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Biological aspects of new organotin(IV) compounds of 3-maleimidopropionic acid

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Abstract

Four new compounds of organic mono carboxylic acid, 3-maleimidopropionic acid; with $Bu_2Sn(IV)^{2+}$, $Ph_3Sn(IV)^+$ and $Cychex_3Sn(IV)^+$ having ligand to metal ratio 1:2 and 1:1 were prepared. The spectrophotometric techniques used for structure determination like ^1H-, ^{13}C- and ^{119}Sn-NMR, FT IR and ^{119m}Sn Mössbauer have demonstrated that the organotin(IV) moieties establish chemical bonding with the ligand through carboxylic oxygen atom. The percent CHN analyses and MS data also corroborates the spectroscopic results. During in vitro LD_{50}, anti-fungal, anti-bacterial and anti-yeast bioassays promising results were exhibited. In vitro anti-tumour activity assays against five human tumor cell lines, MCF-7 Breast cancer–EVSA-T Breast cancer–WiDr Colon cancer–IGROV Ovarian cancer–M226 Non small cell lung cancer and anti-inflammatory screenings furnished the significant toxicities of the title complexes. In addition the triorganotin(IV) complexes were comparatively less toxic than the diorganotin(IV) complexes.

Keywords: 3-Maleimidopropionic acid; Dibutyltin complexes; Triphenyltin complex; Tricyclohexyltin complex

1. Introduction

The increasing interest in organotin(IV) carboxylates that has arisen in the last few decades is attributed to their significantly important biological properties like antiviral and anticancer agents, in vitro anti-bacterial and anti-fungal agents, wood preservatives and pesticides, etc., [1–6]. Further organotin(IV) carboxylates of *N*-protected amino acids have a number of interesting therapeutic applications as anti-tumour agents, etc. [5–9], whereas only one tributyltin(IV) derivative of 3-maleimidopropionic acid has been reported [10]. Literature divulges that little is known about the mode/mechanism of action of such complexes, etc., and requires structural information for better understanding. As an outcome of several attempts it has been assumed that the organic ligand facilitates the transportation of the complexes across the cell membrane, while the anti-tumour activity would be wielded by the dissociated organotin(IV) moieties [1–3].

Based on these facts, we have extended previous work, with the synthesis and characterization of new organotin(IV) complexes containing 3-maleimidopropionic acid [7,8]. The choice of the ligand has been made keeping in view the biological significance [11] and to increase the hydrolysability of the organotin(IV) precursors due to formation of Sn–O bonds, permitting the attack of hydrolyzed R'_2Sn and R'_3Sn moieties on the tumour cells, thus enhancing the anti-tumour activity [3]. All the complexes and the ligand were tested for in vitro

Abbreviations: Bu; butyl; Ph; phenyl; Cychex; cyclohexyl.

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cytotoxicity against five human tumoural cell lines in order to correlate it with the interactions between organotin(IV) cations (R_2Sn^{++} and R_3Sn^{+}) and the ligand. Moreover, anti-fungal, anti-bacterial, anti-yeast and anti-inflammatory screening results have also been reported.

2. Results and discussion

2.1. Syntheses

The ligand 3-maleimidopropionic acid (compound V, Scheme 1) was synthesized according to a reported procedure [11]. Di-*n*-butyltin(IV)di-3-maleimidopropionato (compound I), bis[di-*n*-butyl{3-maleimidopropionato}-tin(IV)] oxide (compound II), triphenyltin(IV)3-maleimidopropionato (compound III), and tricyclohexyltin (IV)3-maleimidopropionato (compound IV) were synthesized as given in Scheme 1.

2.2. Spectroscopy of diorganotin(IV) derivatives I and II

Vibrational data obtained for the compounds I–V are depicted in Table 1 which are in good agreement with the one reported by others [12,13] for similar compounds and that the hydroxyl group absorption of the ligand disappeared in compounds I and II. The asymmetric and symmetric stretching vibrations of the maleimido, carbonyl, of M–C (Metal–Carbon) and M–O (Metal–Oxygen) groups were exhibited as reported [13]. The asymmetric and symmetric stretching of the CO group in compound I (monomer) showed following trend:

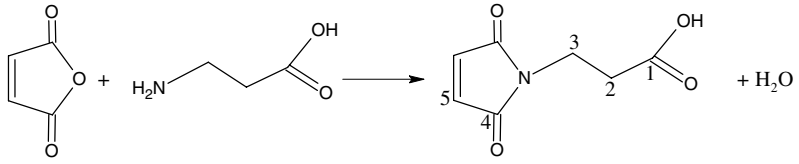
$$\nu_{\text{asym (compound)}} > \nu_{\text{asym (ligand)}},$$
$$\nu_{\text{s (compound)}} < \nu_{\text{s (ligand)}}, \quad \Delta\nu_{(\text{compound})} > \Delta\nu_{(\text{ligand})}.$$

Compound I showed unidentate or weak bidentate bonding with Sn(IV) atom. Two types of CO absorption bands were observed at 1680–1376 cm^{-1} for bonding behavior and 1721–1690 cm^{-1} for non-bonding behavior, which indicated two dissimilar tin sites for compound II. The order of asymmetric and symmetric stretching of CO group of compound II with respect to ligand is as:

$$\nu_{\text{asym (compound)}} < \nu_{\text{asym (ligand)}},$$
$$\nu_{\text{s (compound)}} < \nu_{\text{s (ligand)}}, \quad \Delta\nu_{(\text{compound})} > \Delta\nu_{(\text{ligand})}.$$

The butyl protons in mono and dimer were resolved on appropriate positions as reported [14–16]. The compound I exhibited a single triplet for methylenic protons of Sn(IV) atoms, signifying one tin site, conversely two triplets of methylenic protons in compound II are due to the unequivalent surroundings of the same protons bonded to *endo*- and *exo*-tin(IV) atoms. In the ^{13}C NMR spectrum for compound I only one signal was observed for each methylenic carbon of the butyl group; on contrary a pair of signals in II around *exo*- and *endo*-cyclic Sn(IV). Furthermore, the covalently attached R group to Sn furnished a trend $[^1J] \gg [^2J] < [^3J]$ for the coupling constants $^nJ(^{119}Sn–^{13}C)$ ably supported by the literature [17–20].

Ligand Compound V:



Compound I:

$$Bu_2SnO + 2RCOOH \longrightarrow Bu_2Sn(OOCR)_2 + H_2O$$

Compound II:

$$4Bu_2SnO + 4RCOOH \longrightarrow [\{Bu_2Sn(OOCR)\}_2O]_2 + 2H_2O$$

Compounds III & IV:

$$R'_3SnCl + RCOOHNEt_3 \longrightarrow RCOOSnR'_3 + Et_3NHCl$$

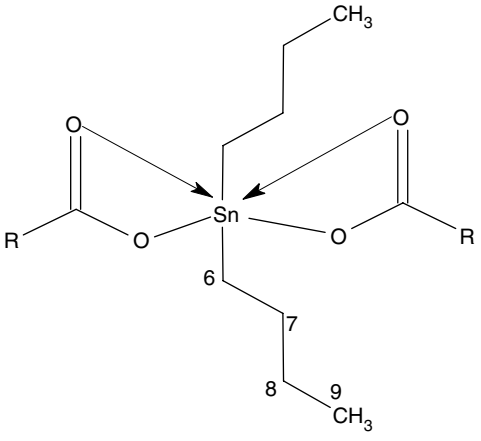
Where R'= phenyl or cyclohexyland

RCOOH = 3-maleimidopropionic acid (V).

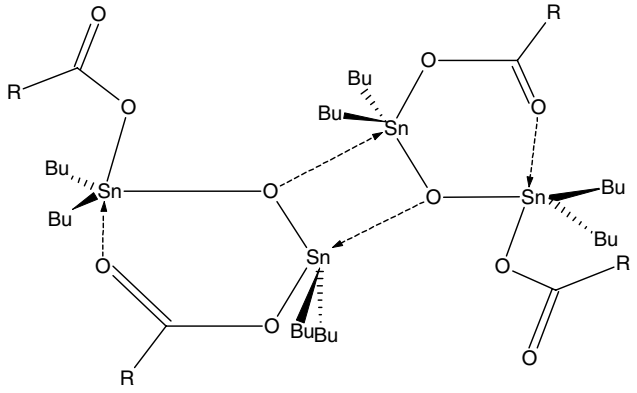
Scheme 1.

Table 1
Characteristic FT IR (cm^{-1}) spectroscopic bands of ligand and complexes formed with different di- and triorganotin(IV) cations (s, strong; sp, sharp; b, broad; v, very; m, medium; w, weak; –, absent)

Assigned	I	II	III	IV	V
ν(Sn–O)	510 wsp	490 sp	503 w	509 w	–
ν(Sn–C)	521 sp	535 wsp	545 sp	540 sp	–
$\nu_s(C_2O_2N)$ Maleimido	1720 ssp	1721 ssp	1716 sb	1700 sb	1718 sb
$\nu_{asym}(C_2O_2N)$ Maleimido	1778 sp	1779 sp	1772 sp	1770 sp	1779 mb
$\nu_s(COO^-)$ Carbonyl	1379 sb	1376/1690 sb/sp	1350 sb	1381 sb	1685 ssp
ν_{asym} (COO^-) Carbonyl	1722 sp	1680/1721 sb/sp	1684 sp	1690 sp	1715 mb
$\Delta\nu$	325	304	334	309	30



Scheme 2.



Bu = Butyl (-$\overset{6}{C}H_2$-$\overset{7}{C}H_2$-$\overset{8}{C}H_2$-$\overset{9}{C}H_3$)

Scheme 3.

^{119}Sn NMR spectra of compound I displayed a solitary resonance at −149.8 ppm; whilst for compound II a pair of resonances of equal intensities at −213.1 and −215.2 confirming *endo*- and *exo*-cyclic tin atoms, respectively [8]. The Mössbauer parameters were around 3.42 mm s^{-1} for compound I supporting octahedral geometry around tin atom of compound I in solid (Scheme 2) [14,15,17–20]. The large quadrupole splitting value (QS = 3.67 mm s^{-1}) for compound II, recommended penta-coordinate environment in solid state, indicating a tetrabutyl bis(2-maleimidoacetato) distannoxane dimer type (Scheme 3).

Merely Mössbauer spectra cannot distinguish two different tin atoms since this method is less sensitive to small variations to the tin environment than ^{119}Sn NMR spectroscopy [8]. The carboxylates (R) linked with *exo*- and *endo*-cyclic tins should produce different R signals; however, in the NMR spectra there is only one set of signals for R group obviously due to very similar environments. To date there is no report dealing with the non-equality of carboxylate groups in such compounds. There may be fast exchange in the coordination behavior of carboxylate groups attached to *endo*- and *exo*-cyclic tin atoms as reflected by different butyl signals in NMR spectra. A possible mechanism to explain this fluxional behavior is proposed in Scheme 4.

The salient feature of MS studies is the cleavage of O–Sn (Oxygen–Tin) bond because it is the most labile one in both the complexes. This cleavage results in two complementary ions, we call cationic and the anionic parts of the molecule. The cationic part (m/z = 233) is identical for both the molecules (see observed ions in Section 5). The structures of the observed ions are easily proposed by correlation with the known structure of the cationic part. The ^{1}H-, ^{13}C-, ^{119}Sn NMR, QS and FT IR data substantially authenticate the structures of compounds I and II in Schemes 2 and 3, respectively. The %CHN analysis and MS data also confirms the mono and dimeric composition of compounds I and II.

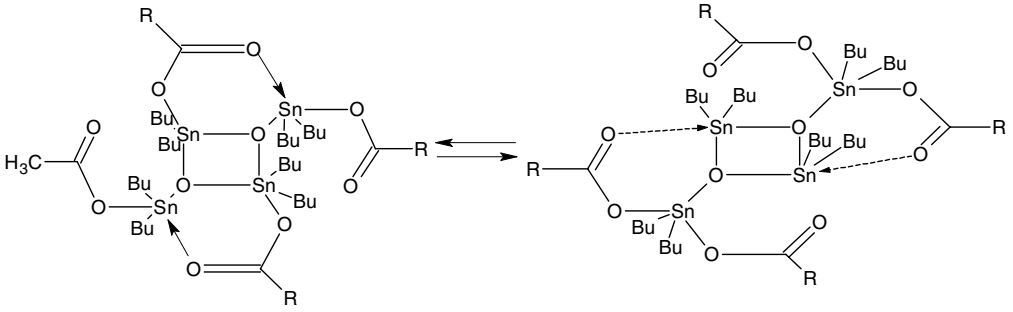
2.3. Spectroscopic discussion of triorganotin(IV) derivatives III and IV

In the solid state FT IR spectra, penta coordination of tin was indicated via shifting of the CO band for compound III at 1684_{asym} and 1350_{sym} and for compound IV at 1690_{asym} and 1381_{sym} [16] (Scheme 5).

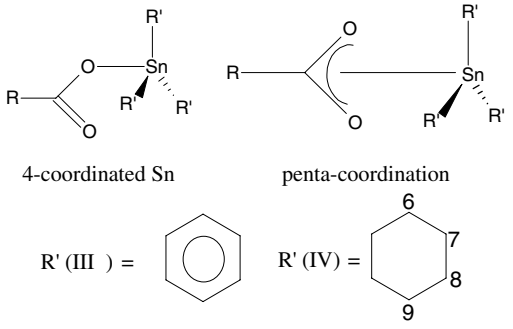
The Carbonyl (CO) stretching of compounds III and IV followed a trend like:

$$\nu_{asym\ (compound)} < \nu_{asym\ (ligand)},$$

$$\nu_{s\ (compound)} < \nu_{s\ (ligand)}, \quad \Delta\nu_{(compound)} > \Delta\nu_{(ligand)}.$$



Scheme 4.

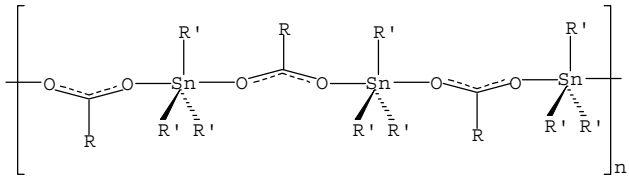


Scheme 5.

Multinuclear NMR techniques fell short in providing any clue about such mode of coordination in inert solvent rather exhibit 4-coordinated monomeric species consistently as suggested for comparable systems (Scheme 5) [14,21–23].

The anticipated NMR resonances are assigned by the intensity, multiplicity and coupling constant pattern. The exhibited $^{1}J(^{119}\mathrm{Sn}–^{13}\mathrm{C})$ coupling constants in solution are characteristic of tetrahedral compounds, being of the order of 651 Hz for triphenyltin(IV) and 359 Hz for tricyclohexyltin(IV) esters [9].

The ^{119}Sn NMR signals are in the range of −115.8 ppm for compound III and 9.3 ppm for the compound IV recommends also 4-coordinate environment around tin(IV) atom. Based on the spectroscopic data and literary evidences, the compounds III and IV lead to a 5-coordinated polymeric trigonal bipyramidal geometry in the solid (Scheme 6) and a tetrahedral geometry in inert solvent [22].



Scheme 6.

The ^{119m}Sn Mössbauer spectra of compounds III and IV display quadrupole splitting values of 3.40 and 3.58 mm s^{-1}, respectively. Relying on reported data the compounds having QS values between 3.40 and 3.70 mm s^{-1}, have 5-coordinated chain structure, trigonal bipyramidal geometry with a bridging carboxyl group in solid (Scheme 6) [9,21] and a tetrahedral geometry in inert solvents (Scheme 5) [3,6,21]. The ρ = QS/IS also supports the same geometry [9,21]. In the mass spectra of III and IV $R'_3Sn–O$ fragments gave peaks of considerable intensities, confirming the spectroscopic data. Due to lack of XRD facility, the X-ray studies of compounds I–V could not be carried out.

3. Bioassays

The diorganotin compounds I and II exhibited considerable anti-fungal and anti-bacterial activities as compared to triorganotin(IV) compounds III and IV and the reference drugs in clinical use (Tables 2 and 3). The ED_{50} values in the anti-fungal bioassay for I, II and III, IV are <1 and 0.01–10.80 ppm, respectively. It demonstrates that the compounds III and IV possess a higher degree of selectivity in their fungal toxicity against all pathogens. Similar trend was observed for diorganotin(IV) compounds I and II during the in vitro Brine shrimp and anti-yeast bio-assays [Tables 4 and 5].

Triorganotin(IV) compounds III and IV in comparison with diorganotin(IV) compounds I and II, found to be moderately toxic in anti-tumour and anti-inflammatory biological activity screenings (Tables 6 and 7). Whereas literature reveals that R'_3SnR complexes have a better capacity than other classes like R'_2SnR_2, $R'SnR_3$, while the tetraalkyltins (R'_4Sn) are very toxic to many species including humans, which can be explained in terms of ligand's toxicity and the degree of hydrophilicity of the complexes. [1–6]. In addition diorganotin(IV) compounds can affect the cellular metabolism, while the triorganotin(IV) compounds mediate an exchange of hydroxyl ions across the mitochondrial membranes [24–26]. There-

Table 2
ED_{50} values for compounds I–V against selected plant-, human- and animal pathogenic fungi

Fungus	I	II	III	IV	V	A	B
Alternaria padwicki[a]	0.891	0.451	1.126	7.891	8.914	1.619	3.022
Botryodiplodia theobromae 122	0.659	0.328	2.043	6.357	2.585	1.014	0.014
Colletotrichum mause	0.585	0.519	0.218	3.553	3.654	0.935	0.924
Colletotrichum mause 246	0.872	0.203	1.251	9.989	10.12	1.087	1.396
Colletotrichum mause 273	0.211	0.397	3.018	8.255	11.04	2.105	0.613
Colletotrichum gloeosporiodes 282	0.027	0.012	2.022	6.363	36.27	1.004	7.035
Pestalotiposis guepini	0.361	0.567	0.410	7.295	2.368	0.528	0.197
Phytopohothora palmivora	0.299	0.882	0.040	8.096	0.291	1.094	9.127
Phytopohothora palmivora 139	0.031	1.213	4.060	9.087	0.986	2.909	2.178
Pyricularia oryzae	0.012	1.111	1.087	8.025	0.645	0.897	0.034
Trichophyton schoenlem[b]	0.015	0.141	1.248	5.013	1.253	0.935	0.807
Pseudallescheria boydii	0.093	1.122	4.011	3.915	2.965	6.872	0.397
Candida albicans	0.247	0.390	3.149	10.80	3.629	2.405	1.735
Aspergillus niger	0.598	0.822	3.363	1.817	0.852	0.034	6.341
Microsporum canis[c]	0.022	0.947	2.945	2.095	0.999	0.005	5.938
Trichophyton mantagrophytes	0.027	0.686	4.912	3.082	9.368	0.947	0.197
Trichophyton rubrum	0.012	0.692	5.010	5.671	14.84	0.386	3.108

Incubation temperature, 27 (28 ± 1 °C); incubation period 7 (7–10 days); reference drugs: (A) Miconazole and (B) Amphotericin B.
[a] Plant pathogens.
[b] Human pathogens.
[c] Animal pathogens.

Table 3
Anti-bacterial bioassay

Bacteria	Activity of compounds							
	I	II	III	IV	V	A	B	C
Bacillus cereus[a]	+++	++++	++	+	+	++	+	++
Bacillus subtilis	++++	++++	++	+	++	+	++	+
Cornyebacterium diphtheriae	+++	++++	+	++	++	++	+	+
Escherichia coli ETEC	++	+++	++	+++	+	+++	+++	+
Klebsiella pneumoniae	+++	++++	++	+	+	++	+	++
Salmonella typhi	++++	++++	+++	+	++	+	+	+++
Staphylococcus aureus	+++	+++	+	+	++	++	++	+
Shigella boydii	++++	+++	++	+	+	+	+	++
Pseudomons aeroginosa	++++	++	+	++	+	++	++	+++
Proteus mirabillis	+++	+++	++	+	++	++	++	+
Streptococcus pyogenes	++++	+++	++	++	+	+	+	++

Key: ++++, significant; +++, good; ++, moderate; +, weak activity; reference drug: (A) Amoxicillin (H_2O), (B) Ampicillin (H_2O), (C) Cephlaxin Na.
[a] Human pathogens; incubation period: 8 h, 37 °C; colony forming unit = 10^4–10^6; size of well = 5 mm radius.

Table 4
Brine shrimp bioassay

Compounds	% Deaths at doses			LD_{50} μg/ml
	0.1 μg/ml	0.05 μg/ml	0.025 μg/ml	
I	20	15	83	0.0527
II	10	26	77	0.0581
III	0	4	7	56.0396
IV	5	7	8	51.0022
V	11	8	4	45.0124

Table 5
Anti-yeast bioassay

Name of yeast[a]	Activity					
	I	II	III	IV	V	Streptonigrin
(m). RS 322Y (RAD52)	++++	++++	++	+	+	++
(w). LF 15 (RAD_+)	++++	++++	++	++	++	++

Key: ++++, very high; ++, optimum; +, no activity.
[a] *Saccharomyces cerevisiae*.

fore, the difference in overall response of the reported complexes in reference to toxicity is presumably due to the difference in the degree of hydrolyzability, which in a way is a function of the ligand attached and the geometry attained by the compounds in the solution [1,3].

Table 6
In vitro anti-tumour screening (ng/ml) of compounds I–V together with those of some reference drugs in clinical use

Compounds	MCF-7	EVSA-T	WiDr	IGROV	H226
I	31	23	15	25	34
II	25	18	55	24	36
III	124	355	232	155	>300
IV	115	101	122	182	84
V	1500	490	720	360	980
Cisplatin	1220	940	1160	960	880
5-Fluorouracil	1130	720	890	850	470
Methotraxate	48	96	52	32	44
Doxorubicin	190	85	44	76	170

Table 7
Anti-inflammatory activity on Albino mice

Dose (mg/kg)	No. of writhes[a]	Percentage of inhibition by compounds					
		I	II	III	IV	V	Aspirin[b]
Control	62						–
10		24(47)	44(35)	21(49)	06(58)	18(51)	–
50		63(23)	42(36)	34(41)	39(38)	37(39)	–
100		87(8)	82(11)	39(38)	77(14)	34(41)	–
150							35(44)

Note. Writhes remained are given in parentheses.
[a] Acetic acid.

4. Conclusions

The ^{119}Sn–NMR spectra revealed only one sharp signal for compound I, while compound II exhibited two signals due to non-equivalent *exo*- and *endo*-Sn(IV) atoms. The behavior of CO groups of monomer (compound I) in IR supports weak bidentate coordination to Sn(IV), which also gives clue about its octahedral geometry in solid, aptly supported by Mössbauer data too. Dimer (compound II) shows two signals of equal intensity in the ^{119}Sn NMR spectrum. The *exo*-tin(IV) atom may be bonded in monodentate mode with carboxylic oxygen of ligand, while the *endo*-cyclic tin(IV) atom in bidentate mode. This mode of coordination with *exo*-cyclic tin atoms results in penta coordination, trigonal bipyramidal geometry [16].

Tetrahedral geometry is assigned to triorganotin(IV) monomers in inert solvent and polymeric trigonal bipyramidal in solid state.

The bioassays of triorganotin(IV) class of compounds exhibited strange behavior in present chemistry when compared with previous work [7–9]; normally this class of organotins is more active than the diorganotin(IV) compounds. But this time round diorganotins remarkably proved to be more potent than the triorganotins; which may be to due the complexation of bioactive 3-maleimidopropionic acid [11]. Toxicity also increases due to the attached R group, in the $R_{n-1}SnL$ unit; the L (RCOO) plays an important role after hydrolysis for the transportation of the organotin(IV) moiety to an action site [1–4,7,27,28].

5. Experimental

5.1. Materials

Maleic anhydride, 3-aminopropionic acid, di-*n*-butyltin(IV) oxide, triphenyltin(IV) chloride, tricyclohexyltin(IV) chloride and triethylamine are Merck Chemicals (AR Grade) used as such. Standard procedures were adopted for drying of all the organic solvents used during the synthesis of compounds I–V [28].

5.2. Instruments

Elemental analyses (C, H, N) were performed on a Yanaco high-speed CHN analyzer; antipyrene was used as a reference. Melting points were taken on Reichert Thermovar of F.G.Bode Co. Austria.

The FT IR spectra of the ligand and the complexes in the KBr pellets were measured on a Perkin–Elmer FTIR 1605 Spectrophotometer in the range of 4000–400 cm^{-1}. ^{1}H, ^{13}C and ^{119}Sn spectra were recorded on a multinuclear FT NMR 200 MHz spectrometer of JEOL operating at room temperature (200 MHz for ^{1}H, 50 MHz for ^{13}C and 93.28 MHz for ^{119}Sn) in deutero-chloroform ($CDCl_3$). The proton and carbon chemical shifts, δ, were measured with respect to $SiMe_4$, whereas tin chemical shifts were measured with respect to $SnMe_4$.

For Mössbauer measurements, the solid samples were maintained at liquid nitrogen temperature (77.3 K) V.G. Micromass 7070 F Cryolid liquid nitrogen cryostat. The multichannel calibration was performed with an enriched iron foil using ^{57} Co–Pd source, while the zero point of the Doppler velocity scale was determined through the absorption spectra of $CaSnO_3$ (^{119}Sn = 0.5 mg cm^{-2}). The resulting 5×105 count spectra were refined to obtain the isomeric shift, IS (mm s^{-1}), the nuclear quadrupole splitting QS, ρ (mm s^{-1}) and the width at half-height of the resonant peaks, Γ (mm s^{-1}). Mass spectra were recorded using model MAT 112 and 113, Double Focusing Mass Spectrometer (Finnigan) connected to IBM at compatible PC based system.

The ED_{50} values have been calculated based on the colony growth (radial extension) measurements of the test fungus over a 6-day period using Miconazole and Amphotericin B as reference drugs [29]. The organotin(IV) test solutions were freshly prepared in chloroform and aseptically added to malt agar extract to have a final concentration 1–100 μg cm^{-3}. Mixture was placed in Petri dishes, inoculated with fungal cultures growing on malt agar extract or corn meal agar and incubated for 6 days. Colony diameter was taken as the mean of two perpendicular diameters. A probit-log

concentration analysis was performed to calculate the effective doses for 50% inhibition of fungal growth (ED_{50}) [30]. The anti-bacterial activity was measured by agar-well diffusion method, Amoxicillin (H_2O), Ampicillin (H_2O) and Cephlaxin Na were used as reference drugs [7,32]. Brine shrimp hatching method was adopted for determination of LD_{50} of all the compounds as reported [12]. The in vitro anti-tumour activity tests against five human tumoral cell lines, MCF-7 Breast cancer–EVSA-T Breast cancer–WiDr Colon cancer–IGROV Ovarian cancer–M226 Non-small cell lung cancer, were measured using Cisplatin, 5-Flourouracil, Methatroxate and Doxurubicin as reference drugs, implying the standard procedure [31]. The anti-yeast bioassay of I–V against mutant (*Saccharomyces cerevisiae*, Rs 322Y RAD52) and wild types strains (*Saccharomyces cerevisiae* LF15RAD$_+$) was determined; using Streptonigrin as a reference drug [32]. Anti-inflammatory activity tests were conducted on Albino mice. A number of writhing responses for each animal were recorded. Aspirin and acetic acid was used as a reference drug and writhe producer, respectively [32].

6. Spectroscopic data

%CHN Analyses: calculated values are given in parenthesis, antipyrene was standard.

NMR: Solvent used: $CDCl_3$; standard $SiMe_4$ and $SnMe_4$; abbreviations: s, singlet; d, doublet; t, triplet; m, complex pattern; no, not observed; coupling constants are given in Hz between parenthesis for $^nJ(^{119}Sn–^{13}C)$.

Mössbauer data: QS: quadrupole splitting; IS: isomer shift, all in mm s^{-1}.

Selected cationic fragments of I–V have been given (in *m/z*) taking C = 12, H = 1, N = 14, O = 16 and Sn = 119, percent relative abundances of fragments are given in parenthesis.

6.1. Compound I

The monomer compound I was prepared by dissolving 1.00 g (8.034 mM) di-*n*-butyltin oxide to 1.3589 g (4.017 mM) ligand in 150 cm^3 of toluene and 50 cm^3 ethanol. The homogeneous solution was refluxed for 6 h and the ternary azeotrope water/ethanol/toluene was distilled off with Dean–Stark funnel. Solvent was removed on a rotary evaporator. The oily residue obtained was solidified from methanol.

Yield: 2.808 g (91%), m.p.: >350 °C (from CH_3OH), %CHN Analyses: C, 46.39(46.41); H, 5.35(5.38); N, 4.90(4.92). δ_H: H2: 2.69, t (7.8); H3: 3.5, t (6.3); H5: 7.0, s; H6: 2.93, m; H7: 1.95, m; H8: 1.43, m and H9: 0.95, m. δ_C: C1, 195.3; C2, 35.9; C3, 41.6; C4, 168.1; C5, 135.0; C6, 12.2 [$^1J(^{119}Sn–^{13}C) = 571$]; C7, 27 [$^2J(^{119}Sn–^{13}C) = 43$]; C8, 26.1 [$^3J(^{119}Sn–^{13}C) = 79$]; C9, 15.1. δ_{Sn}: −149.8. ^{119m}Sn Mössbauer data (mm s^{-1}): QS, 3.42; IS, 1.33; Γ_1, 1.15; Γ_2, 1.20; ρ = QS/IS, 2.57. MS: $[Bu_2Sn]^+$, *m/z* = 233 (73%); $[R - C]^+$, *m/z* = 136 (56%); $[COOH]^+$, *m/z* = 45 (39%); $[Bu]^+$, *m/z* = 57 (65%); $[CH_3]^+$, *m/z* = 15 (21%); $[CH_3–CH_2]^+$, *m/z* = 29 (68%).

6.2. Compound II

Di-*n*-butyltin oxide 1.00 g (4.017 mM) and the ligand 0.3404 g (4.017 mM) in equimolar ratios were dissolved in chloroform and dry benzene, refluxed for 4 h, water formed was removed as ternary azeotrope water/benzene/chloroform using a Dean–Stark funnel. After the completion of the reaction, the solvent was removed on a rotary evaporator leaving a brownish gel, which was dissolved in acetone and treated with animal charcoal giving a clear filterate. The acetone was removed under vacuo at room temperature; giving fine crystals of dimer compound II.

Yield: 1.4314 g (87%), m.p.: 158 °C (from C_6H_6/C_6H_{12}), %CHN Analyses: C, 44.99(44.02); H, 5.87(5.91); N, 3.40(3.42). δ_H: H2: 2.91, t (4); H3: 4.23, t (9); H5: 7.13, s; H6: 3.52/3.26, m; H7: 2.17/2.19, m); H8: 1.65/1.71, m and H9: 0.92/0.97, m. δ_C: C1, 174.1/176.3; C2, 23.9/25.1; C3, 36.2/35.4; C4, 168.3; C5, 134.2; C6, 20.51/10.2 [$^1J(^{119}Sn–^{13}C) = 57$/no]; C7, 13.9/16.8 [$^2J(^{119}Sn–^{13}C) = 51/48$]; C8, 24.02/21.8 [$^3J(^{119}Sn–^{13}C) = 79/83$]; C9, 14.4/13.6. δ_{Sn}: −213.1, −215.2. ^{119m}Sn Mössbauer data (mm s^{-1}): QS, 3.67; IS, 1.30; Γ_1, 0.88; Γ_2, 0.85; ρ = QS/IS, 2.82. MS: $[Bu_2Sn]^+$, *m/z* = 233(89%); $[Bu_2SnO_2]^+$, *m/z* = 265 (47%); $[R–CO]^+$, *m/z* = 152 (36%); $[Bu_2SnO]^+$, *m/z* = 249 (54%).

6.3. Compounds III and IV

The triorganotin(IV) complexes III and IV were synthesized by refluxing the equimolar quantities of triethylammonium salt of ligand [11] with triphenyltin(IV) chloride and tricyclohexyltin(IV) chloride, respectively, in toluene for 3 h. The precipitated triethylammonium hydrochloride formed during the course of this reaction was filtered off. The solvent was removed under vacuum and the solid mass left was crystallized from dichloromethane and benzene.

6.4. III

Yield: 1.23 g (92%), m.p.: 141 °C (from CH_2Cl_2), %CHN Analyses: C, 57.80(57.83); H, 4.25(4.27); N, 2.67(2.70). δ_H: H2: 2.68, t (10); H3: 3.81, t (7); H5: 7.01, s; H7: 7.54, m; H8: 7.21, m and H9: 7.36, m. δ_C: C1, 178.5; C2, 35.11; C3, 39.4; C4, 167.9; C5, 135.1; C6, 134.83 [$^1J(^{119}Sn–^{13}C) = 671$]; C7, 132.8 [$^2J(^{119}Sn–^{13}C)$ =

45]; C8, 130.3 [$^3J(^{119}Sn–^{13}C) = 48$]; C9, 131.5. δ_{Sn}: −115.8. ^{119m}Sn Mössbauer data (mm s^{-1}): QS, 3.40; IS, 1.50; Γ_1, 0.89; Γ_2, 0.81; ρ = QS/IS, 2.26. MS: $[R'_3Sn–O]^+$: $m/z = 366$ (31%); $[R'_3Sn]^+$: $m/z =$ 196 (48%); $[R']^+$: $m/z =$ 77 (17%); $[R'_3COOSn]^+$: $m/z = 287$ (53%).

6.5. IV

Yield: 1.13 g (85%), m.p.: 170 °C (from CH_2Cl_2+C_6H_6), %CHN Analyses: C, 44.99(44.02); H, 5.87(5.91); N, 3.40(3.42). δ_H: H2: 2.79, t (11); H3: 3.93, t (8); H5: 1.03, s; H6: 1.11, m; H7: 1.69, m; H8: 1.49, m and H9: 1.89, m. δ_C: C1, 171.21; C2, 35.2; C3, 39.1; C4, 170.0; C5, 134.3; C6, 22.9 [$^1J(^{119}Sn–^{13}C) = 421$]; C7, 26.2 [$^2J(^{119}Sn–^{13}C) = 23$]; C8, 28.4 [$^3J(^{119}Sn–^{13}C) = 69$]; C9, 26.6. δ_{Sn}: 9.3 ^{119m}Sn Mössbauer data (mm s^{-1}): QS, 3.58; IS, 1.45; Γ_1, 0.91; Γ_2, 01.20; ρ = QS/IS, 2.47. MS: $[R'_3Sn–O]^+$: $m/z = 384$ (53%); $[R'_3Sn]^+$: $m/z =$ 368 (50%); $[R'_2SnO]^+$: $m/z = 301$(78%); $[R']$: $m/z =$ 83 (63%).

6.6. Compound V

The compound V (ligand) 3-maleimidopropionic acid was synthesized according to a reported procedure [11].

Yield: 1.23 g (92%), m.p.: 108–109 °C (from C_6H_6), %CHN Analyses: C, 57.93 (57.94); H, 5.88 (5.91); N, 3.42 (3.44).

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