APPLIED ORGANOMETALLIC CHEMISTRY
Appl. Organometal. Chem. 2005; **19**: 980–987
Published online in Wiley InterScience (www.interscience.wiley.com). DOI:10.1002/aoc.940

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

Laijin Tian[1]*, Bochu Qian[2,3], Yuxi Sun[1], Xiaoliang Zheng[2], Min Yang[1], Huijun Li[2] and Xueli Liu[2]

[1]Department of Chemistry, Qufu Normal University, Qufu 273165, People's Republic of China
[2]Institute of Materia Medica, Zhejiang Academy of Medical Science, Hangzhou 310013, People's Republic of China
[3]Institute of Materia Medica, Zhejiang University City College, Hangzhou 310015, People's Republic of China

Received 14 February 2005; Revised 10 March 2005; Accepted 8 April 2005

Fourteen new diorganotin(IV) complexes of *N*-(5-halosalicylidene)-α-amino acid, R'_2Sn(5-X-2-$OC_6H_3CH{=}NCHRCOO$) (where X = Cl, Br; R = H, Me, i-Pr; R′ = *n*-Bu, Ph, Cy), were synthesized by the reactions of diorganotin halides with potassium salt of *N*-(5-halosalicylidene)-α-amino acid and characterized by elemental analysis, IR and NMR (^1H, ^{13}C and ^{119}Sn) spectra. The crystal structures of Bu_2Sn(5-Cl-2-$OC_6H_3CH{=}NCH$(i-Pr)COO) and Ph_2Sn(5-Br-2-$OC_6H_3CH{=}NCH$(i-Pr)COO) 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. Bioassay results of a few compounds indicated that the compounds have strong cytotoxic activity against three human tumour cell lines, i.e. HeLa, CoLo205 and MCF-7, and the activity decreased in the order Cy>*n*-Bu>Ph for the R′ group bound to tin. Copyright © 2005 John Wiley & Sons, Ltd.

KEYWORDS: organotin complex; α-amino acid; cytotoxic activity; crystal structure

INTRODUCTION

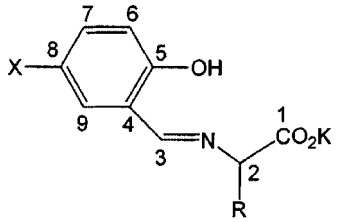
Organotin compounds have numerous applications, including their use as biocides and antifouling agents.[1] Recently, a number of organotin compounds have been investigated for their antitumour activity against a series of tumour cell lines.[2–6] The organotin complexes with Schiff bases derived from α-amino acids continue to receive attention owing to their structural features and biological properties.[7–18] The structural studies have shown that the diorganotin complexes of Schiff bases derived from salicylal,[13,15,17,18] 2-hydroxyacetophenone[9] or 2-hydroxynaphthaldehyde[14] and α-amino acids have isolated monomeric structures with a distorted trigonal bipyramidal tin atom[9,13–15,17,18] and the trimeric and polymeric structures have a distorted octahedral tin atom[18] in the solid state. In order to continue to expand the chemistry of the diorganotin(IV) Schiff base complexes and build structure–activity relationships, we selected *N*-(5-halosalicylidene)-α-amino acid salt as a ligand (Scheme 1), synthesized 14 new diorganotin(IV) complexes R'_2Sn(5-X-2-$OC_6H_3CH{=}NCHRCOO$), and determined their cytotoxic activity.

*Correspondence to: Laijin Tian, Department of Chemistry, Qufu Normal University, Qufu, Shandong 273165, People's Republic of China.
E-mail: laijintian@sohu.com
Contract/grant sponsor: Natural Science Foundation of Shandong Province; Contract/grant number: Z2002F01.
Contract/grant sponsor: Qufu Normal university.

EXPERIMENTAL

Materials and physical measurements

Dicyclohexyltin dichloride (Cy_2SnCl_2) was prepared according to a method reported in the literature.[19] Di-*n*-butyltin dichloride (Bu_2SnCl_2; Fluka), diphenyltin dichloride (Aldrich) 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 analyser. Melting points were measured on an X-4 microscopic melting-point apparatus. Optical activities were



Abbreviation	R	X
L^1HK	Me	Cl
L^2HK	i-Pr	Cl
L^3HK	H	Br
L^4HK	Me	Br
L^5HK	i-Pr	Br

Scheme 1. The structure of ligands LHK (H is the hydroxyl proton).

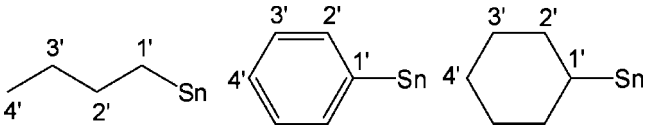
determined by using Wzz-3 digital auto-polarimeter. IR spectra were recorded on a Nicolet 470 FT-IR spectrophotometer using KBr discs in the range 4000–400 cm^{-1}. ^1H and ^{13}C NMR spectral data were collected using a Bruker Avance DMX500 FT-NMR spectrometer with $CDCl_3$ as solvent and tetramethylsilane as internal standard. ^{119}Sn NMR spectra were recorded in $CDCl_3$ on a Varian Mercury Vx300 spectrometer using Me_4Sn internal reference.

Synthesis of potassium salt of *N*-(5-halosalicylidene)-α-amino acid (LHK)

50 mmol α-amino acid (glycine, L-alanine or L-valine) was added to a 50% EtOH–H_2O solution (60 ml) containing KOH (2.80 g, 50 mmol). The mixture was stirred at room temperature for 30 min and a clear solution was obtained. An ethanol solution (30 ml) of 5-chlorosalicylaldehyde (7.82 g, 50 mmol) or 5-bromosalicylaldehyde (10.05 g, 50 mmol) was added dropwise and stirring of the yellow solution was continued for 1 h. After removal of the solvent, the resulting residue was washed with diethyl ether and recrystallized from ethanol. The yellow solid obtained was dried in vacuum for 24 h at 65 °C. L^1HK: yield 50%, m.p. 159–160 °C. L^2HK: yield 62%, m.p. 234–235 °C. L^3HK: yield 77%, m.p. 238 °C (dec.). L^4HK: yield 68%, m.p. 156–157 °C. L^5HK: yield 60%, m.p. 223–224 °C.

Synthesis of the organotin(IV) complexes

A benzene solution (30 ml) of 1.5 mmol diorganotin dichloride were dropped into a stirred absolute ethanol solution (30 ml) containing 1.5 mmol LHK and Et_3N (1.52 g, 1.5 mmol). The reaction mixture was refluxed for 3 h, and then filtered to remove KCl and $Et_3N \cdot HCl$. The yellow filtrate was evaporated under reduce pressure. The yellow solid obtained was washed with petroleum ether, extracted into dichloromethane, and filtered. A yellow product was obtained by removal of solvent using a rotary evaporator, and then recrystallized from chloroform–hexane (1 : 1, v/v) and dried in vacuum. The numbering scheme of the Sn–R′ skeleton in the diorganotins is shown below:



Bu_2SnL^1 (*1*)

Yield 72%; m.p.: 88–90 °C. $[\alpha]_D^{23}$ (EtOH) = −35.3°. Anal. Found: C, 47.29; H, 5.65; N, 3.08. Calc. for $C_{18}H_{26}ClNO_3Sn$: C, 47.15; H, 5.71; N, 3.05%. IR (cm^{-1}): 1625 ($\nu_{as}(CO_2)$), 1586 (ν(C=N)), 1391 ($\nu_s(CO_2)$), 564 (ν(Sn–O)). ^1H NMR δ: 0.86 (t, J = 7.3 Hz, 3H, H-4′), 0.94 (t, J = 7.3 Hz, 3H, H-4′), 1.28–1.83 (m, 12H, H-1′+ H-2′ + H-3′), 1.64 (d, J = 7.2 Hz, 3H, CH_3 in R), 4.18 (q, J = 7.2 Hz, 1H, H-2), 6.76 (d, J = 9.1 Hz, 1H, H-6), 7.17 (d, J = 2.7 Hz, 1H, H-9), 7.36 (dd, J = 2.7, 9.1 Hz, 1H, H-7), 8.31 (s, $^3J(^{119}Sn-^1H)$ = 48.5 Hz, 1H, H-3). ^{13}C NMR 173.95 (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-3), 117.44 (C-6), 64.19 (C-2), 22.54 (CH_3 in R), 27.19 (C-2′), 27.04 (C-2′), 26.86 ($^3J(^{119}Sn-^{13}C)$ = 86 Hz, C-3′), 26.67 ($^3J(^{119}Sn-^{13}C)$ = 90 Hz, C-3′), 22.29 ($^1J(^{119/117}Sn-^{13}C)$ = 618/591 Hz, C-1′), 21.95 ($^1J(^{119/117}Sn-^{13}C)$ = 603/578 Hz, C-1′), 13.78 (C-4′), 13.66 (C-4′). ^{119}Sn NMR δ: −214.2.

Ph_2SnL^1 (*2*)

Yield 60%, m.p.: 114–115 °C. $[\alpha]_D^{23}$ (EtOH) = −11.9°. IR (cm^{-1}): 1636 ($\nu_{as}(CO_2)$ + ν(C=N), an unresolved broad band), 1386 ($\nu_s(CO_2)$), 552 (ν(Sn–O)). ^1H NMR δ: 1.49 (d, J = 7.2 Hz, 3H, CH_3 in R), 4.24 (q, J = 7.2 Hz, 1H, H-2), 7.08 (d, J = 9.1 Hz, 1H, H-6), 7.18 (d, J = 2.6 Hz, 1H, H-9), 7.37–7.40 (m, 3H, H-3′+ H-4′), 7.43–7.46 (m, 4H, H-3′+ H-4′+ H-7), 7.78–7.80 (m, 2H, H-2′), 7.91–7.93 (m, 2H, H-2′), 8.34 (s, $^3J(^{119}Sn-^1H)$ = 57.1 Hz, 1H, H-3). ^{13}C NMR 173.62 (C-1), 170.89 (C-3), 168.01 (C-5), 137.96 (C-7), 133.78 (C-9), 124.63 (C-8), 122.01 (C-3), 117.75 (C-6), 137.58, 137.46 (C-1′), 136.76 ($^2J(^{119}Sn-^{13}C)$ = 57 Hz, C-2′), 136.48 ($^2J(^{119}Sn-^{13}C)$ = 59 Hz, C-2′), 131.23 ($^4J(^{119}Sn-^{13}C)$ = 18 Hz, C-4′), 131.10 ($^4J(^{119}Sn-^{13}C)$ = 19 Hz, C-4′), 129.34 ($^3J(^{119}Sn-^{13}C)$ = 89 Hz, C-3′), 129.23 ($^3J(^{119}Sn-^{13}C)$ = 89 Hz, C-3′), 64.24 (C-2), 22.59 (CH_3 in R). ^{119}Sn NMR δ: −348.2.

Bu_2SnL^2 (*3*)

Yield 75%, m.p.: 147–148 °C. $[\alpha]_D^{23}$ (EtOH) = −348.1°. Anal. Found: C, 49.22; H, 6.02; N, 2.83. Calc. for $C_{20}H_{30}ClNO_3Sn$: C, 49.36; H, 6.21; N, 2.88%. IR (cm^{-1}): 1671 ($\nu_{as}(CO_2)$), 1617 (ν(C=N)), 1393 ($\nu_s(CO_2)$), 547 (ν(Sn–O)). ^1H NMR δ: 0.81 (t, J = 7.3 Hz, 3H, H-4′), 0.95 (t, J = 7.3 Hz, 3H, H-4′), 1.05, (d, J = 6.8 Hz, 3H, CH_3 in R), 1.09 (d, J = 6.8 Hz, 3H, CH_3 in R), 1.25–1.78 (m, 12H, H-1′ + H-2′ + H-3′), 2.30–2.35 (m, 1H, CH in R), 3.86 (d, J = 4.9 Hz, $^3J(^{119/117}Sn-^1H)$ = 39.1/29.3 Hz, 1H, H-2), 6.78 (d, J = 9.0 Hz, 1H, H-6), 7.20 (d, J = 2.6 Hz, 1H, H-9), 7.34 (dd, J = 2.6, 9.0 Hz, 1H, H-7), 8.23 (s, $^3J(^{119}Sn-^1H)$ = 44.8 Hz, 1H, H-3). ^{13}C NMR δ: 172.68 (C-1), 171.23 (C-3), 168.04 (C-5), 137.40 (C-7), 133.38 (C-9), 124.21 (C-8), 121.39 (C-4), 117.46 (C-6), 74.61 (C-2),

34.38 (CH in R), 18.90 (CH_3 in R), 18.16 (CH_3 in R), 26.77 ($^2J(^{119}Sn-^{13}C) = 24$ Hz, C-2′), 26.75 ($^2J(^{119}Sn-^{13}C) = 24$ Hz, C-2′), 26.47 ($^3J(^{119}Sn-^{13}C) = 94$ Hz, C-3′), 26.33 ($^3J(^{119}Sn-^{13}C) = 92$ Hz, C-3′), 22.62 ($^1J(^{119/117}Sn-^{13}C) = 626/602$ Hz, C-1′), 20.89 ($^1J(^{119/117}Sn-^{13}C) = 588/561$ Hz, C-1′), 13.40 (C-4′), 13.31 (C-4′). ^{119}Sn NMR δ: −220.2.

Ph_2SnL^2 (**4**)

Yield 73%, m.p.: 250–251 °C. $[\alpha]_D^{23}$ (EtOH) = −225.4°. Anal. Found: C, 54.79; H, 4.17; N, 2.68. Calc. for $C_{24}H_{22}ClNO_3Sn$: C, 54.74; H, 4.21; N, 2.66%. IR (cm^{-1}): 1677 ($\nu_{as}(CO_2)$), 1616 (ν(C═N)), 1389 ($\nu_s(CO_2)$), 542 (ν(Sn–O)). ^{1}H NMR δ: 0.86 (d, $J = 6.8$ Hz, 3H, CH_3 in R), 0.97 (d, $J = 6.8$ Hz, 3H, CH_3 in R), 2.29 (m, $J = 6.8$ Hz, 1H, CH in R), 3.95 (d, $J = 4.4$ Hz, $^3J(^{119/117}Sn-^1H) = 44.0/34.9$ Hz, 1H, H-2), 7.12 (d, $J = 9.1$ Hz, 1H, H-6), 7.19 (d, $J = 2.7$ Hz, 1H, H-9), 7.33–7.37 (m, 3H, H-3′ + H-4′), 7.45–7.47 (m, 3H, H-3′ + H-4′), 7.48 (dd, $J = 2.7$, 9.1 Hz, 1H, H-7), 7.69–7.71 (m, $^3J(^{119}Sn-^1H) = 84.6$ Hz, 2H, H-2′), 7.99–8.01 (m, $^3J(^{119}Sn-^1H) = 82.6$ Hz, 2H, H-2′), 8.21 (s, $^3J(^{119}Sn-^1H) = 56.6$ Hz, 1H, H-3). ^{13}C NMR 173.52 (C-1), 170.83 (C-3), 168.11 (C-5), 138.06 (C-7), 133.85 (C-9), 124.89 (C-8), 122.38 (C-4), 117.86 (C-6), 137.44, 137.38 (C-1′), 136.80 ($^2J(^{119}Sn-^{13}C) = 57$ Hz, C-2′), 136.49 ($^2J(^{119}Sn-^{13}C) = 56$ Hz, C-2′), 131.31 ($^4J(^{119}Sn-^{13}C) = 18$ Hz, C-4′), 131.16 ($^4J(^{119}Sn-^{13}C) = 19$ Hz, C-4′), 129.36 ($^3J(^{119}Sn-^{13}C) = 88$ Hz, C-3′), 129.27 ($^3J(^{119}Sn-^{13}C) = 88$ Hz, C-3′), 74.21 (C-2), 34.03 (CH in R), 19.01 (CH_3 in R), 18.26 (CH_3 in R). ^{119}Sn NMR δ: −348.7.

Cy_2SnL^2 (**5**)

Yield 45%, m.p.: 166–167 °C. $[\alpha]_D^{23}$ (EtOH) = −205.8°. Anal. Found: C, 53.55; H, 6.34; N, 2.56. Calc. for $C_{24}H_{34}ClNO_3Sn$: C, 53.51; H, 6.36; N, 2.60%. IR (cm^{-1}): 1668 ($\nu_{as}(CO_2)$), 1615 (ν(C═N)), 1392 ($\nu_s(CO_2)$), 537 (ν(Sn–O)). ^{1}H NMR δ: 1.05 (d, $J = 6.8$ Hz, 3H, CH_3 in R), 1.11 (d, $J = 6.8$ Hz, 3H, CH_3 in R), 2.23–2.28 (m, 1H, CH in R), 1.23–2.36 (m, 22 H, 2Cy), 3.80 (d, $J = 5.4$ Hz, $^3J(^{119/117}Sn-^1H) = 36.5/25.8$ Hz, 1H, H-2), 6.79 (d, $J = 9.0$ Hz, 1H, H-6), 7.16 (d, $J = 2.7$ Hz, 1H, H-9), 7.35 (dd, $J = 2.7$, 9.1 Hz, 1H, H-7), 8.19 (s, $^3J(^{119}Sn-^1H) = 40.8$ Hz, 1H, H-3). ^{13}C NMR δ: 173.40 (C-1), 171.32 (C-3), 169.02 (C-5), 137.65 (C-7), 133.72 (C-9), 124.56 (C-8), 121.35 (C-4), 117.91 (C-6), 75.32 (C-2), 41.60 ($^1J(^{119/117}Sn-^{13}C) = 567/545$ Hz, C-1′), 39.95 ($^1J(^{119/117}Sn-^{13}C) = 580/557$ Hz, C-1′), 30.47, 30.28 (C-2′), 28.88, 28.67 (C-3′), 26.71, 26.56 (C-4′), 34.83 (CH in R), 19.33, 18.77 (CH_3 in R). ^{119}Sn NMR δ: −289.8.

Bu_2SnL^3 (**6**)

Yield: 72%, m.p.: 90–92 °C. Anal. Found: C, 41.48; H, 4.73; N, 2.81. Calc. for $C_{17}H_{24}BrNO_3Sn$: C, 41.76; H, 4.95; N, 2.86%. IR (cm^{-1}): 1639 ($\nu_{as}(CO_2)$), 1609 (ν(C═N)), 1386 ($\nu_s(CO_2)$), 545 (ν(Sn–O)). ^{1}H NMR δ: 0.87 (t, $J = 7.1$ Hz, 6H, H-4′), 1.34 (sextet, $J = 7.1$ Hz, 4H, H-3′), 1.52–1.61 (m, 8H, H-2′ + H-1′), 4.35 (s, $^3J(^{119}Sn-^1H) = 15.4$ Hz, 2H, H-2), 6.72 (d, $J = 9.2$ Hz, 1H, H-6), 7.28 (d, $J = 2.6$ Hz, 1H, H-9), 7.46 (dd, $J = 2.6$, 9.2 Hz, 1H, H-7), 8.32 (s, $^3J(^{119}Sn-^1H) = 38.7$ Hz, 1H, H-3). ^{13}C NMR δ: 172.74 (C-1), 171.11 (C-3), 167.92 (C-5), 139.60 (C-7), 136.60 (C-3), 124.80 (C-8), 118.80 (C-4), 107.45 (C-6), 58.04 (C-2), 27.13 ($^2J(^{119}Sn-^{13}C) = 37$ Hz, C-2′), 26.39 ($^3J(^{119}Sn-^{13}C) = 101$ Hz, C-3′), 22.75 ($^1J(^{119/117}Sn-^{13}C) = 590/562$ Hz, C-1′), 13.48 (C-4′). ^{119}Sn NMR δ: −216.8.

Ph_2SnL^3 (**7**)

Yield: 66%, m.p.: 170–172 °C. Anal. Found: C, 47.69; H, 2.93; N, 2.61. Calc. for $C_{21}H_{16}BrNO_3Sn$: C, 47.68; H, 3.05; N, 2.65%. IR (cm^{-1}): 1627 ($\nu_{as}(CO_2) + \nu$(C═N), an unresolved broad band), 1398 ($\nu_s(CO_2)$), 550 (ν(Sn–O)). ^{1}H NMR δ: 4.38 (s, $^3J(^{119}Sn-^1H) = 21.9$ Hz, 2H, H-2), 7.04 (d, $J = 9.2$ Hz, 1H, H-6), 7.30 (d, $J = 2.5$ Hz, 1H, H-9), 7.42–7.46 (m, 6H, H-3′ + H-4′), 7.58 (dd, $J = 2.5$, 9.2 Hz, 1H, H-7), 7.86 (dd, $J = 2.3$, 9.2 Hz, 4H, $^3J(^{119/117}Sn-^1H) = 88.1/76.4$ Hz, H-2′), 8.34 (s, $^3J(^{119}Sn-^1H) = 55.1$ Hz, 1H, H-3). ^{13}C NMR δ: 172.09 (C-1), 170.28 (C-3), 168.02 (C-5), 140.06 (C-7), 137.03 (C-9), 124.78 (C-8), 118.83 (C-4), 107.85 (C-6), 136.87 (C-1′), 136.50 ($^2J(^{119}Sn-^{13}C) = 55$ Hz, C-2′), 131.36 ($^4J(^{119}Sn-^{13}C) = 19$ Hz, C-3′), 129.47 ($^3J(^{119}Sn-^{13}C) = 88$ Hz, C-4′), 57.76 (C-2). ^{119}Sn NMR δ: −349.1.

Cy_2SnL^3 (**8**)

Yield: 57%, m.p.: 99–100 °C. Anal. Found: C, 46.54; H, 5.01; N, 2.47. Calc. for $C_{21}H_{28}BrNO_3Sn$: C, 46.62; H, 5.22; N, 2.59%. IR (cm^{-1}): 1620 ($\nu_{as}(CO_2) + \nu$(C═N), an unresolved broad band), 1400 ($\nu_s(CO_2)$), 540 (ν(Sn–O)). ^{1}H NMR δ: 1.27–1.96 (m, 22 H, 2Cy), 4.30 (s, $^3J(^{119}Sn-^1H) = 15.0$ Hz, 2H, H-2), 6.91 (d, $J = 9.1$ Hz, 1H, H-6), 7.25 (d, $J = 2.5$ Hz, 1H, H-9), 7.45 (dd, $J = 2.5$, 9.1 Hz, 1H, H-7), 8.31 (s, $^3J(^{119}Sn-^1H) = 38.1$ Hz, 1H, H-3). δ: 173.39 (C-1), 171.54 (C-3), 168.03 (C-5), 139.87 (C-7), 136.72 (C-9), 125.05 (C-8), 121.35 (C-4), 119.10 (C-6), 57.89 (C-2), 41.65 ($^1J(^{119}Sn-^{13}C) = 567$ Hz, C-1′), 41.11 ($^1J(^{119}Sn-^{13}C) = 556$ Hz, C-1′), 30.33, 30.21 (C-2′), 28.83, 28.72 ($^3J(^{119}Sn-^{13}C) = 89$ Hz, C-3′), 26.59, 26.51 (C-4′). ^{119}Sn NMR δ: −279.9.

Bu_2SnL^4 (**9**)

Yield: 73%, m.p.: 98–99 °C. $[\alpha]_D^{23}$ (EtOH) = −29.7°. Anal. Found: C, 43.11; H, 5.17; N, 2.70. Calc. for $C_{18}H_{26}BrNO_3Sn$: C, 42.98; H, 5.21; N, 2.78%. IR (cm^{-1}): 1625 ($\nu_{as}(CO_2) + \nu$(C═N), an unresolved broad band), 1400 ($\nu_s(CO_2)$), 560 (ν(Sn–O)). ^{1}H NMR δ: 0.84 (t, $J = 7.3$ Hz, 3H, H-4′), 0.93 (t, $J = 7.3$ Hz, 3H, H-4′), 1.29–1.73 (m, 12H, H-3′ + H-2′ + H-1′), 1.64 (d, $J = 7.2$ Hz, 3H, CH_3 in R), 4.17 (q, $J = 7.2$ Hz, 1H, H-2), 6.70 (d, $J = 9.1$ Hz, 1H, H-6), 7.30 (d, $J = 2.5$ Hz, 1H, H-9), 7.46 (dd, $J = 2.5$, 9.1 Hz, 1H, H-7), 8.28 (s, $^3J(^{119}Sn-^1H) = 44.0$ Hz, 1H, H-3). ^{13}C NMR δ: 173.99 (C-1), 171.11 (C-3), 168.23 (C-5), 140.23 (C-7), 136.58 (C-3), 124.53 (C-8), 118.34 (C-4), 107.85 (C-6), 63.86 (C-2), 22.36 (CH_3, in R), 26.89, 26.78 (C-2′), 26.59 ($^3J(^{119}Sn-^{13}C) = 90$ Hz, C-3′), 26.47 ($^3J(^{119}Sn-^{13}C) = 86$ Hz, C-3′), 22.49 ($^1J(^{119/117}Sn-^{13}C) = 590/570$ Hz, C-1′), 22.15 ($^1J(^{119/117}Sn-^{13}C) = 578/556$ Hz, C-1′), 13.47, 13.45 (C-4′). ^{119}Sn NMR δ: −213.6.

Ph_2SnL^4 (**10**)

Yield: 70%, m.p.: 180–182 °C. $[\alpha]_D^{23}$ (EtOH) = −13.5°. Anal. Found: C, 48.56; H, 3.23; N, 2.60. Calc. for $C_{22}H_{18}BrNO_3Sn$: C,

48.66; H, 3.34; N, 2.58%. IR (cm^{-1}): 1626 ($\nu_{as}(CO_2) + \nu$(C═N), an unresolved broad band), 1400 ($\nu_s(CO_2)$), 554 (ν(Sn–O)). ^{1}H NMR δ: 1.52 (d, $J = 7.3$ Hz, 3H, CH_3 in R), 4.24 (q, $J = 7.2$ Hz, 1H, H-2), 7.04 (d, $J = 9.1$ Hz, 1H, H-6), 7.32 (d, $J = 2.6$ Hz, 1H, H-9), 7.38–7.40 (m, 3H, H-3′ + H-4′), 7.45–7.47 (m, 3H, H-3′ + H-4′), 7.57 (dd, $J = 2.6$, 9.1 Hz, 1H, H-7), 7.79–7.81 (m, $^3J(^{119}Sn-^1H) = 83.3$ Hz, 2H, H-2′), 7.92–7.94 (m, $^3J(^{119}Sn-^1H) = 83.6$ Hz, 2H, H-2′), 8.29 (s, $^3J(^{119}Sn-^1H) = 56.3$ Hz, 1H, H-3). ^{13}C NMR 174.02 (C-1), 171.63 (C-3), 168.55 (C-5), 140.23 (C-7), 137.11 (C-9), 125.00 (C-8), 119.09 (C-3), 107.38 (C-6), 136.99, 136.74 (C-1′), 136.66 ($^2J(^{119}Sn-^{13}C) = 56$ Hz, C-2′), 136.52 ($^2J(^{119}Sn-^{13}C) = 57$ Hz, C-2′), 131.35, 131.23 (C-4′), 129.24 ($^3J(^{119}Sn-^{13}C) = 91$ Hz, C-3′), 129.15 ($^3J(^{119}Sn-^{13}C) = 89$ Hz, C-3′), 64.17 (C-2), 22.80 (CH_3 in R). ^{119}Sn NMR δ: −352.0.

Cy_2SnL^4 (**11**)

Yield: 60%, m.p.: 177–179 °C. $[\alpha]_D^{23}$ (EtOH) = −9.3°. Anal. Found: C, 47.69; H, 5.47; N, 2.48. Calc. for $C_{22}H_{30}BrNO_3Sn$: C, 47.60; H, 5.45; N, 2.52%. IR (cm^{-1}): 1617 ($\nu_{as}(CO_2) + \nu$(C═N), an unresolved broad band), 1386 ($\nu_s(CO_2)$), 552 (ν(Sn–O)). ^{1}H NMR δ: 1.30–1.97 (m, 25 H, 2Cy + CH_3 in R), 4.15 (q, $J = 7.2$ Hz, 1H, H-2), 6.72 (d, $J = 9.1$ Hz, 1H, H-6), 7.27 (d, $J = 2.6$ Hz, 1H, H-9), 7.46 (dd, $J = 2.6$, 9.1 Hz, 1H, H-7), 8.26 (s, $^3J(^{119}Sn-^1H) = 42.2$ Hz, 1H, H-3). ^{13}C NMR δ: 174.47 (C-1), 172.09 (C-3), 168.52 (C-5), 139.17 (C-7), 136.42 (C-9), 124.67 (C-8), 118.09 (C-4), 107.12 (C-6), 64.08 (C-2), 41.61, 41.05 (C-1′), 30.19, 30.06 (C-2′), 28.72, 28.63 (C-3′), 26.60, 25.52 (C-4′), 22.59 (CH_3 in R). ^{119}Sn NMR δ: −282.4.

Bu_2SnL^5 (**12**)

Yield: 65%, m.p.: 122–124 °C. $[\alpha]_D^{23}$(EtOH) = −181.4°. Anal. Found: C, 45.06; H, 5.50; N, 2.51. Calc. for $C_{20}H_{30}BrNO_3Sn$: C, 45.23; H, 5.69; N, 2.64%. IR (cm^{-1}): 1671 ($\nu_{as}(CO_2)$), 1615 (ν(C═N)), 1389 ($\nu_s(CO_2)$), 544 (ν(Sn–O)). ^{1}H NMR δ: 0.82 (t, $J = 7.4$ Hz, 3H, H-4′), 0.95 (t, $J = 7.4$ Hz, 3H, H-4′), 1.05 (d, $J = 6.9$ Hz, 3H, CH_3 in R), 1.09 (d, $J = 6.9$ Hz, 3H, CH_3 in R), 1.25–1.34 (m, 8H, H-3′ + H-2′), 1.66–1.70 (m, $^2J(^{119}Sn-^1H) = 88.0$ Hz, 2H, H-1′), 1.75–1.81 (m, $^2J(^{119}Sn-^1H) = 92.2$ Hz, 2H, H-1′), 2.28–2.36 (m, 1H, CH in R), 3.84 (dd, $J = 0.6$, 4.8 Hz, $^3J(^{119/117}Sn-^1H) = 39.4/29.5$ Hz, 1H, H-2), 6.73 (d, $J = 9.2$ Hz, 1H, H-6), 7.33 (d, $J = 2.8$ Hz, 1H, H-9), 7.48 (dd, $J = 2.8$, 9.2 Hz, 1H, H-7), 8.19 (s, $^3J(^{119}Sn-^1H) = 45.4$ Hz, 1H, H-3). ^{13}C NMR δ: 172.83 (C-1), 171.51 (C-3), 168.49 (C-5), 140.07 (C-7), 136.71 (C-9), 124.66 (C-8), 118.45 (C-4), 108.07 (C-6), 74.61(C-2), 34.51 (CH in R), 18.98, 18.31 (CH_3 in R), 26.88 ($^2J(^{119}Sn-^{13}C) = 29$ Hz, C-2′), 26.86 ($^2J(^{119}Sn-^{13}C) = 30$ Hz, C-2′), 26.57 ($^3J(^{119}Sn-^{13}C) = 95$ Hz, C-3′), 26.43 ($^3J(^{119}Sn-^{13}C) = 90$ Hz, C-3′), 22.71 ($^1J(^{119/117}Sn-C) = 601/573$ Hz, C-1′), 21.03 ($^1J(^{119/117}Sn-C) = 589/564$ Hz, C-1′), 13.51, 13.43 (C-4′). ^{119}Sn NMR δ: −213.6.

Ph_2SnL^5 (**13**)

Yield: 76%, m.p.: 259–260 °C. $[\alpha]_D^{23}$ (EtOH) = −321.3°. Anal. Found: C, 50.46; H, 3.79; N, 2.48%. Calc. for $C_{24}H_{22}BrNO_3Sn$: C, 50.48; H, 3.88; N, 2.45%. IR (cm^{-1}): 1676 ($\nu_{as}(CO_2)$), 1612 (ν(C═N)), 1400 ($\nu_s(CO_2)$), 544 (ν(Sn–O)). ^{1}H NMR δ: 0.86 (d, $J = 6.8$ Hz, 3H, CH_3 in R), 0.97 (d, $J = 6.8$ Hz, 3H, CH_3 in R), 2.26–2.32 (m, 1H, CH in R), 3.94 (d, $J = 4.6$ Hz, $^3J(^{119/117}Sn-^1H) = 43.8/34.9$ Hz, 1H, H-2), 7.07 (d, $J = 9.0$ Hz, 1H, H-6), 7.33 (d, $J = 2.5$ Hz, 1H, H-9), 7.35–7.38 (m, 3H, H-3′ + H-4′), 7.45–7.50 (m, 3H, H-3′ + H-4′), 7.59 (dd, $J = 2.5$, 9.0 Hz, 1H, H-7), 7.68–7.71 (m, 2H, $^3J(^{119}Sn-H) = 84.7$ Hz, H-2′), 7.99–8.01 (m, 2H, $^3J(^{119}Sn-^1H) = 84.4$ Hz, H-2′), 8.20 (s, $^3J(^{119}Sn-^1H) = 56.4$ Hz, 1H, H-3). ^{119}Sn NMR δ: −338.7.

Cy_2SnL^5 (**14**)

Yield: 64%, m.p.: 170–172 °C. $[\alpha]_D^{23}$ (EtOH) = −209.5°. Anal. Found: C, 49.74; H, 5.77; N, 2.29%. Calc. for $C_{24}H_{34}BrNO_3Sn$: C, 49.43; H, 5.88; N, 2.40%. IR (cm^{-1}): 1668 ($\nu_{as}(CO_2)$), 1615 (ν(C═N)), 1392 ($\nu_s(CO_2)$), 547 (ν(Sn–O)). ^{1}H NMR δ: 1.05 (d, $J = 6.8$ Hz, 3H, CH_3 in R), 1.10 (d, $J = 6.8$ Hz, 3H, CH_3 in R), 1.23–2.36 (m, 23 H, 2Cy + CH in R), 3.83 (d, $J = 5.0$ Hz, $^3J(^{119/117}Sn-^1H) = 38.5/27.6$ Hz, 1H, H-2), 6.75 (d, $J = 9.1$ Hz, 1H, H-6), 7.32 (d, $J = 2.6$ Hz, 1H, H-9), 7.47 (dd, $J = 2.6$, 9.1 Hz, 1H, H-7), 8.19 (s, $^3J(^{119}Sn-^1H) = 42.8$ Hz, 1H, H-3). ^{13}C NMR δ: 173.42 (C-1), 171.56 (C-3), 169.32 (C-5), 140.25 (C-7), 137.01 (C-9), 124.94 (C-8), 118.12 (C-4), 108.41 (C-6), 75.26 (C-2), 34.81 (CH in R), 19.31, 18.75 (CH_3 in R), 41.56, 39.93 (C-1′), 30.45, 30.27 (C-2′), 28.89, 28.65 (C-3′), 26.70, 26.55 (C-4′). ^{119}Sn NMR δ: −288.0.

X-ray crystallography

Yellow single crystals of compounds **3** ($0.14 \times 0.20 \times 0.26$ mm^3) and **13** ($0.11 \times 0.22 \times 0.25$ mm^3) were obtained from the slow evaporation of dichloromethane–petroleum ether (60–90 °C) (1:1, v/v) solutions of the respective compounds. The intensity data for crystals of complexes **3** and **13** were measured at 295(2) K on a Bruker Smart Apex area-detector fitted with graphite monochromatized Mo Kα radiation (0.710 73 Å) using the omega scan technique so that $\theta_{max} = 27.5°$. Empirical corrections were made using the SADABS program.[20] The structures were solved by direct methods[21] and refined by a full-matrix least-squares procedure based on F^2 using SHELXL-97.[22] The non-hydrogen atoms were refined anisotropically and hydrogen atoms were placed at calculated positions in the riding model approximation. Disorder was noted in the refinement of **13** so that the C13-phenyl and C5-methyl groups were disposed over two positions each; from refinement, these had 50% site occupancies. The absolute configurations were confirmed by the X-ray study.[23] The crystallographic parameters and refinements are summarized in Table 1.

Cytotoxic assays

The samples were prepared by dissolving compounds **3**, **4**, **5**, and **13** in ethanol, and by diluting the solution obtained with water. In the assays, the final concentration of the solvent (ethanol) was less than 0.1% (this concentration of ethanol used was found to be non-cytotoxic against the tumour cells). *cis*-Platin was purchased from Mayne Pharma Pty Ltd (Australia). Three human tumour cell lines, HeLa (cervix

Table 1. Crystallographic and refinement data for **3** and **13**

	3	**13**
Empirical formula	$C_{20}H_{30}ClNO_3Sn$	$C_{24}H_{22}BrNO_3Sn$
Formula weight	486.59	571.03
Crystal system	Orthorhombic	Monoclinic
Space group	$P2_12_12_1$	$P2_1$
a (Å)	8.9939(11)	9.5459(13)
b (Å)	10.4290(13)	11.4154(16)
c (Å)	23.854(3)	10.5677(15)
β (°)	90	92.602(2)
Volume (Å^3)	2237.5(5)	1150.4(3)
Z	4	2
D_c(g/cm^3)	1.445	1.649
μ(mm^{-1})	1.279	2.872
Independent reflections	5027 ($R_{int} = 0.028$)	4735 ($R_{int} = 0.025$)
Observed data [$I > 2\sigma(I)$]	3765	4127
Flack x	0.00(3)	0.00(1)
Final R[$I > 2\sigma(I)$]	$R = 0.043$, $Rw = 0.100$	$R = 0.035$, $Rw = 0.063$
CCDC deposition no.	253 231	253 232

tumour cell), CoLo 205 (colon carcinoma cell) and MCF-7 (mammary tumour cell), were obtained from the Tumour Institute of Zhejiang University. Cytotoxic activities of the compounds were measured by the 3-[4,5-dimethylthiazol-2-yl]-2,5-diphenyltetrazolium bromide (MTT) assay according to the literature.[24,25] All cells cultured in Dulbecco's modified Eagle's medium (DMEM) supplemented with 10% heat-inactivated new-born calf serum at 37 °C in a humidified 5% CO_2 incubator and were seeded into each well of 96-well plate and were allowed to attach for 24 h. The following day, different concentrations of the test compounds were added. After incubation with various concentrations of the test materials for 96 h, the inhibition on cell proliferation was measured with MTT assay. The experiments were repeated in triplicate for each tin compound concentration tested. Statistical significance was tested using Student's t-test ($p < 0.05$ was considered statistically significant). The dose causing 50% inhibition of cell growth (IC_{50}) was calculated by NDST software as described previously.[26]

RESULTS AND DISCUSSION

The reaction of diorganotin(IV) dichloride with potassium salt of *N*-(5-halosalicylidene)-α-amino acid, derived from the condensation of 5-halosalicylaldehyde and α-amino acid in the presence of KOH, in 1 : 1 molar ratio, afforded the products. The reaction equation was as follows:

$$R'_2SnCl_2 + LHK + Et_3N \longrightarrow R'_2SnL + KCl + Et_3N \cdot HCl$$

where L = L^1, L^2, L^3, L^4, L^5

The complexes are yellow crystalline solids that are soluble in benzene and in polar organic solvents such as chloroform, dichloromethane, ethanol, acetone and tetrahydrofuran, but they are insoluble in water and in saturated aliphatic hydrocarbons. With the exception of R'_2SnL^3 (**6, 7** and **8**) the complexes possess optical activity, which indicates that the chiralities of the α-amino acid were still retained after two-step reactions, condensation and substitution.

IR spectra

None of the IR spectra of the organotin(IV) complexes show a strong band at ~3200 cm^{-1} assigned to ν(OH), indicating the deprotonation of the phenolic oxygen of the ligand upon complexation with tin atom.[11,17] This is further confirmed by the appearance of a sharp band at ~550 cm^{-1} assignable to the Sn–O stretching vibration.[11,13,27] In some complexes, the ν(C═N) band appears as a single sharp band at ~1615 cm^{-1} and is assigned as being due to C═N → Sn coordination in the solid state.[9] However, in some complexes, the ν(C═N) and $\nu_{as}(CO_2)$ appear as an unresolved broad band at ~1625 cm^{-1}. The $\Delta\nu(\nu_{as}(CO_2) - \nu_s(CO_2))$ value is used to determine the nature of the bonding of the carboxylate to the tin(IV) atom.[28] It is generally believed that the Δν value is below 200 cm^{-1} for the bidentate carboxylate moiety and above 200 cm^{-1} for the monodentate carboxylate moiety. The difference between the $\nu_{as}(CO_2)$ and $\nu_s(CO_2)$ bands in the complexes is in the range 220–288 cm^{-1}, indicating monodentate bonding through the carboxylate moiety.[11,14] Thus, it may be suggested that the compounds are five-coordinated to tin in the solid.

NMR spectra

The ^{1}H and ^{13}C chemical shift assignments of the diorganotin moiety are straightforward from the multiplicity patterns

and/or resonance intensities, whereas the ligand skeletons were assigned by multiplicity patterns and/or resonance intensities of the signals and also by the related literature.[8,29] The ^{1}H NMR spectra of the complexes show that the signal assigned to the azomethine proton N=CH (H-3) appears in the range 8.19–8.34 ppm. The appearance of spin–spin coupling between the azomethine proton and the tin nucleus ($^3J(^{119}\text{Sn}-^1\text{H}) = 39-56$ Hz) further confirms the presence of nitrogen–tin coordination in all complexes. The signals of the carboxyl carbon (C-1) and imine carbon (C-3) appear in the ranges 174.47–172.28 ppm and 172.09–170.28 ppm respectively. The signal of N–C (C-2) appears in the range 75.26–57.76 ppm, depending on the nature of the substituent R. With the exception of R'_2SnL^3, the complexes displayed two resonances for the protons and carbon atoms of organic group (R′)-bonded tin, which may be due to the presence of the chiral centre (C-2) in these complexes.[30] The $^1J(^{119}\text{Sn}-^{13}\text{C})$ values of di-*n*-butyltin complexes and dicyclohexyltin complexes **5** and **8** are in the range of 567–626 Hz, which indicates five-coordination around the tin atom.[10,30] However, the $^1J(^{119}\text{Sn}-^{13}\text{C})$ couplings of the dicyclohexyltin complexes **11** and **13** and the diphenyltin complexes are not observed, probably due to the dilute solutions and the short time of taking spectra. The ^{119}Sn chemical shifts depend on the number and nature of alkyl or aryl groups coordinated to the tin central atom.[31] The ^{119}Sn chemical shifts of the di-*n*-butyltin and dicyclohexyltin complexes are in the ranges −213.6 to −220.2 ppm and −282.4 to −289.8 ppm respectively. The ^{119}Sn chemical shifts of the di-*n*-butyltin complexes fall between the ranges of five-coordinate and six-coordinate tin centres.[32,33], suggesting that an equilibrium structure[32] could be present from a fast equilibrating process between the monomeric structure with five-coordinate tin and the polymeric structure with six-coordinate tin formed by the intermolecular interaction of carbonyl oxygen with the tin atom (C=O → Sn). Diphenyltin complexes show a resonance between −338.7 and −352.0 ppm, indicating a penta-coordinated tin structure in solution, which is consistent with earlier reports.[9,17]

Crystal structures of 3 and 13

The molecular structures for compounds **3** and **13** are shown in Figs 1 and 2 respectively, and selected geometric parameters are given in the respective figure captions. The molecular structures of **3** and **13** are similar: the tin atom is in a distorted trigonal bipyramidal geometry with two organic groups and the imino-nitrogen atom occupying the equatorial positions, and with the axial positions being occupied by a phenoxide-oxygen atom and a monodentate carboxylate-oxygen atom. The distance between tin and the carboxylate oxygen is longer than that between tin and the phenoxide oxygen. The axial bond angles in **3** and **13** are 154.20(15)° and 157.73(12)° respectively, values that are comparable to those observed in $Bu_2Sn(OC_6H_4CH{=}NCH(i\text{-}Pr)COO)$,[15] $Bu_2Sn(OC_6H_4CH{=}NCH(CH_2Indole\text{-}3)COO)$,[17] $Ph_2Sn(OC_6H_4C(CH_3){=}NCH_2COO)$,[9] $Ph_2Sn(OC_6H_4CH{=}NCH_2COO)$,[13]

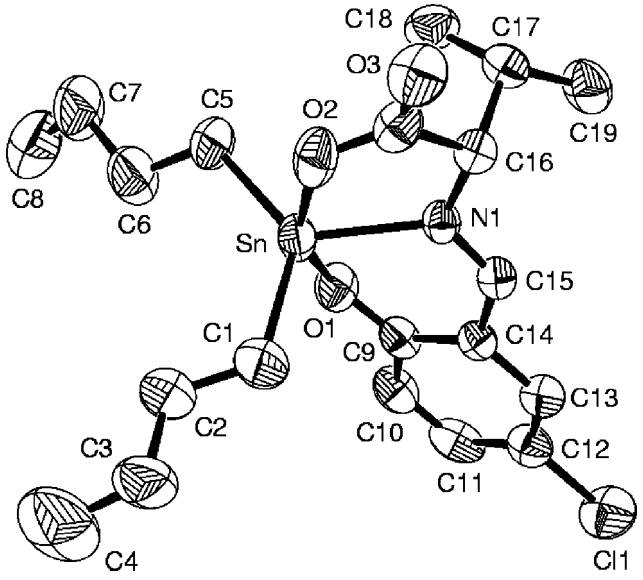


Figure 1. The molecular structure of **3**; hydrogen atoms are omitted for clarity. Selected bond lengths (Å) and angles (°): Sn–O1 2.103(5), Sn–O2 2.158(5), Sn–N1 2.164(4), Sn–C1 2.131(6), Sn–C5 2.109(6); O1–C9 1.308(7), O2–C20 1.274(8), O3–C20 1.218(7), N1–C15 1.285(6), N1–C16 1.472(6); O1–Sn–O2 154.20(15), O1–Sn–N1 81.32(16), O2–Sn–N1 74.12(16), Sn–O1–C9 126.1(3), Sn–O2–C20 121.2(4), Sn–N1–C15 123.6(3), Sn–N1–C16 116.0(3).

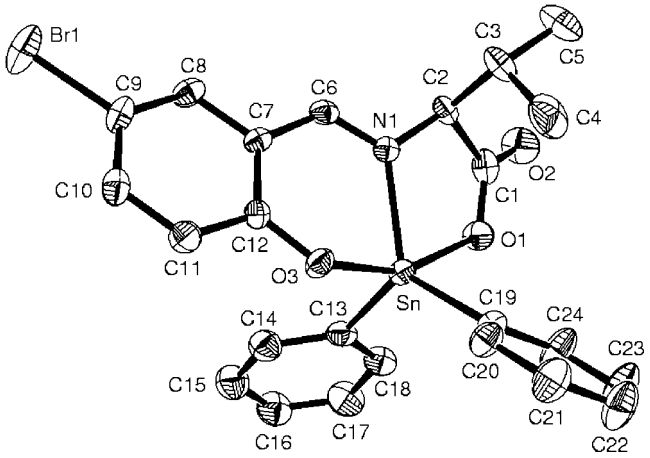


Figure 2. The molecular structure of **13**; hydrogen atoms are omitted for clarity. Selected bond lengths (Å) and angles (°): Sn–O1 2.128(3), Sn–O3 2.070(3), Sn–N1 2.158(3), Sn–C13 2.115(7) (average value), Sn–C19 2.105(4), O1–C1 1.296(6), O2–C1 1.210(6), O3–C12 1.314(5), N1–C2 1.472(6), N1–C6 1.290(5); O1–Sn–O3 157.73(12), O1–Sn–N1 75.22(12), O3–Sn–N1 82.93(12), Sn–O1–C1 120.4(3), Sn–O3–C12 128.1(3), Sn–N1–C2 115.6(3), Sn–N1–C6 124.8(3).

Table 2. Cytotoxic assays results against HeLa, CoLo205 and MCF-7 of some compounds

Compound	IC_{50} (μg ml^{-1})[a]		
	HeLa	CoLo205	MCF-7
3	$0.31 \pm 0.08^{b,c}$ (0.69 ± 0.13)	$1.40 \pm 0.08^{b,c,e}$ (2.88 ± 0.16)	$2.1 \pm 0.5^{b,e}$ (4.4 ± 0.9)
4	2.9 ± 0.5^{b} (5.4 ± 1)	2.72 ± 0.07^{b} (5.16 ± 0.13)	2.97 ± 0.15^{b} (5.62 ± 0.29)
5	$0.25 \pm 0.06^{b,c}$ (0.47 ± 0.11)	$0.61 \pm 0.10^{b,c,d}$ (1.14 ± 0.19)	$0.21 \pm 0.03^{b,c,d}$ (0.38 ± 0.05)
13	$0.77 \pm 0.11^{b,f}$ (1.35 ± 0.19)	$3.15 \pm 0.43^{b,e}$ (5.51 ± 0.75)	$2.68 \pm 0.54^{b,e}$ (4.68 ± 0.95)
cis-Platin	1.44 ± 0.33 (4.8 ± 1.1)	4.61 ± 0.86 (13.9 ± 0.5)	5.46 ± 0.35 (18.7 ± 0.6)

[a] The data represent mean plus/minus standard deviation and the numbers in parentheses represent IC_{50} values expressed as μM. All assays were performed in triplicate for three independent experiments.
[b] $p < 0.01$ versus *cis*-platin in each cell line.
[c] $p < 0.01$ vs compound **4** in each cell line.
[d] $p < 0.01$ versus compound **3** in each cell line.
[e] $p < 0.01$ versus the IC_{50} of HeLa in compound **3** and **13**.
[f] $p < 0.01$ versus compound **4** in HeLa (*t*-test).

and $Ph_2Sn(OC_{10}H_6CH{=}NCH_2COO)$.[14] Distortions from the ideal geometry may be rationalized partly by the restricted bite angles of the tridentate ligand. Neither of the five- or six-membered rings formed upon chelation are planar in **3** and **13**, as seen in the following torsion angles: 18.6(5)° for Sn–N1–C16–C20, 1.3(6)° for Sn–O2–C20–C16, 19.2(6)° for Sn–N1–C15–C14, and −29.7(7)° for Sn–O1–C9–C14 for **3**; 12.4(6)° for Sn–N1–C2–C1, 6.4 (6)° for Sn–O1–C1–C2, 12.4(6)° for Sn–N1–C6–C7, and −28.4(6)° for Sn–O3–C12–C7 for **13**. The closest non-hydrogen intermolecular contacts in the lattices of **3** and **13** are $C15\cdots O3^{i}$ (3.290(6) Å) (symmetry code i: $-x$, $1/2+y$, $1/2-z$) and $C6\cdots O2^{ii}$ (3.145(6) Å) (symmetry code ii: $-x$, $1/2+y$, $1-z$) respectively. The differences in the coordination geometries between **3** and **13** are reflected in the bond distances around tin (longer in **3**) and the C–Sn–C angle (128.2(3)° for **3** and 121.5(3)° for **13** respectively), reflecting the nature of the tin-bound organic substituents. The Sn–N bond length (2.164(4) Å) of **3** is similar to that found in the dibutytin compounds $Bu_2Sn(OC_6H_4CH{=}NCH(i\text{-}Pr)COO)$ (2.158(8) Å)[15] and $Bu_2Sn(OC_6H_4CH{=}NCH(CH_2Indole\text{-}3)COO)$ (2.161(3) Å).[17] The Sn–N bond length (2.158(3) Å) of compound **13** is shorter than that of $Ph_2Sn(OC_6H_4C(CH_3){=}NCH_2COO)$ (2.190(5) Å)[9] and longer than that of $Ph_2Sn(OC_6H_4CH{=}NCH_2COO)$ (2.086(3) Å).[13]

Cytotoxic activity

In order to observe the effects of the alkyl bound to tin on the cytotoxic activity, complexes **3, 4, 5** and **13** were selected for the cytotoxic assays. The results of these assays and the reference drug, *cis*-platin, against the three human tumour cell lines HeLa, CoLo205 and MCF-7 are shown in Table 2. The compounds belong to the efficient cytostatic agents and their cytotoxic activities were higher than those of the clinically widely used *cis*-platin, except compound **4** against HeLa. However, they were less active than the di-*n*-butyltin and diphenyltin complexes of (2-hydroxynaphthalidene)glycine (IC_{50} against MCF-7 is 75 ng ml^{-1} and 170 ng ml^{-1} respectively).[11] As observed in previous studies,[3,4] both the organotin moiety (R′) and the ligand (L) appear to play an important role. The data from Table 2 reveal that dicyclohexyltin derivatives are the most active against the three cell lines and that the activity decreases in the order Cy > *n*-Bu > Ph for the R′ group bound to tin.

REFERENCES

1. Davies AG. *Organotin Chemistry*, 2nd edn. Wiley–VCH: Weinheim, 2004; 383.
2. Narayanan V, Nasr M, Paull KD. In *Tin-Based Anti-Tumor Drugs*, Gielen M (ed.). Springer-Verlag: Berlin, 1990; 201.
3. Gielen M. *Coord. Chem. Rev.* 1996; **15**: 41.
4. Yang P, Guo M. *Coord. Chem. Rev.* 1999; **185–186**: 189.
5. Gielen M, Biesemans M, Vos DD, Willem R. *J. Inorg. Biochem.* 2000; **79**: 139.
6. Gielen M. *Appl. Organometal. Chem.* 2002; **16**: 481.
7. Basu Baul TS, Dutta S, Masharing C, Rivarola E, Englert U. *Heteroat. Chem.* 2003; **14**: 149.
8. Basu Baul TS, Dutta S, Rivarola E, Scopelliti M, Choudhuri S. *Appl. Organometal. Chem.* 2001; **15**: 947.
9. Dakternieks D, Basu Baul TS, Dutta S, Tiekink ERT. *Organometallics* 1998; **17**: 3058.
10. Basu Baul TS, Dutta S, Rivarola E, Butcher R, Smith FE. *J. Organometal. Chem.* 2002; **654**: 100.
11. Nath M, Yadav R, Gielen M, Dalil H, Vos DD, Eng G. *Appl. Organometal. Chem.* 1997; **11**: 727.
12. Ogwuru N, Khoo LE, Eng G. *Appl. Organometal. Chem.* 1998; **12**: 409.
13. Wang J, Zhang Y, Xu Y, Wang Z. *Heteroat. Chem.* 1992; **3**: 599.
14. Smith FE, Koo LE, Goh NK, Hynes RC, Eng G. *Can. J. Chem.* 1996; **74**: 2041.
15. Smith FE, Hynes RC, Ang TT, Khoo LE, Eng G. *Can. J. Chem.* 1992; **70**: 1114.
16. Tian L, Liu X, Shang Z, Li D, Yu Q. *Appl. Organometal. Chem.* 2004; **18**: 483.
17. Yin H, Wang Q, Xue S. *J. Organometal. Chem.* 2004; **689**: 2480.
18. Beltran HI, Zamudio-Rivera LS, Mancilla T, Santillan R, Farfan N. *Chem. Eur. J.* 2003; **9**: 2291.
19. Langer HG. *Tetrahedron Lett.* 1967; 43.

20. SADABS, program for empirical absorption correction of area detector data. Bruker AXS Inc., Madison, WI, USA, 2002.
21. Sheldrick GM. SHELX 97, program for crystal structure solution. University of Göttingen, Germany, 1997.
22. Sheldrick GM. SHELXL-97, program for the crystal structure refinement. University of Göttingen, Germany, 1997.
23. Flack HD. *Acta Crystallogr. Sect. A* 1983; **39**: 876.
24. Denizot F, Lang R. *J. Immunol. Methods* 1986; **89**: 271.
25. Bonire JJ, Fricker SP. *J. Inorg. Biochem.* 2001; **83**: 217.
26. Zheng XL, Sun HX, Liu XL, Chen YX, Qian BC. *Acta Pharmacol. Sin.* 2004; **25**: 109.
27. Tian L, Zhou Z, Zhao B, Zhang C. *Main Group Met. Chem.* 1998; **21**: 735.
28. Ho BYK, Zuckerman JJ. *Inorg. Chem.* 1973; **12**: 1552.
29. Liu S, Gelmini L, Rettig SJ, Thompson RC, Orvig C. *J. Am. Chem. Soc.* 1992; **114**: 6081.
30. Van Koten G, Noltes JG. *J. Am. Chem. Soc.* 1976; **98**: 5393.
31. Davies AG. *Organotin Chemistry*, 2nd edn. Wiley–VCH: Weinheim, 2004; 18.
32. Holecek J, Nadvornik M, Handlir K. *J. Organometal. Chem.* 1986; **315**: 297.
33. Saraswat BS, Mason J. *Polyhedron* 1986; **5**: 1449.

