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Diphenyltin(IV) complexes of the 5-[(*E*)-2-(aryl)-1-diazenyl]quinolin-8-olates: Synthesis and multinuclear NMR, ^{119}Sn Mössbauer, electrospray ionization MS, X-ray characterization and assessment of in vitro cytotoxicity

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Abstract

A series of *cis*-bis{5-[(*E*)-2-(aryl)-1-diazenyl]quinolinolato}diphenyltin(IV) complexes have been synthesized and characterized by ^{1}H, ^{13}C, ^{119}Sn NMR, ESI-MS, IR and ^{119m}Sn Mössbauer spectroscopic techniques in combination with elemental analysis. The structures of a ligand L^6H (i.e., 5-[(*E*)-2-(4-ethoxyphenyl)-1-diazenyl]quinolin-8-ol) and three diphenyltin(IV) complexes, viz., $Ph_2Sn(L^1)_2 \cdot (CH_3)_2CO$ (**1**), $Ph_2Sn(L^4)_2$ (**4**) and $Ph_2Sn(L^5)_2$ (**5**) (L = 5-[(*E*)-2-(aryl)-1-diazenyl]quinolin-8-ol: aryl = phenyl – (L^1H); 4′-methylphenyl – (L^4H) and 4′-bromophenyl – (L^5H)) were determined by single crystal X-ray diffraction. In general, the complexes were found to adopt a distorted *cis*-octahedral arrangement around the tin atom. These complexes retain their solid-state structure in non-coordinating solvent as evidenced by ^{119}Sn NMR spectroscopic results. The in vitro cytotoxicity of **1** is reported and compared with $Ph_2Sn(Ox)_2$ (Ox = deprotonated quinolin-8-ol) against seven well characterized human tumor cell lines.

Keywords: 5-[(*E*)-2-(aryl)-1-diazenyl]quinolin-8-ol; Diphenyltin(IV) complexes; NMR; ESI-MS; ^{119m}Sn Mössbauer; Cytotoxicity; Crystal structures

1. Introduction

Functionally substituted 5-azoxines, hereafter 5-[(*E*)-2-(aryl)-1-diazenyl]quinolin-8-ol, are long known as analytical reagents for qualitative detection of metal ions [1–3]. This class of azo-dyes forms complexes in solution with a wide variety of metals [3] and later these reagents have attracted the attention of several workers in recent years. Consequently, some of the earlier publications have dealt with the coordinating behavior of such reagents towards organotin [4–6], transition metals [7], mixed organotin-transition metals [7], mercury [8] and uranium [9]. Among the organotin(IV) compounds, bis{5-[(*E*)-2-(phenyl)-1-diazenyl]-8-quinolinolato}diphenyltin(IV), [$Ph_2Sn(L^1)_2$] has been studied by IR, UV–Vis, ^{1}H NMR [5] and ^{119m}Sn Mössbauer [4] spectroscopic techniques to indicate the

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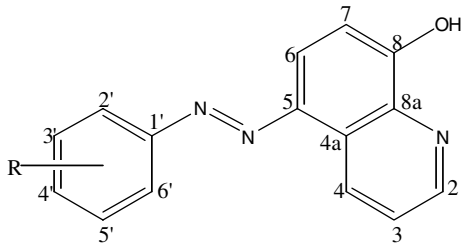


Fig. 1. Generic structure of the ligand (*Abbreviations*. L^1H: R = H; L^2H: R = 2′-CH_3; L^3H: R = 3′-CH_3; L^4H: R = 4′-CH_3; L^5H: R = 4′-Br; L^6H: R = 4′-OC_2H_5, where H represents hydroxyl proton.).

mode of coordination. The diverging results reported may reflect the different experimental conditions associated with each method. However, the closeness of the Mössbauer parameters for $[Ph_2Sn(L^1)_2]$ and bis(8-quinolinato)diphenyltin(IV), $[Ph_2Sn(Ox)_2]$, (where Ox = deprotonated quinolin-8-ol) [10] suggests that they have the same structure. To resolve these issues, firstly the X-ray structure of $[Ph_2Sn(Ox)_2]$ has been determined. The X-ray results indicate a distorted *cis*-octahedral geometry where two phenyl ligands are *cis* to one another and *trans* to the nitrogen atoms of the oxinate ligands [11]. A systematic approach was then followed to study the diphenyltin(IV) complexes of 5-[(*E*)-2-(aryl)-1-diazenyl]quinolin-8-ol ligand system (Fig. 1). Further, organotin compound Ph_2SnOx_2 has been reported to possess cytotoxic properties [12] and, for this reason the cytotoxicity tests of a representative compound was performed along with Ph_2SnOx_2.

2. Experimental

2.1. Materials

Ph_3SnCl (Fluka AG), Ph_2SnCl_2 (Aldrich), Oxine (Merck) and the substituted anilines (reagent grade) were used without further purification. The solvents used in the reactions were of AR grade and dried using standard procedures. Benzene was distilled from sodium benzophenone ketyl.

2.2. Physical measurements

Carbon, hydrogen and nitrogen analyses were performed with a Perkin–Elmer 2400 series II instrument. IR spectra in the range 4000–400 cm^{-1} were obtained on a BOMEM DA-8 FT-IR spectrophotometer with samples investigated as KBr discs. The two-dimensional experiments for the ligands were performed on a Bruker Avance 500 spectrometer equipped with a triple ($^1H/^{13}C$/broad band) 5 mm inverse probe operating at 500.13 and 125.76 MHz, respectively. For the organotin compounds, the ^1H, ^{13}C and ^{119}Sn NMR spectra were recorded on a Bruker Avance 500 spectrometer and measured at 500.13, 125.76 and 186.18 MHz, respectively. The ^1H, ^{13}C and ^{119}Sn chemical shifts were referred to Me_4Si set at 0.00 ppm, $CDCl_3$ set at 77.0 ppm and Me_4Sn set at 0.00 ppm, respectively. Positive-ion and negative-ion electrospray ionization (ESI) mass spectra of unsolvated compounds were measured on an ion trap analyzer Esquire 3000 (Bruker Daltonics, Bremen, Germany) in the mass range m/z 50–1500. The samples were dissolved in acetonitrile and analyzed by direct infusion at the flow rate 5 μl/min. The selected precursor ions were further analyzed by MS/MS analyses under the following conditions: the isolation width $m/z = 8$, the collision amplitude in the range 0.8–1.0 V depending on the precursor ion stability, the ion source temperature 300 °C, the tuning parameter compound stability 100%, the flow rate and the pressure of nitrogen 4 l/min and 10 psi, respectively [13,14]. Mössbauer spectra were recorded on solid samples at liquid nitrogen temperature by using a conventional constant acceleration spectrometer, coupled with a multichannel analyser (a.e.n., Ponteranica (BG), Italy) equipped with a cryostat Cryo (RIAL, Parma, Italy). A $Ca^{119}SnO_3$ Mössbauer source, 10 mCi (from Ritverc, St. Petersburg, Russia) moving at room temperature with constant acceleration in a triangular waveform was used. The velocity calibration was made using a ^{57}Co Mössbauer source, 10 mCi, and an iron foil as absorber (from Ritverc, St. Petersburg, Russia).

2.3. Synthesis of 5-[(E)-2-(aryl)-1-diazenyl]quinolin-8-ols

2.3.1. Preparation of 5-[(E)-2-(phenyl)-1-diazenyl]quinolin-8-ol (L^1H)

Aniline (5.0 g, 53.7 mmol) was mixed with HCl (16 ml) and water (16 ml) and digested in a water bath for an hour. The hydrochloride was cooled to 5 °C and diazotized with ice-cold aqueous $NaNO_2$ solution (3.7 g, 53.6 mmol, 25 ml). A cold solution of 8-hydroxyquinoline (7.78 g, 53.6 mmol), previously dissolved in 10% NaOH solution (5 g, 50 ml), was then added to the cold diazonium salt solution with vigorous stirring. A yellow colour developed almost immediately and the stirring is continued for 1 h. The reaction mixture was kept overnight in a refrigerator followed by 2 h at room temperature. The precipitate was filtered, washed several times with water to remove soluble starting materials, and then dried in air. The crude product was washed with hexane to remove any tarry materials and recrystallized from methanol to yield yellow precipitate of L^1H (5.75 g, 42.9%), m.p. 182–183 °C. Anal. Calc. for $C_{15}H_{11}N_3O$: C, 72.28; H, 4.45; N, 16.86%. Found: C, 72.35; H, 4.57; N, 16.90%. ^1H NMR ($CDCl_3$); δ_H: 9.31 [dd. 1H, H4], 8.88 [d, 1H, H2], 8.06 [d, 1H, H6], 7.99 [d, 2H, H2′ and H6′], 7.62 [m, 1H, H-3], 7.54 [m, 2H, H3′ and H5′], 7.48 [m, 1H, H4′], 7.27 [d, 1H, H7] ppm. The signal for the phenol was exchanged due to presence of water in the solvent. ^{13}C NMR ($CDCl_3$); δ_C: 155.4 [C8], 153.2 [C1′], 148.4 [C2], 139.9 [C5], 137.7 [C8a], 132.9 [C4], 130.6 [C4′], 129.1 [C3′ and C5′], 127.3 [C4a], 122.81 [C2′ and C6′], 122.80 [C3], 115.5 [C6], 109.9 [C-7] ppm.

The other 5-[(*E*)-2-(aryl)-1-diazenyl]quinolin-8-ols, viz., L^2H–L^6H were prepared analogously with appropriate anilines and their analytical and spectroscopic data are presented below.

2.3.2. Preparation of 5-[(E)-2-(2-methylphenyl)-1-diazenyl]quinolin-8-ol (L^2H)

Recrystallized from a mixture of methanol and benzene to give brown crystalline product in 69.4% yield; m.p. 184–185 °C. Anal. Calc. for $C_{16}H_{13}N_3O$: C, 72.99; H, 4.98; N, 15.96%. Found: C, 73.10; H, 4.97; N, 16.21%. ^{1}H NMR ($CDCl_3$); δ_H: 9.33 [dd, 1H, H4], 8.87 [dd, 1H, H2], 8.03 [d, 1H, H6], 7.74 [d, 1H, H6′], 7.61 [m, 1H, H3], 7.36 [d, 2H, H4′ and H5′], 7.30 [m, 1H, H-3′], 7.27 [d, 1H, H7], 2.77 [s, 3H, CH_3] ppm. The signal for the phenol was exchanged due to presence of water in the solvent. ^{13}C NMR ($CDCl_3$); δ_C: 155.2 [C8], 151.2 [C1′], 148.4 [C2], 140.4 [C5], 137.9 [C2′], 137.7 [C8a], 133.0 [C4], 131.5 [C3′], 130.6 [C4′], 127.2 [C4a], 126.4 [C-5′], 122.8 [C3], 115.8 [C6′], 115.6 [C6], 109.9 [C7], 17.7 [CH_3] ppm.

2.3.3. Preparation of 5-[(E)-2-(3-methylphenyl)-1-diazenyl]quinolin-8-ol (L^3H)

Recrystallized from a mixture of methanol and benzene to give brown crystalline product in 64.8% yield; m.p. 159–160 °C. Anal. Calc. for $C_{16}H_{13}N_3O$: C, 72.99; H, 4.98; N, 15.96%. Found: C, 73.20; H, 5.03; N, 16.20%. ^{1}H NMR ($CDCl_3$); δ_H: 9.30 [dd, 1H, H4], 8.86 [dd, 1H, H2], 8.03 [d, 1H, H6], 7.79 [d, 2H, H2′ and 6′], 7.60 [m, 1H, H3], 7.41 [d, 1H, H5′], 7.28 [d, 1H, H4′], 7.26 [d, 1H, H7], 2.48 [s, 3H, CH_3] ppm. The signal for the phenol was exchanged due to the presence of water in the solvent. ^{13}C NMR ($CDCl_3$); δ_C: 155.3 [C8], 153.2 [C1′], 148.4 [C2], 139.9 [C5], 138.9 [C-3′], 137.7 [C8a], 132.9 [C4], 131.4 [C4′], 128.9 [C5′], 127.2 [C4a], 123.2 [C2′], 122.7 [C3], 120.2 [C6′], 115.4 [C6], 110.0 [C7], 21.4 [CH_3] ppm.

2.3.4. Preparation of 5-[(E)-2-(4-methylphenyl)-1-diazenyl]quinolin-8-ol (L^4H)

Recrystallized from chloroform to give brick red microcrystalline product in 63% yield; m.p. 188–189 °C. Anal. Calc. for $C_{16}H_{13}N_3O$: C, 72.99; H, 4.98; N, 15.96%. Found: C, 72.88; H, 5.01; N, 15.86%. ^{1}H NMR ($CDCl_3$); δ_H: 9.29 [dd, 1H, H4], 8.86 [dd, 1H, H2], 8.03 [d, 1H, H6], 8.01 [m, 2H, H2′ and H6′], 7.59 [m, 1H, H3], 7.32 [m, 2H, H3′ and H5′], 7.26 [d, 1H, H7], 2.44 [s, 3H, CH_3] ppm. The signal for the phenol was exchanged due to the presence of water in the solvent. ^{13}C NMR ($CDCl_3$); δ_C: 155.1 [C8], 151.3 [C1′], 148.3 [C2], 141.1 [C4′], 139.9 [C5], 137.7 [C8a], 132.9 [C4], 129.7 [C3′ and C5′], 127.2 [C4a], 122.8 [C2′ and C6′], 122.6 [C3], 115.2 [C6], 109.9 [C7], 21.5 [CH_3] ppm.

2.3.5. Preparation of 5-[(E)-2-(4-bromophenyl)-1-diazenyl]quinolin-8-ol (L^5H)

Recrystallized from a mixture of ethanol and benzene to give yellowish brown precipitate in 65.5% yield; m.p. 210–211 °C. Anal. Calc. for $C_{15}H_{10}BrN_3O$: C, 54.99; H, 3.07; N, 12.80%. Found: C, 55.23; H, 3.12; N, 12.86%. ^{1}H NMR (DMSO-d_6); δ_H: 9.34 [dd, 1H, H4], 9.04 [dd, 1H, H2], 8.05 [d, 1H, H6], 7.99 [m, 2H, H2′ and H6′], 7.67 [m, 2H, H3′ and H5′], 7.82 [m, 1H, H3], 7.25 [d, 1H, H7] ppm. The signal for the phenol was exchanged due to the presence of water in the solvent. ^{13}C NMR (DMSO-d_6); δ_C: 158.1 [C8], 151.5 [C1′], 149.1 [C2], 138.7 [C5], 137.9 [C8a], 132.5 [C3′ and C5′], 131.9 [C4], 127.6 [C4a], 124.4 [C2′ and C6′], 124.1 [C4′], 123.4 [C3], 115.2 [C6], 111.8 [C7] ppm.

2.3.6. Preparation of 5-[(E)-2-(4-ethoxyphenyl)-1-diazenyl]quinolin-8-ol (L^6H)

Recrystallized from chloroform to give dark brown microcrystalline product in 64.6% yield; m.p. 180–181 °C. Anal. Calc. for $C_{17}H_{15}N_3O_2$: C, 69.61; H, 5.15; N, 14.33%. Found: C, 69.50; H, 5.11; N, 14.52%. ^{1}H NMR ($CDCl_3$); δ_H: 9.29 [dd, 1H, H4], 8.84 [dd, 1H, H2], 8.01 [d, 1H, H6], 7.93 [m, 2H, H2′ and H6′], 7.58 [m, 1H, H3], 7.23 [d, 1H, H7], 6.99 [m, 2H, H3′ and H5′], 4.12 [q, 2H, OCH_2CH_3], 1.48 [t, 3H, OCH_2CH_3] ppm. The signal for the phenol was exchanged due to the presence of water in the solvent. ^{13}C NMR ($CDCl_3$); δ_C: 161.2 [C8], 154.7 [C1′], 148.4 [C2], 147.4 [C4′], 140.0 [C5], 137.7 [C8a], 132.9 [C4], 124.6 [C3′ and C5′], 127.0 [C4a], 114.6 [C2′ and C6′], 122.6 [C3], 114.5 [C6], 110.0 [C7], 63.6 [OCH_2CH_3], 14.8 [OCH_2CH_3] ppm.

2.4. Synthesis of the diorganotin complexes

A typical method is described below.

*2.4.1. Synthesis of $Ph_2Sn(L^4)_2$ (**4**)*

L^4H (1.0 g, 3.80 mmol) in hot anhydrous benzene (45 ml) was added drop-wise with continuous stirring to a hot anhydrous benzene solution (30 ml) containing Ph_3SnCl (1.46 g, 3.80 mmol). The reaction mixture was refluxed for 2 h, then triethylamine (0.38 ml, 3.80 mmol) was added and reflux was continued for additional 1.5 h. The reaction mixture was cooled to room temperature and filtered to remove $Et_3N{\cdot}HCl$. The filtrate was collected; volatiles were removed and dried in vacuo. The residue was extracted into hexane and filtered while hot. The crude product was obtained after evaporation of the hexane. This was then recrystallized from a mixture of benzene–hexane (1:1), which upon slow evaporation afforded red crystalline product. Yield: 1.02 g (66.2%), m.p. 239–240 °C. Anal. Calc. for $C_{44}H_{34}N_6O_2Sn$: C, 66.27; H, 4.30; N, 10.54%. Found: C, 66.35; H, 4.35; N, 10.60%. IR (cm^{-1}): 1248 ν(C(aryl)O). ^{1}H NMR ($CDCl_3$, 500.13 MHz) δ_H: Ligand skeleton: 9.27 [dd, 2H, H4], 8.61 [dd, 2H, H2], 8.22 [d, 2H, H6], 7.80 [m, 4H, H2′ and H6′], 7.24 [m, 2H, H3], 7.25 [m, 4H, H3′ and H5′], 7.46 [d, 2H, H7], 2.41 [s, 6H, CH_3]; Sn–Ph skeleton: 7.59 [m, 4H, H2*], 7.23 [m, 6H, H3* and H4*] ppm. ^{13}C NMR ($CDCl_3$, 125.76 MHz); δ_C: 161.1 [C8], 151.4 [C1′], 143.4 [C2], 140.6 [C4′], 136.5 [C5], 135.4 [C8a], 136.1 [C4], 129.7 [C3′ and C5′], Not observed, possibly overlapped by a CH signal [C4a], 122.2 [C2′, C6′ and C3], 118.5 [C6], 114.5 [C7], 21.4 [CH_3]; Sn–Ph skeleton ($^nJ(^{119}Sn, ^{13}C)$, Hz): 148.7 [C-1* (927)], 134.9 [C-2* (55)], 128.5 [C-4*(17)], 128.3 [C-3* (81)] ppm. ^{119}Sn NMR ($CDCl_3$,

186.18 MHz) δ_{Sn}: −385.8 ppm. ^{119}Sn Mössbauer: $\delta = 0.81$, $\Delta = 1.77$, $\Gamma_1 = 1.00$, $\Gamma_2 = 1.00$ mm s^{-1}, $\rho = 2.18$. Positive-ion ESI mass spectra: *m/z* 837 $[M + K]^+$; *m/z* 821 $[M + Na]^+$; *m/z* 799 $[M + H]^+$; *m/z* 721 $[M - Ph]^+$; *m/z* 536 $[M - L^4]^+$, 100%. MS/MS of *m/z* 837: *m/z* 574 $[M + K - L^4H]^+$; *m/z* 536 $[M - L^4]^+$. MS/MS of *m/z* 821: *m/z* 558 $[M + Na - L^4H]^+$; *m/z* 536 $[M - L^4]^+$. MS/MS of *m/z* 799: *m/z* 536 $[M - L^4]^+$. MS/MS of *m/z* 721: *m/z* 645 $[M - 76 - Ph]^+$; *m/z* 603 $[M - Ph - N_2 - 90]^+$; *m/z* 525 $[M - Ph - benzene - N_2 - 90]^+$; *m/z* 458 $[M - L^4H - Ph]^+$; *m/z* 382 $[L^4Sn]^+$; *m/z* 263 $[L^4H]^{+\cdot}$. MS/MS of *m/z* 536: *m/z* 458 $[M - L^4 - benzene]^+$; *m/z* 444 $[M - L^4 - toluene]^+$; *m/z* 417 $[M - L^4 - toluene - N_2]^{+\cdot}$; *m/z* 382 $[M - L^4 - benzene - 76]^+$. Negative-ion ESI mass spectra: *m/z* 262 $[L^4]^-$, 100%.

The other diphenyltin complexes were prepared by reacting ligands, viz., L^1H, L^2H, L^3H, L^5H and L^6H with Ph_3SnCl by following analogous procedure. The characterization and spectroscopic data of the complexes are presented below.

2.4.2. Synthesis of $[Ph_2Sn(L^1)_2] \cdot C_3H_6O$ (1)

Dark-red crystals of **1** were obtained from acetone. Yield: 0.74 g (74%), m.p. 140–141 °C. Anal. Calc. for $C_{45}H_{36}N_6O_3Sn$: C, 65.31; H, 3.85; N, 10.16%. Found: C, 65.34; H, 4.90; N, 11.09%. IR (cm^{-1}): 1248 *ν*(C(aryl)O). ^{1}H NMR ($CDCl_3$, 500.13 MHz); δ_H: 9.34 [dd, 2H, H4], 8.68 [d, 2H, H2], 8.26 [d, 2H, H6], 7.91 [d, 4H, H2′ and H6′], 7.48 [m, 2H, H-3], 7.60 [m, 4H, H3′ and H5′], 7.43 [m, 2H, H4′], 7.36 [d, 2H, H7]; Sn–Ph skeleton: 7.48 [m, 4H, H2*], 7.25 [m, 6H, H3* and H4*] ppm. ^{13}C NMR ($CDCl_3$, 125.76 MHz); δ_C: 161.4 [C8], 153.3 [C1′], 143.4 [C2], 136.4 [C5], 136.2 [C8a], 135.4 [C4], 128.6 [C4′], 128.3 [C3′ and C5′], 128.0 [C4a], 122.5 [C2′ and C6′], 122.5 [C3], 118.8] [C6], 114.5 [C-7]; Sn–Ph skeleton (^nJ(^{119}Sn, ^{13}C), Hz): 148.7 [C-1*(920)], 135.0 [C-2*(52)], 130.1 [C-4*(20)], 129.0 [C-3*(80)] ppm. ^{119}Sn NMR ($CDCl_3$, 186.18 MHz) δ_{Sn}: −385.9 ppm. ^{119}Sn Mössbauer: $\delta = 0.82$, $\Delta = 1.86$, $\Gamma_1 = 0.86$, $\Gamma_2 = 0.86$ mm s^{-1}, $\rho = 2.27$. Positive-ion ESI mass spectra of unsolvated compound: *m/z* 809 $[M + K]^+$; *m/z* 793 $[M + Na]^+$; *m/z* 693 $[M - Ph]^+$; *m/z* 522 $[M - L^1]^+$, 100%. MS/MS of *m/z* 809: *m/z* 522 $[M - L^1]^+$. MS/MS of *m/z* 793: *m/z* 522 $[M - L^1]^+$. MS/MS of *m/z* 522: *m/z* 417 $[M - L^1 - benzene - N_2]^{+\cdot}$; *m/z* 368 $[M - L^1 - benzene - 76]^+$. Negative-ion ESI mass spectra: *m/z* 248 $[L^1]^-$, 100%.

2.4.3. $Ph_2Sn(L^2)_2$ (2)

Red crystals of **2** were obtained from a mixture of benzene and hexane (v/v 1:1). Yield: 0.87 g (56.5%), mp: 80–81 °C. Anal. Calc. for $C_{44}H_{34}N_6O_2Sn$: C, 66.27; H, 4.30; N, 10.54%. Found: C, 66.30; H, 4.31; N, 10.50%. IR (cm^{-1}): 1248 *ν*(C(aryl)O). ^{1}H NMR ($CDCl_3$, 500.13 MHz) δ_H: 9.35 [dd, 2H, H4], 8.64 [dd, 2H, H2], 8.24 [d, 2H, H6], 7.66 [m, 2H, H6′], 7.49 [m, 2H, H3], 7.30–7.40 [m, 8H, H3′, H4′, H5′ and H7], 2.75 [s, 6H, CH_3]]; Sn–Ph skeleton: 7.59 [m, 4H, H2*], 7.24 [m, 6H, H3* and H4*] ppm. ^{13}C NMR ($CDCl_3$, 125.76 MHz); δ_C: 161.2 [C8], 151.3 [C1′], 143.3 [C2], 137.5 [C5], 137.0 [C2′], 136.2 [C8a], 136.1 [C4], 131.2 [C3′], 128.5 [C4′], 128.5 [C4a], 126.3 [C5′], 122.5 [C3], 119.1 [C6′], 115.5 [C6], 114.4 [C7], 17.6 [CH_3]; Sn–Ph skeleton (^nJ(^{119}Sn, ^{13}C), Hz): 148.7 [C-1*(925)], 135.2 [C-2*(52)], 130.1 [C-4*(20)], 128.2 [C-3*(80)] ppm. ^{119}Sn NMR ($CDCl_3$, 186.18 MHz) δ_{Sn}: −386.0 ppm. ^{119}Sn Mössbauer: $\delta = 0.81$, $\Delta = 1.77$, $\Gamma_1 = 0.83$, $\Gamma_2 = 0.84$ mm s^{-1}, $\rho = 2.18$. Positive-ion ESI mass spectra: *m/z* 837 $[M + K]^+$; *m/z* 821 $[M + Na]^+$; *m/z* 799 $[M + H]^+$; *m/z* 536 $[M - L^2]^+$, 100%. MS/MS of *m/z* 837: *m/z* 574 $[M + K - L^2H]^+$; *m/z* 536 $[M - L^2]^+$. MS/MS of *m/z* 821: *m/z* 558 $[M + Na - L^2H]^+$; *m/z* 536 $[M - L^2]^+$. MS/MS of *m/z* 799: *m/z* 536 $[M - L^2]^+$. MS/MS of *m/z* 536: *m/z* 458 $[M - L^2 - benzene]^+$; *m/z* 444 $[M - L^2 - toluene]^+$; *m/z* 417 $[M - L^2 - toluene - N_2]^{+\cdot}$; *m/z* 382 $[M - L^2 - benzene - 76]^+$.

2.4.4. $Ph_2Sn(L^3)_2$ (3)

Maroon crystals of **3** were obtained from a mixture of benzene and hexane (v/v 1:1). Yield: 0.77 g (50%), mp: 194–195 °C. Anal. Calc. for $C_{44}H_{34}N_6O_2Sn$: C, 66.27; H, 4.30; N, 10.54%. Found: C, 66.20; H, 4.38; N, 10.60%. IR (cm^{-1}): 1251 *ν*(C(aryl)O). ^{1}H NMR ($CDCl_3$, 500.13 MHz) δ_H: 9.32 [dd, 2H, H4], 8.63 [dd, 2H, H2], 8.26 [d, 2H, H6], 7.71 [m, 4H, H2′ and H6′], 7.48 [m, 2H, H3], 7.32–7.42 [m, 4H, H4′ and H5′], 7.25 [d, 2H, H7], 2.50 [s, 6H, CH_3]; Sn–Ph skeleton: 7.60 [m, 4H, H2*], 7.25 [m, 6H, H3* and H4*] ppm. ^{13}C NMR ($CDCl_3$, 125.76 MHz); δ_C: 161.4 [C8], 153.5 [C1′], 143.4 [C2], 138.9 [C5], 136.6 [C3′], 136.3 [C8a], 128.6 [C4 and C4′], 128.3 [C5′ and C4a], 123.0 [C2′], 122.6 [C3], 119.9 [C6′], 118.9 [C6], 114.5 [C7], 21.4 [CH_3]; Sn–Ph skeleton (^nJ(^{119}Sn, ^{13}C), Hz): 148.8 [C-1*(920)], 134.9 [C-2*(52)], 131.0 [C-4*(18)], 128.9 [C-3*(78)] ppm. ^{119}Sn NMR ($CDCl_3$, 186.18 MHz) δ_{Sn}: −386.4 ppm. ^{119}Sn Mössbauer: $\delta = 0.79$, $\Delta = 1.77$, $\Gamma_1 = 0.88$, $\Gamma_2 = 0.80$ mm s^{-1}, $\rho = 2.24$. Positive-ion ESI mass spectra: *m/z* 837 $[M + K]^+$; *m/z* 821 $[M + Na]^+$, 100%; *m/z* 536 $[M - L^3]^+$. MS/MS of *m/z* 837: *m/z* 574 $[M + K - L^3H]^+$; *m/z* 536 $[M - L^3]^+$. MS/MS of *m/z* 821: *m/z* 558 $[M + Na - L^3H]^+$; *m/z* 536 $[M - L^3]^+$. MS/MS of *m/z* 799: *m/z* 536 $[M - L^3]^+$. MS/MS of *m/z* 536: *m/z* 458 $[M - L^3 - benzene]^+$; *m/z* 444 $[M - L^3 - toluene]^+$; *m/z* 417 $[M - L^3 - toluene - N_2]^{+\cdot}$; *m/z* 382 $[M - L^3 - benzene - 76]^+$. Negative-ion ESI mass spectra: *m/z* 262 $[L^3]^-$, 100%.

2.4.5. $Ph_2Sn(L^5)_2$ (5)

Orange crystals of **5** were obtained from a mixture of benzene and hexane (v/v 1:1). Yield: 0.28 g (45.7%), mp: 275–276 °C. Anal. Calc. for $C_{42}H_{28}Br_2N_6O_2Sn$: C, 54.40; H, 3.04; N, 9.06%. Found: C, 54.28; H, 3.33; N, 8.89%. IR (cm^{-1}): 1248 *ν*(C(aryl)O). ^{1}H NMR ($CDCl_3$, 500.13 MHz) δ_H: 9.33 [dd, 2H, H4], 8.17 [dd, 2H, H2], 7.70 [d, 2H, H6], 7.54 [m, 4H, H2′ and H6′], 7.22 [m, 4H, H3′ and H5′], 7.34 [d, 2H, H3], 7.10 [d, 2H, H7]; Sn–Ph skeleton: 7.40 [m, 4H, H2*], 7.22 [m, 6H, H3* and H4*] ppm. ^{13}C NMR ($CDCl_3$, 125.76 MHz); δ_C: 161.8 [C8], 151.6

Table 1
Crystal data, data collection parameters and convergence results for L^6H, **1** · $(CH_3)_2CO$, **4** and **5**

	L^6H	**1** · $(CH_3)_2CO$	**4**	**5**
Empirical formula	$C_{17}H_{15}N_3O_2$	$C_{45}H_{36}N_6O_3Sn$	$C_{44}H_{34}N_6O_2Sn$	$C_{42}H_{28}Br_2N_6O_2Sn$
Formula weight	293.32	827.49	797.46	927.21
Crystal size (mm)	$0.4 \times 0.3 \times 0.1$	$0.60 \times 0.55 \times 0.50$	$0.30 \times 0.15 \times 0.08$	$0.60 \times 0.15 \times 0.10$
Crystal shape	Plate	Prism	Plate	Rod
Temperature (K)	223(2)	110(2)	293(2)	228(2)
Crystal system	Monoclinic	Monoclinic	Monoclinic	Monoclinic
Space group	$P2_1/c$	$P2_1/c$	$C2/c$	$C2/c$
a (Å)	10.5775(14)	20.063(3)	19.880(3)	20.1514(17)
b (Å)	11.1957(12)	11.4413(19)	10.1913(10)	10.082(2)
c (Å)	12.7553(14)	16.417(3)	19.014(3)	18.785(3)
β (°)	107.840(11)	91.096(3)	103.534(13)	104.340(12)
V (Å^3)	1437.9(3)	3767.8(11)	3745.3(9)	3697.6(10)
Z	4	4	4	4
D_x (g cm^{-3})	1.355	1.459	1.414	1.666
μ (mm^{-1})	0.091	0.729	0.728	2.898
Transmission factors (min, max)	–	0.67, 0.71	0.81, 0.94	0.76, 0.60
Diffractometer	Nonius CAD4	Bruker SMART APEX	Nonius CAD4	Nonius CAD4
$2\theta_{max}$ (°)	26.5	28.3	26.0	27.0
Reflections measured	11496	50915	14289	12596
Independent reflections (R_{int})	2959 (0.076)	9374 (0.029)	3686 (0.193)	4026 (0.049)
Independent reflections with $I > 2\sigma(I)$	1668	8626	1887	2970
Number of parameters	200	498	241	254
$R(F)$ ($I > 2\sigma(I)$ refIns)	0.0530	0.0242	0.0689	0.0443
$wR_2(F^2)$ (all data)	0.1213	0.0622	0.1576	0.1025
GOF(F^2)	1.00	1.06	1.01	1.03
Max, min $\Delta\rho$ (e/Å^3)	0.167, −0.160	0.59, −0.33	0.84, −0.88	0.98, 1.02

[C1′], 143.4 [C2], 136.1 [C4], 135.9 [C5], 135.2 [C8a], 132.2 [C3′ and C5′], 128.7 [C4a], 124.6 [C4′], 123.9 [C2′ and C6′], 122.7 [C3], 118.9 [C6], 114.6 [C7]; Sn–Ph skeleton (^nJ(^{119}Sn, ^{13}C), Hz): 148.4 [C-1*(925)], 134.8 [C-2*(55)], 128.6 [C-4*(17)], 128.3 [C-3*(82)], ppm. ^{119}Sn NMR ($CDCl_3$, 186.18 MHz) δ_{Sn}: −385.0 ppm. ^{119}Sn Mössbauer: $\delta = 1.10$, $\Delta = 2.20$, $\Gamma_1 = 1.00$, $\Gamma_2 = 1.00$ mm s^{-1}, $\rho = 2.00$. Positive-ion ESI mass spectra: m/z 965 $[M + K]^+$; m/z 949 $[M + Na]^+$; m/z 600 $[M - L^5]^+$; m/z 351 $[SnPh_3]^+$, 100%; m/z 197 $[SnPh]^+$. MS/MS of m/z 949: m/z 600 $[M - L^5]^+$. MS/MS of m/z 600: m/z 446 $[M - L^5 - 76 - \text{benzene}]^+$; m/z 417 $[M - L^5 - 76 - HBr - N_2]^{+\cdot}$.

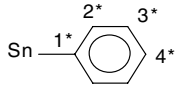
2.4.6. $Ph_2Sn(L^6)_2$ (**6**)

Orange crystals of **6** were obtained from a mixture of benzene and hexane (v/v 1:1). Yield: 0.33 g (45.8%), mp: 125–126 °C. Anal. Calc. for $C_{46}H_{38}N_6O_4Sn$: C, 64.43; H, 4.47; N, 9.80%. Found: C, 64.53; H, 4.50; N, 10.01%. IR (cm^{-1}): 1248 ν(C(aryl)O). ^{1}H NMR ($CDCl_3$, 500.13 MHz) δ_H: 9.24 [dd, 2H, H4], 8.60 [dd, 2H, H2], 8.17 [d, 2H, H6], 7.86 [m, 4H, H2′ and H6′], 7.27 [m, 2H, H3], 7.44 [m, 2H, H7], 6.95 [m, 4H, H3′ and H5′], 3.97 [q, 4H, OCH_2CH_3], 1.31 [t, 6H, OCH_2CH_3]; Sn–Ph skeleton: 7.58 [m, 4H, H2*], 7.22 [m, 6H, H3* and H4*] ppm. ^{13}C NMR ($CDCl_3$, 125.76 MHz); δ_C: 160.9 [C4′], 160.7 [C8], 143.4 [C2], 143.3 [C1′], 136.5 [C5], 136.1 [C4], 135.4 [C8a], 128.4 [C4a], 124.3 [C2′ and C6′], 122.3 [C3], 118.1 [C6], 114.7 [C3′ and C5′], 114.4 [C7], 63.8 [OCH_2CH_3], 14.8 [OCH_2CH_3]; Sn–Ph skeleton (^nJ (^{119}Sn, ^{13}C), Hz): 148.8 [C-1*(925)], 134.9 [C-2*(55)], 128.5 [C-4*(16)], 128.2 [C-3*(82)] ppm. ^{119}Sn NMR ($CDCl_3$, 186.18 MHz) δ_{Sn}: −386.1 ppm. ^{119}Sn Mössbauer: $\delta = 0.80$, $\Delta = 1.82$, $\Gamma_1 = 0.91$, $\Gamma_2 = 0.91$ mm s^{-1}, $\rho = 2.27$. Positive-ion ESI mass spectra: m/z 897 $[M + K]^+$; m/z 881 $[M + Na]^+$; m/z 566 $[M - L^6]^+$; m/z 351 $[SnPh_3]^+$. MS/MS of m/z 881: m/z 566 $[M - L^6]^+$. MS/MS of m/z 566: m/z 412 $[M - L^6 - 76 - \text{benzene}]^{+\cdot}$.[1]

2.5. X-ray crystallography

Crystals of ligand L^6H and diphenyltin(IV) compounds **1** · $(CH_3)_2CO$, **4** and **5** suitable for an X-ray crystal structure determination were obtained from benzene, acetone, hexane and benzene–hexane mixture (1:1 v/v), respectively. Intensity data were collected with graphite-monochromated Mo Kα radiation ($\lambda = 0.71073$ Å), either on Nonius CAD4 diffractometers (for L^6H, **4** and **5**) or a Bruker SMART APEX (for **1**). Crystal data, data collection parameters and convergence results are listed in Table 1. For the tin complexes **1** · $(CH_3)_2CO$, **4** and **5**, empirical absorption corrections based on a multiscan approach [15] or on azimuthal scans [16] were applied to the data sets before averaging over symmetry-related reflections; no absorption correction was made for the intensity data of

[1] Ligand numbering scheme as shown in Fig. 1 and numbering scheme for Sn–Ph skeleton as shown below:



ligand L^6H. The structures were solved by direct methods with the help of the SHELXS-97 program [17] and refined on reflection intensities F^2 using the SHELXL-97 program [18]. In the final least-squares refinements, all non-hydrogen atoms were refined with anisotropic displacement parameters, and hydrogen atoms were placed in idealized positions and included as riding on the corresponding atoms. Further details on the structures are available as supplementary material in CIF format, see below.

2.6. Biological tests

The in vitro cytotoxicity test of compound **1** and $Ph_2Sn(Ox)_2$ were performed using the SRB test for the estimation of cell viability. The cell lines WIDR (colon cancer), M19 MEL (melanoma), A498 (renal cancer), IGROV (ovarian cancer) and H226 (non-small cell lung cancer) belong to the currently used anticancer screening panel of the National Cancer Institute, USA [19]. The MCF7 (breast cancer) cell line is estrogen receptor (ER)+/progesterone receptor (PgR)+ and the cell line EVSA-T (breast cancer) is (ER)−/(Pgr)−. Prior to the experiments, a mycoplasma test was carried out on all cell lines and found to be negative. All cell lines were maintained in a continuous logarithmic culture in RPMI 1640 medium with Hepes and phenol red. The medium was supplemented with 10% FCS, penicillin 100 μg/ml and streptomycin 100 μg/ml. The cells were mildly trypsinized for passage and for use in the experiments. RPMI and FCS were obtained from Life technologies (Paisley, Scotland). SRB, DMSO, Penicillin and streptomycin were obtained from Sigma (St. Louis MO, USA), TCA and acetic acid from Baker BV (Deventer, NL) and PBS from NPBI BV (Emmer-Compascuum, NL).

The test compounds **1** and $Ph_2Sn(Ox)_2$, and reference compounds were dissolved to a concentration of 250 000 ng/ml in full medium, by 20-fold dilution of a stock solution which contained 1 mg of compound **1**/200 μl. Compound **1** and $Ph_2Sn(Ox)_2$ were dissolved in absolute ethanol. Cytotoxicity was estimated by the microculture sulforhodamine B (SRB) test [20].

2.6.1. Experimental protocol and cytotoxicity tests

The experiment was started on day 0. On day 0, 150 μl of trypsinized tumor cells (1500–2000 cells/well) were plated in 96-wells flat-bottomed microtiter plates (falcon 3072, BD). The plates were pre-incubated for 48 h at 37 °C, 8.5% CO_2 to allow the cells to adhere. On day 2, a 3-fold dilution sequence of ten steps was made in full medium, starting with the 250 000 ng/ml stock solution. Every dilution was used in quadruplicate by adding 50 μl to a column of four wells. This results in a highest concentration of 62 500 ng/ml being present in column 12. Column 2 was used for the blank. To column 1, PBS was added to diminish interfering evaporation. On day 7, washing the plate twice with PBS terminated the incubation. Subsequently, the cells were fixed with 10% trichloroacetic acid in PBS and placed at 4 °C for an hour. After five washings with tap water, the cells were stained for at least 15 min with 0.4% SRB dissolved in 1% acetic acid. After staining, the cells were washed with 1% acetic acid to remove the unbound stain. The plates were air-dried and the bound stain was dissolved in 150 μl (10 mM) tris–base. The absorbance was read at 540 nm using an automated microplate reader (Labsystems Multiskan MS). Data were used for construction of concentration–response curves and the determination of ID_{50} values by use of Deltasoft 3 software.

3. Results and discussion

3.1. Syntheses

The diphenyltin(IV) complexes of the 5-[(*E*)-2-(aryl)-1-diazenyl]quinolin-8-ol ligand (LH) could be prepared by reacting stoichiometric amounts of Ph_2SnCl_2 and LH in a suitable solvent under conditions described by Blake et al. [21] and Ghuge et al. [4]. These reactions proceeded smoothly but results into a complex mixture in both the cases that could be separated with great difficulty. In view of this, an effort have been made to develop a new synthetic strategy via disproportionation dearylation reaction (reaction (1)) which proved to be convenient for synthesizing *cis*-bis{5-[(*E*)-2-(aryl)-1-diazenyl]-8-quinolinolato}diphenyltin(IV) compounds. The complexes could be isolated by fractional crystallization with high purity in moderate yield. The work-up detail and characterization data for the complexes is described in Section 2.4.

$$2LH + 2Ph_3SnCl + 2Et_3N \xrightarrow[\text{(conditions: reflux, 3–4 h, } Et_3N)]{\text{Benzene}} Ph_2Sn(L)_2 + Ph_4Sn + 2Et_3N \cdot HCl \quad (1)$$

The complexes are crystalline in nature, stable in air but slowly loose the solvent of crystallization and become amorphous. These amorphous solids retain their chemical composition and properties as evidenced by spectroscopic results. The complexes are soluble in all common organic solvents.

3.2. IR spectra

The IR spectra of the ligands, L^1H–L^6H and their diphenyltin(IV) complexes, **1**–**6** are very complex due to the presence of a large number of vibrational modes due to ring stretches, deformation, in-plane and out-of-plane ring and CH deformations, etc. However, these modes are of little value in understanding the structure and bonding of the complexes. Valuable information can, however, be obtained from the frequencies of ν(OH) and ν(Ar–O) modes. The ν(OH) in L^1H–L^6H occurs at around 3380 cm^{-1} as broad band which is assigned due to the presence of intermolecular H-bonding interactions involving

the O–H···N bonds and also has been detected in the structure determined by X-ray crystallography on the analogous system, i.e., 5-[(2-ethoxyphenyl)diazenyl]quinolin-8-ol [22] and 5-[(*E*)-2-(4-ethoxyphenyl)-1-diazenyl]quinolin-8-ol (L^6H) (vide infra, see X-ray discussion). The ν(OH) band is found to be absent in the diphenyltin complexes, **1**–**6**, confirming bonding through the O-atom of the ligand. A strong band at around 1235 cm^{-1} in the ligands is found to be shifted to around 1250 cm^{-1} in the complexes, is assigned to the ν(C(aryl)–O) (i.e., C_8–O). An upward shift of this stretching frequency is expected in the complexes because the large polarity of –O–SnR_2 bond increases the conjugative interaction of the oxygen atom with the π-ring, resulting in an increase of the C–O bond order [23]. The ν(C=N) vibration could not be assigned with certainty. Thus, IR spectroscopy provides only information of C_8–O–Sn linkage in the complexes.

3.3. ^{119}Sn Mössbauer data

In order to resolve the structural issues (*cis*- or *trans*-structure), ^{119}Sn Mössbauer spectroscopy have been performed on the complexes, **1**–**6** in the solid state. The Mössbauer data, i.e., isomer shift (δ), quadrupole splittings (Δ) and the line widths at half-peak height (Γ) for the diphenyltin complexes are given in Section 2.4. Generally, δ values can differentiate between a *cis*- or a *trans*-R_2SnX_4 octahedral system. The *cis*-complexes have lower δ values than the *trans*-complexes [24], however, the δ values could not be utilized for characterizing the complexes since there are no reference compounds of the type $[Ph_2Sn(Ox)_2]$ known having *trans*-R_2SnX_4 structure. On the other hand, Δ has proved useful in distinguishing between a *cis*- and a *trans*-configuration in the complexes. The Δ values in the range between 1.7–2.2 and 3.5–4.2 mm s^{-1} have been classified for a *cis*- and *trans*-octahedral geometry, respectively [25,26]. The complexes **1**–**6** display a doublet nature of spectrum and Δ values are in the range 1.77–2.20 mm s^{-1}. The observed Δ values lie inside the range delimited for *cis*-R_2Sn octahedral geometry. The Δ values compare well with the data for $[Ph_2Sn(Ox)_2]$ complex ($\Delta = 1.70$ [25]) having a *cis*-R_2Sn octahedral geometry [11]. Furthermore, the ratio ρ of the Δ to the δ has been found to be useful in determining the coordination number of tin [27] and in the complexes, ρ is $\geqslant 2.0$, which indicate that the complexes have six-coordinate structure. Similar magnitude of δ and Δ values in all the complexes, further indicate that the complexes are isostructural. Thus, Mössbauer spectroscopic data suggest a *cis*-R_2Sn octahedral geometry where equatorial positions defined by two oxygen, a nitrogen and a phenyl group while axial site is occupied by a phenyl and a nitrogen atom.

3.4. ^{1}H, ^{13}C and ^{119} Sn NMR data

The ^{1}H and ^{13}C NMR signals of L^1H–L^6H were assigned by the use of correlated spectroscopy (COSY), heteronuclear single-quantum correlation (HSQC) and heteronuclear multiple-bond connectivities (HMBC) experiments. The conclusions drawn from the ligand assignments were then subsequently extrapolated to the complexes **1**–**6** owing to the data similarity. The ^{1}H NMR integration values were completely consistent with the formulation of the products. The ^{1}H and ^{13}C NMR chemical shift assignment of the diphenyltin moiety is straight forward from the multiplicity pattern, resonance intensities and also by examining the $^nJ(^{13}C–^{119/117}Sn)$ coupling constants [28]. In the ^{1}H and ^{13}C NMR spectra of the complexes, **1**–**6**, there is only one set of NMR signals for both the phenyl groups (Sn–Ph) and for the ligands, which provides evidence for the magnetic equivalence of both the phenyls and both ligands on the NMR time scale. This indicates their relative symmetrical arrangement in the coordination sphere of the central tin atom in solution. The chemical shifts δ (^{13}C) of the carbon atoms of the phenyl substituents (Sn–Ph) are not very sensitive to changes in the coordination of central tin atom. Nevertheless, the values $\delta(^{13}C(1^*))$, which are shifted mostly by 5 ppm downfield, in comparison with those in compounds having four coordinate tin atom [29]. The value of the coupling constants $^nJ(^{119}Sn–^{13}C(Sn–Ph))$ ($n = 1$–4) matches closely with the data for hexa-coordinated $[Ph_2Sn(Ox)_2]$ complex in $CDCl_3$ solution [30]. In order to provide further structural evidence to establish the structure of the complexes in solution, we further recorded ^{119}Sn NMR spectra. The complexes **1**–**6**, all display a sharp singlet at around −386 ppm and the $\delta(^{119}Sn)$ chemical shifts lie inside the range (between −125 and −515 ppm) delimited for six coordinate diorganotin compounds [31]. The $\delta(^{119}Sn)$ values are comparable with the shift observed for $[Ph_2Sn(Ox)_2]$ complex (−397 ppm in $CHCl_3$ solution [30] and −394.2 in $CDCl_3$ [30]). Thus, ^{119}Sn NMR data indicate that the complexes retain their solid state structures (see Mössbauer and X-ray discussion) in solution.

3.5. Mass spectrometry

The typical positive-ion ESI mass spectra of studied compounds **1**–**6** consist of molecular adducts with sodium and potassium ions, i.e., $[M + Na]^+$ and $[M + K]^+$ ions, together with the product of tin–oxygen bond cleavage $[M - L]^+$, which is the base peak of spectra for **1**, **2** and **4**. In the case of **1** and **4**, the product of tin–carbon cleavage is observed as well leading to the $[M - Ph]^+$ ion. The ligand ion $[L]^-$ is formed in the negative-ion ESI-MS as a complementary species to $[M - L]^+$ observed in the positive-ion mode, but the spectra of **2**, **5** and **6** are very noisy. All discussed mechanisms of the ion formation were already reported previously [13,14,32]. The molecular weight of all studied compounds can be confirmed from the information obtained from both positive-ion and negative-ion first-order spectra. Tandem mass spectra (MS/MS) provide the characteristic neutral losses, which can be correlated with particular structural features, such as neutral losses of 90

or 92 (toluene) for **2**, **3** and **4**, 76 or 78 (benzene) for **1** and **5**, 79 (HBr) for **5**, etc.

3.6. Structural results from single crystal X-ray diffraction

The molecular structures of the ligand L^6H and organotin(IV) complexes **1** (obtained as **1** · $(CH_3)_2CO$), **4** and **5** are depicted in Figs. 2–5 [33], respectively, while selected geometric parameters are given in Table 2.

The ligand L^6H exists as the *trans*-isomer. In the solid state, both intra and intermolecular H bonds occur. The intramolecular hydrogen bond between the hydroxy H and the N atom (O···N = 2.755(2) Å, O–H···N = 115°) can be assigned the graph set symbol $S_1^1(5)$ [34], whereas the intermolecular H bond (O···N = 2.865(2) Å, O–H···N = 137°) corresponds to the formation of a $R_2^2(10)$ ring and links neighboring molecules around inversion centres to dimers (Fig. 2). The same hydrogen bond pattern

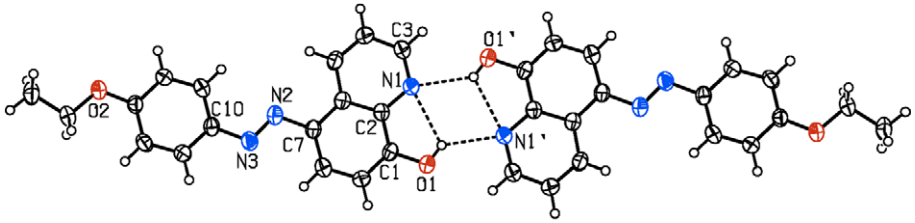


Fig. 2. Structure of a molecule of L^6H in the crystal.

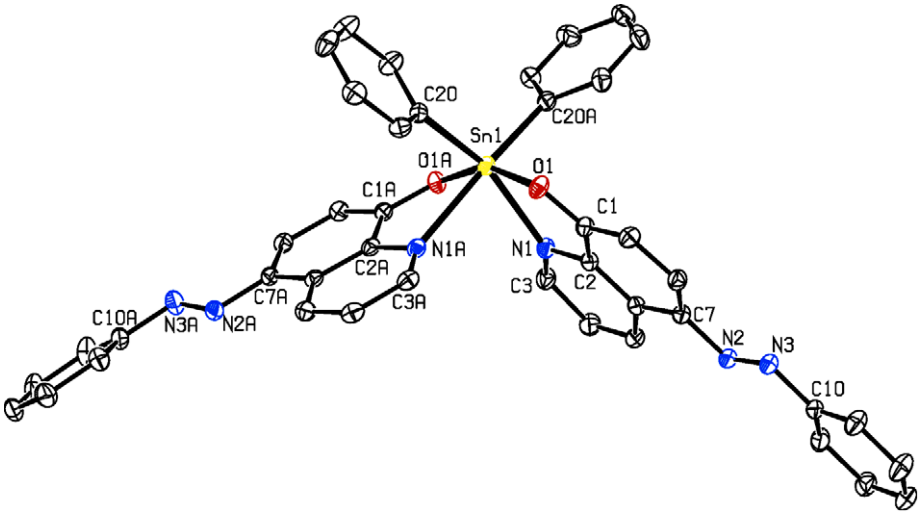


Fig. 3. Structure of a molecule of **1** in the crystal **1** · $(CH_3)_2CO$. The solvent molecule in the crystal and the hydrogen atoms have been omitted for clarity.

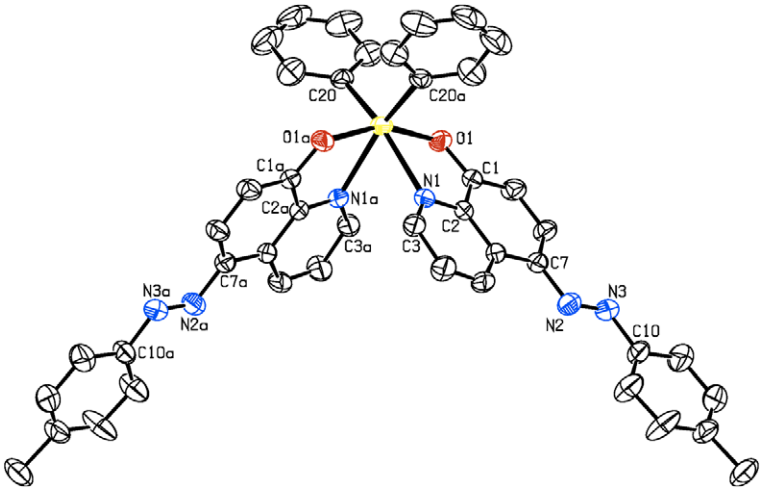


Fig. 4. Structure of a molecule of **4** in the crystal. The hydrogen atoms have been omitted for clarity.

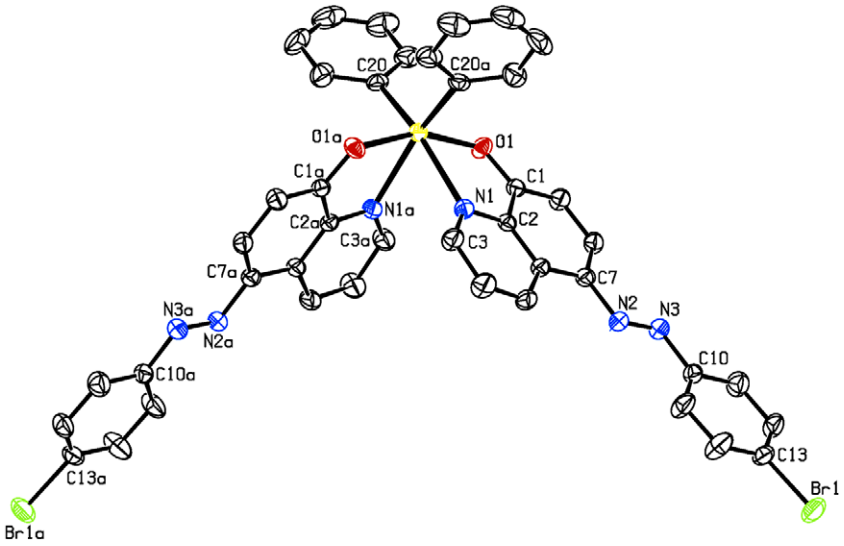


Fig. 5. Structure of a molecule of **5** in the crystal. The hydrogen atoms have been omitted for clarity.

Table 2
Selected bond lengths (Å), angles (°), and torsion angles (°) for L^6H and **1**, **4** and **5**

	L^6H	**1** · $(CH_3)_2CO$ (2 independent ligands)	**4**	**5**
Sn–C20		2.1463(14), 2.1509(15)	2.134(7)	2.149(4)
Sn–O1		2.0961(11), 2.0968(10)	2.093(5)	2.099(3)
Sn–N1		2.2833(13), 2.3868(13)	2.359(6)	2.345(3)
O1–C1	1.352(2)	1.3240(17), 1.3185(17)	1.326(8)	1.313(5)
N1–C2	1.366(2)	1.3662(19), 1.3680(18)	1.345(8)	1.361(5)
N1–C3	1.312(3)	1.3218(19), 1.3198(19)	1.306(8)	1.315(5)
N2–N3	1.262(2)	1.2619(18), 1.2596(18)	1.250(8)	1.253(5)
C20–Sn–C20A		107.48(5)	109.6(4)	110.0(2)
O1–Sn–N1		75.18(4), 73.53(4)	73.68(19)	73.66(11)
O1–Sn–O1A		157.19(4)	158.1(2)	159.04(16)
C20–Sn–N1		159.15(5), 164.06(5)	158.0(2)	157.06(14)
N1–Sn–N1A		79.99(4)	73.1(3)	73.02(17)
C7–N2–N3–C10	−179.24(18)	179.56(12), 178.43(12)	−179.6(6)	178.8(3)

is observed for the isomer 5-[(2-ethoxyphenyl)-1-diazenyl]-quinolin-8-ol described by Chen et al. [22].

In contrast to ligand L^6H, the organotin complexes **1** · $(CH_3)_2CO$, **4** and **5** represent van der Waals crystals without remarkably short intermolecular interactions. Shortest contacts are associated with C···H distances of 2.8 Å and CH···O distances of 2.5 Å. No short inter-halogen distances occur in the bromine containing compound **5**.

The organotin complexes **4** and **5** show very similar lattice parameters and share all relevant packing features; they are most probably isomorphous. In both structures, the molecules are located on 2-fold crystallographic axes. In **1** · $(CH_3)_2CO$, the organotin complex and the solvent molecule are in general positions; the molecule of the former does not exhibit local C_2 symmetry. In the chelating ligand coordinated to tin via the atoms O1A and N1A, the 10 membered quinolinol ring N1A–C9A and the phenyl moiety C10A–C15A subtend a dihedral angle of 20° whereas the corresponding groups are significantly closer to coplanarity in the other ligand (O1/N1) as well as in L^6H, **4**, and **5** with dihedral angles in the range of 5–7°. Apart from these differences in conformation, all three organotin complexes show essentially the same arrangement of donor atoms found in $Ph_2Sn(Ox)_2$ [11]. The oxygen atoms of the two chelating ligands occupy *trans* positions in a strongly distorted octahedron; the nitrogen donors are situated in *trans* geometry with respect to the tin-coordinating phenyl C. The so-formed O–Sn–O and N–Sn–C angles range between 157° and 164°. The *ipso*-carbon atoms of the phenyl ligands form angles of 107.48(5)° (**1**), 109.6(4)° (**4**) and 110.0(2)° (**5**) at the tin atom, in good agreement with the angle reported for $[Ph_2Sn(Ox)_2]$ (108.61 (9)°) with *cis*-R_2Sn octahedral geometry [11].

3.7. In vitro cytotoxicity

Ph_2SnOx_2 has shown antitumour activity in the National Cancer Institute (USA) test panel [12]. The results of the in vitro cytotoxicity test in human tumour cell lines on Ph_2SnOx_2 and compound **1** are given as ID_{50} values in

Table 3
ID_{50} values (ng/ml) of test compounds **1** and Ph_2SnOx_2 in vitro (using as cell viability test) in seven human tumour cell lines

Test compound[a]	Cell lines						
	A498	EVSA-T	H226	IGROV	M19	MCF-7	WIDR
1	16902	8677	8950	4774	10104	7332	8441
Ph_2SnOx_2	304	103	314	113	131	127	183
DOX	51	26	20	120	80	21	36
CPT	539	251	650	72	980	480	491
5-FU	146	382	531	799	495	373	556
MTX	44	10	168	285	45	15	15
ETO	119	395	159	1387	1513	296	457
TAX	25	4	5	78	14	3	5

[a] *Abbreviations*. **1**, $Ph_2Sn(L^1)_2$; Ph_2SnOx_2, bis(8-quinolinato)diphenyltin(IV); DOX, doxorubicin; CPT, cisplatin; 5-FU, 5-fluorouracil; MTX, methotrexate; ETO, etoposide; TAX, paclitaxel.

Table 3, and compared with the data for some compounds that are in current clinical use as antitumour agents. The table clearly shows that Ph_2SnOx_2 is more active in vitro than cisplatin against all seven human cancer cell lines. Compound **1** is less active than cisplatin. The compound tested may be used as a model for modification in order to improve cytotoxic and dissolution properties.

4. Supplementary material

CCDC Nos. 266988–266991 contain the supplementary crystallographic data for complexes L^6H, **5**, **1** · $(CH_3)_2CO$ and **4**, respectively. These data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033; e-mail: deposit@ccdc.cam.ac.uk).

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