and Synonyms	**Stannane, dioctylbis[(1-oxoisononyl)oxy]-** bis(isononanoyloxy)dioctylstannane
CAS Number	93965-21-0
Structural Formula	
Molecular Formula	C34H68O4Sn
Molecular Weight	659.62

Chemical Name in the Inventory and Synonyms	**Stannane, dioctylbis[(1-oxoisodecyl)oxy]-** bis(isodecanoyloxy)dioctylstannane

CAS Number	93965-26-5
Structural Formula	
Molecular Formula	C36H72O4Sn
Molecular Weight	687.67

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