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Homobimetallic organotin(IV) complexes with hexadentate Schiff base: Synthesis, crystal structure and antimicrobial studies

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ABSTRACT

This article describes the synthesis of four new homobimetallic organotin(IV) complexes: $[Et_2Sn]_2L$ (**1**), $[Bu_2Sn]_2L$ (**2**), $[Oct_2Sn]_2L$ (**3**) and $[BuClSn]_2L$ (**4**) ($\mathbf{H_4L}$ = $N^{1\prime},N^{6\prime}$-bis(5-bromo-2-hydroxybenzylidene)adipodihydrazide) and their structural elucidation by means of elemental analysis, mass spectroscopy, FT-IR, NMR (^1H, ^{13}C, ^{119}Sn) and single crystal X-ray analysis. Spectroscopic studies indicate coordination of hexadentate ligand to the diorganotin(IV) moieties via ONO–ONO donor sites and pentacoordinated tin centers. Single crystal X-ray analysis of (**1**) and (**2**) revealed homobimetallic nature of complexes with each Sn atom in a distorted square pyramidal coordination geometry. Packing diagrams suggest the seminal role of Sn···N and Br···π interactions in generating supramolecular assembly. The synthesized compounds were screened for their antimicrobial activity and cytotoxicity. Compound (**2**) exhibit highest activity against several pathogenic microbes.

1. Introduction

The study of organotin(IV) complexes of Schiff bases has been a subject of interest mainly due to their wide applications in various fields like catalysis, biotechnology, analytical and medicinal chemistry [1–6]. Several organotin(IV) hydrazones have been investigated for their structural diversity [7,8]. The tin atom in these complexes is usually pentacoordinate with a trigonal bipyramidal or square pyramidal geometry and can act as a Lewis acid. The coordination number can be increased by addition of molecules with donor atoms and the geometry around tin changes to pentagonal bipyramidal [9]. Moreover, supramolecular architectures can be achieved through self-assembly of molecules by hydrogen bonding, hydrophobic, hydrophilic effects, electrostatic and π–π interactions etc. [10,11].

The metal complexes of diacylhydrazones exhibit pronounced biological and pharmaceutical activities as antitumor, antimicrobial, antituberculosis and antimalarial agents [12–17]. The presence of two coordinating units connected by hydrocarbon linkers with varying degrees of flexibility in the ligand may yield supramolecular architectures such as double helices, grids, racks or coordination polymers [18]. However, few studies have been reported for the synthesis of bis-diorganotin(IV) complexes of diacylhydrazones with double set of ONO donor atoms [19]. The diacylhydrazones can either act as monobasic bis-bidentate, monobasic bis-tridentate, dibasic bis-tridentate chelators or they may form polymeric chain [20]. In continuation with our studies on diorganotin(IV) complexes derived from ONO donor ligands [21,22], and triggered by the need for potent antimicrobial agents to mitigate or eliminate the infections, we report herein the synthesis, spectroscopic characterization and antimicrobial activities of four new centrosymmetric homobimetallic organotin(IV) derivatives of $N^{1\prime},N^{6\prime}$-Bis(5-bromo-2-hydroxybenzylidene)adipodihydrazide, a potential tetrabasic

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0022-328X/

hexadentate ligand with ONO–ONO donor atoms. The single crystal X-ray structure and intermolecular interactions generating supramolecular architecture for complex **1** and **2** have also been discussed.

2. Experimental

2.1. Chemicals and instrumentations

Organotin(IV) dichlorides, dioctyltin(IV) oxide, butyltin(IV) chloridedihydroxide, adipic hydrazide and 5-bromo-2-hydroxybenzaldehyde were procured from Aldrich and the organic solvents used were of Merck, Germany. These solvents were freshly dried using standard procedures [23]. The melting points were recorded on an electrothermal melting point apparatus, model MP-D Mitamura Rieken Kogyo (Japan) by using capillary tubes and are uncorrected. The infrared (IR) spectra were recorded as neat liquids, using NaCl cells or as KBr pellets for solids on a Bio-Rad Excaliber FT-IR, model FTS 300 MX spectrophotometer (USA) in the frequency range of 4000–400 cm^{-1}. Multinuclear NMR (^1H, ^{13}C, and ^{119}Sn) spectra were recorded on a Bruker ARX 300 MHz-FT-NMR and a Bruker 400 MHz-FT-NMR spectrometers Switzerland using $CDCl_3$ as an internal reference. Chemical shifts (δ) are given in ppm and coupling constants (J) are given in Hz. The multiplicities of signals in ^1H NMR are given with chemical shifts; (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, bs = broad signal). The mass spectra were recorded on a MAT-311A Finnigan (Germany). The m/z values were evaluated assuming that H = 1, C = 12, N = 14, O = 16, Cl = 35 and Sn = 120.

The X-ray diffraction data were collected on a Bruker SMART APEX CCD diffractometer, equipped with a 4 K CCD detector. Data integration and global cell refinement was performed with the program SAINT. The program suite SAINTPLUS was used for space group determination (XPREP). The structure was solved by Patterson method; extension of the model was accomplished by direct method and applied to different structure factors using the program DIRDIF. All refinement calculations and graphics were performed with the program PLUTO and PLATON package [24–28].

2.2. Synthesis

2.2.1. Synthesis of $N^{1\prime},N^{6\prime}$-bis(5-bromo-2-hydroxybenzylidene) adipodihydrazide (***H_4L***)

The synthesis of $N^{1\prime},N^{6\prime}$-bis(5-bromo-2-hydroxybenzylidene) adipodihydrazide was carried out by a reported method [29]. To a solution (25 mL) of adipic dihydrazide, 1.0 g (5.74 mmol) in ethanol was added a solution (25 mL) of 5-bromo-2-hydroxybenzaldehyde 2.47 g (11.48 mmol) in ethanol. The mixture was stirred and refluxed for 2 h. A white solid product was obtained (Scheme 1). Yield 77%. Anal. Calc. for $C_{20}H_{20}Br_2N_4O_4$ (M = 538): C, 44.47; H, 3.73; N, 10.37 Found: C, 44.50; H, 3.70; N, 10.40%. EI-MS, m/z (%): $[C_{20}H_{20}Br_2N_4O_4]^+$ 538(20.7), $[C_{13}H_{14}BrN_2O_3]^+$ 325(81.4), $[C_8H_6BrN_2O_2]^+$ 241(9.1), $[C_7H_4BrNO]^+$ 197(100.0), $[C_7H_4NO]^+$ 118(4.5), $[C_7H_3BrN]^+$ 180 (3.8), $[C_6H_4BrO]^+$ 171(18.7), $[C_6H_5]^+$ 77(16.7).

2.2.2. Bis[diethyltin(IV)][$N^{1\prime},N^{6\prime}$-bis(5-bromo-2-oxidobenzylidene) adipodihydrazide](Et$_2$Sn)$_2$L (***1***)

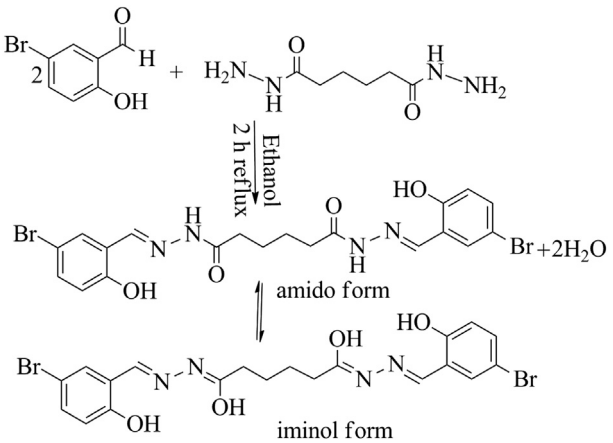
The triethylammonium salt of ligand (H_4L) was synthesized by reacting $N^{1\prime},N^{6\prime}$-bis(5-bromo-2-hydroxybenzylidene)adipodihydrazide 0.81 g (1.5 mmol) and triethylamine 0.84 mL (6.0 mmol) in dry toluene. The mixture was stirred for 15 min at room temperature and diethyltin(IV) dichloride 0.74 g (3.0 mmol) was added. The solution turned yellow and was further stirred for 5 h. The white precipitates of Et_3NHCl formed during the reaction were filtered. The filtrate was concentrated by rotary evaporator under reduced pressure to obtain yellow solid. The product was recrystallized from chloroform n-hexane (4:1) mixture (Scheme 2a).

Yield 78%. mp 194–196 °C. Anal. Calc. for $C_{28}H_{36}Br_2N_4O_4Sn_2$ (M = 890): C, 37.79; H, 4.08; N, 6.30 Found: C, 37.77; H, 4.10; N, 6.32% EI-MS, m/z (%): $[(C_8H_4BrN_2O_2)_2C_4H_8Sn_2(C_2H_5)_3]^+$ 861(100.0), $[(C_8H_4BrN_2O_2)Sn(C_2H_5)_2]^+$ 417(6.3), $[(C_8H_4BrN_2O_2)Sn(C_2H_5)]^+$ 388(6.9), $[(C_2H_5)_2\,Sn]^+$ 178 (3.1), $[C_2H_5Sn]^+$ 149(5.4), $[Sn]^+$ 120(7.1) IR (cm^{-1}): 1609 ν(C=N), 1079 ν(N–N), 569 ν(Sn–O), 460 ν(Sn–N), ^1H NMR (ppm): 8.49 (s, 2H, CH=N, $^3J(^{119}Sn-^1H)$ = 41 Hz), 2.34 (bs, 4H, $2CH_2$), 1.72 (bs, 4H, $2CH_2$), 6. 64 (d, 2H, Ar–H, $^3J_{H-H}$ = 9.0), 7.32 (dd, 2H, Ar–H, $^3J_{H-H}$ = 9.0), 7.18 (s, 2H, Ar–H), 1.42 (q, 8H, H_α–SnEt, $^3J_{H-H}$ = 7.2), 1.24 (t, 12H, H_β–SnEt, $^3J_{H-H}$ = 7.5) ^{13}C NMR (ppm): 159.3 (CH=N), 176.5 (NCO), 34.2, 26.1 ($-CH_2CH_2$), 166.0, 137.4, 135.3, 123.5, 118.0, 107.7 (Ar–C), 14.2 (C_α–SnEt, $^1J[^{119/117}Sn-^{13}C]$ = 614, 587 Hz), 9.2 (C_β–SnEt, $^2J[^{119}Sn-^{13}C]$ = 42 Hz), ^{119}Sn NMR: δ (ppm) = −192.5.

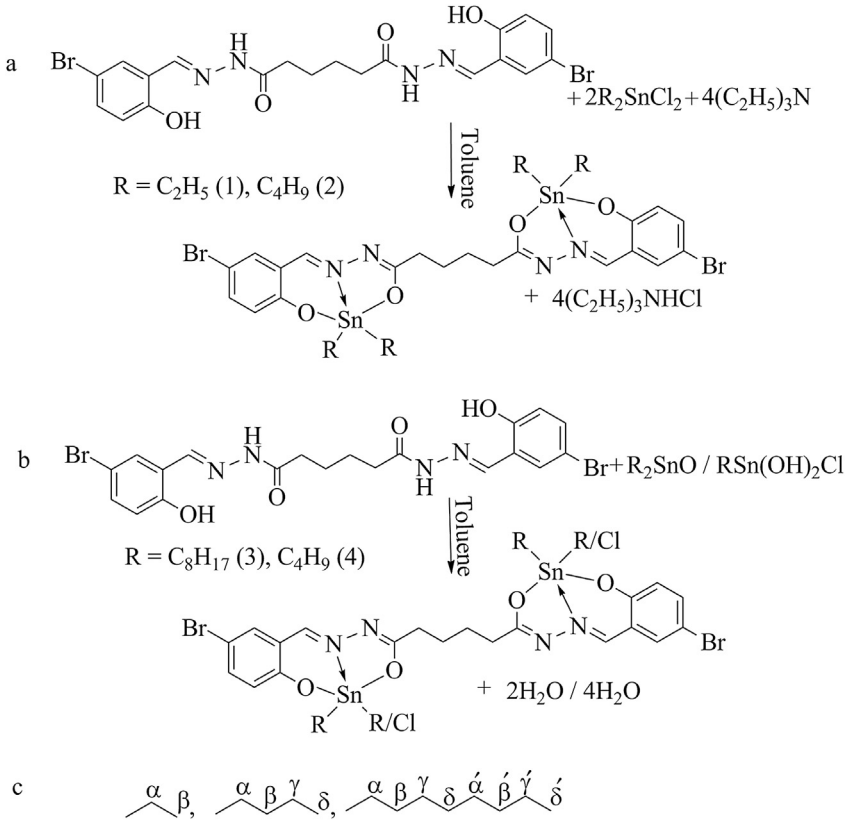
2.2.3. Bis[di-n-butyltin(IV)][$N^{1\prime},N^{6\prime}$-bis(5-bromo-2-oxidobenzylidene) adipodihydrazide] (***2***)

Compound **2** was prepared in the same way as **1**, using following precursors quantities: $N^{1\prime},N^{6\prime}$-bis(5-bromo-2-hydroxy benzylidene)adipodihydrazide 0.81 g (1.5 mmol), dibutyltin(IV) dichloride 0.91 g (3.0 mmol) and triethylamine 0.84 mL (6.0 mmol) were reacted in a 1:2:4 ratio. The solid product was recrystallized from a chloroform n-hexane (4:1) mixture.

Yield 78%. mp 99–101 °C. Anal. Calc. for $C_{36}H_{54}Br_2N_4O_4Sn_2$ (M = 1004): C, 43.06; H, 5.42; N, 5.58 Found: C, 43.17; H, 5.20; N, 5.61% EI-MS, m/z (%): $[(C_8H_4BrN_2O_2)_2C_4H_8Sn_2(C_4H_9)_3]^+$ 945(100.0), $[(C_8H_4BrN_2O_2)CNC_4H_8Sn(C_4H_9)_2]^+$ 555(23.5), $[(C_8H_4BrN_2O_2)Sn(C_4H_9)_2]^+$ 473(3.1), $[(C_8H_4BrN_2O_2)Sn(C_4H_9)]^+$ 416(6.1), $[(C_8H_4BrN_2O_2)Sn]^+$ 281(8.0), $[(C_4H_9)_2Sn]^+$ 234(4.3), $[C_4H_9Sn]^+$ 177(18.4), $[Sn]^+$ 120(7.0), $[C_6H_5]^+$ 77(3.4), $[C_4H_9]^+$ 57(74.5) IR (cm^{-1}): 1609 ν(C=N), 1078 ν(N–N), 590 ν(Sn–O), 453 ν(Sn–N), ^1H NMR (ppm): 8.48 (s, 2H, CH=N, $^3J(^{119}Sn-^1H)$ = 41 Hz), 2.35 (bs, 4H, $2CH_2$), 1.72 (bs, 4H, $2CH_2$), 6. 65 (d, 2H, Ar–H, $^3J_{H-H}$ = 9.0), 7.35 (dd, 2H, Ar–H, $^3J_{H-H}$ = 9.0), 7.20 (s, 2H, Ar–H), 1.57–1.67 (m, 8H, H_α–SnBu), 1.44–1.49 (m, 8H, H_β–SnBu), 1.28–1.40 (m, 8H, H_γ–SnBu), 0.88 (t, 12H, H_δ–SnBu, $^3J_{H-H}$ = 7.2) ^{13}C NMR (ppm): 159.2 (CH=N), 176.3 (NCO), 34.2, 25.8 ($-CH_2CH_2$), 165.8, 137.4, 135.3, 123.6, 118.0, 107.6 (Ar–C), 22.1 (C_α–SnBu, $^1J[^{119/117}Sn-^{13}C]$ = 599, 574 Hz), 26.8 (C_β–SnBu, $^2J[^{119/117}Sn-^{13}C]$ = 34 Hz), 26.4 (C_γ–SnBu, $^3J[^{119/117}Sn-^{13}C]$ = 86 Hz), 13.4 (C_δ–SnBu), ^{119}Sn NMR: δ (ppm) = −190.3.



Scheme 1. Synthesis of $N^{1\prime},N^{6\prime}$-bis(5-bromo-2-hydroxybenzylidene)adipodihydrazide (H_4L).



Scheme 2. Synthesis of bis[diorganotin(IV)] and bis[butylchlorotin(IV)] derivatives (a, b). Numbering scheme of alkyl groups bonded to tin atom in bis[dialkyltin(IV)] derivatives of H_4L (c).

2.2.4. Bis[di-n-octyltin(IV)][$N^{1\prime}$,$N^{6\prime}$-bis(5-bromo-2-oxidobenzylidene)adipodihydrazide](**3**)

Compound **3** was prepared by refluxing $N^{1\prime}$,$N^{6\prime}$-bis(5-bromo-2-hydroxybenzylidene)adipodihydrazide 0.81 g (1.5 mmol) and dioctyltin(IV) oxide 1.09 g (3.0 mmol) in 100 mL dry toluene in 1:2 ratio. The water formed during the reaction was removed by Dean-Stark apparatus. The yellow solution obtained was rotary evaporated under reduced pressure. A viscous liquid product was obtained (Scheme 2b).

Yield 76%. mp viscous liquid. Anal. Calc. for $C_{52}H_{84}Br_2N_4O_4Sn_2$ (M = 1226): C, 50.92; H, 6.90; N, 4.57 Found: C, 50.89; H, 6.87; N, 4.55% EI-MS, m/z (%): $[(C_8H_4BrN_2O_2)CNC_4H_8Sn(C_8H_{17})_2]^+$ 667(4.8), $[(C_8H_4BrN_2O_2)Sn(C_8H_{17})]^+$ 472 (4.5), $[(C_8H_4BrN_2O_2)Sn]^+$ 359(3.9), $[C_7H_4NOSn]^+$ 238(29.8), $[Sn]^+$ 120(6.5), $[C_4H_9]^+$ 57(100.0) IR (cm^{-1}): 1621 ν(C=N), 1082 ν(N–N), 578 ν(Sn–O), 466 ν(Sn–N) ^{1}H NMR (ppm): 8.46 (s, 2H, CH=N, $^3J(^{119}Sn-^1H)$ = 41 Hz), 2.32 (bs, 4H, $2CH_2$), 1.71 (bs, 4H, $2CH_2$), 6. 62 (d, 2H, Ar–H, $^3J_{H-H}$ = 8.7), 7.30 (dd, 2H, Ar–H, $^3J_{H-H}$ = 9.0), 7.17 (s, 2H, Ar–H), 1.57–1.64 (m, 8H, H_α–SnOct), 1.42–1.47 (m, 8H, H_β–SnOct), 1.20–1.29 (bs, 40H, $H_{\gamma-\gamma'}$–SnOct), 0.85 (t, 12H, $H_{\delta'}$–SnOct, $^3J_{H-H}$ = 7.2) ^{13}C NMR (ppm): 159.2 (CH=N), 176.3 (NCO), 34.2, 26.1 ($-CH_2CH_2$), 165.7, 137.4, 135.3, 123.5, 118.0, 107.7 (Ar–C), 22.7 (C_α–SnOct, $^1J[^{119/117}Sn-^{13}C]$ = 627, 599 Hz), 24.7 (C_β–SnOct, $^2J[^{119/117}Sn-^{13}C]$ = 36 Hz), 33.4 (C_γ–SnOct, $^3J[^{119/117}Sn-^{13}C]$ = 78 Hz), 29.2, 29.0, 31.8, 22.5 ($C_{\delta-\gamma'}$–SnOct), 14.1 (C_δ–SnOct), ^{119}Sn NMR: δ (ppm) = −198.

2.2.5. Bis[n-butylchlorotin(IV)][$N^{1\prime}$,$N^{6\prime}$-bis(5-bromo-2-oxidobenzylidene)adipodihydrazide] (**4**)

Compound **4** was prepared in the same way as **3**, using following precursors quantities: $N^{1\prime}$,$N^{6\prime}$-bis(5-bromo-2-hydroxybenzylidene) adipodihydrazide 0.81 g (1.5 mmol) and butyldihydroxidetin(IV) chloride 0.73 g (3.0 mmol) were reacted in a 1:2 ratio. The solid product was recrystallized from a chloroform and n-hexane (4:1) mixture.

Yield 70%. mp 140–143 °C. Anal. Calc. for $C_{28}H_{34}Br_2Cl_2N_4O_4Sn_2$ (M = 958): C, 35.08; H, 3.57; N, 5.84 Found: C, 35.05; H, 3.60; N, 5.80% EI-MS, m/z (%): $[(C_8H_4BrN_2O_2)_2C_4H_8Sn_2(C_4H_9)_2Cl]^+$ 923(73.8), $[(C_8H_4BrN_2O_2)_2C_4H_8Sn_2(C_4H_9)Cl_2]^+$ 901 (32.2), $[(C_8H_4BrN_2O_2)_2C_4H_8Sn_2(C_4H_9)Cl]^+$ 866(9.1), $[(C_8H_4BrN_2O_2)CNC_4H_8Sn(C_4H_9)Cl]^+$ 533(5.6), $[(C_8H_4BrN_2O_2)Sn(C_4H_9)Cl]^+$ 451(7.0), $[(C_8H_4BrN_2O_2)Sn(C_4H_9)]^+$ 416(5.2), $[(C_8H_4BrN_2O_2)SnCl]^+$ 394(3.9), $[(C_8H_4BrN_2O_2)Sn]^+$ 359(4.6), $[(C_4H_9)ClSn]^+$ 212(8.5), $[ClSn]^+$ 155(23.4), $[Sn]^+$ 120(6.7), $[C_4H_9]^+$ 57(100.0) IR (cm^{-1}): 1609 ν(C=N), 1072 ν(N–N), 560 ν(Sn–O), 451 ν(Sn–N) ^{1}H NMR (ppm): 8.51 (s, 2H, CH=N), 2.37 (bs, 4H, $2CH_2$), 1.72 (bs, 4H, $2CH_2$), 6. 81 (d, 2H, Ar–H, $^3J_{H-H}$ = 9.0), 7.41 (bs, 2H, Ar–H), 7.21 (s, 2H, Ar–H), 1.68–1.72 (m, 4H, H_α–SnBu), 1.43–1.50 (m, 4H, H_β–SnBu), 1.34–1.41 (m, 4H, H_γ–SnBu), 0.94 (t, 6H, H_δ–SnBu, $^3J_{H-H}$ = 7.5) ^{13}C NMR (ppm): 159.7 (CH=N), 175.1 (NCO), 34.2, 25.6 ($-CH_2CH_2$), 64.7, 135.3, 132.4, 124.4, 118.2, 107.5 (Ar–C), 23.7 (C_α–SnBu), 27.2 (C_β–SnBu), 26.3 (C_γ–SnBu), 13.7 (C_δ–SnBu), ^{119}Sn NMR: δ (ppm) = −200.

2.3. Antibacterial activity

The synthesized compounds were tested for antibacterial activity against *Escherichia coli* ATCC 11229, *Bacillus subtilis* ATCC 11774, *Shigella flexneri* ATCC 10782, *Staphylococcus aureus* ATCC 25923, *Pseudomonas aeruginosa* ATCC 10245 and *Salmonella typhi* ATCC 10749 using the agar well diffusion method [30]. Imipenum was used as standard drug and 6 mm diameter wells were dug in the media with the help of a sterile metallic borer. Eight hours old bacterial inoculums containing approximately 10^4–10^6 colony forming units (CFU)/mL were spread on the surface of nutrient agar with the help of a sterile cotton swab. The recommended

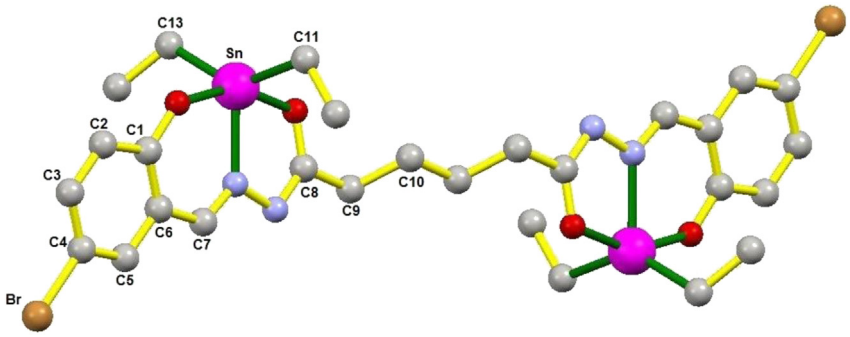


Fig. 1. Molecular structure of compound **1**, hydrogen atoms are omitted for clarity.

concentration of the test sample (2 mg/mL in DMSO) was introduced into the respective wells. Other wells supplemented with DMSO and reference antibacterial drug served as negative and positive controls, respectively. The plates were incubated immediately at 37 °C for 20 h. The activity was determined by measuring the diameter of the inhibition zone (in mm), showing complete inhibition. Growth inhibition was calculated with reference to the positive control.

2.4. Antifungal activity

The *in vitro* antifungal activity of synthesized compounds was also investigated against six fungal strains [*Trichophyton longifusus* ATCC 22397, *Candida albicans* ATCC 2192, *Aspergillus flavus* ATCC 1030, *Microsporum canis* ATCC 9865, *Fusarium solani* ATCC 11712, *Candida glabrata* ATCC 90030] using the agar tube dilution test [31]. Miconazole and Amphotericin B were used as standard drugs for comparison.

Stock solutions of pure compounds (200 μg/mL) were prepared in sterilized DMSO. Sabouraud dextrose agar was prepared by mixing Sabouraud (32.5 g), glucose agar (4%) and agar–agar (20 g) in 500 mL of distilled water followed by dissolution at 90–95 °C on a water bath. The media (4 mL) was dispensed into screw-capped tubes and autoclaved at 121 °C for 15 min. Known amounts of test compounds were added from the stock solution to non-solidified Sabouraud agar media (50 °C). The contents of the tubes were then solidified at room temperature and inoculated with 4 mm diameter portion of inoculums derived from a 7 days old respective fungal culture. For non-mycelial growth, an agar surface streak was employed. The tubes were incubated at 27–29 °C for 7–10 days and growth in the compound containing media was determined by measuring the linear growth (in mm) and growth inhibition with reference to the respective control.

2.5. Cytotoxicity

The cytotoxicity of the compounds was studied by the Brine shrimp lethality bioassay [31]. Brine shrimps (*Artemia salina*) were hatched using brine shrimp eggs in a vessel, filled with sterile simulated seawater (prepared using sea salt 38 g $L^{-1}$and adjusted to pH 8.5 using 1 M NaOH) at room temperature 22–29 °C under constant aeration for two days. After hatching, thirty active nauplii were drawn through a glass capillary and placed in a vial containing 4.5 mL of brine solution and a drop of yeast suspension. In each experiment, 0.5 mL of the test solution was added to the vial and maintained at ambient temperature for 24 h, the surviving larvae were counted. All the experiments with different concentrations (1, 10, 100 μg/mL) of the test substances were conducted in triplicate and compared with the control. Data were analyzed with Finney's probit analysis to determine the LD_{50} [32]. Etoposide was used as the standard drug.

3. Results and discussion

3.1. Spectroscopic studies

The absorption bands observed due to the stretching vibrations of –OH, –NH and C=O groups in the IR spectrum of ligand

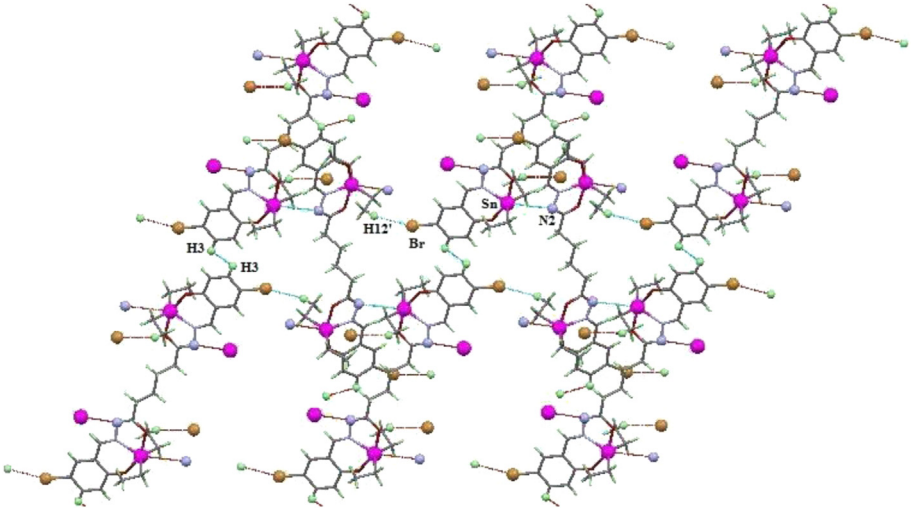


Fig. 2. Supramolecular layer of compound **1** mediated by Sn···N2(3.573 Å), Br···H12′(2.900 Å) and H3···H3(2.384 Å) intermolecular non-covalent interactions.

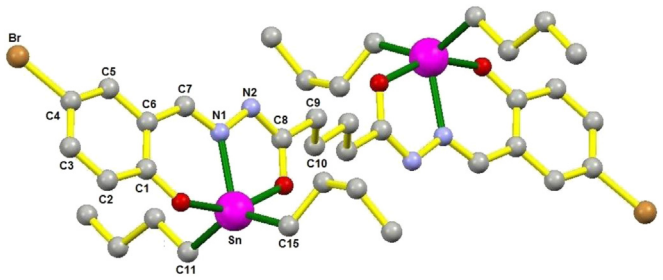


Fig. 3. Molecular structure of compound **2**, hydrogen atoms are omitted for clarity.

disappear in all the complexes. This suggests coordination of phenolic and enolic oxygens to the diorganotin(IV) moieties after enolization and subsequent deprotonation processes. The υ(C=N) band is shifted to lower frequency indicating the coordination of azomethine nitrogen to tin center [33]. The band due to υ(N–N) is shifted to higher frequencies at 1072–1082 cm^{-1} in the spectra of organotin(IV) complexes (1–4). An increase in the frequency of this band is attributed to an increase in bond length and decrease in repulsion of the lone pairs of electrons on the nitrogen atoms [19,34]. The presence of IR bands in the regions of 560–590 cm^{-1} and 451–466 cm^{-1} indicate the formation of Sn–O and Sn–N bonds, respectively [35].

The ^{1}H NMR signals in the ligand due to –OH, CHO and –NHN = protons disappeared in the diorganotin(IV) complexes (**1**–**4**), due to the conversion of amido form of the ligand to iminol form (Scheme 1a) and subsequent deprotonation. The downfield shift in the –CH=N proton resonance to 8.46–8.51 ppm with ^{3}J (^{119}Sn, ^{1}H) coupling constant of 41 Hz confirmed the shift of electron density from azomethine nitrogen to Sn atom. This coordination was further confirmed by the single crystal X-ray structures of compounds **1** and **2**. All the other protons of the ligand and the Sn bonded R groups have also been assigned, which are in good agreement with reported values [36].

The characteristic resonance peaks in ^{13}C NMR spectra of the complexes were recorded in $CDCl_3$. The ^{13}C NMR spectra of the complexes show a downfield shift of all carbon resonances, compared with that of the ligand. This may be a consequence of an electron density shift from the ligand to the diorganotin(IV) moieties. In organotin(IV) compounds, the ^{1}J [^{119}Sn, ^{13}C] value is an important parameter and is used to establish the coordination around tin in solution. The calculated coupling constants for compounds **1**–**4** were found to be in the range 599–627 Hz, which further support the idea of penta-coordination around the Sn atom in solution for complexes **1**–**4** [37].

The ^{119}Sn NMR spectra of diethyl, di-*n*-butyl, di-*n*-octyl and butylchlorotin(IV) complexes show only one sharp resonance at –192.5, –190.3, –198 and –200 ppm, respectively. The ^{119}Sn chemical shift values are typical of five-coordinated diorganotin(IV) compounds and indicate similar environment around the two tin atoms in each complex [38–41].

Table 1
Crystal data and structure refinement parameters for complexes **1** and **2**.

Complex no.	**1**	**2**
Empirical formula	$(C_{14}H_{18}BrN_2O_2Sn)_2$	$(C_{18}H_{26}BrN_2O_2Sn)_2$
Formula mass	889.84	1002.06
Crystal system	Monoclinic	Orthorhombic
Space group	*C2/c*, 15	*Pbca*
a (Å)	19.115(2)	9.705(17)
b (Å)	10.389(13)	16.165(3)
c (Å)	17.299(2)	24.704(4)
α (°)	90.00	90.00
β (°)	113.35(15)	90.00
γ (°)	90.00	90.00
V (Å^3)	3154.2(6)	3875.4(12)
Z	4	4
Crystal habit	Block	Block
Size (mm)	0.41 × 0.33 × 0.28	0.47 × 0.23 × 0.14
T (K)	100 (1)	100 (1)
ρ (g cm^{-3})	1.874	1.717
μ (Mo $K_α$) (cm^{-1})	41.56	33.93
F(000)	1736	1992
Total reflections	14,013	23,508
Independent reflections	3866	3913
For ($F_o \geq \sigma(F_o)$)	3259	3189
$R(F) = \Sigma(\|\|F_o\| - \|F_c\|\|)/\Sigma\|F_o\|$, for $F_o > \sigma(F_o)$	0.0290	0.0334
$wR(F^2) = [\Sigma[w(F_o^2 - F_c^2)^2]/\Sigma[w(F_o^2)^2]]^{1/2}$	0.0712	0.0827
Goodness-of-fit	1.051	1.091
θ Range (deg)	2.56–29.43	2.58–29.42
Data/restrictions/params	3866/0/183	3913/0/219

Table 2
Selected bond lengths (Å) and bond angles (°) of complex **1**.

Bond lengths			
Sn–O(1)	2.119(2)	Sn–C(13)	2.129(3)
Sn–O(2)	2.159(2)	N(1)–N(2)	1.403(4)
Sn–N(1)	2.194(2)	N(1)–C(7)	1.293(3)
Sn–C(11)	2.127(3)	N(2)–C(8)	1.314(3)
Bond angles			
O(1)–Sn–O(2)	154.91(7)	N(1)–Sn–C(13)	112.86(9)
O(1)–Sn–N(1)	82.55(8)	C(11)–Sn–C(13)	137.73(10)
O(1)–Sn–C(11)	92.07(11)	Sn–O(1)–C(1)	133.15(18)
O(1)–Sn–C(13)	94.14(11)	Sn–O(2)–C(8)	114.83(19)
O(2)–Sn–N(1)	72.43(8)	Sn–N(1)–N(2)	116.43(16)
O(2)–Sn–C(11)	94.53(10)	Sn–N(1)–C(7)	128.7(2)
O(2)–Sn–C(13)	97.11(11)	Sn–C(11)–C(12)	109.7(2)
N(1)–Sn–C(11)	109.40(11)	Sn–C(13)–C(14)	112.29(19)

3.2. X-ray crystal structure of complexes (*1* and *2*)

The asymmetric unit of centrosymmetric binuclear complexes **1** and **2** consists of half of the molecule. The molecular structure and atomic numbering scheme for the two molecules is given in Figs. 1 and 3. The crystallographic data, selected bond lengths and angles of the homobimetallic molecule of complex **1** and **2** are listed in Tables 1–3. The structure of binuclear complexes **1** and **2** consists of a deprotonated ONO tetrabasic hexadentate ligand bonded to two $R_2Sn(IV)$ moieties via two oxygen and a nitrogen atom, forming a O_2NC_2 core around each Sn atom. The Sn–O(1) and Sn–O(2) bond lengths {2.119(2) and 2.159(2) Å for **1** and {2.120(2) and 2.143(2) Å for **2**} are less than the sum of van der Waals radii of Sn and O (3.68 Å). The O(1)–Sn–N(1), O(1)–Sn(1)–O(2) and O(2)–Sn–N(1) angles are 82.55(8)°, 154.91(7)° and 72.43(8)° for **1** and 81.92(9)°, 154.53(8)° and 72.91(9)° for **2**, respectively. The Sn–N(1) bond distance is 2.194(2) and 2.189(2) Å for **1** and **2**, respectively, comparable with the sum of the covalent radii of Sn and N (2.15 Å) and

Table 3
Selected bond lengths (Å) and bond angles (°) of complex **2**.

Bond lengths			
Sn–O(1)	2.120(2)	Sn–C(15)	2.108(3)
Sn–O(2)	2.143(2)	N(1)–N(2)	1.403(4)
Sn–N(1)	2.189(2)	N(1)–C(7)	1.293(4)
Sn–C(11)	2.121(3)	N(2)–C(8)	1.316(4)
Bond angles			
O(1)–Sn–O(2)	154.53(8)	N(1)–Sn–C(15)	113.64(11)
O(1)–Sn–N(1)	81.92(9)	C(11)–Sn–C(15)	137.49(12)
O(1)–Sn–C(11)	95.19(11)	Sn–O(1)–C(1) 1	32.0(2)
O(1)–Sn–C(15)	90.56(11)	Sn–O(2)–C(8)	114.59(19)
O(2)–Sn–N(1)	72.91(9)	Sn–N(1)–N(2)	116.19(18)
O(2)–Sn–C(11)	96.54(11)	Sn–N(1)–C(7)	128.6(2)
O(2)–Sn–C(15)	95.88(11)	Sn–C(11)–C(12)	111.9(2)
N(1)–Sn–C(11)	108.87(11)	Sn–C(15)–C(16)	112.2(2)

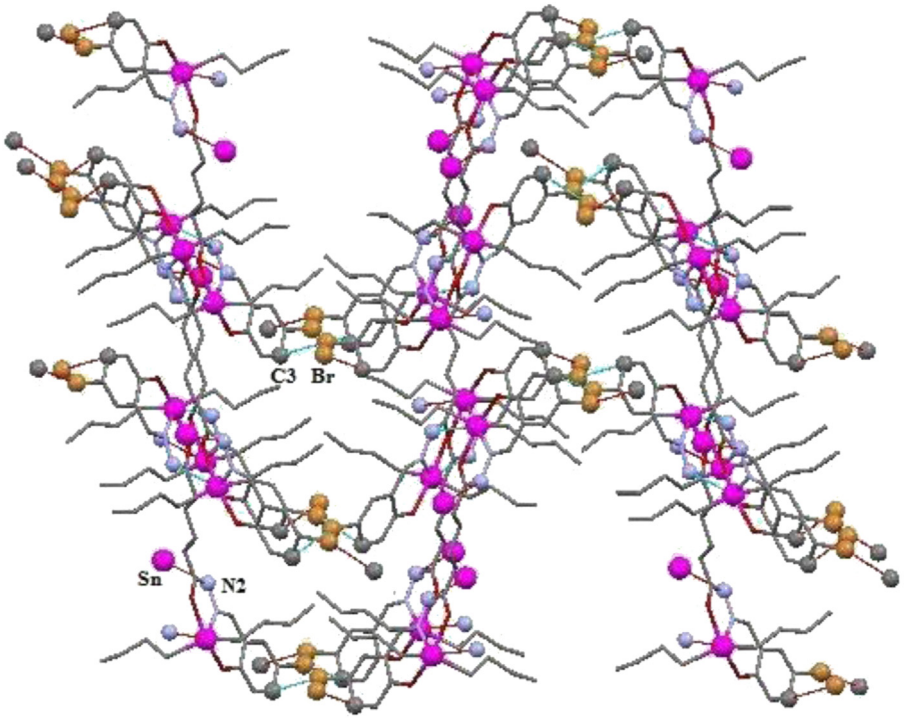


Fig. 4. Supramolecular wavy layers of compound **2** mediated by Sn···N2(3.632 Å) and Br···π(3.539 Å) intermolecular interactions.

less than the sum of the van der Waals radii (3.75 Å) confirming a strong tin–nitrogen bond. The Sn atom and the O(1), C(1), C(6), C(7), N(1) atoms form a six membered ring, while the Sn atom and O(2), C(8), N(2) and N(1) atoms form a five membered ring. The flexibility present in the butylene linker allows the complexes to adopt different orientations when relating the two diorganotin(IV) moieties. The extended structures of **1** and **2** reveal that the butylene chains of these structures adopt an antiperiplanar or zigzag conformation [42]. The $R_2Sn(IV)$ groups are disposed at trans conformation in the crystalline structure due to packing effects and it can be supposed that in solution there is a fast dynamic equilibrium between the different possible conformations [43].

The τ value is an important parameter to decide the geometry of five-coordinated metal and can be calculated by using equation $\tau = (\beta - \alpha)/60$ [39], where β and α are the consecutive largest of the basal angles around the Sn atom. For five-coordinated Sn with perfect trigonal-bipyramidal geometry τ value is one whereas a value of zero corresponds to a perfect square-pyramidal structure. The τ value 0.5 for a molecule indicates a geometry midway between trigonal bipyramidal and square-pyramidal. The calculated τ values 0.29 and 0.28 (**1** and **2**) indicates a highly distorted square pyramidal arrangement around each tin atom.

Packing diagram offers a supramolecular structure to compound (**1**) mediated by Sn···N2 (3.573 Å), Br···H12′(2.900 Å) and H3···H3(2.384 Å) intermolecular non-covalent interactions (Fig. 2). Similarly complex (**2**) also exhibit a supramolecular wavy layer structure mediated by Sn···N2(3.632 Å) and Br···π(3.539 Å) intermolecular interactions (Fig. 4).

4. Biological activities

4.1. Antibacterial activity

The need for more potent and specific antimicrobial agents continues to grow, since the pathogenic microbes develop resistance against such compounds due to gene mutation. Thus, the synthesized bis[diorganotin(IV)] complexes (**1**–**4**) were screened for their antibacterial activity against 2 g positive (*B. subtilis*, *S. aureus*) and 4 g negative bacteria (*E. coli*, *S. flexenari*, *P. aeruginosa* and *S. typhi*). The bacterial activity of ligand is reported in a previous study [29]. The results of present investigation are presented in Fig. 5. The bis[diorganotin(IV)] complexes (**1**–**4**) exhibited elevated inhibitory activity against gram positive bacteria as their polyglycane outer layer is loosely packed to facilitate deep penetration of the complex inside the cell to interact with the cytoplasmic membrane. On the other hand, a Gram-negative bacterial cell with a bilayer phospholipid structure protects the inner cytoplasmic membrane to a greater degree against the inhibitory action of the organotin(IV) complex. However, none of the synthesized complex is more active than the reference drug. Bis[dibutyltin(IV)] complex (**2**) was found to be the most potent bactericide and showed the highest antibacterial activity against *B. subtilis*, *S. aureus* and *S. typhi*. Bis[chlorodibutyltin(IV)] complex (**4**) exhibited mild toxicity to all bacterial strains. *S. typhi* was resistant against all compounds except bis[dibutyltin(IV)] complex (**2**). Survey of literature shows that other organotin(IV) resistant bacteria have also been isolated and characterized. However, details of bacterial

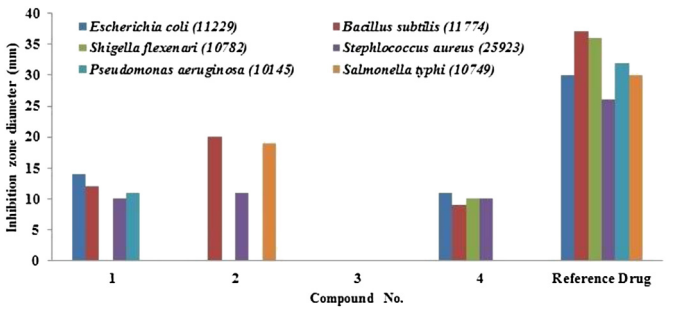


Fig. 5. Antibacterial activity of H_4L and its organotin(IV) derivatives against various bacteria.

resistance mechanisms are still poorly understood [44,45]. Bis [dioctyltin(IV)] complex (**3**) showed insignificant antibacterial activity against all tested bacteria.

The bacterial growth inhibition may be due to bactericide effects or bacteriostatic effects of compounds. The inhibitory action of organotin(IV) derivatives can be understood by considering chelation theory and is believed to be due to their ability to inhibit cellular respiration and ATP synthesis. The parent ligand on chelation reduces the polarity of the central tin atom primarily because of the partial sharing of its positive charge with the donor groups and possible π-electron delocalization within the whole chelate ring. The lipophilic nature of the central Sn atom increases, which favors the permeation of the complexes through the lipid layer of the cell membrane. The alkyl groups bonded to the tin atom also play a significant role in the diffusion of metal complex through the bacterial cell wall [46,47].

4.2. Antifungal activity

The *in vitro* antifungal activities of ligand H_4L and bis[diorganotin(IV)] complexes (**1**–**4**) were evaluated against six human pathogenic fungal strains including yeasts (*C. albicans* ATCC 2192, *C. glabrata* ATCC 90030), dermatophytes (*M. canis* ATCC 9865, *T. longifusus* ATCC 22397), opportunistic molds (*A. flavus* ATCC 1030 and *F. solani* ATCC 11712) using the agar tube dilution Test. Amphotericin-B and Miconazole were used as standard drug. The results are depicted in Fig. 6. The ligand was found active only against *A. flavus*. All the complexes were active against *F. solani* and the highest antifungal activity was shown by bis[dibutyltin(IV)] complex (**2**). However, all the compounds have lower activity than the standard drug. The bis[diorganotin(IV)] complexes (**1**,**3**,**4**) showed 20–30% inhibition against *A. flavus*. *T. longifusus*, *C. albicans*, and *M. canis*. The complete mechanism of antifungal activity is not fully understood, however, the activity of ligand and complexes can be rationalized in terms of hydrogen bond formation between the azomethinic nitrogen of the synthesized compound and some bioreceptors in the cells of microorganisms causing disruption in the movement of ribosome along with RNA consequently the synthesis of protein and DNA in the cell nucleus is blocked [48,49].

4.3. Cytotoxicity

Organotin(IV) complexes exert their toxic effects on cells by preventing the mitochondrial oxidative phosphorylation, inducing DNA damage, apoptosis or necrosis. The *in vivo* lethality to brine shrimp nauplii was used to assess the cytotoxicity of synthesized

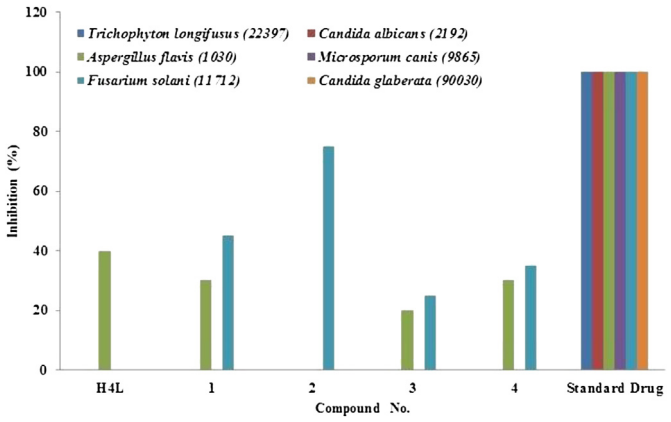


Fig. 6. Antifungal activity of H_4L and its organotin(IV) derivatives against various bacteria.

Table 4
Brine Shrimp (*Artemia salina*) lethality bioassay of $N^{1\prime},N^{6\prime}$-bis(5-bromo-2-hydroxybenzylidene)adipodihydrazide and its bis[diorganotin(IV)] complexes.

Sample code	H_4L	1	2	3	4
LD_{50} (μg/mL)	–	–	24.65	–	–

Standard drug etoposide, LD50 7.46 μg/mL.

compounds. The results are presented in Table 4. The toxicity of the organotin(IV) compounds vary significantly according to their substitution and within the same substituent series depends on the lipophilic character of alkyl group [50]. Compound (**2**) show highest toxicity with LD_{50} 24.65 μg/mL.

5. Conclusions

Four new homobimetallic diorganotin(IV) derivatives compounds of $N^{1\prime},N^{6\prime}$-bis(5-bromo-2-hydroxybenzylidene)adipodihydrazide have been synthesized and characterized by FT-IR, NMR, mass spectroscopy and elemental analysis. The single crystal analysis of the bis[diethyl] (**2**) and bis[dibutyltin(IV)] (**3**) derivatives showed homobimetallic nature of these compounds in which each Sn atom is in distorted square pyramidal geometry. The tendency towards the said geometry may be due to intermolecular Sn···N interaction. Moreover, Sn···N and Br···π interactions were found to assemble molecules to form fancy supramolecular architecture in both compounds. These compounds were found active against studied bacteria, and fungi. The highest cytotoxicity was noted for complex **2** (LD_{50} 24.65 μg/mL).

Acknowledgments

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Appendix A. Supplementary material

CCDC 962695 for $(Et_2Sn)_2L$ (**1**) and 962694 for $(Bu_2Sn)_2L$ (**2**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

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