

PROCESS FOR THE PREPARATION OF LIQUID TIN(II) ALKOXIDES

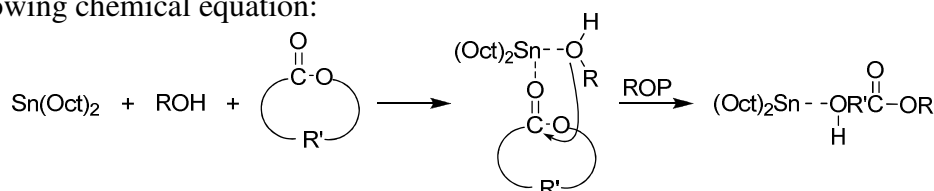
FIELD OF THE INVENTION

This invention is pertaining to organic chemistry focusing on the preparation and spectroscopic characterization of novel liquid tin(II) alkoxides.

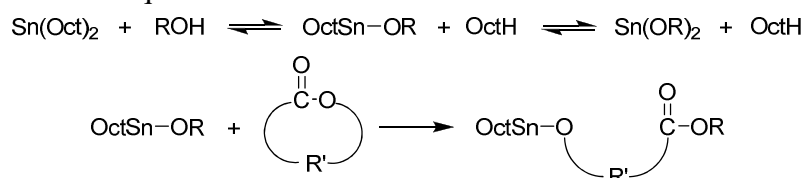
BACKGROUND OF THE INVENTION

Recently, the uses of poly(*l*-lactide), poly(*d*-lactide), poly(*dl*-lactide), poly(ϵ -caprolactone), polyglycolide, and other high molecular weight copolymers in the production of biodegradable containers have increased dramatically due to concerns regarding non-degradable petrochemical products which cause severe environmental problems.

Generally, the synthesis of high molecular weight polyester requires ring-opening polymerization (ROP) of a cyclic ester monomer using tin(II) octoate ($\text{Sn}(\text{Oct})_2$) and an alcohol as the initiating system. There are two proposed mechanisms in this well-known process as suggested by 1) Kricheldorf and co-workers [Hans R. Kricheldorf, I. Kreiser-Saunders, and Caroline Boettcher, *Polymer* 1995, 36, 1253–1259, and Hans R. Kricheldorf, Ingrid Kreiser-Saunders, and Andrea Stricker, *Macromolecules* 2000, 33, 702–709] and 2) Penczek and co-workers [Adam Kowalski, Andrzej Duda, and Stanislaw Penczek, *Macromol. Rapid Commun.* 1998, 19, 567–572; Adam Kowalski, Andrzej Duda, and Stanislaw Penczek, *Macromolecules* 2000, 33, 689–695, and Adam Kowalski, Andrzej Duda, and Stanislaw Penczek, *Macromolecules* 2000, 33, 7359–7370]. Kricheldorf proposed the coordination of $\text{Sn}(\text{Oct})_2$ and the alcohol with the initial cyclic ester following by ring-opening polymerization. The former serves as a catalyst whereas the latter is an initiator, as depicted in the following chemical equation:

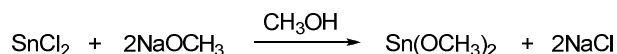


In contrast, Penczek suggested the reaction between $\text{Sn}(\text{Oct})_2$ and the alcohol, resulting in the formation of $\text{Sn}(\text{Oct})(\text{OR})$ and $\text{Sn}(\text{OR})_2$, the true initiators of this reaction as shown in the following chemical equations:

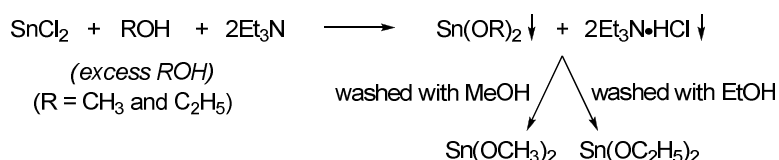


The latter mechanism has been widely accepted as the most reasonable mechanistic pathway. To produce high molecular weight polyesters via ring-opening polymerization, it is extremely important to know the exact concentration of the tin(II) alkoxide initiator which should be highly soluble in the cyclic ester monomer. For these reasons, our research group has been focusing on liquid tin(II) alkoxide derivatives which are soluble in common organic solvents and cyclic ester monomers.

Tin(II) alkoxides were firstly prepared by Amberger and Kula [Eberhard Amberger, Maria-Regina Kula, *Chem. Ber.* 1963, 96, 2562–2565] in 1963, using anhydrous tin(II) chloride to react with sodium methoxide (NaOCH_3) in methanol as shown in the following equation:

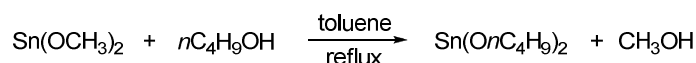


White, hygroscopic solid tin(II) methoxide ($\text{Sn}(\text{OCH}_3)_2$) was obtained from this preparation. Later in 1967, Morrison and Haendler [James S. Morrison and Helmut M. Haendler, *J. Inorg. Nucl. Chem.* 1967, 29, 393–400] developed a more convenient synthetic method using tin(II) chloride dihydrate ($\text{SnCl}_2 \cdot 2\text{H}_2\text{O}$, 6.0 g, 0.032 mol) dried with acetic anhydride ($(\text{CH}_3\text{CO})_2\text{O}$). Dry tin(II) chloride was dissolved in anhydrous methanol (anh. CH_3OH , 200 mL), under a nitrogen atmosphere. A solution of triethylamine (Et_3N) was added slowly until the precipitation was complete. The resulting solution was filtered, washed several times with methanol to remove triethylamine hydrochloride and then washed with diethyl ether. The product was subsequently dried under reduced pressure. The overall chemical equation for this preparation may be represented as:



Tin(II) ethoxide ($\text{Sn}(\text{OCH}_2\text{CH}_3)_2$) can be synthesized in a similar fashion. Tin(II) chloride dihydrate (3.0 g, 0.015 mol) was dissolved in anhydrous ethanol ($\text{CH}_3\text{CH}_2\text{OH}$, 75 mL). The white solid obtained turned yellow rapidly, even when the product was dried and kept under vacuum. Solubility tests showed that both tin(II) methoxide and tin(II) ethoxide dissolved only slightly in several organic solvents.

In 1975, Gsell and Zeldin [Ray Gsell and Martel Zeldin, *J. Inorg. Nucl. Chem.* **1975**, 37, 1133–1137] prepared tin(II) *n*-butoxide ($\text{Sn}(\text{OC}_4\text{H}_9)_2$) via transesterification of tin(II) methoxide. Tin(II) methoxide was refluxed with excess *n*-butanol (*n*- $\text{C}_4\text{H}_9\text{OH}$) in toluene ($\text{C}_6\text{H}_5\text{CH}_3$) until the solution became clear and colorless. Toluene and *n*-butanol were removed until the volume of solution was about 100 mL. The solution was cooled to room temperature and crystalline tin(II) *n*-butoxide was obtained, as shown in the following equation:



The tin(II) *n*-butoxide product was a white solid with a melting point of 171–172 °C and was extremely moisture and oxygen sensitive. As the alkyl chain became longer, such as in changing from CH₃ to C₂H₅, the solubility of the product in organic solvents increased slightly. The physical and chemical properties relating to tin(II) methoxide, tin(II) ethoxide and tin(II) *n*-butoxide are summarized in Table 1, while their ¹H-NMR spectroscopic data are shown in Table 2.

Table 1 Molecular formulae, physical appearances, melting points and solubilities of solid tin(II) alkoxides synthesized by Gsell and Zeldin.

Tin(II) alkoxide	Molecular formula	Physical appearance	m.p. (°C) / Solubility
Tin(II) methoxide	Sn(OCH ₃) ₂	White solid	242–243 °C / slightly dissolves in organic solvents at room temperature but hardly dissolves in polar solvents at high temperature
Tin(II) ethoxide	Sn(OC ₂ H ₅) ₂	White solid	Decomposes at T > 200 °C before the melting point / insoluble in most organic solvents at room temperature but dissolves in polar solvents such as <i>o</i> -dichlorobenzene at high temperature
Tin(II) <i>n</i> -butoxide	Sn(O- <i>n</i> -C ₄ H ₉) ₂	White solid	171–172 °C / partially soluble in organic solvents

Table 2 ^1H -NMR data (220 MHz) of solid tin(II) alkoxides synthesized by Gsell and Zeldin.

Tin(II) alkoxide	Solvent	Temp ($^{\circ}\text{C}$)	Chemical shift (δ , ppm)
Tin(II) methoxide	<i>o</i> -C ₆ H ₄ Cl ₂	75	6.5 (s, br)
	<i>o</i> -C ₆ H ₄ Cl ₂	150	6.48 (s)
Tin(II) ethoxide*	<i>o</i> -C ₆ H ₄ Cl ₂	35	1.17 (t), 1.23 (t), 3.80 (q), 3.99 (q)
	<i>o</i> -C ₆ H ₄ Cl ₂	150	1.20 (t), 3.85 (q) [†]
Tin(II) <i>n</i> -butoxide* ^{‡,§}	C ₆ H ₆	35	0.85 (t) [‡] , 1.30 (h, γ), 1.65 (q, β), 3.80 (t, α)
	<i>o</i> -C ₆ H ₄ Cl ₂	100	0.96 (t, δ) [‡] , 1.45 (h, γ), 1.72 (q, β), 4.09 (t, α) (spectrum shown in the following figure)

Note: * $J = 7$ Hz

[†] The ratio of t/q = 1.5

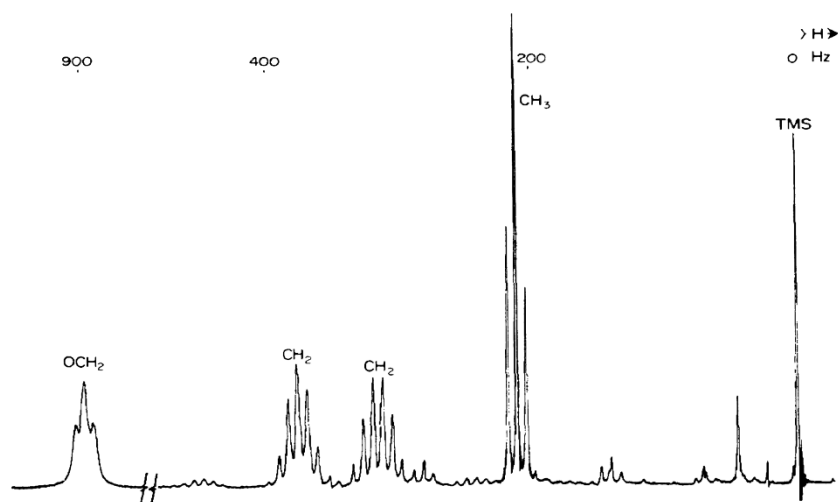
[‡] Recorded on NMR 220 MHz

[§] Proton positions of CH₃-CH₂-CH₂-CH₂- are α , γ , β , and δ respectively

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In accordance with the US Patent 6,414,174 B1 (July 2, 2002), Boyle and co-workers reported the preparation of a tin complex from the hydrolysis of tin(II) *tert*-butylmethoxide in the presence of a basic catalyst. (Sn(N(CH₃)₂)₂)₂ was dissolved in hexane and two mole equivalence of *tert*-butylmethanol ((CH₃)₃CCH₂OH) were added. The reaction mixture was stirred for 24 hours and then warmed for an additional 1 hour. All solvents were removed *in vacuo* and the product washed with hexane and recrystallized from hot tetrahydrofuran

(THF). Tin(II) *tert*-butylmethoxide was obtained as a white solid in its polymeric form of $((\text{Sn}(\text{OCH}_2\text{C}(\text{CH}_3)_3)_2)_n$, which barely dissolved in tetrahydrofuran. Later, Boyle and co-workers carried out the hydrolysis of $(\text{Sn}(\text{OCH}_2\text{C}(\text{CH}_3)_3)_2)_n$ using water in the amounts of 0.50–0.75 and 0.30–0.50 mole equivalence relative to the starting material. The results showed that tin(II) *tert*-butylmethoxide was obtained in the forms of $\text{Sn}_6(\text{O})_4(\text{OCH}_2\text{C}(\text{CH}_3)_3)_4$ and $\text{Sn}_5(\text{O})_2(\text{OCH}_2\text{C}(\text{CH}_3)_3)_6$, respectively.

The major drawback of these tin(II) compounds, such as tin(II) alkoxide $(\text{Sn}(\text{OR})_2)$ where $\text{R} = \text{CH}_3$, C_2H_5 , and $n\text{-C}_4\text{H}_9$, as reported by Morrison and Haendler, and Gsell and co-workers, is their poor solubility in common organic solvents in the temperature range of 25–35 °C. Solubility increases in highly polar solvents and at higher temperatures. Moreover, tin(II) alkoxides synthesized by Morrison and Haendler's procedure using several alcohols such as CH_3OH , $\text{C}_2\text{H}_5\text{OH}$, $n\text{-C}_3\text{H}_7\text{OH}$, $n\text{-C}_4\text{H}_9\text{OH}$, $n\text{-C}_6\text{H}_{13}\text{OH}$, and $n\text{-C}_8\text{H}_{17}\text{OH}$, are all white solids. Solubility test results for these tin(II) alkoxides in general organic solvents are summarized in Table 3. All of the tin(II) alkoxides are insoluble in all ten non-polar aprotic solvents but are slightly soluble in polar solvents when heated.

Table 3 Solubility test results of tin(II) alkoxides in normal organic solvents.

Tin(II) alkoxide	Chloroform/toluene/ <i>n</i> -heptane	Methanol/acetone/ tetrahydrofuran	Dimethyl sulfoxide/ <i>o</i> -dichlorobenzene
$\text{Sn}(\text{OCH}_3)_2$ (solid)	x	x	x
$\text{Sn}(\text{OC}_2\text{H}_5)_2$ (solid)	x	x	x
$\text{Sn}(\text{O}-n\text{-C}_3\text{H}_7)_2$ (solid)	x	x	○
$\text{Sn}(\text{O}-n\text{-C}_4\text{H}_9)_2$ (solid)	x	x	○
$\text{Sn}(\text{O}-n\text{-C}_6\text{H}_{13})_2$ (solid)	x	x	○
$\text{Sn}(\text{O}-n\text{-C}_8\text{H}_{17})_2$ (solid)	x	x	○

Note: Solid tin(II) alkoxides were synthesized by the method reported by Morrison and Haendler.

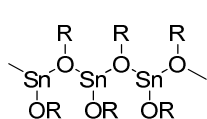
x is insoluble even when heat was applied

○ is slightly soluble upon heating

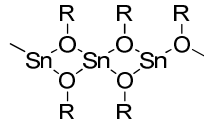
✓ is completely soluble in the temperature range of 25–35 °C

The inventors have tried to synthesize tin(II) alkoxides with R groups of $n\text{-C}_4\text{H}_9$, $n\text{-C}_6\text{H}_{13}$ and $n\text{-C}_8\text{H}_{17}$ using the procedure reported by Gsell and Zeldin but no liquid tin(II) alkoxides could be obtained due to the tendency for self-aggregation of the tin(II) alkoxide molecules, as illustrated in the following figure:

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(a) Linear aggregation



(b) Angular aggregation

The self-aggregation of tin(II) alkoxide molecules makes them insoluble and also inhibits their transesterification with the desired alcohols. Additionally, solid tin(II) alkoxides synthesized by the procedure reported by Morrison and Haendler contain significant amounts of triethylamine hydrochloride. This requires large quantities of alcohol to remove the salt by-product in the washing step, producing unnecessary and unwanted alcohol waste. Only moderate percent yields (~50%) were obtained after the washing step. Due to their low solubility in most organic solvents and cyclic ester monomers, the polymerizations of monomers such as *l*-lactide, *d*-lactide, *dl*-lactide, ϵ -caprolactone and other cyclic esters are relatively slow and ineffective. Furthermore, it is difficult to effectively control the molecular weight of the final polymer product which is also contaminated with some residual solid tin(II) alkoxide initiator.

20 SUMMARY OF THE INVENTION

The main advantage of the liquid tin(II) alkoxides prepared in this invention is that they are soluble in general organic solvents by 1) using anhydrous tin(II) chloride instead of tin(II) chloride dehydrate, 2) using diethylamine as a base or ligand in the 2.0–2.1 mole equivalence of anhydrous tin(II) chloride and 3) using *n*-heptane, which is a non-polar aprotic solvent. *N*-heptane can solvate the molecules of tin(II) alkoxide produced from the reaction and prevent both self-aggregation of the tin(II) alkoxide and aggregation of bridging alcohols with tin(II) alkoxide molecules. Aggregation is the major cause of the relative poor solubility of tin(II) alkoxides in normal organic solvents and cyclic ester monomers.

The primary objective of this synthetic process of liquid tin(II) alkoxides is to prepare a suitable catalyst/initiator for the synthesis of *l*-lactide, *d*-lactide, *dl*-lactide, polylactide, poly(ϵ -caprolactone), polyglycolide, and other co-polyesters. Liquid tin(II) alkoxides can be homogeneously dissolved or mixed with many monomers such as lactide, ϵ -caprolactone, glycolide and other cyclic esters during the melting process. When these tin(II) alkoxides are

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used as initiators in polymerization, it is possible to control the molecular weight of the polymer formed and also obtain high molecular weights. These advantages can be applied to the production of biodegradable polyesters for use in both biomedical and environmental applications.

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BRIEF DESCRIPTION OF DRAWINGS For a fuller understanding of the invention, reference is made to the following description, taken in connection with the accompanying drawings, in which:

Fig. 1 shows the physical appearances of liquid tin(II) alkoxides: (A) tin(II) *n*-butoxide, (B) tin(II) *n*-hexoxide, and (C) tin(II) *n*-octoxide

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Fig. 2 shows the IR spectra (neat) of liquid tin(II) alkoxides: (A) tin(II) *n*-butoxide, (B) tin(II) *n*-hexoxide, and (C) tin(II) *n*-octoxide

Fig. 3 shows the comparison of the ¹H-NMR spectra (400 MHz, CDCl₃, 25 °C) of liquid tin(II) alkoxides: (A) tin(II) *n*-butoxide, (B) tin(II) *n*-hexoxide, and (C) tin(II) *n*-octoxide

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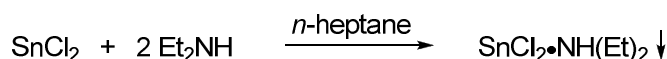
Fig. 4 shows the comparison of the ¹³C-NMR spectra (100 MHz, CDCl₃, 25 °C) of liquid tin(II) alkoxides: (A) tin(II) *n*-butoxide, (B) tin(II) *n*-hexoxide, and (C) tin(II) *n*-octoxide

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

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This invention describes the development of the synthetic process of liquid tin(II) alkoxides which are soluble in organic solvents for the preparation of lactide and polyesters by using anhydrous tin(II) chloride instead of tin(II) chloride dehydrate, 2) changing from triethylamine to diethylamine or other amines such as dimethylamine, diisopropylamine, and trimethyl-amine as a base or ligand to enhance the nucleophilicity on the substitution of chlorine atoms, resulting in the formation of SnCl₂•HNEt₂ in high yield, as shown in the following equation:

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This also allows the alcohol to react with the tin atom of SnCl₂•HNEt₂ better than that of SnCl₂•NEt₃. Finally, 3) by using one of the following nonpolar aprotic solvents: *n*-heptane, *n*-hexane, cyclohexane, benzene, toluene, xylene, and tetrahydrofuran instead of an excess of a polar, protic solvent such as an alcohol., the nonpolar aprotic solvent molecules can surround the molecules of tin(II) alkoxide, thereby preventing their self-aggregation. If excess alcohol is used, it can result in the formation of tin(II) alkoxide with bridging alcohol molecules leading to the poor solubility of tin(II) alkoxide in most common organic solvents. Moreover,

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the use of nonpolar aprotic solvents causes the precipitation of $\text{Et}_2\text{NH}\cdot\text{HCl}$ from the soluble tin(II) alkoxide so that purification of tin(II) alkoxide prior to use is not necessary.

The objective of the synthetic process of liquid tin(II) alkoxides is to obtain products which can act as catalysts in the synthesis of lactides such as *l*-lactide, *d*-lactide, and *dl*-lactide and as initiators in the synthesis of polyesters from cyclic esters such as polylactide, poly-(ϵ -caprolactone), polyglycolide, and co-polyesters. This procedure is the first successful process to produce liquid tin(II) alkoxides with no such procedure having yet been reported in the literature. All three tin(II) alkoxides: tin(II) *n*-butoxide ($\text{Sn}(\text{O}-n\text{-C}_4\text{H}_9)_2$), tin(II) *n*-hexoxide ($\text{Sn}(\text{O}-n\text{-C}_6\text{H}_{13})_2$), and tin(II) *n*-octoxide ($\text{Sn}(\text{O}-n\text{-C}_8\text{H}_{17})_2$), which were synthesized from this process, are viscous, dark yellow liquids. They could be mixtures of monomer, dimer, trimer, and/or oligomers that are still soluble in common organic solvents in the temperature range of 25–38 °C. They can be stored under a nitrogen or argon atmosphere without any significant effect on their reactivity. Moreover, the products from this process do not require any further purification and can be used either as a catalyst or initiator in the solution phase.

The synthetic process of liquid tin(II) alkoxides in this invention is composed of several important steps which are 1) the use of anhydrous tin(II) chloride instead of tin(II) chloride dihydrate, 2) the use of dimethylamine, diisopropylamine, trimethylamine or triethylamine in the 2.0–2.1 mole equivalence of anhydrous tin(II) chloride to enhance the nucleophilicity or ligand ability in the substitutions of chloride compared to the use of triethylamine, resulting in the formation of $\text{SnCl}_2\cdot\text{HNEt}_2$ in high yield and giving a better reaction between the alcohol molecule and the tin atom of $\text{SnCl}_2\cdot\text{HNEt}_2$ than that of $\text{SnCl}_2\cdot\text{NEt}_3$, and most importantly, 3) the use of one of the suggested nonpolar aprotic solvents such as *n*-heptane, *n*-hexane, cyclohexane, benzene, toluene, xylene, and tetrahydrofuran instead of polar protic solvents such as alcohols to inhibit the formation of tin(II) alkoxide self-aggregates. Moreover, nonpolar aprotic solvent also allow for the precipitation and therefore easy separation of $\text{Et}_2\text{NH}\cdot\text{HCl}$ from the tin(II) alkoxide in solution. Thus, no further purification of tin(II) alkoxide is required; 4) the amount of alcohol used in this process is about 2.0–2.1 mole equivalence of the anhydrous tin(II) chloride to reduce the aggregation of tin(II) alkoxide in the presence of excess alcohol.

Examples 1 for chemicals used in process for the preparation of liquid tin(II) alkoxides ($\text{Sn}(\text{OR})_2$) are:

1. Anhydrous tin(II) chloride, purity > 98%, purchased from Aldrich. Molecular weight = 189.62 g/mol, boiling point = 652 °C, and melting point = 246 °C

2. Diethylamine ((C₂H₅)₂NH). Molecular weight = 73.14 g/mol, boiling point = 55 °C, melting point = -50 °C, density = 0.707 g/mL (25 °C). Must be purified by refluxing with sodium (Na) or calcium hydride (CaH₂) for 1 hour and distilled prior to use. Dry diethylamine is kept under nitrogen or argon, or kept in a container with molecular sieves.

5 3. *N*-butanol (*n*-C₄H₉OH). Molecular weight = 74.12 g/mol, boiling point = 116–118 °C, melting point = -90 °C, density = 0.81 g/mL (25 °C). Must be purified by refluxing with sodium (Na) for 1 hour and distilled prior to use. Dry *n*-butanol is kept under nitrogen or argon, or kept in a container with molecular sieves.

10 4. *N*-hexanol (*n*-C₆H₁₃OH). Molecular weight = 102.17 g/mol, boiling point = 156–157 °C, melting point = -52 °C, density = 0.814 g/mL (25 °C). Must be purified by refluxing with sodium (Na) for 1 hour and distilled prior to use. Dry *n*-hexanol is kept under nitrogen or argon, or kept in a container with molecular sieves.

15 5. *N*-octanol (*n*-C₈H₁₇OH). Molecular weight = 130.23 g/mol, boiling point = 196 °C, melting point = -15 °C, density = 0.827 g/mL (25 °C). Must be purified by refluxing with sodium (Na) for 1 hour and distilled prior to use. Dry *n*-octanol is kept under nitrogen or argon, or kept in a container with molecular sieve.

20 6. *N*-heptane (*n*-C₇H₁₆). Molecular weight = 100.20 g/mol, boiling point = 98 °C, melting point = -91 °C, density = 0.684 g/mL (25 °C). Must be purified by refluxing with sodium (Na) for 1 hour and distilled prior to use. Dry *n*-heptane is kept under nitrogen or argon, or kept in a container with molecular sieves.

To fully understand this invention, the following further details are given:

Example 2 for the preparation of liquid tin(II) *n*-butoxide (Sn(O-*n*-C₄H₉)₂)

25 1. A three-necked round bottom flask is equipped with a magnetic bar, an oven-dried gas-inlet, and a dropping funnel. It is placed on a magnetic stirrer. A gas-inlet is connected to a volumetric gauge-controlled nitrogen or argon source via a plastic tube.

2. Anhydrous tin(II) chloride 4.84 g (25.01 mmol) is added to the reaction flask.

3. Dry *n*-heptane (ca.100 mL) is added into the reaction vessel at the temperature range of 25–38 °C. The mixture was well-stirred for 30–60 minutes.

30 4. Dry diethylamine (5.43 mL, 52.53 mmol) is then added into the reaction vessel in the temperature range of 15–20 °C. The reaction mixture is stirred for 3–6 hours.

5. Solution of dry *n*-butanol 4.81 mL (52.53 mmol) in dry *n*-heptane (ca. 50 mL) was added to the reaction mixture in the temperature range of 25–38 °C. The resulting solution is stirred for another 12 hours.

6. The reaction mixture is filtered under nitrogen or argon, and the solid residue is thoroughly washed with dry *n*-heptane (100–200 mL).

7. The filtrate is concentrated and evaporated to dryness on a rotary evaporator.

8. The residue of tin(II) *n*-butoxide is further dried using a high vacuum pump for
5 another 3–6 hours.

9. Tin(II) *n*-butoxide is obtained as viscous, dark yellow liquid, in 4.89 g, 73.79 % yield.

Example 3 for the preparation of liquid tin(II) *n*-hexoxide (Sn(O-*n*-C₆H₁₃)₂)

1. A three-necked round bottom flask is equipped with a magnetic bar, an oven-dried gas-inlet, and a dropping funnel. It is placed on a magnetic stirrer. A gas-inlet is connected
10 to a volumetric gauge-controlled nitrogen or argon source via a plastic tube.

2. Anhydrous tin(II) chloride 4.84 g (25.01 mmol) is added to the reaction flask.

3. Dry *n*-heptane (ca.100 mL) is added into the reaction vessel at the temperature range of 25–38 °C. The mixture was well-stirred for 30–60 minutes.

4. Dry diethylamine (5.43 mL, 52.53 mmol) is then added into the reaction vessel in the
15 temperature range of 15–20 °C. The reaction mixture is stirred for 3–6 hours.

5. Solution of dry *n*-hexanol 6.59 mL (52.53 mmol) in dry *n*-heptane (ca. 50 mL) was added to the reaction mixture in the temperature range of 25–38 °C. The resulting solution is stirred for another 12 hours.

6. The reaction mixture is filtered under nitrogen or argon, and the solid residue is
20 thoroughly washed with dry *n*-heptane (100–200 mL).

7. The filtrate is concentrated and evaporated to dryness on a rotary evaporator.

8. The residue of tin(II) *n*-hexoxide is further dried using a high vacuum pump for another 3–6 hours.

9. Tin(II) *n*-hexoxide is obtained as viscous, dark yellow liquid, in 6.97 g, 86.73 %
25 yield.

Example 4 for the preparation of liquid tin(II) *n*-octoxide (Sn(O-*n*-C₈H₁₇)₂)

1. A three-necked round bottom flask is equipped with a magnetic bar, an oven-dried gas-inlet, and a dropping funnel. It is placed on a magnetic stirrer. A gas-inlet is connected
30 to a volumetric gauge-controlled nitrogen or argon source via a plastic tube.

2. Anhydrous tin(II) chloride 4.84 g (25.01 mmol) is added to the reaction flask.

3. Dry *n*-heptane (ca.100 mL) is added into the reaction vessel at the temperature range of 25–38 °C. The mixture was well-stirred for 30–60 minutes.

4. Dry diethylamine (5.43 mL, 52.53 mmol) is then added into the reaction vessel in the temperature range of 15–20 °C. The reaction mixture is stirred for 3–6 hours.

5. Solution of dry *n*-octanol 8.27 mL (52.53 mmol) in dry *n*-heptane (ca. 50 mL) was added to the reaction mixture in the temperature range of 25–38 °C. The resulting solution is stirred for another 12 hours.

6. The reaction mixture is filtered under nitrogen or argon, and the solid residue is thoroughly washed with dry *n*-heptane (100–200 mL).

7. The filtrate is concentrated and evaporated to dryness on a rotary evaporator.

8. The residue of tin(II) *n*-octoxide is further dried using a high vacuum pump for another 3–6 hours.

9. Tin(II) *n*-octoxide is obtained as viscous, dark yellow liquid, in 7.00 g, 74.18 % yield.

Products from the syntheses of liquid tin(II) alkoxides, their molecular formula, physical appearances, percentage yields and solubilities are summarized in Figure 1 and Table 4–5.

Table 4 Molecular formula, physical appearances, and percentage yields of tin(II) alkoxides.

Tin(II) alkoxide	Molecular formula	Physical appearances	Percent yield
Tin(II) <i>n</i> -butoxide	Sn(O- <i>n</i> -C ₄ H ₉) ₂	Viscous, dark yellow liquid	73.79
Tin(II) <i>n</i> -hexoxide	Sn(O- <i>n</i> -C ₆ H ₁₃) ₂	Viscous, dark yellow liquid	86.73
Tin(II) <i>n</i> -octoxide	Sn(O- <i>n</i> -C ₈ H ₁₇) ₂	Viscous, dark yellow liquid	74.18

Table 5 Solubilities of liquid tin(II) alkoxides in various organic solvents.

Tin(II) alkoxide	Chloroform/toluene/ <i>n</i> -heptane	Methanol/acetone/ tetrahydrofuran	Dimethyl sulfoxide/ <i>o</i> -dichlorobenzene
Tin(II) <i>n</i> -butoxide	✓	x	x
Tin(II) <i>n</i> -hexoxide	✓	x	x
Tin(II) <i>n</i> -octoxide	✓	x	x

Note: x is insoluble even when heated.

✓ is soluble at room temperature.

IR characterization data of the liquid tin(II) alkoxides synthesized as described in the invention compared with that of solid tin(II) alkoxides are shown in Figure 2 and Table 6.

Table 6 IR characterization data of liquid tin(II) alkoxides and their respective solid forms.

Assignment	Wavenumber (ν , cm^{-1})					
	$\text{Sn}(\text{O}-n\text{-C}_4\text{H}_9)_2$		$\text{Sn}(\text{O}-n\text{-C}_6\text{H}_{13})_2$		$\text{Sn}(\text{O}-n\text{-C}_8\text{H}_{17})_2$	
	Solid*	Liquid	Solid*	Liquid	Solid*	Liquid
CH_3	2911 (w)	2956 (s) 2862 (s)	2911 (w)	2950 (s)	2911 (w)	2953 (s)
CH_2		2922 (s) 2851 (s)		2925 (s) 2858 (s)		2922 (s) 2851 (s)
CH_3 (def)		1369 (m)	1377 (w)	1378 (m)	1377 (w)	1373 (m)
CH_2 (def)		1455 (m)		1455 (m)		1455 (m)
C-O (stretch)	1014 (w)	1067 (m) 1039 (m)	1007 (w)	1052 (m) 1025 (m)	1007 (w)	1049 (m) 1014 (m)
Sn-O-Sn (stretch)		740 (w)		740 (w)		740 (w)
Sn-O (stretch)	541 (s)	573 (br s) 512 (br s)	541 (s)	505 (br m)	541 (s)	581 (br m) 528 (br m)

Note:* Solid tin(II) alkoxides were synthesized by the method reported by Morrison and Haendler.

5 def = deformation; s = strong; m = medium; br = broad; w = weak

Molecular weights of liquid tin(II) alkoxide analyzed by GC-MS and LC-MS techniques are tabulated in Table 7.

Table 7 Molecular ions of liquid tin(II) alkoxides from GC-MS and LC-MS techniques.

Tin(II) alkoxide	Found molecular ion (m/z)	Structure of found molecular ion	
Sn(O- <i>n</i> -C ₄ H ₉) ₂ (MW = 264)	264 [†]	M ⁺	= [Sn(OnC ₄ H ₉) ₂] ⁺
	265 [‡]	[M + H] ⁺	= [Sn(OnC ₄ H ₉) ₂ + H] ⁺
	287 [‡]	[M + Na] ⁺	= [Sn(OnC ₄ H ₉) ₂ + Na] ⁺
Sn(O- <i>n</i> -C ₆ H ₁₃) ₂ (MW = 320)	320 [†]	M ⁺	= [Sn(OnC ₆ H ₁₃) ₂] ⁺
	321	[M + H] ⁺	= [Sn(OnC ₆ H ₁₃) ₂ + H] ⁺
	343 ^{‡‡}	[M + Na] ⁺	= [Sn(OnC ₆ H ₁₃) ₂ + Na] ⁺
Sn(O- <i>n</i> -C ₈ H ₁₇) ₂ (MW = 376)	376 [†]	M ⁺	= [Sn(OnC ₈ H ₁₇) ₂] ⁺
	377 [‡]	[M + H] ⁺	= [Sn(OnC ₈ H ₁₇) ₂ + H] ⁺
	399 [‡]	[M + Na] ⁺	= [Sn(OnC ₈ H ₁₇) ₂ + Na] ⁺

Note: [†] is molecular ion from GC-MS.

[‡] is molecular ion from LC-MS.

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¹H-NMR characterization data are shown in Figure 3 and Table 8, while the ¹³C-NMR characterization data are summarized in Figure 4 and Table 9.

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Table 8 ^1H -NMR data of liquid tin(II) alkoxides (400 MHz, CDCl_3 , 25 °C).

Sn(OCH ₂ CH ₂ CH ₂ CH ₃) ₂				Sn(OCH ₂ CH ₂ CH ₂ CH ₂ CH ₂ CH ₃) ₂						Sn(OCH ₂ CH ₂ CH ₂ CH ₂ CH ₂ CH ₂ CH ₂ CH ₃) ₂							
1'	2'	3	4	1'	2'	3	4	5	6	1'	2'	3	4	5	6	7	8
1"	2"			1"	2"					1"	2"						
Type of proton	Chemical shift (δ, ppm)																
	Sn(O- <i>n</i> -C ₄ H ₉) ₂				Sn(O- <i>n</i> -C ₆ H ₁₃) ₂						Sn(O- <i>n</i> -C ₈ H ₁₇) ₂						
H-8	-				-						0.89 (t, <i>J</i> = 7.1 Hz)						
H-7	-				-						1.18–1.41 (br m)						
H-6	-				0.89 (t, <i>J</i> = 6.9 Hz)												
H-5	-				1.17–1.48 (br m)												
H-4	0.92 (t, <i>J</i> = 7.3 Hz)																
	0.93 (t, <i>J</i> = 7.3 Hz)																
H-3	1.27–1.47 (m)																
H-2''	1.48–1.60 (m)				1.48–1.61 (m)						1.50–1.61 (m)						
H-2'	1.60–1.74 (m)				1.61–1.80 (br m)						1.61–1.75 (m)						
H-1''	3.64 (br t)				3.63 (br t, <i>J</i> = 6.2 Hz)						3.63 (br t, <i>J</i> = 6.2 Hz)						
H-1'	3.80 (t, <i>J</i> = 6.7 Hz)				3.80 (t, <i>J</i> = 6.7 Hz)						3.80 (t, <i>J</i> = 6.7 Hz)						
	3.87 (t, <i>J</i> = 7.1 Hz)				3.83 (t, <i>J</i> = 7.1 Hz)						3.83 (t, <i>J</i> = 7.1 Hz)						

Note: t = triplet, m = multiplet, br = broad

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Table 9 ^{13}C -NMR data of liquid tin(II) alkoxides (100 MHz, CDCl_3 , 25 °C).

Sn(OCH ₂ CH ₂ CH ₂ CH ₃) ₂				Sn(OCH ₂ CH ₂ CH ₂ CH ₂ CH ₂ CH ₃) ₂						Sn(OCH ₂ CH ₂ CH ₂ CH ₂ CH ₂ CH ₂ CH ₃) ₂							
1'	2'	3	4	1'	2'	3	4	5	6	1'	2'	3	4	5	6	7	8
1"	2"			1"	2"					1"	2"						
Type of carbon	Chemical shift (δ, ppm)																
	Sn(O- <i>n</i> -C ₄ H ₉) ₂				Sn(O- <i>n</i> -C ₆ H ₁₃) ₂					Sn(O- <i>n</i> -C ₈ H ₁₇) ₂							
C-8	-				-					14.0							
C-7	-				-					22.6							
C-6	-				14.0					25.6 (w), 25.7							
C-5	-				22.6, 22.5 (w)					29.2, 29.1 (w)							
C-4	13.9, 13.8				25.6 (w), 25.4					29.4, 29.3 (w)							
C-3	19.1, 18.9				31.6, 31.5(w)					31.8, 31.8 (w)							
C-2',2"	36.8, 34.8				34.7 (w), 32.8					34.7 (w), 32.7							
C-1',1"	64.3, 62.7				64.6 (w), 63.1					64.5 (w), 62.8							

Note: w = weak

In conclusion, the synthetic process for producing liquid tin(II) *n*-butoxide, tin(II) *n*-hexoxide, and tin(II) *n*-octoxide can be successfully accomplished via the following important steps: 1) enough diethylamine in 2 or 3 mole equivalence of anhydrous tin(II) chloride to act as a base or ligand in the formation of $\text{SnCl}_2 \cdot \text{HNEt}_2$ in high yield, and 2) the use of nonpolar aprotic solvents such as *n*-heptane instead of alcohols such as methanol and ethanol. Molecules of *n*-heptane can solvate the tin(II) alkoxide, thereby preventing its self-aggregation during the reaction. Another important advantage of using nonpolar aprotic solvent systems is that they facilitate the precipitation and separation of the $\text{Et}_2\text{NH} \cdot \text{HCl}$ by-product from the soluble tin(II) alkoxide. Therefore, no further purification of the tin(II) alkoxide is required prior to its use as either a catalyst or initiator. Finally, 3) the use of a suitable amount of alcohol of about 2–3 mole equivalence of the anhydrous tin(II) chloride can reduce the aggregation between the tin(II) alkoxide and the bridging alcohol. Tin(II) alkoxides produced from this process are viscous, dark yellow liquids, soluble in common organic solvents at room temperature, and can be stored for a long time under nitrogen or argon without any significant change in their reactivity. In addition, the products from the process can be used either as a catalyst or an initiator without any extra purification and can be used either neat or in solution form.

Claim

1. Process for the preparation of liquid tin(II) alkoxides consists of the use of base or ligand in 2–3 mole equivalence of anhydrous tin(II) chloride in nonpolar, aprotic solvents. The solvent surrounds the newly formed tin(II) alkoxide molecules from the reaction and thus prevents their unwanted self-aggregation and also the possible multi-aggregation between the bridging alcohol and tin(II) alkoxide molecules when excess anhydrous alcohol is used, typically in 2-3 mole equivalence of the anhydrous tin(II) chloride.
2. Process for the preparation of liquid tin(II) alkoxides, as described in Claim 1, can use a base or ligand from any of: dimethylamine, diethylamine, diisopropylamine, trimethylamine, and triethylamine.
3. Process for the preparation of liquid tin(II) alkoxides, as described in Claim 1, shows that the most suitable base or ligand is diethylamine.
4. Process for the preparation of liquid tin(II) alkoxides, as described in Claim 1, can use a nonpolar, aprotic solvent from any of: *n*-heptane, *n*-hexane, cyclohexane, benzene, toluene, xylene, and tetrahydrofuran.
5. Process for the preparation of liquid tin(II) alkoxides, as described in Claim 1, shows that the most suitable nonpolar, aprotic solvent is *n*-heptane.
6. Process for the preparation of liquid tin(II) alkoxides, as described in Claim 1, also includes the following appropriate steps:
 - a. Anhydrous tin(II) chloride is dissolved in dry *n*-heptane under a nitrogen or argon atmosphere.
 - b. Dry diethylamine is added into the reaction mixture of anhydrous tin(II) chloride in dry *n*-heptane.
 - c. The mixture is well-stirred under a nitrogen or argon atmosphere.
 - d. Alcohol (ROH), where R = CH₃, C₂H₅, *n*-C₃H₇, *n*-C₄H₉, *n*-C₅H₁₁, *n*-C₆H₁₃, *n*-C₇H₁₅, and *n*-C₈H₁₇, is added to the reaction mixture of anhydrous tin(II) chloride and dry diethylamine in dry *n*-heptane in the temperature range of 25–38 °C under a nitrogen or argon atmosphere.
 - e. The reaction mixture is stirred for 12 hours under a nitrogen or argon atmosphere.
 - f. The reaction mixture is filtered under a nitrogen or argon atmosphere.
 - g. The solid residue is washed with dry *n*-heptane.
 - h. The combined organic layer is evaporated to dryness.

7. Process for the preparation of liquid tin(II) alkoxides, as described in Claim 1 or 4, also includes the following best procedure:

a. Anhydrous tin(II) chloride is dissolved in dry *n*-heptane in the temperature range of 25–38 °C. The solution is stirred for 30-60 minutes under a nitrogen or argon atmosphere.

b. Dry diethylamine in 2 or 3 mole equivalence of anhydrous tin(II) chloride is added into the reaction vessel in the temperature range of 15 – 20 °C. The resulting solution is stirred for 36 hours under a nitrogen or argon atmosphere.

c. Dry alcohol (where R = *n*-C₄H₉, *n*-C₆H₁₃, *n*-C₈H₁₇) in 2 or 3 mole equivalence of anhydrous tin(II) chloride is added under nitrogen or argon. The temperature is controlled in the range of 25–38 °C.

d. The reaction mixture is stirred for 12 hours under a nitrogen or argon atmosphere.

e. The reaction mixture is filtered under nitrogen or argon.

f. The solid residue is washed with dry *n*-heptane (100–150 mL)

g. The combined organic phase is evaporated to dryness and nitrogen or argon is purged into the evaporation flask before removing from an evaporator.

8. Liquid tin(II) alkoxides, as obtained from one of the Claim 1-5, are viscous, dark yellow liquids. They are soluble in common organic solvents. The general molecular formula of these compounds is Sn(OR)₂ where R is CH₃, C₂H₅, *n*-C₃H₇, *n*-C₄H₉, *n*-C₅H₁₁, *n*-C₆H₁₃, *n*-C₇H₁₅, and *n*-C₈H₁₇.