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Synthesis, structural characterization and *in vitro* cytotoxicity of diorganotin complexes with Schiff base ligands derived from 3-hydroxy-2-naphthoylhydrazide

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A series of diorganotin complexes with Schiff base ligands, (*E*)-*N'*-(5-bromo-2-hydroxybenzylidene)-3-hydroxy-2-naphthohydrazide, H_2L1, and (*E*)-*N'*-(5-chloro-2-hydroxybenzylidene)-3-hydroxy-2-naphthohydrazide, H_2L2, were synthesized and characterized by elemental analysis, IR, ^1H, ^{13}C and ^{119}Sn NMR spectroscopy. The molecular structures of the complexes, [(5-bromo-2-oxidobenzylidene)-3-hydroxy-2-naphthohydrazidato]di(*o*-chlorobenzyl)tin(IV) 6 and [(5-chloro-2-oxidobenzylidene)-3-hydroxy-2-naphthohydrazidato]dibutyltin(IV) 9, were determined through single-crystal X-ray diffraction and revealed a distorted trigonal-bipyramidal configuration. The *in vitro* cytotoxic activity of the Schiff bases and their diorganotin complexes was also evaluated against several human carcinoma cell lines, namely HT29 (human colon carcinoma cell line), SKOV-3 (human ovarian cancer cell line), MCF7 (hormone-dependent breast carcinoma cell line) and MRC5 (non-cancer human fibroblast cell line). [(5-Bromo-2-oxidobenzylidene)-3-hydroxy-2-naphthohydrazidato]dibutyltin(IV) 2 and [(5-bromo-2-oxidobenzylidene)-3-hydroxy-2-naphthohydrazidato]dibenzyltin(IV) 5 were the most active diorganotin complexes of H_2L1 ligand. Among the diorganotin complexes of H_2L2 ligand, [(5-chloro-2-oxidobenzylidene)-3-hydroxy-2-naphthohydrazidato] dicyclohexyltin(IV) 11 showed good cytotoxic activity against all the tested cell lines. As such, the above compounds can be considered agents with potential anticancer activities, and can therefore be investigated further in *in vitro* or *in vivo* anticancer studies. Copyright © 2012 John Wiley & Sons, Ltd.

Keywords: diorganotin; crystal structures; cytotoxic activity

Introduction

In the literature many Schiff bases have been synthesized and widely studied because of their various characteristics for use in medicine and their biological properties. Lately, studies of Schiff base metal complexes with salicylaldehyde or substituted salicylaldehyde derivatives have been of interest because of their potential DNA binding properties.[1,2]

In recent years, studies of organotin(IV) compounds have gained interest because of their potential industrial and biocidal applications.[3–6] Among these compounds, the chemistry and applications of organotin(IV) complexes with monodentate, bidentate, tridentate and multidentate Schiff bases are extensively studied because of their structural diversity, thermal stability and biological properties such as antifungal,[7,8] antibacterial,[7,8] antitumour,[7,9–11] antioxidant,[11] insecticidal[12] and anti-inflammatory.[11,13] The biological activities of the compounds are largely related to the molecular structure of the organotin(IV) complexes, their coordination number, extent of alkylation, and the nature and number of organic groups attached to the tin atom. The coordination chemistry of diorganotin(IV) complexes with *ONO*, *ONS* and *NNO* terdentate ligands has been widely discussed for their biological and pharmacological properties.[14–16] Schiff bases derived from 3-hydroxy-2-naphthoylhydrazide are reported to have good antimicrobial activities.[17]

The present work focuses on Schiff bases prepared from the condensation reaction of 3-hydroxy-2-naphthoylhydrazide and substituted salicylaldehydes. The synthesis of the diorganotin (IV) complexes derived from these terdentate *ONO* ligands is discussed. It is our aim to investigate the structural features and biological properties of the Schiff bases and their diorganotin (IV) complexes. The crystal structures of some of the diorganotin(IV) complexes have been reported elsewhere. The *in vitro* cytotoxicity of the Schiff bases and their diorganotin(IV) complexes against three human carcinoma cell lines (HT29, SKOV-3 and MCF7) and non-carcinoma human cell line (MRC5) is evaluated and the results are discussed.

Experimental

Materials and Physical Measurements

All chemicals and reagents used in the synthesis were of reagent grade. Dimethyltin oxide (Acros), dibutyltin dichloride (Fluka), diphenyltin oxide (Acros), dicyclohexyltin oxide (Acros), 3-hydroxy-

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2-naphthoylhydrazide (Aldrich), 5-bromosalicylaldehyde (Fluka) and 5-chlorosalicylaldehyde (Aldrich) are commercially available. Dibenzyltin dichloride, di(*o*-chlorobenzyl)tin dichloride and di(*p*-chlorobenzyl)tin dichloride were prepared in accordance with the literature method.[18] The solvents used in the reaction were of AR grade and dried using standard literature procedures.[19] The melting points of the ligands and the diorganotin complexes were determined using an Electrothermal digital melting point apparatus and were uncorrected. The IR spectra for the compounds were recorded in KBr pellets on a PerkinElmer Spectrum RX1 FT-IR spectrophotometer. ^{1}H and ^{13}C NMR spectra were recorded on a JEOL JNM GX-270 FT NMR System spectrometer, while the ^{119}Sn NMR spectra were recorded on a JEOL ECA-400MHz spectrometer. The chemical shifts were recorded in ppm with reference to Me_4Si for ^{1}H and ^{13}C NMR and Me_4Sn for ^{119}Sn NMR. Elemental analyses were carried out on a PerkinElmer EA2400 CHNS Elemental Analyzer.

Synthesis of the Ligands

(E)-N′-(5-Bromo-2-hydroxybenzylidene)-3-hydroxy-2-naphthohydrazide ***[H_2L1]***

3-Hydroxy-2-naphthoylhydrazide (2.03 g, 0.01 mol) and 5-bromosalicylaldehyde (2.05 g, 0.01 mol) were dissolved in 200 ml methanol and refluxed for 2 h. Upon cooling to room temperature, a yellow solid was obtained and used without further purification.

Yield: 2.31 g, 60%; m.p. 316–318°C. Anal. Calc for $C_{18}H_{13}N_2O_3Br$: C, 56.12: H, 3.40: N, 7.27. Found: C, 56.05: H, 3.15: N, 7.08% IR (cm^{-1}): 3432 ν(OH, NH), 1642 ν(CO), 1629 ν(CN), 1077 ν(CO).

(E)-N′-(5-Chloro-2-hydroxybenzylidene)-3-hydroxy-2-naphthohydrazide ***[H_2L2]***

3-Hydroxy-2-naphthoylhydrazide (2.03 g, 0.01 mol) and 5-chlorosalicylaldehyde (1.57 g, 0.01 mol) were dissolved in 200 ml methanol and refluxed for 2 h. Upon cooling to room temperature, a yellow solid was obtained and used without further purification.

Yield: 2.35 g, 69%; m.p. 310–312°C. Anal. Calc for $C_{18}H_{13}N_2O_3Cl$: C, 63.45: H, 3.85: N, 8.22. Found: C, 63.72: H, 3.57: N, 8.06% IR (cm^{-1}): 3390 ν(OH, NH), 1647 ν(CO), 1630 ν(CN), 1091, 1072 ν(CO).

Synthesis of the Diorganotin Complexes, 1–14

The preparation method used for diorganotin compound **1** was repeated for compounds **3**, **4**, **8**, **10** and **11** with the appropriate diorganotin oxides and Schiff base ligands. The preparation method used for diorganotin compound **2** was repeated for compounds **5**, **6**, **7**, **9**, **12**, **13** and **14** with the appropriate diorganotin chlorides and Schiff base ligands.

[(5-Bromo-2-oxidobenzylidene)-3-hydroxy-2-naphthohydrazidato]dimethyltin (IV), Me_2SnL1, ***1***

Ligand **H_2L1** (0.39 g, 1.0 mmol) in 20 ml dry toluene was added to a suspension of dimethyltin oxide (0.17 g, 1.0 mmol) in 40 ml dry toluene. The mixture was heated under reflux in a Dean–Stark apparatus for 8 h to remove water formed during the reaction. The solvent was gradually removed by evaporation under vacuum until a precipitate was obtained. The precipitate was recrystallized from a 1:1 mixture of dichloromethane–hexane to yield yellow crystals.

Yield: 0.41 g, 77%; m.p. 218–220°C. Anal. Calc for $C_{20}H_{17}N_2O_3BrSn$: C, 45.16; H, 3.22; N, 5.27%. Found: C, 45.58; H, 3.16; N, 5.40%. IR (cm^{-1}): 3431 ν(OH), 1638 ν(CN), 1601 ν(CNNC), 1080, 1051 ν(CO).

[(5-Bromo-2-oxidobenzylidene)-3-hydroxy-2-naphthohydrazidato]dibutyltin (IV), Bu_2SnL1, ***2***

The ligand **H_2L1** (0.39 g, 1.0 mmol), and triethylamine (0.14 ml, 1.0 mmol) were added to 50 ml absolute ethanol and the mixture was heated under reflux for 2 h. Dibutyltin dichloride (0.30 g, 1.0 mmol) in 30 ml absolute ethanol was added and the mixture was further refluxed for 5 h and filtered. The filtrate was evaporated until a precipitate was obtained. The precipitate was recrystallized from toluene and the by-product, triethylammonium chloride, was removed through filtration. Yellow crystals suitable for X-ray crystallographic studies were obtained from the slow evaporation of the filtrate.

Yield: 0.50 g, 81%; m.p. 123–124°C. Anal. Calc for $C_{26}H_{29}N_2O_3BrSn$: C, 50.68; H, 4.74; N, 4.55%. Found: C, 51.04; H, 4.62; N, 4.26%. IR (cm^{-1}): 3422 ν(OH), 1638 ν(CN), 1602 ν(CNNC), 1076, 1056 ν(CO).

[(5-Bromo-2-oxidobenzylidene)-3-hydroxy-2-naphthohydrazidato]diphenyltin (IV), Ph_2SnL1, ***3***

Yield: 0.49 g, 75%; m.p. 264–266°C. Anal. Calc for $C_{30}H_{21}N_2O_3BrSn$: C, 54.92; H, 3.23; N, 4.27%. Found: C, 54.52; H, 3.57; N, 4.47%. IR (cm^{-1}): 3386 ν(OH), 1638 ν(CN), 1602 ν(CNNC), 1076, 1054 ν(CO).

[(5-Bromo-2-oxidobenzylidene)-3-hydroxy-2-naphthohydrazidato]dicyclohexyltin (IV), Cy_2SnL1, ***4***

Yield: 0.44 g, 66%; m.p. 156–158°C. Anal. Calc for $C_{30}H_{33}N_2O_3BrSn$: C, 53.92; H, 4.98; N, 4.19%. Found: C, 54.38; H, 4.98; N, 4.05%. IR (cm^{-1}): 3400 ν(OH), 1638 ν(CN), 1601 ν(CNNC), 1077, 1052 ν(CO).

[(5-Bromo-2-oxidobenzylidene)-3-hydroxy-2-naphthohydrazidato]dibenzyltin (IV), Bz_2SnL1, ***5***

Yield: 0.41 g, 60%; m.p. 144–146°C. Anal. Calc for $C_{32}H_{25}N_2O_3BrSn$: C, 56.18; H, 3.68; N, 4.09%. Found: C, 55.93; H, 3.44; N, 4.29%. IR (cm^{-1}): 3422 ν(OH), 1639 ν(CN), 1607 ν(CNNC), 1082, 1057 ν(CO).

[(5-Bromo-2-oxidobenzylidene)-3-hydroxy-2-naphthohydrazidato]di(o-chlorobenzyl)tin(IV), (o-ClBz)$_2$SnL1, ***6***

Yield: 0.52 g, 69%; m.p. 140–142°C. Anal. Calc for $C_{32}H_{23}N_2O_3BrCl_2Sn$: C, 51.04; H, 3.08; N, 3.72 %. Found: C, 51.45; H, 3.25; N, 3.76 %. IR (cm^{-1}): 3402 ν(OH), 1638 ν(CN), 1604 ν(CNNC), 1079, 1057 ν(CO).

[(5-Bromo-2-oxidobenzylidene)-3-hydroxy-2-naphthohydrazidato]di(p-chlorobenzyl)tin(IV), (p-ClBz)$_2$SnL1, ***7***

Yield: 0.37 g, 49%; m.p. 80–82°C. Anal. Calc for $C_{32}H_{23}N_2O_3BrCl_2Sn$: C, 51.04; H, 3.08; N, 3.72%. Found: C, 50.87; H, 3.28; N, 3.47%. IR (cm^{-1}): 3392 ν(OH), 1639 ν(CN), 1606 ν(CNNC), 1078, 1036 ν(CO).

[(5-Chloro-2-oxidobenzylidene)-3-hydroxy-2-naphthohydrazidato]dimethyltin (IV), Me_2SnL2, ***8***

Yield: 0.37 g, 75%; m.p. 220–222°C. Anal. Calc for $C_{20}H_{17}N_2O_3ClSn$: C, 49.27; H, 3.51; N, 5.75%. Found: C, 49.54; H, 3.38; N, 5.36%. IR (cm^{-1}): 3431 ν(OH), 1638 ν(CN), 1604 ν(CNNC), 1093, 1054 ν(CO).

[(5-Chloro-2-oxidobenzylidene)-3-hydroxy-2-naphthohydrazidato]dibutyltin (IV), Bu_2SnL2, ***9***

Yield: 0.47 g, 82%; m.p. 118–120°C. Anal. Calc for $C_{26}H_{29}N_2O_3ClSn$: C, 54.63; H, 5.11; N, 4.90%. Found: C, 54.35; H, 5.26; N, 4.65%. IR (cm^{-1}): 3430 ν(OH), 1638 ν(CN), 1610 ν(CNNC), 1090, 1056 ν(CO).

[(5-Chloro-2-oxidobenzylidene)-3-hydroxy-2-naphthohydrazidato]diphenyltin (IV), Ph_2SnL2, ***10***

Yield: 0.47 g, 77%; m.p. 264–266°C. Anal. Calc for $C_{30}H_{21}N_2O_3ClSn$: C, 58.91; H, 3.46; N, 4.58%. Found: C, 59.12; H, 3.48; N, 4.66%. IR (cm^{-1}): 3428 ν(OH), 1639 ν(CN), 1610 ν(CNNC), 1075, 1054 ν(CO).

[(5-Chloro-2-oxidobenzylidene)-3-hydroxy-2-naphthohydrazidato]dicyclohexyltin (IV), Cy_2SnL2, ***11***

Yield: 0.34 g, 55%; m.p. 320–322°C. Anal. Calc for $C_{30}H_{33}N_2O_3ClSn$: C, 57.77; H, 5.33; N, 4.49%. Found: C, 58.01; H, 5.51; N, 4.57%. IR (cm^{-1}): 3400 ν(OH), 1640 ν(CN), 1602 ν(CNNC), 1084, 1054 ν(CO).

[(5-Chloro-2-oxidobenzylidene)-3-hydroxy-2-naphthohydrazidato]dibenzyltin (IV), Bz_2SnL2, ***12***

Yield: 0.41 g, 64%; m.p. 154–156°C. Anal. Calc for $C_{32}H_{25}N_2O_3ClSn$: C, 60.08; H, 3.94; N, 4.38%. Found: C, 60.25; H, 3.77; N, 4.09%. IR (cm^{-1}): 3428 ν(OH), 1640 ν(CN), 1615 ν(CNNC), 1079, 1057 ν(CO).

[(5-Chloro-2-oxidobenzylidene)-3-hydroxy-2-naphthohydrazidato]di(o-chlorobenzyl)tin(IV), $(o\text{-}ClBz)_2SnL2$, ***13***

Yield: 0.50 g, 70%; m.p. 145–146°C. Anal. Calc for $C_{32}H_{23}N_2O_3Cl_3Sn$: C, 54.24; H, 3.27; N, 3.95%. Found: C, 53.97; H, 3.19; N, 3.74%. IR (cm^{-1}): 3380 ν(OH), 1640 ν(CN), 1608 ν(CNNC), 1068, 1038 ν(CO).

[(5-Chloro-2-oxidobenzylidene)-3-hydroxy-2-naphthohydrazidato]di(p-chlorobenzyl)tin(IV), $(p\text{-}ClBz)_2SnL2$, ***14***

Yield: 0.43 g, 60%; m.p. 134–136°C. Anal. Calc for $C_{32}H_{23}N_2O_3Cl_3Sn$: C, 54.24; H, 3.27; N, 3.95%. Found: C, 54.01; H, 3.38; N, 3.90%. IR (cm^{-1}): 3422 ν(OH), 1639 ν(CN), 1617 ν(CNNC), 1093, 1037 ν(CO).

X-Ray Structural Studies

X-ray crystallographic data for [(5-bromo-2-oxidobenzylidene)-3-hydroxy-2-naphthohydrazidato]di(*o*-chlorobenzyl)tin(IV) **6** and [(5-chloro-2-oxidobenzylidene)-3-hydroxy-2-naphthohydrazidato] dibutyltin(IV) **9** were collected at 100 K using graphite-monochromated MoKα ($\lambda = 0.71073$) radiation on a Bruker SMART APEX2 CCD diffractometer. The structures were solved by direct method and refined using the full-matrix least-squares procedure based on F^2 using the SHELXL-97 program.[20]

The positions of hydrogen atoms were calculated and included in the structure factor calculations. Crystallographic data for the structures have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication numbers CCDC 765256 and CCDC 787617. Copies of available materials can be obtained on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: +44 1223 336 033; or e-mail: deposit@ccdc.cam.ac.uk).

In Vitro Cytotoxicity

The *in vitro* cytotoxicity of the complexes was determined by Neutral Red cytotoxicity assay.[21] HT29 (human colon carcinoma cell line), SKOV-3 (human ovarian cancer cell line), MCF7 (hormone-dependent breast carcinoma cell line) and MRC5 (non-cancer human fibroblast cell line) were purchased from the American Tissue Culture Collection (ATCC, USA). The HT29 and MCF7 cells were maintained in RPMI 1640 medium (Sigma), SKOV-3 cells in Dulbecco's Modified Eagle's Medium (DMEM; Sigma) and MRC5 cells in Eagle Minimum Essential Medium (EMEM; Sigma), supplemented with 10% fetal bovine serum (FBS; PAA Lab, Austria), 100 μg ml^{-1} penicillin or streptomycin (PAA Lab, Austria) and 50 μg ml^{-1} Fungizone (PAA Lab). The cells were cultured in a 5% CO_2 incubator (Shel Lab water-jacketed) kept at 37°C in a humidified atmosphere.

The cells (1×10^4 per well) were seeded in 96-well microtitre plates (Nunc) and allowed to grow for 24 h before treatment with test compounds. After incubation, the cells were treated with six different concentrations (0.1–100 μg ml^{-1}) of test compounds in three replicates. The plates were further incubated for 72 h at 37°C in the 5% CO_2 incubator. Stock solutions were initially obtained by dissolving the test compounds in DMSO. Further dilutions to different test concentrations were carried out to ensure that the final concentration of DMSO in the test and control wells did not exceed 1% (v/v). The concentration of DMSO used did not reveal any cytotoxic activity. Cisplatin was used as positive control and the wells containing untreated cells were the negative control. Cytotoxicity of each sample is expressed as IC_{50}, value which refers to the average concentration of test compounds that causes 50% inhibition or cell death from the three experiments. The IC_{50} value was obtained from the graph of percentage inhibition (%) versus concentration of test compounds (μg ml^{-1}).

Statistical Analysis

Data are presented as mean $\pm$ SEM. The IC_{50} values were obtained by nonlinear regression using GraphPad Prism statistical software.

Results and Discussion

Synthesis

The Schiff base ligands (*E*)-*N*′-(5-bromo-2-hydroxybenzylidene)-3-hydroxy-2-naphthohydrazide $\mathbf{H_2L1}$ and (*E*)-*N*′-(5-chloro-2-hydroxybenzylidene)-3-hydroxy-2-naphthohydrazide $\mathbf{H_2L2}$ were prepared from the condensation reaction of 5-bromosalicylaldehyde and 5-chlorosalicylaldehyde with 3-hydroxy-2-naphthoylhydrazide (Fig. 1). These Schiff base ligands are polydentate with five potential donor atoms (two nitrogen atoms and three oxygens from hydroxy groups) which can readily form coordination bonds with the tin atom. The ligands can be enolized in solution state as shown in Fig. 2, with the enolized form providing three acidic protons which can react with the diorganotin oxides and diorganotin dichlorides. Subsequently, the diorganotin complexes are prepared from the reactions of the Schiff base ligands with diorganotin oxides and diorganotin dichlorides as shown in Fig. 3.

The coordination of one of the imine nitrogens to the tin atom further stabilizes the overall structure. The structural features of the diorganotin complexes were characterized using various spectroscopic techniques.

Spectroscopic Characterization

The characteristic infrared absorption bands of the ligands and its diorganotin complexes are given in the Experimental section. The IR spectra of ligands $\mathbf{H_2L1}$ and $\mathbf{H_2L2}$ show strong and broad bands at 3432 and 3390 cm^{-1}, respectively, which can be attributed to the overlapping of the hydroxy and amine functional groups. In the IR spectra of the diorganotin complexes, the presence of a smaller band in the same region suggests the presence of an uncoordinated hydroxy group. Accordingly, the Schiff base

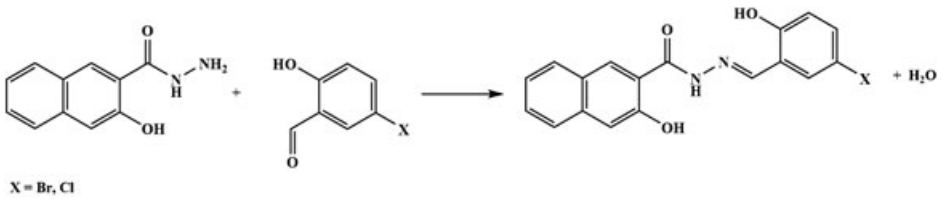


Figure 1. Reaction scheme for the synthesis of Schiff base ligands

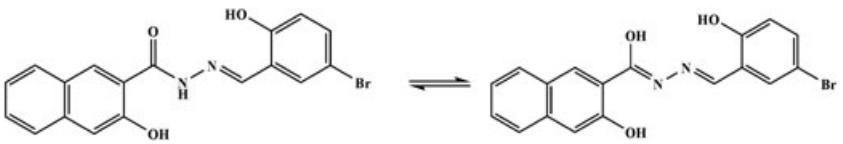


Figure 2. Keto-enol form of Schiff base ligand, **H_2L1**

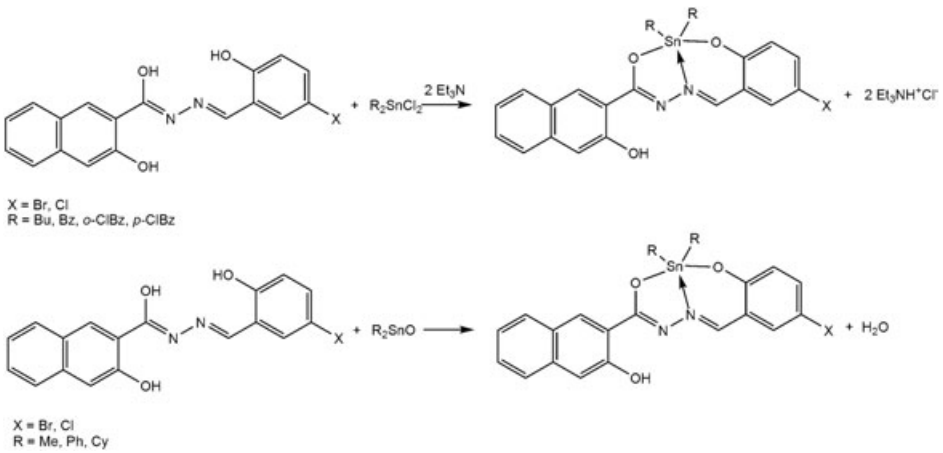


Figure 3. Reaction scheme for the synthesis of Schiff base ligands with diorganotin dichlorides and diorganotin oxides

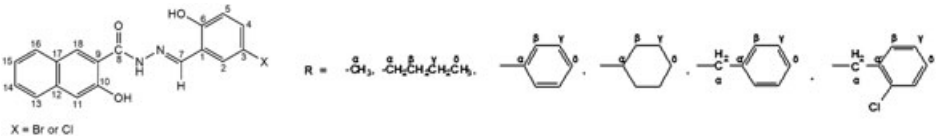
ligands display strong to medium absorption within the range 1620–1650 cm^{-1} due to the CO and CN stretching frequencies, while the diorganotin complexes show medium absorption in the 1600–1640 cm^{-1} region due to the CN and CNNC stretching frequencies.[22–25]

The ^{1}H NMR spectral data of the Schiff base ligands and its diorganotin complexes are presented in Table 1, and the chemical shifts for the aliphatic and aromatic protons are found within the expected range. The azomethine proton HCN of the Schiff bases is observed as a sharp singlet between 8.60 and 8.70 ppm. The ^{1}H NMR signal of azomethine protons for the complexes are shifted by about 0.2–0.5 ppm and this is due to the coordination of azomethine nitrogen to the tin atom, which leads to a significant deshielding effect of the protons.[26–28] The signals at 6.50–7.90 and 8.00–8.50 ppm are assigned to aryl protons of the Schiff base ligands and the diorganotin complexes. In the ^{1}H NMR spectra of the ligands, a singlet at 12.20 ppm is assigned to the NH proton, while the signals at 11.23 and 11.24 ppm are assigned to the OH protons. In the diorganotin complexes, the presence of a singlet in the region of 11.10–12.10 ppm suggests that an OH proton on the naphthalene ring does not participate in the coordination to the tin atom.

The ^{13}C NMR spectral data of the Schiff base ligands and its diorganotin complexes are tabulated in Table 2. The aromatic carbons of the ligand as well as the diorganotin complexes are found in the expected range, and their chemical shifts are in close agreement with reported values.[24,25,29,30] The aromatic carbon resonances are assigned by two-dimensional proton-detected heteronuclear single bond chemical shift correlation (HSBC) using the values corresponding to $^1J_{(C,H)}$, heteronuclear multiple bond correlation (HMBC) using the values corresponding to $^2J_{(C,H)}$ or $^3J_{(C,H)}$ between the carbons and protons and DEPT (distortionless enhancement by polarization transfer) spectra. The signals of the azomethine carbons C-7 and C-8 of the ligands appear in the range 156–158 and 171–172 ppm, respectively. For the diorganotin complexes, downfield chemical shifts in the signals of the azomethine carbons C-7 and C-8 support the formation of the coordination SnO bond.

The heteronuclear coupling constant is useful in providing information on the geometry and coordinating environment of the diorganotin complexes. The satellite signals caused by the hydrogen–tin coupling and carbon–tin coupling are observed in most of the diorganotin complexes except in diphenyltin, dibenzyltin, di(*o*-chlorobenzyl)tin and di(*p*-chlorobenzyl)tin derivatives, where the spin–spin coupling peak between the tin nucleus and neighbouring carbons are not well resolved. The coupling constant values of the hydrogen–tin coupling $^2J(^{119}Sn^1H)$ and carbon–tin coupling, $^1J(^{119}Sn^{13}C)$, are given in Tables 1 and 2. The CSnC angles of the diorganotin complexes, as calculated

Table 1. ^{1}H NMR chemical shifts (δ, ppm) of the Schiff base ligands and their diorganotin(IV) complexes



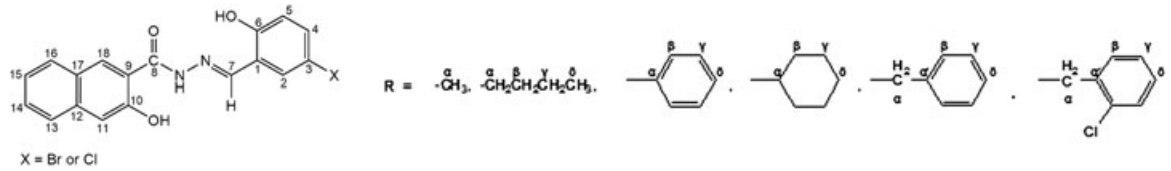
Compound No.	H-3, H-4, H-6, H-11, H-13, H-14, H-15, H-16, H-18 (aromatic protons)	−CH=N−	−OH	−NH	Sn−R
H_2L1	6.90, d (1H, J = 8.3 Hz), 7.30–7.49, m (4H), 7.70–7.91, m (3H), 8.43, s (1H)	8.62, s (1H)	11.24, s (2H)	12.20, s (1H)	—
1[a]	6.68, d (1H, J = 8.1 Hz), 7.26–7.45, m (4H), 7.65–7.82, m (3H), 8.49, s (1H)	8.59, s (1H)	11.48, s (1H)	—	0.79, s (6H, H_α, $^2J(^{119/117}Sn-^1H)$ = 78, 75 Hz)
2[a]	6.70, d (1H, J = 8.2 Hz), 7.28–7.45, m (4H), 7.50–7.84, m (3H), 8.50, s (1H)	8.58, s (1H)	11.58, s (1H)	—	1.66, t (4H, H_α, J = 6.3 Hz, $^2J(^{119/117}Sn-^1H)$ = 75, 71 Hz), 1.62, sbr (4H, H_β, $^3J(^{119}Sn-^1H)$ = 27 Hz), 1.42, sbr (4H, H_γ, $^4J(^{119/117}Sn-^1H)$ = 52, 50 Hz), 0.88, t (6H, H_δ, J = 6.9 Hz, $^5J(^{119}Sn-^1H)$ = 10 Hz)
3[b]	7.02, d (1H, J = 8.5 Hz), 7.10–7.26, m (4H), 7.64–7.85, m (3H), 8.50, s (1H)	8.78, s (1H)	11.39, s (1H)	—	7.30-7.40, m (4H), 7.42–7.55, m (6H)
4[a]	6.98, d (1H, J = 8.2 Hz), 7.17–7.42, m (4H), 7.60–7.87, m (3H), 8.53, s (1H)	8.57, s (1H)	11.67, s (1H)	—	2.22, t (2H, H_α, J = 6.5 Hz, $^2J(^{119/117}Sn-^1H)$ = 75, 72 Hz), 1.30–1.94 (m, 20H, H_β, H_γ, H_δ)
5[c]	6.92, d (1H, J = 8.3 Hz), 7.10–7.46, m (4H), 7.80–8.05, m (3H), 8.46, s (1H)	8.92, s (1H)	11.53, s (1H)	—	2.70, t (4H, H_α, J = 6.6 Hz, $^2J(^{119/117}Sn-^1H)$ = 83, 80 Hz), 7.51-7.75, m (10H)
6[c]	6.94, d (1H, J = 8.3 Hz), 7.12–7.40, m (4H), 7.78–7.95, m (3H), 8.15, s (1H)	8.35, s (1H)	11.47, s (1H)	—	2.75, t (4H, H_α, J = 6.5 Hz, $^2J(^{119/117}Sn-^1H)$ = 82, 78 Hz), 7.50-7.66, m (8H)
7[c]	6.89, d (1H, J = 8.3 Hz), 7.18–7.40, m (4H), 7.85–8.00, m (3H), 8.31, s (1H)	8.60, s (1H)	11.80, s (1H)	—	2.85, t (4H, H_α, J = 6.6 Hz, $^2J(^{119/117}Sn-^1H)$ = 81, 78 Hz), 7.45-7.72, m (8H)
H_2L2	6.97, d (1H, J = 8.4 Hz), 7.32–7.50, m (4H), 7.70–7.92, m (3H), 8.43, s (1H)	8.63, s (1H)	11.23, s (2H)	12.20, s (1H)	—
8[a]	6.73, d (1H, J = 8.1 Hz), 7.13–7.38, m (4H), 7.65–7.82, m (3H), 8.49, s (1H)	8.56, s (1H)	11.49, s (1H)	—	0.79, s (6H, $^2J(^{119/117}Sn-^1H)$ =76, 72 Hz)
9[a]	6.72, d (1H, J = 8.2 Hz), 7.20–7.45, m (4H), 7.70–7.95, m (3H), 8.50, s (1H)	8.54, s (1H)	11.60, s (1H)	—	1.66, t (4H, H_α, J = 6.4 Hz, $^2J(^{119/117}Sn-^1H)$ = 78, 75 Hz), 1.62, sbr (4H, H_β, $^3J(^{119}Sn-^1H)$ = 28 Hz), 1.44, sbr (4H, H_γ, $^4J(^{119/117}Sn-^1H)$ = 52, 50 Hz), 0.88, t (6H, H_δ, J = 6.9 Hz, $^5J(^{119}Sn-^1H)$ = 10 Hz)
10[b]	6.88, d (1H, J = 8.4 Hz), 7.04–7.25, m (4H), 7.62–7.90, m (3H), 8.53, s (1H)	8.77, s (1H)	11.38, s (1H)	—	7.31–7.42, m (4H), 7.45–7.58, m (6H)
11[a]	6.92, d (1H, J = 8.3 Hz), 7.10–7.34, m (4H), 7.60–7.84, m (3H), 8.47, s (1H)	8.94, s (1H)	12.05, s (1H)	—	2.20, t (2H, H_α, J = 6.6 Hz, $^2J(^{119/117}Sn-^1H)$ = 74, 71 Hz), 1.20–1.94, m (20H, H_β, H_γ, H_δ)
12[c]	6.90, d (1H, J = 8.2 Hz), 7.12–7.40, m (4H), 7.80–8.02, m (3H), 8.48, s (1H)	8.98, s (1H)	12.14, s (1H)	—	2.70, t (4H, H_α, J = 6.6 Hz, $^2J(^{119/117}Sn-^1H)$ = 80, 77 Hz), 7.45–7.70, m (10H)
13[c]	6.90, d (1H, J = 8.2 Hz), 7.10–7.35, m (4H), 7.75–7.98, m (3H), 8.17, s (1H)	8.66, s (1H)	11.81, s (1H)	—	2.80, t (4H, H_α, J = 6.5 Hz, $^2J(^{119/117}Sn-^1H)$ = 81, 77 Hz), 7.40–7.65, m (8H)
14[c]	6.78, d (1H, J = 8.3 Hz), 7.26–7.40, m (4H), 7.72–7.92, m (3H), 8.20, s (1H)	8.67, s (1H)	11.84, s (1H)	—	2.72, t (4H, H_α, J = 6.5 Hz, $^2J(^{119/117}Sn-^1H)$ = 76, 73 Hz), 7.42–7.68, m (8H)

s, singlet; sbr, singlet broad; d, doublet; t, triplet; m, complex pattern.
[a]Spectra recorded in $CDCl_3$.
[b]Spectra recorded in DMSO-d_6.
[c]Spectra recorded in 1,4-dioxane + 2–3 drops of $CDCl_3$.

from the Lockhart and Manders equation, $\theta(CSnC) = 0.0161|^2J(^{119}Sn^1H)|^2 - 1.32\ |^2J(^{119}Sn^1H)| + 133.4$,[31,32] are found in the range 118–138°, which corresponds to diorganotin complexes with trigonal-bipyramidal geometry. Furthermore, the CSnC angle of the diorganotin complexes can also be estimated from the $^1J(^{119}Sn, ^{13}C)$ coupling constants using the Lockhart equation, $\theta(CSnC) = [|^1J(^{119}Sn^{13}C)| + 875]/11.4$.[32] Overall, the calculated CSnC angles show slight deviation from the values obtained by X-ray diffractometry studies.[33–37] This is probably due to the presence of weak interaction with the solvent molecules.

The ^{119}Sn NMR spectral data of the diorganotin complexes are tabulated in Table 3. ^{119}Sn NMR chemical shifts have long been

Table 2. ^{13}C NMR chemical shifts (δ, ppm) of the Schiff base ligands and their corresponding diorganotin(IV) complexes



Compound no.	C-1, C-3, C-4, C-5, C-6	C-8	C-7	C-9, C-10, C-11, C-12, C-13, C-14, C-15, C-16, C-17, C-18	C-2	Sn&—(C_α to C_δ)
H_2L1	118.8, 126.0, 133.9, 110.6, 136.0	171.2	156.5	121.3, 154.0, 110.9, 138.5, 124.2, 124.0, 126.8, 128.5, 128.8, 130.5	163.8	—
1[a]	117.7, 126.1, 135.8, 108.5, 136.8	170.1	160.2	122.0, 155.4, 111.2, 138.3, 123.8, 123.2, 127.3, 128.1, 128.8, 131.0	165.5	1.9 (C_α, $^1J(^{119/117}Sn\text{-}^{13}C)$ = 555, 525 Hz)
2[b]	118.0, 126.4, 135.5, 108.1, 136.6	170.3	160.0	121.8, 155.6, 111.1, 138.2, 123.8, 123.3, 127.3, 128.0, 128.9, 130.9	166.1	22.8 (C_α, $^1J(^{119/117}Sn\&-^{13}C)$ = 565, 540 Hz), 26.9 (C_β, $^2J(^{119}Sn\&-^{13}C)$ = 28 Hz), 26.4 (C_γ, $^3J(^{119/117}Sn\&-^{13}C)$ = 77, 69 Hz), 13.6 (C_δ)
3[b]	117.3, 126.2, 135.3, 108.4, 136.4	169.7	160.2	121.4, 154.9, 110.9, 138.1, 123.7, 123.1, 126.9, 127.9, 129.2, 131.0	167.7	137.5 (C_α, $^1J(^{119/117}Sn\&-^{13}C)$ = 510, 485 Hz), 130.4 (C_β, $^2J(^{119}Sn\&-^{13}C)$ = 22 Hz), 127.5 (C_γ, $^3J(^{119/117}Sn\&-^{13}C)$ = 56, 50 Hz), 131.6 (C_δ)
4[a]	117.8, 126.1, 135.5, 107.8, 136.7	170.4	159.7	121.1, 155.5, 111.0, 138.1, 123.8, 123.3, 127.3, 128.0, 128.8, 130.8	166.7	41.0 (C_α, $^1J(^{119/117}Sn\&-^{13}C)$ = 574, 548 Hz), 29.9 (C_β, $^2J(^{119}Sn\&-^{13}C)$ = 22 Hz), 28.4 (C_γ, $^3J(^{119/117}Sn\&-^{13}C)$ = 76, 69 Hz), 26.4 (C_δ)
5[c]	117.9, 126.2, 135.4, 110.1, 136.0	170.1	160.3	121.0, 155.2, 111.1, 138.3, 124.0, 123.6, 126.9, 128.1, 129.0, 130.6	167.1	12.7 (C_α, $^1J(^{119/117}Sn\&-^{13}C)$ = 602, 580 Hz), 136.4, 125.3, 124.2, 129.6
6[c]	117.7, 126.4, 135.2, 108.4, 136.7	169.8	160.0	121.1, 155.2, 110.9, 137.9, 123.9, 123.3, 126.8, 128.0, 128.8, 130.2	166.8	10.8 (C_α, $^1J(^{119/117}Sn\&-^{13}C)$ = 575, 550 Hz), 129.9, 134.8, 131.0 (C_β'), 125.0, 127.8 (C_γ'), 128.5
7[c]	117.4, 126.8, 135.0, 109.2, 136.8	169.5	160.6	121.4, 155.5, 110.9, 138.0, 123.8, 123.3, 127.2, 128.1, 128.8, 130.6	167.6	10.9 (C_α, $^1J(^{119/117}Sn\&-^{13}C)$ = 596, 575 Hz), 133.3, 127.5, 124.9, 131.2
H_2L2	117.6, 126.6, 133.3, 110.6, 135.4	171.9	157.2	121.3, 154.0, 117.4, 136.0, 124.0, 123.2, 126.9, 128.4, 128.8, 130.5	163.8	—
8[a]	117.5, 126.1, 132.4 109.0, 135.6	170.1	160.3	121.8, 155.3, 116.9, 136.8, 123.4, 122.1, 127.2, 128.1, 128.8, 131.0	165.1	1.9 (C_α, $^1J(^{119/117}Sn\text{-}^{13}C)$ = 590, 560 Hz)
9[a]	117.8, 126.0, 132.9, 108.1, 135.5	170.3	160.0	121.7, 155.4, 117.0, 136.8, 123.8, 122.4, 127.3, 128.0, 128.9, 130.9	165.7	22.8 (C_α, $^1J(^{119/117}Sn\&-^{13}C)$ = 593, 565 Hz), 26.7 (C_β, $^2J(^{119}Sn\&-^{13}C)$ = 31 Hz), 26.4 (C_γ, $^3J(^{119/117}Sn\&-^{13}C)$ = 78, 70 Hz), 13.5 (C_δ)
10[b]	117.9, 126.2, 132.7, 108.4, 135.7	170.1	160.3	122.2, 155.7, 117.1, 136.5, 123.5, 122.7, 127.4, 128.0, 128.3, 130.7	165.8	136.9 (C_α, $^1J(^{119/117}Sn\&-^{13}C)$ = 498, 475 Hz), 130.2 (C_β, $^2J(^{119}Sn\&-^{13}C)$ = 24 Hz), 128.7 (C_γ, $^3J(^{119/117}Sn\&-^{13}C)$ = 56, 50 Hz), 131.2 (C_δ)
11[a]	117.7, 126.2, 132.5, 108.3, 135.8	169.9	162.0	121.3, 155.6, 117.1, 136.9, 123.5, 122.0, 127.4, 128.3, 129.0, 131.2	168.4	43.8 (C_α, $^1J(^{119/117}Sn\&-^{13}C)$ = 530, 505 Hz), 29.9 (C_β, $^2J(^{119}Sn\&-^{13}C)$ = 22 Hz), 28.8 (C_γ, $^3J(^{119/117}Sn\&-^{13}C)$ = 78, 69 Hz), 26.5 (C_δ)
12[c]	117.6, 126.0, 132.5, 108.8, 135.2	170.2	162.4	121.7, 155.1, 117.3, 136.5, 123.6, 122.5, 127.1, 128.5, 129.3, 131.0	168.0	8.6 (C_α, $^1J(^{119/117}Sn\&-^{13}C)$ = 587, 565 Hz), 135.0, 128.2, 124.5, 129.9
13[c]	118.0, 126.2, 132.3 107.9, 135.1	172.0	162.6	120.7, 154.8, 116.8, 136.6, 123.4, 122.2, 127.0, 128.6, 130.2, 131.7	167.2	9.4 (C_α, $^1J(^{119/117}Sn\&-^{13}C)$ = 596, 570 Hz), 129.5, 138.1, 131.2(C_β'), 124.0, 127.5 (C_γ'), 128.3
14[c]	117.9, 126.4, 132.0, 108.5, 135.2	171.4	162.7	121.1, 155.0, 117.2, 136.3, 123.3, 122.3, 126.8, 128.0, 130.0, 131.2	167.4	9.2 (C_α, $^1J(^{119/117}Sn\&-^{13}C)$ = 606, 589 Hz), 138.2, 128.4, 127.3, 129.5

[a]Spectra recorded in $CDCl_3$.
[b]Spectra recorded in DMSO-d_6.
[c]Spectra recorded in 1,4-dioxane + 2–3 drops of $CDCl_3$.

used as an indicator to predict the coordination environment of tin in complexes.[38,39] The ^{119}Sn NMR chemical shifts for the dimethyltin complexes **1** and **8**, dibutyltin complexes **2** and **9**, and dicyclohexyltin complexes **4** and **11** are found at −157 ppm, −196 ppm and −262 ppm, respectively. The ^{119}Sn NMR chemical shift for diphenyltin complexes **3** and **10** are observed further upfield at −340 ppm. The ^{119}Sn NMR chemical shifts for dibenzyltin and substituted dibenzyltin complexes are found in the range −217 to −296 ppm. The ^{119}Sn NMR chemical shifts are found in the range reported for five-coordinated diorganotin complexes.[40–45]

Table 3. ^{119}Sn NMR spectral data of the synthesized diorganotin(IV) complexes

Compound no.	δ (ppm)
1[a]	−157.5
2[a]	−196.5
3[b]	−340.5
4[a]	−262.7
5[c]	−217.6
6[c]	−274.5
7[c]	−288.8
8[a]	−157.5
9[a]	−196.4
10[b]	−340.4
11[a]	−262.7
12[c]	−220.1
13[c]	−263.2
14[c]	−295.2

[a]Spectra recorded in $CDCl_3$.
[b]Spectra recorded in DMSO-d_6.
[c]Spectra recorded in 1,4-dioxane + 2–3 drops of $CDCl_3$.

Table 5. Selected bond lengths (Å) and angles (°) for [(5-bromo-2-oxidobenzylidene)-3-hydroxy-2-naphthohydrazidato]di(*o*-chlorobenzyl)tin(IV) **6** and [(5-chloro-2-oxido-benzylidene)-3-hydroxy-2-naphthohydrazidato]dibutyltin(IV) **9**

	6	9
Sn(1)N(1)	2.196(3)	2.1869(19)
Sn(1)O(1)	2.076(3)	2.0900(16)
Sn(1)O(2)	2.142(3)	2.1583(16)
Sn(1)C_i	2.142(4)	2.128(2)
Sn(1)C_i′	2.142(4)	2.129(2)
N(1)C(7)	1.294(5)	1.295(3)
N(2)C(8)	1.330(5)	1.316(3)
O(1)C(2)	1.326(5)	1.319(3)
O(2)C(8)	1.291(5)	1.290(3)
O(1)Sn(1)O(2)	153.25(11)	154.09(6)
C_iSn(1)N(1)	110.68(16)	106.61(8)
C_i′Sn(1)N(1)	114.59(15)	126.77(9)
C_iSn(1)C_i′	134.30(18)	126.40(9)

C_i refers to Ci_{pso}.
C_i and C_i′ for compound **6** is C-19 and C-26, while C_i and C_i′ for compound **9** is C-19 and C-23.

X-ray crystallography

[(5-Bromo-2-oxidobenzylidene)-3-hydroxy-2-naphthohydrazidato]di(o-chlorobenzyl)tin(IV), (o-ClBz)$_2$SnL1 ***6*** *and [(5-chloro-2-oxidobenzylidene)-3-hydroxy-2-naphthohydrazidato]dibutyltin(IV), Bu$_2$SnL2* ***9***

The crystallographic data and refinement details of compounds **6** and **9** are shown in Table 4, while the selected bond lengths and bond angles are given in Table 5. The molecular structures of compounds **6** and **9** show that the Schiff base behaved as a terdentate ligand when it reacted with di(*o*-chlorobenzyl)tin dichloride and dibutyltin dichloride, giving rise to a five-coordinated tin structure (Figs 4 and 5). The overall geometry of tin is a distorted trigonal-bipyramidal where the equatorial plane is formed from the imine nitrogen and two alkyl groups of the diorganotin moieties, while the phenoxy oxygen and hydroxy oxygen occupy the axial position. Distortion from the ideal trigonal-bipyramidal geometry for compounds **6** and **9** can be observed from the small O(1)SnO(2) axial angles of 153.25° and 154.09°, respectively, and the extent of the distortion is estimated from the τ-value. The τ-value is defined as $\tau = (\beta - \alpha)/60$, where α and β are the two largest donor–metal–donor angles in the five-coordinated environment.[46,47] The τ-value is expected to be zero for perfect square-pyramidal

Table 4. Crystallographic data of [(5-bromo-2-oxidobenzylidene)-3-hydroxy-2-naphthohydrazidato]di(*o*-chlorobenzyl)tin(IV) **6** and [(5-chloro-2-oxidobenzylidene)-3-hydroxy-2-naphthohydrazidato]dibutyltin(IV) **9**

Compound	6	9
Empirical formula	$C_{32}H_{23}BrCl_2N_2O_3Sn$	$C_{26}H_{29}ClN_2O_3Sn$
Formula weight	753.02	571.65
Crystal system, space group	Monoclinic, $P2_1/n$	Triclinic, $P\bar{1}$
a (Å)	17.6531(12)	10.0704 (1)
b (Å)	6.7016(5)	11.9259(1)
c (Å)	24.2085(16)	12.7460(2)
α (°)	90	62.957(1)
β (°)	96.069(1)	84.504(1)
γ (°)	90	66.574(1)
Volume (Å^3)	2847.9(3)	1244.25(3)
Z	4	2
Calculated density (mg m^{-3})	1.756	1.526
μ (mm^{-1})	2.526	1.164
θ range (°) for data collection	1.36–27.50	1.80–25.00
Reflections collected / unique 26 730 / 6546 [$R_{(int)} = 0.0712$] 9781 / 4376 [$R_{(int)} = 0.0183$]		
Max. and min. transmission	0.8841 and 0.6320	0.9261 and 0.6930
Data / restraints / parameters	6546 / 0 / 371	4376 / 1 / 301
Goodness-of-fit on F^2	1.05	1.08
Final R indices [$I > 2\sigma(I)$]	$R_1 = 0.037$, $wR_2 = 0.079$	$R_1 = 0.022$, $wR_2 = 0.055$
R indices (all data)	$R_1 = 0.069$, $wR_2 = 0.101$	$R_1 = 0.025$, $wR_2 = 0.057$
$\Delta\rho_{max}/\Delta\rho_{min}$ (e Å^{-3})	0.64 and −0.91	0.84 and −0.37

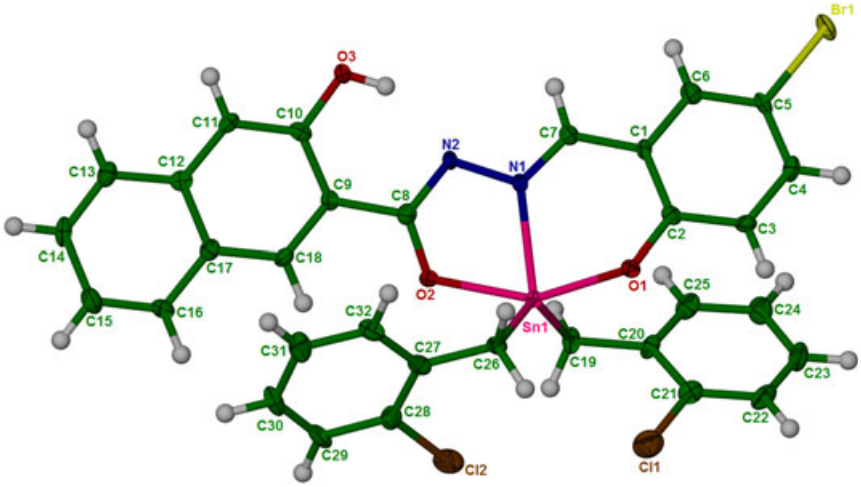


Figure 4. Molecular structure and crystallographic numbering scheme for [(5-bromo-2-oxidobenzylidene)-3-hydroxy-2-naphthohydrazidato]di(*o*-chlorobenzyl)tin(IV) **6**

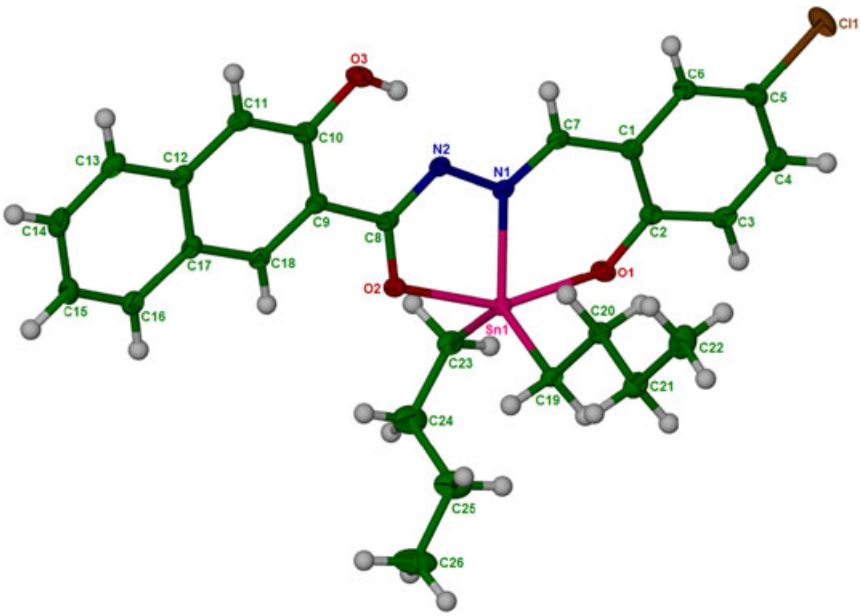


Figure 5. Molecular structure and crystallographic numbering scheme for [(5-chloro-2-oxidobenzylidene)-3-hydroxy-2-naphthohydrazidato] dibutyltin(IV) **9**

geometry and unity for perfect trigonal-bipyramidal geometry. The τ-value for compound **6** is 0.32, indicating a square-pyramidal geometry. For compound **9**, the τ-value (0.46) indicates that the coordination should be intermediate between a trigonal-bipyramidal and square-pyramidal geometry.

The two chelating planes, O(2)Sn(1)N(1)N(2)C(8) and O(1)Sn(1)N(1)C(7)C(1)C(2), in compound **6** are not planar and have a root mean square (RMS) deviation from planarity of 0.11 Å and 0.18 Å, respectively. The two rings form a dihedral angle of 15.4°. Conversely, the O(2)Sn(1)N(1)N(2)C(8) and O(1)Sn(1)N(1)C(7)C(1)C(2) planes in compound **9** are more planar, with RMS deviation from planarity of 0.01 Å and 0.07 Å, respectively. Unlike compound **6**, the O(2)Sn(1)N(1)N(2)C(8) and O(1)Sn(1)N(1)C(7)C(1)C(2) rings in compound **9** form a smaller dihedral angle of 4.3°.

Overall, the strong intramolecular hydrogen bonding interactions between O(3)H(3) and N(2) [OH···N 2.604(4) Å for compound **6** and 2.590(2) Å for compound **9**] whereby the bond distance is lower than the sum of the van der Waals radii (3.07 Å) help to stabilize the overall structures. The SnC, SnO and SnN bond distances for both complexes are comparable to the values reported for similar five-coordinated diorganotin complexes.[48–50]

Cytotoxic Activity of the Schiff Base Ligands and its Diorganotin Complexes

The *in vitro* Neutral Red cytotoxicity assay determines the accumulation of the Neutral Red dye in the lysosomes of viable and uninjured cells. Cisplatin is used as positive control and is found to exhibit remarkable growth inhibitory activities with mean IC_{50} values ranging from 1.4 to 5.7 $\mu g\ ml^{-1}$ on the studied cancer cell lines. The results of the cytotoxicity screening of the Schiff base ligands and the diorganotin complexes are summarized in Table 6.

Table 6. Cytotoxic activity of the Schiff base ligands and its diorganotin complexes

Compound	Cell lines (IC_{50} μg ml^{-1})[a]			
	HT29	**MCF7**	**SKOV3**	**MRC5**
cisplatin	5.0 ± 0	2.4 ± 0.6	1.4 ± 0	5.7 ± 0.6
H_2L1	34.7 ± 1.5	28.3 ± 2.9	33.0 ± 1.7	8.7 ± 1.5
1	5.0 ± 0	17.0 ± 3.6	1.3 ± 0.6	1.3 ± 0.6
2	6.7 ± 0.6	5.3 ± 0.6	3.7 ± 0.6	1.0 ± 0
3	54.3 ± 3.1	28.0 ± 4.0	8.3 ± 0.6	26.7 ± 9.1
4	26.7 ± 0.6	25.0 ± 2.0	16.0 ± 1.0	4.0 ± 0
5	8.0 ± 0	9.0 ± 0	9.3 ± 0.6	3.3 ± 0.6
6	9.0 ± 0	9.7 ± 0	34.0 ± 1.7	4.0 ± 0
7	24 ± 0.9	7.4 ± 0	30.7 ± 0.6	—
H_2L2	39.8 ± 1.0	26.0 ± 1.7	55.3 ± 0.6	55.0 ± 8.7
8	6.0 ± 0	71.0 ± 4.6	15.0 ± 6.2	16.7 ± 3.5
9	2.3 ± 1.2	8.5 ± 0.5	14.7 ± 4.5	36.7 ± 6.4
10	19.3 ± 1.5	> 100	8.0 ± 0	7.0 ± 0
11	4.8 ± 0.3	7.7 ± 0.6	6.0 ± 0	4.7 ± 0.6
12	21.0 ± 0	9.0 ± 0	39.0 ± 1.0	16.0 ± 0
13	27.3 ± 1.2	18.3	15.3 ± 1.2	60.3 ± 4.9
14	29.7 ± 1.2	9.0 ± 0	> 100	5.0 ± 0

[a]IC_{50} values (μg ml^{-1}) = inhibition concentration at 50%, i.e., concentration to reduce growth of cancer cells by 50%.

The **H_2L1** ligand is found to be less cytotoxic against all the tested cell lines when compared to its diorganotin derivatives. However, the diphenyltin derivative **3** shows weak cytotoxic activity against HT29 and MCF7 cell lines. The dimethyltin, dibutyltin and dibenzyltin derivatives of **H_2L1** (compounds **1**, **2** and **5**) have good cytotoxic activity with IC_{50} values which are comparable to those of the cisplatin in all the cell lines, except for compound **1** against MCF7 cell line.

As shown in Table 6, the **H_2L2** ligand is found to be less cytotoxic against all the tested cell lines. The dimethyltin and dibutyltin derivatives of **H_2L2** (compounds **8** and **9**) display good cytotoxic activity in all the tested cell lines, except for compound **8** against MCF7 cell line. Compound **11**, the dicyclohexyltin derivative, shows remarkable cytotoxic activity in all the tested cell lines.

In general, most of the diorganotin complexes display good cytotoxic activity against all the tested human cell lines when compared to their Schiff base ligands. Furthermore, most of the tested compounds show high cytotoxicity against normal cells (MRC5), with the exception of ligand **H_2L2** and compounds **3**, **8**, **9**, **12** and **13**.

Conclusion

The diorganotin complexes are five-coordinated, as shown by the X-ray structures and spectroscopic data. An increase in cytotoxic activity of the diorganotin complexes is observed when compared to the ligands. In the case of the diorganotin complexes of **H_2L1** ligand, [(5-bromo-2-oxidobenzylidene)-3-hydroxy-2-naphthohydrazidato]dibutyltin(IV) **2** and [(5-bromo-2-oxidobenzylidene)-3-hydroxy-2-naphthohydrazidato]dibenzyltin(IV) **5** are the most active. For the diorganotin complexes of **H_2L2** ligand, [(5-chloro-2-oxidobenzylidene)-3-hydroxy-2-naphthohydrazidato] dicyclohexyltin(IV) **11** shows remarkable cytotoxic activity against all tested cell lines.

Our findings indicate that the diorganotin complexes could be considered as agents with potential anticancer activity, and this can be further investigated through *in vitro* or *in vivo* anticancer studies.

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