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Spectral and Biological Studies of Newly Synthesized Organotin(IV) Complexes of 4-({[(E)-(2-Hydroxyphenyl)methylidene]amino}methyl)cyclohexane Carboxylic Acid Schiff Base

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The new organotin(IV) complexes with 4-({[(E)-(2-hydroxyphenyl)methylidene]amino}methyl)cyclohexane carboxylic acid (**HL**, Schiff base) were synthesized by the reaction of di- and triorganotin salts in the presence of triethylamine as base or dioctyltin oxide using Dean and Stark trap for the removal of azeotropic water. All complexes were characterized by elemental analysis, IR, NMR (^{1}H and ^{13}C) and mass spectrometry. The IR data indicate that in both di- and triorganotin(IV) carboxylates, the ligand moiety -COO acts as a bidentate group in solid state. Multinuclear NMR data show that triorganotin complexes exhibit the four-coordinated geometry, while diorganotin(IV) complexes show the coordination number greater than four, probably five or six, in solution state. These compounds were screened for antibacterial activities against six pathogenic bacterial strains. The activities were measured in terms of inhibition zones (mm). Antifungal activity was determined against six pathogenic fungal strains, cytotoxicity by the brine shrimp lethality assay. Results for antibacterial and antifungal activity, and cytotoxicity of these compounds demonstrate that complexes exhibit significant biological activity with few exceptions.

Keywords: Organotin(IV) carboxylates, Schiff base, Spectral characterization, Biological activity

INTRODUCTION

The chemistry of organotin(IV) derivatives is a field of growing interest [1] because of their great structural diversity, the nature of organic ligand and the ratio of the reactant [2]. The increasing importance of organotin(IV) compounds is not only because of its extensive commercial use [3] in industry such as PVC stabilizing agent and anti-neoplastic agent, and in agriculture such as a wood preservative, fungicide and pesticide, but also due to the environmental consequences of the widespread use of these complexes [4]. The organotin(IV) compounds are also used for pharmacological applications such as bactericides [3], as an anti-tumour [5], as an anti-inflammatory agent [6], and as an antituberclosis [7,8].

Many Schiff bases are biologically active and show significant anti-microbial and anti-tumor activities [9,10]. These compounds also possess a wide range of structural diversity. Molecules having hetero-atoms, other than nitrogen, can be easily synthesized and successfully used for metal complexation [11,12]. The role of Schiff base as extractant in radioisotope enrichment and manufacturing of radiopharmaceutical is worth mentioning [13]. Due to the clinical importance of tranexamic acid and in order to pursue our studies of biologically active organotin(IV) derivatives [14,15], we attempted to synthesize the Schiff base by using tranexamic acid as reactant (Fig. 1) and then their organotin(IV)

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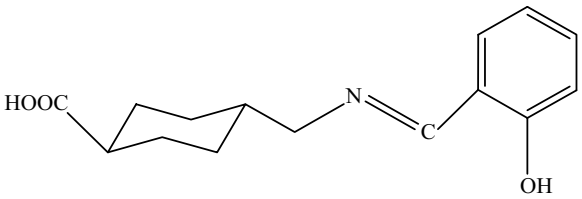


Fig. 1. 4-({[(E)-(2-Hydroxyphenyl)methylidene]amino} methyl)cyclohexane carboxylic acid (Schiff base).

complexes assuming that the complexes can be used as new prodrug of tranexamic acid. To check this, we screened these complexes against different bacterial and fungal strains and also checked their cytotoxicity. These complexes were characterized by IR, NMR and mass spectrometry.

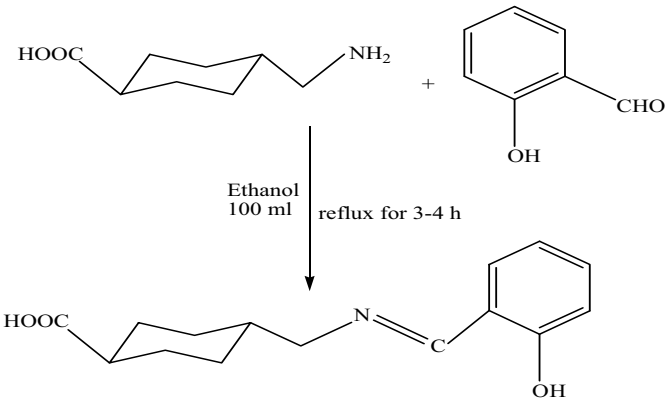
EXPERIMENTAL

Materials and Methods

All the glass apparatus with standard quick fit joints was used throughout the work after cleaning and drying at 120 °C. 2-Hydroxybenzaldehyde, organotin(IV) chlorides and organotin(IV) oxide from Aldrich and toluene from Fluka were purchased. Solvents were purified by standard methods [16], while other chemicals were used as supplied. Melting points were determined with a Mitamura Rikero Kogyo (Japan) and are uncorrected. Mass spectra were recorded on a MAT 8500 Finngin (Germany). Elemental analysis was carried out with a Perkin-Elmer 2400 Series II instrument. IR spectra in the range 4000-400 cm^{-1} were recorded as neat liquids, using KBr pellets (for solid compounds) on a Bio-Rad FT-IR spectrometer. The ^{1}H and ^{13}C NMR spectra were recorded on a Bruker AM-300 MHz spectrometer using $CDCl_3$ as internal reference.

Synthesis of 4-({[(E)-(2-Hydroxyphenyl)methylidene] amino}methyl)cyclohexane Carboxylic Acid (Schiff Base)

An aqueous hot (100 °C) solution (100 ml) of tranexamic acid (1 mmol) was added dropwise to an ethanolic (100 ml) solution of 4-hydroxybenzaldehyde (1 mmol) in round bottom flask equipped with water condenser with constant stirring. Reaction mixture was left under reflux for 3-4 h and then the solution was kept at room temperature for 48 h to get the yellow solid product (Scheme 1).



Scheme 1

Synthesis of Organotin(IV) Complexes of 4-({[(E)-(2-Hydroxyphenyl)methylidene]amino}methyl)cyclohexane Carboxylic Acid

a. 4-({[(E)-(4-Hydroxyphenyl)methylidene]amino} methyl)cyclohexane carboxylic acid (1 g, 3.83 mmol) was suspended in 250 ml round bottom two necked flask in dry toluene (100 ml) and treated with triethylamine (0.386 ml, 3.83 mmol). The mixture was refluxed for 2-3 h. Then 2 mmol diorganotindichloride (R_2 = Me_2, Bu_2, Ph_2 and Oct_2) or 1 mmol triorganotinchloride (R_3 = Me_3, Bu_3 and Ph_3) was added as solid to a reaction flask with constant stirring and reaction mixture was refluxed for 8-10 h. The reaction mixture contained Et_3NHCl and was filtered off in such a way that filtrate had the organotin derivative. The solvent was removed through rotary apparatus. The mass left behind was recrystallized from $CHCl_3$ and *n*-hexane mixture (1:1).

b. 4-({[(E)-(4-Hydroxyphenyl)methylidene]amino} methyl)cyclohexane carboxylic acid (1 g, 3.83 mmol) was suspended in dry toluene, (100 ml). To this solution, Oct_2SnO (dioctyltin(IV) oxide) (0.67 g, 1.91 mmol) was added as solid with constant stirring and refluxed for 8-10 h. Water formed during the reaction was removed *via* Dean and Stark trap. The solvent was removed under reduced pressure through rotary apparatus and the product obtained was recrystallized in $CHCl_3$:*n*-hexane (1:1) mixture.

The resulting organotin(IV) complexes of 4-({[(E)-(2-hydroxyphenyl)methylidene]amino}methyl)cyclohexane carboxylic acid are **1** (Me_2), **2** (Bu_2), **3** (Ph_2), **4** (Oct_2), **5** (Me_3),

6 (Bu_3) and **7** (Ph_3). Some typical synthetic routs for the organotin(IV) complexes of the Schiff base HL are as follows:

$$R_2SnCl_2 + 2Et_3NHL \xrightarrow[\text{ii) Reflux for 8-10 hrs}]{\text{i) Toluene}} R_2SnL_2 + 2Et_3NHCl \quad (\mathbf{1})$$

$$R_3SnCl + Et_3NHL \xrightarrow[\text{ii) Reflux for 8-10 hrs}]{\text{i) Toluene}} R_3SnL + Et_3NHCl \quad (\mathbf{2})$$

$$Oct_2SnO + 2HL \xrightarrow[\text{ii) Reflux for 8-10 hrs}]{\text{i) Toluene}} Oct_2SnL_2 + H_2O \quad (\mathbf{3})$$

RESULTS AND DISCUSSION

The Schiff base ligand is yellow in color and is soluble in almost all organic solvents. While, the corresponding metal complexes obtained in 1:1 and 1:2 molar ratios (Eqs. 1-3) were found to be dark yellow in color. The reported compounds (**1**)-(**7**) were prepared by the reaction of ligand acid with organotin(IV) halides or oxide in the presence of triethylamine. All the synthesized compounds were stable having sharp melting points and were soluble in common organic solvents. The complexes were analyzed by IR, MS and NMR to propose their geometry in the solid and solution state. The physical data are given in Table 1.

Infrared Spectroscopy

IR spectra of the complexes (**1**)-(**7**) were recorded as KBr pellets or neat liquid (for liquid sample) in the range 4000-400 cm^{-1}. The collected data are summarized in Table 2. The ν(C=N) band of Schiff base appears in the range 1613-1622 cm^{-1} which is in close agreement with the values reported in literature for such systems [17].

Assignment of different vibrational bands was made by the comparison of free acid spectrum with the organotin(IV) derivatives. The absorption bands ν(Sn-C) in the spectra of the reported compounds lie in the range of 510-526 cm^{-1} which indicate the presence of Sn-C bond. The absence of a broad band due to ν(OH) stretching frequency in the organotin(IV) derivatives and the presence of ν(Sn-O) stretching frequency at 403-459 cm^{-1} is indicative of complex formation [18].

The values of IR stretching vibration frequencies of carboxylic group [(ν(COO_{asym}) and ν(COO_{sym})] in organotin(IV) carboxylates are helpful in elucidation of the structure and bonding behaviour of the ligand [19-21]. In all complexes the difference Δν is less than 200 cm^{-1} which indicates the bidentate nature of the ligand. Diorganotin(IV) dicarboxylates exhibit the hexa coordinated geometry, while triorganotin(IV) carboxylates show the trigonal bipyramidal geometry in solid state. Polymeric structure is supported by trigonal bipyramidal geometry.

^{1}H NMR Spectroscopy

The characteristic resonance peaks for the reported complexes (**1**)-(**7**) have been recorded in $CDCl_3$ and data are given in Table 3. The expected resonances are assigned by their peak multiplicity, intensity pattern and integration. The integration of spectra shows good agreement with the composition of the compounds.

The ^{1}H NMR spectral data of the ligand show single resonance at 11.4 ppm, which is absent in the spectra of the complexes, indicating the replacement of the carboxylic acid proton by the organotin(IV) moiety.

In addition, the resonance appearing in the range 5.20-5.21 ppm as a singlet is attributed to the -N=CH proton and aromatic protons appearing in the expected region as doublets and triplets. However, cyclohexyl protons appear at relatively upfield shift value in the range of 1.20-1.73 ppm, while four protons of aromatic ring of the ligand appear as doublet and a triplet with $^3J(^1H,^1H)$ 8.1 and 8.2 Hz, respectively. The phenyl groups attached to metal atom come into view as a multiplet at 7.26-7.30 and 7.28-7.39 ppm for compound (**3**) and (**7**), respectively.

The CH_2 protons of di-n-butyltin compound (**2**) are significant as a triplet at 0.87 ppm with $^3J[^1H,^1H]$ = 7.5 Hz, while -CH_2-CH_2- protons appear as a multiplet. Terminal protons of di-butyltin(IV) also show a triplet at 0.95 ppm with ^3J $[^1H,^1H]$ = 7.8 Hz.

The most important information obtained from ^{1}H NMR values is $^2J[^{119}Sn\text{-}^1H]$ coupling constant values in these compounds. The coupling value of 81 Hz in compound (**1**)

Table 1. Physical Parameters of Organotin(IV) Complexes of Schiff Base

Compound	Empirical formula	m.p. (ºC)	Yield (%)	Molecular weight	Elemental analysis; calculated (found) (%)		
					C	H	N
HL	$C_{15}H_{19}O_3N$	120	-	261	68.96 (68.93)	6.89 (6.92)	5.36 (5.32)
(**1**)	$C_{32}H_{42}O_6N_2Sn$	168	80	669	57.39 (57.33)	6.27 (6.23)	4.18 (4.22)
(**2**)	$C_{38}H_{54}O_6N_2Sn$	154	75	753	60.55 (60.50)	7.17 (7.20)	3.71 (3.75)
(**3**)	$C_{42}H_{46}O_6N_2Sn$	143	79	793	63.55 (63.50)	5.80 (5.82)	3.53 (3.57)
(**4**)	$C_{46}H_{62}O_6N_2Sn$	-	70	857	64.41 (64.37)	7.23 (7.19)	3.26 (3.22)
(**5**)	$C_{18}H_{27}O_3NSn$	166	81	424	50.94 (50.90)	6.36 (6.40)	3.30 (3.35)
(**6**)	$C_{27}H_{45}O_3NSn$	67	83	550	58.90 (58.86)	8.18 (8.21)	2.54 (2.58)
(**7**)	$C_{33}H_{33}O_3NSn$	134	80	610	64.91 (64.96)	5.40 (5.37)	2.29 (2.23)

Table 2. Characteristic Infrared Bands (cm^{-1}) for Organotin(IV) Complexes of Schiff Base

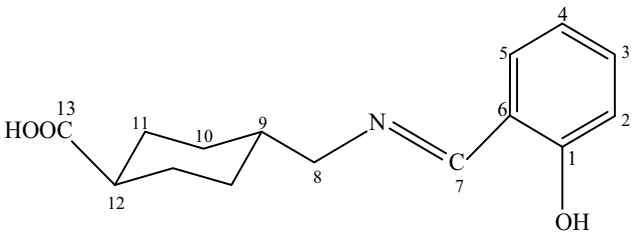
Compound	ν_{asym}(COO)	ν_{sym}(COO)	$\Delta\nu$	ν(Sn-C)	ν(Sn-O)
HL	1635	1372	263	-	-
(**1**)	1641	1447	194	516	403
(**2**)	1634	1450	184	525	459
(**3**)	1645	1452	193	-	456
(**4**)	1633	1449	184	526	452
(**5**)	1635	1495	140	510	449
(**6**)	1637	1488	149	520	457
(**7**)	1645	1480	165	-	453

demonstrates that diorganotin(IV) derivatives show the coordination number greater than four, probably five or six, in non-coordinating solvent. The coupling value of 57 Hz in the compound (**5**) signifies that triorganotin(IV) derivatives show distorted tetrahedral geometry [22,23] in the solution form. Furthermore, it is observed that the aldehyde phenyl protons appear upfield as a two doublet and a triplet due to the electron donating effect of the hydroxy group. The hydroxy proton gives singlet in the range of 5.1-5.3 ppm for the complexes (**1**)-(**7**).

^{13}C NMR Spectroscopy

The characteristic resonance peaks in the ^{13}C NMR spectra of the complexes (**1**)-(**7**) recorded in $CDCl_3$, are reported in Table 4. The position of the phenyl carbons of the ligand undergo a minor variation in the complexes as compared to

Table 3. ^{1}H NMR Data[a,b] (ppm) for Organotin(IV) Complexes of Schiff Base

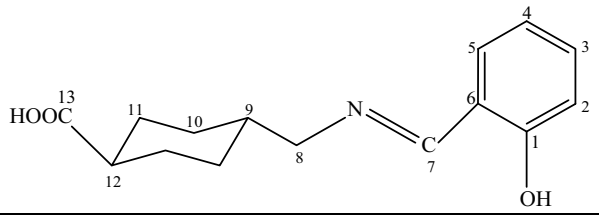


H No.	**HL**	(**1**)	(**2**)	(**3**)	(**4**)	(**5**)	(**6**)	(**7**)
2	6.93d	6.92d	6.91d	6.92d	6.90d	6.94d	6.93d	6.91d
	(8.1)	(8.1)	(8.1)	(8.1)	(8.1)	(8.1)	(8.1)	(8.1)
3	6.94t	6.91t	6.92t	6.94t	6.91t	6.93t	6.92t	6.93t
	(8.3)	(8.3)	(8.3)	(8.3)	(8.3)	(8.3)	(8.3)	(8.3)
4	6.95t	6.92t	6.93t	6.95t	6.91t	6.94t	6.93t	6.91t
	(8.3)	(8.1)	(8.1)	(8.1)	(8.1)	(8.1)	(8.1)	(8.1)
5	6.93d	6.94d	6.93d	6.94d	6.92d	6.94d	6.93d	6.94d
	(8.2)	(8.1)	(8.1)	(8.1)	(8.1)	(8.1)	(8.1)	(8.1)
7	5.20s	5.20s	5.20s	5.21s	5.20s	5.20s	5.21s	5.20s
8	1.57s	1.58s	1.57s	1.58s	1.59s	1.57s	1.58s	1.58s
9	1.20m	1.22m	1.21m	1.23m	1.21m	1.20m	1.21m	1.22m
10	1.62m	1.61m	1.60m	1.61m	1.62m	1.61m	1.60m	1.60m
11	1.72m	1.70m	1.71m	1.71m	1.72m	1.72m	1.71m	1.73m
12	1.80m	1.83m	1.82 m	1.81m	1.82 m	1.81m	1.83m	1.84m
COOH	11.4s	-	-	-	-	-	-	-
OH	5.1s	5.3s	5.2s	5.1s	5.2s	5.2s	5.2s	5.1s

[a]Compound (**1**): Sn-CH_3, 0.27s ^{2}J[81]. Compound (**2**): Sn-$CH_2CH_2CH_2CH_3$, 0.87t (7.5), 1.30-1.41m. Compound (**3**): Sn-C_6H_5, 7.26-7.30m. Compound (**4**): Sn-$CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_3$, 0.91-1.82m. Compound (**5**): Sn-CH_3, -0.05s [57]. Compound (**6**): Sn-$CH_2CH_2CH_2CH_3$, 0.95t (7.8), 1.31-1.42m. Compound (**7**): Sn-C_6H_5, 7.28-7.39m. [b]Chemical shifts (δ) in ppm. ^{2}J[^{119}Sn, ^{1}H] and ^{3}J(^{1}H, ^{1}H) in Hz are listed in square brackets and parenthesis, respectively. Multiplicity is given as: s = singlet, d = doublet, t = triplet, m = multiplet.

those observed in free acid. The carboxylate carbon shows a downfield shift in the complexes, indicating the contribution of the carboxylic group (COO) in coordination to tin(IV) [24]. The coupling constants, ^{n}J[^{119}Sn,^{13}C] are important parameters for the structure characterization of organotin(IV) compounds. For triorganotin compound (**5**), the magnitude of ^{1}J[^{119}Sn,^{13}C] coupling values is 397 Hz, which suggests the typical tetrahedral geometry around the tin atom in solution [24]. This is further supported by the C-Sn-C bond angles (Table 5) calculated from the ^{2}J[^{119}Sn, ^{1}H] and ^{1}J[^{119}Sn, ^{13}C] values, using the literature methods [25]. Since the geometry of the diorganotin dicarboxylates in non-coordinating solvents is concerned from ^{1}J[^{119}Sn,^{13}C] coupling value, as in case of compound (**3**), it is not defined with certainty because of the fluxional behavior of the carboxylate oxygen in their coordination with the tin atom. However, most of alkyl diorganotin(IV) dicarboxylates appear as skew trapezoidal geometry which is in between five and six coordination

Table 4. ^{13}C NMR Data[a,b] (ppm) for Organotin(IV) Complexes of Schiff Base



C No.	**HL**	(**1**)	(**2**)	(**3**)	(**4**)	(**5**)	(**6**)	(**7**)
1	138.2	138.3	138.4	138.8	138.2	138.3	138.4	138.4
2	129.3	129.2	129.2	129.3	129.1	129.4	129.2	129.2
3	125.2	125.1	125.4	125.4	125.3	125.4	125.4	125.4
4	120.6	120.7	120.5	120.4	120.3	120.6	120.7	120.5
5	129.2	129.4	129.1	129.3	129.2	129.2	129.3	129.1
6	137.8	137.7	137.5	137.6	137.5	137.1	137.7	137.5
7	122.6	122.8	122.7	122.8	122.6	122.2	122.5	122.2
8	31.2	31.5	31.4	31.5	31.6	31.5	31.3	31.4
9	38.2	38.5	38.3	38.3	38.2	38.3	38.4	38.3
10	34.8	34.6	34.5	34.6	34.6	34.5	34.6	34.6
11	34.2	34.4	34.3	34.1	34.2	34.3	34.3	34.3
12	33.6	33.5	33.5	33.5	33.4	33.2	33.3	33.6
13	180.1	182.7	182.4	182.3	182.3	182.7	182.6	182.9

[a]Compound (**1**): Sn-CH_3, (C-α)-2.23 ^1J[641,664]. Compound (**2**): Sn-$CH_2CH_2CH_2CH_3$, (C-α) 28.6, (C-β) 27.4 ^2J[22], (C-γ) 26.8 ^3J[63], (C-δ) 14.5. Compound (**3**): Sn-C_6H_5, (C-α) 138.4, (C-β) 137.7 ^2J[48], (C-γ) 136.5, (C-δ) 130.2. Compound (**4**): Sn-$CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_3$, (C-α) 37.6 ^1J[555, 580], (C-β) 31.3 ^2J[37] (C-γ) 30.5 ^3J [91], (C-δ) 29.8 (C-α*) 29.3, (C-β*) 26.4, (C-γ*), 22.1, (C-δ*) 14.8. Compound (**5**): Sn-CH_3, (C-α)-2.3 ^1J[377, 397]. Compound (**6**): Sn-$CH_2CH_2CH_2CH_3$, (C-α) 29.2, (C-β) 27.3 ^2J[22], (C-γ) 26.4 ^3J[63], (C-δ) 14.6. Compound (**7**): Sn-C_6H_5, (C-α) 138.8, (C-β) 137.9 ^2J[47], (C-γ) 136.9, (C-δ) 130.8. [b]Chemical shifts (δ) in ppm. ^nJ[^{119}Sn, ^{13}C] in Hz are listed in square brackets.

Table 5. (C-Sn-C) Angles (°) Based on NMR Parameters of Selected Organotin(IV) Complexes of Schiff Base

Compound	^1J[^{119}Sn, ^{13}C] (Hz)	^2J[^{119}Sn, ^{1}H] (Hz)	Angle (°)	
			^1J	^2J
(**1**)	-	81	-	132.1
(**5**)	397	57	111.6	110.5

numbers [24]. Deshielding of C(13) observed in complexes (**1**)-(**7**) should be related to the electrophilicity of the tin.

Mass Spectrometry

The fragment ions with their m/z (%) values for compounds (**1**)-(**7**) have been reported in Table 6. It can be observed that large organotin molecules suffer considerable fragmentation in the mass spectrometer, while small organotin(IV) molecules often show the molecular ion peaks. Molecular ion peak is not observed for the reported complexes

Table 6. Mass Spectral Data for Organotin(IV) Complexes of Schiff Base

Fragment ion	(**1**) m/z(%)	(**2**) m/z(%)	(**3**) m/z(%)	(**4**) m/z(%)	(**5**) m/z(%)	(**6**) m/z(%)	(**7**) m/z(%)
$[C_{15}H_{19}NO_3]^+$	263(90)	263(87)	263(90)	263(15)	263(38)	263(21)	263(92)
$[C_{14}H_{18}NO]^+$	216(70)	216(45)	216(70)	216(18)	216(60)	216(50)	216(40)
$[C_{11}H_{12}NO]^+$	174(35)	174(39)	174(65)	174(18)	174(10)	174(10)	174(30)
$[C_8H_8NO]^+$	134(100)	134(100)	134(100)	134(55)	134(45)	134(20)	134(48)
$[SnH]^+$	121(25)	121(20)	121(25)	121(55)	121(20)	121(18)	121(20)
$[C_5H_4O_2Sn]^+$	216(42)	216(45)	216(32)	216(17)	216(65)	216(18)	216(29)
$[C_8H_{12}O_2Sn]^+$	260(25)	260(88)	260(70)	260(35)	260(100)	260(25)	260(55)
$[C_4H_9]^+$	-	57(44)	-	57(24)	-	57(64)	-
$[C_6H_5]^+$	77(18)	77(18)	77(35)	77(100)	77(8)	77(100)	77(100)
$[R_3Sn]^+$	-	-	-	-	165(22)	291(31)	351(24)
$[R_2Sn]^+$	150(11)	234(21)	274(15)	346(14)	150(13)	234(17)	274(16)
$[RSn]^+$	135(6)	177(14)	197(7)	233(11)	135(4)	177(9)	197(10)

(**1**)-(**7**). In these compounds, primary decomposition is due to either loss of R group or ligand, while secondary decomposition is a consequence of loss of either R group or CO_2 molecules [26,27]. However, the latter is the more frequent and probable pathway. Base peak for compounds (**1**)-(**3**) is observed due to $[C_8H_8NO]^+$ fragment, while for compounds (**4**), (**6**) and (**7**) it is due to $[C_6H_5]^+$.

Biological Studies

The cytotoxicity (LD_{50}) data have also been determined using the Brine-shrimp (*Artemia salina*) method [28], and results are listed in Table 7. The highest toxicity is observed for compound (**7**), whereas compounds (**5**) and (**6**) were found to be the least and moderate toxic, respectively, and the other synthesized compounds showed no cytotoxicity.

All synthesized complexes of Schiff base were evaluated for their microbial toxicity against a set of fungal strain. The antifungal results of the investigated compounds are given in Table 8. Compounds (**5**) and (**7**) are found to show significant antifungal activity against the test fungi. Compound (**3**) also shows good antifungal activity. Compounds (**2**) and (**4**) show no fungal activity. The activity varies with variation of R groups, attached with the Sn. Apparently, the function of the ligand is only to support the transport of the active organotin(IV) moiety to the site of action where it is released by hydrolysis [29].

The synthesized reported compounds were screened for antibacterial activity by the agar well diffusion method [28] at concentration of 10 mg ml^{-1} of DMSO. The zone of inhibition diameter was measured in mm and the reference drug used was Imipenum. All bacterial strains have clinical implication; *Escherichia coli*, infection of wounds, urinary tract and dysentery; *Bacillus subtilis*, food poisoning; *Shigella flexenari*, blood diarrhea with fever and severe prostration; *Staphlococcus aureus*, food poisoning, scaled skin syndrome, endrocarditis; *Pseudomonas aeruginosa*, infection of wounds, eyes, septicemia and *Salmonella typhi*, typhoid fever, localized infection. The antibacterial data are given in Table 9. Compound (**2**) shows excellent activity and compounds (**6**) and (**7**) show good activity against all of these tested becteria. From the biological screeing results, it is concluded that (i) triphenyltin(IV) derivative has high toxicity but good antifungal activity, (ii) trimethyltin(IV) derivative is least toxic as well as good antifungal, (iii) compound (**2**) is excellent antibacterial and has no fungal activity.

Proposed Structure

The possible structures for organotin(IV) complexes of Schiff base HL, concluded based on the spectroscopic data given in Tables 2-6, are given in Fig. 2.

Table 7. Brine Shrimp (Artemia Salina) Lethality Bioassay for Organotin(IV) Complexes of Schiff Base

Compound	Dose ($\mu g\ ml^{-1}$)	No. of Shrimps	No. of Survivors	LD_{50} ($\mu g\ ml^{-1}$)	Standard drug	LD_{50} ($\mu g\ ml^{-1}$)
	100	30	0			
HL	10	30	0	-	Etoposide	7.46
	1	30	1			
	100	30	22			
(**1**)	10	30	24	-	Etoposide	7.46
	1	30	27			
	100	30	24			
(**2**)	10	30	25	-	Etoposide	7.46
	1	30	27			
	100	30	26			
(**3**)	10	30	26	-	Etoposide	7.46
	1	30	28			
	100	30	24			
(**4**)	10	30	24	-	Etoposide	7.46
	1	30	29			
	100	30	0			
(**5**)	10	30	1	1.12	Etoposide	7.46
	1	30	18			
	100	30	0			
(**6**)	10	30	0	3.72	Etoposide	7.46
	1	30	0			
	100	30	0			
(**7**)	10	30	0	5.98	Etoposide	7.46
	1	30	1			

Table 8. Antifungal Activity[a-c] (%Inhibition) for Organotin(IV) Complexes of Schiff Base

Fungus (ATCC No.)	Inhibition (%)								MIC ($\mu g\ ml^{-1}$)
	HL	(**1**)	(**2**)	(**3**)	(**4**)	(**5**)	(**6**)	(**7**)	
Trichophyton longifusus (22397)	0	30	0	80	0	80	20	80	70.0
Candida albicans (2192)	0	0	0	0	0	20	0	90	110.8
Aspergillus flavis (1030)	0	0	0	0	0	50	50	90	20.0
Microsporum canis (9865)	0	50	0	80	0	80	0	80	98.4
Fusarium solani (11712)	0	0	0	0	0	50	50	40	73.2
Candida glaberata	0	0	0	0	0	20	20	90	110.8

[a]Concentration: 100 $\mu g\ ml^{-1}$ of DMSO. [b]MIC: Minimum inhibitory concentration. [c]Percent inhibition (standard drug) = 100.

Table 9. Antibacterial Activity[a-c] (Diameter of Inhibition Zone after 20 h) for Organotin(IV) Complexes of Schiff Base

Bacterium (ATCC No.)	Inhibition zone diameter (mm)								Reference drug
	HL	(**1**)	(**2**)	(**3**)	(**4**)	(**5**)	(**6**)	(**7**)	
Escherichia coli	-	15	22	0	0	0	12	12	35
Bacillus subtilis (11774)	-	0	24	0	0	0	12	12	38
Shigella flexenari (700390)	-	0	17	0	0	0	12	12	32
Stephlococcus aureus (25923)	-	0	18	0	0	0	0	0	38
Pseudomonas aeruginosa (10145)	-	12	14	12	0	23	14	15	29
Salmonella typhi (10749)	-	10	20	16	10	20	18	22	28

[a]*In vitro*, agar well diffusion method, conc. 3 mg ml^{-1} of DMSO. [b]Reference drug, Imipenum. [c]Clinical Implication: *Escherichia coli*, infection of wounds, urinary tract and dysentery; *Bacillus subtilis*, food poisoning; *Shigella flexenari*, blood diarrhea with fever and severe prostration; *Staphlococcus aureus*, food poisoning, scaled skin syndrome, endrocarditis; *Pseudomonas aeruginosa*, infection of wounds, eyes, septicemia, *Salmonella typhi*, typhoid fever, localized infection.

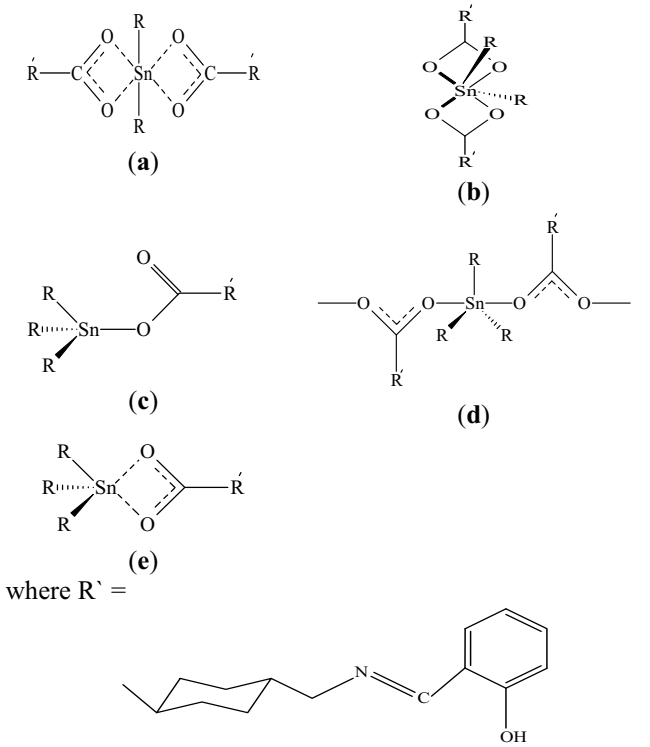


Fig. 2. Proposed structures (a), (b) for diorganotin(IV) derivatives, and (c), (d), (e) for triorganotin(IV) carboxylates.

CONCLUSIONS

Elemental analysis shows a good agreement between the calculated and observed % of C, H and N. The FT-IR spectra clearly demonstrate that the organotin(IV) moieties react with [O,O] atoms of the ligand and ligand behaves as bidentate for coordination to tin. Detailed studies of the reported complexes in solution state indicate that their structure is tetrahedral for triorganotin(IV) complexes, while the polymeric structure was exhibited by triorganotin(IV) complexes having a penta coordinated geometry around tin atom. Diorganotin(IV) complexes show the coordination number greater than four, probably five or six, in solution state. Mass spectral data are also in agreement with the proposed molecular formulae of all the synthesized compounds with no molecular ion peak. Organotin(IV) complexes are found to be active against tested Brine Shrimp larvae, bacteria and fungi with few exceptions.

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REFERENCES

[1] L. Pellerito, L. Nagy, Coord. Chem. Rev. 224 (2002) 111.

[2] E.R.T. Tiekink, Appl. Organomet. Chem. 1 (1991) 5.

[3] C.J. Evans, S. Karpel, J. Organomet. Chem. 1 (1985) 16.

[4] M.F. Mahon, K.C. Molloy, P.C. Waterfield, J. Organomet. Chem. 361 (1989) C5.

[5] P. Quevauviller, R. Ritsema, R. Morabit, W.M.R. Dirkx, Appl. Organomet. Chem. 541 (1994) 8.

[6] S. Belwal, R.K. Saini, R.V. Singh, Indian J. Chem. 37A (1998) 245.

[7] A.J. Crowe, Appl. Organomet. Chem. 1 (1987) 143.

[8] E.R.T. Tiekink, Appl. Organomet. Chem. 1 (1991) 5.

[9] I. Sakiyan, E. Logoglu, S. Arslan, N. Sari, N. Sakiyan, Bio-Met. 17 (2004) 115.

[10] Z.H. Chohan, M. Hassan, K.M. Khan, C.T. Supuran, J. Enz. Inhib. Med. Chem. 20 (2005) 183.

[11] M. Danish, S. Choudhary, M.R. Churchill, K.M. Keil, A.V. Eliseev, J.R. Morrow, Inorg. Chem. 40 (2001) 1591.

[12] R. Karmakar, C.R. Choudhury, S. Mitra, L. Dahlenburg, Struct. Chem. 16 (2005).

[13] S.K. Sahu, V. Chakravortty. J. Radioanal. Nucl. Chem. 227 (1998) 163.

[14] S. Shahzadi, K. Shahid, S. Ali, Russian. J. Coord. Chem. 33 (2007) 403.

[15] K. Shahid, S. Shahzadi, S. Ali, M. Mazhar, Bull. Korean Chem. Soc. 27 (2006) 44.

[16] W.L.F. Armarego, C.L.L. Chai, Purification of Laboratory Chemicals, 5th ed., Butterworth-Heinemann, London, 2003.

[17] H. Unver, Spectrosc. Lett. 34 (2001) 783.

[18] M. Parvez, S. Ahmad, S. Ali, M.H. Bhatti, M. Mazhar, Acta Cryst. E60 (2004) m554.

[19] L.Q. Xie, Z.Q. Yang, Z.X. Zhang, D.K. Zhang, Appl. Organomet. Chem. 6 (1992) 193.

[20] Q. Xie, Z. Yang, L. Jiang, Main Group Met. Chem. 19 (1996) 509.

[21] H.D. Yin, C.H. Wang, Y. Wang, C.L. Ma, J.X. Shao, J.H. Zhang, Acta Chim. Sinica 60 (2002) 143.

[22] M. Danish, S. Ali, A. Badshah, M. Mazhar, H. Masood, A. Malik, G. Kehr, Synth. React. Inorg. Met.-Org. Chem. 27 (1997) 863.

[23] H.O. Kalinowski, S. Berger, S. Braun, Carbon NMR Spectroscopy, Chichester, John Wiley & Sons, UK, 1988.

[24] M. Nadvornik, J. Holecek, K. Handlir, A. Lycka, J. Organomet. Chem. 275 (1984) 43.

[25] J. Holeček, A. Lycka, Inorg. Chim. Acta 118 (1986) L15.

[26] M. Danish, S. Ali, M. Mazhar, A. Badshah, M.I. Choudhary, H.G. Alt, G. Kehr, Polyhedron, 14 (1995) 3115.

[27] M. Gielen, M. Boualam, E.R.T. Tiekink, Appl. Organomet. Chem. 8 (1994) 19.

[28] A. Rahman, M.I. Choudhary, W.J. Thomsen, Bioassay Techniques for Drug Development, Hardward Academic Press, Amsterdam, 2001.

[29] M. Jain, S. Gaur, V.P. Singh, R.V. Singh, Appl. Organomet. Chem. 18 (2004) 73.