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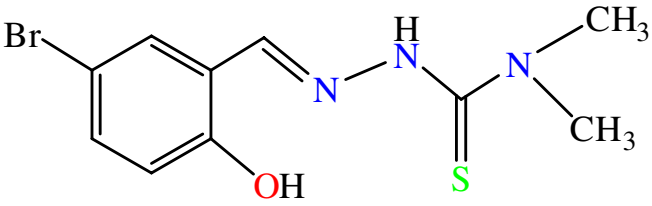

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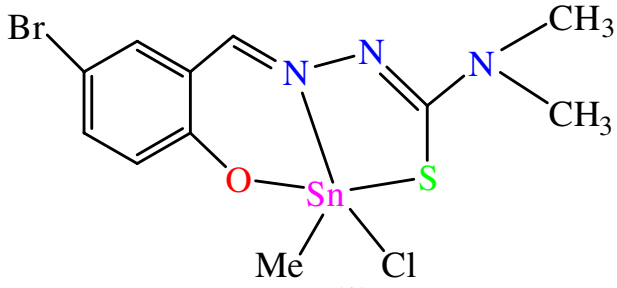

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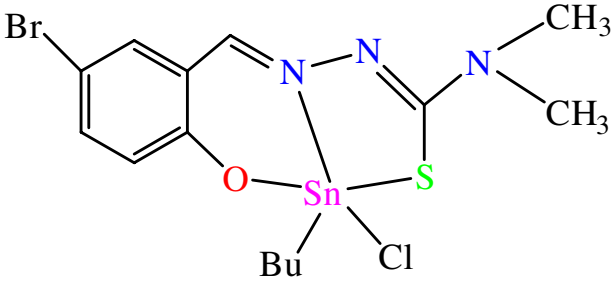

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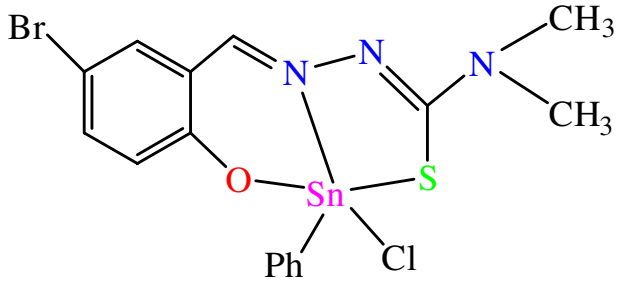

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INORGANIC CHEMISTRY | RESEARCH ARTICLE

Synthesis, spectroscopic properties and biological activity of new mono organotin(IV) complexes with 5-bromo-2-hydroxybenzaldehyde-4, 4-dimethylthiosemicarbazone

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Synthesis, spectroscopic properties and biological activity of new mono organotin(IV) complexes with 5-bromo-2-hydroxybenzaldehyde-4, 4-dimethylthiosemicarbazone

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Abstract: The organotin(IV) complexes [RSn(L)] (where R = Me (**2**), R = n-Bu (**3**), R = Ph (**4**); H_2L (**1**) = 5-bromo-2-hydroxybenzaldehyde-4,4-dimethylthiosemicarbazone) have been synthesized by the reaction of organotin(IV) chloride(s) with H_2L (**1**). All the compounds have been characterized by CHN analyses, UV–vis, FT-IR, ^{1}H, ^{13}C and ^{119}Sn NMR spectral studies. The molecular structure of H_2L (**1**) has been confirmed by X-ray crystallography. The infrared spectrum gives confirmation for the compound (H_2L) in the thione form, which is supported with the observed bond lengths from the crystal structure. Spectral studies revealed that the dinegative tridentate ligand is bonded to the tin(IV) atom via phenolic-O, azomethine-N and thiolate-S atoms. ^{119}Sn NMR data in DMSO-d_6 suggested penta-coordinated Sn(IV) atom in solutions for all complexes (**2–4**). The compound, H_2L (**1**) crystallizes into a monoclinic lattice with the space group $P2_1/c$, Z = 4, V = 1,191.75(8)Å^3. The compounds were also tested for their antiproliferative activity against human colon cancer cell line (HCT 116) and displayed strong cytotoxic activities.

Subjects: Chemical Spectroscopy; Chemistry; Inorganic Chemistry

Keywords: 5-bromo-2-hydroxybenzaldehyde-4,4-dimethylthiosemicarbazone; organotin(IV) complexes; spectral analyses; crystal structure; cytotoxicity

ABOUT THE AUTHORS

The authors are involved in the research work mainly focused on the synthesis of organotin(IV) complexes with different types of substituted thiosemicarbazone ligands and investigate their structural and cancer-/bacteria-inhibiting properties. The group is also engaged in synthesis and characterization of metal complexes of *N*-heterocyclic carbenes (NHC). The characterization techniques includes elemental analysis, FT-IR, ^{1}H ^{13}C, ^{119}Sn NMR, UV–visible spectroscopy and X-ray diffraction analysis. Organotin(IV) complexes possess a wide variety of potential biological activities such as antibacterial, antifungal, antitumor DNA interaction and enzyme inhibition. They are used as stabilizers for plastics and paints, industrial catalysts, textile and wood preservation. As a part of our ongoing studies, herein, we reported the synthesis, structural characterization and antitumor activities of organotin(IV) complexes with 5-bromo-2-hydroxybenzaldehyde-4,4-dimethylthiosemicarbazone.

PUBLIC INTEREST STATEMENT

Three new organotin(IV) complexes of 5-bromo-2-hydroxybenzaldehyde-4,4-dimethylthiosemicarbazone have been synthesized and characterized by elemental analysis, UV–vis, FT-IR, ^{1}H, ^{13}C and ^{119}Sn NMR techniques. Thiosemicarbazone ligand in its deprotonated forms coordinate to tin(IV) via phenolic oxygen, azomethine nitrogen and thiolate sulphur atoms. The tin atom is a five-coordinated geometry. Biological studies carried out *in vitro* against human colon cancer cell line (HCT 116) have shown different organic groups (R) attached to tin(V) centre, which showed distinctive differences in the biological property. Therefore, complexes may be considered as new anticancer agents.

1. Introduction

Thiosemicarbazones have received interest because of their activities, which can be predominantly classified according to their antitumor, antiviral, antitubercular, antibacterial, antihypertensive and antimalarial activities (Campbell, 1975; Liberta & West, 1992; Pandeya & Dimmork, 1993; Reddy, Sambasiva Reddy, & Ravindra Babu, 1999; Wang et al., 2009; West et al., 1993). Thiosemicarbazone with tridentate-ONS donor ligands play a vital role in the field of coordination chemistry as they readily form complexes with certain metal ions (Affan, Salam, Ahmad, White, & Ali, 2012; Alomar, Khan, Allain, & Bouet, 2009; Maurya, Kumar, Abid, & Azam, 2006; Vieites, Otero, & Santos, 2009). Substituted thiosemicarbazones and their transition and main group metal complexes have been extensively studied and found to be associated with biological activities (John, Sreekanth, Rajakannan, Ajith, & Kurup, 2004; Joseph et al., 2004; Kasuga et al., 2001; Rebolledo et al., 2005). Recent studies showed that the substitution on the terminal *N*(4) of thiosemicarbazones much improved their anticancer activity. The terminal *N*(4) dimethylation of thiosemicarbazone of 2-acetylpyridine *N*,*N*-dimethyl thiosemicarbazone and acetylpyrazine *N*,*N*-dimethyl thiosemicarbazone increased their cytotoxcity (Kowol et al., 2007). In earlier studies on the biological applications of metal complexes of thiosemicarbazone derivatives, Dilworth et al. highlighted various biological roles exhibited by this class of compound (Dilworth & Hueting, 2012). In the context of biological importance, Tan et al. have reported that the ligand coordinated as a tridentate ONS-dianion to zinc(II) and the resultant complex explored for activity against prostate cancer cell (Tan et al., 2012). In addition, biological studies have been reported for some transition-metal and other main group metal thiosemicarbazone derivatives. But based on the literature survey, there is very limited information available regarding the synthesis, structure and biological studies of organotin(IV) complexes with ONS donor containing thiosemicarbazone derivatives. As a part of our ongoing studies, in the present research work, we reported the synthesis, spectral and biological studies of organotin(IV) complexes with 5-bromo-2-hydroxybenzaldehyde-4,4-dimethylthiosemicarbazone. X-ray crystal structure of ligand (**1**) is also reported.

2. Experimental

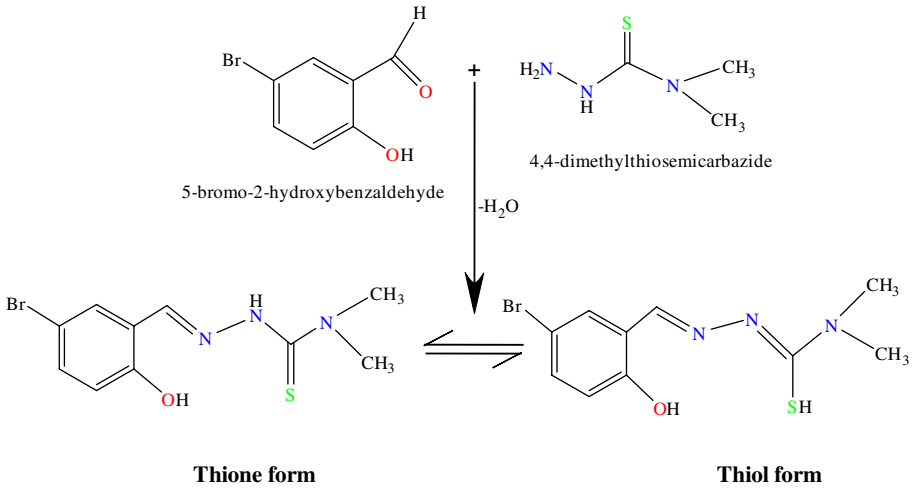
2.1. Materials and methods

All reagents were purchased from Fluka, Aldrich and Sigma. All solvents were received as reagent grade and used without further purification. Melting point was measured by the Stuart Scientific SMP1 melting point apparatus. Infrared (IR) spectra were recorded by the Perkin Elmer System 2000 spectrophotometer by using the KBr disc method in the range 4,000–400 cm^{-1}. ^{1}H, ^{13}C and ^{119}Sn NMR spectra were recorded on a Bruker 500 and 400 MHz NMR spectrophotometer relative to $SiMe_4$ and $SnMe_4$ in DMSO-d_6 solvent. Elemental analysis was conducted by the Perkin Elmer 2400 Series-11 CHN analyzer. The crystals suitable for X-ray diffraction studies were obtained by the slow evaporation of its solution in DMF. X-ray crystallographic data were recorded on a Bruker SMART APEXII CCD area-detector diffractometer using graphite monochromated MoKα radiation (λ = 0.71073 Å) at 100 K. A crystal with dimension 0.43 × 0.20 × 0.09 mm was used. The data were collected and reduced using APEX2 and SAINT programs. The structure of all compounds was solved using the SHELXS-97 programme package, and refined using the SHELXL-97 programme package. All nonhydrogen atoms were anisotropically refined. The molecular graphics were created using SHELXTL-97.

2.2. Synthesis of 5-bromo-2-hydroxybenzaldehyde-4,4-dimethylthiosemicarbazone (H_2L) (1)

A solution of 5-bromo-2-hydroxybenzaldehyde (0.84 g, 4.19 mmol) in ethanol (20 ml) was added to a solution of 4,4-dimethylthiosemicarbazide (0.5 g, 4.19 mmol) in ethanol (20 ml). The resulting yellow solution was refluxed with stirring for 2 h (Scheme 1). A white product was formed when the solution cooled down to room temperature, then filtered, washed with ethanol and dried *in vacuo* over silica gel. Colourless crystals were obtained by slow evaporation of a DMF solution at room temperature. M.p: 203–205°C, (1.05 g, 83%). UV–vis (DMSO) λ_{max} nm^{-1}: 254, 317, 369: FT-IR (KBr, cm^{-1}) ν_{max}: 3,372 (s, OH), 3,190 (s, NH), 1,622 (m, C=N), 1,561 (s, C_{aro}–O), 1,360, 858 (w, C–S), 985 (m, N–N). ^{1}H NMR (DMSO-d_6, ppm): 11.41 (s, 1H, OH), 10.47 (s, 1H, N–NH), 8.44 (s, 1H, CH=N), 7.47 (d, 1H, *J* = 7.2 Hz, PhC3–H), 7.29 (d, 1H, *J* = 6.2 Hz, PhC4–H), 6.92 (s, 1H, PhC6–H), 3.30 (s, 6H, CH_3). ^{13}C NMR

Scheme 1. Synthesis of 5-bromo-2-hydroxybenzaldehyde-4,4-dimethylthiosemicarbazone [H_2L, (1)].



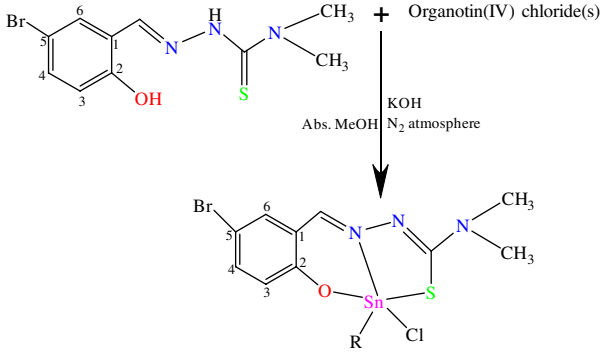
(DMSO-d_6, ppm): 189.16 (C=S), 155.67 (C=N), 151.45, 145.44, 136.55, 130.15, 124.32, 118.38 (Ph–C2, Ph–C5, Ph–C3, Ph–C4, Ph–C6, Ph–C1), 29.16 (CH_3). Anal. Calc. for $C_{10}H_{12}BrN_3OS$: C, 39.70; H, 3.97; N, 13.89. Found: C, 39.47; H, 3.71; N, 14.11%.

2.3. Synthesis of [MeSnCl(L)] (2)

H_2L (**1**) (0.302 g, 1.0 mmol) was dissolved in dry methanol (10 mL) under a nitrogen atmosphere in a round-bottomed reaction flask. KOH (0.11 g, 2.0 mmol) dissolved in methanol was added dropwise to the ligand solution. The resulting mixture was refluxed under nitrogen for 1 h. Then, a methanolic solution of methyltin(IV) trichloride (0.24 g, 1.0 mmol) was added dropwise. The resulting reaction mixture was refluxed for 4 h (Scheme 2) and cooled to room temperature. The yellow microcrystals were obtained from slow evaporation of the resulting solution at room temperature. The microcrystals were filtered off, washed with a small amount of cold methanol and dried in *vacuo* over silica gel. M.p: 255–257°C, (1.05 g, 83%). UV–vis (DMSO) λ_{max} nm^{-1}: 255, 322, 381, 482: FT-IR (KBr, cm^{-1}) ν_{max}: 1,591 (m, C=N–N=C), 1,528 (s, C_{aro}–O), 1,325, 830 (w, C–S), 1,027 (m, N–N), 599 (w, Sn–C), 559 (w, Sn–O), 462 (w, Sn–N). ^{1}H NMR (DMSO-d_6, ppm): 8.56 (s, 1H, CH=N), 7.65 (d, 1H, J = 7.3 Hz, PhC3–H), 7.30 (d, 1H, J = 6.4 Hz, PhC4–H), 6.95 (s, 1H, PhC6–H), 3.35 (s, 6H, CH_3), 1.10 (s, 3H, Sn–CH_3). ^{13}C NMR (DMSO-d_6, ppm): 176.51 (C=S), 164.48 (C=N), 155.50, 148.22, 138.31, 131.75, 125.45, 120.19 (Ph–C2, Ph–C5, Ph–C3, Ph–C4, Ph–C6, Ph–C1), 30.81 (CH_3), 18.62 (Sn–CH_3). ^{119}Sn NMR (DMSO-d_6, ppm): −162.61. Anal. Calc. for $C_{11}H_{13}BrClN_3OSSn$: C, 28.15; H, 2.79; N, 8.95. Found: C, 28.20; H, 2.93; N, 9.11%.

The other organotin(IV) complexes (**3**–**4**) were synthesised following the same procedure by using the appropriate organotin(IV) chloride(s) (Scheme 2).

Scheme 2. Reaction scheme for the synthesis of organotin(IV) complexes (2–4).



2.4. Synthesis of [BuSnCl(L)] (3)

M.p: 261–263°C, (1.05 g, 83%). UV–vis (DMSO) λ_{max} nm^{-1}: 250, 320, 371, 454: FT-IR (KBr, cm^{-1}) ν_{max}: 1,594 (m, C=N–N=C), 1,531 (s, C_{aro}–O), 1,322, 834 (w, C–S), 1,028 (m, N–N), 607 (w, Sn–C), 567 (w, Sn–O), 480 (w, Sn–N). ^{1}H NMR (DMSO-d_6, ppm): 8.59 (s, 1H, CH=N), 7.71 (d, 1H, J = 7.4 Hz, PhC3–H), 7.33 (d, 1H, J = 6.3 Hz, PhC4–H), 7.01 (s, 1H, PhC6–H), 3.38 (s, 6H, CH_3), 1.60–1.51 (t, 2H, Sn–CH2–CH_2–CH_2–CH_3), 1.31–1.22 (m, 2H, Sn–CH_2–CH2–CH_2–CH_3), 1.20–1.12 (m, 2H, Sn–CH_2–CH_2–CH2–CH_3), 1.05–0.98 (t, 3H, Sn–CH_2–CH_2–CH_2–CH3). ^{13}C NMR (DMSO-d_6, ppm): 172.36 (C=S), 162.39 (C=N), 149.07, 141.28, 135.92, 129.74, 123.16, 122.94 (Ph–C2, Ph–C5, Ph–C3, Ph–C4, Ph–C6, Ph–C1), 30.11 (CH_3), 24.09, 22.15, 19.64, 17.22 (Sn–CH_2–CH_2–CH_2–CH_3). ^{119}Sn NMR (DMSO-d_6, ppm): −174.94. Anal. Calc. for $C_{14}H_{19}BrClN_3OSSn$: C, 32.88; H, 3.74; N, 8.22. Found: C, 32.98; H, 3.85; N, 8.13%.

2.5. Synthesis of [PhSnCl(L)] (4)

M.p: 249–251°C, (1.05 g, 83%). UV–vis (DMSO) λ_{max} nm^{-1}: 251, 325, 378, 418: FT-IR (KBr, cm^{-1}) ν_{max}: 1,599 (m, C=N–N=C), 1,530 (s, C_{aro}–O), 1,326, 827 (w, C–S), 1,019 (m, N–N), 600 (w, Sn–C), 569 (w, Sn–O), 472 (w, Sn–N). ^{1}H NMR (DMSO-d_6, ppm): 8.62 (s, 1H, CH=N), 7.58–7.01 (m, 8H, Ph–H), 3.29 (s, 6H, CH_3). ^{13}C NMR (DMSO-d_6, ppm): 169.48 (C=S), 160.77 (C=N), 152.79–123.44 (Ph–C), 30.87 (CH_3). ^{119}Sn NMR (DMSO-d_6, ppm): −170.81. Anal. Calc. for $C_{16}H_{15}BrClN_3OSSn$: C, 36.16; H, 2.85; N, 7.91. Found: C, 36.22; H, 2.90; N, 8.05%.

2.6. Anticancer activity evaluation by MTT assays

The cytotoxic effects of **1–4** against human colorectal cancer (HCT 116) cell line were evaluated with MTT assay procedures (Mosmann, 1983). Human colorectal cancer (HCT 116) cell lines (1.5×10^5 cells mL^{-1}, 100 µL $well^{-1}$) were seeded in a 96-well microtiter plate. The plate was incubated in a CO_2 incubator overnight to allow cell attachment. After 24 h from seeding, the cells were incubated with 100 µL of test organotin(IV) complexes into each well containing the cells. The test compounds were diluted with media into various concentrations from the stock. The plates were incubated at 37°C with an internal atmosphere of 5% CO_2 for 3 days. Then, 20 µL of MTT reagent was added into each well and the plates were incubated for 4 h. After this incubation period, 50 µL of MTT lysis solution (DMSO) was added into the wells. The plates were further incubated for 5 min in a CO_2 incubator. Finally, the absorbance was measured at 570 nm with the use of a standard ELISA microplate reader. Data were recorded and analysed to assess the effects of test compound on cell viability. The drug concentration required to reduce cell number to 50% of controls following a 72 h continuous drug exposure (IC_{50}) was obtained from semilogarithmic dose-response plots. The medium containing without samples were served as control and 5-flourouracil was used as standard reference drug. IC_{50} values of the compounds (**1**-**4**) and reference drug are given in Table 1.

3. Results and discussion

5-bromo-2-hydroxybenzaldehyde-4,4-dimethylthiosemicarbazone was prepared by the condensation reaction of 5-bromo-2-hydroxybenzaldehyde and 4,4-dimethylthiosemicarbazide. The ligand has two tautomerization features within the structure (Scheme 1). Organotin(IV) complexes (**2–4)** were synthesized by reacting a methanolic solution of appropriate organotin chloride(s) with methanolic solution of the H_2L (**1**) containing an 1: 2 M amount of potassium hydroxide. They are

Table 1. IC_{50} values (µM) for synthesized compounds 1–4 against human colorectal cancer (HCT 116) cell lines

No.	Compound	IC_{50} (µM)
1	H_2L	6.20
2	[MeSnCl(L)]	4.12
3	[BuSnCl(L)]	5.46
4	[PhSnCl(L)]	3.23
R	5-fluorouracil	6.41

stable under nitrogen atmosphere and soluble in common organic solvents such as MeOH, CH_2Cl_2, $CHCl_3$, DMF and DMSO. The structural features of the organotin(IV) complexes were characterized by different spectroscopic techniques.

3.1. UV–visible spectra

The electronic spectrum was recorded in DMSO. The ligand (H_2L) displayed three absorption bands at 254, 317, 369 nm which have π–π* and n–π* transition bands. There is a slight shift in the energy of these bands upon complexation. The new band for the complexes in the region at 482–418 nm assigned to ligand to metal charge transfer (LMCT) transition bands (Silverstein, Bassler, & Morrill, 1981). Therefore, shift in the λ_{max} is clear indication coordination occurred between metal and ligand.

3.2. Infrared spectra

The IR spectrum of H_2L (**1**) shows a broad band at 3,372 and 3,190 cm^{-1}, which are due to the stretching vibrations of the ν(OH) and ν(NH) groups, respectively. A medium bands at 1,622 cm^{-1} are attributed to ν(C=N) and a very strong absorption at 1,561 cm^{-1}, which can be assigned to the $\nu(C_{aro}–O)$ group. The other bands observed in the H_2L (**1**) spectrum at 1,360, 858 and 985 cm^{-1} due to ν(C=S) and ν(N–N), respectively. The nonappearance of ν(S–H) band around 2,700 cm^{-1} proposed that ligand (**1**) remains in the thione form in the solid state (Nakamoto, 1986). No bands due to ν(OH) and ν(NH) vibrations are observed in the IR spectra of the complexes (**2–4**), indicating deprotonation of ligand and coordinated to tin(IV) atom. The appearance of peaks at 1,599–1,591 cm^{-1} for all complexes corresponding to the newly formed C=N–N=C bond which indicated coordination of azomethine nitrogen to tin(IV) atom (Costa et al., 2005). The absorption bands within the range 1,528–1,531 cm^{-1} due to $\nu(C_{aro}–O)$ are shifted to lower frequencies compared to those of H_2L (**1**), implying coordination through phenolic oxygen (Rajan & Chakravorty, 1981). Furthermore, increase in ν(N–N) on coordination of H_2L (**1**) also supported the coordination of azomethine nitrogen to tin(IV) atom (Garg, Prathapachandra Kurup, Jain, & Bhoon, 1988). The ν(C=S) bands are shifted to lower frequencies in the complexes (**2–5**), supporting coordination via the thiolate sulphur after deprotonation of the ligand (Mendes et al., 2007). The peaks at 607–599 cm^{-1} can be assigned to ν(Sn–C) vibrations, whereas the peaks at 569–559 cm^{-1} are due to ν(Sn–O) vibrations (Ma, Li, Zhang, & Wang, 2006; Xanthopoulou et al., 2003). The bands at 480–462 cm^{-1} are assigned to the ν(Sn–N) bond vibrations. It is completely evident from these IR data that the ligand (**1**) is bound to tin(IV) atom as dinegative tridentate agent via phenolic-O, azomethine-N and thiolate-S atoms.

3.3. ^{1}H, ^{13}C and ^{119}Sn NMR spectra

The ^{1}H, ^{13}C and ^{119}Sn NMR data of the free ligand and its organotin complexes are given in the experimental section. ^{1}H NMR spectrum of H_2L (**1**) showed resonance signals at 11.41 and 10.47 ppm which are corresponded to δ(OH) and δ(N–NH) protons, respectively. After complexation, these signal are absent suggest ligand is bonded to the tin(IV) centre with phenolic oxygen and thiolate sulphur atoms. The signal due to δ(CH=N) proton, present in the free ligand appeared at 8.44 ppm, while for the complexes δ shifted slightly downfield indicating azomethine nitrogen coordinated to tin(IV) atom. The aromatic protons were observed in the 7.47–6.92 region for H_2L (**1**). These signals are slightly shifted to downfield region for complexes (**2–4**) due to complexation. The dimethyl group protons signal appeared at 3.38–3.29 ppm range for the ligand and its complexes. The chemical shifts of the methyl and butyl groups attached to the organotin(IV) complexes **2** and **3,** appeared within the expected range.

In the ^{13}C NMR spectra, the C=S signal appeared at upfield region in the spectra of the complexes (**2–4**) compared to those of free ligand (**1**), supporting coordination of the tin(IV) centre to the N=C–S group. The chemical shift due to the (C=N) carbon is found to have shifted downfield in the complexes relative to the free ligand (**1**), supported coordination via the azomethine nitrogen to tin(IV) centre. The aromatic carbon signals were observed in the 151.45–118.38 ppm region for free ligand while for the organotin complexes, its chemical shift is observed downfield region due to complexation.

The chemical shift of carbon in $(CH_3)_2$ group was found in the 29.16–30.87 ppm region for ligand and its complexes. The chemical shifts due to the (Sn–CH_3) and (Sn–Bu) for complexes **2** and **3** were clearly observed within the expected region.

The coordination of Sn can also be determined through $\delta(^{119}Sn)$ values by fingerprinting (Huber et al., 1997; Otera, Kusaba, Hinoishi, & Kawasaki, 1982). ^{119}Sn NMR spectra of complexes (**2–4**), $\delta(^{119}Sn)$ values were found at −174.94 to −162.61 ppm, indicating that the tin(IV) atom is five-coordinate in these complexes (Holeček, Nádvorník, Handlíř, & Lyčka, 1986; Yin & Chen, 2006).

3.4. Crystallographic study of H_2L (1)

The molecular structure of H_2L (**1**) along with the atomic numbering scheme and its packing in the crystal lattice are given in Figures 1 and 2, respectively. Table 2 summarizes crystal data and structure refinement results of the H_2L compound. Selected bond lengths (Å) and angles(°) are shown in Table 3. The compound crystallizes into a monoclinic lattice with space group $P2_1/c$. According to the crystal structure, the compound exists in the thione form with S1 and N1 in the E configuration with respect to the N2–C8 bond. This is confirmed by the torsion angle of −0.1(4)° of the N1–N2–C8–S1 moiety (Chattopadhyay, Banerjee, Majumdar, Ghosh, & Kuroda, 1987) and the torsion angle of N1–N2–C8–N3 is −179.9(2)°. Similarly, the N1–N2 bond length (1.368 Å) is closer to single bond length (1.45 Å) than to double bond length (1.25 Å) (Huheey, Keiter, & Keiter, 1993). The C8–S1 bond distance (1.677 Å) is close to that expected of a C=S double bond (1.60 Å) (March, 1992) than to C–S bond length (1.81 Å) and the C7–N1 bond length (1.279 Å) is nearly the same as that of the C=N double bond (1.28 Å) (Vrdoljak et al., 2005). These bond distances are in strong support of the existence of 5-bromo-2-hydroxybenzaldehyde-4,4-dimethylthiosemicarbazone in the thione form in the solid state. The molecular structure of the H_2L can be divided into two planar moieties that are connected by a single N1–N2 bond. The first plane, the N-ethylthioureide plane, includes N2, S1, N3 and C8–C10, whereas the second plane, the salicylaldimine plane, includes N1, O1 and C1–C7. Dihedral angle between these two planes is 11.8(3)°. In the title compound (H_2L), the C7–N1–N2–C8 torsion angle is 176.6(3)°. The N2–H hydrogen atom is approximately *syn* to the C7–H hydrogen atom. In the crystal lattice, the packing of the molecules is stabilized by intra and intermolecular hydrogen bonding interactions. The semicarbazones, as exemplified by the salicylaldehyde 4-methylthiosemicarbazone homolog (Xanthopoulou et al., 2003), feature an N–H···S hydrogen bond that connects two molecules into a hydrogen-bonded dimer. The hydroxy-O– and amide-N-bound H atoms form intramolecular hydrogen bonds to the imine-N atom. The amino H atom of the chain is hydrogen-bond donor to the S atom of an inversion-related molecule to form a dimer. The H atom of the hydroxyl unit is hydrogen bond donor to the azomethine N atom. This arrangement leads to supramolecular

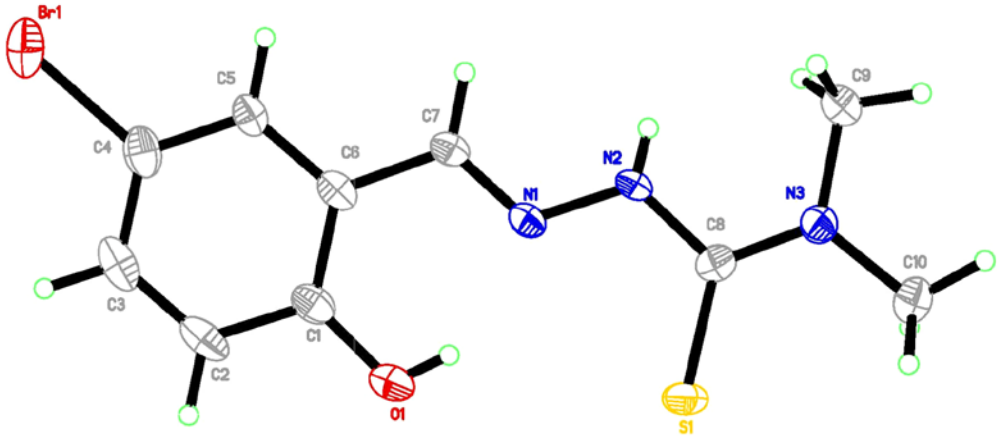


Figure 1. Molecular structure of H_2L (1) showing displacement ellipsoids at the 50% probability level.

structures and sustained by N–H···O, O–H···S and N–HS hydrogen bonds. Further stabilization is provided by C–H...π and π...π [ring centroid(hydroxybenzene)] interactions.

3.5. Anticancer activity

The compounds **1–4** were tested against HCT 116 cell line. The organotin(IV) complexes showed strong cytotoxic activity (IC_{50} = 3.23–5.46 μM) than the parent ligand (IC_{50} = 6.20 μM) and standard drug, 5-Flourouracil (IC_{50} = 6.41 μM). As for the identical coordination geometry, the organotin(IV) complexes (**2–4**) exhibited cytotoxic activity in the order of **4 > 2** > **3** > . This study has been demonstrated that complex activity is dependent on the organo group attached to the metal centre in the order Ph > Me > Bu. This is might be due to the bulky organo group which increases lipophilicity of these complexes. Furthermore, phenyltin(IV) complex (**4**) showed stronger cytotoxic activity than the other organotin(IV) derivatives. Between methyltin(IV) (**2**) and butyltin(IV) (**3**) complexes of H_2L ligand, complex **2** showed stronger cytotoxic activity (**2 > 3**).

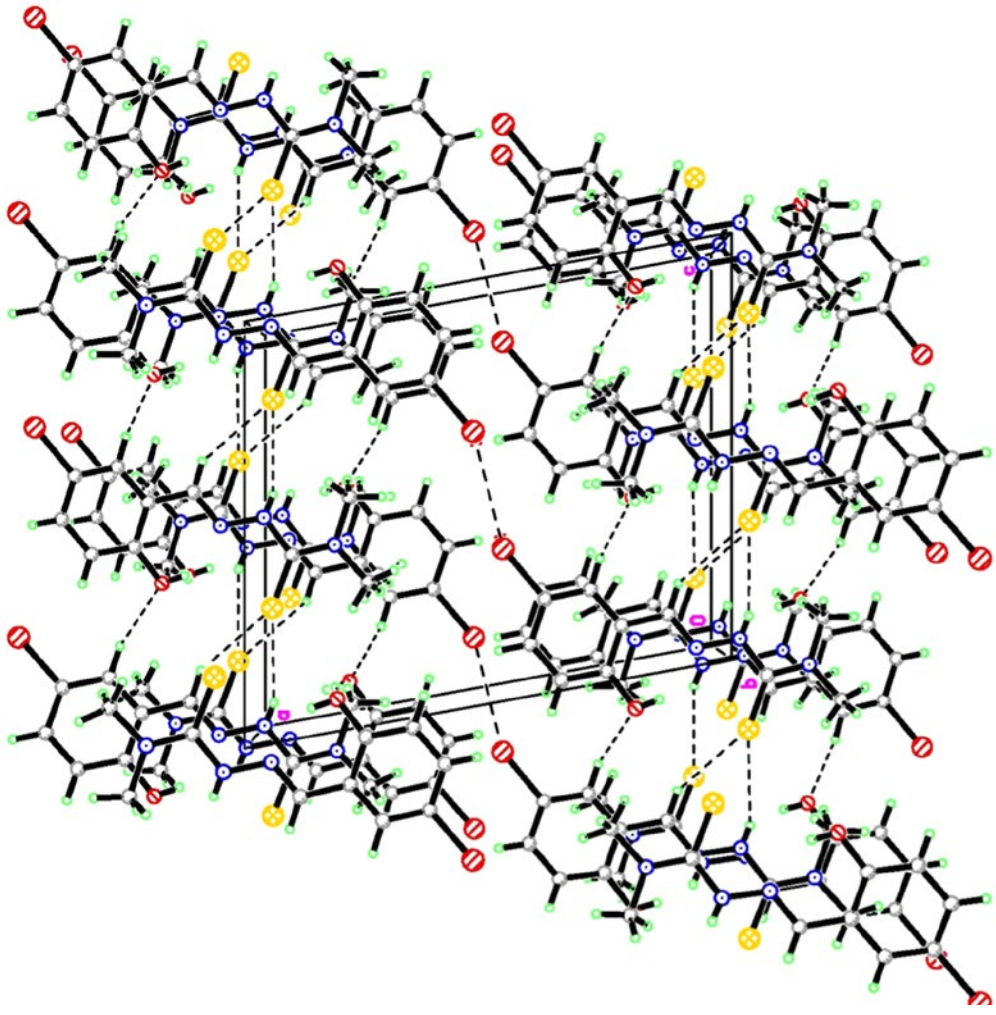


Figure 2. The packing diagram of H_2L (1) in the crystal lattice.

Notes: Intermolecular hydrogen bonds are shown as dotted lines.

4. Conclusion

Three new mono organotin(IV) complexes of 5-bromo-2-hydroxybenzaldehyde-4,4-dimethylthiosemicarbazone (H_2L) were synthesized and characterized successfully. From spectroscopic results, it can be concluded that dinegative tridentate ligand coordinated to the tin(IV) centre via ONS donor

Table 2. Crystal data and structure refinement parameters for H_2L (1)

Compound	**H_2L (1)**
Empirical formula	$C_{10}H_{12}BrN_3OS$
Formula weight	302.20
Temperature (K)	100
Wavelength (Å)	0.71073
Crystal system	Monoclinic
Space group	$P2_1/c$
Unit cell dimensions	
a (Å)	14.1524(5)
b (Å)	7.0159(3)
c (Å)	12.2016(5)
α (°)	90.00
β (°)	100.366(3)
γ (°)	90.00
Volume (Å^3)	1,191.75(8)
Z	4
Calculated density (mg m^{-3})	1.684
Radiation type λ (Å)	M_0K/α
F(0 0 0)	608
Crystal size (mm)	0.43 × 0.20 × 0.09
Crystal colour	Colourless
Scan range θ(°)	2.93–31.12
Absorption coefficient (μ) (mm^{-1})	3.607
Max. and min. transm	0.3061 and 0.7326
Goodness-of-fit on F^2	1.030
Data/restrains/parameters	3,803/0/156
Final *R* indices [$I > 2\sigma(I)$]	R_1 = 0.0466, wR_2 = 0.0897
R indices (all data)	R_1 = 0.1002, wR_2 = 0.1038

Table 3. Selected bond lengths (Å) and angles (°) of H_2L (1)

Bond lengths (Å)			
S1–C8	1.677(3)	O1–C1	1.353(4)
N1–C7	1.279(3)	N1–N2	1.368(3)
N2–C8	1.374(4)	N3–C8	1.340(3)
N3–C10	1.464(3)	N3–C9	1.467(3)
Br1–C4	1.905(3)	C6–C7	1.459(4)
Bond angles (°)			
C7–N1–N2	119.4(2)	N1–N2–C8	118.0(2)
C8–N3–C10	120.4(2)	C8–N3–C9	121.5(2)
C10–N3–C9	118.1(2)	O1–C1–C2	117.3(3)
C2–C1–C6	119.6(3)	C3–C2–C1	121.0(3)
N1–C7–C6	117.6(2)	N3–C8–N2	115.6(2)
N3–C8–S1	123.9(2)	N2–C8–S1	120.5(2)

atoms in all complexes. ^{119}Sn chemical shifts of all the compounds confirmed penta-coordinate tin(IV) centre. All the organotin(IV) complexes exhibited higher cytotoxicity than their parent ligand and the standard drug, 5-fluorouracil. The cytotoxic activity of the complexes with their structure relationship we found that the bulky organic group (R) bonded to tin(IV), increases the degree of cytotoxicity. Furthermore, phenyltin(IV) complex **4** displayed good cytotoxic activities than other organotin(IV) derivatives against the tested cell lines.

Supplementary material
CCDC reference number 965806 contains the supplementary crystallographic data for H2L (1). This data can be obtained free of charge from the Cambridge Crystallographic data center via www.ccdc.ac.uk/data_request/cif or from the Cambridge Crystallographic data center, 12 Union Road, Cambridge CB2 1EZ, UK; fax: (+44) 1223-336-033; or e-mail: deposit@ccdc.cam.ac.uk.

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