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Organotin(IV) Derivatives as Biocides: An Investigation of Structure by IR, Solution NMR, Electron Impact MS and Assessment of Structure Correlation with Biocidal Activity

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A brief account is given of the synthesis, structural chemistry and the antibacterial, antifungal and cytotoxic effects of organotin complexes of 2-[(2,4-dichloroanilinocarbonyl)]benzoic acid. The unimolar and bimolar substitution products have been characterized by elemental analysis and spectral studies, including IR, ^{1}H NMR, ^{13}C NMR, ^{119}Sn NMR, and mass spectra. The data support the binding of the oxygen atom to the tin atom in $[R_2Sn(OOCR^{/})_2]$ and $[R_3Sn(OOCR^{/})]$ (R = Me, Bu, and Ph, $R^{/}$ = 2-[(2,4-dichloroanilinocarbonyl)]benzoic acid). Based on these studies, with a coordination number of four, a distorted tetrahedral geometry has been proposed for the resulting derivatives in solution. The free ligand ($R^{/}COOH$) and its respective tin complexes were tested *in vitro* against a number of microorganisms to assess their biocidal properties and to correlate them with the structures of the derivatives.

Keywords: Structure correlation, Biocidal activity, Organotin(IV) complexes, Spectroscopic analysis

INTRODUCTION

Tin(IV) and organotin(IV) compounds, a deceptively simple area of inorganic and metal-organic chemistry, have been receiving more attention due to the important industrial [1,2] and environmental applications. Nitrogen, oxygen, and sulfur donor ligands have been used to enhance the biological activity of organotin derivatives [3]. Also organotin compounds with such ligands have widely been tested for their possible use in cancer chemotherapy. The coordination chemistry of tin is extensive with various geometries and coordination numbers known for both inorganic and organometallic complexes [4]. Higher coordination numbers can be generated by inter-/intramolecular interaction, especially in complexes where tin bonds to electronegative atoms, such as oxygen, nitrogen, and sulfur. Organotin compounds have gained an edge over other organometallics due to their bioavailability in the ecosystem and entrance into the food chain. Organotin compounds are now the active components in a number of biocidal formulations, finding applications in such diverse areas as fungicides, miticides, molluscicides, marine antifouling paints, surface disinfectants and wood preservatives [5].

Information on the structures of organotin complexes continues to accumulate, and new applications of organotin compounds are being discovered in industry, ecology and medicine. In recent years, investigations have been carried out to test their anti-tumor activity and it has been observed that indeed several diorganotin and triorganotin species show potential as antineoplastic agents [6].

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In view of the diverse fields of applications of organotin complexes, we have synthesized some new organotin(IV) derivatives with 2-[(2,4-dichloroanilinocarbonyl)]benzoic acid in continuation of our previous work [7-13]. Our aim is to determine the possible use of these compounds as biocides, as well as the structural correlation, *i.e.,* whether the biocidal activity is related to the organic part of the ligand or the organotin moiety. Further, we aim to investigate the spectroscopic behavior and elucidate the structure.

EXPERIMENTAL

Apparatus

Fourier transform infrared spectra of the ligand and its metal complexes were recorded as KBr pellets on a Bio-Rad FTIR spectrometer. ^{1}H, ^{13}C, and ^{119}Sn NMR spectra were recorded on a Bruker AM 250 spectrometer (Germany). ^{119}Sn NMR spectra were obtained with Me_4Sn as an external reference. Mass spectral data have been measured on a MAT 8500 Finnigan mass spectrometer (Germany). Melting points were determined by using an MP-D Mitamura Riken Kogyo (Japan) electrothermal melting point apparatus as open tubes and are uncorrected. C, H, and N were performed with an organic elemental analyzer, model EA 1110, CE Instrument, Italy. All the glass apparatuses used throughout the experimental work had standard quick fit joints and were dried at 120 °C.

Materials and Methods

Diorganotin dichloride and triorganotin chloride were purchased from Aldrich and were used without any further purification. Anhydrous toluene was obtained using a previously published method [14].

Synthesis of 2-[(2,4-Dichloroanilinocarbonyl)]benzoic Acid (Scheme 1)

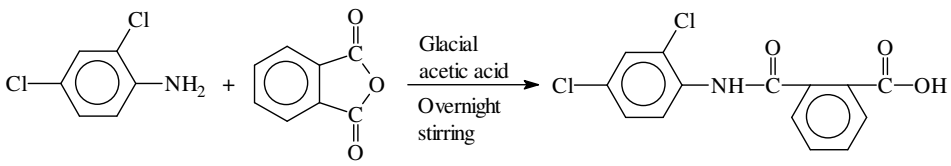
A solution of phthalic anhydride (10 mg, 67.5 mmol) in HOAc (300 ml) was added to a solution of 2,4-dichloroaniline (10.9 mg, 67.6 mmol) in HOAc (150 ml) in a 500 ml round bottom flask equipped with a water condenser and the mixture was stirred overnight at room temperature. The light grey precipitate was filtered, washed with cold distilled water (200 ml) and air dried.

Synthesis of Organotin(IV) Complexes of 2-[(2,4-Dichloroanilinocarbonyl)]benzoic Acid

2-[(2,4-Dichloroanilinocarbonyl)]benzoic acid (1 mg, 3.23 mmol) was suspended in a 250 ml round bottom two necked flask in dry toluene (100 ml) and treated with triethylamine (0.45 ml, 3.23 mmol). The mixture was refluxed for 2-3 h. Then diorganotindichloride (1.61 mmol) or triorganotin-chloride (3.23 mmol) was added as a solid to a reaction flask with constant stirring and the reaction mixture was refluxed for 8-10 h. The reaction mixture containing Et_3NHCl was filtered off such that the filtrate had the organotin derivative. The solvent was removed using a rotary apparatus. The mass left behind was recrystallized from a $CHCl_3$ and n-hexane mixture (1:1).

Cytotoxicity Studies

The cytotoxicity of the reported organotin compounds was studied by the Brine Shrimp method [15]. Thirty shrimp were transferred to each sample vial using a 9 inch disposable pipette (Scientific Products, diSPo pipettes), and artificial sea water was added to make the total volume in each vial 5 ml. The nauplii were counted macroscopically in the stem of the pipette against a lighted background. A drop of dry yeast suspension (Red Star, 3 mg in 5 ml artificial sea water) was added as food to each vial. The vials were maintained under illumination. Survivors were counted, with a 3 × magnifying glass, after 6 and 24 h, and the percent deaths at each dose and control were determined. The 24 h counts were more useful. In cases where control deaths occurred, the data were corrected using Abbott's formula [16]: %Dead = [(test-control)/control]



Scheme 1

× 100. The LD_{50} was determined from the 24 h counts using the probit analysis method described by Finney [17].

Antibacterial Activity

The antibacterial activities of the reported organotin compounds against *Escherichia coli*, *Bacillus subtilis* ATCC 11774, *Shigella flexneri* ATCC 700930, *Staphylococcus aureus* ATCC 25923, *Pseudomonas aeruginosa* ATCC 10145 and *Salmonella typhi* ATCC 10749 bacterial strains were screened using the agar well diffusion method [18,19]. Ampicillin $(H_2O)_3$ and Cephalexin Na were used as standard drugs. The wells were dug in the media using a sterile metallic borer with the centers at least 24 mm apart. Two- to eight-hour-old bacteria inoculums containing approximately 10^4-10^6 colony forming units (CFU)/ml were spread on the surface of nutrient agar using sterile cotton swabs. The recommended concentration of the test sample (2 mg ml^{-1} in DMSO) was introduced into the respective wells. Other wells were supplemented with DMSO and reference antibacterial drugs serving as negative and positive controls, respectively. The plates were incubated immediately at 37 ^oC for 20 h. The activity was determined by measuring the diameter of zones showing complete inhibition in millimeters. Growth inhibition was calculated with reference to positive control.

Antifungal Activity

The antifungal activities of synthesized compounds were tested against various pathogens, namely *Trichophyton longifusum* ATCC 22397, *Candida albicans* ATCC 2192, *Aspergillus flavipes* ATCC 1030, *Microsporum canis* ATCC 9865, *Fusarium solani* ATCC 11712 and *Candida glabrata,* by using the tube diffusion test [13,14]. Micoanazole (200 mg ml^{-1}), Ketoconazole (200 mg ml^{-1}), Amphotericin B (200 mg ml^{-1}) and Flucytosine (200 mg ml^{-1}) were used as standards drugs. Stock solutions of pure compounds (12 mg ml^{-1}) were prepared in sterile DMSO. Sabouraud dextrose agar was prepared by mixing Sabouraud agar (32.5 g), glucose agar (4%) and agar-agar (4 g) in 500 ml of distilled water followed by steamed dissolution. Into screw-capped tubes, media (4 ml) was dispensed and autoclaved at 121 ^oC for 15 min. Test compound (66.6 mg ml^{-1}) was added from the stock solution to nonsolidified Sabouraud agar media (50 ^oC). The tubes were allowed to solidify at room temperature and were inoculated with 4 mm diameter portion of inoculums derived from a 7-day-old respective fungal culture. For nonmycelial growth, an agar surface streak was employed. The tubes were incubated at 27-29 ^oC for 7-10 days and the growth in the compound containing media was determined by measuring the linear growth (in mm) and growth inhibition and comparing it to the respective control. The amount of growth inhibition was calculated as:

$$\text{Inhibition (\%)} = [(A-B)/B] \times 100$$

A = Diameter of fungal colony in control plate
B = Diameter of fungal colony in test plate

RESULTS AND DISCUSSION

The elemental analyses agree well with the proposed formula of the complexes. All the reported compounds were prepared by a reaction of the ligand with the respective organotin dichloride/chloride in an anhydrous toluene medium, as given in Scheme 2 to give organotin compounds, stable in air and soluble in most common organic solvents. All compounds have sharp melting points and were characterized by various instrumental techniques. The experimental and physical data are given in Table 1.

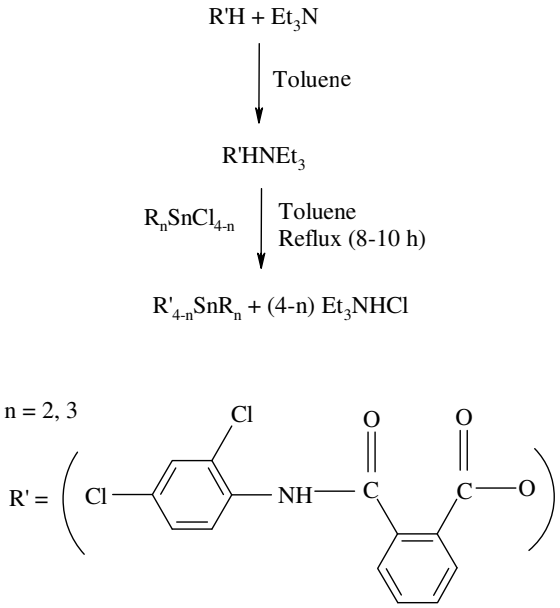
Infrared Spectroscopy

In order to clarify the mode of the ligand coordination to the tin center, IR spectra in the 4000-400 cm^{-1} range were recorded. The most important bands, presented and assigned in Table 2, show the following characteristics:

-The complexation of tin with the ligand is confirmed by the absence of a broad band in the range of 2650-2950 cm^{-1} due to ν (OH).

-The C=O band of the peptide group appears at 1716 cm^{-1} in the ligand; the complexes show this band in the range 1742-1721 cm^{-1}.

-A carboxylate ligand can bind to the metal as either a monodentate or bidentate ligand, resulting in changes in the relative positions of the asymmetric and symmetric stretching vibrations [20]. The IR spectra of the complexes give a separation value (Δν) less than 200 cm^{-1} which confirms the bidentate nature of carboxylate group (Fig. 1) [21,22].



compound	n	R
(1)	2	Me
(2)	2	Bu
(3)	2	Ph
(4)	3	Me
(5)	3	Bu
(6)	3	Ph

Scheme 2

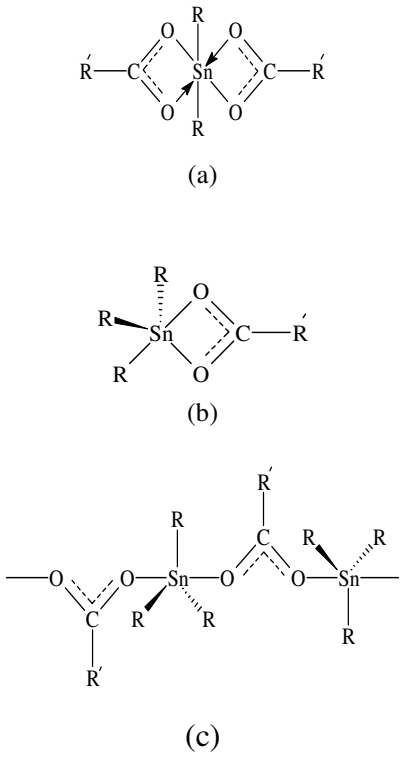


Fig. 1. Proposed structures of (a) diorganotin(IV) dicarboxylates (b) triorganotin(IV) carboxylates (c) polymeric structure of triorganotin(IV) carboxylates.

-Bands in the range of 585-512 cm^{-1} and 480-420 cm^{-1} indicate the presence of Sn-C and Sn-O bonds for the metal complexes (absent in the free ligand).

-A strong band at 3386-3359 cm^{-1}, characteristic for the NH group and present in the spectrum of the ligand, is also persists in the spectra of the complexes, which shows that the NH group does not participate *via* intra- or intermolecular modes of interactions. This observation parallels the NMR results.

Mass Spectrometry

The electron impact (EI) mass spectral data at 70 eV for the reported compounds are given in Table 3. The general fragmentation patterns are given in Schemes 3 and 4.

-The molecular ion peak is observed in all triorgnotin(IV) carboxylates, while it is absent in all diorganotin(IV) dicarboxylates [23].

- The fragment ions agree well with the expected structures of the compounds.

-For the diorganotin(IV) dicarboxylates, the primary fragmentation is due to the loss of the R group, where R is methyl, butyl, and phenyl. The base peaks for compounds (1) and (2) are due to $[C_{14}H_8O_3Cl]^+$ and $[C_6H_4Cl_2N]^+$ respectively. While in compound (3), it is due to $[C_6H_6N]^+$.

-For the triorganotin(IV) carboxylates, the primary fragmentation is also due to the loss of the R group, where the R is methyl, butyl and phenyl and the base peak for compounds (4) and (6), is due to the $[C_6H_6N]^+$ fragment. The base peak for compound (5) is due to $[C_{14}H_8O_3Cl]^+$. A secondary fragmentation pathway is characterized by the loss of all R groups by different routes, followed by the liberation of CO_2, which is more probable than the first one.

Table 1. Experimental and Physical Data for the Organotin(IV) Compounds

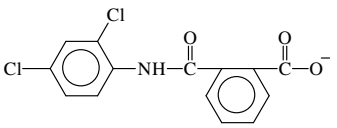
Comp. No.	Reactants in mg (mmol)			Product physical state	Yield (%)	M.P. (^oC)	Mol. Wt.	Found (Calcd.) C (%)	Found (Calcd.) H (%)	Found (Calcd.) N (%)
	Organotin(IV) chlorides	Ligand	Molar ratio							
(1)	Me_2SnCl_2 0.35 (1.61)	1.00 (3.22)	1:2	$C_{30}H_{24}N_2O_6Cl_4Sn$ Me_2SnL_2 White solid	80	124	767	46.9 (47.1)	3.12 (3.01)	3.67 (3.70)
(2)	Bu_2SnCl_2 0.48 (1.61)	1.00 (3.22)	〃	$C_{36}H_{34}N_2O_6Cl_4Sn$ Bu_2SnL_2 Grey solid	65	72	849	50.8 (50.2)	4.00 (3.91)	3.29 (3.30)
(3)	Ph_2SnCl_2 0.55 (1.61)	1.00 (3.22)	〃	$C_{40}H_{28}N_2O_6Cl_4Sn$ Ph_2SnL_2 White solid	72	85	891	53.8 (54.0)	3.14 (3.32)	3.14 (3.18)
(4)	Me_3SnCl 0.64 (3.22)	1.00 (3.22)	1:1	$C_{17}H_{18}NO_3Cl_2Sn$ Me_3SnL White solid	67	52	473	43.1 (42.9)	3.80 (3.90)	2.95 (3.01)
(5)	Bu_3SnCl 1.04 (3.22)	1.00 (3.22)	〃	$C_{26}H_{36}NO_3Cl_2Sn$ Bu_3SnL Brown solid	59	62	599	52.0 (52.8)	6.01 (5.90)	2.33 (2.39)
(6)	Ph_3SnCl 1.24 (3.22)	1.00 (3.22)	〃	$C_{32}H_{23}NO_3Cl_2Sn$ Ph_3SnL White solid	76	110	658	58.3 (58.9)	3.49 (3.61)	2.12 (2.16)

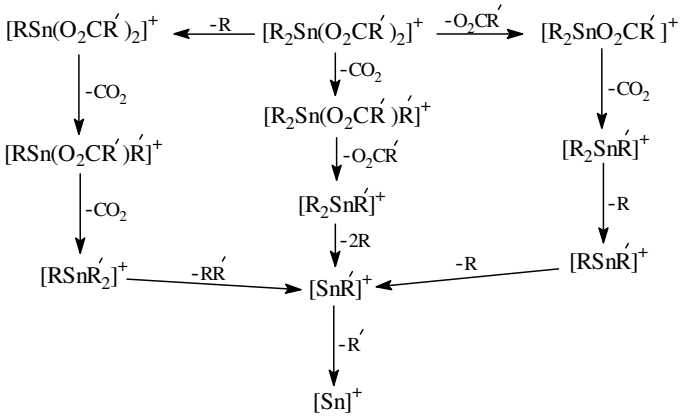
Table 2. Characteristic IR Frequencies (cm^{-1}) for Organotin(IV) Compounds and Their Ligand[a]

Comp. No.	Compound	ν_{NH}	$\nu_{C=O}$	$\nu_{(COO)asym}$	$\nu_{(COO)sym}$	$\Delta\nu$	ν_{Sn-C}	ν_{Sn-O}
HL	Ligand	3386 s	1716 s	1598 s	1365 s	233	–	–
(1)	$Me_2Sn(OOCR^/)_2$	3376 s	1725 m	1570 s	1380 s	190	585 s	430 s
(2)	$Bu_2Sn(OOCR^/)_2$	3380 s	1738 s	1575 s	1397 s	178	512 m	452 w
(3)	$Ph_2Sn(OOCR^/)_2$	3370 s	1721 s	1564 s	1398 s	166	–	461m
(4)	$Me_3SnOOCR^/$	3365 s	1725 s	1560 s	1375 s	185	535 s	420 m
(5)	$Bu_3SnOOCR^/$	3359 s	1730 m	1585 s	1392 s	193	522 w	472 s
(6)	$Ph_3SnOOCR^/$	3382 s	1742 s	1542 s	1390 s	152	–	480 s

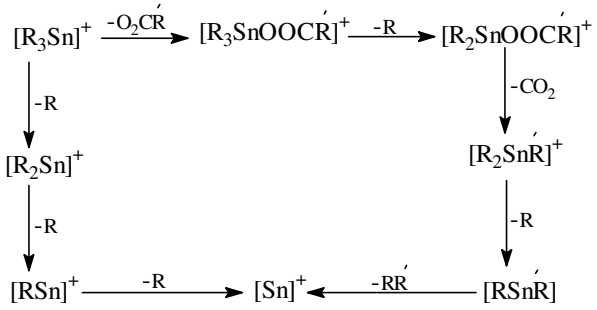
[a]s = strong, m = medium, w = weak

$(R^/)$ =





Scheme 3. Fragmentation Pattern of Diorganotin Dicarboxylates.



Scheme 4. Fragmentation Pattern of Triorganotin Carboxylates.

NMR SPECTROSCOPY

^{1}H NMR Spectroscopy

^{1}H NMR spectral data of reported compounds are given in Table 4. The signals are assigned by their peak multiplicity, intensity pattern, integration and satellites.

-In the ^{1}H NMR spectra of all the complexes studied, the CO(OH) resonance of the ligand is absent, which suggests the replacement of the carboxylic proton by the organotin(IV) moiety.

-The -NH signal remains almost unchanged which indicates that this group is not involved in intramolecular hydrogen bonding or in bonding to organotin moiety.

-All the protons present in the compounds have been identified by position and number with the protons calculated from the incremental method [24] tallies with that were expected from the molecular formula.

-The different R groups give signals within the expected range, thus confirming the complexation.

^{13}C NMR Spectroscopy

^{13}C NMR data of the studied compounds are given in Table 5.

-The aromatic resonances were assigned by comparison with values calculated from the incremental method [24].

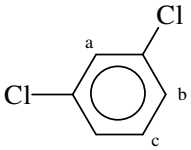
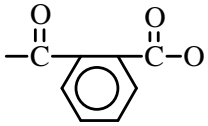
-The involvement of the carboxylate group in bonding to tin is confirmed by the resonance ascribed to C(12), which exhibits a shift after coordination.

-The carbons of the phenyl and alkyl groups attached to tin are observed at similar positions in the experimental data as

Table 3. Mass Spectral Data of the Organotin(IV) Compounds

Fragment ion	**(1)** m/z (%)	**(2)** m/z (%)	**(3)** m/z (%)	**(4)** m/z (%)	**(5)** m/z (%)	**(6)** m/z (%)
$R_3SnCOO\,R'$	–	–	–	473 (4)	599 (6)	658 (7)
$RSnOOCR'$	443 (4)	484 (6)	504 (5)	443 (11)	484 (24)	504 (10)
$SnOOCR'$	428 (7)	428 (9)	428 (2)	428 (4)	428 (18)	428 (5)
R_3Sn^+	–	–	–	164 (4)	290 (12)	347 (2)
R_2Sn^+	149 (11)	233 (2)	271 (3)	149 (8)	233 (14)	271 (3)
$C_6H_6N^+$	91(3)	91(1)	91 (100)	91 (6)	91 (2)	91 (4)
Sn^+	120 (4)	120 (2)	120 (3)	120 (3)	120 (6)	120 (10)
$C_{14}H_8O_3Cl^+$	256 (100)	256 (7)	256 (6)	256 (17)	256 (100)	256 (2)
$C_6H_4Cl_2N^+$	161 (6)	161 (100)	161 (21)	161 (100)	161 (16)	161(100)

Table 4. ^{1}H NMR Spectral Data[a] (δ ppm) of Organotin(IV) Compounds

Comp. No.		–NH		R
HL	(a) 7.63 s, (b) 7.25 d (7.65) (c) 6.97 d (2.6)	5.2 s	7.77-7.80 d,d (8.69) 7.92-7.96 d,d (8.69)	–
(1) Me_2	(a) 7.65 s, (b) 7.27 d (7.70) (c) 6.95 d (2.5)	5.2 s	7.76-7.79 d,d (8.68) 7.91-7.94 d,d (8.68)	0.46 s ^{2}J [79.8]
(2) Bu_2	(a) 7.68 s, (b) 7.28 d (7.72) (c) 6.94 d (2.4)	5.2 s	7.83-7.84 d,d (8.65) 7.99-8.00 d,d (8.65)	0.96 t, 1.27 m, 1.34-1.37 m, 2.62 t
(3) Ph_2	(a) 7.58 s, (b) 7.30 d (7.74) (c) 6.98 d (2.7)	5.2 s	7.78-7.83 d,d (8.60) 7.97-8.01 d,d (8.60)	7.47-7.52 m
(4) Me_3	(a) 7.60 s, (b) 7.24 d (7.67) (c) 6.95 d (2.5)	5.2 s	7.76-7.80 d,d (8.50) 7.91-7.95 d,d (8.50)	-0.08 s ^{2}J [55.8, 58.6]
(5) Bu_3	(a) 7.75 s, (b) 7.32 d (7.75) (c) 6.99 d (2.7)	5.2 s	7.94-7.97 d,d (8.67) 8.51-8.55 d,d (8.67)	0.84t, 1.29 m, 1.15-1.29 m, 2.47t
(6) Ph_3	(a) 7.80 s, (b) 7.38 d (7.90) (c) 6.93 d (2.3)	5.2 s	7.97-7.98 d,d (8.58) 8.00-8.02 d,d (8.58)	7.25-7.38 m

[a] ^{2}J [$^{117/119}$Sn, ^{1}H]; ^{2}J [^{119}Sn, ^{1}H] and ^{3}J (^{1}H, ^{1}H) in Hz are listed in square brackets and parentheses, respectively.

those calculated from the incremental method [24] and reported in the literature [7-11].

-Carbons 2,4 and 8,11 have two signals that are very close to each other and are therefore difficult to assign to a particular carbon so they are reported together in Table 5.

^{119}Sn NMR Spectroscopy

The value of δ ^{119}Sn defines the region of various coordination numbers of the central tin atom [5]. These results are given in Table 5.

-In all complexes, ^{119}Sn spectra show only a sharp singlet indicating the formation of a single species.

-In general, ^{119}Sn chemical shifts move to a lower frequency with an increasing coordination number. Although the shift ranges are somewhat dependent on the nature of the substituents of the tin atom.

-In all the complexes, ^{119}Sn chemical shift values lie in the tetrahedral environment around the tin atom and the non-coordinating solvent.

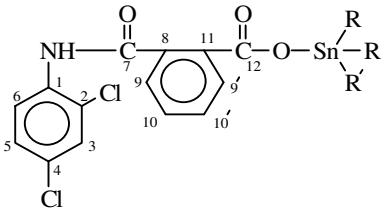
BIOLOGICAL ACTIVITY

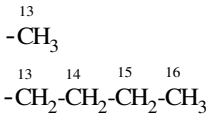
Cytotoxicity

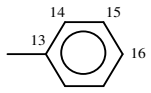
The Brine Shrimp method [15] was used to check the toxicity of the synthesized compounds using etoposide as a standard cytotoxic drug. This data is presented in Table 6 and

Table 5. ^{13}C and ^{119}Sn NMR Data of Organotin(IV) Compounds

Carbon No.	**HL**	**(1) Me_2**	**(2) Bu_2**	**(3) Ph_2**	**(4) Me_3**	**(5) Bu_3**	**(6) Ph_3**
1	136.0	136.7	136.4	136.2	136.2	136.5	136.4
2,4	128.21	128.5	128.7	128.4	128.3	128.4	128.6
3/5	134.6	134.0	134.0	134.4	134.7	133.9	134.0
6	130.3	130.3	130.2	130.2	130.5	130.8	130.3
7	166.3	166.3	166.2	167.7	166.5	168.1	166.9
8,11	131.31	131.3	131.3	131.9	131.9	131.3	131.6
9,9′	124.2	124.0	124.5	124.9	124.1	124.6	124.9
10,10′	114.0	114.1	114.8	114.1	114.1	114.5	114.9
12	174.6	175.7	175.8	175.9	175.6	175.5	175.3
13	–	14.12	29.6	129.9	14.3	29.6	137.2
14	–	–	27.4	127.4	–	27.7	136.0 [49]
15	–	–	26.6	126.9	–	26.5	134.5
16	–	–	13.6	125.4	–	13.5	129.1 [63]
^{119}Sn	-	-98.0	-88.45	-81.50	170.55	69.44	-46.37







$R' = R$ for triorganotin

$R' = L$ for diorganotin

Fig. 2.

The highest toxicity was shown by compound (5), whose LD_{50} value is 4.7261 mg ml^{-1}, while the lowest toxicity is shown by compound (1) whose LD_{50} value is 2.3878 mg ml^{-1} as compared to the standard drug. 2-[(2,4-dichloroanilino-carbonyl)]benzoic acid and compounds (2), (3), (4), and (6) do not show any toxicity against the brine shrimp larvae.

Antibacterial Activity

The synthesized compounds were screened for antibacterial activity by the agar well diffusion method [20] and the zone of inhibition was measured in millimeters (Table 7 and Fig. 3).

-All of the compounds showed significant antibacterial activity against the tested bacteria.

-The ligand was found to be active and its organotin carboxylates showed more significant antibacterial activity than the ligand.

Antifungal Activity

The percent inhibition data is given in Table 8 and Fig.4. When the reported compounds were screened against different plant pathogens using the tube diffusion method [19], the

Table 6. Brine Shrimp (*Artemia salina*) Lethality Bioassay[a] of Organotin(IV) Compounds

Comp. No.	Dose (mg ml^{-1})	No. of shrimps	No. of survivors	LD_{50} (mg ml^{-1})
	100	30	10	
HL	10	30	10	–
	1	30	10	
	100	30	0	
(1) Me_2	10	30	0	2.3878
	1	30	9	
	100	30	10	
(2) Bu_2	10	30	10	–
	1	30	10	
	100	30	0	
(3) Ph_2	10	30	10	–
	1	30	10	
	100	30	10	
(4) Me_3	10	30	10	–
	1	30	10	
	100	30	0	
(5) Bu_3	10	30	2	4.7261
	1	30	10	
	100	30	0	
(6) Ph_3	10	30	10	–
	1	30	10	

[a]Standard drug (Etoposide); LD_{50} (mg ml^{-1}) = 7.4625.

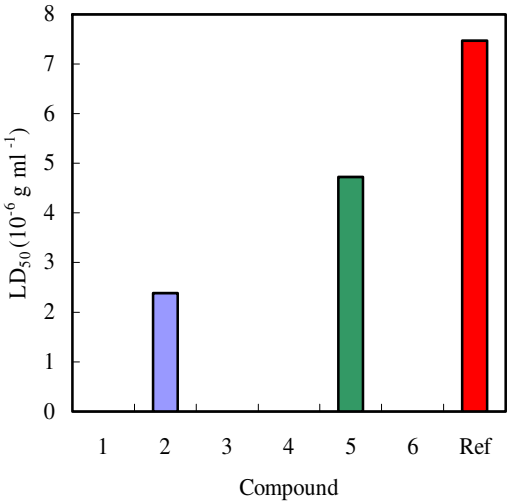


Fig. 2. Cytotoxicity of organotin(IV) derivatives.

order of degree of activity was: Me_3< Bu_3 < Ph_3. The most probable reason is the association of the activity with the length of R group. As the length of the R group increases, activity also increases [25].

Compound (5) caused the most inhibition of fungal growth except in the case of *Trichophyton longifusum*.

MODE OF ACTION

The degradative enzymes produced by the microorganisms are important in host infection, food deterioration and breakdown of organic matter. Enzyme production is here intended to mean both synthesis of the enzymes by the microorganisms and activity of the enzymes in the medium after it is produced. Since the organotin(IV) complexes inhibit the growth of organisms, it is assumed that the production of

Table 7. Antibacterial Activity of Organotin(IV) Compounds

Name of bacteria ATCC No.	Zone of inhibition (mm)							Standard drug (Ref.)
	HL	**(1) Me_2**	**(2) Bu_2**	**(3) Ph_2**	**(4) Me_3**	**(5) Bu_3**	**(6) Ph_3**	
Escherichia coli	10	–	–	11	12	–	–	Ampicillin $(H_2O)_3$ Cephalexin Na
Bacillus subtilis (11774)	10	21	18	–	–	20	11	"
Shigella flexneri (700930)	–	–	–	–	–	9	–	"
Staphylococcus aureus (25923)	–	22	–	–	12	16	–	"
Pseudomonas aeruginosa (10145)	12	10	13	11	12	13	12	"
Salmonella typhi (10749)	–	14	–	–	–	14	14	"

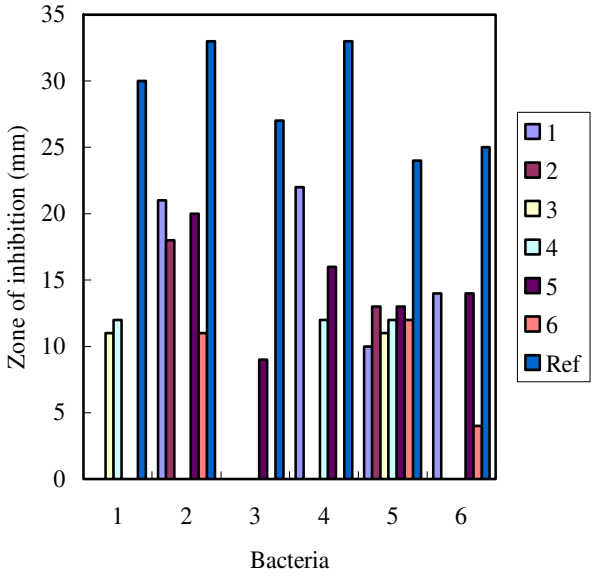


Fig. 3. Antibacterial activity of organotin(IV) derivatives against various bacteria: (1) *Escherichia coli*, (2) *Bacillus subtilis*, (3) *Shigella flexneri*, (4) *Staphylococcus aureus*, (5) *Pseudomonas aeruginosa*, (6) *Salmonella typhi*.

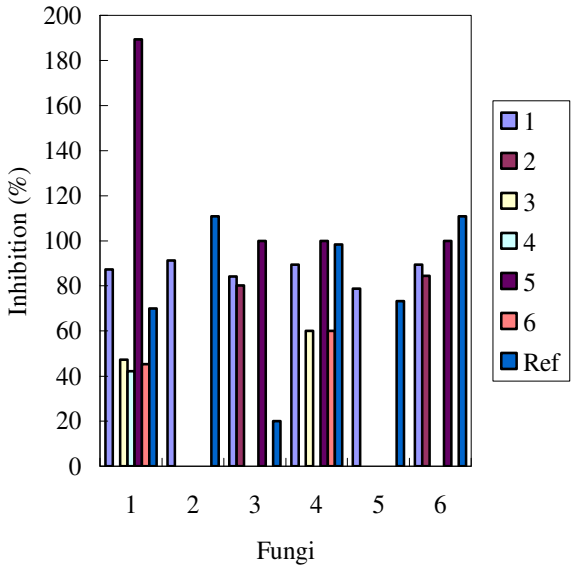


Fig. 4. Antifungal activity of organotin(IV) derivatives against various fungi: (1)*Trichophyton longifusum*, (2) *Candida albicans*, (3) *Aspergillus flavipes*, (4) *Microsporum canis*, (5) *Fusarium solani*, (*6*) *Candida glabrata.*

Table 8. Antifungal Activity[a] of Organotin(IV) Derivatives

Name of fungi (ATCC No.)	Percent inhibition							Standard drug (Ref.)
	HL	**(1) Me_2**	**(2) Bu_2**	**(3) Ph_2**	**(4) Me_3**	**(5) Bu_3**	**(6) Ph_3**	
Trichophyton longifusum (22397)	0	87.3	0	47.3	42.1	89.4	45.2	Miconazole Ketoconazole
Candida albicans (2192)	0	91.5	0	0	0	100	0	Miconazole Ketoconazole
Aspergillus flavipes (1030)	0	84.2	80.2	0	0	100	0	Amphotericin.B Flucytosine
Microsporum canis (9865)	80	89.4	0	60	0	100	60	Miconazole Ketoconazole
Fusarium solani (11712)	0	78.9	0	0	0	100	0	Miconazole
Candida glabrata	0	84.5	84.5	0	0	100	0	Miconazole

[a]Concentration: 200 (mg ml^{-1}).

the enzymes is being affected; hence the organisms are unable to utilize the food and, consequently, the growth ceases [26].

The variation in the effectiveness of different biocidal agents against different organisms, as suggested by Sexena and Singh [27], depends on the impermeability of the cell. The effect of resonating rings on the toxicity may be appraised in the light of modern electronic theory. The resonant energy is the energy in excess of the sum of the energy of the separate bonds making up the molecules. Resonating structures, such as benzene rings (in the present case), may serve as powerhouses to activate potentially reactive groupings. If the toxicity is dependent on one or more chemical reactions, then the molecule that would increase the rate of chemical reactions must enhance toxicity [28].

From the bactericidal activity, it is apparent that the complexes were more toxic toward Gram (+) strains than Gram (-) strains. The reason is the difference in the structure of the cell walls. The walls of Gram (-) cells are more complex than those of Gram (+) cells. The lipopolysaccharide forms an outer-lipid membrane and contributes to the complex antigenic specificity of Gram (-) cells.

STRUCTURAL CORRELATION WITH BIOCIDAL ACTIVITY

From the results of biological activity, it is concluded that:

-There is a direct relationship between the biocidal activity and the coordination environment of the metal.

-The function of the ligand is to support the transport of the active organotin moiety to the site of the action where it is released by hydrolysis [29].

-The anionic ligand also plays an important role in determining the degree of the activity of organotin compounds.

-As all complexes showed tetrahedral geometry in solution and, with few exceptions, showed significant activity, our results are consistent with the literature that states species generating a tetrahedral geometry in solution are more active

[29].

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