Synthesis, Characterization and Antimicrobial Activity of Potential Bioactive Organotin(IV) Dithiocarboxylates

[1, 2] Syed Mustansar Abbas, [1] Muhammad Sirajuddin, [1] Farooq Ali Shah
[1] Saqib Ali* and [1] Sajjad Ahmad
[1]*Department of Chemistry, Quaid-i-Azam University, Islamabad 45320, Pakistan.*
[2]*Nanoscience and Catalysis Division, National Centre for Physics, Quaid-i-Azam University Campus, Islamabad, Pakistan.*
drsa54@yahoo.com*

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Summary: A series of newly synthesized organotin(IV) compounds; Me_2SnClL **(1)** Bu_2SnClL **(2)**, Ph_2SnClL **(3)**, Me_3SnL **(4)**, Ph_3SnL **(5)** have been derived from the reaction of organotin(IV) chlorides with 4-formylpiperazinium 4-formylpiperazine-1-carbodithioate **(L)** in the appropriate molar ratio. Their spectroscopic investigations have been carried out in solution state. Based on spectroscopic results, the ligand appeared to coordinate to the Sn atom through the CSS moiety. Bioassay results have revealed that these compounds have good antibacterial and antifungal activities and may well be the basis for a new class of antimicrobial drugs. The triorganotin(IV) derivatives in particular, were found to be more active than diorganotin(IV) compounds.

Keywords: Organotin(IV) dithiocarboxylate; Antibacterial activity; Antifungal activity.

Introduction

The chemistry of organotin(IV) compounds has grown with prolific speed on account of diverse chemical, physical and especially their biological properties like antiviral and anticancer agents, *in vitro* antibacterial and antifungal agents [1]. Out of various classes of organotin(IV) compounds, dithiocarboxylates are extensively used in biology [2], medicine [3], organic synthesis [4], analytical chemistry [5], as antioxidants [6], polymer photo stabilizers [7], and precursors for creating sulfide film semiconductors [8]. Among various sulfur containing ligands the dithiocarboxylate moiety has proved as a useful structural motif showing exceptional coordination ability to form stable complexes with range of metal ions [9] as they are considered soft donors. Due to small bite angle (2.8–2.9A°) they efficiently stabilize unusual oxidation states of a variety of metal ions by stabilization of definite stereochemistry in their metal complexes [10].

Piperazine based ligands generate novel supramolecular structures due to possible hydrogen bonding of such nitrogen containing aliphatic heterocyles [11]. The chair form generally exists in 17.2 kJ/mol higher thermodynamic stability than the other readily convertible boat conformation of piperazine and its substituted derivatives [12].

Generally speaking the biological behavior of organotin(IV) dithiocarboxylates is inclined by the structure of the molecule and by the coordination number of the tin atom. Consequently, some metal-based dithiocarboxylates like ziram (zinc-dimethyldithiocarboxylate) and zineb (zinc ethylene-1,2-bis-dithiocarboxylate) are marketed as fungicides [13]. Organotin(IV) dithiocarboxylates have been largely tested for their antifungal activity and of the presence of tin was illustrated by the fact that all the organotin(IV) compounds investigated had activities greater than those exhibited by the uncoordinated dithiocarboxylate ligand [14]. The rapid appearance of bacterial infections that are resistant to many drugs argues the need for new therapeutic agents. Here in we report the synthesis, characterization and antimicrobial activity of some new organotin(IV) dithiocarboxylate derivatives.

Results and Discussion

FT-IR

The comparison was carried out between the spectra of complexes formed and the precursor. The disappearance of a vibration signal at 3200 cm^{-1} in L-salt due to N-H bond stretching in R_2NH (secondary amine) indicates, the formation of a ligand. The disappearance of NH_2^+ bond stretching at 2485 cm^{-1} of free ligand, in all the complexes indicate that cationic portion of the L-salt is detached, which in turn is replaced by more electropositive tin metal. There are two significant bands observed in the IR spectra of dithiocarboxylates, one of them predicts the nature of binding of 1,1-dithioate moiety of

*To whom all correspondence should be addressed.

ligand in the range of 950-1050 cm^{-1} [15] and the other one helps to allot the shift of electron density towards the coordinating metal ion in the range of 1450-1600 cm^{-1} and is termed as thioureide band [16]. In our present study we have observed a single sharp band at 995 ± 20 cm^{-1} for all the complexes, which according to literature [17] is indicative of bidentate coordination of L-salt. The ν(C-N) at 1434 cm^{-1} in L-salt was found to be shifted to such a wave number in complexes which is intermediate between C-N single bond (1250-1360 cm^{-1}) and C=N double bond (1640-1690 cm^{-1}) [18], owing to the electron delocalization towards the tin metal. The unaltered strong band due to aldehydic carbonyl group at 1666 cm^{-1} confirms the non-involvement of this group in coordination [19]. In case of compounds **3**, **5** the sharp bands due to $–C_6H_5$ further supports the formation of these complexes.

NMR

In the ^{1}H-NMR spectra of the complexes (Table-1), the disappearance of duplicate peak pattern due to 4-formylpiperazinium ion at 7.89, 2.93-3.02 and 3.48-3.52 ppm due to aldehydic and methylene protons, respectively, of cationic portion of L-salt, and appearance of new signals for the organic groups attached to Sn deep rooted our findings for complexes **1-5**. The anionic aldehydic part of L-salt at 7.95 ppm in the ligand shows a slight shift to 8.12-8.18 ppm in the complexes, indicating that it is not affected by complexation. The methylene proton of piperazine ring showed a slight downfield shift from 3.31-3.44 ppm, because of electron density shift to central tin [20-22]. For complex **2**, the terminal methyl protons of butyl group emerge as a clear triplet at 0.93 ppm while multiplets are observed at 1.48-1.21 ppm for methylene protons. The aromatic protons in complexes **3** and **5** were observed at 7.10-7.94 ppm.

The detachment of cationic part of L-salt results in vanishing of duplicate peak pattern in ^{13}C-NMR spectra of complexes **1-5** (Table-2). A substantial shift is observed for C(1) for all the complexes due to deshielding of –CSS moiety upon coordination with Sn centre. A slight variation for aldehydic carbon at 163.5 ppm in L-salt in all the complexes confirms its non-involvement in coordination. Organic species attached to tin centre give signals in the expected regions. The magnitude of the ^1J[^{119}Sn, ^{13}C] coupling constant in complexes **3** and **4** are 798 and 570 Hz, respectively, which is an indication of 5-coordinated geometry around the tin atom [23-28]. The ^2J(^{119}Sn, ^{1}H) value for complexes **1** and **4** were 79 and 70 Hz, respectively, which is a normal tendency for 5-coordinated tin [23-28] and is in agreement with C-Sn-C angle of 129.6^o and 119.9^o (Table-3).

Mass Spectrometry

The conventional EI mass spectral data for the ligand and compounds **1–5** are recorded and different fragmentation patterns have been proposed and are listed in Scheme-1 along with m/z and % intensity. The different fragments are found to be in close correlation with the structures expected, on the basis of various spectroscopic techniques discussed earlier. In the mass spectrum of L-salt, molecular ion peak is observed at m/z (%), 304 (40.3) while a base peak at m/z (%), 56 (100) for a four member heterocycle.

Table-1: ^{1}H-NMR chemical shifts[a,b] of the compounds 1-5 (in ppm).

^{1}H	(1)	(2)	(3)	(4)	(5)
4	8.16 (s)	8.18 (s)	8.12 (s)	8.13 (s)	8.17 (s)
2,2´	3.99–4.07 (m)	4.20–4.46 (m)	4.13–4.29 (m)	4.47–4.54 (m)	4.26–4.34 (m)
3,3´	3.71–3.74 (m)	3.51–3.68 (m)	3.49–3.53 (m)	3.49–3.51 (m)	3.58–3.61 (m)
	3.55–3.59 (m)	3.69–3.73 (m)	3.55–3.60 (m)	3.52–3.59 (m)	3.38–3.41 (m)
α	(1.44) (s) [79]	1.48-1.21 (m)	-	0.65 (s) [70, 68]	-
β	-	1.48-1.21 (m)	7.94 (bs)	-	7.40 (m)
γ	-	1.48-1.21 (m)	7.46 (bs)	-	7.29 (m)
δ	-	0.93 (t) (7.5)	7.10 (bs)	-	7.25 (m)

a) Chemical shift (δ) in ppm. ^2J [^{119}Sn, ^{1}H], ^3J (^{1}H, ^{1}H) in Hz are listed in square brackets and parenthesis, respectively. Multiplicity is given as s = singlet, m = muliplet, bs = broad signal. b) Numbering in accordance with Scheme 2.

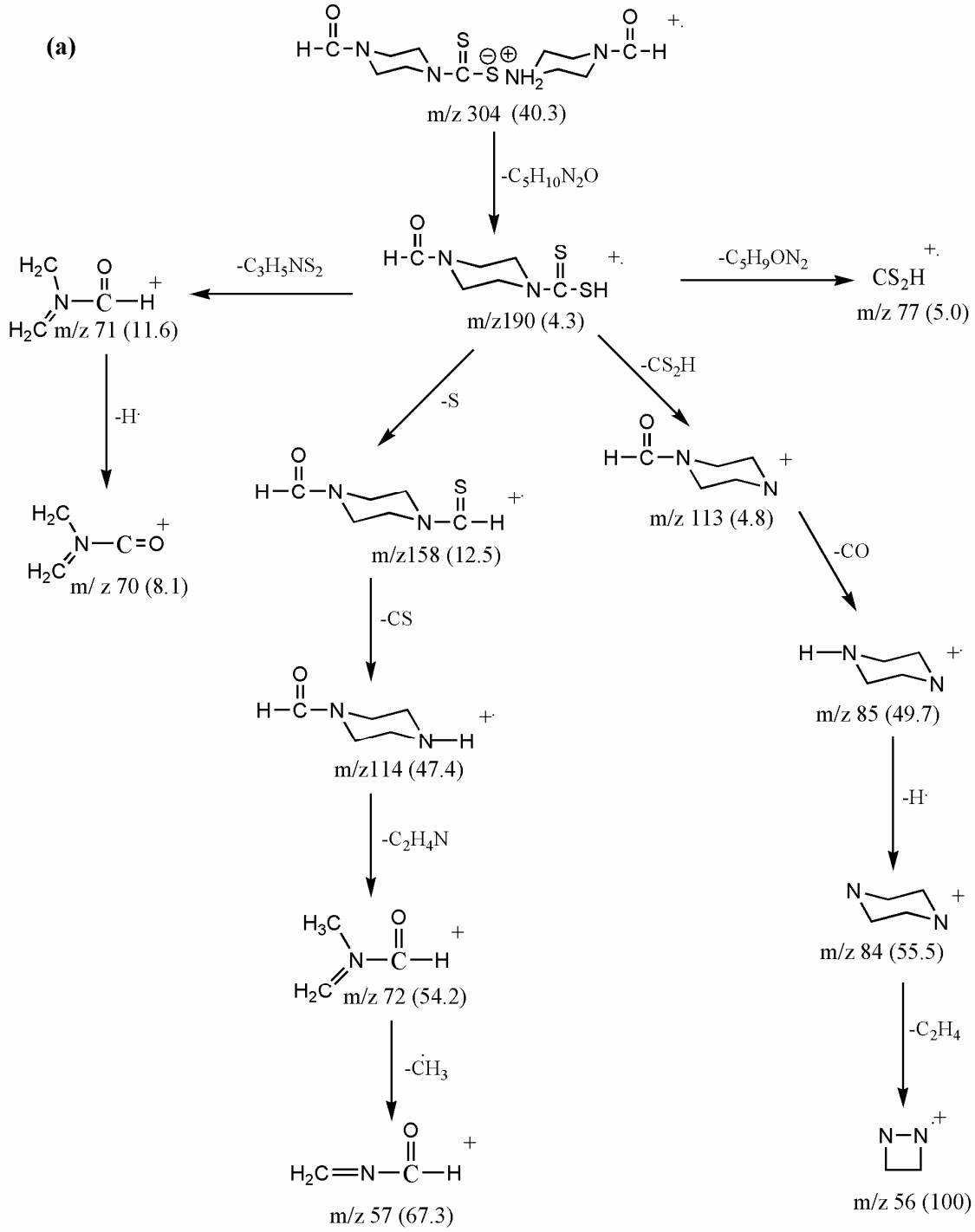
Table-2: ^{13}C-NMR chemical shifts of the compounds 1-5 (in ppm).

^{13}C	(1)	(2)	(3)	(4)	(5)
4	160.8	160.8	161.0	162.0	161.0
3,3´	44.3, 39.1	44.4, 39.8	45.0, 39.7	45.0, 39.5	45.0, 39.7
2,2´	51.8, 50.8	51.8, 50.8	51.2, 50.2	50.6, 49.3	51.2, 50.2
1	198.8	200.3	189.7	183.9	185.3
α	10.1	32.8	133.7	29.4	134.0
	[560, 552]	[523, 517]	[798, 789]	[570, 565]	[605, 600]
β	-	29.5 [46]	131.6	-	129.7 [65]
γ	-	27.1 [63]	130.8	-	128.7 [73]
δ	-	26.5	129.3	-	128.5

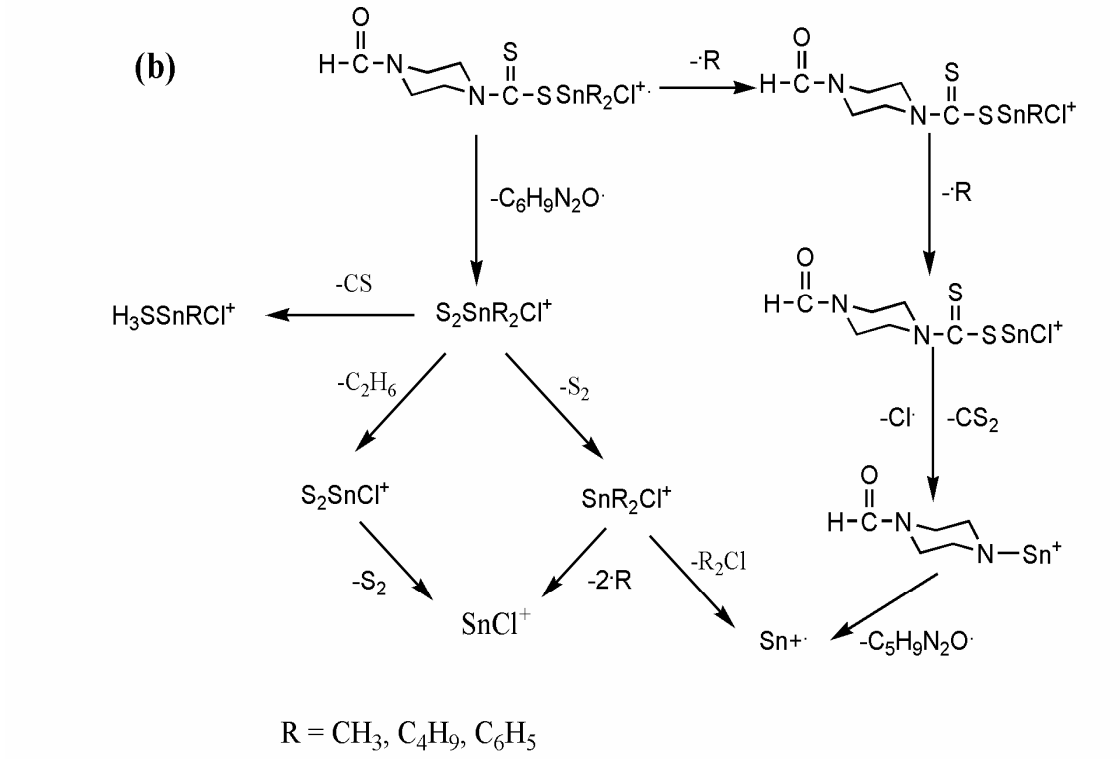
a) Chemical shifts (δ) in ppm. ^nJ [^{119}Sn, ^{13}C] in Hz are listed in square brackets. b) Number in accordance with Scheme 2.

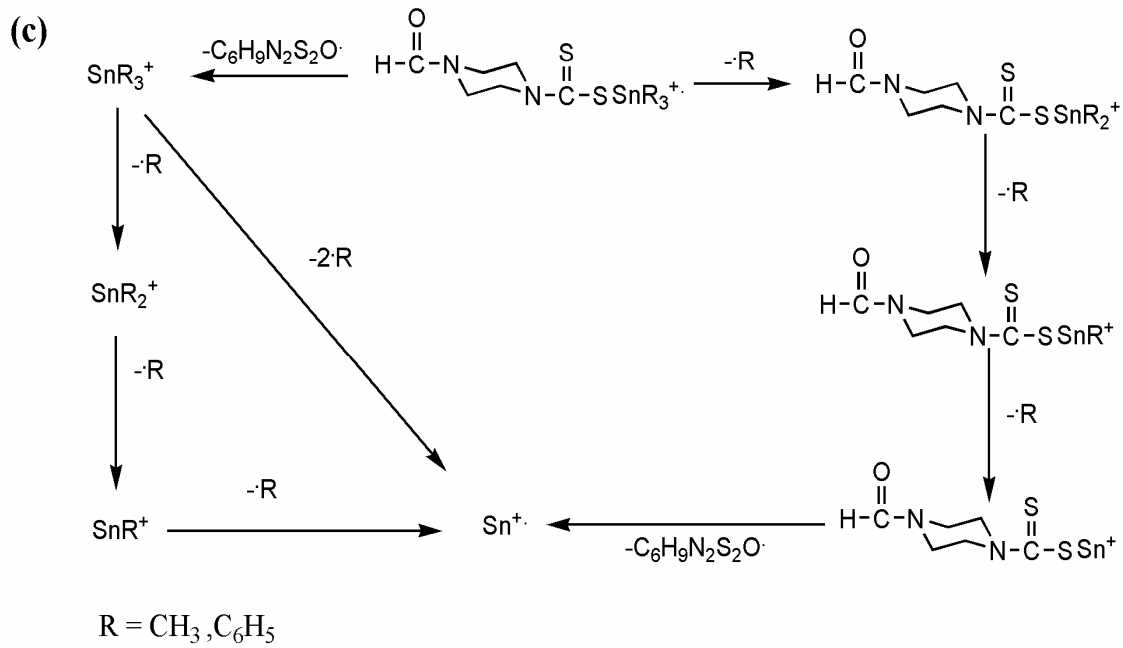
Table-3: (C-Sn-C) angles (°) based on NMR parameters of selected organotin(IV) derivatives.

Compound	$^{1}J(^{119}Sn-^{13}C)$ (Hz)	$^{2}J(^{119}Sn-^{1}H)$ (Hz)	Angle(◦)	
			$\theta(^{1}J)$	$\theta(^{2}J)$
1	560	79	125.9	129.6
2	523	-	127	-
3	798	-	125.8	-
4	506	70	126.8	119.9
5	605	-	129.8	-



Scheme-1 continue..





Scheme-1: Proposed mass fragmentation patterns for (a) L-salt (b) Chlorodiorganotin(IV) dithiocarboxylates (c) Triorganotin(IV) dithiocarboxylates
[Mass (% of the total positive current carried by identified tin-containing ions)].

As a general trend for organotin compounds, the molecular ion (M^+) was not cited for complexes **1-5**. Due to tin isotopes cluster of peaks appear in mass spectral data, but for simplicity only principle isotope ^{120}Sn is well thought out [29]. In triorganotin(IV) dithiocarboxylates, the primary fragmentation occurs *via* two routes either by the loss of ligand or tin-bonded R group. In both fragmentation routes, the daughter ion of the primary fragmentation, loss R groups in successive steps to give $[Sn]^+$ ion as the end product.

For chlorodiorganotin(IV) dithiocarboxylates, fragmentation also commence either by loss of R^+ or the organic part of the anion. For dimethyltin(IV) derivatives, an abundant tin-containing sulphonium ion, $H_3SSn(CH_3)Cl^+$ is formed *via* dimethyl species $S_2Sn(CH_3)_2Cl$, [30] which in sequence undergoes fragmentation to the terminal $SnCl^+$ and Sn^+ species, the latter perhaps derived from $SnCH_3^+$. Dibutyltin(IV) and diphenyltin(IV) derivatives also adopt a similar fragmentation behaviour except that the steric effects of the these larger groups compared to smaller methyl may be sufficient to account for the ease of losing R^+ groups. Hence ions formed by loss of CH_3^+ provide only minor amount of current (<3.0) for tin-containing ions, while it is significantly larger for $C_6H_5^+$ and $C_4H_9^+$.

Biological Activities

Antibacterial Activity

Free ligand and its organotin(IV) complexes were tested against five different strains of bacteria by agar well diffusion method (Table-4). The activity of the organotin(IV) derivatives is higher than its ligand. The higher activity of the organotin(IV) derivatives can be explained on the basis of chelation theory of metals which assigns this activity to reduction in polarity of central Sn atom upon coordination with the ligand and hence high lipophilicity for infiltration through the bacterial lipid bilayer. This reduction in polarity is thought to be achieved due to partial sharing of metal positive charge with donor groups and secondly due to *p*-electrons delocalization within the whole chelating ring [31, 32].

Table-4: Antibacterial activity of the free ligand salt and its di and triorganotin(IV) complexes.

Bacterium	Zone of Inhibition of samples in diameter (mm)						Standard Drug[a]
	L-salt	(1)	(2)	(3)	(4)	(5)	
Bacillus subtilis	**20**	**41**	**39**	**32**	**47**	**42**	**30**
Stephlococcus aureus	**23**	**40**	**42**	**42**	**49**	**43**	**37**
Shigella flexenaria	**22**	**35**	**24**	**22**	**41**	**41**	**35**
Salmonella typhi	**12**	**37**	**13**	**14**	**40**	**39**	**32**
Escherichia coli	**15**	**36**	**16**	**16**	**44**	**42**	**30**

a) Standard drug = Imipenem

In general, triorganotin(IV) derivatives are more active than the diorganotin(IV) compounds which may be due the greater lipophilic character of triorganotin(IV) because of greater number of alkyl groups attached to the tin atom. Lipopolysaccharides form an outer lipid membrane and contribute to the complex antigenic specificity of gram-negative cells. The effect of various compounds may then vary among microorganisms due to difference in the structures of the cell [33, 34]. Also, activity decreases with increasing length of alkyl group, which may be due to slow movement and greater hydrophobic character of bulky groups. This trend shows dependence of antibacterial activity on number and nature of alkyl group attached to tin [35]. Most of the diorganotin(IV) derivatives significantly inhibit gram-positive bacterial growth. This may be due to the ease of permeation of the complexes owing to the simplicity of the cell wall of these strains. Most probably, this is also because of the development of small interaction by halo substituents. These small interactions may cause increase in hydrolysis and up to some extent lipophilicity, which are the main factors for the improvement of potency of these compounds. The high activity of chloromethyldiorganotin(IV) derivatives than the corresponding diorganotin(IV) compounds may be described on the basis of labile nature of the chloro group and also due be the Efflux effect (a mechanism responsible for moving out of toxic substances and antibiotics outside the cell).

Antifungal Activity

The agar tube dilution protocol method was employed to test the antifungal activities of the synthesized compounds against five different strains of fungi, and the results are shown in Table-5. Both the triorganotin(IV) and chlorodimethyltin(IV) derivatives are active against the fungi tested. In fact, few compounds have activities higher than that of the standard drug (*Clotrimazole*).

In general triorganotin(IV) are more active than chlorodiorganotin(IV) complexes against all fungi. However, chlorodimethyltin(IV) derivative is more active against *Aspergillus fumigates* and *Fusarium solani*. High activity of triorganotin(IV) and chlorodimethylorganotin(IV) is probably due to high lipophilicity and feasible permeability to cytoplasm where compounds interact to cause extensive K^+ discharge and the organism dies. Since few of our synthesized compounds are more active than is the standard drug (*Clotrimazole*) against fungi so these compounds have potential to be used as antifungal drug in future.

Table-5: Antifungal activity of the free ligand salt and its di and triorganotin(IV) complexes.

Sample	Tested fungi									
	Fusarium moniliformis		Aspergillus niger		Fusarium solani		Aspergillus fumigatus		Alternaria specie	
	Linear growth	% inhibition	Linear growth	% inhibition	Linear growth	% inhibition	Linear growth	% inhibition	Linear growth	% inhibition
Control[b]	86	-	85	-	85	-	86	-	90	-
L-salt	76	11.6	78	8.2	82	3.5	86	0.0	82	8.9
(1)	26	69.7	28	67.0	29	65.8	10	88.4	16	82.3
(2)	68	20.9	79	7.0	70	17.6	83	3.5	77	14.5
(3)	60	30.2	76	10.5	76	10.6	80	7.0	69	23.4
(4)	22	74.4	26	69.4	32	62.3	16	81.4	16	82.3
(5)	29	66.2	32	62.3	36	57.6	23	73.2	18	80.0
Clotrimazole[a]	58	32.5	62	27.0	56	34.1	69	19.8	76	15.6

a) Concentration: 200 µL/mL of DMSO. b) Control = DMSO

Experimental

Materials and Methods

Me_2SnCl_2, Me_3SnCl, *n*-Bu_2SnCl_2, Ph_2SnCl_2, Ph_3SnCl, 1-formylpiperazine were procured from Aldrich chemical company and carbon disulphide from Riedal-de-Haën. Various solvents such as chloroform, diethyl ether, toluene, n-hexane, ethanol and DMSO of analytical grade were purchased from E-Merk and Fluka. All the organic solvents were dried before use according to standard procedures [37].

Melting points were determined in a capillary tube using a Gallenkamp (U.K) electrothermal melting point apparatus. IR spectrum in the range of 4000-400 cm^{-1} was obtained on a Thermo Nicolet-6700 FT-IR Spectrophotometer equipped with DTGS (deuterated triglycine sulphate) detector. Microanalysis was done using a Leco CHNS 932 apparatus. ^1H and ^{13}C-NMR were recorded on a Bruker-300 MHz FT-NMR Spectrometer, using $CDCl_3$ as an internal reference [^1H ($CDCl_3$) = 7.25 and ^{13}C ($CDCl_3$) = 77]. Chemical shifts are given in ppm and coupling constants (*J*) values are given in Hz. The multiplicities of signals in ^1H-NMR are given with chemical shifts; (s = singlet, d = doublet, t = triplet, m = multiplet). Electron impact (70 ev) mass spectra were recorded on a Kratos MS25RFA. The m/z values were evaluated assuming that H = 1, C = 12, N = 14, O = 16, Cl = 35 and Sn = 120.

Synthesis

Synthesis of 4-formylpiperazinium 4-formylpiperazine-1-carbodithioate (L-salt)

Dropwise addition of 1.20 mL (0.02 mol) CS_2 in ethanol (20 mL) to 0.04 mol of 1-formylpiperazine in ethanol (50 mL) followed by stirring for 6h at 273K gave the white product. This was filtered and washed with diethyl ether and finally air dried.

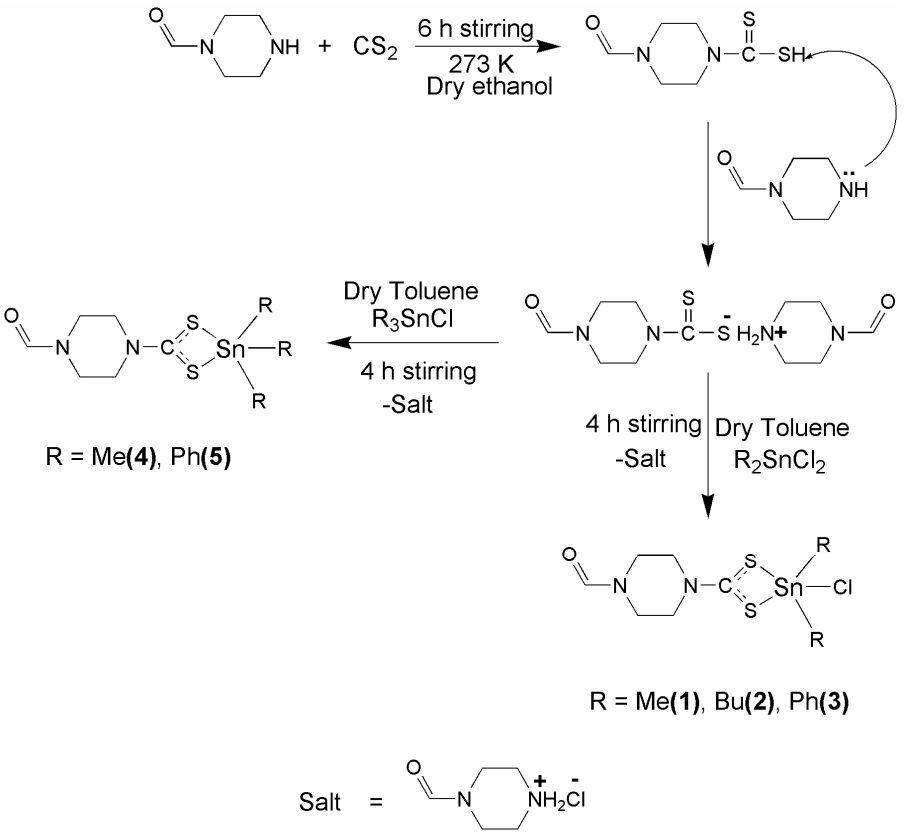
Yield: 5.6g, 92%. M.p. 180-182 ^oC. Elemental Anal. Calc. for $C_{11}H_{20}N_4O_2S_2$: C, 43.4; H, 6.6; N, 18.4; S, 21.1. Found: C, 43.1; H, 6.6; N, 18.5; S, 21.4. FT-IR (cm^{-1}): 995 ν(C-S), 1434 ν(C-N), 1666 ν(C=O), 2485 ν(NH_2^+). EI-MS, m/z (%): $[C_5H_{10}N_2O]^+$ 114 (68.2), $[C_4H_9N_2]^+$ 85 (49.7), $[CS_2H]^+$ 77 (5.0), $[C_3H_5NO]^+$ 71 (11.6), $[C_2H_3NO]^+$ 57 (67.3), $[C_2H_4N_2]^+$ 56 (100.0). ^1H-NMR ($CDCl_3$; ppm): 7.95,7.89 (s, $H_{4,4a}$), 3.39–3.44, 3.48-3.52 (m, H3,3´,3a,3´a), 4.24-4.69, 2.93-3.02 (m, H2,2´,2a,2´a). ^{13}C-NMR ($CDCl_3$; ppm): 210.2 (C-1), 51.0, 49.7, 42.4, 38.1 (C-2,2´,2a,2´a), 45.2, 39.7 , 44.0, 42.9 (C-3,3´,3a,3´a), 163.5, 163.3 (C-4,4a)

General Procedure for Synthesis of Complexes

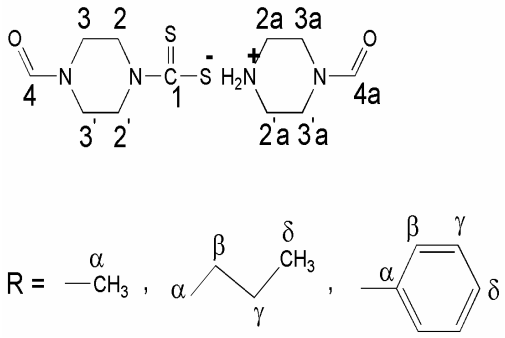
Appropriate molar ratios of R_3SnCl/R_2SnCl_2 in toluene (30 mL) were added dropwise to ligand in toluene (50 mL) and the mixture was refluxed for 4h with constant stirring. Soluble product was isolated by filtration and the solvent was rotary evaporated to get the desired products (Scheme-2). All the complexes were white solids, stable in air and were soluble in $CHCl_3$ and DMSO. The numbering scheme of ligand-salt and alkyl groups attached to tin is given in Scheme-3.

Synthesis of chlorodimethylstannyl 4-formylpiperazine-1-carbodithioate **(1)**

Yield: 0.6g, 76%. M.p. 152-155 ^oC. Elemental Anal. Calc. for $C_8H_{15}N_2OS_2SnCl$: C, 25.7; H, 4.1; N, 7.5; S, 17.2. Found: C, 25.7; H, 4.0; N, 7.5; S, 17.1. IR (cm^{-1}): 987 ν(C-S), 1492 ν(C-N), 1649 ν(C=O), 365 ν(Sn–S), 464 ν(Sn–C), 263 ν(Sn–Cl). EI-MS, m/z (%): $[C_7H_{12}N_2OS_2SnCl]^+$ 359 (1.2), $[C_6H_9N_2OS_2SnCl]^+$ 344 (0.9), $[CH_6SSnCl]^+$ 205 (59.6), $[C_2H_6SnCl]^+$ 185 (24.7), $[SnCl]^+$ 155 (38.3), $[CH_3Sn]^+$ 135 (4.3), $[Sn]^+$ 120 (11.2).



Scheme-2: Synthesis of ligand-salt and their organotin(IV) compounds.



Scheme-3: Numbering scheme of ligand-salt and organic groups.

Synthesis of chlorodibutylstannyl 4-formylpiperazine-1-carbodithioate **(2)**

Yield: 0.41 g, 63%. M.p. 108-110 °C. Elemental Anal. Calc. for $C_{14}H_{27}N_2OS_2SnCl$: C, 36.7; H, 6.0; N, 6.1; S, 14.0. Found: C, 36.7; H, 5.9; N, 6.1; S, 14.0. IR (cm^{-1}): 987 ν(C-S), 1475 ν(C-N), 1666 ν(C=O), 355 ν(Sn–S), 467 ν(Sn–C), 261 ν(Sn–Cl). EI-MS, m/z (%): $[C_{10}H_{17}N_2OS_2SnCl]^+$ 400 (1.9), $[C_6H_8N_2OS_2SnCl]^+$ 343 (8.3), $[C_8H_{18}SnCl]^+$ 269 (70.1), $[S_2SnCl]^+$ 219 (28.1), $[SnCl]^+$ 155 (39.5), $[Sn]^+$ 120 (17.0), $[C_4H_9Sn]^+$ 177 (2.0).

Synthesis of chlorodiphenylstannyl 4-formylpiperazine-1-carbodithioate **(3)**

Yield: 0.42 g, 64%. M.p. 202-204 °C. Elemental Anal. Calc. for $C_{18}H_{19}N_2OS_2SnCl$: C, 43.4; H, 3.9; N, 5.6; S, 12.9. Found: C, 43.4; H, 3.8; N, 5.6; S, 13.0. IR (cm^{-1}): 978 ν(C-S), 1467 ν(C-N), 1657 ν(C=O), 3059 ν(C_6H_5), 357 ν(Sn–S), 466 ν(Sn–C),

260 ν(Sn–Cl). EI-MS, m/z (%): $[C_6H_9N_2OS_2SnCl]^+$ 344 (1.2), $[C_5H_9N_2OSn]^+$ 233 (7.8), $[C_{12}H_{10}SnCl]^+$ 309 (43.0), $[C_6H_5SnCl]^+$ 232 (6.1), $[SnCl]^+$ 155 (62.3), $[C_6H_5Sn]^+$ 197 (3.6), $[Sn]^+$ 120 (11.9).

Synthesis of trimethylstannyl 4-formylpiperazine-1-carbodithioate **(4)**

Yield: 0.52g, 71%. M.p. 127-130 °C. Elemental Anal. Calc. for $C_9H_{18}N_2OS_2Sn$: C, 30.6; H, 5.1; N, 7.9; S, 18.2. Found: C, 30.6; H, 5.1; N, 7.9; S, 18.1. IR (cm^{-1}): 985 ν(C-S), 1417 ν(C-N), 1649 ν(C=O), 358 ν(Sn–S), 468 ν(Sn–C). EI-MS, m/z (%): $[C_8H_{15}N_2OS_2Sn]^+$ 339 (9.7), $[C_7H_{12}N_2S_2OSn]^+$ 324 (18.9), $[C_6H_9N_2S_2OSn]^+$ 309 (40.0), $[C_3H_9Sn]^+$ 165 (61.9), $[C_2H_6Sn]^+$ 150 (27.4), $[Sn]^+$ 120 (13.6).

Synthesis of triphenylstannyl 4-formylpiperazine-1-carbodithioate **(5)**

Yield: 0.35g, 59%. M.p. 122-125 °C. Elemental Anal. Calc. for $C_{24}H_{24}N_2OS_2Sn$: C, 53.5; H, 4.5; N, 5.2; S, 11.9. Found: C, 53.4; H, 4.5; N, 5.2; S, 11.7. IR (cm^{-1}): 985 ν(C-S), 1475 ν(C-N), 1649 ν(C=O), 3123 ν(C_6H_5), 358 ν(Sn–S), 466 ν(Sn–C). EI-MS, m/z (%): $[C_{18}H_{19}N_2OS_2Sn]^+$ 463 (5.2), $[C_{18}H_{15}Sn]^+$ 351 (41.8), $[C_{12}H_{10}Sn]^+$ 274 (3.7), $[C_6H_5Sn]^+$ 197 (25.9), $[Sn]^+$ 120 (20.4).

Antibacterial Assay

The synthesized compounds **(1-5)** were tested for antibacterial activity against five different bacterial strains including, two gram-positive: *Staphylococcus aureus, Bacillus subtilis*, and three gram-negative: *Escherichia coli, Salmonella typhi,* and *Shigella flexenari*, using the agar well diffusion method [38] with *Imipenem* as a standard drug for comparison. 0.75 mL of the broth culture containing ~10^5 colony forming units per mL of the test strain was added to the 75 mL of nutrient agar medium at 37 °C, mixed well, and then poured into a 14 cm sterile Petri plate. The media were allowed to solidify, and wells were dug with a sterile metallic borer having 8mm diameter. Then a dimethyl sulphoxide (DMSO) solution of test compounds at 2 mg/mL was added to the respective wells. DMSO served as negative control and the standard antibacterial drug *Imipenem* (1 mg/mL) was used as positive controls. The plates were incubated aerobically at 37 °C for 24h. Test compounds were checked at 200 µg/mL, 100 µg/mL and 50 µg/mL as final concentrations. The activity was determined by measuring the diameter of zone showing complete inhibition (mm). Thereby zones were precisely measured with the aid of a vernier caliper (precision ± 0.1 mm).

Antifungal Assay

Antifungal activity against five fungal strains *Fusarium moniliformis*, *Alternaria species*, *Aspergillus niger*, *Fusarium solani*, and *Aspergillus fumigatus* was determined with the agar tube dilution method [38]. Screw caped test tubes containing Sabouraud dextrose agar (SDA) medium (4 mL) were autoclaved at 121 °C for 15 min. Tubes were allowed to cool at 50 °C and non solidified SDA was loaded with 66.6 µL of compound from the stock solution (12 mg mL^{-1} in DMSO) to make 200 µg mL^{-1} final concentration. Tubes were then allowed to solidify in slanting position at room temperature. Each tube was inoculated with 4 mm diameter piece of inoculum from seven days old fungal culture. The media supplemented with DMSO and *Clotrimazole* (200 µg mL^{-1}) were used as negative and positive control, respectively. The tubes were incubated at 28 °C for 7 days and growth was determined by measuring linear growth (mm) and growth inhibition was calculated with reference to growth in vehicle control using the Vincent equation [39]:

$$\text{Inhibition \%} = 100(C-T)/C$$

where C is the diameter of fungal growth for a control and T is the diameter of fungal growth for the sample.

Conclusions

Five new organotin compounds of 4-formylpiperazinium 4-formylpiperazine-1-carbodithioate were synthesized by reacting it with respective organotin(IV) chlorides and fully characterized by different analytical techniques. All the compounds have been tested against biological organisms and were found to be active however the activity is maximum for complexes **4** and **5.** The primary role of the metal and alkyl/aryl groups during biological testing is credited as compared to ligand, as it helps in ease of diffusion and creating secondary interaction with cell constituents. This study provides a further step in designing novel antifungal metal-based drugs.

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