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Preparation, Spectroscopic Studies and Biological Activity of Mono-organotin(IV) Derivatives of Non-Steroidal Anti-inflammatory Drugs

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A set of 14 mono-organotin(IV) derivatives of general formulae n-$BuSnClL_2$ and n-$BuSnL_3$, where 'L' are various non-steroidal anti-inflammatory drugs (NSAIDs), were synthesized and structurally characterized by vibrational, ^{1}H, ^{13}C and ^{119}Sn spectroscopies and mass spectrometry to propose their structure. Biological activity data (antibacterial, antifungal and cytotoxicity) of the synthesized complexes were compared with the precursors to establish the significance of the complexes.

Key Words: Mono-organotin(IV) derivatives, non-steroidal anti-inflammatory drugs, biological activity.

Introduction

Organic ligands with sulfur, nitrogen, oxygen and fluorine substituents have long been used to enhance the biological activity of organotin(IV) carboxylates[1]. Organotin compounds with such ligands have been widely tested for their possible use in cancer chemotherapy[2].

Non-steroidal anti-inflammatory drugs (NSAIDs) are frequently used medicinal drugs. They are utilized primarily as analgesics, anti-inflammatories and antipyretics[3] and their side effects have been well studied. Their main known mode of action is through inhibition of the cyclo-oxygenase-mediated production of prostaglandins, but this is not deemed to be sufficient to explain their wide variety of actions[4,5]. Several NSAIDs, such as mefenamic acid, indomethacin or sulindac, have been used in combination with a number of cytotoxic drugs, e.g., cyclophosphamide and melphalanor. The effect on clinically important NSAIDs with a variety of chemotherapeutics was studied in different human cancer cells.

It was thought to explore the chemistry of organotin (IV) carboxylates due to the pharmacological importance of drugs, e.g., Ibuprofen and neproxene, and the potential biological activity of organotin carboxylates. Previously[6,7], it was reported that di- and tri-organotin(IV) derivatives of NSAIDs show

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significant biological activity against bacteria and plant pathogens. We synthesized the mono-organotin(IV) derivatives of NSAIDs to check their biological activity. These complexes were characterized by IR, ^{1}H, ^{13}C and ^{119}Sn NMR spectroscopy and mass spectrometry. These complexes were screened for different animal and plant pathogens to check their antibacterial, antifungal activity and cytotoxicity effects.

Experimental

n-Butyltin(IV) chloride dihydroxide and n-butyltin(IV) oxyhydroxide were purchased from Aldrich Chemicals (USA) and were used without further purification. Solvents were dried out by reported methods[8] before use.

Melting points were determined in a capillary tube on an electrothermal melting point apparatus model MP-D Mitamura Rikero Kogyo (Japan) and were uncorrected. Infrared spectra were recorded in the range 4000-400 cm^{-1} as KBr pellets or thin film (Nujol) on a Bio-Rad Elmer 16FPc FT-IR and 4000-250 cm^{-1} on a Hitachi 250-50 spectrophotometer.

Electron impact mass spectra (EIMS) were recorded on a Finnigan MAT-312 or a Varian MAT-112 double focusing mass spectrophotometer connected to a DPD 11/34 (DEC) computer system. The ^{1}H NMR spectra were recorded on a Bruker AM-400 MHz using $CDCl_3$ as internal reference. ^{13}C and ^{119}Sn NMR spectra were recorded on a Bruker AM-250 MHz using $CDCl_3$ as internal reference.

Synthesis

General Procedure for the Synthesis of n- BuSnCl(OOCR′)$_2$

A stoichiometric amount of organic acid was added to $BuSnCl(OH)_2$ in 100 mL of toluene in a 2:1 molar ratio. The mixture was stirred for 15 min and refluxed for 4 h. The water formed was removed through a Dean and Stark apparatus. After cooling, the solvent was evaporated on a rotary apparatus. The mass left was recrystallized in $CHCl_3$ and petroleum ether in a 1:1 molar ratio. The general chemical reaction is given as equation (1) in Scheme 1.

General Procedure for the Synthesis of n-BuSn(OOCR′)$_3$

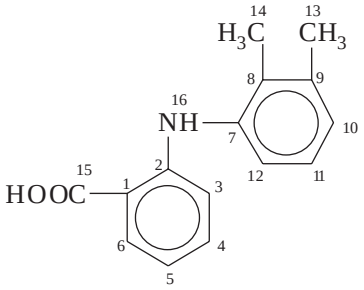
A stoichiometric amount of organic acid was added to BuSnO(OH) in 100 mL of toluene in a 3:1 molar ratio. The remaining procedure was the same as above. The general reaction is given as equation (2) in Scheme 1.

$$\text{n-BuSnCl(OH)}_2 + 2\text{R}'\text{COOH} \xrightarrow[\text{Reflux for 4 h}]{\text{Toluene}} \text{n-BuSnCl(OOCR}')_2 + 2\text{H}_2\text{O} \quad (1)$$

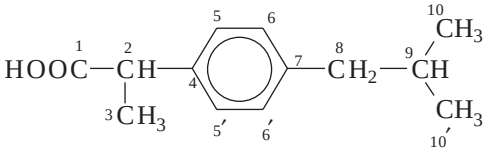
$$\text{n-BuSnO(OH)} + 3\text{R}'\text{COOH} \xrightarrow[\text{Reflux for 4 h}]{\text{Toluene}} \text{n-BuSn(OOCR}')_3 + 2\text{H}_2\text{O} \quad (2)$$

where

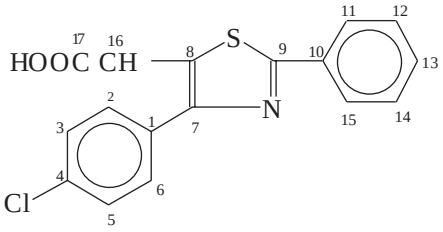
R′COOH =



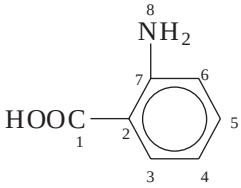
L^1



L^2



L^3



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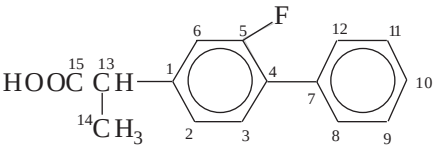
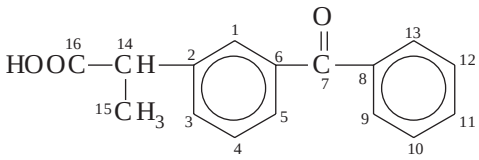
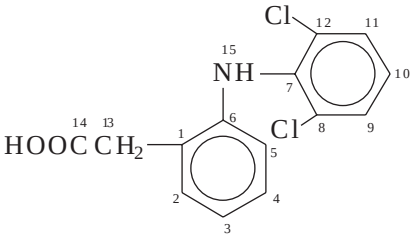


L^5



L^6



L^7

Scheme

The monoisotopic mass fragmentations of compounds 1-14 are as follows:

Compound-1

MS, m/z(%) [Fragment]

$[BuSn(Cl)L_2^1]^+$ 691 (n.o), $[Sn(Cl)L^1]^+$ 395 (2)

$[OOCC_6H_4NHC_6H_3CH_3]^+$ 225 (4), $[C_6H_4NHC_6H_3CH_3]^+$ 181 (19)

$[C_6H_4NHC_6H_3]^+$ 166 (4), $[Sn\text{-}C_6H_4NHC_6H_3(CH_3)_2]^+$ 315 (5), $[SnC_6H_4]^+$ 195 (17)

$[Bu\text{-}C_6H_4NHC_6H_3]^+$ 223 (100), $[SnC_6H_9]^+$ 177 (1), $[C_4H_9]^+$ 57 (3)

$[C_6H_4]^+$ 76 (n.o), $[Sn]^+$ 120 (n.o)

Compound-2

MS, m/z(%) [Fragment]

$[BuSn(L^1)_3]^+$ 896 (n.o), $[BuSn(L^1)_2OOCNH]^+$ 715 (33), $[BuSn(L^1)_2]^+$ 656 (24)

$[Sn(L^1)_2]^+$ 599 (15), $[SnL^1C_6H_4C_6H_3]^+$510 (4),$[Sn\text{-}C_6H_4NHC_6H_3(CH_3)_2]^+$315 (53)

$[SnC_6H_4]^+$ 195 (63), $[BuSn(L^1)]^+$ 416 (3), $[Bu\text{-}L^1]^+$ 297 (47)

$[Bu\text{-}C_6H_4NHC_6H_3(CH_3)_2]^+$ 253 (9), $[BuC_6H_4NHC_6H_3]^+$ 223 (100)

$[Bu\text{-}C_6H_4C_6H_3]^+$ 208 (77), $[C_6H_4C_6H_3]^+$ 151 (8), $[SnL^1]^+$ 359 (14)

$[C_6H_4NHC_6H_3(CH_3)_2]^+$ 196 (74), $[C_6H_4NHC_6H_3]^+$ 166 (15), $[C_4H_9]^+$ 57 (50)

$[Sn]^+$ 120 (42)

Compound-3

MS, m/z(%) [Fragment]

$[BuSn(Cl)L_2^2]^+$ 621 (n.o), $[L^2H]^+$ 206 (42), $[CHCH_3C_6H_4\text{-iso-}Bu]^+$ 161 (98)

$[C_6H_4CH_2CH(CH_3)]^+$ 118 (35), $[C_6H_4CH_2CH_3]^+$ 105 (12), $[C_6H_4CH_3]^+$ 91 (86)

$[CH_3(CH_2)_2Sn]^+$ 162 (100), $[C_6H_9]^+$ 57 (22), $[Sn]^+$ 120 (3)

Compound-4

MS, m/z(%) [Fragment]

$[BuSn(L_3^2)]^+$ 791 (n.o), $[L^2H]^+$ 206 (42), $[CHCH_3C_6H_4\text{-iso-}Bu]^+$ 161 (36)

$[C_6H_4CH_2CH(CH_3)]^+$ 118 (4), $[C_6H_4CH_2CH_3]^+$ 105 (5), $[C_6H_4CH_3]^+$ 91 (14)

$[CH_3(CH_2)_2Sn]^+$ 162 (4), $[C_6H_9]^+$ 57 (100), $[Sn]^+$ 120 (n.o)

Compound-5

MS, m/z(%) [Fragment]

$[BuSn(Cl)L_2^3]^+$ 867 (n.o), $[C_{24}H_{23}NCl_2SO_4Sn]^+$ 599 (10)

$[C_{23}H_{23}NClSO_4Sn]^+$ 563 (44), $[C_{17}H_{11}NO_2ClSSn]^+$ 447 (3)

$[C_{17}H_{12}NO_2ClS]^+$ 329 (44), $[C_{16}H_{11}NClS]^+$ 284 (56), $[C_9H_6Cl]^+$ 181 (57)

$[C_9H_6S]^+$ 146 (48), $[C_9H_6]^+$ 114 (3), $[C_4H_9Sn]^+$ 177 (29)

$[C_{17}H_{10}NOClS]^+$ 311 (100), $[C_{17}H_{10}NOS]^+$ 276 (54), $[C_{13}H_5NOS]^+$ 223 (36)

$[C_{13}H_5S]^+$ 193 (4), $[C_4H_9]^+$ 57 (19), $[Sn]^+$ 120 (5)

Compound-6

MS, m/z(%) [Fragment]

$[BuSnL_3^3]^+$ 1160 (n.o), $[C_{31}H_{27}N_2ClS_2O_4Sn]^+$ 677 (4)

$[C_{25}H_{22}N_2ClO_2S_2Sn]^+$ 600 (10), $[C_{25}H_{22}N_2O_2S_2Sn]^+$ 565 (5)

$[C_{18}H_{17}N_2S_2Sn]^+$ 444 (2), $[C_{12}H_{13}N_2S_2Sn]^+$ 368 (27)

$[C_8H_4S_2N_2Sn]^+$ 311 (100), $[C_{16}H_{11}NSCl]^+$ 284 (28)

$[C_4H_9]^+$ 57 (1), $[C_6H_5]^+$ 77 (1), $[Sn]^+$ 120 (n.o)

Compound-7

MS, m/z(%) [Fragment]

$[BuSn(Cl)L_2^4]^+$ 483 (n.o), $[BuSn(Cl)(L^4)C_6H_4NH2]^+$ 439 (2), $[SnL^4]^+$ 255 (1)
$[Sn\text{-}C_6H_4NH_2]^+$ 211 (1), $[OOCC_6H_4NH_2]^+$ 136 (6), $[C_6H_4NHCO]^+$ 119 (50)
$[C_6H_4NH]^+$ 91 (44), $[C_2H_3Sn\text{-}NH]^+$ 161 (100), $[C_4H_9Sn]^+$ 177 (n.o)
$[C_4H_9]^+$ 57 (60), $[Sn]^+$ 120 (15)

Compound-8

MS, m/z(%) [Fragment]
$[BuSn(L^4)_3]^+$ 584 (n.o), $[Bu\text{-}SnC_6H_4NH_2]^+$ 268 (3), $[Sn\text{-}C_6H_4NH_2]^+$ 211 (1)
$[Sn\text{-}OOCC_6H_4NH_2]^+$ 255 (3), $[C_6H_4CONH]^+$ 119 (73), $[C_6H_4CO]^+$ 104 (3)
$[C_6H_4NH]^+$ 91 (62), $[C_2H_3\text{-}SnNH]^+$ 161 (89), $[C_4H_9]^+$ 57 (100), $[Sn]^+$ 120 (24)

Compound-9

MS, m/z(%) [Fragment]
$[BuSn(Cl)(L^5)_2]^+$ 697 (n.o), $[Sn\text{-}L^5]^+$ 362 (10), $[Sn\text{-}OOCCH(CH_3)C_6H_5]^+$268 (2)
$[Sn\text{-}C_6H_5]^+$ 196 (6), $[L^5]^+$ 243 (28), $[CH(CH_3)C_6H_3FC_6H_5]^+$ 199 (100)
$[C_4H_9Sn]^+$ 177 (15), $[C_4H_9]^+$ 57 (18), $[Sn]^+$ 120 (n.o)

Compound-10

MS, m/z(%) [Fragment]
$[Bu\text{-}Sn(L^5)_3]^+$ 906 (n.o), $[L^5]^+$ 243 (28), $[C_6H_3FC_6H_5]^+$ 171 (4)
$[CH(CH_3)C_6H_3FC_6H_5]^+$ 199 (100), $[C_6H_5C_6H_3]^+$ 152 (7)
$[C_4H_9Sn]^+$ 177 (3), $[C_4H_9]^+$ 57 (12), $[Sn]^+$ 120 (1)

Compound-11

MS, m/z(%) [Fragment]
$[Bu\text{-}Sn(Cl)(L^6)_2]^+$ 717.5 (n.o), $[L^6]^+$ 253 (26), $[C_6H_5COC_6H_4CH(CH_3)]^+$ 209 (29)
$[C_6H_5COC_6H_4]^+$ 181 (8), $[C_6H_5CO]^+$ 105 (100), $[C_6H_5]^+$ 77 (87), $[C_6H_4]^+$ 76 (4)
$[Bu\text{-}Sn]^+$ 177 (34), $[C_4H_9]^+$ 57 (7), $[Sn]^+$ 120 (n.o)

Compound-12

MS, m/z(%) [Fragment]
$[Bu\text{-}Sn(L^6)_3]^+$ 935 (n.o), $[L^6]^+$ 253 (17), $[C_6H_5COC_6H_4CH(CH_3)]^+$ 209 (19)
$[C_6H_5COC_6H_4]^+$ 181 (8), $[C_6H_5CO]^+$ 105 (90), $[C_6H_5]^+$ 177 (100)
$[C_6H_4]^+$ 76 (7), $[C_4H_9]^+$ 57 (2), $[Sn]^+$ 120 (n.o)

Compound-13

MS, m/z(%) [Fragment]
$[Bu\text{-}SnCl(L^7)_2]^+$ 799(n.o), $[Bu\text{-}Sn(L^7)CH_2COO]^+$ 529 (2)
$[Bu\text{-}SnC_6H_4NHC_6H_3Cl_2]^+$ 413 (6), $[CH_3CH_2SnC_6H_4NHC_6H_3Cl_2]^+$ 370 (14)
$[CH_3CH_2SnC_6H_3Cl_2]^+$ 294 (20), $[L^7]^+$ 295 (4), $[C_6H_3ClNHC_6H_4CH_2CO]^+$243 (29)
$[C_6H_3ClNHC_6H_4CCO]^+$ 241 (100), $[Bu\text{-}Sn]^+$ 177 (10), $[C_4H_9]^+$ 57 (36)
$[C_6H_4]^+$ 36 (9), $[Sn]^+$ 120 (n.o)

Compound-14

MS, m/z(%) [Fragment]

$[Bu\text{-}Sn(L^7)_3]^+$ 1058 (n.o), $[Bu\text{-}Sn(L^7)CH_2COO]^+$ 529 (2)

$[BuSnC_6H_4NHC_6H_3Cl_2]^+$ 413 (3), $[CH_3CH_2SnC_6H_4NHC_6H_3Cl_2]^+$ 370 (6)

$[CH_3CH_2SnC_6H_3Cl_2]^+$ 294 (19), $[L^7]^+$ 295 (4), $[C_6H_3ClNHC_6H_4CH_2CO]^+$243 (27)

$[C_6H_3ClNHC_6H_4CCO]^+$ 241 (100), $[Bu\text{-}Sn]^+$ 177 (9), $[C_4H_9]^+$ 57 (15)

$[C_6H_4]^+$ 76 (5), $[Sn]^+$ 120 (n.o)

Results and Discussion

Organotin(IV) carboxylates were prepared by treating ligand acid with stochiometric amounts of corresponding organotin(IV) precursors in dry toluene. The reported compounds were crystalline solid, amorphous powder or gel-like in appearance. All compounds were soluble in common organic solvents like chloroform and acetone etc., and solids having definite melting points.

The physical properties of the ligands and reported compounds are given in Table 1.

Infrared spectroscopy

Infrared spectral data of free ligands, L^1-L^7 and their organotin complexes are given in Table 2. The free ligands and their organotin complexes contain a large number of weak to strong absorptions, which made assignment difficult. In general, the L^1-L^7 ligand skeletons possess one potential donor site for bond formation with tin, the carboxyl oxygen.

Table 1. Physical data Of mono n-butyltin(IV) carboxylates.

Comp. No.	Molecular Formula	Molecular Weight	Melting Point (C^0)	Yield (%)
L^1	$C_{15}H_{15}NO_2$	241.28	230-231	—-
1	$C_{34}H_{37}N_2O_4ClSn$	691.5	120-123	90
2	$C_{49}H_{51}N_3O_6Sn$	896	285	70
L^2	$C_{13}H_{18}O_2$	206.29	58-60	—-
3	$C_{30}H_{43}O_4ClSn$	621.5	*	50
4	$C_{43}H_{60}O_6Sn$	791	*	59
L^3	$C_{17}H_{12}NO_2ClS$	329.81	161-162	—-
5	$C_{38}H_{31}N_2Cl_3S_2O_4Sn$	868.5	110-115	78
6	$C_{55}H_{42}Cl_3S_3N_3O_6Sn$	1161.5	140-142	76
L^4	$C_7H_7NO_2$	137.13	144-146	—-
7	$C_{18}H_{21}ClO_4N_2Sn$	483.5	105-110	84
8	$C_{25}H_{27}N_3O_6Sn$	584	112-117	86
L^5	$C_{15}H_{13}FO_2$	244	110-111	—-
9	$C_{34}H_{33}F_2O_4ClSn$	697.5	*	60
10	$C_{49}H_{45}F_3O_6Sn$	905	*	50
L^6	$C_{16}H_{14}O_3$	254	94	—-
11	$C_{36}H_{35}ClO_6Sn$	717.5	*	53
12	$C_{52}H_{48}O_9Sn$	935	*	55
L^7	$C_{14}H_{11}NCl_2O_2$	296	156-158	—-
13	$C_{32}H_{29}N_2O_4Cl_5Sn$	801.5	125-128	72
14	$C_{46}H_{39}N_3O_6Cl_6Sn$	1061	196-198	69

* Physical state is gel-like

Table 2. Infrared data (cm^{-1}) of mono n-butyltin(IV) carboxylates.

Code No.	ν (NH)	ν $(COO)_{asym}$	ν $(COO)_{sym}$	$\Delta\nu$	ν (Sn-C)	ν (Sn-O)	ν (Sn-Cl)
L^1	3312	1651	1329	322	-	-	-
Compound 1	3328	1611	1390	221	515	461	329
Compound 2	3337	1612	1395	217	526	485	-
L^2	-	1719	1321	398	-	-	-
Compound 3	-	1587	1367	220	520	453	386
Compound 4	-	1597	1366	231	516	469	-
L^3	-	1717	1406	311	-	-	-
Compound 5	-	1699	1412	287	516	438	329
Compound 6	-	1707	1418	289	531	453	-
L^4	3324	1662	1369	293	-	-	-
Compound 7	3374	1619	1392	227	520	491	329
Compound 8	3372	1620	1387	233	521	488	-
L^5	-	1699	1323	376	-	-	-
Compound 9	-	1701	1416	285	530	489	340
Compound 10	-	1711	1413	298	565	415	-
L^6	-	1695	1370	325	-	-	-
Compound 11	-	1655	1413	242	532	477	329
Compound 12	-	1658	1411	247	531	469	-
L^7	3335	1652	1335	317	-	-	-
Compound 13	3337	1611	1336	275	514	474	345
Compound 14	3335	1612	1336	276	555	459	-

In view of this, a few vibrations that provide reasonable support in establishing bonding were selected and are discussed below. The IR spectra of the free ligands (L^1-L^7) in KBr exhibit a broad band centered at 2900-2600 cm due to v(OH), which are absent in organotin complexes, suggesting the deprotonation of the COOH group upon complexation[9]. The ν_{Sn-C}, ν_{Sn-O} and ν_{Sn-Cl} bands were appeared 500-585, 420-490 and 315-335 cm^{-1}, respectively[10].

It is known that the denticity of the COO^- group can be determined with a high level of probability on the basis of v_{asym}(COO) and v_{sym}(COO) values and/or their difference. $\Delta\nu$(COO) = ν_{asym}(COO) $-\nu_{sym}$(COO). The Δv(COO) values of all compounds studied are in the range 217 to 298 cm^{-1}.Thus these cases can be described as an intermediate state between monodentate and bidentate carboxylate groups, which are called anisobidentate.

^{1}H NMR spectra

The comparative study of the ^{1}H NMR spectra of the starting materials and the complexes showed that the proton resonance signals due to the –OH group were absent in the respective metal complexes, suggesting that the proposed complexation to the tin atom was formed. The characteristic resonance peaks in the ^{1}H NMR spectra of the complexes were recorded in deutero chloroform and are presented in Table 3.

The ^{1}H NMR spectral data of ligands are also included in Table 3 for comparison. In the spectra of the synthesized complexes the resonance peaks of protons were assigned on the basis of their intensity and multiplicity pattern. The ring proton signals were assigned by the comparison of experimental data and calculated data by the incremental method[11].

Table 3. ^{1}H NMR data^{a,b,c,d,e} of mono n-butyltin(IV) carboxylates.

Proton No.	L^1	(1)	(2)	Proton No.	L^2	(3)	(4)	Proton No.	L^3	(5)
3	7.13 m	6.54 m	6.99 m	2	3.71-3.66 q(7.2)	3.72 m	3.63-3.48 m	2,6	7.61-7.60 m	7.63 m
4	7.26 t (12)	7.28-7.24 m	7.47 m	3	1.49-1.47 d(7.2)	1.51-1.50 m	1.53-1.51 m	3,5	7.95-7.92 m	7.86 m
5	7.04-7.03 m	7.11-7.03 m	7.08-7.03 m	5,5	7.09-7.07d (8.0)	7.12-7.10 d(7.2)	7.06-7.00 m	11,15	7.59-7.58 m	7.59-7.58 m
6	7.99-8.00 m	7.89 m	7.81-7.79 m	6,6	7.19-7.21 d(8.0)	7.23 s	7.22-7.20 m	12,14	7.44-7.40 m	7.48-7.46 m
10	6.64 m	6.50 m	6.42-6.39 d(8.4)	8	2.44-2.42 d(7.2)	2.47-2.46 d(6.8)	2.45-2.42 t (20)	13	7.24 s	7.24 m
11	6.68 m	6.67 m	7.01 m	9	1.81-1.84 m	1.88-1.83 m	1.88-1.83 m	16	3.93 s	3.97 s
12	7.28 m	7.28-7.24 m	7.24 m	10,10	0.89-0.87 d(6.4)	0.93-0.91 d(6.4)	0.91 m	α	——	1.79-1.70 m
13	2.3 s	2.29s	2.3 s	α	——	1.88-1.83 m	1.88-1.83 m	β	——	1.60-1.54 m
14	2.16 s	2.11s	2.1 s	β	——	1.51-1.50 m	1.53-1.51 m	γ	——	1.39-1.34 m
α	——	1.85-1.76 m	1.85-1.77 m	γ	——	1.30 s	1.30 s	δ	——	0.69 m
β	——	1.47-1.45 m	1.52-1.47 m	δ	——	0.93-0.91 m	0.91 m			
γ	——	1.36-1.32 m	1.36-1.32 m							
δ	——	0.88-0.85 m	0.81-0.77 m							
NH	9.09 s (bd)	8.7 s (bd)	9.13 s (bd)							

[a]Chemical shift (δ) in ppm. [b]Multiplicity is given as s, singlet; d, doublet; t, triplet; q, quartet, m, multiplet. [c]Coupling constants are in parentheses $^{3}J(^{1}H, ^{1}H)$, [d]bd is "broad signal", [e]For numbering see structures of R′ groups
in Scheme 1 and α, β, γ, δ are given below:
$^{\alpha}CH_2^{\beta}CH_2^{\gamma}CH_2^{\delta}CH_3$

Table 3. Contunied

ProtonNo.	(6)	ProtonNo.	L^4	(7)	(8)	Proton No.	L^5	(9)	(10)
2,6	7.59 m	3	7.92 m	7.87 s	7.93 m	2	7.12 d(1.6)	7.13 m	7.13-7.10 d(9.6)
3,5	7.90 m	4	6.67 s	6.66 m	7.21 m	3	7.17 d (1.6)	7.17 m	7.18 s
11,15	7.57 m	5	7.28-7.27 m	7.24 m	7.26 m	6	7.24 s	7.24 m	7.24 s
12,14	7.46-7.38 m	6	6.67-6.64 m	5.97 m	6.61 m	8,12	7.52-7.50 m	7.48 m	7.50-7.48 m
13	7.24 s	α	——	1.78-1.76 m	1.84-1.74 m	9,11	7.44-7.42 m	7.42-7.40 m	7.43-7.39 t(20)
16	3.9 s	β	——	1.38 m	1.61-1.59 m	10	7.40-7.38 m	7.35-7.32 m	7.36-7.33 m
α	n.o	γ	——	1.38 m	1.47-1.38 m	13	3.80-3.74 q(7.2)	3.7 m	3.7-3.69 d(6.8)
β	1.52 m	δ	——	0.86 m	0.90-0.87 m	14	1.55-1.53 d(6.8)	1.52 m	n.o
γ	1.38-1.35 m	NH	5.28 s (bd)	5.27 s (bd)	5.70 s (bs)	α	——	1.79-1.73 m	n.o
δ	0.84 m					β	——	1.52 m	1.48-1.46 d(6.8)
						γ	——	1.41 m	1.36-1.34 m
						δ	——	0.89-0.87 m	0.89-0.87 m

[a]Chemical shift (δ) in ppm. [b]Multiplicity is given as s, singlet; d, doublet; t, triplet; q, quartet, m, multiplet. [c]Coupling constants are in parentheses^{3}J(^{1}H, ^{1}H), [d]bd is "broad signal", [e] n.o is "not observed", [f]For numbering see structures of R′ groups in Scheme 1 and α, β, γ, δ are given below:
-$^{\alpha}CH_2^{\beta}CH_2^{\gamma}CH_2^{\delta}CH_3$

Table 3. Contunied

Proton No.	L^6	(11)	(12)	Proton No.	L^7	(13)	(14)
1	7.76 s	7.77-7.76 d(6.8)	7.74-7.76 d(6.8)	2	6.78 m	6.76 m	7.02 s
3	7.58 m	7.56-7.54 d(7.2)	7.43-7.40 m	3	6.76-6.74 t	6.64-6.55 m	6.77-6.74 t
4	7.43-7.42 m	7.46-7.42 m	7.36-7.32 m	4	7.12-7.10 d(8.4)	7.11-7.09 d(7.2)	7.08-7.06 d(8)
5	7.68-7.65 m	7.66-7.65 m	7.62-7.60 d(7.6)	5	6.32-6.30 d(8.4)	6.28-6.23 m	6.31-6.29 d(8.4)
9,13	7.78-7.76 m	7.77-7.76 m	7.74-7.72 d(8)	9,11	7.28 m	7.28 d(6.4)	7.24 s
10,12	7.43-7.42 m	7.46-7.42 t	7.43-7.40 m	10	7.24 s	7.24 s	7.24 s
11	7.47-7.44 m	7.56-7.54 d(7.2)	7.55-7.51 t(60)	13	2.55 s	2.37 s	2.40 s
14	3.8-3.78 q(7.2)	3.81-3.80 m	3.69-3.67 m	α	——	1.85 m	1.81 m
15	1.54-1.52 d(7.2)	1.53-1.52 d(6.4)	1.42-1.40 d(6.8)	β	——	1.68-1.64 m	1.58-1.53 m
α	——	1.67-1.65 m	n.o	γ	——	1.33 m	1.36 m
β	——	1.53-1.52 d(6.4)	1.42-1.40 d	δ	——	0.95-.91 m	0.88 m
γ	——	1.32 m	1.24 s	NH	8.05-.03 d,d(1.6)	8.6 s	9.0-8.9 d(36)
δ	——	0.87-0.84 m	0.88 m				

[a]Chemical shift (δ) in ppm. [b]Multiplicity is given as s, singlet; d, doublet; t, triplet; q, quartet, m, multiplet. [c]Coupling constants are in parentheses $^3J(^1H, ^1H)$,
[d] n.o is "not observed". [e]For numbering see structures of R′ groups in Scheme 1 and α, β, γ, δ are given below:
$^{\alpha}CH_2^{\beta}CH_2^{\gamma}CH_2^{\delta}CH_3$

The integration of the spectra revealed a good agreement with the expected composition of the protons in the complex molecules. The proton signals of butyl groups appeared as a multiplet in the range δ 1.85-0.77 ppm whereas $^{n}J[^{119/117}\text{Sn}-\text{H}]$ coupling cannot be assigned due to complex multiplets.

^{13}C NMR spectra

The ^{13}C NMR spectra of L^1-L^7 and the corresponding tin(IV) complexes were also recorded in $CDCl_3$ and are presented in Table 4.

The ^{13}C NMR data of ligands are also included in Table 4 for comparison. The number of signals in the spectra correspond with the number of magnetically non-equivalent carbon atoms. The aromatic carbon's resonance peaks were assigned by comparison of the experimental chemical shifts with those calculated by the incremental method[11]. The resonance of carbonyl carbon in complexes 1-14 are observed at larger δ 174.0-181.9 ppm compared to the respective ligands δ 170.4-180.28 ppm[12], suggesting the coordination of the ligands through the carboxylic oxygen to organotin(IV) moiety[13]. The butyl groups display 4 resonances in the range δ 29.7-13.4 ppm, which is in good agreement with the reported value[14,15].

^{119}Sn NMR spectra

Table 5 contains the $\delta(^{119}\text{Sn})$ values of the studied compounds in a solution of non- coordinating solvent deutero chloroform ($CDCl_3$). These values demonstrate that all the reported compounds exhibit 4 coordination around the central tin atom in solution state. However, inspection of the^{119}Sn NMR data shows that the peak attributed to Sn-Cl in compounds 3, 5, 7, 9, 11 and 13 in the mono-organotin(IV) chlorides carboxylates has also been shifted upfield. One factor that can account for this observation is that the chloride ion attached to the central tin atom remains almost intact upon complexation.

Biological activity

All the synthesized compounds were screened for their microbial toxicity against a set of bacterial and fungal strains. The antifungal results of compounds 1-14 along with ligands are given in Table 6. The complexes were tested against 6 different plant fungal strains. Among the 6, 4 are standard strains whose ATCC numbers are 22397, 2192, 1030 and 11712 and 2 are non- standard strains, namely, *Microsporum cannis,* and *Candida glaberata. Miconazole* and *Amphotericin B* were used as standard drugs. All the complexes showed good anti-fungal activity against the strain with ATCC number 22397 and *M. cannis*. Complexes showed moderate activity against the strains with the ATCC numbers 1030 and 11712 but no activity against strain with the ATCC number 2192 and *C. glaberata*.

The reported compounds were also screened for their antibacterial effects against 4 standard bacterial strains and 2 non- standard bacterial strains. The standard strain's ATCC numbers are 6539, 25923, 12695 and 12696 and the non- standard strains are *Shigella flexenari* and *Pseudomonas aeruginosa* using the agar well diffusion method[16]. None of the complexes showed antibacterial activity.

LD_{50} data were determined for selective compounds by brine shrimp assay[17] and the results are summarized in Table 7. Compounds 6, 8, 12, 13 and 14 showed no positive lethality, while the compounds 4 and 7 showed cytotoxicity.

Table 4. ^{13}C NMR data of mono n-butyltin(IV) carboxylates.

C^{13}	L^1	(1)	(2)	C^{13}	L^2	(3)	(4)	C^{13}	L^3
1	109.2	115.7	115.7	1	181.3	181.5	181.9	1	134.4
2	150.3	149.0	149.6	2	45.0	47.9	47.8	2,6	130.2
3	113.7	113.4	113.7	3	18.0	18.3	19.3	3,5	128.9
4	135.2	136.0	133.7	4	140.8	140.6	139.6	7	124.1
5	116.1	116.0	115.7	5	129.3	129.3 (113.7)	128.8	8	167.0
6	132.4	131.5	133.0	6	127.2	127.3	127.4	9	152.9
7	138.2	138.3	138.9	7	136.9	137.2	139.0	10	132.8
8	132.9	132.1	127.2	8	30.1	30.2	30.2	11,15	128.8
9	138.0	138.7	138.0	9	45.0	45.0	45.1	12,14	126.5
10	123.0	122.5	124.8	10	22.4	22.4	22.4	13	124.1
11	126.0	126.7	126.1	α	—-	18.3	19.0	16	n.o
12	127.0	129.0	126.0	β	—-	29.7	29.7	17	175.3
13	20.5	20.0	20.6	γ	—-	22.7	22.4	α	—-
14	14.0	14.0	14.3	δ	—-	13.6	13.6	β	—-
15	173.6	n.o	174.5					γ	—-
α	—-	20.6	20.6					δ	—-
β	—-	28.0	29.7 (41.6)						
γ	—-	25.4	27.5 (33.1)						
δ	—-	14.0	13.3						

[a]Chemical shift (δ) in ppm, [b]For numbering see structures of R$^{/}$ groups in scheme1 and α, β, γ, δ are given below: -$^{\alpha}CH_2^{\beta}CH_2^{\gamma}CH_2^{\delta}CH_3$

Table 4. Contunied

C^{13}	(5)	(6)	C^{13}	L^4	(7)	(8)	C^{13}	L^5	(9)
1	134.4	134.3	1	173.2	175.o	174.0	1	148.9	141.0
2,6	130.0	130.1	2	128.0	130.0	132.5	2	123.6	123.7
3,5	128.9	128.9	3	132.1	132.0	133.8 (81)	3	128.9	128.9
7	124.5	124.1	4	116.7	117.0	116.5	4	127.6	127.6
8	166.7	166.6	5	135.0	135.0	135.3	5	161.6 (248)	161.6 (248.5)
9	152.5	153.0 (219.1)	α	—-	22.6	22.7	6	115.1	115.2
10	132.5	132.6	β	—-	29.6	29.6	7	135.4	135.4
11,15	128.8	128.7	γ	—-	25.5	25.6	8,12	128.2	128.4
12,14	126.3	126.4	δ	—-	13.5	13.6	9,11	130.8	130.8
13	124.5	124.1					10	128.0	127.0
16	14.1	n.o					13	44.8	47.8
17	178.6	176.3					14	17.9	18.1
α	25.6	25.8					15	180.28	180.7
β	29.6	29.6					α	—-	18.2
γ	26.8	27.5					β	—-	29.7
δ	13.4	n.o					γ	—-	25.5
							δ	—-	13.5

[a]Chemical shift (δ) in ppm, [b]For numbering see structures of R$'$ groups in Scheme 1 and α, β, γ, δ are given below: -$^{\alpha}CH_2^{\beta}CH_2^{\gamma}CH_2^{\delta}CH_3$

Table 4. Contunied

C^{13}	(10)	C^{13}	L^6	(11)	(12)	C^{13}	L^7	(13)	(14)
1	141.8	1	128.7	128.5	128.3	1	136.8	136.4 (196.9)	136.3
2	123.8	2	142.2	140.3	141.0	2	131.9	133.3	133.1
3	128.9	3	132.2	132.6	132.4	3	117.7	117.5	117.4
4	127.9	4	128.9	129.3	129.3	4	128.4	127.6	127.8
5	161.6 (248)	5	128.7	128.5	128.2	5	113.3	113.8	113.6
6	115.5	6,8	137.4	137.7	137.6	6	147.5	147.5	146.8
7	135.4	7	196.0	196.7	196.3	7	147.5	148.2	148.2
8,12	128.4	9,13	130.0	131.7	130.0	8,12	129.7	128.6	128.6
9,11	130.7	10,12	130.0	131.7	131.7	9,11	130.9	131.3	131.4
10	127.6	11	132.4	132.6	132.5	10	115.2	115.0	115.4
13	45.9	14	44.8	45.1	46.5	13	n.o	n.o	n.o
14	18.3	15	18.9	18.4	18.5	14	170.4	174.9	174.3
15	182.0	16	175.5	179.8	181.8	α		20.6	20.6
α	18.4	α	—-	18.4	18.5	β		29.6	29.6
β	29.7	β	—-	29.6 (41.62)	29.6 (41.27)	γ		26.9	26.7
γ	25.8	γ	—-	25.3	25.7	δ		13.4	13.3
δ	13.6	δ	—-	13.5	13.5				

[a]Chemical shift (δ) in ppm, [b]For numbering see structures of R′ groups in Scheme 1 and α, β, γ, δ are given below: -$^{\alpha}CH_2^{\beta}CH_2^{\gamma}CH_2^{\delta}CH_3$

Table 5. ^{119}Sn NMR data of mono-n-butyltin(IV) carboxylates.

Compound No.	δ (^{119}Sn)
L^1	–
(1)	–
(2)	+54.26
L^2	–
(3)	-20.18
(4)	+52.47
L^3	–
(5)	+146.28
(6)	-127.8
L^4	–
(7)	+164.2
(8)	+53.4
L^5	–
(9)	+45.6
(10)	-8.51
L^6	–
(11)	-20.2
(12)	–
L^7	–
(13)	+52.8
(14)	+55.8

Table 6. Antifungal Activity of mono-n-butyltin(IV) carboxylates

Fungus (ATCC #)	Percent Inhibition										Standard Drug
	L^1	(1)	(2)	L^2	(3)	(4)	L^3	(5)	(6)	L^4	
Trichophyton longifusus (22397)	60	60	60	85	80	60	75	65	80	75	Miconazole
Candida albicans (2192)	0	0	0	0	0	0	0	0	0	0	Miconazole
Aspergillus flavus (1030)	0	20	0	35	50	20	50	37	0	0	Amphotericin B.
Microsporum canis	75	68	63	80	79	65	60	50	75	85	Miconazole
Fusarium solani (11712)	35	30	0	65	50	10	70	26	20	20	Miconazole
Candida glaberata	0	0	0	0	0	0	0	0	0	0	Miconazole

Table 6. Contunied

Fungus (ATCC #)	Percent Inhibition										Standard Drug
	(7)	(8)	L^5	(9)	(10)	L^6	(11)	(12)	L^7	(13)	(14)	
Trichophyton longifusus (22397)	0	0	60	70	80	65	60	75	20	0	0	Miconazole
Candida albicans (2192)	0	0	0	0	0	0	0	0	0	0	0	Miconazole
Aspergillus flavus (1030)	0	58	65	0	10	0	79	40	0	16	0	Amphotericin B
Microsporum canis	45	55	65	85	85	70	6	55	30	0	50	Miconazole
Fusarium solani (11712)	40	16	60	30	30	10	0	10	35	0	0	Miconazole
Candida glaberata	0	0	0	0	0	0	0	0	0	0	0	Miconazole

Mass spectrometry

Mass spectra of all the compounds and the ligands were recorded on a Finnigan MAT-312 or a Varian MAT-112 double focusing mass spectrometer. No molecular ion peak was observed in the complexes with a few exceptions. Fragmentation for the investigated compounds is reported in the Experimental section.

Table 7. Cytotoxicity[a] data of selective mono n-butyltin(IV) carboxylates.

Compound No.	(4)	(6)	L^4	(7)	(8)	(12)	L^7	(13)	(14)
$LD_{50}(\mu g/mL)$	(+) 1015.1430	(-)	(-)	(+) 120.5259	(-)	(-)	(+)1.5379	(-)	(-)

[a]Against brine shrimp (Artemia salina)

(+) Positive lethality

(-) No positive lethality

Standard drug Etoposide

$LD_{50}$of standard drug is 7.4625(μg/mL)

LD_{50}= Lethal dose at which 50% organisms die

Conclusions

It is concluded that Δv(COO) of the complexes falls in the range 398-215, which indicates the anisobidentate nature of the carboxylate group in solid state. Mass spectral data show that no molecular ion peak is observed in the complexes with a few exceptions. Multinuclear NMR data show that mono-organotin(IV) carboxylates exhibits 4 coordination around the central tin atom in solution state. The biological studies reveal that the compounds do not show antibacterial activity, but they show significant antifungal activity and cytotoxicity.

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