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Synthesis, structural characterization and cytotoxic activity of diorganotin(IV) complexes of *N*-(5-halosalicylidene)tryptophane

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Four new diorganotin(IV) complexes of *N*-(5-halosalicylidene)tryptophane, R_2Sn[5-X-2-OC_6H_3CH=NCH(CH_2Ind)COO] [Ind = 3-indolyl; R, X = Et, Cl (1); Et, Br(2); *n*-Bu, Cl (3); *n*-Bu, Br (4)], were synthesized and characterized by elemental analysis, IR and NMR (^{1}H, ^{13}C and ^{119}Sn) spectra. The crystal structures of complexes 1–3 were determined by X-ray single crystal diffraction and showed that the tin atoms are in a distorted trigonal bipyramidal geometry and form five- and six-membered chelate rings with the tridentate ligand. Intermolecular weak interactions in 1–3 link molecules, respectively, into a two-dimensional array, a one-dimensional infinite chain and a one-dimensional double-chain supramolecular structure. Bioassay results of the compounds indicated that the dibutyltin complexes 3 and 4 have potent *in vitro* cytotoxic activity against two human tumor cell lines, CoLo205 and Bcap37, while the diethyltin complexes 1 and 2 display weak cytotoxic activity.

Supporting information may be found in the online version of this article.

Keywords: organotin complex; α-amino acid; tryptophane; *in vitro* cytotoxic activity; crystal structure

Introduction

In recent years, organotin carboxylates have received considerable attention due to their structural diversity[1–4] and biological properties, particularly cytotoxicity/antitumor activity[5–7]. *N*-Salicylidene-α-amino acid and its analogs are very versatile ligands, creating the possibility of a variety of coordination modes, and some of their diorganotin complexes have been synthesized and structurally characterized by several groups.[8–17] Structural studies have shown that the diorganotin complexes of these ligands adopt isolated monomeric structures with the tin atom in a distorted trigonal bipyramid and the dimeric, trimeric and polymeric structures with the tin atom in a distorted octahedron or a distorted pentagonal bipyramid in solid state.[8–12,14–17] Bioassay studies showed that the class of diorganotin complexes possesses significant cytotoxic activity against some human tumor cell lines.[13] In general, the organotin moiety, the ligand and the number of tin atoms appear to play an important role in determining their cytotoxicity activity.[5–7] In order to continue to expand the chemistry and therapeutic potential of the diorganotin(IV) complexes of the ligands and develop a correlation between structure and cytotoxic activity, more recently, we have reported the synthesis and cytotoxicity of some diorganotin(IV) complexes with *N*-(halosalicylidene)-α-amino acid.[18–20] As a continuation of our work, here we selected *N*—(5-halosalicylidene)tryptophane containing the nitrogen-heterocycle as a ligand, synthesized four new dialkyltin complexes, R_2Sn[5-X-2-OC_6H_3CH=NCH(CH_2Ind)COO] [Ind = 3-indolyl; R, X = Et, Cl (**1**); Et, Br(**2**); *n*-Bu, Cl (**3**); *n*-Bu, Br (**4**)] (Scheme 1), discussed their supramolecular structures and determined their cytotoxic activity.

Experimental

Materials and physical measurements

Diethyltin dichloride was prepared according to method reported in the literature.[21] Dibutyltin dichloride (Fluka) and other chemicals were of reagent grade and were used without further purification. Carbon, hydrogen and nitrogen analyses were obtained using a Perkin Elmer 2400 Series II elemental analyzer. The melting points were measured on a WRS-1A digital melting point apparatus. IR spectra were recorded on a Nicolet 470 FT-IR spectrophotometer using KBr discs in the range 4000–400 cm^{-1}. ^{1}H NMR spectral data were collected using a Bruker Avance DPX300 FT-NMR spectrometer with $CDCl_3$ as solvent and TMS as internal standard. ^{119}Sn NMR spectra were recorded in $CDCl_3$ on a Varian Mercury Vx300 spectrometer using Me_4Sn external reference.

Synthesis of the title complexes 1–4

Potassium hydroxide (0.112 g, 2 mmol) and L-tryptophan (0.408 g, 2 mmol) were added in methanol (60 ml). The mixed solution

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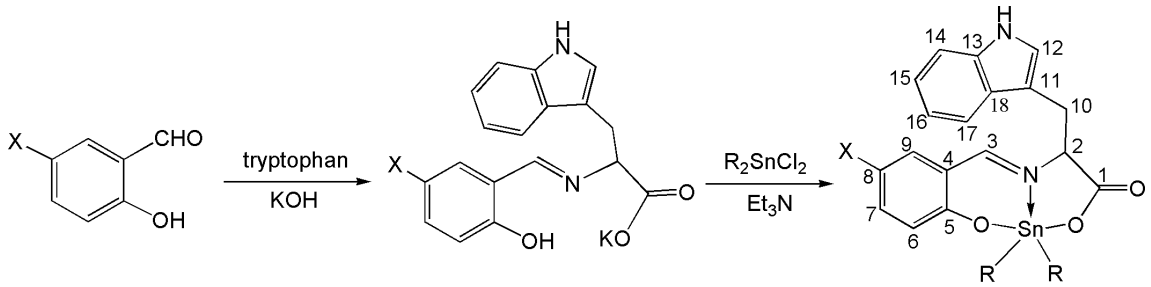

Scheme 1. Synthetic route of compounds **1**–**4**.

was heated with continuous stirring until the solid disappeared, and then a methanolic solution (20 ml) of 5-halosalicylaldehyde (2 mmol) was added dropwise. A deep-yellow color developed almost immediately and stirring was continued for 30 min at room temperature. A methanol solution (15 ml) of diethyltin dichloride (0.496 g, 2 mmol) or dibuthyltin dichloride (0.608 g, 2 mmol) and Et_3N (0.202 g, 2 mmol) was added to the yellow mixture. The reaction mixture was refluxed for 2 h, and the solvent was then removed using a rotary evaporator. The residues was extracted into dichloromethane and filtered. A yellow product was obtained by removal of solvent under reduced pressure, and recrystallized from methanol and dried in vacuum.

*Et_2Sn[5-Cl-2-OC_6H_3CH=NCH(CH_2Ind)COO] (**1**)*

Yield 74%, m.p. 188.3–190.0 °C. Anal. calcd for $C_{22}H_{23}N_2O_3ClSn$: C, 51.06; H, 4.48; N, 5.41. Found: C, 50.98; H, 4.36; N, 5.38. IR (KBr) cm^{-1}: 3257 (N–H), 1668 [$(COO)_{as}$], 1615 (C=N), 1458 [$(COO)_s$], 1297 (Ph–O), 553 (Sn–O). ^{1}H NMR δ: 1.13 (t, J = 8.0 Hz, 3H, CH_3), 1.31–1.44 (m, 7H, CH_3 + $2CH_2Sn$), 3.01 (dd, J = 10.0, 14.6 Hz, 1H, H-10), 3.82 (dd, J = 3.1, 14.6 Hz, 1H, H-10), 4.21(dd, J = 3.1, 10.0 Hz, 1H, H-2), 6.46–7.65 (m, 8H, Ar–H), 7.06 [s, $J(^{119}Sn–H)$ = 50.0 Hz, 1H, H-3], 8.33 (br, s, 1H, NH) ppm. ^{119}Sn NMR δ: −193.2 ppm. ^{13}C NMR δ: 174.04 (C-1), 171.37 (C-3), 167.96 (C-5), 137.66 (C-7), 133.44 (C-9), 124.32 (C-8), 121.25 (C-4), 117.45 (C-6), 136.82, 126.89, 124.97, 123.04, 120.50, 118.91, 112.06, 109.13 (indole-C), 69.04 (C-2), 32.62 (C-10), 14.40 [$^1J(^{119/117}Sn–^{13}C)$ = 601/572 Hz, CH_2Sn], 14.02 [$^1J(^{119/117}Sn–^{13}C)$ = 584/557 Hz, CH_2Sn], 9.58 [$^2J(^{119}Sn–^{13}C)$ = 30 Hz, CH_3], 9.28 [$^2J(^{119}Sn–^{13}C)$ = 29 Hz, CH_3] ppm.

*Et_2Sn[5-Br-2-OC_6H_3CH=NCH(CH_2Ind)COO] (**2**)*

Yield 72%, m.p. 178.4–179.6 °C. Anal. calcd for $C_{22}H_{23}N_2O_3BrSn$: C, 47.01; H, 4.12; N, 4.98. Found: C, 46.89; H, 4.06; N, 4.90. IR (KBr, cm^{-1}): 3260 (N–H), 1664 [$(COO)_{as}$], 1610 (C=N), 1408 [$(COO)_s$], 1293 (Ph–O), 547 (Sn–O). ^{1}H NMR δ: 1.14 (t, J = 7.8 Hz, 3H, CH_3), 1.33–1.49 (m, 7H, CH_3 + $2CH_2Sn$), 3.00 (dd, J = 10.1, 14.7 Hz, 1H, H-10), 3.83 (dd, J = 3.2, 14.7 Hz, 1H, H-10), 4.23 (dd, J = 3.2, 10.1 Hz, 1H, H-2), 6.73–7.65 (m, 8H, Ar–H), 7.02 [s, $J(^{119}Sn–H)$ = 41.3 Hz, 1H, H-3], 8.39 (br, s, 1H, NH) ppm. ^{119}Sn NMR δ: −192.2 ppm. ^{13}C NMR δ: 174.04 (C-1), 171.32 (C-3), 168.01 (C-5), 140.06 (C-7), 136.44 (C-9), 124.56 (C-8), 118.35 (C-4), 108.09 (C-6), 136.82, 126.71, 124.89, 123.01, 120.46, 118.81, 111.96, 109.19 (indole-C), 69.14 (C-2), 32.58 (C-10), 21.38 [$^1J(^{119/117}Sn–^{13}C)$ = 608/578 Hz, CH_2Sn], 21.02 [$^1J(^{119/117}Sn–^{13}C)$ = 589/560 Hz, CH_2Sn], 12.26 [$^2J(^{119}Sn–^{13}C)$ = 30 Hz, CH_3], 12.09 [$^2J(^{119}Sn–^{13}C)$ = 30 Hz, CH_3] ppm.

*n−Bu_2Sn[5-Cl-2-OC_6H_3CH=NCH(CH_2Ind)COO] (**3**)*

Yield 63%, m.p. 169.3–170.1 °C. Anal. calcd for $C_{26}H_{31}ClN_2O_3Sn$: C, 54.43; H, 5.45; N, 4.88. Found: C, 54.59; H, 5.36; N, 4.87. IR (KBr) cm^{-1}: 3255 (N–H), 1670 [$(COO)_{as}$], 1613 (C=N), 1441 [$(COO)_s$], 1291 (Ph–O), 560 (Sn–O). ^{1}H NMR δ: 0.79 (t, J = 7.3 Hz, 3H, CH_3), 0.93 (t, J = 7.3 Hz, 3H, CH_3), 1.23–1.88 [m, 12H, $(CH_2CH_2CH_2)_2Sn$], 3.05 (dd, J = 9.7, 14.7 Hz, 1H, H-10), 3.77 (dd, J = 3.2, 14.7 Hz, 1H, H-10), 4.23 (dd, J = 3.2, 9.6 Hz, 1H, H-2), 6.54–7.59 (m, 8H, Ar–H), 7.16 [s, $J(^{119}Sn–H)$ = 47.1 Hz, 1H, H-3], 8.65 (br, s, 1H, NH) ppm. ^{119}Sn NMR δ: −199.3 ppm. ^{13}C NMR 173.96 (C-1), 171.16 (C-3), 167.92 (C-5), 137.46 (C-7), 133.34 (C-9), 124.22 (C-8), 121.25 (C-4), 117.44 (C-6), 136.77, 126.73, 124.87, 122.98, 120.45, 118.79, 111.96, 109.14 (indole-C), 69.15 (C-2), 32.59 (C-10), 27.19 [$^2J(^{119}Sn–^{13}C)$ = 28 Hz, CH_2-β], 27.04 (CH_2-β), 26.86 [$^3J(^{119}Sn–^{13}C)$ = 92 Hz, CH_2-γ], 26.67 [$^3J(^{119}Sn–^{13}C)$ = 90 Hz, CH_2-γ], 22.29 [$^1J(^{119/117}Sn–^{13}C)$ = 613/587 Hz, CH_2-α], 21.95 [$^1J(^{119/117}Sn–^{13}C)$ = 598/571 Hz, CH_2-α], 13.78 (CH_3), 13.66 (CH_3) ppm.

*n−Bu_2Sn[5-Br-2-OC_6H_3CH=NCH(CH_2Ind)COO] (**4**)*

Yield 68%, m.p. 175.6–177.3 °C. Anal. calcd for $C_{26}H_{31}BrN_2O_3Sn$: C, 50.52; H, 5.05; N, 4.53. Found: C, 50.59; H, 4.93; N, 4.36. IR (KBr) cm^{-1}: 3240 (N–H), 1658 [$(COO)_{as}$], 1606 (C=N), 1415 [$(COO)_s$], 1301 (Ph–O), 558 (Sn–O). ^{1}H NMR δ: 0.82 (t, J = 7.3 Hz, 3H, CH_3), 0.96 (t, J = 7.3 Hz, 3H, CH_3), 1.24–1.74 (m, 12H, $(CH_2CH_2CH_2)_2Sn$], 3.01 (dd, J = 10.0, 14.7 Hz, 1H, H-10), 3.81 (dd, J = 3.1, 14.7 Hz, 1H, H-10), 4.24 (dd, J = 3.1, 10.0 Hz, 1H, H-2), 6.94–7.62 (m, 8H, Ar–H), 7.08 [s, $J(^{119}Sn–H)$ = 39.6 Hz, 1H, H-3], 8.51 (br, s, 1H, NH) ppm. ^{119}Sn NMR δ: −198.4 ppm. ^{13}C NMR 173.95 (C-1), 171.14 (C-3), 168.49 (C-5), 140.07 (C-7), 136.42 (C-9), 124.56 (C-8), 118.40 (C-4), 108.07 (C-6), 136.76, 126.71, 124.87, 122.96, 120.45, 118.80, 112.01, 109.12 (indole-C), 69.13 (C-2), 32.56 (C-3), 26.89 [$^2J(^{119}Sn–^{13}C)$ = 27 Hz, CH_2-β], 26.78 (CH_2-β), 26.57 [$^3J(^{119}Sn–^{13}C)$ = 88 Hz, CH_2-γ], 26.43 [$^3J(^{119}Sn–^{13}C)$ = 86 Hz, CH_2-γ], 22.71 [$^1J(^{119/117}Sn–^{13}C)$ = 604/576 Hz, CH_2-α], 22.03 [$^1J(^{119/117}Sn–^{13}C)$ = 592/565 Hz, CH_2-α], 13.51 (CH_3), 13.43 (CH_3) ppm.

X-ray crystallography

Yellow single crystals of compounds **1** (0.12 × 0.28 × 0.26 mm), **2** (0.02 × 0.18 × 0.30 mm) and **3** (0.11 × 0.28 × 0.32 mm) were obtained from the slow evaporation of methanol solution of the respective compounds. Intensity data for the crystals were measured at 295(2) K on a Bruker Smart Apex area-detector fitted with graphite monochromatized Mo–$K\alpha$ radiation (0.71073 Å) using the φ and ω scan technique. Empirical corrections for absorption effects were made using the SADABS program.[22] The structures were solved by direct-methods[23] and refined by a

Table 1. Crystallographic and refinement data for **1**, **2** and **3**

	1	**2**	**3**
Empirical formula	$C_{22}H_{23}ClN_2O_3Sn$	$C_{22}H_{23}BrN_2O_3Sn$	$C_{26}H_{31}ClN_2O_3Sn$
Formula weight	517.56	562.02	573.67
Crystal system	Monoclinic	Monoclinic	Triclinic
Space group	$C2/c$	$P2_1/c$	$P-1$
a (Å)	32.167(2)	13.649(4)	10.4386(13)
b (Å)	11.0328(8)	9.074(2)	11.9157(15)
c (Å)	13.0435(9)	18.422(5)	12.2683(15)
α (deg)	90	90	67.534(2)
β (deg)	110.340(1)	101.441(4)	76.326(2)
γ (deg)	90	90	64.489(2)
Volume (Å^3)	4340.5(5)	2236.3(10)	1267.9(3)
Z	8	4	2
D_c(g/cm^3)	1.584	1.669	1.503
μ(mm^{-1})	1.326	2.954	1.142
F(000)	2080	1112	584
θ range for data collection (deg)	1.4–26.0	1.5–26.0	1.8–25.0
Reflections collected	16 630	16 813	6166
Independent reflections	4260 ($R_{int} = 0.018$)	4381 ($R_{int} = 0.032$)	4219 ($R_{int} = 0.016$)
Data with $I > 2\sigma$ (I)	3923	3735	3886
Goodness-of-fit on F^2	1.05	1.05	1.04
Final R indices [$I > 2\sigma$ (I)]	$R = 0.023$, $Rw = 0.061$	$R = 0.032$, $Rw = 0.077$	$R = 0.032$, $Rw = 0.081$
R indices (all data)	$R = 0.025$, $Rw = 0.062$	$R = 0.039$, $Rw = 0.081$	$R = 0.035$, $Rw = 0.083$
CCDC deposition no.	698 875	698 874	685 522

full-matrix least squares procedure based on F^2 using SHELXL-97.[23] The non-hydrogen atoms were refined anisotropically and hydrogen atoms were placed at calculated positions in the riding model approximation. Crystallographic parameters and refinements are listed in Table 1.

In vitro cytotoxicity

Cytotoxic activity was assayed against two human tumor cell lines, CoLo 205 (colon carcinoma cell) and Bcap37 (mammary tumor cell). The samples were prepared by dissolving the test compounds in DMSO, and by diluting the resultant solutions with water. In the assays, the final concentration of DMSO was less than 0.1% (the concentration used was found to be non-cytotoxic against tumor cells). *In vitro* cytotoxic activity of the compounds was measured by the MTT (3-[4,5-dimethylthiazol-2-yl]-2,5-diphenyltetrazolium bromide) assay according to the literature.[24] All cells were cultured in DMEM (Dulbecco's modified eagle medium) supplemented with 10% heat-inactivated newborn calf serum at 37 °C in a humidified 5% CO_2 incubator and were seeded into each well of 96-well plate and were fixed for 24 h. The following day, different concentrations of the test compounds were added. After incubation with various concentrations of test compounds for 72 h, the inhibition on cell proliferation was measured. The experiments were conducted in triplicate for each tested concentration. The dose causing 50% inhibition of cell growth (IC_{50}) was calculated by NDST software as previously described.[25]

Results and Discussion

Diethyltin or dibutyltin dichloride reacted with potassium *N*-(5-halosalicylidene)tryptophanate *in situ* formed by condensation of 5-halosalicylaldehyde and L-tryptophan in the presence of KOH, to afford compounds **1–4**, respectively (Scheme 1). The complexes are yellow crystalline solids that are soluble in common organic solvents such as benzene, chloroform, dichloromethane, methanol, ethanol, acetone and tetrahydrofuran, but insoluble in water and in saturated aliphatic hydrocarbons.

IR spectra

The infrared spectra do not show a strong band at 3500–3300 cm^{-1} indicating the deprotonation of the phenolic oxygen upon complexation.[13] This conclusion is further supported by the appearance of a sharp band at ~550 cm^{-1}, assignable to the Sn–O stretching vibration.[13,26] The NH stretching vibration of indolyl in the tryptophan fragment as a medium strong band lies in the range of 3240–3260 cm^{-1}. In all compounds, the ν(C=N) absorption appears as a strong band at ~1610 cm^{-1} and is consistent with C=N → Sn coordination.[9] The stretching frequencies of carboxylate have been used to distinguish the coordination mode of the carboxylate group and to identify the nature of bonding[27,28] as the $\Delta\nu[\nu_{as}(CO_2) - \nu_s(CO_2)]$ value is below 200 cm^{-1} for bidentate coordination and above 200 cm^{-1} for the unidentate coordination. The difference between the $\nu_{as}(CO_2)$ and $\nu_s(CO_2)$ bands in **1–4** is in the range 210–256 cm^{-1}, indicating an unidentate carboxylate moiety. Thus, it is concluded that the compounds feature five-coordinated tin in the solid, consistent with the X-ray structural analysis (see below). In chloroform, $\Delta\nu[\nu_{as}(CO_2) - \nu_s(CO_2)]$ value of **1–4** is 222, 263, 238 and 250 cm^{-1}, respectively, indicating that the carboxylate group is also unidentate coordination to tin in solution.

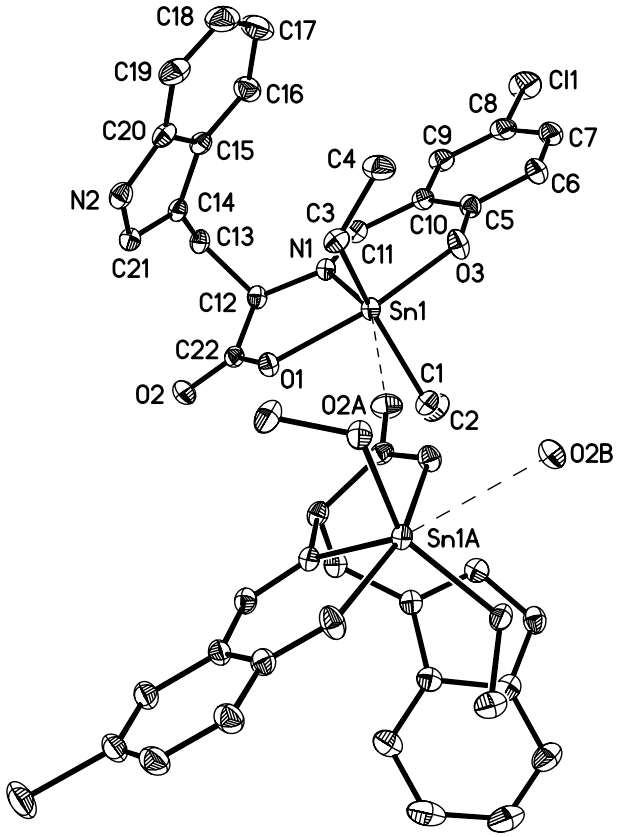

Figure 1. The molecular structure of **1** showing a weak Sn1$\cdots$ O2$^{\#1}$ (symmetry code #1: $^1/_2 - X, ^1/_2 + Y, 1^1/_2 - Z$ interaction; hydrogen atoms are omitted for clarity.

NMR spectra

The ^{1}H and ^{13}C chemical shift assignments of the compounds are straightforward from the multiplicity of patterns and resonance intensities, and are consistent with the literature.[16,18] The NH proton of the indole ring appears as a broad singlet in the range of δ 8.33–8.65 ppm. The signal assigned to azomethine proton N=CH (H-3) lies in the range δ 7.06–7.16 ppm which is shifted to lower frequencies compared with the general chemical shift value of N=CH proton ($\delta\sim$8.25) owing to the shielding effect of the indole ring.[16,18] The appearance of spin–spin coupling between the azomethine proton and the tin nucleus [$^3J(^{119}\text{Sn}-\text{H}) = 40-50$ Hz] further confirms the presence of nitrogen-tin coordination in all complexes. The CH–N (H-2) proton exhibits a doublet of doublets at about δ 4.23 ppm. The signals of the carboxyl carbon (C-1), imine carbon (C-3), and C-N (C-2) appear at *ca* 174, 171 and 69 ppm, respectively. In **1**–**4**, the coupling between tin nuclear and carbon can be observed, and the $^1J(^{119}\text{Sn}-^{13}\text{C})$, $^2J(^{119}\text{Sn}-^{13}\text{C})$ and $^3J(^{119}\text{Sn}-^{13}\text{C})$ is respectively in the range 613–584, 27–30 and 86–92 Hz. The value of $^1J(^{119}\text{Sn}-^{13}\text{C})$ indicates that the tin atom of each complex is five-coordinated in the $CDCl_3$ solution.[10] According to the equation, $^1J(^{119}\text{Sn}-^{13}\text{C}) = 9.99\ (\pm 0.73)\theta - 746\ (\pm\ 100)$,[29] the estimated value of the C–Sn–C angle (θ) from $^1J(^{119}\text{Sn}-^{13}\text{C})$ is 136.0–133.1°, suggesting that the tin atom has a slightly distorted trigonal bipyramid geometry in non-coordinating solvents. The complexes **1**–**4** display two sets of ^{1}H and ^{13}C NMR signals from the Sn–R groups (R = Et, *n*-Bu), indicating that the two R groups experience different environments on the NMR time scale due to the presence of a stereogenic carbon in the ligand.[10,16] 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.[30] The ^{119}Sn chemical shifts of the complexes are in the range δ −192.2 to −199.3 ppm, further confirming a five-coordinated tin structure in solution.[29]

Crystal structures of compounds 1–3

The molecular structures of compounds**1**–**3** is shown in Figs 1–6, and the selected geometric parameters are given in Table 2. In **1**, the coordination geometry of the tin atom is a distorted trigonal bipyramid with two carbons of ethyl groups and an N1 atom from the ligand defining the trigonal plane and a phenolic O3 and a carboxylic O1 atom occupying the axial positions (Fig. 1). The tin atom is 0.0401(1) Å out of the NC_2 trigonal plane in the direction of the more tightly held O3 atom. The tin atom forms a five-membered and a six-membered chelate ring with the tridentate ligand. The six-membered ring is nearly planar with the largest deviation of −0.042(2) Å at N1 from the mean plane. The Sn1–O3–C5–10 and Sn1–N1–C11–C10 torsion angles are 0.5(4) and −6.9(4)°, respectively. The five-membered ring formed upon chelation is not planar as seen in the following torsion angles Sn1–O1–C22–C12 [−14.1(4)°] and Sn1–N1–C12–C22 [−8.0(2)°]. The Sn1–N1 [2.1934(16) Å] and Sn1–O1[2.1754(15) Å] bond distances are longer than those found in $Bu_2Sn[OC_6H_4CH{=}NCH(CH_2Ind)COO]$ [2.161(3) and 2.162(3) Å] and $Bu_2Sn[OC_6H_4CH{=}NCH(i\text{-}Pr)COO]$ [2.154(8) and 2.158(8) Å].[16,17] The axial bond angle O1–Sn–O3 [158.33(6)°] is consistent with that of the literature structures[16,17] [158.75(11) and 156.0(4)°, respectively], but the three angles, C1–Sn1–N1 [106.00(8)°], C3–Sn1–N1 [109.70(8)°] and C1–Sn1–C3 [144.18(9)°], in the trigonal plane are clearly different from those in the two structures [113.12(15), 120.24(14), 126.55(17)° and 108.6(5), 124.9(4), 126.1(6)°].[16,17] This key difference is explained in the following terms. In **1**, there exists a long Sn1$\cdots$ O2$^{\#1}$ contact of 3.017(2) Å between the Sn1 and the carbonyl O2 (symmetry code #1: −x + 1/2, *y* + 1/2, −*z*+ 1/2) of the ligand of a neighboring complex, which is considerably longer

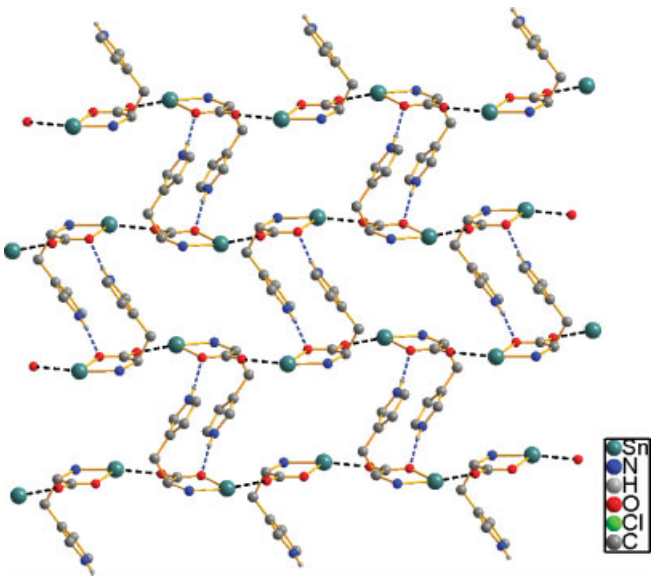

Figure 2. The two-dimensional supramolecular array along the *a* axis in **1**. Except for the partial atoms of tryptophane fragments, other atoms around tin are omitted for clarity.

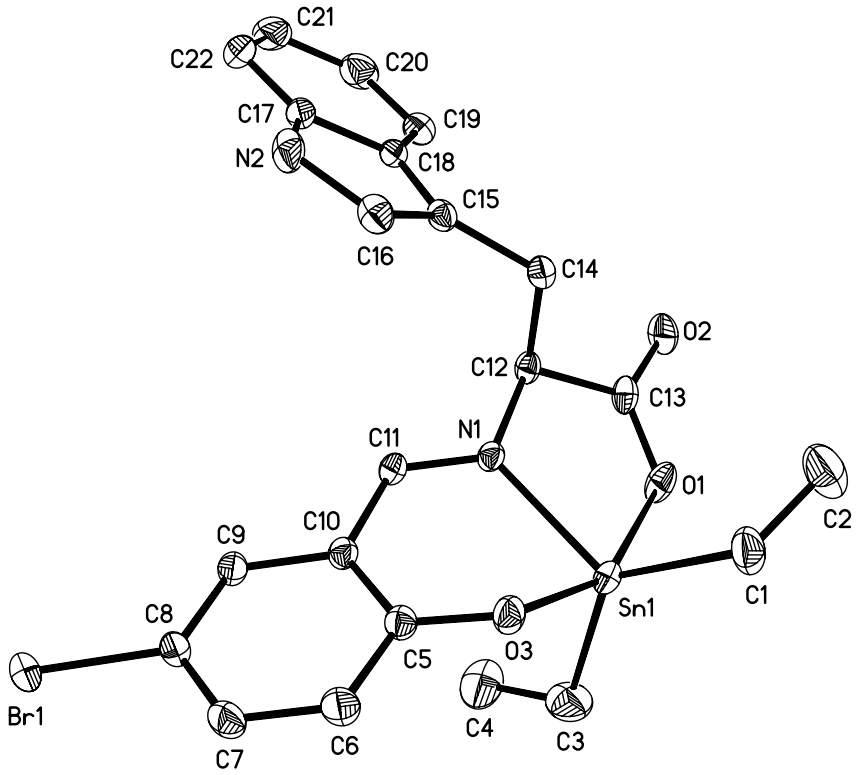

Figure 3. The molecular structure of **2**; hydrogen atoms are omitted for clarity.

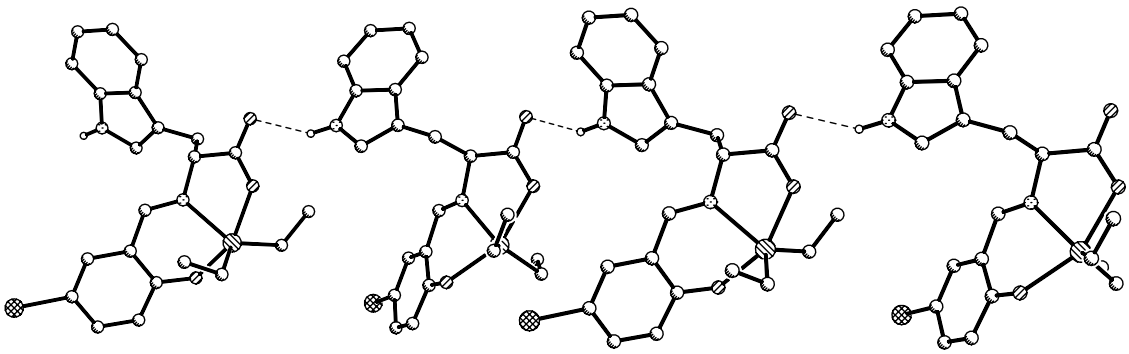

Figure 4. The one-dimensional chain in **2** formed by intermolecular N–H· · · O hydrogen bonds along the *b* axis; hydrogen atoms are omitted for clarity.

than a normal Sn ← O coordination bond (∼2.40 Å),[10,11] but much shorter than the sum of the van der Waals radii of these atoms (3.77 Å).[31] The major stereochemical role of the $O2^{\#1}$ atom is to distort the trigonal bipyramid geometry by opening up the C1–Sn1–C3 angle with concomitant reduction of the C1–Sn1–N1 and C3–Sn1–N1 angles. By the weak Sn· · · O interaction the distorted trigonal bipyramidal units are linked into infinite zigzag bridged chains. Two molecules between the one-dimensional chains are arranged about a center of inversion and produced a cyclic dimmer by two N–H· · · O hydrogen bonds involving the indolyl N–H and carboxylate O1 atom [H2· · · $O1^{\#2}$ 2.08 Å, N2· · · $O1^{\#2}$ 2.932(2) Å, N2–H2· · · $O1^{\#2}$ 174°, symmetry code #2: $-x+1/2, -y+1/2+1, -z+1$]. Thus, in the crystal of **1**, a two-dimensional supramolecular network was formed by the Sn1· · · $O2^{\#1}$ weak interaction and intermolecular N–H· · · O hydrogen bonds, N2–H2· · · $O1^{\#2}$ and $N2^{\#2}$–$H2^{\#2}$· · · O1 (Fig. 2). The dihedral angle between the salicylidene fragment and indole ring is 57.79(4)°. The unidentate mode of coordination of carboxylate group is also reflected in the disparate C22–O1 and C22–O2 bond lengths of 1.287(3) and 1.224(3) Å, respectively.

As shown in Fig. 3 the tin atom of compound **2** also is five-coordinated and has distorted trigonal bipyramidal geometry. The tin atom lies 0.0587(3) Å out of the NC_2 trigonal plane in the direction of the more tightly held O3 atom. The bond angles and bond distances around tin atom are comparable to those observed in the related dibutyltin complexes such as $Bu_2Sn[OC_6H_4CH{=}NCH(i\text{-}Pr)COO]$,[15,16] $Bu_2Sn[OC_6H_4CH{=}NCH(CH_2Ind)COO]$,[17] $Bu_2Sn[OC_6H_4CH{=}NCH(s\text{-}Bu)COO]$,[16] $Bu_2Sn[5\text{-}Cl\text{-}2\text{-}OC_6H_4CH{=}NCH(i\text{-}Pr)COO]$,[18] and $Bu_2Sn[3,5\text{-}Br_2\text{-}2\text{-}OC_6H_4CH{=}NCH(i\text{-}Pr)COO]$.[20] However, the values are clearly different from those of compound **1**. In compound **2**, the closest intermolecular Sn and O contact is Sn1· · · $O2^{\#1}$ (symmetry code #1: $-x$, $1\frac{1}{2}+y$, $\frac{1}{2}-z$) 4.587(4) Å, indicating no significant interaction exists. Neither the five- nor six-membered chelate rings are planar; the most deviated atom from the five-membered ring mean plane and the six-membered ring mean

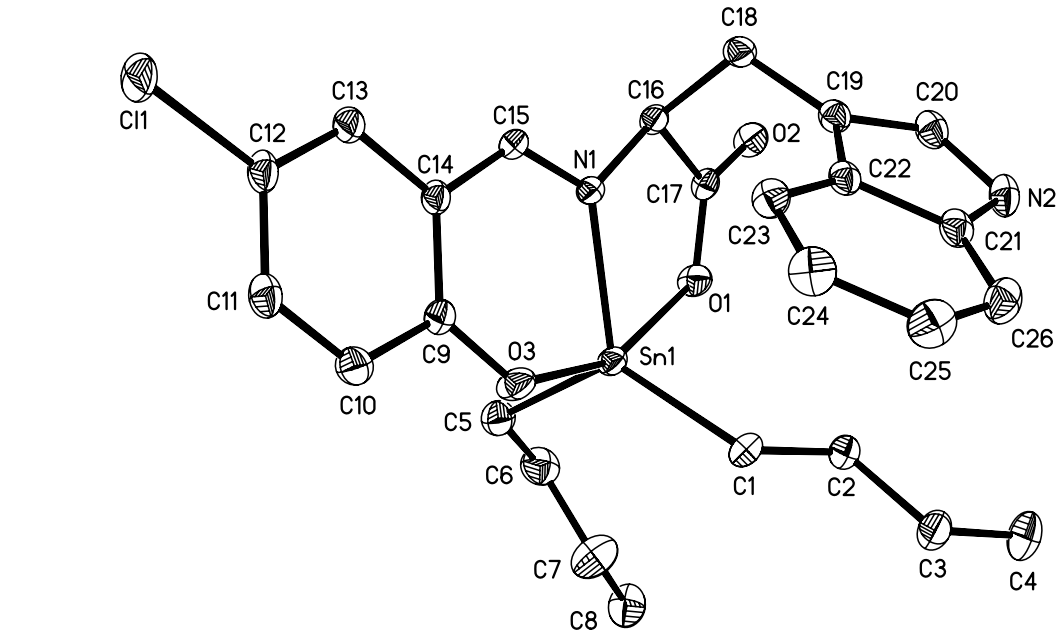

Figure 5. The molecular structure of **3**; hydrogen atoms are omitted for clarity.

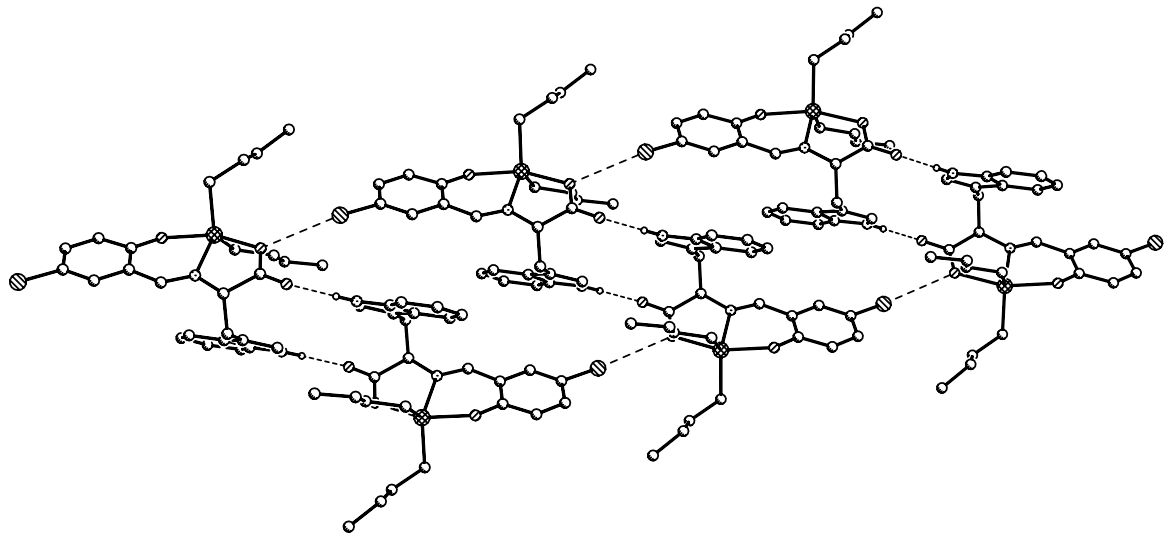

Figure 6. The one-dimensional supramolecular double-chain along the *b*-axis in **3** formed by intermolecular N–H···O hydrogen bonds and weak C–Cl···O interactions; hydrogen atoms are omitted for clarity.

plane is O1 [0.159(3) Å] and O3 [−0.409(2) Å], respectively. The torsion angles, Sn1–N1–C12–C23 [17.3(3)°], Sn1–O1–C13–C12 [−16.3(4)°], Sn1–N1–C11–C10 [15.9(4)°] and Sn1–O3–C5–C10 [−37.7(4)°], are much greater than the corresponding values in **1**. Compound **2** is linked into a one-dimensional supramolecular chain through intermolecular N–H···O hydrogen bonds involving the hydrogen atom on N2 of indolyl and $O2^{\#2}$ atom of carbonyl [H2···$O2^{\#2}$ 2.17 Å, N2···$O2^{\#2}$ 2.945(4) Å, N2–H2···$O2^{\#2}$ 151°, symmetry code #2: x, $1\frac{1}{2} - y$, $\frac{1}{2} + z$] (Fig. 4). The dihedral angle between the salicylidene fragment and the indole ring is 42.02(7)°.

The structure of **3** is similar but not isomorphous to **2** (Fig. 5). The tin atom is 0.0087(2) Å out of the NC_2 trigonal plane in the direction of the O3 atom. The axial bond angle O1–Sn1–O3 [157.67(10)°] is slightly wider than that of **2** [154.31(9)°], and the C1–Sn1–C3 [126.98(15)°] on the equatorial positions is narrower than that in **2**. The torsion angles, Sn1–N1–C16–C17 [8.7(3)°], Sn1–O1–C17–C16 [−2.5(4)°], Sn1–N1–C15–C14 [12.1(5)°] and Sn1–O3–C9–C14 [−19.3(5)°], indicate that the five- and six-membered chelate rings are non-planar. The dihedral angles between the salicylidene fragment and indole ring is 55.59(7)°. The Sn–donor atom bond lengths are in agreement with those found in **2** and related compounds.[15–17,20] Two molecules of the compound **3** are linked by a pair of intermolecular N–H···O hydrogen bonds between the hydrogen atom on N2 of indolyl and O2 atom of carbonyl over a center of inversion to form a centrosymmetric cyclic dimmer [H2···$O2^{\#1}$ 2.08 Å, N2···$O2^{\#1}$ 2.932(4) Å, N2–H2···$O2^{\#1}$ 174°, symmetry code #1: $-x + 1, -y, -z$]. The 16-membered cyclic dimmers are further joined by two weak intermolecular C12–Cl1···$O1^{\#2}$ [Cl1···$O1^{\#2}$ 3.205(2) Å, C12–Cl1···$O1^{\#2}$ 155.07(4)°, symmetry code #2:

Table 2. Selected bond lengths (Å) and angles (deg) of **1**, **2** and **3**

	1	2	3
Bond lengths			
Sn1–O1	2.1754(15)	2.155(2)	2.141(2)
Sn1–O2$^{\#1}$	3.0170(16)		
Sn1–O3	2.1022(16)	2.087(2)	2.097(2)
Sn1–N1	2.1934(16)	2.168(2)	2.171(2)
Sn1–C1	2.113(2)	2.119(4)	2.118(3)
Sn1–C3(C5)	2.116(2)	2.121(4)	2.130(4)
Bond angles			
O3–Sn1–C1	91.57(9)	92.30(14)	91.39(11)
O3–Sn1–C3(C5)	95.11(8)	99.68(15)	95.70(13)
C1–Sn1–C3(C5)	144.18(9)	130.4(2)	126.98(15)
O1–Sn1–O3	158.33(6)	154.31(9)	157.67(10)
C1–Sn1–O1	90.99(8)	93.21(13)	97.96(11)
C3(C5)–Sn1–O1	95.35(8)	95.72(16)	94.76(12)
O3–Sn1–N1	83.63(7)	81.41(8)	82.97(9)
C1–Sn1–N1	106.00(8)	120.37(15)	120.26(12)
C3(C5)–Sn1–N1	109.70(8)	108.95(15)	112.75(12)
O1–Sn1–N1	74.99(6)	74.17(8)	74.80(9)

Symmetry code #1: $^1/_{2-x}, ^1/_{2+y}, 1^1/_{2-z}$.

Table 3. Cytotoxic activity [IC_{50} (μg ml^{-1})] of **1**–**4** against CoLo205 and Bcap37

Compound	CoLo205	Bcap37
1	>10	3.12 ± 0.79
2	>10	>10
3	0.52 ± 0.03	0.16 ± 0.01
4	0.82 ± 0.10	0.32 ± 0.07
cis-Platin	4.12 ± 0.12	1.78 ± 0.25

$x-1, y+1, z$] contacts over a center of inversion into a one-dimensional supramolecular double-chain (Fig. 6).

In vitro cytotoxicity

The results of the cytotoxic assay against CoLo205 and Bcap37 are shown in Table 3. The dibutyltin compounds **3** and **4** displayed the potent *in vitro* activity, and are more active than clinically used *cis*-platin. By contrast, the diethyltin compounds **1** and **2** were less active than *cis*-platin. The disparate activity between the dibutyl- and diethyltin compounds is in accord with earlier reports.[5,32] The activity against CoLo205 of complexes **3** and **4** are slightly greater than those of our previous reported dibutyltin analogues Bu_2Sn[5-Cl-2-$OC_6H_3CH{=}NCH(i\text{-}Pr)COO$] ($IC_{50}$ 1.40 μg ml^{-1})[18] and Bu_2Sn[3,5-Br_2-2-$OC_6H_2CH{=}NCH(i\text{-}Pr)COO$] ($IC_{50}$ 1.35 μg ml^{-1})[20], indicating that the fragment of α-amino acid in the ligand appears to influence the cytotoxic activity. The dibutyltin complex of (2-hydroxynaphthalidene)glycine, $Bu_2Sn(2\text{-}OC_{10}H_6CH{=}NCH_2COO)$, reported by Nath *et al.*[13] also showed quite promising cytotoxicity; the IC_{50} values against cancer cell lines MCF-7, EVSA-T, WiDr, IGROV, MI9, MEL, A498, and H226 is 0.075, 0.035, 0.480, 0.075, 0.090, 0.170, 0.190 and 0.170 μg ml^{-1}, respectively. Thus, further structure modification and optimization of diorganotin compounds of the Schiff base derived from α-amino acid are highly recommended in order to improve cytotoxic properties.

Conclusion

In summary, four new diorganotin(IV) compounds of *N*—(5-halosalicylidene)tryptophane have been synthesized and characterized. The tin atoms of the complexes are five-coordinated and exhibit a distorted trigonal bipyramidal geometry, and compounds **1**, **2** and **3** self-assemble, respectively, into a two-dimensional array, a one-dimensional infinite chain and a one-dimensional double-chain supramolecular structure by intermolecular interactions. The dibutyltin compounds have potent *in vitro* cytotoxic activity against two human tumor cell lines, i.e. CoLo205 and Bcap37, which were better than clinically used *cis*-platin, while the diethyltin complexes display the weak cytotoxic activity. Further structure modification to enhance the cytotoxicity of the class of diorganotin complexes is desirable.

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Supporting information

Supporting information may be found in the online version of this article.

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