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Synthesis, structural characterization, and antibacterial activity of tricyclohexyltin aryloxyacetates

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Abstract: Three tricyclohexyltin aryloxyacetates, *p*-$YC_6H_4OCH_2COOSn(C_6H_{11}\text{-}c)_3$ (where Y=H, **1**; CHO, **2**; CH_2OH, **3**), have been synthesized and characterized by means of elemental analysis, IR, and NMR (^1H, ^{13}C, and ^{119}Sn) spectroscopy. The crystal structures of complexes **1** and **3** are determined by X-ray single-crystal diffraction. The carboxylate in the compounds is monodentate. The tin atom of compound **1** adopts distorted tetrahedral coordination geometry. In the crystal lattice of compound **3**, there is a four-coordinated tin and a five-coordinated tin in which the fifth coordination site is occupied by a water molecule, and the molecules are linked by $R_3^3(30)$ and $R_5^5(28)$ hydrogen bonds into a two-dimensional supramolecular network. Bioassay results have shown that the compounds have good *in vitro* antibacterial activity against *Escherichia coli*.

Keywords: antibacterial activity; aryloxyacetic acid; crystal structure; organotin; organotin carboxylate.

Introduction

Organotin carboxylates have been widely researched because of their novel structures and various applications in the last few decades (Tiekink, 1991, 1994; Davies et al., 2008). Many organotin carboxylates display good activities against tumors, fungi, bacteria, and other microorganisms (Davies et al., 2008; Hadjikakou and Hadjiliadis, 2009; Shang et al., 2011; Amir et al., 2014; Carraher and Roner, 2014; Wang et al., 2014; Mao et al., 2015). The organotin moiety and ligands appear to play an important role in determining their biological activity (Davies et al., 2008; Hadjikakou and Hadjiliadis, 2009; Amir et al., 2014). In general, the toxicity of organotin compounds seems to increase with the chain length of the organic alkyl groups, which are often more active than aryl ones. To design new active tin compounds, it is necessary to balance some factors such as solubility and lipophilicity to achieve efficacy (Hadjikakou and Hadjiliadis, 2009; Arjmand et al., 2014).

Aryloxyacetic acid derivatives possess a wide array of diverse bioactivities such as antimicrobacterial, anti-inflammatory, antibacterial, analgesic, antisickling, antipaemic, antiplatelet, non-prostanoid prostacyclin mimetic, diuretic, and growth regulators (Fracchiolla et al., 2007; Bala et al., 2010; Kumar et al., 2013). The synthesis, structure, and property of some organotin complexes with ligands have been reported, such as dibutyltin bis(2-naphthoxyacetate) (Ma et al., 2004), tris(2-methyl-2-phenylpropyl)tin phenoxyacetate (Bao et al., 1998), tributyltin 2,4-dichlorophenoxyacetate (Yu et al., 2010), and triphenyltin 8-quinolyloxyacetate (Das et al., 1987). To continue to increase the chemistry and therapeutic potential of the organotin complexes of aryloxyacetic acids, we select phenoxyacetic acid with polar substituent groups as ligands (Scheme 1) and synthesized three new tricyclohexyltin complexes, *p*-$YC_6H_4OCH_2COOSn(C_6H_{11}\text{-}c)_3$ (where Y=H, CHO, and CH_2OH), and determined their *in vitro* antibacterial activity.

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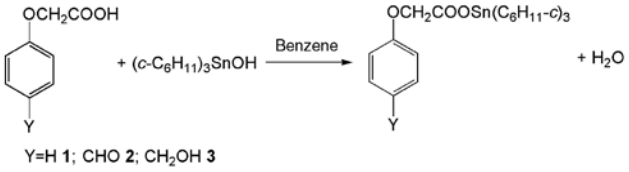
Results and discussion

Synthesis

The reaction of tricyclohexyltin hydroxide with phenoxyacetic acid or *p*-substituted phenoxyacetic acid in a 1:1 molar ratio in anhydrous benzene afforded products **1–3**, with a yield of 65–81% (Scheme 2).

Scheme 1: The structure of the ligand.



Scheme 2: Synthesis of compounds **1–3**.

These compounds are white crystals, air stable, and soluble in benzene and in common polar organic solvents such as methanol, ethanol, dichloromethane, chloroform, acetone, and *N*,*N*-dimethylformamide, but insoluble in water and saturated hydrocarbons such as hexane and petroleum ether.

Spectroscopic analysis

In the IR spectra of compounds **1–3**, the bands at ~3450 and ~1760 cm^{-1} assigned to ν (O-H) and ν (C=O), respectively, of free aryloxyacetic acid do not appear, and new strong bands at ~1660 and ~1350 cm^{-1} are assigned to the asymmetrical, $\nu_{as}(CO_2^-)$, and symmetrical stretching vibrations, $\nu_s(CO_2^-)$, of the aryloxyacetate, respectively. The difference between the $\nu_{as}(CO_2^-)$ and the $\nu_s(CO_2^-)$ bands, $\Delta\nu(CO_2^-)$, is 313 cm^{-1} for **1**, 272 cm^{-1} for **2**, and 331 cm^{-1} for **3**, which is larger than 200 cm^{-1}, suggesting that the carboxylate group is coordinated to tin in the monodentate mode in the solid state (Deacon and Phillips, 1980; Li et al., 2010).

In ^{1}H NMR spectra of **1–3**, the single resonances of COOH in the spectra of the free ligands are not observed at ~12 ppm, which further confirms the replacement of the carboxylic acid protons by the tricyclohexyltin moiety on complex formation. The complexes show multiplets in the range of 1.17–1.97 ppm due to the cyclohexyl protons and singlets at 4.43–4.71 ppm assigned to the OCH_2 protons. The resonances in the range between 6.76 and 7.82 ppm are assigned to the aryl protons.

The ^{13}C chemical shifts of the carboxyl and methylene carbon atoms in **1–3** appear at 172.21–173.36 and 65.56–66.41 ppm, respectively. The signals of the cyclohexyl carbon atoms are in the range of 26.97–36.49 ppm, and the $^1J(^{119}Sn\text{-}^{13}C)$, $^2J(^{119}Sn\text{-}^{13}C)$, and $^3J(^{119}Sn\text{-}^{13}C)$ coupling constants are ~330, 20, and 60 Hz, respectively. The coordination number of the tin atom in the organotin compounds has been related to the $^1J(^{119}Sn\text{-}^{13}C)$ coupling constants (Nadvornik et al., 1984). The $^1J(^{119}Sn\text{-}^{13}C)$ coupling of the compounds is close to that of other four-coordinate tricyclohexyltin carboxylates, such as 2-$HOC_6H_4N{=}NC_6H_4COOSn(C_6H_{11}\text{-}c)_3$ (335 Hz) (Willem et al., 1998), $C_4H_3SCOOSn(C_6H_{11}\text{-}c)_3$ (333 Hz) (Abbas et al., 2013), $(c\text{-}C_6H_{11})_3SnO_2CCH_2CH_2COCH_2CH_2CO_2Sn(C_6H_{11}\text{-}c)_3$ (325 Hz) (Chalupa et al., 2006), and (2-$C_6H_5C_2HN_3$)$COOSn(C_6H_{11}\text{-}c)_3$ (330 Hz) (Tian et al., 2015). Data suggest that the tin atom in these compounds is four-coordinated in $CDCl_3$ solution.

The ^{119}Sn chemical shifts primarily depend on the coordination number and the nature of the donor atom directly bonded to the central tin atom (Davis, 2004). The ^{119}Sn chemical shifts of **1–3** (30.0–33.0 ppm) are in accord with the values of the four-coordinated tricyclohexyltin carboxyl ester in the solution of the non-coordinating solvent (Tian et al., 2005, 2015; Chalupa et al., 2006).

Structure analysis of 1 and 3

The structures of complexes **1** and **3** are shown in Figures 1–3, and the selected geometric parameters are given in Table 1. Compound **1** crystallizes with two independent molecules in the crystallographic asymmetric unit that do not differ from each other significantly. The coordination geometry of the tin atom is a distorted tetrahedron shaped by three carbon atoms from the cyclohexyl groups and one carboxyl O atom [O(1) and O(4)] from the carboxylate ligand. The separation between the other O atom of the carboxylate ligand and Sn atom is Sn(1)···O(2) 3.017(4) Å and Sn(2)···O(5) 2.994(4) Å. The weak interaction distorts the tetrahedral geometry by opening up the

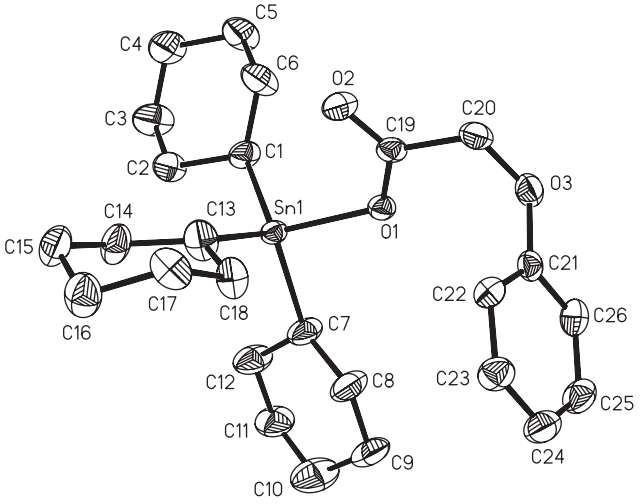


Figure 1: The molecular structure of **1**. Hydrogen atoms are omitted for clarity.

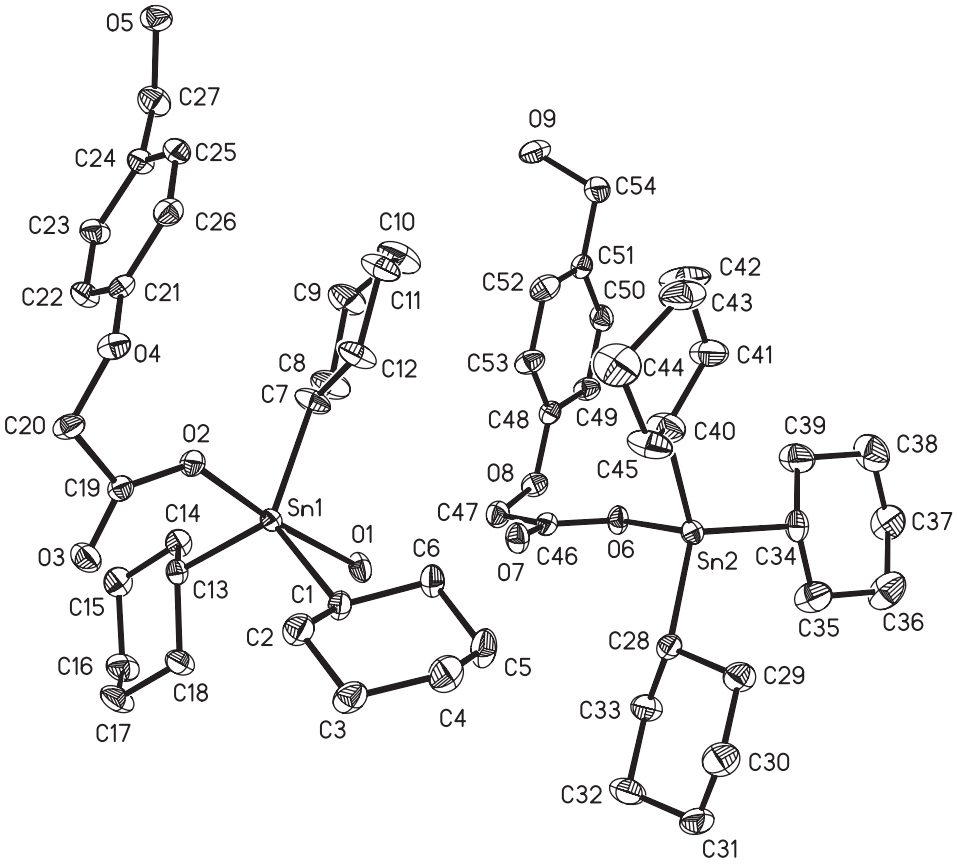


Figure 2: The molecular structure of **3**.
Hydrogen atoms are omitted for clarity.

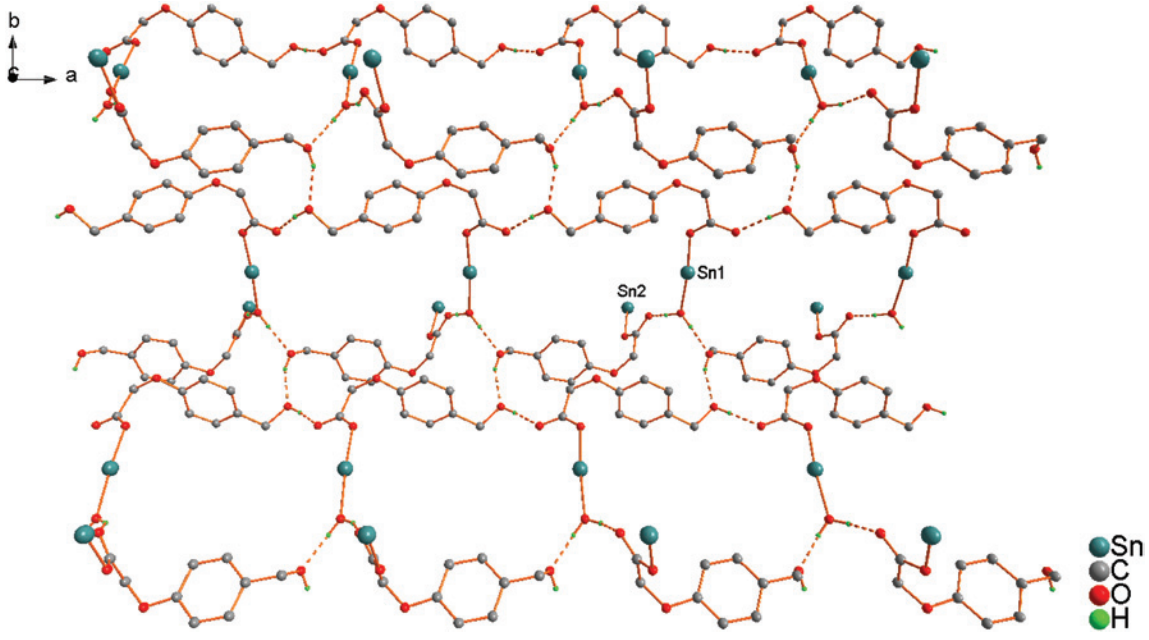


Figure 3: The 2D supramolecular network of **3** formed by the intermolecular O-H···O hydrogen bonds.

Table 1: Selected bond lengths (Å) and angles (°) for compound **1** and **3**.

1					
Sn(1)-O(1)	2.052(3)	Sn(2)-O(4)	2.062(3)	C(19)-O(2)	1.206(6)
Sn(1)-C(1)	2.122(6)	Sn(1)-C(27)	2.151(5)	C(19)-O(1)	1.294(6)
Sn(1)-C(7)	2.137(7)	Sn(1)-C(33)	2.160(5)	C(45)-O(5)	1.210(7)
Sn(1)-C(13)	2.143(7)	Sn(1)-C(39)	2.139(6)	C(45)-O(4)	1.282(6)
O(1)-Sn(1)-C(1)	107.8(2)	C(1)-Sn(1)-C(13)	117.2(4)	O(4)-Sn(2)-C(33)	106.43(19)
O(1)-Sn(1)-C(7)	94.0(2)	C(7)-Sn(1)-C(13)	116.7(3)	C(39)-Sn(2)-C(27)	110.1(3)
O(1)-Sn(1)-C(13)	107.0(2)	O(4)-Sn(2)-C(39)	107.0(2)	C(39)-Sn(2)-C(33)	121.1(3)
C(1)-Sn(1)-C(7)	111.1(3)	O(4)-Sn(2)-C(27)	95.65(17)	C(27)-Sn(2)-C(33)	113.2(2)
3					
Sn(1)-O(1)	2.432(4)	Sn(2)-O(6)	2.081(5)	C(19)-O(2)	1.287(7)
Sn(1)-O(2)	2.175(4)	Sn(2)-C(28)	2.148(6)	C(19)-O(3)	1.222(7)
Sn(1)-C(1)	2.159(6)	Sn(2)-C(34)	2.127(6)	C(46)-O(6)	1.282(7)
Sn(1)-C(7)	2.132(5)	Sn(2)-C(40)	2.126(7)	C(46)-O(7)	1.221(7)
Sn(1)-C(13)	2.143(5)				
C(7)-Sn(1)-C(13)	119.2(2)	C(7)-Sn(1)-O(1)	87.4(2)	O(6)-Sn(2)-C(34)	97.3(2)
C(7)-Sn(1)-C(1)	123.0(3)	C(13)-Sn(1)-O(1)	85.81(18)	C(40)-Sn(2)-C(34)	114.5(3)
C(13)-Sn(1)-C(1)	116.2(2)	C(1)-Sn(1)-O(1)	84.3(2)	O(6)-Sn(2)-C(28)	107.8(2)
C(7)-Sn(1)-O(2)	87.4(2)	O(2)-Sn(1)-O(1)	174.52(15)	C(40)-Sn(2)-C(28)	116.9(3)
C(13)-Sn(1)-O(2)	98.34(19)	O(6)-Sn(2)-C(40)	102.1(3)	C(34)-Sn(2)-C(28)	115.0(3)
C(1)-Sn(1)-O(2)	96.9(2)				

C(1)-Sn(1)-C(13) and C(33)-Sn(2)-C(39) to 117.2(4)° and 121.1(3)°, respectively, and reducing the O(1)-Sn(1)-C(7) and O(5)-Sn(2)-C(27) to 94.0(2)° and 95.65(17)°, respectively. The monodentate mode of the carboxylate coordination is expressed in two disparate C-O bond distances (Table 1). The four bond distances around Sn are similar to those found in other reported tricyclohexyltin carboxylates, such as tricyclohexyltin indole-3-acetate (Molloy et al., 1986), 2-(4-chlorophenyl)-3-methylbutyrate (Song et al., 2003), and ferrocene carboxylate (Dong et al., 2014).

Compound **3** crystallizes in the monoclinic space group $P2_1$, and the crystal structure reveals that there are two crystallographically non-equivalent molecules in the crystallographic asymmetric unit. The tin atom Sn(1) of one molecule (**A**) is five-coordinated, and the tin atom Sn(2) of the other molecule (**B**) is four-coordinated. In **A**, the coordination geometry of the tin center displays a distorted *trans*-O_2SnC_3 trigonal bipyramid with three carbon atoms [C(1), C(7), and C(13)] of cyclohexyl groups defining the trigonal plane and a unidentate carboxylate O(2) and a O(1) atom from the water molecule occupying the axial positions. The C-Sn-C angles were in the range of 116.2(2)–123.0(3)°. The O(1)-Sn(1)-O(2) angle is 174.52(15)°, which is similar to that observed in related tricyclohexyltin analogues, such as 3-$C_5H_4NCO_2Sn(C_6H_{11}$-*c*$)_3(H_2O)$ [176.11(11)°] (Teoh et al., 1999), (4-$MeC_6H_4)_3GeCH(C_6H_4$OMe-4)$CH_2CO_2Sn(C_6H_{11}$-*c*$)_3(H_2O)$ [170.35(6)°] (Din et al., 2003), and 2-Cl-3-$C_5H_4NCO_2Sn(C_6H_{11}$-*c*$)_3(H_2O)$ [176.40(11)°] (Yu et al., 2012). The bond length of Sn(1)-O(1) [2.432(4) Å] is significantly longer than that of Sn(1)-O(2) [2.175(4)Å], so that the Sn(1) atom is displaced out of the C_3 trigonal plane of the *trans*-C_3SnO_2 trigonal bipyramidal polyhedron in the direction of O(2) by 0.155(2) Å.

The structure of molecule **B** is similar to compound **1**, and Sn(2) has also a distorted tetrahedral geometry with the angles range of 97.3(2)–116.9(3)°. As expected, the C-O bond distances [C(19)-O(3) 1.222(7) Å and C(46)-O(7) 1.221(7) Å] associated with the non-coordinating carbonyl O atoms are shorter than the coordinating C-O bond distances [C(19)-O(2) 1.287(7) Å and C(46)-O(6) 1.282(7) Å]. Although not involved in coordination to tin, the O(3) and O(7) atoms form significant intermolecular contacts in the crystal lattice. Through the coordinated water molecules and the hydroxyl groups of ligands, the monomeric structures (**A** and **B**) get into contact with each other *via* hydrogen bonds (Table 2), and a two-dimensional (2D) network containing $R_3^3(30)$ and $R_5^5(28)$ hydrogen bonding patterns is formed (Figure 3).

Antibacterial activity

The antibacterial activities of the compounds and the reference drug (penicillin sodium and cefazolin sodium) are listed in Table 3. Results show that complexes **1–3** is active against *Escherichia coli*, which is comparable with the reported tricyclohexyltin

Table 2: Hydrogen bonds in compound **3**.

D-H···A	D-H (Å)	H···A (Å)	D···A (Å)	D-H···A (°)	Symmetry code
O(1)-H(1A)···O(7)	0.85	1.987	2.744(6)	147.8	
O(5)-H(5)···O(3)$^{\#1}$	0.82	1.874	2.655(7)	158.7	#1: *x*-1, *y*, *z*
O(1)-H(1B)···O(9)$^{\#2}$	0.85	1.817	2.656(7)	169.0	#2: *x*+1, *y*, *z*
O(9)-H(9)···O(5)$^{\#3}$	0.82	1.963	2.708(7)	150.8	#3: -*x*, *y*-1/2, -*z*+2

Table 3: Antibacterial activity (MIC, μg/mL) of the synthesized compounds.

	Compound			Penicillin sodium	Cefazolin sodium
	1	**2**	**3**		
E. coli	25.22	16.50	14.78	8.03	2.01

2-phenyl-1,2,3-triazole-4-carboxylate (MIC=13.50 μg/mL) (Tian et al., 2005) and ferrocenecarboxylate (MIC=23.98 μg/mL) (Dong et al., 2014). The activity of the three compounds against *E. coli* decreased in the order **3**>**2**>**1** under experimental conditions. However, the activity is lower than that of the reference drugs.

Conclusion

Three tricyclohexyltin aryloxyacetates have been synthesized from triorganotin hydroxide and aryloxyacetic acid and characterized. In both the solid state and the $CDCl_3$ solution, the carboxylate moiety coordinates the tin center in a monodentate fashion. The tin atom of compound **1** possesses a distorted tetrahedral geometry. In the crystal lattice of compound **3**, there is a four-coordinated tin and a five-coordinated tin possessing a trigonal bipyramidal environment with the axial positions occupied by a carboxylate oxygen atom and an oxygen atom of a water molecule and the 2D supramolecular network is formed by $R_3^3(30)$ and $R_5^5(28)$ hydrogen bonds. In the $CDCl_3$ solution, the tin atoms of the compounds are all four-coordinated. The compounds have activity against *E. coli* and can be considered as antibacterial compounds to further study.

Experimental

General

All chemicals used in the syntheses were of analytical grade and were purchased from commercial sources (Sinopharm Chemical Reagent Company, Shanghai, China) and used as received. Carbon and hydrogen analyses were determined using a Perkin Elmer 2400 Series II elemental analyzer (Perkin Elmer, Waltham, MA, USA). The IR spectra were recorded on a Nicolet Nexus 470 FT-IR spectrophotometer using KBr discs in the range of 4000–400 cm^{-1} (Thermo Nicolet, Madison, WI, USA). ^1H and ^{13}C NMR spectral data were collected using a Bruker Avance DPX300 NMR spectrometer (Bruker, Fallanden, Switzerland) with CD_3SOCD_3 or $CDCl_3$ as solvent and TMS as internal standard. ^{119}Sn NMR spectra were recorded in $CDCl_3$ on a Varian Mercury Vx300 spectrometer. Me_4Sn was used as external reference (Varian, Palo Alto, USA).

Synthesis of ligands

Synthesis of *p*-formylphenoxyacetic acid: The ligand was prepared by a modified literature procedure (Liu et al., 2005). To a stirred solution of *p*-hydroxybenzaldehyde (1.22 g, 10 mmol) and bromoacetic acid (1.67 g, 12 mmol) in water (20 mL) was dropwise added 20 mL water solution of sodium hydroxide (0.96 g, 24 mmol) within 30 min at room temperature. Stirring of the reaction mixture continued for 1.5 h under reflux and then cooled to room temperature. The solution was acidified with concentrated hydrochloric acid to pH 1–2, and the resulting solid was filtered and recrystallized from 95% alcohol to give *p*-formylphenoxyacetyl acid as a white solid (1.40 g, 78%); m.p. 200–201°C. Anal. calcd. for $C_9H_8O_4$ (%): C, 60.00; H, 4.48. Found: C, 59.94; H, 4.42. IR (KBr): 3460 (br, OH), 1755 (COOH), 1718 (CHO), 1226 (Ar-O) cm^{-1}. ^1H NMR (CD_3SOCD_3) δ 12.46 (s, 1H, COOH), 9.85 (s, 1H, CHO), 7.80 (d, *J*=8.4 Hz, 2H, *m*-H-C_6H_4), 7.08 (d, *J*=8.4 Hz, 2H, *o*-H-C_6H_4), 4.81 (s, 2H, OCH_2) ppm.

Synthesis of *p*-(hydroxymethyl)phenoxyacetic acid: To a solution of *p*-formylphenoxyacetic acid (1.80 g, 10 mmol) in water (15 mL) containing KOH (0.56 g, 10 mmol) was slowly added an excess of sodium borohydride (0.46 g, 12 mmol) in water (10 mL) containing a few drops of sodium hydroxide solution within 15 min in an ice bath. The reactive mixture was stirred for 1 h at room temperature and then acidified with concentrated HCl to a pH of 2–3. The resulting white solid was filtered off, washed with cold water, dried, and was recrystallized from ethyl acetate/*n*-hexane (1:1, v/v). Yield 1.56 g (86%); m.p. 116–117°C. Anal. calcd. for $C_9H_{10}O_4$ (%): C, 59.34; H, 5.53. Found: C, 59.36; H, 5.56. IR (KBr): 3500 (br, OH), 1761 (COOH), 1235 (Ar-O) cm^{-1}. ^1H NMR (CD_3SOCD_3) δ 12.31 ((s, 1H, COOH), 7.22 (d, *J*=8.0 Hz, 2H, *m*-H-C_6H_4), 6.82 (d, *J*=8.0 Hz, 2H, *o*-H-C_6H_4), 4.85 (s, 1H, OH), 4.50 (s, 2H, OCH_2), 4.42 (s, 2H, OCH_2Ar) ppm.

Synthesis of the complexes

Tricyclohexyltin phenoxyacetate (1): To a suspension of tricyclohexyltin hydroxide (0.77 g, 2 mmol) in 50 mL of benzene was added phenoxyacetic acid (0.30 g, 2 mmol). Under magnetic stirring, the

reaction mixture heated at reflux for 5 h with a Dean-Stark separator and then allowed to cool to room temperature. The solution was filtered, and the solvent was removed under reduced pressure by a rotary evaporator. The resulting white solid was recrystallized from methanol and dried in a vacuum dryer for 24 h to afford colorless crystal of **1** (0.81 g, 78%); m.p. 70–71°C. Anal. calcd. for $C_{26}H_{40}O_3Sn$ (%): C, 60.13; H, 7.76. Found: C, 59.94; H, 7.52. IR (KBr): 1665 [$\nu(COO^-)_{as}$], 1352 [$\nu(COO^-)_s$] cm^{-1}. ^1H NMR ($CDCl_3$) δ 7.27 (t, 2H, *m*-H-C_6H_5), 7.10–6.89 (m, 3H, *o*-H-, *p*-H-C_6H_5), 4.56 (s, 2H, OCH_2), 1.21–1.90 (m, 33H, *c*-C_6H_{11}) ppm. ^{13}C NMR ($CDCl_3$) δ 173.36 (COOSn), 158.17 (*i*-C-C_6H_5), 129.26 (*m*-C-C_6H_5), 121.04 (*p*-C-C_6H_5), 114.56 (*o*-C-C_6H_5), 65.56 (OCH_2), 34.04 [$^1J(^{119}Sn\text{-}^{13}C)$=332 Hz, C-$\alpha$], 31.01 [$^2J(^{119}Sn\text{-}^{13}C)$=20 Hz, C-$\beta$], 28.86 [$^3J(^{119}Sn\text{-}^{13}C)$=62 Hz, C-$\gamma$], 26.97 (C-$\delta$) ppm. ^{119}Sn NMR ($CDCl_3$) δ 30.0 ppm.

Tricyclohexyltin *p*-formylphenoxyacetate (2): This compound was prepared in the same way as **1** by the reaction of tricyclohexyltin hydroxide (0.77 g, 2 mmol) with *p*-formylphenoxyacetic acid (0.36 g, 2 mmol). Yield 0.71 g (65%); m.p. 88–89°C. Anal. calcd for $C_{27}H_{40}O_4Sn$: C, 59.25; H, 7.37. Found: C, 59.19; H, 7.25. IR (KBr): 1720 (CHO), 1668 [$\nu(COO^-)_{as}$], 1396 [$\nu(COO^-)_s$] cm^{-1}, ^1H NMR ($CDCl_3$) δ 9.86 (1H, s, CHO), 7.82 (d, *J*=8.2 Hz, 2H, *m*-H-C_6H_4), 7.01 (d, *J*=8.2 Hz, 2H, *o*-H-C_6H_4), 4.71 (s, 2H, OCH_2), 1.30–1.97 (m, 33H, *c*-C_6H_{11}). ^{13}C NMR ($CDCl_3$) δ 191.76 (CH=O), 172.21 (COOSn), 164.87 (*i*-C-C_6H_4), 131.92 (*m*-C-C_6H_4), 129.93 (*p*-C-C_6H_4), 114.48 (*o*-C-C_6H_4), 65.76 (OCH_2), 34.12 [$^1J(^{119}Sn\text{-}^{13}C)$=320 Hz, C-$\alpha$], 30.92 [$^2J(^{119}Sn\text{-}^{13}C)$=20 Hz, C-$\beta$], 28.83 [$^3J(^{119}Sn\text{-}^{13}C)$=62 Hz, C-$\gamma$], 27.54 (C-$\delta$) ppm. ^{119}Sn NMR ($CDCl_3$) δ 33.0 ppm.

Tricyclohexyltin *p*-(hydroxymethyl)phenoxyacetate (3): Complex **3** was prepared by the same procedure as **1** by the reaction of tricyclohexyltin hydroxide (0.77 g, 2 mmol) with *p*-(hydroxymethyl)phenoxyacetic acid (0.36 g, 2 mmol). Yield 0.89 g (81%); m.p. 91–92°C. Anal. calcd. for $C_{27}H_{42}O_4Sn$ (%): C, 59.03; H, 7.71. Found: C, 58.77; H, 7.64. IR (KBr): 3452 (br, OH), 1656 [$\nu(COO^-)_{as}$], 1325 [$\nu(COO^-)_s$] cm^{-1}. ^1H NMR ($CDCl_3$) δ 7.14 (d, *J*=8.0 Hz, 2H, *m*-H-C_6H_4), 6.76 (d, *J*=8.0 Hz, 2H, *o*-H-C_6H_4), 5.01 (s, 1H, OH), 4.43 (s, 2H, OCH_2COO), 4.36 (s, 2H, OCH_2Ar), 1.17–1.83 (m, 33H, *c*-C_6H_{11}). ^{13}C NMR ($CDCl_3$) δ 172.37 (COOSn), 157.57 (*i*-C-C_6H_4), 134.78 (*m*-C-C_6H_4), 127.90 (*p*-C-C_6H_4), 114.41 (*o*-C-C_6H_4), 66.14 (OCH_2), 62.98 ($HOCH_2$), 36.49 [$^1J(^{119}Sn\text{-}^{13}C)$=332 Hz, C-$\alpha$], 30.88 [$^2J(^{119}Sn\text{-}^{13}C)$=20 Hz, C-$\beta$], 29.17 [$^3J(^{119}Sn\text{-}^{13}C)$=64 Hz, C-$\gamma$], 27.07 (C-$\delta$) ppm. ^{119}Sn NMR ($CDCl_3$) δ 30.8 ppm.

X-ray crystallography

The colorless single crystals of **1** and **3** were obtained from methanol by slow evaporation at room temperature. Diffractions measurements were performed on a Bruker Smart Apex imaging plate area detector fitted with graphite monochromatized Mo-Kα radiation (0.71073 Å) using the φ and ω scan technique at 295(2) K. The structures were solved by direct methods and refined by a full-matrix least-squares procedure based on F^2 using SHELXL-97 (Sheldrick, 2008). The non-hydrogen atoms were refined anisotropically, and the hydrogen atoms were placed at calculated positions in the riding model approximation, with C-H=0.93 Å for aromatic and formyl H atoms, C-H=0.97 Å for methylene H atoms, C-H=0.98 Å for methine H atoms, O-H=0.82 Å for hydroxy H atoms, and O-H=0.85(1) Å for water H atoms. In complex **1**, two cyclohexyl groups are disordered over two positions, and their site occupancies were refined to 0.54(6):0.46(6) for C(13)-C(18) and 0.70(2):0.30(2) for C(39)-C(44). In complex **3**, the site occupancies of the cyclohexyls were refined to 0.802(10):0.198(10) for C(7)-C(12) and 0.65(2):0.35(2) for C(40)-C(45), respectively. In refinements, the C-C bonds and 1,3-distances of the disorderly cyclohexyl groups were restrained to 1.52(1) and 2.50(2) Å, respectively. Crystal data, collection procedures, and refinement results are shown in Table 4. The crystallographic data of compounds **1** and **3** were deposited at the Cambridge Crystallographic Data Centre as supplementary publication numbers CCDC 1014268 and 1043087.

Antibacterial activity

The antibacterial activity of compounds **1**–**3** against *E. coli* was determined by the microcalorimetric method according to the literature (Zhang et al., 2004). A 2277 Thermal Activity Monitor (Thermometric AB, Jarfalla, Sweden) was used to determine the power-time curves of bacterial growth at 310 K. After a stable baseline was obtained, the bacterial sample, a beef-extract-soluble medium (pH=7.2–7.4) containing NaCl (1 g), peptone (2 g), beef extract (1 g), and different concentrations of organotin medicine in each 200 mL were pumped into the flow cell system and the monitor began to record the power-time curves of continuous growth for bacteria. When the recording pen returned to the baseline, the process of bacterial growth was completed. Based on the data of power-time curves and theoretical model, the growth rate constants were calculated (Zhang et al., 2004). The relationship between the growth rate constants (μ) and the concentration (*C*) of the organotin medicine was fitted using a computer (μ=a*C*+b). When the growth rate constant is 0, the minimum inhibitory concentration (MIC) was confirmed.

Table 4: Crystallographic data and structure refinement for **1** and **3**.

	Compound	
	1	**3**
Empirical formula	$C_{26}H_{40}O_3Sn$	$C_{54}H_{86}O_9Sn_2$
Formula weight	519.27	1116.61
Crystal system	Monoclinic	Monoclinic
Space group	$P2_1/c$	$P2_1$
a (Å)	9.7697(12)	10.6609(14)
b (Å)	28.546(4)	18.274(2)
c (Å)	18.427(2)	14.1107(18)
α (°)	90	90
β (°)	92.028(2)	90.016(2)
γ (°)	90	90
Volume ($Å^3$)	5135.9(11)	2749.1(6)
Z	8	2
D_c (g/cm^3)	1.343	1.349
μ (mm^{-1})	1.017	0.959
F(000)	2160	1164
θ range	1.32–26.00	1.44–25.50
Crystal size (mm)	0.20×0.07×0.05	0.20×0.18×0.10
Unique reflections	10,020 (R_{int}=0.045)	10,186 (R_{int}=0.031)
Reflections [$I>2\sigma(I)$]	6422	8986
Goodness of fit on F^2	1.024	1.028
R indices [$I>2\sigma(I)$]	*R*=0.050, *wR*=0.126	*R*=0.044, *wR*=0.098
R indices (all data)	*R*=0.087, *wR*=0.147	*R*=0.052, *wR*=0.102
$\Delta\rho_{max}$, $\Delta\rho_{min}$ ($e/Å^3$)	0.710, -0.414	0.803, -0.392

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