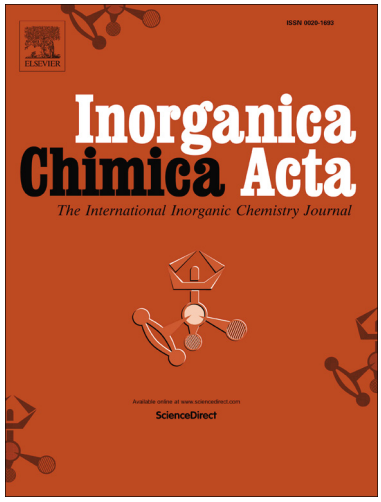

Research paper

Synthesis, spectroscopic characterization, X-ray diffraction studies and *in-vitro* antibacterial activities of diorganotin(IV) derivatives with *N*-methyl-4-bromobenzohydroxamic acid

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Synthesis, spectroscopic characterization, X-ray diffraction studies and *in-vitro* antibacterial activities of diorganotin(IV) derivatives with *N*-methyl-4-bromobenzohydroxamic acid

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Abstract

Three new diorganotin(IV) complexes $(CH_3)_2Sn(mbbha)_2$ (**2**), $(C_4H_9)_2Sn(mbbha)_2$ (**3**), $(C_6H_5)_2Sn(mbbha)_2$ (**4**), of *N*-methyl-4-bromobenzohydroxamic acid (Hmbbha) (**1**) have been synthesized by 2:1 condensation ratio of the parent hydroxamic acid with $(CH_3)_2SnO$, $(C_4H_9)_2SnO$ and $(C_6H_5)_2SnO$ in toluene. Ligand has been synthesized by the reaction of 4-bromobenzoyl chloride and *N*-methylhydroxylamine hydrochloride. Elemental analysis, IR, multinuclear ^{1}H, ^{13}C, ^{119}Sn NMR spectroscopic techniques have been utilized to investigate the bonding and coordination modes of the ligand and its derivatives. It is found on the basis of spectroscopic and structural investigations that hydroxamate ligand acts as a bidentate chelator and coordinated to tin via carbonyl oxygen and deprotonated hydroxy group. The structures of complexes (**3**) and (**4**) have been deduced by X-ray crystallography which reveals octahedral geometry around tin in $(C_4H_9)_2Sn(mbbha)_2$ (**3**) and $(C_6H_5)_2Sn(mbbha)_2$ (**4**) derivatives. The *in-vitro* antibacterial activities of ligand and its derivatives have been evaluated against one Gram positive and three Gram negative bacterial strains. The derivative (**2**) has displayed remarkable potency against both Gram positive and Gram negative strains. Anti-pathogenic results have been verified statistically.

Keywords: Diorganotin(IV) hydroxamate; NMR; X-ray diffraction; antibacterial activity.

1. Introduction

Hydroxamic acids (R-CO-NH-OH) have received explosion of interest owing to their potent biological activities. Hydroxamic acids usually act as mineral collectors, antibacterial agents, growth factors, enzyme inhibitors, antimalarial drugs and fungicide agents due to their low toxicity and high bioactivity [1-3]. Many of the chemotherapeutic entities such as histone deacetylase (HDAC), matrix metalloproteinase (MMP) inhibitors and iron-based antibiotics contain hydroxamic acids as a significant component [4-7]. The chelating ability of these ligands with metal ions, particularly with transition metals enhances their bioactivities [8-9]. These ligands frequently use the *O, O* donor sites to give bidentate chelates. Deportation of these acids imparts two anionic forms; mono-deprotonated (hydroxamato) and di-deprotonated (hydroximato). Hydroxamic acids are synthesized by a number of synthetic ways, which are well depicted in literature [10], but some of these methods have been found pain staking, time consuming and much costly. Hydroxmic acids are usually synthesized by the reaction of hydroxylamines with esters or carboxylic acid salts [11]. The metal-organic framework has gained considerable attraction owing to essential industrial, environmental and biological applications [12-13]. In the area of organometallic chemistry, the organotin compounds have gained extensive interest in industrial and basic research over the recent years. There is a dramatic increase in the industrial utilization of organotin compounds due to their biocidal and industrial applications [14-15]. Dioganotin(IV) complexes have displayed moderate antitumour activity against human cell lines [16]. Tin exhibits a variety of coordination numbers and geometries for both organometallic and inorganic complexes because of its rich coordination chemistry [17-18]. The sulphur, nitrogen and oxygen donor ligands augment the bioactivity of organotin moiety [19-20]. In view of the biological and structural diversity of organotin oxygen donor ligands (hydroxamates), herein we are interested to report the synthesis, structural analyses and antimicrobial activities of a new ligand *N*- methyl–4-bromobenzo-hydroxamic acid (Hmbbha) and its three diorganotin(IV) complexes; $Ph_2Sn(mbbha)_2$, $Bu_2Sn(mbbha)_2$ and $Me_2Sn(mbbha)_2$.

2. Experimental

2.1 *Materials and methods*

All materials were purchased from Sigma Aldrich and used without further purification. All the chemicals were of analytical grade. TLC technique was used to assure the purity of the

ligand and its complexes. Uncorrected melting points were noted by open capillary method using an electro-thermal 9300 digital melting point apparatus. Elemental analysis of C, H and N were determined using Elemental Fison EA 1108 CHNS-O Analyzer. Estimation of tin was carried out gravimetrically. Vibrational spectra of the compounds were obtained on KBr disc by pressed pellet technique using Perkin-Elmer Spectrophotometer, in the range 4000-400 cm^{-1}. ^{1}H, ^{13}C and ^{119}Sn NMR spectra were recorded with a BRUKER FT-NMR 600 MHz Cryo-Prob spectrophotometer. DMSO-d_6 was used as a solvent, while TMS as an internal reference.

2.2 *Synthesis of ligand*

The preparation of ligand was carried out by adding *N*-methylhydroxylamine hydrochloride (10 mmol) to a well stirred solution of sodium hydrogen carbonate (20 mmol) and 4-bromobenzoyl chloride (10 mmol). Sodium hydrogen carbonate was added as a catalyst. Stirring was further continued for about 25 min below 4ºC. The solution was evaporated under reduced pressure after filtration. Solid residue was purified by dissolving in a suitable solvent and placed in a refrigerator to afford suitable crystals [21]. The synthesis of ligand is shown in scheme 1.

2.3 *Synthesis of complexes*

Diorganotin (IV) complexes of ligand were obtained by refluxing 2:1 molar ratio of ligand (2 mmol) and diorganotin (IV) oxide (1 mmol) in toluene, respectively. Refluxing was continued for approximately 5-6 hours and the water formed during reaction was eliminated using a Dean *Stark Trap* to drive the reaction in forward direction. After cooling and filtration, the mother liquour was evaporated under reduced pressure. The solid residue was purified and recrystallized in ethanol [22].Synthesis of complexes is shown in scheme 2.

2.4. *X-ray crystallography*

Suitable single crystals of dibutyltin(IV) *N*-methyl-4-bromobenzohydroxamate and diphenyltin(IV) *N*-methyl-4-bromobenzohydroxamate were each fixed and placed on BRUKER SMART 1000 CCD diffractometer, furnished with the radiation source (λ = 0.71073 Å). SMART software was used to collect data and interpretation was made on SAINT. Empirical absorption correction was performed by means of SADABS. Direct method was used to solve the structure and F^2 based full matrix least square procedure was used to refine, using

SHELXTL, based on SHELX 97. The particulars of structure solution, data collection and crystallographic information are summarized in Table 5.

2.5. *Antibacterial activity*

Agar well method were used for the determination of antibacterial effects of the synthesized compounds against different pathogenic bacterial strains including *Salmonella typhi, Staphylococcus aureus, Klebsiella pneumoniae and Escherichia coli.* Moller Hinton Agar were prepared following the manufacturer's instructions and sterilized at 15 lbs. (121°C) pressure for 15 minutes. After sterilization, the molten medium was spreaded on 100 mm (millimeter) petri plates. Petri plates containing 25 mL of medium were seeded with fresh (24 hours) culture of bacterial strains. Wells (6mm) were made in the medium with sterilized borers and 100 µL of stock solutions (4mg/mL in DMSO) of compounds were poured in each well. Pure DMSO and antimicrobial drug Doxycycline (DO 30µg) were employed as negative and positive controls, respectively. The petri plates were then incubated for 24 hours at 37 ^{0}C. Antibacterial activities of the compounds were assayed by measuring the inhibition zone diameter in mm around each well [23-24].

3. Results and Discussion

3.1. *Synthesis of ligand*

The preparation of *N*-methyl-4-bromobenzohydroxamic acid was carried out by reacting *N*-methylhydroxylamine hydrochloride with 4-bromobenzoyl chloride. Sodium hydrogen carbonate was used as catalyst. Purity of the synthesized ligand and its organotin complexes was assured by TLC, and silica gel-G was used as a stationary phase. The physical properties and analytical data of ligand and its complexes are given in Table 1. The calculated values are found close to the experimental ones.

3.2 Infra-Red Spectroscopy

Vibrational spectra of ligand *N*-methyl-4-bromobenzohydroxamic acid and its diorganotin(IV) complexes have been recorded in solid state in the range 4000-370 cm^{1-}. The key stretching absorptions are given in Table 2. In free hydroxamic acid, the main stretching vibrations are ν(O-H), ν(C=O), ν(N-C) and ν(N-O). The ν(C=O) absorption is observed at 1600 cm^{-1}, lower than the simple carbonyl group ν(C=O) positioned at 1700 cm^{-1}. The location of ν(O-H) stretching frequency at 3123 cm^{-1} as a broad peak indicates the presence of

intramolecular hydrogen bonding between the proton of hydroxy group and lone pair of carbonyl oxygen. The presence of carbonyl peak at lower value along with the broad ν(O-H) peak is a strong evidence of formation of hydroxamic acid. The sharp spectral bands at 1398 and 915 cm^{-1} indicate the presence of ν(N-C) and ν(N-O) bonds, respectively [25]. In IR spectra of hydroxamate complexes, the absence of the hydroxyl ν(O-H) frequency and shifting of carbonyl group absorption to lower frequencies are main characteristic peaks. The absence of ν(O-H) peak in the spectra of complexes implies the replacement of (OH) proton by tin and existence of ligand in deprotonated form in complexes [26]. The carbonyl group absorptions shift to the lower value range (1600-1584 cm^{-1}) in spectra of organotin derivatives, which confirm the formation of complexes. This shifting of stretching frequency of carbonyl group to lower value range and the absence of ν(O-H) vibrational frequency indicates the existence of hydroxamic acid as a bidentate chelating ligand in complexes. Furthermore, the shifting of ν(N-O) stretching frequencies to higher values in spectra of complexes, excludes the ligation of hydroxamic acid through nitrogen atom. The frequencies of ν(Sn-C) and ν(Sn-O) are observed in the range (573-521 cm^{-1}) and (458-443 cm^{-1}), respectively [27].

3.3. *NMR Spectroscopy*

The ligand and its organotin complexes are dissolved in DMSO at room temperature to record their ^{1}H NMR spectra. ^{1}H NMR spectral values of ligand and its complexes are documented in Table 3. The low field absorption of OH proton at 10.34 ppm in ^{1}H-NMR spectrum of free ligand supports the presence of intramolecular hydrogen bonding between the hydroxy proton and oxygen of carbonyl group. The complete disappearance of OH absorption in the spectra of complexes implies occurrence of ligand in deprotonated form in organotin(IV) derivatives. The protons of methyl group attached to nitrogen atom in the ligand appear in the region 3.22 ppm in spectra of complexes and their unaffected position strongly indicates the non-involvement of nitrogen atom in complex formation. The resonance frequency of methyl protons bonded with tin atom in dimethyltin(IV) complex is observed as a singlet in the range 0.32 ppm accompanied with tin satellites. The value of two bond heteronuclear coupling constant $^{2}J(^{119}Sn-^{1}H)$ = 85.2 Hz has been calculated from tin satellites present in the ^{1}H NMR spectrum of dimethyltin(IV) complex which lies in the range of hexa-coordinated complexes [28]. Methyl and methylene protons of dibutyl group occur as a triplet and multiplet in the regions 0.82 ppm and 1.24-1.30 ppm, respectively [29]. Aromatic protons of the free ligand appear as a multiplet

in the range 7.51-7.61 ppm. However, arromatic protons of ligand and diphenyltin(IV) moiety occur as a complex multiplet in the region 7.31-7.69 ppm.

^{13}C NMR studies have been carried out in DMSO-d_6. The carbonyl C=O absorption is the main characteristic peak in ^{13}C NMR spectra of ligand and its complexes. In ligand spectrum, carbonyl group resonates at 168.3 ppm. In spectra of complexes, carbonyl signal exists in the range 161.1-161.7 ppm. This upfield shift of the carbonyl resonance frequency in diorganotin(IV) complexes is due to increase in shielding at carbon and substantially indicates the coordination of carbonyl group with tin via oxygen atom of carbonyl group [30]. The singlet of methyl carbon attached to nitrogen atom fall in the range 39.08-39.2 ppm and its unaltered position on complexation is in conformity with ^{1}H NMR spectral interpretation. In ^{13}C NMR spectrum of dimethyltin(IV) derivative, the carbons of methyl group attached to tin atom resonate at 6.57 ppm. The chemical shifts of dibutyl carbons bonded to tin atom fall in the range 7.3-28.2 ppm.

^{119}Sn NMR studies have been carried out in DMSO-d_6 at room temperature in decoupling mode. ^{119}Sn NMR is one of the sensitive techniques to determine the coordination geometry around tin [31]. Substituent effects, coordination number around tin, oxidation state of tin and isotope effect mainly influence the chemical shift of ^{119}Sn NMR. ^{119}Sn NMR resonating frequencies of diorganotin(IV) complexes are found in the range -405 to -407 ppm which substantially reflects octahedral geometry around tin in solution for the reported complexes [32]. This larger upfield shift of ^{119}Sn NMR in spectra of complexes as compared to simple analogues; Me_2SnCl_2 (+137 ppm) and Ph_2SnCl_2 (-32 ppm) is due to higher coordination number of tin and increase in shielding at tin centre [33]. ^{13}C and ^{119}Sn NMR data for ligand and diorganotin(IV) complexes are documented in Table 4.

3.4. *X-ray crystallography*

The suitable quality single crystals of complexes (**3**) and (**4**) were each fixed and placed on the BRUKER SMART 1000 CCD diffractometer, furnished with the radiation source (λ = 0.71073 Å). The ranges 2.67-25.50° for (**2**) and 2.78-25.98° for (**3**) were selected for data collection. SHELXTL-97 program system was used to perform the calculations. The refining parameters and data collection are reported in Table 5. The molecular structures of complexes **(3)** and **(4)** are shown in Fig 1 and 3, respectively. Selected bond distances and bond angles of the compounds are recorded in the Tables 6 and 7, respectively. The crystal structures of (**3**) and

(**4**) organotin(IV) complexes exhibit that two *N*-methyl-4-bromobenzohydroxamate ligands are bonded to tin as a chelator through oxygens of carbonyl and deprotonated hydroxy groups. The molecular structures of (**3**) and (**4**) have shown similar crystal characteristics where tin atom is coordinated with two ligands in a complex through two oxygen atoms and two carbon atoms of butyl or phenyl moieties imparting a six-coordinated tin structure. *N*-methyl-4-bromo-benzohydroxamate ligand acts as a bidentate ligand. The selected bond lengths of Sn(1)–O(1), Sn(1)–O(2), Sn(1)–O(3) Sn(1)–O(4) are 2.110(2), 2.193(2)Å, 2.110(2) Å and 2.217(2) Å, for the complex (**3**), Sn1–O1 Sn1–O2 Sn1–O3, Sn1–O4 are 2.105(2)Å, 2.363(2) Å, 2.121(2)Å and 2.398(3) Å, respectively, which are in consistent with the bond distances of identical compounds reported in literature [34]. The shorter bond length of tin and oxygen is measured very close to sum of their covalent radii (2.098(6)Å) [35], while the longer bond length 2.398(3) Å is found much shorter as compared to van der Waals radii (4.00 Å). This is substantial indication of strong bond formation between tin and oxygens of carbonyl and deprotonated hydroxy group of ligand, as speculated by infrared and NMR spectral interpretation. The complex $Bu_2Sn(mbbha)_2$ (**3**) crystalizes as colourless block shaped crystal in triclinic space group P-1, while $Ph_2Sn(mbbha)_2$ (**4**) crystallizes as block shaped crystal in orthorhombic space group.

3.5. *Antibacterial activity*

The *in-vitro* antibacterial activities of ligand (Hmbbha), its complexes; $Me_2Sn(mbbha)_2$, $Bu_2Sn(mbbha)_2$, $Ph_2Sn(mbbha)_2$ and doxycycline (a standard drug) have been assayed by agar-well and disc diffusion methods against four different pathogenic bacterial strains; Gram positive (*Staphylococcus aureus*) and Gram negative (*Escherichia coli, Salmonella typhi, Klebsiella pneumoniae*) [36]. The inhibition zone values for tested agents are recorded in mm and presented in Table 8. Zone inhibitions of diameter less than 10 mm are referred as weak; 10-16 mm are considered moderate and higher than 16 mm are active [37]. Ligand (Hmbbha) exhibits moderate activity against *Salmonella typhi* and significant activity against three other strains. The potent biological effectiveness of hydroxamic acid (ligand) is attributed to the presence of OH and CO groups. Although, hydroxamic acids inhibit the activity of enzymes essential for bacterial growth but probably their antibacterial activity is due to interaction with deoxyribose nucleic acid (DNA) of bacteria. The greater potency of hydroxamic aicds may also be related with their hydrophobicity [38-40].The results of antimicrobial screening of compounds reveal

that $Me_2Sn(mbbha)_2$ has displayed significant effectiveness against both Gram positive and Gram negative tested strains in comparison to ligand and other complexes [41]. This significant activity of $Me_2Sn(mbbha)_2$ is associated with its lower molecular weight than other organotin compounds, because of which it has greater rate of diffusion across the membrane [42- 43]. It may also attribute to the ligand's role, which adds in transportation of organotin moiety to the site of action [44-45]. Fig 3 shows the inhibition zone of $Me_2Sn(mbbha)_2$ complex. $Bu_2Sn(mbbha)_2$ complex possesses strong activity against all the tested pathogens as compared to other compounds except $Me_2Sn(mbbha)_2$. The lower potency of $Bu_2Sn(mbbha)_2$ complex in comparison to $Me_2Sn(mbbha)_2$ may be ascribed to its lower permeability through the bacterial cell membrane owing to its greater molecular weight and increase in carbon chain length [46-47]. $Ph_2Sn(mbbha)_2$ has displayed moderate activity against all the pathogens but found least active as compared to other tested compounds. In general, the bioactivity of organotin(IV) complexes is influenced both by nature and number of organic groups on tin centre and the donor ligand. Furthermore, the permeability of compound through the bacterial cell is essential for the effectiveness of a bactericidal agent. Thus, each factor which adds in passage of the compound through microorganism membrane may increase the activity [48]. The current work is also in consistent with the decreasing order of antibacterial activity of diorganotins; dimethyltin > dibutyltin > diphenyltin as reported earlier [49-50]. As a whole, the dimethyltin(IV) complex has been observed as a promising agent which is strongly active against both Gram positive and Gram negative tested strains as represented in Fig 4. Nevertheless, the lack of data on antimicrobial activity of oranotin(IV) hydroxamtes has prevented us to establish a rational comparison of the similar compounds.

3.6. *Statistical* analysis

The statistical information have been generated by IBM SPSS Statistics 20. Important statistical values including mean, standard deviation and confidence interval with variables are given in the summary Table 9. The results of ANOVA analysis are shown in Table 10. The ANOVA table F (4, 15), 8.349, p=0.005) exhibits that there are statistically significant difference between the activity of assayed compounds which may be argued owing to the various organotin moieties in each compound. The existence of significance value (p=0.005), reasonably below 0.05, confirms the rejection of null hypothesis (H_0). The results of Tukey's multiple studies are given in Table 11. The Tukey post hoc analysis displays that the activity of $Me_2Sn(mbbha)_2$

(29.25 ± 2.217, p = 0.002) complex is significantly high as compared to other assayed compounds including ligand (21.25 ± 5.737, p = .084), $Bu_2Sn(mbbha)_2$ (22.25 ± 2.217, p = 0.154), and $Ph_2Sn(mbbha)_2$ (15.50 ± 2.082, p = 0.002) and the standard (Doxycycline) (22.75 ± 5.852, p = 0.025).

4. Conclusion

The new ligand and its dioranotin(IV) derivatives have been synthesized and characterized successfully. Infrared data show the disappearance of the ν(O-H) stretching frequency, lowering of the carbonyl frequency and shifting of the ν(N-O) absorption to higher frequency on chelation indicate that the hydroxamic acid is a bidentate chelator. The new absorption bands appeared in the spectra of complexes are assigned to ν(Sn-O) and ν(Sn-C). ^{1}H NMR spectral data confirm the presence of ligand in deprotonated form in complexes. ^{13}C spectra illustrate minor upfield shift in the position of carbonyl absorption on complexation. Up-field shift of ^{119}Sn NMR absorptions reflects six coordination number for tin in the derivatives. The X-ray diffraction studies confirm the speculated six-coordination environment around tin in **(3)** and **(4)** derivatives. Compound **(2)** has exhibited strong antimicrobial activity against all tested strains as compared to other compounds and its further investigation is proposed as an antibacterial agent.

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Supplementary material

Crystallographic data for structure analysis of compound (**3**) and (**4**) have been deposited with the Cambridge Crystallographic Data Centre, CCDC reference numbers 4171 for (**3**) and 4244 for (**4**). The provided information can be obtained free of charge from the Director, CCDC, 12

Union Road, Cambridge, CB2 1EZ, UK (fax: +44-1223-336033; e-mail:deposit@ccdc.cam.ac.uk; website: http://www.ccdc.cam.ac.uk).

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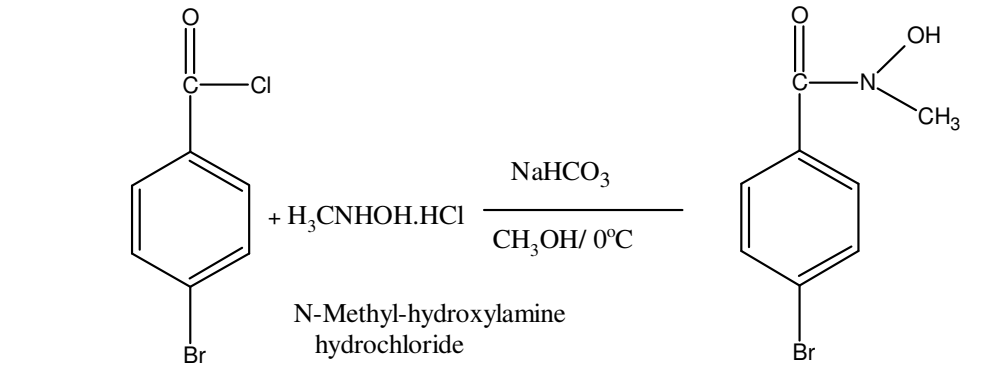
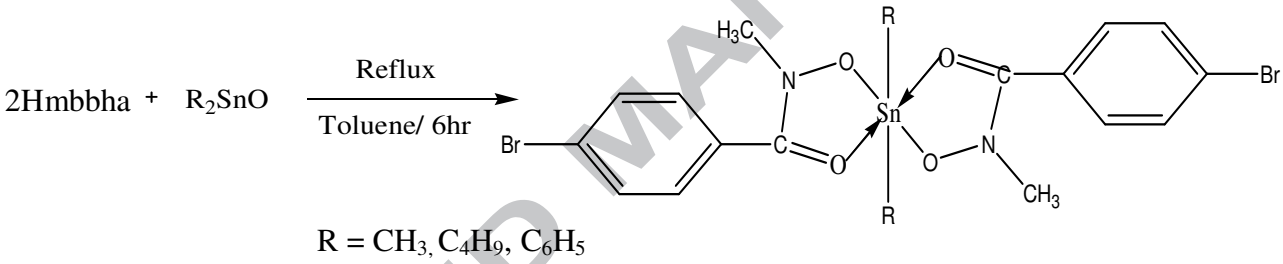


4-Bromobenzoyl chloride

N-Methyl-4-bromobenzohydroxamic acid

(Hmbbha)

Scheme 1 Reaction of Hydroxylamine with Acid Chloride



R = CH_3, C_4H_9, C_6H_5

Scheme 2 Reaction of free Ligand with Diorganotin(IV) oxide

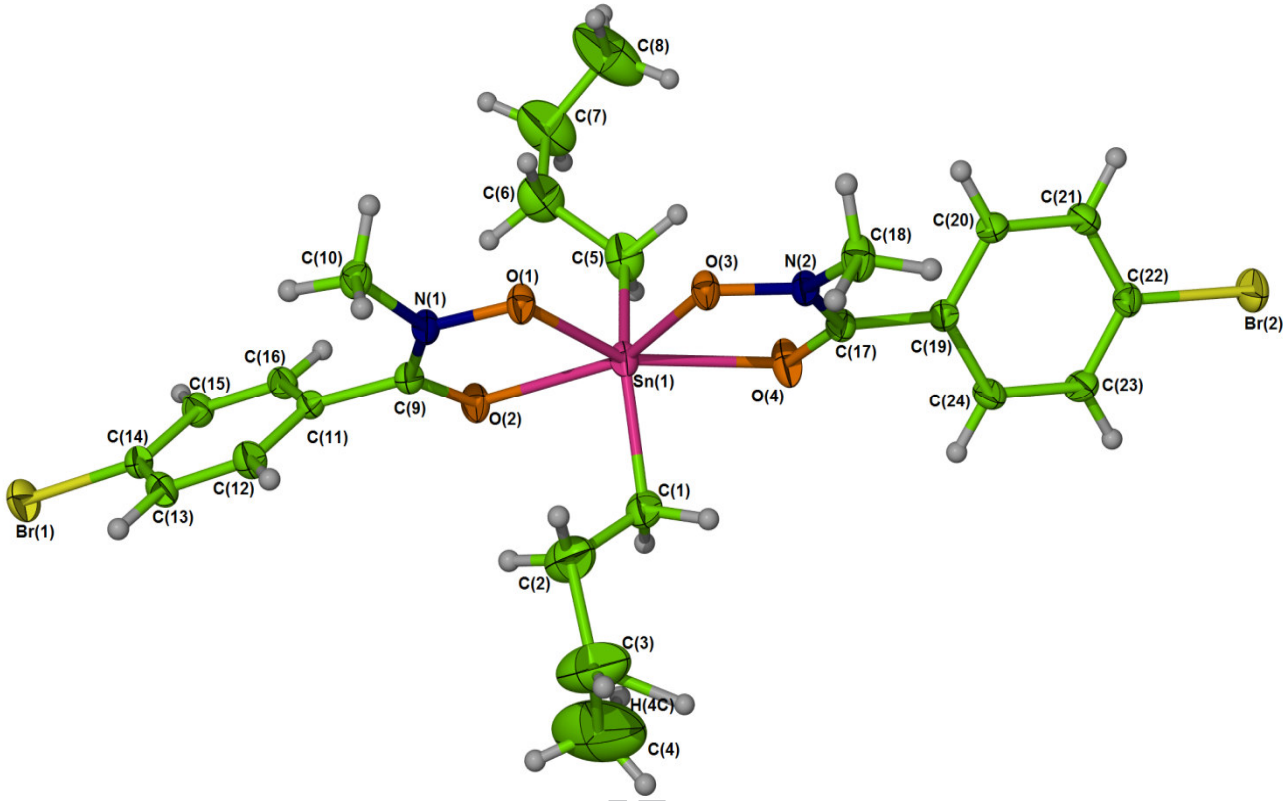


Fig. 1 Thermal ellipsoid plot of $C_{24}H_{32}Br_2N_2O_4Sn$. Displacement ellipsoids are drawn at the 50% probability level, and H atoms are shown as spheres of arbitrary radii

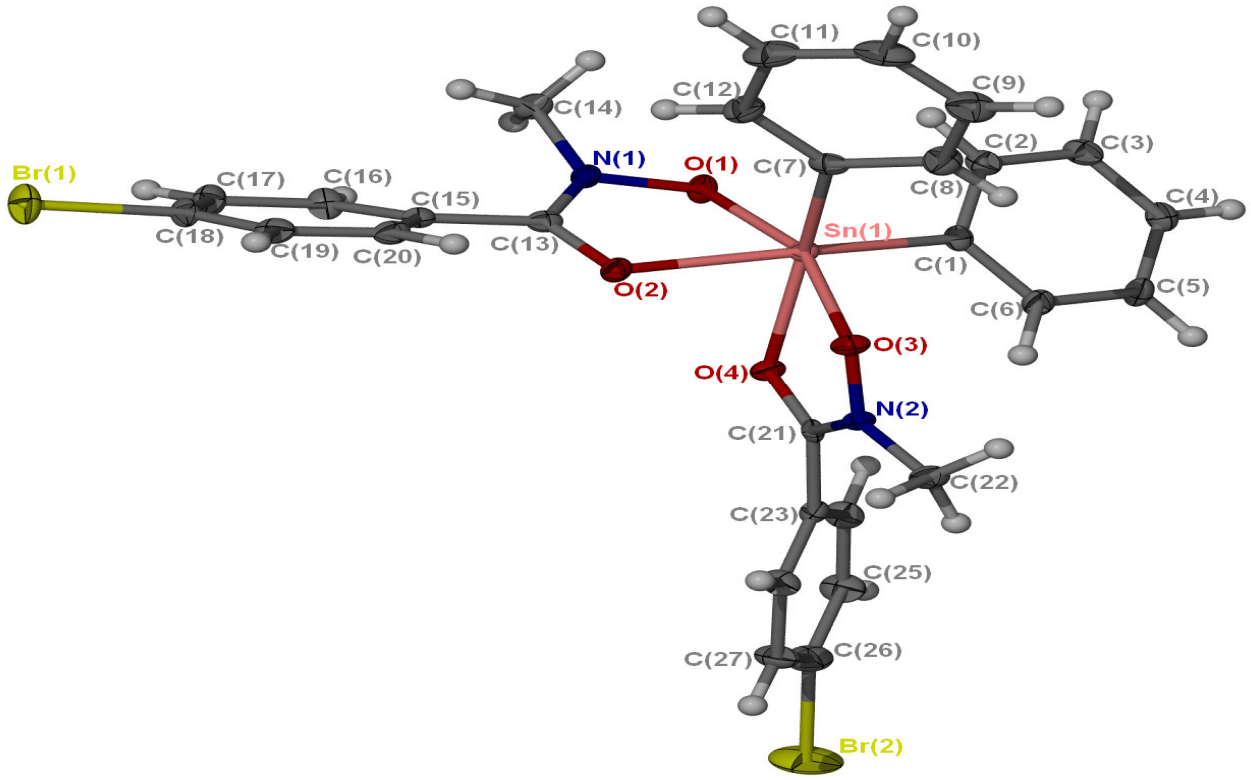


Fig. 2 Thermal ellipsoid plot of $C_{28}H_{24}Br_2N_2O_4Sn$. Displacement ellipsoids are drawn at the 50% probability level, and H atoms are shown as spheres of arbitrary radii.

Fig. 3 A representation of inhibition zones of various bacterial strains.

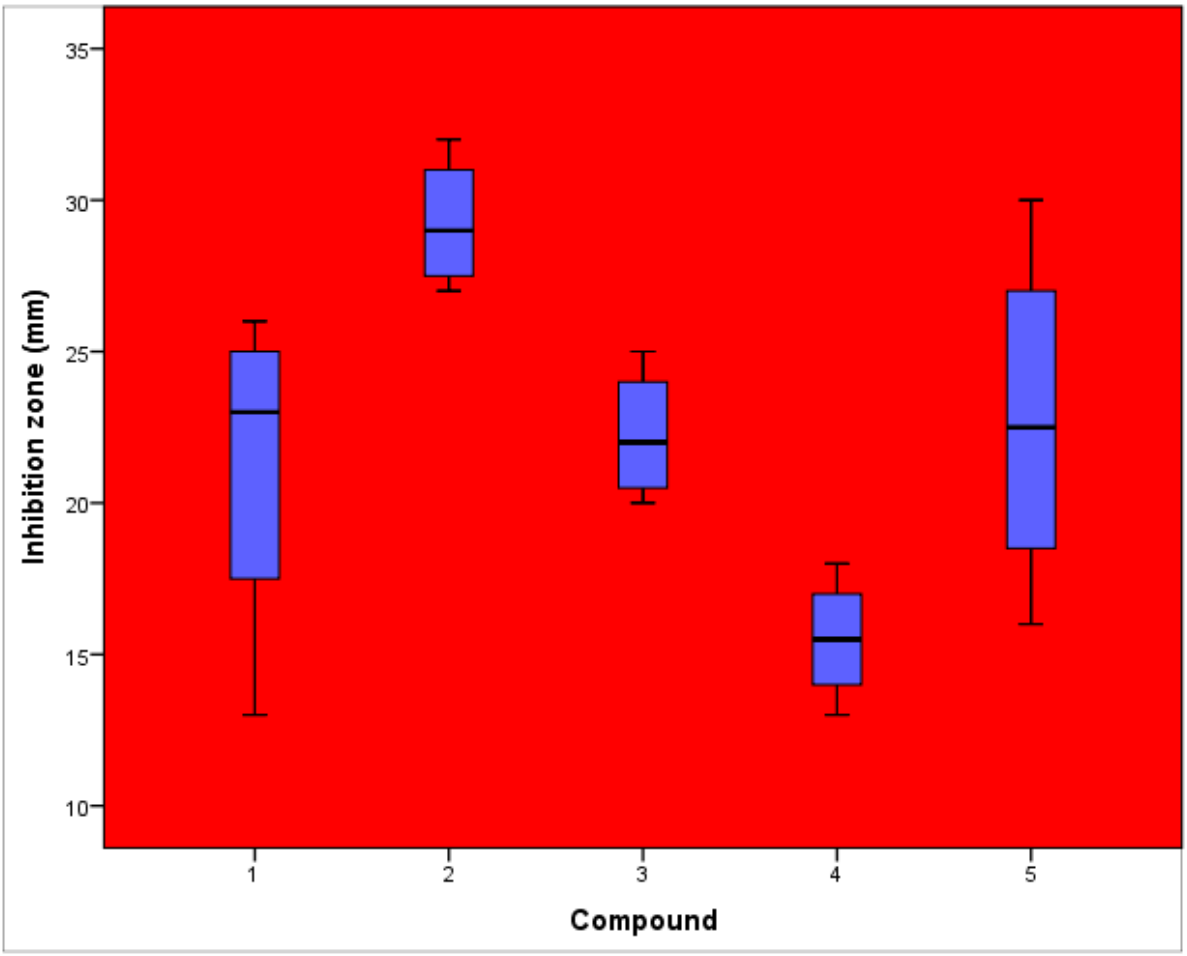


Fig. 4 Boxplot graph of antimicrobial activity of compounds (**1-6**) against various bacteria.

Table 1 Physical data for the prepared ligand and the complexes.

Compound	Colour	Yield (%)	M.P.(ºC)	Found (Calc.) %			
				C	H	N	Sn
(Hmbbha)	Colourless	82	104-105	38.83 (41.76)	3.88 (3.48)	5.90 (6.09)	
$Me_2Sn(mbbha)_2$	White	85	118-119	36.53 (35.59)	2.48 (3.32)	4.48 (4.61)	17.38 (19.60)
$Bu_2Sn(mbbha)_2$	Colourless	76	154-155	41.63 (41.68)	4.66 (4.66)	3.79 (4.05)	15.82 (17.22)
$Ph_2Sn(mbbha)_2$	White	71	151-152	45.46 (45.97)	3.11 (3.31)	3.28 (3.83)	15.01 (16.28)

Table 2: Infrared spectral data for the ligand and its complexes

Compound	?? (O-H) cm^1	?? (C=O) cm^1	?? (C-N) cm^{-1}	?? (N-O) cm^1	?? (Sn-C) cm^{-1}	?? (Sn-O) cm^{1-}
$(Hmbbha)_2$	3123	1600	1436	915	-	-
$Me_2Sn(mbbha)_2$	-	1584	1496	934	524	443
$Bu_2Sn(mbbha)_2$	-	1586	1497	937	521	447
$Ph_2Sn(mbbha)_2$	-	1590	1492	946	573	458

Table 3 ^{1}H NMR data for free ligand and diorganotin(IV) complexes (ppm)

No	Compound	OH	H(Aromatic)	H(Aliphatic)
1	(Hmbbha)	10.34 (H)	7.51-7.61m (4H)	N-CH_3: 3.22 s (3H)
2	$Me_2Sn(mbbha)_2$	-	7.11-7.44m 2(4H)	N-CH_3: 3.41s 2(3H) Sn-$(CH_3)_2$: 0.32
3	$Bu_2Sn(mbbha)_2$	-	7.56-7.70m 2(4H)	N-CH_3: 3.38s 2(3H) 1.24-1.30m 2(6H) -(CH_3):0.82t 2(3H)
4	$Ph_2Sn(mbbha)_2$	-	7.31-7.69m 2(9H)	N-CH_3:3.46s 2(3H)

Table 4 ^{13}C and ^{119}Sn NMR data for free ligand and diorganotin(IV) complexes (ppm)

No	Compound	C=O	Aromatic	Aliphatic	^{119}Sn-R
1	(Hmbbha)	168.3	114- 134	39.0	-
2	$Me_2Sn(mbbha)_2$	161.3	124-131	39.2, 6.5	-404
3	$Bu_2Sn(mbbha)_2$	161.5	115-142	39.2, 7.3-28.2	-407
4	$Ph_2Sn(mbbha)_2$	161.7	124-135	39.2	-405

Table 5 Crystal data of the complexes studied

Compound	**(3)**	**(4)**
Gross formula	C_{28} H_{24} Br_2 N_2 O_4 Sn	C_{24} H_{32} Br_2 N_2 O_4 Sn
M	731	691.06
Crystal system, space group	Triclinic, P-1	Orthorhombic, P21/n
Crystal shape	Block	Block
Colour	Colourless	Colourless
a, Å	9.0565(6)	14.151(6)
b, Å	12.4799(8)	11.692(5)
c, Å	14.0288(9)	17.404(7)
α, deg	66.8960(10)	90.00
β, deg	84.8720(10)	106.109(6)
γ, deg	80.9240(10)	90.00
V, Å ^{3}	1439.50(16)	2766.5(19)
Z	2	4
d_c, g/cm	1.686	1.608
μ (Mo Kα)cm^{-1}	3.698	3.840
T , K	100(2)	100(2)
Crystal size, mm	0.2, 0.9, 0.12	0.33, 0.25, 0.36
measured reflections	17150	32004
independent reflections	5945	5726
reflections with I > 2σ(I)	4771	4238
R_{int}	0.0416	0.0475
θ_{max}	26.50º	26.50º
θ_{min}	1.88º	2.13º
h	-11 →11	-17→17
k	-15→15	-14→14
l	-17→17	-21→21

$R[F^2 > 2\sigma(F^2)]$	0.0322	0.0321
$wR(F^2)$	0.0705	0.0648
S	1.012	1.057
reflections	5945	5726
parameters	336	306
restraints	0	24
$\Delta\rho_{max}$ e Å^{-3}	1.670	0.509
$\Delta\rho_{min}$ e Å^{-3}	-1.215	-0.698

Table 6 Selected bond lengths of the compounds

(**3**)		(**4**)	
Sn1 O3 2.110(2)	C5 C6 1.380(5)	Sn1 O1 2.105(2)	C19 C20 1.384(5)
Sn1 O1 2.110(2)	C7 C12 1.390(5)	Sn1 O3 2.121(2)	C19 C24 1.390(5)
Sn1 C7 2.148(4)	C7 C8 1.395(5)	Sn1 C1 2.123(4)	C19 C17 1.494(5)
Sn1 C1 2.152(3)	C8 C9 1.390(5)	Sn1 C5 2.131(5)	C22 C21 1.370(5)
Sn1 O2 2.193(2)	C9 C10 1.384(6)	Sn1 O2 2.363(2)	C22 C23 1.375(5)
Sn1 O4 2.217(2)	C10 C11 1.382(6)	Sn1 O4 2.398(3)	C9 C11 1.498(5)
Br1 C18 1.905(3)	C11 C12 1.395(6)	Br2 C22 1.900(3)	C11 C12 1.388(5)
Br2 C26 1.897(4)	C13 C15 1.472(5)	Br1 C14 1.895(3)	C11 C16 1.382(5)
N1 C13 1.318(4)	C15 C16 1.398(5)	O1 N1 1.384(3)	C15 C16 1.382(5)
N1 O1 1.375(3)	C15 C20 1.398(5)	N1 C9 1.316(4)	C1 C2 1.500(6)
N1 C14 1.451(4)	C16 C17 1.378(5)	N1 C10 1.451(4)	C24 C23 1.380(5)
N2 C21 1.314(4)	C17 C18 1.376(5)	O4 C17 1.254(4)	C21 C20 1.374(5)

N2 O3 1.373(3)	C18 C19 1.384(5)	O3 N2 1.377(3)	C12 C13 1.379(5)
N2 C22 1.455(4)	C19 C20 1.383(5)	O2 C9 1.263(4)	C5 C6 1.502(6)
O2 C13 1.283(4)	C21 C23 1.486(5)	N2 C17 1.321(4)	C2 C3 1.527(8)
O4 C21 1.276(4)	C23 C28 1.384(5)	N2 C18 1.451(4)	C3 C4 1.264(11)
C1 C2 1.396(5)	C23 C24 1.386(5)	C14 C15 1.372(5)	C6 C7 1.549(7)
C1 C6 1.396(5)	C24 C25 1.380(5)	C14 C13 1.379(5)	C7 C8 1.429(8)
C2 C3 1.384(5)	C25 C26 1.387(5)		
C3 C4 1.385(5)	C26 C27 1.381(5)		
C4 C5 1.381(5)	C27 C28 1.385(5)		

Table 7 Selected bond angles of the compounds

(3)		(4)	
O3 Sn1 O1 157.92(9)	C12 C7 C8 117.3(3)	O1 Sn1 O3 73.99(9)	C21 C22 C23 121.5(3)
O3 Sn1 C7 87.99(11)	C12 C7 Sn1 126.4(3)	O1 Sn1 C1 107.09(13)	C21 C22 Br2 119.3(3)
O1 Sn1 C7 105.37(12)	C8 C7 Sn1 116.2(3)	O3 Sn1 C1 101.40(14)	C23 C22 Br2 119.2(3)
O3 Sn1 C1 104.41(11)	C9 C8 C7 122.1(4)	O1 Sn1 C5 103.49(15)	O2 C9 N1 120.7(3)
O1 Sn1 C1 89.23(11)	C10 C9 C8 119.4(4)	O3 Sn1 C5 103.68(15)	O2 C9 C11 119.3(3)
C7 Sn1 C1 105.16(13)	C11 C10 C9 119.8(4)	C1 Sn1 C5 144.68(18)	N1 C9 C11 120.0(3)
O3 Sn1 O2 88.72(9)	C10 C11 C12 120.3(4)	O1 Sn1 O2 72.08(9)	C12 C11 C16 118.9(3)
O1 Sn1 O2 73.59(9)	C7 C12 C11 121.1(4)	O3 Sn1 O2 145.98(8)	C12 C11 C9 122.4(3)
C7 Sn1 O2 91.94(11)	O2 C13 N1 118.8(3)	C1 Sn1 O2 86.18(13)	C16 C11 C9 118.5(3)

C1 Sn1 O2 158.58(11)	O2 C13 C15 119.3(3)	C5 Sn1 O2 86.76(14)	C14 C15 C16 119.4(4)
O3 Sn1 O4 73.10(9)	N1 C13 C15 121.8(3)	O1 Sn1 O4 144.34(9)	C14 C15 H15 120.3
O1 Sn1 O4 90.37(9)	C16 C15 C20 118.8(3)	O3 Sn1 O4 70.60(9)	C16 C15 H15 120.3
C7 Sn1 O4 159.23(11)	C16 C15 C13 122.8(3)	C1 Sn1 O4 84.24(14)	C2 C1 Sn1 115.9(3)
C1 Sn1 O4 88.21(11)	C20 C15 C13 118.3(3)	C5 Sn1 O4 81.11(15)	Sn1 C1 H1A 108.3
O2 Sn1 O4 79.39(9)	C17 C16 C15 120.2(3)	O2 Sn1 O4 143.42(8)	Sn1 C1 H1B 108.3
C13 N1 O1 117.6(3)	C18 C17 C16 119.7(3)	N1 O1 Sn1 116.71(17)	O4 C17 N2 119.7(3)
C13 N1 C14 130.2(3)	C17 C18 C19 121.6(3)	C9 N1 O1 119.0(3)	O4 C17 C19 119.7(3)
O1 N1 C14 111.7(3)	C17 C18 Br1 119.2(3)	C9 N1 C10 129.3(3)	N2 C17 C19 120.5(3)
C21 N2 O3 117.7(3)	C19 C18 Br1 119.2(3)	O1 N1 C10 111.5(3)	C23 C24 C19 120.0(3)
C21 N2 C22 129.5(3)	C20 C19 C18 118.5(3)	C17 O4 Sn1 112.4(2)	C15 C16 C11 120.6(3)
O3 N2 C22 112.6(3)	C19 C20 C15 121.0(3)	N2 O3 Sn1 117.78(17)	C20 C21 C22 118.5(3)
N1 O1 Sn1 112.86(17)	O4 C21 N2 119.3(3)	C9 O2 Sn1 111.3(2)	C21 C20 C19 121.6(3)
C13 O2 Sn1 113.5(2)	O4 C21 C23 119.1(3)	C17 N2 O3 119.4(3)	C22 C23 C24 119.5(3)
N2 O3 Sn1 113.88(18)	N2 C21 C23 121.6(3)	C17 N2 C18 128.3(3)	C13 C12 C11 121.0(4)
C21 O4 Sn1 113.4(2)	C28 C23 C24 119.7(3)	O3 N2 C18 111.3(3)	C14 C13 C12 118.8(3)
C2 C1 C6 117.2(3)	C28 C23 C21 121.6(3)	C15 C14 C13 121.3(3)	C6 C5 Sn1 117.4(3)
C2 C1 Sn1 120.0(3)	C24 C23 C21 118.6(3)	C15 C14 Br1 119.4(3)	C1 C2 C3 116.2(5)
C6 C1 Sn1 122.8(3)	C25 C24 C23 120.8(3)	C13 C14 Br1 119.4(3)	C4 C3 C2 116.4(11)
C3 C2 C1 121.3(3)	C24 C25 C26 118.5(4)	C20 C19 C24 118.7(3)	C5 C6 C7 115.9(5)
C2 C3 C4 120.3(3)	C27 C26 C25 121.8(4)	C20 C19 C17 122.4(3)	C8 C7 C6 115.6(5)

C5 C4 C3 119.4(3) C6 C5 C4 120.1(3) C5 C6 C1 121.7(3)	C27 C26 Br2 118.6(3) C25 C26 Br2 119.6(3) C26 C27 C28 118.8(4) C23 C28 C27 120.4(3)	C24 C19 C17 118.6(3)	

Table 8 Antibacterial activity of the ligand and its organotin(IV) derivatives

Compound	Inhibition zone (mm)			
	E. coli	*K. pneumoniae*	*S. typhi*	*S. aureus*
Hmbbha (**1**)	22	26	13	24
$Me_2Sn(mbbha)_2$ (**2**)	30	32	27	28
$Bu_2Sn(mbbha)_2$ (**3**)	20	25	21	23
$Ph_2Sn(mbbha)_2$ (**4**)	16	18	15	13
Doxycycline **(5)**	24	21	16	13

Note: *E. coli = Escherichia coli, K. pneumoniae = Klebsiella pneumoniae, S. typhi = Salmonella typhi, S. aureus = Staphylococcus aureus*

Table 9 Summary statistics of statistical analysis

Compounds	N	Mean	Std. Deviation	Std. Error	95% Confidence Interval for Mean		Minimum	Maximum
					Lower Bound	Upper Bound		
(Hmbbha)	4	21.25	5.737	2.869	12.12	30.38	13	26
$Me_2Sn(mbbha)_2$	4	29.25	2.217	1.109	25.72	32.78	27	32
$Bu_2Sn(mbbha)_2$	4	22.25	2.217	1.109	18.72	25.78	20	25
$Ph_2Sn(mbbha)_2$	4	15.50	2.082	1.041	12.19	18.81	13	18
Doxycycline	4	22.75	5.852	2.926	13.44	32.06	16	30
Total	20	22.20	5.745	1.285	19.51	24.89	13	32

Table 10 ANOVA

	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	383.200	4	95.800	5.889	.005
Within Groups	244.000	15	16.267		
Total	627.200	19			

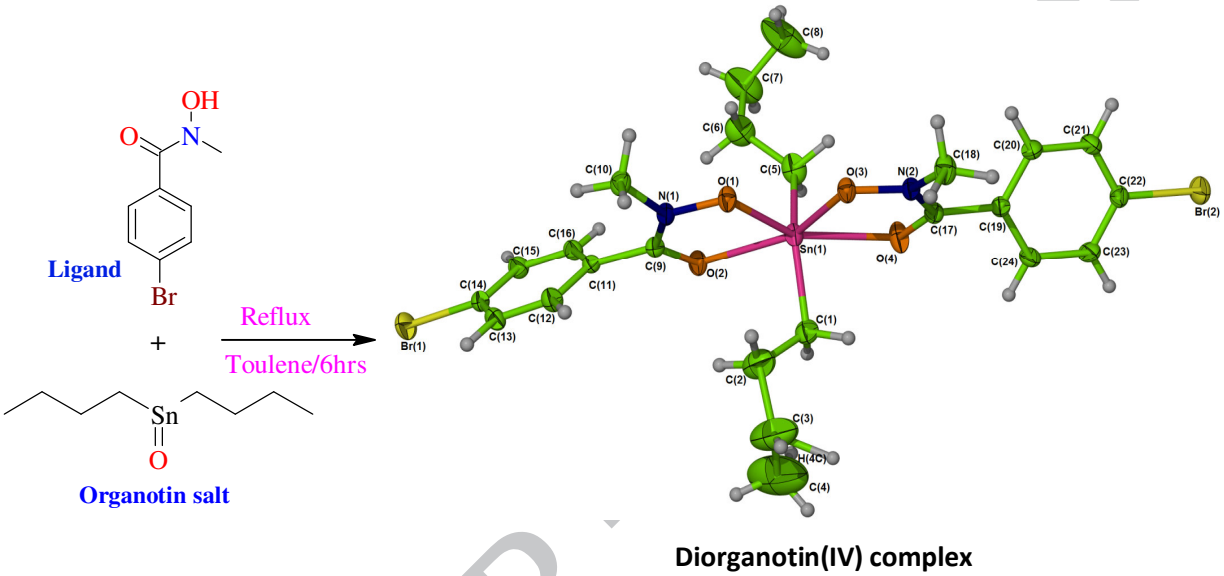
Table 11 Tukey's multiple comparative test results

Compound	(Hmbbha)	$Me_2Sn(mbbha)_2$	$Bu_2Sn(mbbha)_2$	$Ph_2Sn(mbbha)_2$	Doxycycline
Mean	21.25^{a}	29.25^{b}	22.25^{ab}	15.50^{a}	22.75^{ab}

Note: Distinct letters in superscripts show statistically significant difference

Graphical Abstract

Synthesis, spectroscopic characterization, X-ray diffraction studies and *in-vitro* antibacterial activities of diorganotin(IV) derivatives with *N*-methyl-4-bromobenzohydroxamic acid.



HIGHLIGHTS

- The compounds were characterized by CHN, IR, NMR and X-ray methods.
- The ligand in diorganotin(IV) complexes is bidentate.
- The geometry around tin in diorganotin(IV) complexes is octahedral.
- The dimethyltin(IV) complex has exhibited significant antibacterial activity