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Synthesis, characterization, cytotoxic activity and crystal structures of tri- and di-organotin(IV) complexes constructed from the β-{[(E)-1-(2-hydroxyaryl)alkylidene]amino}propionate and β-{[(2Z)-(3-hydroxy-1-methyl-2-butenylidene)]amino}propionate skeletons

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Abstract

Reactions of potassium β-{[(E)-1-(2-hydroxyaryl)alkylidene]amino}propionates (L^1HK-L^3HK) and potassium β-{[(2Z)-(3-hydroxy-1-methyl-2- butenylidene)]amino}propionate (L^4HK) with R_3SnCl (R = Ph and ^nBu) and $^nBu_2SnCl_2$ yielded complexes of composition Ph_3SnL^1H (**1**), Ph_3SnL^2H (**2**), Ph_3SnL^4H (**3**), $^nBu_3SnL^1H$ (**4**), and $\{[^nBu_2Sn(L^2H)]_2O\}_2$ (**5**) and $\{[^nBu_2Sn(L^3H)]_2O\}_2$ (**6**), respectively. These complexes have been characterized by ^1H, ^{13}C, ^{119}Sn NMR, ESI-MS, IR and ^{119m}Sn Mössbauer spectroscopic techniques in combination with elemental analyses. The crystal structures of **1**, **4**, **5** and **6** were determined. In the solid state, compound **1** is a one-dimensional polymer built from $SnPh_3$ moieties bridged by single carboxylate ligands, but two alternating modes of bridging are present along the polymeric chain. Compound **4** is also a one-dimensional polymer built from $SnBu_3$ moieties bridged by the two carboxylate O-atoms of a single ligand, but only one mode of bridging is present. Di-*n*-butyltin compounds **5** and **6** are centrosymmetric tetranuclear bis(dicarboxylatotetrabutyldistannoxane) complexes containing a planar Sn_4O_2 core in which two μ_3-oxo O-atoms connect an Sn_2O_2 ring to two exocyclic Sn-atoms. The four carboxylate ligands display two different modes of coordination where both modes involve bridging of two Sn-atoms. The solution structures were predicted by ^{119}Sn NMR spectroscopy. The in vitro cytotoxic activity of compound **5** against WIDR, M19 MEL, A498, IGROV, H226, MCF7 and EVSA-T human tumor cell lines is reported.
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1. Introduction

Information on the structures of organotin(IV) carboxylates continues to accumulate, and at the same time, new applications of such compounds are being discovered, which are relevant for industrial, ecological and medicinal applications. The increasing interest in the chemistry of

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organotin(IV) compounds has led to extended studies on their reactions with different biomolecules, e.g., carbohydrates [1–3], nucleic acid derivatives [4–6], amino acids [7–11] and peptides [12–16]. In general, triorganotin(IV) compounds display a larger array of biological activity than their di- and mono-organotin(IV) analogues. This has been attributed to their ability to bind proteins [17–19]. Furthermore, many organotin(IV) derivatives have been found to possess anticancer activity in a variety of tumour cells and the structures of these organotin(IV) complexes are well characterized in the solid state [20,21]. Organotin(IV) complexes with Schiff bases, such as organotin(IV) esters of *N*-arylidene-amino acids, have also been shown to exhibit notable antitumour activity against human tumour cell lines [22], as well as fungicidal activity [23]. On the other hand, dialkyltin(IV) compounds have selective effects on lymphocytes [24–26], which can be used in cancer chemotherapy or to control other pathological effects. Among diorganotin(IV) compounds, tetraorganodistannoxanes are an important class of compounds owing to their applications as catalysts [27] and their interesting biological activity [21,28]. In view of this, and the recent reports on the synthesis, characterization and structure elucidation of organotin(IV) complexes of *N*-arylidene-amino acids [29–36], we now report on some organotin(IV) complexes of composition $[R_3SnLH]_n$ (R = ^{n}Bu and Ph) and $\{[^nBu_2Sn(LH)]_2O\}_2$ (refer to Fig. 1 for ligand description). The latter compounds possess a bis(dicarboxylatotetraorganodistannoxane) framework and a representative example, **5**, was tested across a panel of human cell lines viz., WIDR (colon cancer), M19 MEL (melanoma), A498 (renal cancer), IGROV (ovarian cancer) and H226 (non-small cell
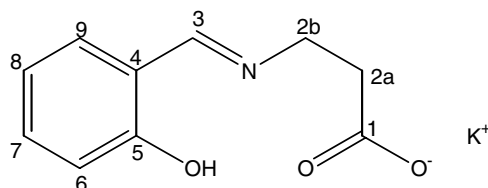
Potassium β-{[(*E*)-1-(2-hydroxyphenyl)methylidene]amino}propionate (L^{1}HK)
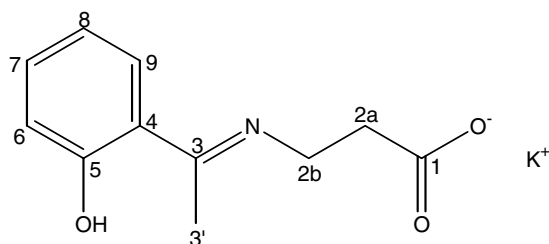
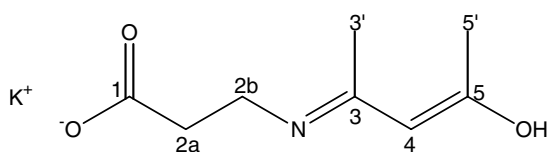Potassium β-{[(*E*)-1-(2-hydroxyphenyl)ethylidene]amino}propionate (L^{2}HK)
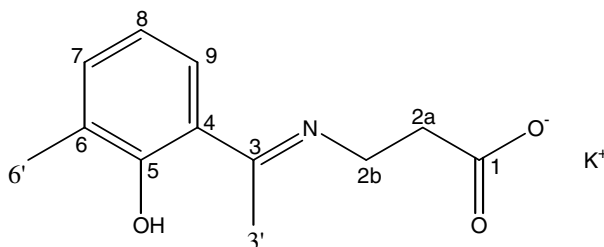
Potassium β-{[(*E*)-1-(2-hydroxy-3-methylphenyl)ethylidene]amino}propionate (L^{3}HK)

Potassium β-{[(2*Z*)-(3-hydroxy-1-methyl-2-butenylidene)]amino}propionate (L^{4}HK)

Fig. 1. Generic structure of the ligands, their abbreviations and numbering scheme.

lung cancer), MCF7 (breast cancer), EVSA-T (breast cancer) to establish the activity.

2. Experimental

2.1. Materials

Ph$_3$SnCl (Fluka AG), ^{n}Bu$_3$SnCl, ^{n}Bu$_2$SnCl$_2$ (Merck), β-alanine, 2-hydroxybenzaldehyde, acetylacetone (Sisco), and 2-hydroxyacetophenone (Aldrich) were used without further purification, while 2-hydroxy-3-methylacetophenone was a gift sample. The solvents used in the reactions were of AR grade and dried using standard procedures. Benzene was distilled from sodium benzophenone ketyl.

2.2. Physical measurements

Carbon, hydrogen and nitrogen analyses were performed with a Perkin–Elmer 2400 series II instrument. IR spectra in the range 4000–400 cm^{-1} were obtained on a BOMEM DA-8 FT-IR spectrophotometer with samples investigated as KBr discs. The ^{1}H and ^{13}C NMR spectra of the ligands were acquired on a Bruker Avance 500 spectrometer operating at 500.13 and 125.76 MHz, respectively. For the organotin compounds, the ^{1}H, ^{13}C and ^{119}Sn NMR spectra were recorded on a Bruker AMX 400 spectrometer and measured at 400.13, 100.62 and 149.18 MHz and on a Bruker AVANCE 500 spectrometer and measured at 500.13, 125.67 and 186.18 MHz, respectively. The ^{1}H, ^{13}C and ^{119}Sn chemical shifts were referred to Me$_4$Si set at 0.00 ppm, CDCl$_3$ set at 77.0 ppm and Me$_4$Sn set at 0.00 ppm, respectively. Positive-ion and negative-ion electrospray ionization (ESI) mass spectra were measured on an ion trap analyzer Esquire 3000 (Bruker Daltonics, Bremen, Germany) in the range m/z 50–2000. The complexes **2**, **4**, **5**, **6** and **1**, **3** were dissolved in acetonitrile and methanol, respectively, and analyzed by direct infusion at a flow rate of 5 μl/min. The selected precursor ions were further analyzed by MS/MS analyses under the following conditions: an isolation width of $m/z = 8$ for ions containing one tin atom and $m/z = 12$ for ions containing more tin atoms, the collision amplitude in the range 0.8–1.0 V depending on the precursor ion stability, an ion source temperature of 300 °C, a tuning parameter of compound stability 100%, a flow rate and pressure of nitrogen of 4 l/min and 10 psi, respectively. Mössbauer spectra were recorded on solid samples at liquid nitrogen temperature by using a conventional constant acceleration spectrometer, coupled with a multichannel analyser (a.e.n., Ponteranica (BG), Italy) equipped with a cryostat Cryo (RIAL, Parma, Italy). A Ca^{119}SnO$_3$ Mössbauer source, 10 mCi (from Ritverc, St Petersburg, Russia) moving at room temperature with constant acceleration in a triangular waveform was used. The velocity calibration was made using a ^{57}Co Mössbauer source, 10 mCi, and an iron foil as absorber (from Ritverc, St Petersburg, Russia).

2.3. Synthesis of ligands

A typical procedure is described below.

2.3.1. Synthesis of potassium β-{[(E)-1-(2-hydroxyphenyl)methylidene]amino}propionate (L^{1}HK)

A cold aqueous solution (3 ml) of KOH (0.36 g, 6.41 mmol) was mixed with a cold aqueous solution (1 ml) containing β-alanine (0.57 g, 6.40 mmol) and was held at 15–20 °C in an ice bath with continuous stirring. A methanolic solution (15 ml) of 2-hydroxybenzaldehyde (0.78 g, 6.40 mmol) was added drop-wise. A deep-yellow colour developed almost immediately and stirring was continued for 1 h, followed by 5 h stirring at room temperature. The volatiles were removed carefully; the yellow mass was stirred in diethylether and filtered. The residue was dissolved in a minimum amount of anhydrous methanol and filtered. The filtrate was precipitated with diethylether, which afforded the crude product. Repeated precipitations from a methanol–diethylether mixture yielded L^{1}HK in 94% (1.40 g) yield. M.p.: 105–106 °C. Anal. Calc. for C$_{10}$H$_{10}$NKO$_3$: C, 51.92; H, 4.35; N, 6.05. Found: C, 52.01; H, 4.43; N, 6.15%. IR (cm^{-1}): 1646 ν(OCO)$_{asym}$, 1592 ν(C=N), 1307 ν(Ph(C–O)).

The other potassium salts (Fig. 1), viz. potassium β-{[(E)-1-(2-hydroxyphenyl)ethylidene]amino}propionate (L^{2}HK), potassium β-{[(E)-1-(2-hydroxy-3-methylphenyl)ethylidene)]amino}propionate (L^{3}HK) and potassium β-{[(2Z)-(3-hydroxy-1-methyl-2-butenylidene)]amino}propionate (L^{4}HK) were prepared analogously by reacting 2-hydroxyacetophenone, 2-hydroxy-3-methylacetophenone and acetylacetone, respectively, with β-alanine.

2.3.2. Potassium β-{[(E)-1-(2-hydroxyphenyl)ethylidene]-amino}propionate (L^{2}HK)

Recrystallized from methanol to give a yellow precipitate in 84% yield. M.p.: 105 °C (decomp.). Anal. Calc. for C$_{11}$H$_{12}$NKO$_3$: C, 53.90; H, 4.93; N, 5.71. Found: C, 54.06; H, 5.01; N, 5.82%. IR (cm^{-1}): 1675 ν(OCO)$_{asym}$, 1614 ν(C=N), 1304 ν(Ph(C–O)).

2.3.3. Potassium β-{[(E)-1-(2-hydroxy-3-methylphenyl)ethylidene]amino}propionate (L^{3}HK)

Recrystallized from methanol to give a yellow precipitate in 70% yield. M.p.: 105 °C (decomp.). Anal. Calc. for C$_{12}$H$_{14}$NKO$_3$: C, 55.57; H, 5.44; N; 5.40. Found: C, 55.70; H, 5.58; N, 5.55%. IR (cm^{-1}): 1667 ν(OCO)$_{asym}$, 1601 ν(C=N), 1269 ν(Ph(C–O)).

2.3.4. Potassium β-{[(2Z)-(3-hydroxy-1-methyl-2-butenylidene)]amino}propionate (L^{4}HK)

Recrystallized from methanol to give a yellow precipitate in 71% yield. M.p.: 95–96 °C (decomp.). Anal. Calc. for C$_8$H$_{12}$NKO$_3$: C, 45.01; H, 5.77; N; 6.69. Found: C, 45.21; H, 6.01; N, 7.10%. IR (cm^{-1}): 1706 ν(OCO)$_{asym}$, 1605 ν(C=N), 1295 ν(Ph(C–O)).

2.4. Synthesis of the organotin complexes

2.4.1. Synthesis of Ph₃SnL¹H (1)

Ph₃SnCl (0.5 g, 1.30 mmol) in 10 ml anhydrous chloroform was added drop-wise to a stirred suspension of L¹HK (0.30 g, 1.30 mmol) in 20 ml chloroform. The stirring was continued for 6 h at ambient temperature and the reaction mixture was filtered. The filtrate was allowed to evaporate at ambient temperature to leave a dry yellow mass which was then triturated with hexane and filtered. The precipitate was washed several times with hexane, dried in vacuo and recrystallized from ethanol to yield yellow crystals of **1** in 70% (0.49 g) yield. M.p.: 131–132 °C. Anal. Calc. for $C_{28}H_{25}NO_3Sn$: C, 62.03; H, 4.64; N, 2.58. Found: C, 62.23; H, 4.60; N, 2.70%. IR (cm⁻¹): 1639 $v(OCO)_{asym}$, 1615 $v(C=N)$, 1281 $v(Ph(CO))$. ¹H NMR (CDCl₃): 13.18 (brs, 1H, OH), 8.33 (s, 1H, H-3), 7.29 (t, 1H, H-7), 7.10 (d, 1H, H-9), 6.93 (d, 1H, H-6), 6.84 (t, 1H, H-8), 3.87 and 2.81 (t, 4H, H-2a and H-2b); Sn–Ph Skeleton: 7.65 (m, 6H, H-2*), 7.37–7.41 (m, 9H, H-3* and H-4*), ppm. ¹³C NMR (CDCl₃): Ligand skeleton: 177.9 (C-1), 166.0 (C-3), 161.2 (C-5), 132.1 (C-7), 131.4 (C-9), 118.7 (C-4), 118.4 (C-6), 117.0 (C-8), 55.5 and 35.4 (C-2b and C-2a); Sn–Ph skeleton: 138.0 (C-1*), 136.7 (C-2*), 130.1 (C-4*), 128.8 (C-3*) ppm. ¹¹⁹Sn NMR (CDCl₃): −108.6 ppm. ¹¹⁹Sn Mössbauer: $\delta = 1.24$, $\Delta = 3.13$, $\Gamma\pm = 0.87$ mm s⁻¹, $\rho = 2.46$. Positive-ion MS: m/z 894 [M+SnPh₃]⁺, 100%; m/z 733 [CH₃OSnPh₃+SnPh₃]⁺; m/z 719 [(SnPh₃)₂O+H]⁺; m/z 582 [M+K]⁺; m/z 566 [M+Na]⁺; m/z 544 [M+H]⁺; m/z 351 [SnPh₃]⁺. MS/MS of m/z 894: m/z 816 [M+SnPh₃-benzene]⁺; m/z 466 [M+H-benzene]⁺; m/z 406 [M+H-benzene−CH₃COOH]⁺; m/z 316 [M+H-2*benzene−CO₂-ethene]⁺. MS/MS of m/z 733: m/z 351 [SnPh₃]⁺. MS/MS of m/z 719: m/z 659 [(SnPh₃)₂O+H-benzene+H₂O]⁺; m/z 581 [(SnPh₃)₂O+H-2*benzene+H₂O]⁺; m/z 351 [SnPh₃]⁺. MS/MS of m/z 566: m/z 488 [M+Na-benzene]⁺; m/z 351 [SnPh₃]⁺. MS/MS of m/z 544: m/z 466 [M+H-benzene]⁺; m/z 406 [M+H-benzene−CH₃COOH]⁺. Negative-ion MS: m/z 735 [M+ligand]⁻; m/z 542 [M−H]⁻; m/z 439 [SnPh₃+Cl₂+H₂O]⁻; m/z 192 [ligand]⁻; m/z 148 [ligand-CO₂]⁻, 100%. MS/MS of m/z 735: m/z 542 [M−H]⁻. MS/MS of m/z 542: m/z 498 [M−H−CO₂]⁻; m/z 351 [SnPh₃]⁻. MS/MS of m/z 439: m/z 351 [SnPh₃]⁻. MS/MS of m/z 192: m/z 148 [ligand-CO₂]⁻.

2.4.2. Synthesis of Ph₃SnL²H (2)

An identical method to that of **1** was followed using Ph₃SnCl and L²HK, except that the reaction was conducted in anhydrous benzene for 4 h. Yellow crystals of compound **2** were obtained from ethanol in 75% yield. M.p.: 161–162 °C. Anal. Calc. for $C_{29}H_{27}NO_3Sn$: C, 62.64; H, 4.89; N, 2.52. Found: C, 62.84; H, 5.05; N, 2.67%. IR (cm⁻¹): 1637 $v(OCO)_{asym}$, 1611 $v(C=N)$, 1281 $v(Ph(CO))$. ¹H NMR (CDCl₃): Ligand skeleton: 16.14 (brs, 1H, OH), 7.40 (m, 1H, H-9), 7.25 (t, 1H, H-7), 6.87 (d, 1H, H-6), 6.75 (t, 1H, H-8), 3.83 and 2.86 (t, 4H, H-2a and H-2b), 2.27 (s, 3H, H-3′); Sn–Ph Skeleton: 7.70 (m, 6H, H-2*), 7.40–7.45 (m, 9H, H-3* and H-4*), ppm. ¹³C NMR (CDCl₃): Ligand skeleton: 178.1 (C-1), 172.0 (C-3), 163.6 (C-5), 132.4 (C-7), 128.9 (C-9), 119.3 (C-4), 118.6 (C-6), 117.0 (C-8), 45.8 and 35.3 (C-2b and C-2a), 14.5 (C-3′); Sn–Ph skeleton: 138.0 (C-1*), 136.7 (C-2*) 130.1 (C-4*), 128.1 (C-3*), ppm. ¹¹⁹Sn NMR (CDCl₃ solution): −108.6 ppm. ¹¹⁹Sn Mössbauer: $\delta = 1.24$, $\Delta = 3.06$, $\Gamma\pm = 0.92$ mm s⁻¹, $\rho = 2.47$. Positive-ion MS: m/z 908 [M+SnPh₃]⁺, 100%; m/z 830 [M+SnPh₃-benzene]⁺; m/z 719 [HOSnPh₃+SnPh₃]⁺; m/z 580 [M+Na]⁺; m/z 369 [SnPh₃+H₂O]⁺; m/z 351 [SnPh₃]⁺. MS/MS of m/z 908: m/z 830 [M+SnPh₃-benzene]⁺; m/z 480 [M+H-benzene]⁺; m/z 420 [M+H-benzene−CH₃COOH]⁺; m/z 351 [SnPh₃]⁺; m/z 330 [M+H-2*benzene−CO₂-ethene]⁺. MS/MS of m/z 830: m/z 420 [M+H-benzene−CH₃COOH]⁺; m/z 351 [SnPh₃]⁺; m/z 330 [M+H-2*benzene−CO₂-ethene]⁺. MS/MS of m/z 719: m/z 659 [(SnPh₃)₂O+H-benzene+H₂O]⁺; m/z 581 [(SnPh₃)₂O+H-2*benzene+H₂O]⁺; m/z 351 [SnPh₃]⁺. MS/MS of m/z 580: m/z 562 [M+Na−H₂O]⁺; m/z 502 [M+Na-benzene]⁺; m/z 443 [M+Na-benzene−CH₃COOH]⁺; m/z 351 [SnPh₃]⁺. MS/MS of m/z 351: m/z 369 [SnPh₃+H₂O]⁺; m/z 197 [SnPh]⁺. Negative-ion MS: m/z 439 [SnPh₃+Cl₂+H₂O]⁻; m/z 351 [SnPh₃]⁻; m/z 206 [ligand]⁻; m/z 162 [ligand-CO₂]⁻; m/z 134 [ligand-CO₂-ethene]⁻. MS/MS of m/z 439: m/z 351 [SnPh₃]⁻. MS/MS of m/z 206: m/z 162 [ligand-CO₂]⁻; m/z 134 [ligand-CO₂-ethene]⁻.

2.4.3. Synthesis of Ph₃SnL⁴H (3)

An identical method to that of **1** was followed using Ph₃SnCl and L⁴HK except that the reaction was conducted in anhydrous methanol and refluxed for 10 h. The solvent was then distilled off to dryness and the residue was dried in vacuo. The solid mass was washed several times with hexane, extracted into warm chloroform and filtered. The yellow-coloured filtrate was concentrated, precipitated with hexane and dried in vacuo. The crude product was recrystallized from a chloroform-ethanol mixture (3:1 v/v) to afford a lemon yellow microcrystalline product in 60% yield. M.p.: 115–116 °C. Anal. Calc. for $C_{26}H_{27}NO_3Sn$: C, 62.03; H, 5.23; N, 2.69. Found: C, 62.10; H, 5.36; N, 2.90%. IR (cm⁻¹): 1639 $v(OCO)_{asym}$, 1606 $v(C=N)$, 1275 $v(Ph(CO))$. ¹H NMR (CDCl₃): Ligand skeleton: 10.80 (brs, 1H, OH), 4.88 (s, 1H, 4-H), 3.49 and 2.62 (t, 4H, H-2a and H-2b), 1.93 and 1.85 (s, 6H, H-3′ and H-5′); Sn–Ph skeleton: 7.74 (m, 6H, H-2*), 7.43 (m, 6H, H-4*), 7.34 (m, 6H, H-3*), ppm. ¹³C NMR (CDCl₃): Ligand skeleton: 194.8 (C-1), 177.0 (C-3), 162.6 (C-5), 95.6 (C-4), 39.3 and 35.3 (C-2b and C-2a); 28.6 and 18.7 (C-3′ and C-5′); Sn–Ph skeleton: 138.3 (C-1*), 136.7 (C-2*), 130.0 (C-4*), 128.8 (C-3*), ppm. ¹¹⁹Sn NMR (CDCl₃): −108.3 ppm. ¹¹⁹Sn Mössbauer: $\delta = 1.27$, $\Delta = 3.04$, $\Gamma\pm = 1.20$ mm s⁻¹, $\rho = 2.47$. Positive-ion MS: m/z 1393 [2*M+SnPh₃]⁺; m/z 1081 [2*M+K]⁺; m/z 1065 [2*M+Na]⁺; m/z 872 [M+SnPh₃]⁺, 100%; m/z 733 [CH₃OSnPh₃+SnPh₃]⁺; m/z 719 [HOSnPh₃+SnPh₃]⁺; m/z 560 [M+K]⁺; m/z 544 [M+Na]⁺; m/z 522

$[M+H]^+$; m/z 351 $[SnPh_3]^+$. MS/MS of m/z 1393: m/z 872 $[M+SnPh_3]^+$. MS/MS of m/z 1081: m/z 560 $[M+K]^+$. MS/MS of m/z 1065: m/z 544 $[M+Na]^+$. MS/MS of m/z 872: m/z 444 $[M-benzene+H]^+$; m/z 384 $[M-benzene-CH_3COOH+H]^+$; m/z 294 $[M+H-2*benzene-CO_2$-ethene$]^+$. MS/MS of m/z 733: m/z 351 $[SnPh_3]^+$. MS/MS of m/z 719: m/z 659 $[(SnPh_3)_2O+H$-benzene$+H_2O]^+$; m/z 581 $[(SnPh_3)_2O+H-2*benzene+H_2O]^+$; m/z 351 $[SnPh_3]^+$. MS/MS of m/z 544: m/z 502 $[M+Na-CH_2=C=O]^+$; m/z 351 $[SnPh_3]^+$; m/z 197 $[SnPh]^+$. MS/MS of m/z 522: m/z 444 $[M-benzene+H]^+$. Negative-ion MS: m/z 691 $[M+ligand]^-$; m/z 439 $[SnPh_3+Cl_2+H_2O]^-$; m/z 170 $[ligand]^-$, 100%; m/z 128 $[ligand-CH_2=C=O]^-$; m/z 98 $[ligand-CO_2$-ethene$]^-$. MS/MS of m/z 691: m/z 520 $[M-H]^-$. MS/MS of m/z 439: m/z 351 $[SnPh_3]^-$. MS/MS of m/z 170: m/z 128 $[ligand-CH_2=C=O]^-$; m/z 98 $[ligand-CO_2$-ethene$]^-$.

2.4.4. Synthesis of $^nBu_3SnL^1H$ (4)

Preparation of compound **4** was accomplished according to the procedure used for **1** by using equimolar amounts of $^nBu_3SnCl$ and L^1HK. Yellow prismatic crystals of **4** were obtained from a hexane–chloroform mixture (4:1 v/v) in 62% yield. M.p.: 79–80 °C. Anal. Calc. for $C_{22}H_{37}NO_3Sn$: C, 54.79; H, 7.73; N, 2.90. Found: C, 55.04; H, 7.67; N, 3.02%. IR (cm^{-1}): 1631 $v(OCO)_{asym}$, 1578 $v(C=N)$, 1281 $v(Ph(CO))$. ^1H NMR (CDCl$_3$): Ligand skeleton: 13.30 (brs, 1H, OH), 8.39 (s, 1H, H-3), 7.26 (t, 1H, H-7), 7.1 (d, 1H, H-9), 6.92 (d, 1H, H-6), 6.85 (t, 1H, H-8), 3.85 and 2.71 (t, 6H, H-2a and H-2b); Sn–^nBu skeleton: 1.56 (m, 6H, 1*), 1.32 (m, 12H, 2* and 3*), 0.87 (t, 9H, 4*), ppm. ^{13}C NMR (CDCl$_3$): Ligand skeleton: 176.7 (C-1), 165.7 (C-3), 161.1 (C-5), 132.1 (C-7), 131.1 (C-9), 118.7 (C-4), 118.3 (C-6), 116.9 (C-8), 55.7 and 35.9 (C-2b and C-2a); Sn–^nBu skeleton: 27.7 (C-2*), 27.0 (C-3*), 16.4 (C-1*), 13.6 (C-4*), ppm. ^{119}Sn NMR (CDCl$_3$): 110.8 ppm. ^{119}Sn Mössbauer: $\delta = 1.46$, $\Delta = 3.56$, $\Gamma\pm = 0.87$ mm s^{-1}, $\rho = 2.44$. Positive-ion MS: m/z 796 $[M+SnPh_3-H+Na]^+$; m/z 774 $[M+SnPh_3]^+$; m/z 522 $[M+K]^+$; m/z 506 $[M+Na]^+$, 100%. MS/MS of m/z 796: m/z 581 $[M+SnPh_3-H+Na-LNa]^+$; m/z 506 $[M+Na]^+$; m/z 334 $[M+Na-2*butane-butene]^+$. MS/MS of m/z 774: m/z 426 $[M-Bu]^+$; m/z 312 $[M-Bu$-butane-butene$]^+$; m/z 291 $[SnBu_3]^+$; m/z 235 $[HSnBu_2]^+$. MS/MS of m/z 506: m/z 448 $[M+Na$-butane$]^+$; m/z 334 $[M+Na-2*butane-butene]^+$; m/z 235 $[HSnBu_2]^+$; m/z 179 $[BuSnH_2]^+$. Negative-ion MS: m/z 482 $[M-H]^-$; m/z 192 $[ligand]^-$; m/z 148 $[ligand-CO_2]^-$, 100%. MS/MS of m/z 482: m/z 438 $[M-H-CO_2]^-$; m/z 289 $[M-H-LH]^-$. MS/MS of m/z 192: m/z 148 $[ligand-CO_2]^-$.

2.4.5. Synthesis of $\{[^nBu_2Sn(L^2H)]_2O\}_2$ (5)

This compound was prepared in the same manner as described for **1** by using $^nBu_2SnCl_2$ (0.4 g, 1.31 mmol) and L^2HK (0.70 g, 2.85 mmol). Yellow crystals of **5** were obtained from a hexane–chloroform mixture (4:1 v/v) in 60% yield. M.p.: 125–126 °C. Anal. Calc. for $C_{76}H_{120}$-

$N_4O_{14}Sn_4$: C, 51.04; H, 6.76; N, 3.13. Found: C, 51.21; H, 6.83; N, 3.21%. IR (cm^{-1}): 1619 $v(OCO)_{asym}$, 1573 $v(C=N)$, 1275 $v(Ph(CO))$, 645 $v(Sn-O-Sn)$. ^1H NMR (CDCl$_3$): Ligand skeleton: 15.84 (brs, 1H, OH), 7.50 (d, 1H, H-9), 7.25 (t, 1H, H-7), 6.87 (d, 1H, H-6), 6.75 (t, 1H, H-8), 3.79 and 2.67 (t, 4H, H-2a and H-2b), 2.35 (s, 3H, H-3′); Sn–^nBu skeleton: 1.60 (m, 4H, H-1*), 1.30–1.41 (m, 8H, H-2* and H-3*), 0.85 (t, 6H, H-4*), ppm. ^{13}C NMR (CDCl$_3$): Ligand skeleton: 177.4 (C-1), 171.7 (C-3), 163.5 (C-5), 132.3 (C-7), 128.0 (C-9), 119.5 (C-4), 118.6 (C-6), 117.0 (C-8), 46.0 and 37.2 (C-2b and C-2a), 14.4 (C-3′); Sn–^nBu skeleton: 27.6, 27.4, 26.8, 26.7, 21.4 (C-2*, C-3* and C-4*), 13.6 br (C-4*), ppm. ^{119}Sn NMR (CDCl$_3$): −200.2, −212.7 ppm , $[^2J(Sn-O-Sn) = 140$ Hz]. ^{119}Sn Mössbauer: $\delta = 1.30$, $\Delta = 3.28$, $\Gamma\pm = 0.95$ mm s^{-1}, $\rho = 2.52$. Positive-ion MS: m/z 958 $[M_{mono}+H+OSn-Bu_2+(OH)_2SnBu_2]^+$; m/z 940 $[M_{mono}+H+2*OSnBu_2]^+$; m/z 751 $[(OSnBu_2)_3+H]^+$; m/z 690 $[M_{mono}+H+OSnBu_2]^+$, 100%; m/z 672 $[M_{mono}+H-H_2O+OSnBu_2]^+$; m/z 501 $[(OSnBu_2)_2+H]^+$; m/z 462 $[M_{mono}+Na]^+$; m/z 440 $[M_{mono}+H]^+$; m/z 326 $[M_{mono}$-butane-butene$+H]^+$. MS/MS of m/z 958: m/z 940 $[M_{mono}+H+2*OSnBu_2]^+$; m/z 690 $[M_{mono}+H+OSnBu_2]^+$. MS/MS of m/z 940: m/z 922 $[M_{mono}+H+2*OSnBu_2-H_2O]^+$; m/z 501 $[(OSnBu_2)_2+H]^+$. MS/MS of m/z 751: m/z 733 $[(OSnBu_2)_3+H-H_2O]^+$; m/z 655 $[(OSnBu_2)_3+H$-butene-butane$+H_2O]^+$; m/z 619 $[(OSnBu_2)_3+H$-butene-butane$-H_2O]^+$; m/z 541 $[(OSnBu_2)_3+H-2*butene-2*butane+H_2O]^+$; m/z 523 $[(OSnBu_2)_3+H-2*butene-2*butane]^+$; m/z 501 $[(OSnBu_2)_2+H]^+$; m/z 465; m/z 427 $[(OSnBu_2)_3+H-3*butene-3*butane+H_2O]^+$; m/z 409 $[(OSnBu_2)_3+H-3*butene-3*butane]^+$; m/z 387 $[(OSnBu_2)_2+H$-butene-butane$]^+$; m/z 273 $[(OSnBu_2)_2+H-2*butane-2*butene]^+$. MS/MS of m/z 690: m/z 672 $[M_{mono}+H-H_2O+OSnBu_2]^+$; m/z 654 $[M_{mono}+H-2*H_2O+OSnBu_2]^+$; m/z 556 $[M_{mono}+H-H_2O+OSnBu_2-2*butane]^+$; m/z 422 $[M_{mono}+H-H_2O]^+$. MS/MS of m/z 672: m/z 654 $[M_{mono}+H-2*H_2O+OSnBu_2]^+$; m/z 556 $[M_{mono}+H-H_2O+OSnBu_2-2*butan]^+$; m/z 538 $[M_{mono}+H-2*H_2O+OSnBu_2-2*butane]^+$; m/z 422 $[M_{mono}+H-H_2O]^+$; m/z 308 $[M_{mono}+H-H_2O$-butane-butene$]^+$. MS/MS of m/z 501: m/z 483 $[(OSnBu_2)_2+H-H_2O]^+$; m/z 445 $[(OSnBu_2)_2+H$-butene$]^+$; m/z 389 $[(OSnBu_2)_2+H-2*butene]^+$; m/z 331 $[(OSnBu_2)_2+H-2*butene-butane]^+$; m/z 289 $[(OSnBu_2)_2+H-3*butane-butene+H_2O]^+$; m/z 273 $[(OSnBu_2)_2+H-2*butane-2*butene]^+$. MS/MS of m/z 462: m/z 348 $[M_{mono}+Na$-butane-butene$]^+$. MS/MS of m/z 440: m/z 422 $[M_{mono}+H-H_2O]^+$; m/z 380 $[M_{mono}+H-HAC]^+$; m/z 369; m/z 326 $[M_{mono}+H$-butane-butene$]^+$; m/z 233 $[BuSn=Bu]^+$; m/z 177 $[SnBu]^+$. Negative-ion MS: m/z 438 $[M_{mono}-H]^-$, 100%. MS/MS of m/z 438: m/z 394 $[M_{mono}-H-CO_2]^-$; m/z 160 $[M_{mono}-H-SnBu_2-CO_2]^-$ (Note: $M_{mono} = LSnBu_2 = 439$).

2.4.6. Synthesis of $\{[^nBu_2Sn(L^3H)]_2O\}_2$ (6)

An identical method to that used for the preparation of **5** was followed by using $^nBu_2SnCl_2$ and L^3HK. Yellow crystals of **6** were obtained from a hexane–chloroform

mixture (4:1 v/v) in 65% yield. M.p.: 159–160 °C. Anal. Calc. for $C_{80}H_{128}N_4O_{14}Sn_4$: C, 52.09; H, 6.99; N, 3.03. Found: C, 52.31; H, 7.18; N, 3.25%. IR (cm^{-1}): 1618 $v(OCO)_{asym}$, 1573 $v(C=N)$, 1268 $v(Ph(CO))$, 645 $v(Sn–O–Sn)$. ^1H NMR (CDCl$_3$): Ligands skeleton: 16.21 (brs, 1H, OH), 7.35 (d, 1H, H-9), 7.14 (t, 1H, H-7), 6.66 (t, 1H, H-8), 3.85 and 2.71 (t, 4H, H-2a and H-2b), 2.35 and 2.22 (s, 6H, H-3′ and H-6′); Sn–^nBu skeleton: 1.59 (m, 4H, H-1*), 1.30–1.42 (m, 8H, H-2* and H-3*), 0.85 (t, 6H, H-4*), ppm. ^{13}C NMR (CDCl$_3$): Ligands skeleton: 177.5 (C-1), 172.0 (C-3), 162.0 (C-5), 133.0 (C-7), 127.2 (C-9), 125.6 (C-4), 118.3 (C-6), 116.3 (C-8), 45.7 and 37.1 (C-2b and C-2a), 15.7 and 14.6 (C-6′ and C-3′); Sn–^nBu skeleton: 27.6, 27.3, 26.8, 26.6, 21.0 (C-2*, C-3* and C-4*), 13.6, 13.5 (C-4*), ppm. ^{119}Sn NMR (CDCl$_3$): −200.7, −213.2 ppm, [$^2J(Sn–O–Sn) = 140$ Hz]. ^{119}Sn Mössbauer: $\delta = 1.17$, $\Delta = 3.28$, $\Gamma\pm = 0.87$ mm s^{-1}, $\rho = 2.80$. Positive-ion MS: m/z 1871 [M+Na]$^+$ a m/z 1887 [M+K]$^+$; m/z 1628 [M−L]$^+$; m/z 1425 [2*M$_{mono}$+H+OSnBu$_2$+(OH)$_2$SnBu$_2$]$^+$; m/z 972 [M$_{mono}$+H+OSn-Bu$_2$+(OH)$_2$SnBu$_2$]$^+$; m/z 954 [M$_{mono}$+H+2*OSnBu$_2$]$^+$; m/z 929 [2*M$_{mono}$+Na]$^+$; m/z 751 [(OSnBu$_2$)$_3$+H]$^+$; m/z 704 [M$_{mono}$+H+OSnBu$_2$]$^+$; m/z 492 [M$_{mono}$+K]$^+$; m/z 476 [M$_{mono}$+Na]$^+$; m/z 454 [M$_{mono}$+H]$^+$, 100%. MS/MS of m/z 1628: m/z 1157 [M−L−M$_{mono}$−H$_2$O]$^+$; m/z 704 [M$_{mono}$+H+OSnBu$_2$]$^+$. MS/MS of m/z 1425: m/z 972 [M$_{mono}$+H+OSnBu$_2$+(OH)$_2$SnBu$_2$]$^+$; m/z 954 [M$_{mono}$+H+OSnBu$_2$+(OH)$_2$SnBu$_2$−H$_2$O]$^+$; m/z 751 [(OSnBu$_2$)$_3$+H]$^+$; m/z 704 [M$_{mono}$+H+OSnBu$_2$]$^+$; m/z 501 [(OSnBu$_2$)$_2$+H]$^+$. MS/MS of m/z 972: m/z 954 [M$_{mono}$+H+2*OSnBu$_2$]$^+$; m/z 936 [M$_{mono}$+H+2*OSnBu$_2$−H$_2$O]$^+$; m/z 751 [(OSnBu$_2$)$_3$+H]$^+$; m/z 704 [M$_{mono}$+H+OSnBu$_2$]$^+$; m/z 501 [(OSnBu$_2$)$_2$+H]$^+$. MS/MS of m/z 954: m/z 936 [M$_{mono}$+H+2*OSnBu$_2$−H$_2$O]$^+$; m/z 501 [(OSnBu$_2$)$_2$+H]$^+$. MS/MS of m/z 929: m/z 476 [M$_{mono}$+Na]$^+$. MS/MS of m/z 751: m/z 733 [(OSnBu$_2$)$_3$+H−H$_2$O]$^+$; m/z 655 [(OSnBu$_2$)$_3$+H-butene-butane+H$_2$O]$^+$; m/z 619 [(OSnBu$_2$)$_3$+H-butene-butane−H$_2$O]$^+$; m/z 541 [(OSnBu$_2$)$_3$+H-2*butene-2*butane+H$_2$O]$^+$; m/z 523 [(OSnBu$_2$)$_3$+H-2*-butene-2*butane]$^+$; m/z 501 [(OSnBu$_2$)$_2$+H]$^+$; m/z 465; m/z 427 [(OSnBu$_2$)$_3$+H-3*butene-3*butane+H$_2$O]$^+$; m/z 409 [(OSnBu$_2$)$_3$+H-3*butene-3*butane]$^+$; m/z 387 [(OSnBu$_2$)$_2$+H-butene-butane]$^+$; m/z 273 [(OSnBu$_2$)$_2$+ H-2*butane-2*butene]$^+$. MS/MS of m/z 704: m/z 686 [M$_{mono}$+H+OSnBu$_2$-H$_2$O]$^+$; m/z 668 [M$_{mono}$+H+ OSnBu$_2$-2*H$_2$O]$^+$; m/z 554 [M$_{mono}$+H+OSnBu$_2$−2*H$_2$O-butene-butane]$^+$; m/z 436 [M$_{mono}$+H-H$_2$O]$^+$. MS/MS of m/z 492: m/z 474 [M$_{mono}$+K−H$_2$O]$^+$; m/z 379 [M$_{mono}$+K-butene-butane]$^{+\cdot}$. MS/MS of m/z 476: m/z 458 [M$_{mono}$+Na−H$_2$O]$^+$; m/z 362 [M$_{mono}$+Na-butene-butane]$^+$. MS/MS of m/z 454: m/z 436 [M$_{mono}$+H−H$_2$O]$^+$; m/z 382 [M$_{mono}$+H−CO$_2$-ethene]$^+$; m/z 340 [M$_{mono}$+H-butene-butane]$^+$; m/z 305 [M$_{mono}$+H-butene-butane-2*H$_2$O]$^{+\cdot}$; m/z 268; m/z 233 [Bu–Sn=Bu]$^+$; m/z 177 [SnBu]$^+$. Negative-ion MS: m/z 452 [M$_{mono}$-H]$^-$; m/z 357 [M$_{mono}$−H-butene-butane+H$_2$O]$^{-\cdot}$; m/z 339 [M$_{mono}$−H-butene-butane]$^{-\cdot}$; m/z 220 [ligand]$^-$; m/z 176 [ligand-CO$_2$]$^-$, 100%; m/z 148 [ligand-

CO$_2$-ethene]$^-$; m/z 133 [ligand-CO$_2$-CH$_3$CHNH]$^-$; m/z 107 [o-cresol-H]$^-$. MS/MS of m/z 452: m/z 408 [M$_{mono}$−H−CO$_2$]$^-$; m/z 380 [M$_{mono}$− H−CO$_2$-ethene]$^-$; m/z 174 [ligand-HCOOH]$^-$. MS/MS of m/z 220: m/z 176 [ligand-CO$_2$]$^-$; m/z 148 [ligand-CO$_2$-ethene]$^-$. MS/MS of m/z 176: m/z 133 [ligand-CO$_2$−CH$_3$CHNH]$^-$; m/z 107 [o-cresol-H]$^-$. MS/MS of m/z 148: m/z 107 [o-cresol-H]$^-$ (Note: M$_{mono}$ = LSnBu$_2$-H = 453).

2.5. X-ray crystallography

Crystals of compounds **1**, **4**, **5** and **6** suitable for an X-ray crystal-structure determination were obtained from ethanol (**1**), hexane (**4**), benzene/hexane (**5**) or hexane/chloroform (**6**). All measurements were made on a Nonius KappaCCD diffractometer [37] with graphite-monochromated Mo Kα radiation ($\lambda = 0.71073$ Å) and an Oxford Cryosystems Cryostream 700 cooler. Data reduction was performed with HKL Denzo and Scalepack [38]. The intensities were corrected for Lorentz and polarization effects, and empirical absorption corrections based on the multi-scan method [39] were applied. Equivalent reflections were merged, other than the Friedel pairs for **1**. The data collection and refinement parameters are given in Table 1, and views of the molecules are shown in Figs. 2–5. The structures were solved by direct methods using sir92 [40] for **1**, **4** and **5**, and shelxs97 [41] for **6**, and the non-hydrogen atoms were refined anisotropically.

For **6**, the molecule sits about a crystallographic centre of inversion. One butyl group on each of the two symmetry-independent Sn-atoms is disordered over two conformations. Two sets of overlapping positions were defined for the atoms of each disordered butyl group and the site occupation factor of the major conformation of these groups refined to 0.647(7) and 0.789(6) for the disordered group at the exo- and endo-cyclic Sn-atoms, respectively. Similarity restraints were applied to the chemically equivalent bond lengths and angles involving all disordered C-atoms, while neighbouring atoms within and between each conformation of the disordered butyl groups were restrained to have similar atomic displacement parameters. In the structure of **5**, the molecule also sits about a crystallographic centre of inversion, but there is no disorder.

The hydroxy and ammonium H-atoms of **1** and the hydroxy H-atoms of **4** and **6** were placed in the positions indicated by a difference electron density map and their positions were allowed to refine together with individual isotropic displacement parameters. All other H atoms in all structures were placed in geometrically calculated positions and refined using a riding model where each H atom was assigned a fixed isotropic displacement parameter with a value equal to $1.2U_{eq}$ of its parent C atom ($1.5U_{eq}$ for the methyl groups). The orientation of each hydroxy O–H vector in **5** was optimised to correspond with the direction that would bring the H-atom closest to the nearest hydrogen

Table 1
Crystallographic data and structure refinement parameters for compounds **1** and **4**–**6**

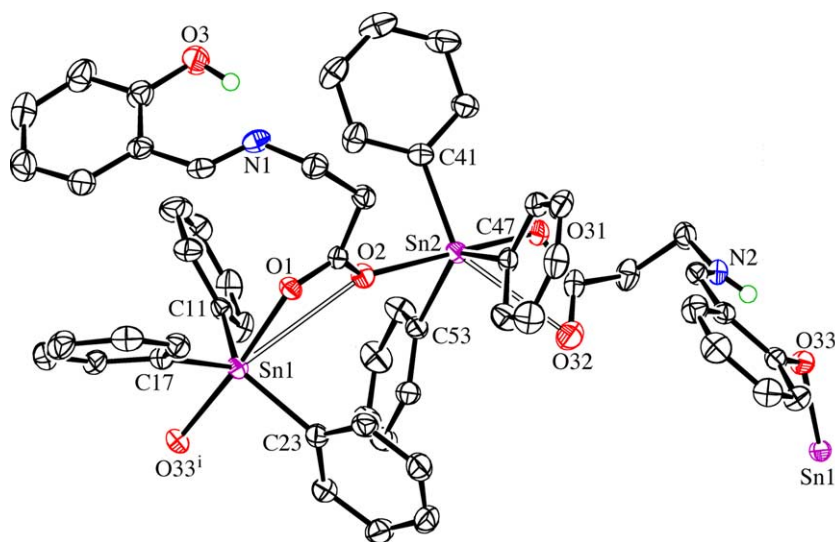|	**1**	**4**	**5**	**6**
Empirical formula	$C_{56}H_{50}N_2O_6Sn_2$	$C_{22}H_{37}NO_3Sn$	$C_{76}H_{120}N_4O_{14}Sn_4$	$C_{80}H_{128}N_4O_{14}Sn_4$
Formula weight	1084.22	482.14	1788.20	1844.30
Crystal size (mm)	$0.08 \times 0.23 \times 0.25$	$0.08 \times 0.12 \times 0.20$	$0.07 \times 0.20 \times 0.25$	$0.10 \times 0.20 \times 0.25$
Crystal shape	Tablet	Prism	Tablet	Prism
Temperature (K)	160(1)	160(1)	160(1)	160(1)
Crystal system	Monoclinic	Monoclinic	Triclinic	Triclinic
Space group	Pc	$P2_1/n$	$P\bar{1}$	$P\bar{1}$
a (Å)	9.8671(1)	13.7830(3)	12.475(1)	13.0368(3)
b (Å)	10.0853(1)	9.9060(2)	13.574(1)	13.6627(3)
c (Å)	24.7096(3)	17.7972(4)	14.212(1)	14.7318(3)
α (°)	90	90	94.149(5)	113.936(1)
β (°)	102.4277(6)	109.616(1)	113.754(5)	102.200(1)
γ (°)	90	90	109.696(5)	108.279(1)
V (Å^3)	2401.30(5)	2288.91(9)	2012.5(3)	2096.86(9)
Z	2	4	1	1
D_c (g cm^{-3})	1.499	1.399	1.475	1.460
μ (mm^{-1})	1.093	1.135	1.287	1.238
Transmission factors (min, max)	0.656, 0.936	0.770, 0.929	0.671, 0.937	0.722, 0.887
$2\theta_{max}$ (°)	60	60	50	55
Reflections measured	59217	56647	22961	43463
Independent reflections; R_{int}	13972; 0.077	6675; 0.076	7078; 0.071	9586; 0.058
Reflections with $I > 2\,\sigma(I)$	11998	5108	5438	7459
Number of parameters	604	251	450	550
Number of restraints	2	0	0	220
$R(F)$ [$I > 2\,\sigma(I)$ reflns]	0.037	0.035	0.053	0.040
$wR(F^2)$ (all data)	0.080	0.079	0.137	0.105
GOF (F^2)	1.04	1.08	1.09	1.03
$\Delta\rho_{max,min}$ (e Å^{-3})	1.07, −0.97	1.59, −0.92	1.47, −1.12	1.07, −1.53

Fig. 2. The unique repeat unit in the polymeric [Ph$_3$SnL^{1}H]$_n$ chain structure of **1** (50% probability ellipsoids).

bond acceptor. The refinement of each structure was carried out on F^2 by using full-matrix least-squares procedures, which minimized the function $\Sigma w(F_o^2 - F_c^2)^2$. Corrections for secondary extinction were not applied. For **1**, refinement of the absolute structure parameter [42] yielded a value of 0.53(1), which indicates that the crystals **1** are inversion twins. All calculations were performed using the SHELXL 97 program [43].

2.6. Biological tests

The in vitro cytotoxicity test of compound **5** was performed using the SRB test for the estimation of cell viability. The cell lines WIDR (colon cancer), M19 MEL (melanoma), A498 (renal cancer), IGROV (ovarian cancer) and H226 (non-small cell lung cancer) belong to the currently used anticancer screening panel of the National
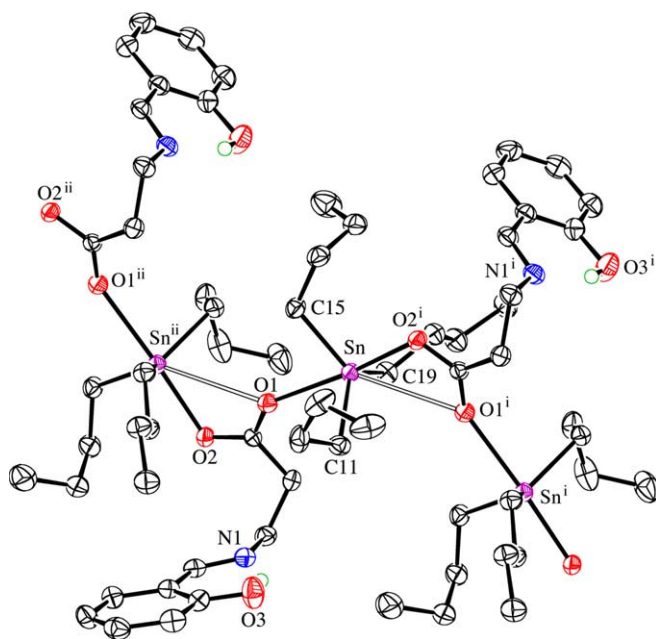
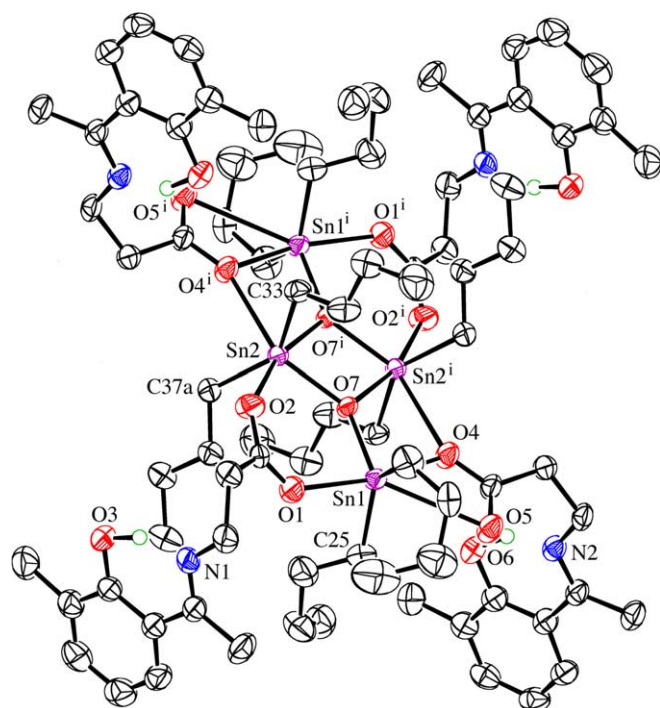Fig. 3. A three-unit segment of the polymeric $[^nBu_3SnL^1H]_n$ chain in **4** (50% probability ellipsoids).

Fig. 5. The molecular structure of $\{[^nBu_2Sn(L^3H)]_2O\}_2$ (**6**) (50% probability ellipsoids).

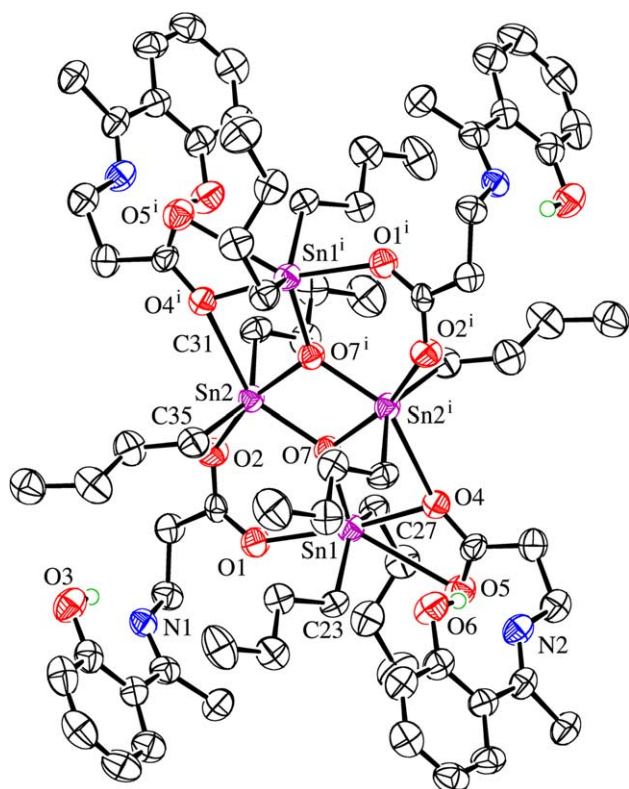Fig. 4. The molecular structure of $\{[^nBu_2Sn(L^2H)]_2O\}_2$ (**5**) (50% probability ellipsoids).

Cancer Institute, USA [44]. The MCF7 (breast cancer) cell line is estrogen receptor (ER)+/progesterone receptor (PgR)+ and the cell line EVSA-T (breast cancer) is (ER)−/(Pgr)−. Prior to the experiments, a mycoplasma test was carried out on all cell lines and found to be nega-

tive. All cell lines were maintained in a continuous logarithmic culture in RPMI 1640 medium with Hepes and phenol red. The medium was supplemented with 10% FCS, penicillin 100 µg/ml and streptomycin 100 µg/ml. The cells were mildly trypsinized for passage and for use in the experiments. RPMI and FCS were obtained from Life Technologies (Paisley, Scotland). SRB, DMSO, Penicillin and streptomycin were obtained from Sigma (St. Louis MO, USA), TCA and acetic acid from Baker BV (Deventer, NL) and PBS from NPBI BV (Emmer-Compascuum, NL).

The test compound **5** and reference compounds were dissolved to a concentration of 250 000 ng/ml in full medium, by 20 fold dilution of a stock solution which contained 1 mg of compound **5**/200 µl. Compound **5** was dissolved in DMSO. Cytotoxicity was estimated by the microculture sulforhodamine B (SRB) test [45].

2.6.1. Experimental protocol and cytotoxicity tests

The experiment was started on day 0. On day 0, 150 µl of trypsinized tumor cells (1500–2000 cells/well) were plated in 96-well flat-bottomed micro-titer plates (falcon 3072, BD). The plates were pre-incubated for 48 h at 37 °C, 5.5% CO_2 to allow the cells to adhere. On day 2, a threefold dilution sequence of ten steps was made in full medium, starting with the 250 000 ng/ml stock solution. Every dilution was used in quadruplicate by adding 50 µl to a column of four wells. This results in a highest concentration of 62 500 ng/ml being present in column 12. Column 2 was used for the blank. To column 1, PBS was added to diminish interfering evaporation. On day 7, washing the plate twice with PBS terminated the incubation.

Subsequently, the cells were fixed with 10% trichloroacetic acid in PBS and placed at 4 °C for an hour. After three washings with tap water, the cells were stained for at least 15 min with 0.4% SRB dissolved in 1% acetic acid. After staining, the cells were washed with 1% acetic acid to remove the unbound stain. The plates were air-dried and the bound stain was dissolved in 150 μl (10 mM) Tris–base. The absorbance was read at 540 nm using an automated microplate reader (Labsystems Multiskan MS). Data were used for construction of concentration-response curves and the determination of ID_{50} values by use of Deltasoft 3 software.

3. Results and discussion

3.1. Synthetic aspects

Organotin(IV) complexes of composition R_3SnLH (R = ^nBu and Ph) and $\{[^nBu_2Sn(LH)]_2O\}_2$ were prepared by reacting potassium salts of the ligands (Fig. 1) with the appropriate organotin(IV) halide(s) in 1:1 and 2:1 molar ratios, respectively. The reactions could be conducted in anhydrous chloroform, benzene or methanol, which resulted in the smooth formation of the complexes 1–6 (see Section 2.4). The synthesis of complexes of the type R_3SnLH is straightforward, however, the formation of diorganotin(IV) complexes deserve specific comments. Recently, we have demonstrated that 2-{[(E)-1-(2-hydroxy-aryl)alkylidene]amino}acetic acid forms a great variety of diorganotin(IV) complexes, viz., $[R_2SnL(OH_2)]_2$ (R = Me [35], Vin [29], ^nBu [35]), $[R_2SnL]_3$ (R = ^nBu [35]), $[R_2SnL]$ (R = Ph [29], Bz [36]) and $[R_2SnL]_n$ (R = Ph [35]). In each case, the labile functional group (phenolic hydrogen atom) is removed, thereby forming a bicycloazadiorganostannox-ides. In the present case, the unsymmetrical bi-functional potassium β-{[(E)-1-(2-hydroxyaryl)alkylidene]amino}pro-pionate and potassium β-{[(2Z)-(3-hydroxy-1-methyl-2-butenylidene)]amino}propionate ligands react with $^nBu_2SnCl_2$ to give a bis(dicarboxylatotetraorganodistan-noxane), $\{[^nBu_2Sn(LH)]_2O\}_2$ (5 and 6), where the labile phenolic group remains intact. The reaction possibly pro-ceeds via the formation of di-n-butyltin dicarboxylates, which can undergo hydrolysis, presumably mediated by adventitious moisture present in the solvent or a slight excess of base present in the starting potassium salt, to yield the product of composition $\{[^nBu_2Sn(LH)]_2O\}_2$ [46]. The complexes were isolated as yellow crystalline solids in good yield (>60 %) and purity. They are stable in air and are soluble in common organic solvents.

3.2. Spectroscopy

Diagnostically important infrared absorption frequen-cies for the carboxylate antisymmetric [v_{asym}(OCO)] stretching vibration of the complexes appears in the range 1630–1640 cm^{-1} (for 1–4) and 1618 cm^{-1} (for 5 and 6).

The assignment of the symmetric [v_{sym}(OCO)] stretching vibration band could not be made owing to the complex pattern of the spectra. In addition, a strong broad band in the region 645 cm^{-1} has been detected for the com-plexes 5 and 6 and is assigned to the v(Sn–O–Sn) mode [47,48].

The ^1H and ^{13}C NMR signals were assigned by the use of homonuclear correlated spectroscopy (COSY), hetero-nuclear single-quantum correlation (HSQC) and heteronu-clear multiple-bond correlation (HMBC) experiments. The ^1H and ^{13}C chemical shift assignment (Section 2.4) of the organotin moiety is straightforward from the multiplicity patterns and resonance intensities. The ^1H NMR integra-tion values were completely consistent with the formulation of the products. The ^{13}C NMR spectra of the ligand and Sn–R skeletons displayed the expected carbon signals in all cases, except for the di-n-butyltin(IV) complexes 5 and 6, which displayed two sets of Sn–^nBu resonances, consis-tent with a dicarboxylatotetraorganodistannoxane struc-ture. Owing to the low intensities of the Sn–^nBu resonances, a poor signal to noise ratio prevented identifi-cation of ^nJ(Sn–C). The ^{119}Sn NMR chemical shifts of the organotin complexes in CDCl$_3$ solution are listed in Sec-tion 2.4. The triorganotin complexes exhibit a single sharp resonance at around −108 ppm for R = Ph (1–3) and 111 ppm for R = ^nBu (4). The δ (^{119}Sn) chemical shifts are consistent with the range specified for tetrahedral triorganotin compounds [49,50,32]. These results demon-strate that the polymeric structure with five-coordinate tin atoms found in the solid state is lost upon dissolution (see Section 3.3). On the other hand, the bis(dicarboxyla-totetraorganodistannoxanes) (5 and 6) exhibit two distinct ^{119}Sn NMR resonances of equal intensities at around −200 and −213 ppm characteristic for the endocyclic and exocy-clic tin atoms [51]. Although it is difficult to assign coordi-nation to the tin atoms with certainty on the basis of their ^{119}Sn chemical shifts, values of δ (^{119}Sn) in the ranges −200 to −400, −90 to −190 and 200 to −60 ppm have been asso-ciated with six-, five- and four-coordinate tin centres, respectively, bearing n-butyl groups [52]. On this basis, two chemically different six-coordinate tin centres (endocy-clic and exocyclic) are present in solution for the di-n-butyl-tin complexes 5 and 6, which is consistent with the X-ray structures (vide infra). Thus, the ^{13}C and ^{119}Sn NMR data for the complexes 5 and 6 provide reasonable support for the formation of a dimeric tetraorganodistannoxane struc-ture [51,53]. Although two different types of carboxylate groups are present (as revealed by the X-ray analysis; see below), only single broad resonances are observed for the COO group in the ^{13}C NMR spectra of 5 and 6, which might also correspond to the situation when two ^{13}C reso-nances of two carboxyl groups exist, however, the differ-ence between them is rather small. ^{119}Sn chemical shifts are much more sensitive to subtle structural changes and the observed difference between two tin resonances was only 13 ppm. The difference in ^{13}C resonances should, therefore, be considerably smaller. This may be due to

the accidental magnetic equivalence of the carbonyl carbon atoms on the NMR time scale.

The triorganotin complexes **1–4** are characterized by a single doublet spectrum in the Mössbauer spectra, revealing the occurrence of only one type of tin atom in the solid state, while the di-*n*-butyltin complexes **5** and **6** displayed two doublets of equal intensities, as expected. These results are in agreement with the ^{119}Sn NMR data. The triorganotin complexes exhibited quadrupole splitting (Δ) values of approximately 3.00 mm s^{-1} (**1–3**) and 3.56 mm s^{-1} (**4**). These values are within the range 3.0–4.1 mm s^{-1}, which are consistent with a *trans*-trigonal bipyramidal geometry with a planar R$_3$Sn unit and two axial carboxylate oxygen atoms [54]. Similar ranges of values were also found in the triorganotin derivatives of cognate ligands with a *trans*-trigonal bipyramidal geometry [32]. In contrast, the Mössbauer data could not be fitted into two doublets, as expected for di-*n*-butyltin complexes of the type {[^{n}Bu$_2$Sn(LH)]$_2$O}$_2$ (**5** and **6**) having *exo*-cyclic and *endo*-cyclic- tin centers [46]. The complexes **5** and **6** both exhibited good single doublet spectra indicating that the two types of tin centers are similar. The isomer shifts of the complexes were found in the usual range of 1.17–1.30 mm s^{-1}, which indicates the presence of quadrivalent tin centers. Further, the ratio of the quadrupole splitting

value to isomer shift value ($\rho = \Delta/\delta$) indicates coordination greater than four [54].

The typical ions in the first-order positive-ion ESI mass spectra of compounds **1–4** are adducts with the SnPh$_3$ group and with alkali metal ions, such as [M+SnPh$_3$]$^+$, [M+K]$^+$ and [M+Na]$^+$ (typical ions for this type of compounds) [55]. The presence of these ions was used for the determination of the molecular weights of the analyzed compounds. The second mechanism of the ion formation is the cleavage of the most labile bond Sn–O in the molecules, which yields two complementary ions, where the cationic part (SnPh$_3$) of the molecule is measured in the positive-ion mode and the anionic part (L) in the negative-ion mode [56]. The ion *m/z* 351 [SnPh$_3$]$^+$ forms the other adduct ion at *m/z* 719 [(SnPh$_3$)$_2$+H]$^+$. The ions observed in the first-order negative-mass spectra are [L−CO$_2$]$^-$ and [M+L]$^-$. On the other hand, compounds **5** and **6** are complex di-*n*-butyltin compounds with four tin atoms. In the case of **6**, low abundant ions corresponding to molecular adducts were identified after longer averaging of mass spectra, which enabled positive confirmation of the tetranuclear structure of this compound. The molecular adducts were not found in the background noise in the case of **5**, so only ions corresponding to the monomeric unit M$_{mono}$ are observed (see Section 2.4 for more details). The typical feature of the spectra is the
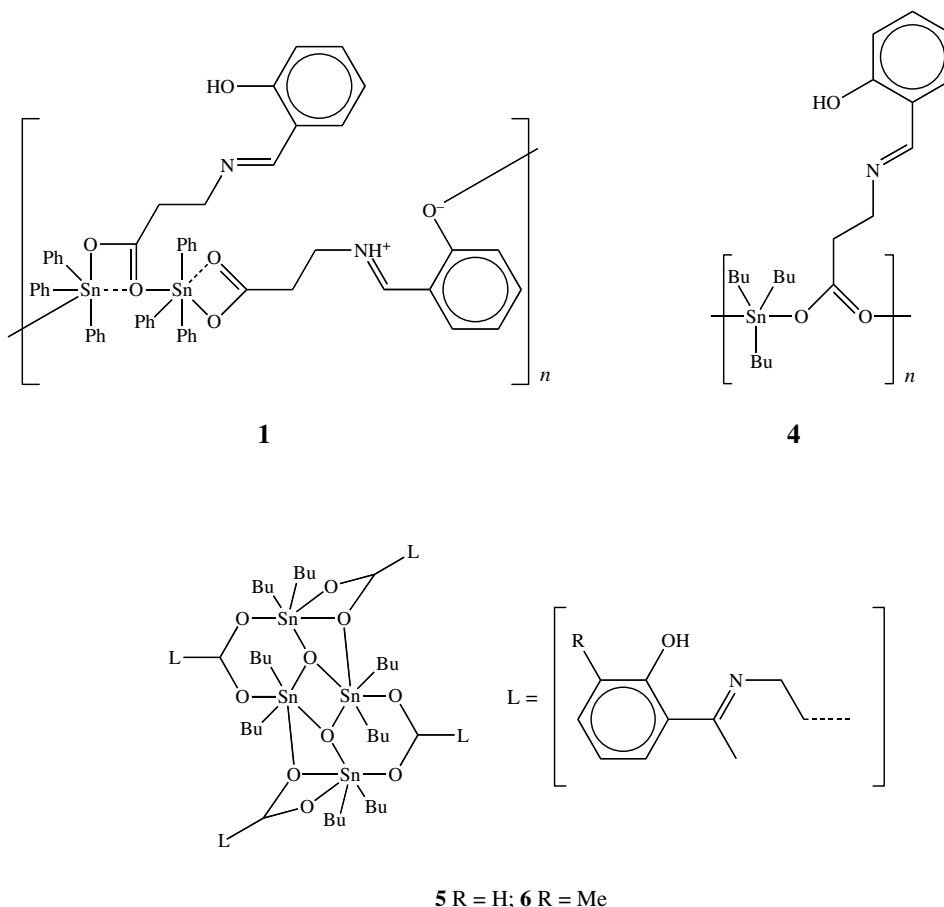
Scheme 1. Structures of the complexes **1**, **4–6**.

formation of adduct ions with tetranuclear character, where the OSnBu$_2$ group is a monomeric unit.

3.3. X-ray crystallography

Views of the structures of compounds **1** and **4**–**6** are shown in Figs. 2–5 (see Scheme 1 for line diagrams), while selected geometric parameters are collected in Tables 2–5. The solid-state structure of complex **1** is a one-dimensional polymer in which the repeat unit contains two Sn-atoms with distinct coordination environments (Fig. 2). The structure is built from SnPh$_3$ moieties bridged by single carboxylate ligands, but two modes of bridging are present with these modes alternating along the polymeric chain. The first bridge links two Sn-atoms via the two carboxylate O-atoms of the carboxylate ligand, while the second bridge links two Sn-atoms via one of the carboxylate O-atoms and the phenoxide O-atom. The pattern then repeats. The repeat Sn$\cdots$Sn distances in this pattern are 5.3882(3) and 8.5119(4) Å, respectively, for the two coordination motifs. The primary coordination sphere of each Sn-atom is trigonal bipyramidal with the phenyl ligands in the equatorial plane. Atom Sn(1) is coordinated by the three phenyl ligands, a carboxylate O-atom from one carboxylate ligand and the phenoxide O-atom from a second carboxylate ligand. In addition, the second carboxylate O-atom of the first carboxylate ligand, which coordinates strongly to Sn(2), also has a weak interaction with Sn(1) with an Sn$\cdots$O distance of 3.202(3) Å (Table 2), thus completing six-coordination of Sn(1) in the extended coordination sphere. Atom Sn(2) is coordinated in the primary coordination sphere by the three phenyl ligands, a carboxylate

Table 2
Selected bond lengths (Å) and angles (°) for compound **1**[a]

Sn(1)–O(1)	2.204(2)	Sn(2)–O(2)	2.396(3)
Sn(1)$\cdots$O(2)	3.202(3)	Sn(2)–O(31)	2.148(3)
Sn(1)–O(33)^i	2.244(2)	Sn(2)$\cdots$O(32)	2.986(3)
Sn(1)–C(11)	2.123(3)	Sn(2)–C(41)	2.141(3)
Sn(1)–C(17)	2.136(3)	Sn(2)–C(47)	2.134(4)
Sn(1)–C(23)	2.135(3)	Sn(2)–C(53)	2.119(4)
O(1)–Sn(1)$\cdots$O(2)	43.93(7)	O(31)–Sn(2)$\cdots$O(32)	47.98(9)
O(1)–Sn(1)–O(33)^i	174.64(9)	O(31)–Sn(2)–O(2)	177.71(9)
O(1)–Sn(1)–C(11)	93.2(1)	O(31)–Sn(2)–C(41)	88.7(1)
O(1)–Sn(1)–C(17)	87.1(1)	O(31)–Sn(2)–C(47)	99.7(1)
O(1)–Sn(1)–C(23)	92.6(1)	O(31)–Sn(2)–C(53)	94.0(1)
O(2)$\cdots$Sn(1)–O(33)^i	135.95(7)	O(32)$\cdots$Sn(2)–O(2)	131.90(8)
O(2)$\cdots$Sn(1)–C(11)	69.0(1)	O(32)$\cdots$Sn(2)–C(41)	136.7(1)
O(2)$\cdots$Sn(1)–C(17)	130.0(1)	O(32)$\cdots$Sn(2)–C(47)	80.8(1)
O(2)$\cdots$Sn(1)–C(23)	78.6(1)	O(32)$\cdots$Sn(1)–C(53)	73.1(1)
O(33)^i–Sn(1)–C(11)	82.5(1)	O(2)–Sn(2)–C(41)	91.3(1)
O(33)^i–Sn(1)–C(17)	91.7(1)	O(2)–Sn(2)–C(47)	82.4(1)
O(33)^i–Sn(1)–C(23)	92.5(1)	O(2)–Sn(2)–C(53)	83.9(1)
C(11)–Sn(1)–C(17)	113.7(1)	C(41)–Sn(2)–C(47)	112.9(1)
C(11)–Sn(1)–C(23)	125.2(1)	C(41)–Sn(2)–C(53)	115.9(1)
C(17)–Sn(1)–C(23)	121.0(1)	C(47)–Sn(2)–C(53)	129.4(1)

[a] Atom labels with superscript "i" refer to atoms from the next symmetrically-related ligand in the polymeric chain (symmetry code: x, $1-y$, $z-\frac{1}{2}$).

Table 3
Selected bond lengths (Å) and angles (°) for compound **4**[a]

Sn–O(1)	2.460(2)	Sn–C(11)	2.147(2)
Sn–O(2)^i	2.181(2)	Sn–C(15)	2.151(2)
Sn$\cdots$O(1)^i	3.043(2)	Sn–C(19)	2.140(2)
O(1)–Sn–O(2)^i	172.11(6)	O(2)^i–Sn–C(19)	100.21(8)
O(1)–Sn$\cdots$O(1)^i	139.44(5)	O(1)^i$\cdots$Sn–C(11)	75.13(9)
O(1)–Sn–C(11)	83.56(8)	O(1)^i$\cdots$Sn–C(15)	140.80(7)
O(1)–Sn–C(15)	79.50(8)	O(1)^i$\cdots$Sn–C(19)	77.80(9)
O(1)–Sn–C(19)	85.47(8)	C(11)–Sn–C(15)	114.5(1)
O(2)^i–Sn$\cdots$O(1)^i	46.58(5)	C(11)–Sn–C(19)	122.3(1)
O(2)^i–Sn–C(11)	96.51(8)	C(15)–Sn–C(19)	118.7(1)
O(2)^i–Sn–C(15)	94.27(8)		

[a] Atom labels with superscript "i" refer to atoms from the next symmetrically-related ligand in the polymeric chain (symmetry code: $1\frac{1}{2} - x$, $\frac{1}{2} + y$, $\frac{1}{2} - z$).

Table 4
Selected bond lengths (Å) and angles (°) for diorganotin(IV) compound **5**[a]

Sn(1)–O(1)	2.278(4)	Sn(2)–O(2)	2.272(4)
Sn(1)–O(4)	2.174(4)	Sn(2)–O(4)^i	2.790(5)
Sn(1)–O(5)	2.810(5)	Sn(2)–O(7)	2.043(4)
Sn(1)–O(7)	2.030(4)	Sn(2)–O(7)^i	2.171(4)
Sn(1)–C(23)	2.132(7)	Sn(2)–C(31)	2.121(7)
Sn(1)–C(27)	2.135(7)	Sn(2)–C(35)	2.140(7)
O(1)–Sn(1)–O(4)	170.4(2)	O(2)–Sn(2)–O(7)^i	164.3(2)
O(1)–Sn(1)–O(5)	138.6(2)	O(2)–Sn(2)–C(31)	82.9(2)
O(1)–Sn(1)–O(7)	90.2(2)	O(2)–Sn(2)–C(35)	91.4(2)
O(1)–Sn(1)–C(23)	84.9(2)	O(4)^i–Sn(2)–O(7)	140.8(2)
O(1)–Sn(1)–C(27)	87.5(2)	O(4)^i–Sn(2)–O(7)^i	65.2(1)
O(4)–Sn(1)–O(5)	50.4(2)	O(4)^i–Sn(2)–C(31)	77.9(2)
O(4)–Sn(1)–O(7)	80.7(2)	O(4)^i–Sn(2)–C(35)	78.5(2)
O(4)–Sn(1)–C(23)	95.8(2)	O(7)–Sn(2)–O(7)^i	75.7(2)
O(4)–Sn(1)–C(27)	98.2(2)	O(7)–Sn(2)–C(31)	109.6(2)
O(5)–Sn(1)–O(7)	131.0(2)	O(7)–Sn(2)–C(35)	106.0(2)
O(5)–Sn(1)–C(23)	76.0(2)	O(7)^i–Sn(2)–C(31)	95.8(2)
O(5)–Sn(1)–C(27)	83.7(2)	O(7)^i–Sn(2)–C(35)	98.6(2)
O(7)–Sn(1)–C(23)	113.0(2)	C(31)–Sn(2)–C(35)	143.9(3)
O(7)–Sn(1)–C(27)	107.5(2)	Sn(1)–O(7)–Sn(2)	135.6(2)
C(23)–Sn(1)–C(27)	138.8(3)	Sn(1)–O(7)–Sn(2)^i	119.7(2)
O(2)–Sn(2)–O(4)^i	129.2(2)	Sn(2)–O(7)–Sn(2)^i	104.3(2)
O(2)–Sn(2)–O(7)	89.9(2)		

[a] Atom labels with superscript "i" refer to symmetrically-related atoms generated by the centre of inversion (symmetry code: $-x$, $-y$, $-z$).

O-atom from one carboxylate ligand and the carboxyl O-atom from a second carboxylate ligand. In addition, the carbonyl O-atom of the second carboxylate ligand coordinates weakly to Sn(2) with an Sn$\cdots$O distance of 2.986(3) Å, thus completing six-coordination in the extended coordination sphere of Sn(2) as well. In the carboxylate ligand that coordinates via its two carboxylate O-atoms, the phenolic hydroxy group forms an intraligand hydrogen bond with the adjacent N-atom. In the carboxylate ligand that coordinates via one carboxylate O-atom and the phenoxide O-atom, the phenolic hydroxy H-atom has migrated to the N-atom, thus forming a zwitterionic ligand. In this ligand, the protonated N-atom then forms an intraligand hydrogen bond back to the phenoxide O-atom.

Table 5
Selected bond lengths (Å) and angles (°) for diorganotin(IV) compound **6**[a]

Sn(1)–O(1)	2.232(3)	Sn(2)–O(7)	2.052(2)
Sn(1)–O(4)	2.174(3)	Sn(2)–O(7)[i]	2.171(2)
Sn(1)–O(5)	2.967(3)	Sn(1)–C(25)	2.138(4)
Sn(1)–O(7)	2.025(2)	Sn(1)–C(29a/b)	2.119(6)/2.120(5)
Sn(2)–O(2)	2.290(3)	Sn(2)–C(33)	2.135(3)
Sn(2)–O(4)[i]	2.676(3)	Sn(2)–C(37a/b)	2.150(5)/2.05(2)
O(1)–Sn(1)–O(4)	167.3(1)	O(2)–Sn(2)–O(7)[i]	164.4(1)
O(1)–Sn(1)–O(5)	144.61(9)	O(2)–Sn(2)–C(33)	84.6(1)
O(1)–Sn(1)–O(7)	89.38(9)	O(2)–Sn(2)–C(37a/b)	90.7(2)/77.1(4)
O(1)–Sn(1)–C(25)	89.8(2)	O(4)[i]–Sn(2)–O(7)	140.77(9)
O(1)–Sn(1)–C(29a/b)	85.9(8)/89.5(4)	O(4)[i]–Sn(2)–O(7)[i]	65.39(8)
O(4)–Sn(1)–O(5)	47.87(9)	O(4)[i]–Sn(2)–C(33)	81.7(1)
O(4)–Sn(1)–O(7)	78.28(9)	O(4)[i]–Sn(2)–C(37a/b)	72.7(1)/86.1(6)
O(4)–Sn(1)–C(25)	93.3(2)	O(7)–Sn(2)–O(7)[i]	75.9(1)
O(4)–Sn(1)–C(29a/b)	100.8(8)/97.1(4)	O(7)–Sn(2)–C(33)	108.0(1)
O(5)–Sn(1)–O(7)	126.00(8)	O(7)–Sn(2)–C(37a/b)	109.3(2)/103.0(7)
O(5)–Sn(1)–C(25)	75.7(1)	O(7)[i]–Sn(2)–C(33)	94.4(1)
O(5)–Sn(1)–C(29a/b)	81.3(7)/78.6(4)	O(7)[i]–Sn(2)–C(37a/b)	99.3(2)/111.3(4)
O(7)–Sn(1)–C(25)	117.0(1)	C(33)–Sn(2)–C(37a/b)	142.4(2)/143.7(6)
O(7)–Sn(1)–C(29a/b)	109.2(2)/109.6(3)	Sn(1)–O(7)–Sn(2)	136.6(1)
C(25)–Sn(1)–C(29a/b)	133.1(4)/133.8(2)	Sn(1)–O(7)–Sn(2)[i]	119.3(1)
O(2)–Sn(2)–O(4)[i]	129.51(9)	Sn(2)–O(7)–Sn(2)[i]	104.1(1)
O(2)–Sn(2)–O(7)	89.64(9)		

[a] Atom labels with superscript "i" refer to symmetrically-related atoms generated by the centre of inversion (symmetry code: $-x$, $1-y$, $-z$). Double entries refer to the alternate positions of atoms in the disordered butyl groups.

Complex **4** also forms a one-dimensional polymer in the solid state, but with only one Sn-atom and coordination motif in the repeat unit. The two carboxylate O atoms of a single alaninate ligand bridge two SnBu$_3$ moieties and the pattern then repeats itself to give a continuous single-stranded polymeric structure, as illustrated in Fig. 3. The primary coordination sphere of the Sn-atom has a slightly distorted *trans*-Bu$_3$SnO$_2$ trigonal bipyramidal geometry (Table 3) with equatorial butyl groups and carboxylate O atoms occupying axial positions, one being from each of two alaninate ligands. The carboxylate C–O bond lengths are not equivalent, which shows some distinction between the carbonyl and carboxylic acid O atoms. Correspondingly, the Sn–O bond lengths involving these O atoms are also not equivalent, with the Sn–O bond to the carbonyl O atom being the longer. The length of the intramolecular Sn···O(1) separation in **4** is 3.043(2) Å. Although this distance is well inside the sum of the van der Waals radii of the Sn and O atoms (ca. 3.6 Å), the trigonal bipyramidal coordination geometry of the primary coordination sphere distorted to only a small extent. The phenolic hydroxy group in each ligand forms an intraligand hydrogen bond with the adjacent N-atom.

The structure of **4** corresponds with the type **II** polymeric motif described by Willem et al. for similar R$_3$SnO$_2$CR′ compounds [50] and observed in the crystal structures of the closely related compounds (^{n}Bu$_3$Sn-[O$_2$CC$_6$H$_4$\{N=N(C$_6$H$_3$-4-OH-5-CHO)\}-o])$_n$ and (^{n}Bu$_3$Sn-[O$_2$CC$_6$H$_4$\{N=N(C$_6$H$_3$-4-OH(C(H)=NC$_6$H$_4$Cl-4))\}-o])$_n$ [57]. In **4**, the repeat Sn···Sn distance is 5.2166(2) Å, which agrees very well with the mean repeat distance found in other type **II** carboxylate-bridged triorganotin species of

5.19 ± 0.21 Å [58] and shows that the repeat distance is independent of the nature of the tin-bound substituents and carboxylate residues. As in the earlier reports [50,57], the polymeric chain in the structure of **4** propagates in a 2$_1$ screw fashion coincident with a crystallographic 2$_1$ screw axis. As complexes **1** and **4** involve the same carboxylate ligand, the different structural motifs observed are most likely a result of the spatial influence of the different R ligands in the SnR$_3$ moiety; i.e., butyl versus phenyl.

The crystal structure determination of **5** and **6** confirmed the bis(dicarboxylatotetraorganodistannoxane) formulation (Figs. 4 and 5). The molecules are centrosymmetric tetranuclear complexes containing a planar Sn$_4$O$_2$ core in which two μ$_3$-oxo O-atoms connect an Sn$_2$O$_2$ ring to two exocyclic Sn-atoms. Two carboxylate ligands each bridge one endocyclic to one exocyclic Sn-centre via the two carboxylate O-atoms, with the Sn–O distances being quite similar (Tables 4 and 5). Two additional carboxylate ligands each have asymmetric bidentate coordination via the two carboxylate O-atoms to an exocyclic Sn-atom, with the longer Sn···O interactions being quite long: 2.810(5) Å in **5** and 2.967(3) Å in **6**. Additionally, the other carboxylate O-atom in each of these ligands coordinates via a second long Sn···O bond [2.790(5) Å in **5** and 2.676(3) Å in **6**] to an endocyclic Sn-atom. Each Sn-atom is also coordinated by two butyl groups. Each Sn-atom, therefore, has six coordination, excluding the central Sn···Sn contact of 3.3277(7) Å in **5** and 3.3320(4) Å in **6**. However, the primary coordination sphere at each Sn-atom looks more like a slightly distorted trigonal bipyramid than an octahedron. In this description, the butyl groups always occupy equatorial positions. The sixth coordination site is then occupied

Table 6
In vitro ID_{50} values (ng/ml) of test compound **5** along with some reported $\{[^nBu_2Sn(L)]_2O\}_2$ compounds used a cell viability test in seven human tumour cell lines[a]

Test compound[b]	Cell lines						
	A498	EVSA-T	H226	IGROV	M19 MEL	MCF-7	WIDR
$\{[^nBu_2Sn(2\text{-}OHC_6H_4C(CH_3)=N(CH_2)_2COO)]_2O\}_2$ (**5**)	376	34	237	174	225	147	895
DOX	51	26	20	120	80	21	36
CDDP	539	251	650	72	980	480	491
5-FU	146	382	531	799	495	373	556
MTX	44	10	168	285	45	15	15
ETO	119	395	159	1387	1513	296	457
TAX	25	4	5	78	14	3	5
$\{[(CH_3CH(OH)COO)^nBu_2Sn]_2O\}_2$ [61]	–	–	–	–	–	60	248
$\{[(C_6H_5CH(OH)COO)^nBu_2Sn]_2O\}_2$ [61]	–	–	–	–	–	54	210
$\{[(C_6H_4(2\text{-}OCH_3)COO)^nBu_2Sn]_2O\}_2$ [62]	–	–	–	–	–	156	1661
CDDP	–	–	–	–	–	850	624
DOX	–	–	–	–	–	63	31
ETO	–	–	–	–	–	187	624
$\{[(C_6H_3(3\text{-}CH_3)(2\text{-}OH)COO)^nBu_2Sn]_2O\}_2$ [63]	–	–	–	–	–	44	330
$\{[(C_6H_3(4\text{-}CH_3)(2\text{-}OH)COO)^nBu_2Sn]_2O\}_2$ [63]	–	–	–	–	–	51	316
$\{[(C_6H_3(4\text{-}OCH_3)(2\text{-}OH)COO)^nBu_2Sn]_2O\}_2$ [64]	–	–	–	–	–	190	1794
$\{[(C_6H_3(5\text{-}OCH_3)(2\text{-}OH)COO)^nBu_2Sn]_2O\}_2$ [63]	–	–	–	–	–	29	122
$\{[(C_6H_3(4\text{-}NH_2)(2\text{-}OH)COO)^nBu_2Sn]_2O\}_2$ [63]	–	–	–	–	–	42	330
$\{[(C_6H_3(5\text{-}Cl)(2\text{-}OH)COO)^nBu_2Sn]_2O\}_2$ [64]	–	–	–	–	–	31	280
CDDP	–	–	–	–	–	850	624
$\{[(C_{23}H_{38}(OH)COO)^nBu_2Sn]_2O\}_2$ [21]	220	60	420	160	120	160	390
CDDP	2253	422	3269	169	558	699	967
DOX	90	8	199	60	16	10	11

[a] *Abbreviation*: DOX, doxorubicin; CDDP, cisplatin; 5-FU, 5-fluorouracil; MTX, methotrexate; ETO, etoposide and TAX, paclitaxel.
[b] Standard drug reference values are cited immediately after the test compounds under identical conditions.

by one of the longer Sn···O interactions, which approaches in rather a skew manner, presumably as a result of bite angle constraints. In **5** and **6**, the *exo*-Sn···*endo*-Sn distances are 3.6322(7) and 3.7711(7) Å and 3.6209(4) and 3.7870(4) Å, respectively. The Sn_4O_{10} core of the molecule forms an essentially planar system, but the remaining atoms of the carboxylate ligands, as well as the butyl ligands extend roughly perpendicular to this plane. In **6**, one butyl group on each Sn-atom is disordered over two conformations. The phenolic hydroxy group in each carboxylate ligand forms an intraligand hydrogen bond with the adjacent N-atom.

The bis(dicarboxylatotetraorganodistannoxane) motif occurs frequently amongst dialkyltin(IV) carboxylate complexes. The Cambridge Structural Database [59] contains 80 entries for such structures and, in all of these structures, the Sn-coordination geometry, as well as the distribution of Sn–O distances, is usually much the same. The structure of the methylidine analogue of the ethylidine complex, **5**, namely bis[(μ₃-oxo)-(μ₂-2-hydroxyphenylmethylimino-β-alaninato-O,O')-(2-hydroxyphenylmethylimino-β-alaninato-O)-tetra-*n*-butylditin], is, apart from the missing methyl group, in all other respects the same as that of **5** [60].

3.4. In vitro cytotoxicity

The results of the in vitro cytotoxic tests performed with a representative compound, **5**, are summarized in Table 6 and the screening results are compared with the results from other related di-*n*-butyltin(IV) compounds of the bis(dicarboxylatotetraorganodistannoxane) type, $\{[^nBu_2Sn(LH)]_2O\}_2$, with respect to the standard drugs that are in current clinical use as antitumour agents. In general, the $\{[^nBu_2Sn(LH)]_2O\}_2$ compounds have shown quite promising antitumour activity (see Table 6) [61–64], especially when compared with CDDP (cisplatin). This encouraging in vitro cytotoxic effect may be predictive of in vivo antitumour activity. Compound **5** may be a suitable candidate for modification in order to improve cytotoxic and dissolution properties.

4. Supplementary material

CCDC nos. 263959–263962 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

Acknowledgments

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