Available online at www.sciencedirect.com
ScienceDirect
European Journal of Medicinal Chemistry 43 (2008) 2380–2385
EUROPEAN JOURNAL OF MEDICINAL CHEMISTRY
http://www.elsevier.com/locate/ejmech

Original article

Synthesis, spectral characterization and bio-analysis of some organotin(IV) complexes

Wajid Rehman [a,*], Musa Kaleem Baloch [b], Amin Badshah [c]

[a] Department of Chemistry, Hazara University, Mansehra, Pakistan
[b] Department of Chemistry, Gomal University, Dera Ismail Khan, Pakistan
[c] Department of Chemistry, Quaid-e-Azam University, Islamabad, Pakistan

Received 1 July 2007; received in revised form 12 December 2007; accepted 10 January 2008
Available online 31 January 2008

Abstract

Five novel organotin(IV) derivatives have been synthesized by refluxing trimethyl, triethyl, tributyl, and triphenyl and tribenzyltin chloride with Schiff base derived from salicylaldehyde and adenine. These compounds were characterized by spectroscopic (IR, ^{1}H, ^{13}C, ^{119}Sn-NMR, ^{119m}Sn Mössbauer) techniques and elemental analysis. Based on these results, trigonal bipyramidal geometry is suggested. The synthesized compounds were also treated with various microorganisms and found to be active.

Keywords: Organotin; Spectra; Salicylaldehyde; Adenine; Schiff base

1. Introduction

Organotin(IV) compounds have fascinated much attention owing to their potential biocidal activities, industrial and agricultural applications [1–5]. In general, the biochemical activity of organotin compounds is influenced greatly by the structure of the molecule and the coordination number of the tin atoms [3–5]. Among these, organotin Schiff bases have gained much importance, as such ligands and their metal complexes are reported to exhibit biocidal and anti-tumor activities [1–4]. It has also been reported that that the Schiff base metal complexes derived from the salicylaldehyde can specially cleave the DNA [6–8]. In order to expand the scope of investigations on the coordination behavior of various donor ligands towards organotins, we carried out the investigations on organotin(IV) compounds containing various ligands and established their bioactivities [9–15]. As an extension of this research field, we are now interested in the development of the chemistry of some novel organotin compounds obtained by the interaction of a number of organotin(IV) halides with the Schiff base derived from salicylaldehyde and adenine. These complexes are also tested against various types of microorganisms in order to establish their bioactivity.

2. Experimental

All the triorganotin(IV) compounds except tribenzyltin chloride were purchased from Fluka and were used as such. Tribenzyltin chloride was synthesized through a known method [16]. All the reactions were carried out under anhydrous and oxygen free atmosphere. The solvents used were dried before use according to the prescribed method [17].

Melting point was measured on a Reichert thermometer of F.G. Bode Co., Austria. IR spectra were obtained in KBr using Perkin–Elmer FT IR-1605 spectrophotometer. An elemental analysis was carried out on a Yanaco MT-3 high-speed CHN analyzer with an anti-pyrene as a reference compound. The amount of tin was determined using an inductively coupled plasma atomic emission spectrometry (ICP-AES) on ARL 3410. The ^{1}H-, ^{13}C- and ^{119}Sn-NMR spectra were recorded on a multinuclear FT NMR 300 MHz of Bruker Biospin using

* Corresponding author. Tel.: +92 997 414136; fax: +92 997 530046.
E-mail address: sono_waj@yahoo.com (W. Rehman).

0223-5234/$ - see front matter © 2008 Elsevier Masson SAS. All rights reserved.
doi:10.1016/j.ejmech.2008.01.019

TMS as an internal standard. The Mössbauer spectra were recorded at 80 K on a Cryophysics instrument equipped with a 15 mCi Ca $^{119}SnO_3$ source.

2.1. Preparation of Schiff base ligand

Schiff base ligand was prepared by taking adenine and salicylaldehyde in ethanol and pouring in a three neck round bottom flask equipped with a reflux condenser, thermometer and a Dean–Stark funnel. The above reaction mixture was heated under reflux for 8 h. Water formed during the reaction was collected through Dean–Stark funnel. The solvent was removed under reduced pressure. The resulting white solid was recrystallized from methanol.

2.2. Preparation of complexes

To a hot methanolic solution of ligand acid (10 mM), triethylamine (10 mM) was added drop wise with constant stirring, then trimethyltin, triethyltin, tributyltin, triphenyltin or tribenzyltin chloride (10 mM) was added and the mixture was refluxed for 4–5 h under nitrogen. The solid formed (triethylamine hydrochloride) during the reaction was centrifuged and filtered. Excess of solvent was then removed under reduced pressure. White solid obtained was recrystallized in mixture of ethanol and petroleum ether (1:2(v/v)) having boiling point 40–60 °C and for further characterization.

2.3. Spectroscopic and other data

Following is the detail of the spectroscopic and other results for each compound. In case of spectroscopic results' presentations, the conventions used are: s, singlet; t, triplet; m, complex pattern; n.o., not observed; sr, strong; med, medium; w, weak; br, broad, sh, shoulder; QS = quadrupole splitting; IS = isomer shift.

2.3.1. Ligand acid

Yield: 82%; m.p.: 184 °C; molecular formula: $C_{12}H_9N_5O$; molecular weight: 239; recrystalization solvent: methanol; elemental analysis: the calculated values are given in parentheses. C: 60.25(60.12); H: 3.77(3.69); N: 29.27(29.20).

IR (KBr, cm^{-1}): 3135 sr (ν C–H); 1590 sr (ν C=N); 3335 br (ν O–H).

^{1}H NMR ($CDCl_3$): H1, H18: 12.2 s [2H, 1NH, 1OH]; H2: 8.1 s [1H, 1CH]; H-7: 8.8 m [1H, 1CH]; H-11: 9.0 s [1H, 1CH]; H-14: 6.8 m [1H, 1CH]; H-15: 7.1 m [1H, 1CH]; H-16: 6.7 m [1H, 1CH]; H-17: 7.5 m [1H, 1CH].

^{13}C NMR ($CDCl_3$): C2: 155; C4: 117; C5: 148.0; C7: 150.5; C9: 151.0, C-11: 166.5; C-12: 118.5; C-13: 158.9; C-14: 120.0; C-15: 135.2; C-16: 121.5; C-17: 132.5.

2.3.2. Trimethyltin complex

Yield: 76%; m.p.: 130 °C; molecular formula: $C_{15}H_{17}N_5OSn$; molecular weight: 403; recrystalization solvent: acetone/chloroform; elemental analysis: the calculated values are given in parentheses. C: 44.59(44.66); H: 4.18(4.22); N: 17.25(17.37); Sn: 29.71(29.78).

IR (KBr, cm^{-1}): 3142 sr (ν C–H); 1598 sr (ν C=N); 545 w (ν Sn–C); 575 sr (ν Sn–O); 484 w (ν Sn ← N).

^{1}H NMR ($CDCl_3$): H1: 12.3 s [1H, 1NH]; H2: 8.1 s [1H, 1CH]; H-7: 8.9 m [1H, 1CH]; H-11: 9.2 s [1H, 1CH]; H-14: 6.7 m [1H, 1CH]; H-15: 7.3 m [1H, 1CH]; H-16: 6.9 m [1H, 1CH]; H-17: 7.5 m [1H, 1CH]; H-α: 0.4 s. $^2J = 70$ Hz.

^{13}C NMR ($CDCl_3$): C2: 157; C4: 116; C5: 150.0; C7: 152.5; C9: 151.5; C-11: 167.5; C-12: 119.0; C-13: 165.7; C-14: 122.5; C-15: 135.9; C-16: 125.5; C-17: 133.7; C-α: 2.5 [$^1J = 552$ Hz].

^{119m}SnNMR($CDCl_3$): −233 ppm.

^{119m}Sn Mössbauer (mm/s): QS = 3.77 ± 0.04; IS = 1.25 ± 0.01.

2.3.3. Triethyltin complex

Yield: 80%; m.p.: 122 °C; molecular formula: $C_{18}H_{23}N_5OSn$; molecular weight: 445; recrystalization solvent: acetone/chloroform; elemental analysis: the calculated values are given in parentheses. C: 48.58(48.53); H: 5.128(5.17); N: 15.65(15.73); Sn: 26.89(26.97).

IR (KBr, cm^{-1}): 3142 sr (ν C–H); 1580 sr (ν C=N); 549 w (ν Sn–C); 582 sr (ν Sn–O); 494 w (ν Sn ← N).

^{1}H NMR ($CDCl_3$): H1: 12.3 s [1H, 1NH]; H2: 8.0 s [1H, 1CH]; H-7: 8.9 m [1H, 1CH]; H-11: 9.4 s [1H, 1CH]; H-14: 6.6 m [1H, 1CH]; H-15: 7.2 m [1H, 1CH]; H-16: 6.8 m [1H, 1CH]; H-17: 7.6 m [1H, 1CH]; H-α: 1.5 t [9H, $3CH_3$]; H-β: 2.2 q [6H, $3CH_2$]; $^2J = 75$ Hz.

^{13}C NMR ($CDCl_3$): C2: 156; C4: 116.5; C5: 149.5; C7: 151; C9: 150.5; C-11: 167.0; C-12: 120.0; C-13: 164.3; C-14: 121.8; C-15: 135.2; C-16: 124.3; C-17: 133.1; C-α: 2.5 $^1J(^{119}Sn-^{13}C) = 560$ Hz; C-β: 22.4 $^2J(^{119}Sn-^{13}C) = 25$ Hz.

^{119m}SnNMR($CDCl_3$): −222 ppm.

^{119m}Sn Mössbauer (mm/s): QS = 3.74 ± 0.04; IS = 1.20 ± 0.01.

2.3.4. Tributyltin complex

Yield: 80%; m.p.: 142 °C; molecular formula: $C_{24}H_{35}N_5OSn$; molecular weight: 529; recrystalization solvent: acetone/chloroform; elemental analysis: the calculated values are given in parentheses. C: 54.38(54.44); H: 6.10(6.16); N: 13.19(13.23); Sn: 22.59(22.68).

IR (KBr, cm^{-1}): 3145 sr (ν C–H); 1576 sr (ν C=N); 540 w (ν Sn–C); 579 sr (ν Sn–O); 490 w (ν Sn ← N).

^{1}H NMR ($CDCl_3$): H1: 12.4 s [1H, 1NH]; H2: 8.2 s [1H, 1CH]; H-7: 8.8 m [1H, 1CH]; H-11: 9.4 s [1H, 1CH]; H-14: 6.7 m [1H, 1CH]; H-15: 7.1 m [1H, 1CH]; H-16: 6.9 m [1H, 1CH]; H-17: 7.6 m [1H, 1CH]; H-α: 0.7 t [9H, $3CH_3$]; H-β: 1.3 se [6H, $3CH_2$]; H-γ: 1.5 qu [6H, $3CH_2$]; H-δ: 1.5 t [6H, $3CH_2$]; $^2J = 78$ Hz.

^{13}C NMR ($CDCl_3$): C2: 156.5; C4: 117.4; C5: 150.1; C7: 151.9; C9: 151.0; C-11: 16.7; C-12: 118.9; C-13: 163.7; C-14: 120.9; C-15: 134.8; C-16: 125.0; C-17: 133.4; C-α: 25.9; $^1J(^{119}Sn-^{13}C) = 555$ Hz; C-β: 26.5; $^2J(^{119}Sn-^{13}C) = 20$ Hz C-γ: 24.5; $^3J(^{119}Sn-^{13}C) =$ C-δ: 12.9.

^{119m}SnNMR($CDCl_3$): −212 ppm.

^{119m}Sn Mössbauer (mm/s): QS = 3.68 ± 0.04; IS = 1.17 ± 0.01.

2.3.5. Triphenyltin complex

Yield: 80%; m.p.: 168 °C; molecular formula: $C_{30}H_{24}N_5OSn$; molecular weight: 590; recrystalization solvent: acetone/chloroform; elemental analysis: the calculated values are given in parentheses. C: 60.98(61.01); H: 3.98(4.06); N: 11.81(11.86); Sn: 20.28(20.33).

IR (KBr, cm^{-1}): 3148 sr (ν C–H); 1585 sr (ν C=N); 555 w (ν Sn–C); 588 sr (ν Sn–O); 495 w (ν Sn ← N).

^{1}H NMR ($CDCl_3$): H1: 12.3 s [1H, 1NH]; H2: 8.3 s [1H, 1CH]; H-7: 8.9 m [1H, 1CH]; H-11: 9.5 s [1H, 1CH]; H-14: 6.8 m [1H, 1CH]; H-15: 7.4 m [1H, 1CH]; H-16: 6.9 m [1H, 1CH]; H-17: 7.7 m [1H, 1CH]; H-α: 7.1 m [3H, 3CH]; H-β: 7.3 m [3H, 3CH]; H-γ: 7.7 m [3H, 3CH]; H-δ: 7.5 m [3H, 3CH]; $^2J = 80$ Hz.

^{13}C NMR ($CDCl_3$): C2: 156.5; C4: 117.4; C5: 150.1; C7: 151.9; C9: 151.0; C-11: 17.5; C-12: 118.9; C-13: 170.3; C-14: 122.0; C-15: 135.2; C-16: 125.4; C-17: 133.8; C-α: 125.2; $^1J(^{119}Sn-^{13}C) = 680$ Hz; C-β: 130.2; $^2J(^{119}Sn-^{13}C) = 24$ Hz; C-γ: 127.5; $^3J(^{119}Sn-^{13}C) = 62$ Hz; C-δ: 124.7.

^{119m}SnNMR($CDCl_3$): −185 ppm.

^{119m}Sn Mössbauer (mm/s): QS = 3.80 ± 0.04; IS = 1.28 ± 0.01.

2.3.6. Tribenzyltin complex

Yield: 85%; m.p.: 152 °C; molecular formula: $C_{33}H_{29}N_5OSn$; molecular weight: 631; recrystalization solvent: chloroform; elemental analysis: the calculated values are given in parentheses. C: 62.70(62.76); H: 4.54(4.59); N: 10.95(11.01); Sn: 18.94(19.02).

IR (KBr, cm^{-1}): 3140 sr (ν C–H); 1580 sr (ν C=N); 542 w (ν Sn–C); 574 sr (ν Sn–O); 479 w (ν Sn ← N).

^{1}H NMR ($CDCl_3$): H1: 12.3 s [1H, 1NH]; H2: 8.0 s [1H, 1CH]; H-7: 8.7 m [1H, 1CH]; H-11: 9.1 s [1H, 1CH]; H-14: 6.6 m [1H, 1CH]; H-15: 7.0 m [1H, 1CH]; H-16: 6.7 m [1H, 1CH]; H-17: 7.7 m [1H, 1CH]; H-α: 1.8 s [6H, $3CH_2$]; H-β: 7.0 m [3H, 3CH]; H-γ: 7.3 m [3H, 3CH]; H-δ: 7.5 m [3H, 3CH]; H-ω: 7.7 m [3H, 3CH]; $^2J = 72$ Hz.

^{13}C NMR ($CDCl_3$): C2: 155.5; C4: 117.0; C5: 150.8; C7: 151; C9: 150.9; C-11: 16.5; C-12: 119.3; C-13: 164.0; C-14: 121.3; C-15: 135.2; C-16: 125.6; C-17: 134.4; C-α: 28.8 $^1J(^{119}Sn-^{13}C) = 570$ Hz; C-β: 125.9 $^2J(^{119}Sn-^{13}C) = 22$ Hz; C-γ: 120.7; $^3J(^{119}Sn-^{13}C) = 50$ Hz; C-δ: 122.5; C-ω: 119.2.

^{119m}SnNMR($CDCl_3$): −220 ppm.

^{119m}Sn Mössbauer ($CDCl_3$ mm/s): QS = 3.71 ± 0.04; IS = 1.16 ± 0.01.

2.4. Anti-bacterial studies

The anti-bacterial activities were investigated using agar well diffusion method [18]. The wells were dug in the media with a sterile borer and eight-hour-old bacterial inoculums containing ca. 10^4–10^6 colony-forming units (CFU)/mL were spread at the surface of the nutrient agar using a sterile cotton swab. The recommended concentration of the test samples (2 mg/ml in DMSO) was introduced into the respective wells. The wells containing DMSO and the reference anti-bacterial drug served as negative and positive controls, respectively. The plates were incubated immediately at 37 °C for 20 h. The activity was determined by measuring the diameter of the inhibition zone (in mm). Growth inhibition was calculated with reference to the positive control.

2.5. Anti-inflammatory activity

A freshly prepared suspension of carrageenin (0.2 ml/2.0, 1.0% in 0.9% saline) was injected subcutaneous into the plantar aponeurosis of the hind paw of the rats of both sexes (body weight 120/160 g) following Winter et al. method [19]. One group of five rats was kept as a control while the other group of five was pretreated with the test drugs administered orally, 30 min before the carrageenin injection. The paw volume was measured by a water plethysmometer socrel at the time of treatment and then at an interval of 1 h for 4 h. The mean increase of paw volume at each time interval was compared with that of control group and percent anti-inflammatory value was calculated as

$$\text{Percent anti-inflammatory value} = (1 - \text{DT}/\text{DC}) \times 100.$$

where DT and DC are the volumes of paw edema in drug treated and control group, respectively.

2.6. Acute toxicity study

ALD50 (average lethal dose at 50% survival) of the compounds was determined over albino mice. The mice of either sex (body weight 20–25 g) were employed for the purpose. The test compounds were injected intraperitoneally at different dose levels to groups of 10 animals and percent mortality in each group was observed after 24 h of drug administration. The ALD50 value (1 mg kg^{-1}) was calculated by applying Smith method [20].

2.7. Cytostatic activity

Cytostatic activity was assessed against the established KB cell lines, which were derived from a human oral epidermoid carcinoma. Stock culture was grown in 25 cm^3 flasks containing 10 ml of buffered Eagle's minimum essential medium (MEM) supplemented with glutamine, non-essential amino acids (1%) and new born calf serum (10%), according to the literature [21]. The cell population doubling time was approximately 24 h. The cells were dissociated with 0.05% trypsin solution, plated at a density of 5×10^5 cells per well in 24-well cell culture clusters (Costar) containing 1.0 ml of MEM per well, and preincubated for 24 h to allow adhesion to the substrate. Subsequently, the compounds to be tested were dissolved immediately before use in DMSO and these solutions were diluted with the growth medium to the desired concentrations before addition to the wells. At least five concentrations

of each compound were used, with eight cell culture wells for each concentration. Each compound was assayed on at least three separate occasions. Each assay included a blank containing complete medium without cells. The cells were incubated with the compounds to be tested at 37 °C in an atmosphere that was 5% CO_2 and had a relative humidity of 100%. The incubation time was 72 h, during the period the control cells showed exponential growth.

Cell growth was terminated by *in situ* fixation, followed by staining with the protein-binding dye sulforhodamine B (SRB) [22]. Specifically, adherent cell cultures were fixed *in situ* by addition of 250 μl of cold 50% (wt/vol) trichloroacetic acid (TCA) and kept for 60 min at 4 °C. The supernatant was then discarded and the plates were washed three times with deionised water and dried. SRB solution (500 μl, 0.4% wt/vol in 1% AcOH) was added to each well, and the cells were allowed to stain for 20–30 min at room temperature. Unbound SRB was removed by washing three times with 1% AcOH, and the plates were then air dried while bound stain was solubilized with unbuffered Tris base [tris(hydoxymethyl)aminomethane]. Optical densities were read at 565 nm on a Perkin–Elmer 550 SE spectrophotometer.

Cytostatic activity was evaluated from the inhibition of cell growth in the treated cultures with respect to the controls. IC_{50}, the concentration of the test compound at which cell proliferation was 50% of that observed in control cultures, was determined by linear regression analysis. The statistical significance of these results was estimated by means of Student's *t*-test ($P < 0.01$).

2.8. Spectroscopy

2.8.1. Infrared spectroscopy

IR spectroscopy is useful tool in structural determination of coordination compounds [23]. A broad peak in the spectrum of ligand at 3335 cm^{-1} was found to be absent in all the complexes, indicating the complexation through the phenolic oxygen [12]. The υ(C=N) band at 1590 cm^{-1} found in the spectrum of free ligand is shifted to 1576, 1580, 1585 in complexes, showing that the azomethinic nitrogen coordinates with the central tin atom [24]. The strong peak appearing at 574–588 cm^{-1} in the respective spectra of the complexes (absent in the spectrum of ligand) was assigned to Sn–O bond [25]. Compared with the ligand peaks appeared at 475–495 and 540–575 cm^{-1} assigned to Sn ← N and Sn–C, respectively, which confirmed the existence of Sn ← N and Sn–C bonds for all the five complexes [26–28].

2.8.2. NMR spectroscopy

In ^{1}H NMR spectroscopy spectra of ligand, single resonance is observed at 12.2 ppm, which is absent in the spectra of all the five complexes, indicating the replacement of phenolic proton by organotin moiety [12]. The $^{2}J(^{119}Sn-^{1}H)$ values are informative in assigning geometries to the coordination complexes, for five-coordinated complexes $^{2}J(^{119}Sn-^{1}H)$ values are 65–80 Hz, for six coordinated 85–110 Hz, the $^{2}J(^{119}Sn-^{1}H)$ values obtained for all the complexes are consistent with the literature [29]. The characteristic signals for all the magnetically non-equivalent alkyl- or phenyl-protons of the organotin moieties have also been assigned, which are in good agreement with reported values [30].

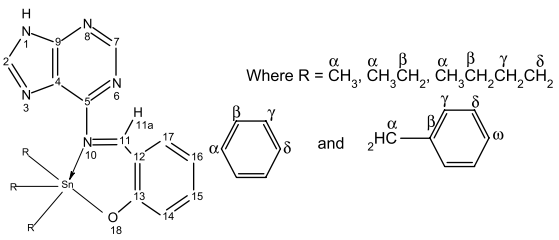
The characteristic resonance peaks in ^{13}C NMR spectra of the complexes were recorded in $CDCl_3$. The ^{13}C NMR spectra of the complexes show a considerable upfield shift of all carbon resonance, compared with the ligand acid. The shift is an outcome of an electron density transfer from the ligand to the acceptor [12]. Coordination of the tin atom in organotins has been related to the $^{1}J(^{119}Sn-^{13}C)$ coupling constants. The $^{1}J(^{119}Sn-^{13}C)$ coupling constants for the synthesized compounds ranged from 755 to 850 Hz, which is indicative of five-coordinated compounds [31].

2.8.3. ^{119}Sn-NMR

Holeček and coworkers' studies result shows that in the di- and triorganotin the ^{119}Sn-NMR spectra can be used as an indicator of the coordination number of the tin atom. In the range of +200 to −60, −90 to −190, −210 to −400, −440 to −540 ppm, the coordinate numbers of the tin are four, five, six and seven, respectively [32–35]. The triorganotin complexes under investigation exhibit the ^{119}Sn spectra under the range of −90 to −190 ppm, indicating the tin atoms are five-coordinated in all the studied complexes.

2.8.4. ^{119m}Sn Mössbauer

The ^{119m}Sn Mössbauer parameters (IS and QS) have been utilized as an analytical tool for proposing the structure that a particular complex can adopt. The spectra of the complexes display a characteristic doublet absorption indicating a single tin site. The R_3Sn derivatives show isomer shift (IS) and the quadrupole splitting (QS) values in the range of 3.72–3.97 mm/s, suggesting trigonal bipyramidal geometry [36].



Proposed structure of trialkyltin (IV) complexes of the ligand.

2.8.5. Bioactivities

The biological activity of the ligand and its tin(IV) complexes and Imipinem (as a standard compound) were tested against bacteria because bacteria can get resistance to antibiotics through biochemical and morphological modifications [37]. The microorganisms used in the present investigations included *Staphylococcus aureus* and *Bacillus subtillis* (as gram-positive bacteria) and *Pseudomonas aeruginosa* and *Escherichia coli* (as gram-negative bacteria). The diffusion agar technique was used to evaluate the anti-bacterial activity

Table 1
Anti-bacterial activity results for R_3SnL (inhibition zone in mm)

Microorganisms	HL	Me_3SnL	Et_3SnL	Bu_3SnL	Ph_3SnL	Bz_3SnL	Standard drug
Gram-positive							
Bacillus subtilis	+	+	+	++	+++	++	++++
S. aureus	n.c.	+	+	++	+++	+	++++
Gram-negative							
E. coli	+	+	++	+	+++	++	++++
Salmonella typhi	+	n.a.	n.a.	++	+++	+	++++
P. aeruginosa	n.c.	+	++	+	+++	++	++++

++++ = Excellent activity (100% inhibition), +++ = good activity (60–70% inhibition), ++ = significant activity (30–50% inhibition), + = negligible activity (10–20% inhibition), n.a. = no activity, n.c. = not checked, size of well: 6 mm (diameter), standard drug: Imipenem.

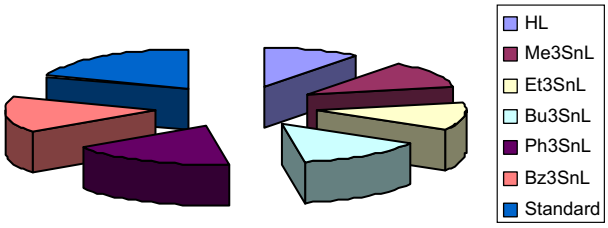


Fig. 1. A comparison of anti-inflammatory activity of ligand acid and triorganotin(IV) complexes.

of the synthesized mixed ligand complexes [38]. The results of the bactericidal study of the synthesized compounds are displayed in Table 1. The data obtained indicate that the ligand has moderate activity in comparison with *S. aureus*, *E. coli* and less active in comparison with *P. aeruginosa*. Ligand also shows a moderate activity towards *B. subtillis*. The remarkable activity of ligand may be due to NH and OH group of the adenine ring, which can play an important role in the anti-bacterial activity [39] and the imine group may impart in elucidating the mechanism of transformation reaction in biological system [40].

Anti-bacterial activity of all complexes at low concentrations towards gram-positive and negative bacteria is quite significant and increases with concentration as noted by others for different cases [41]. Further to it, the ligand showed low, and the complexes moderate to high activities as compared to standard drug towards all the organisms (Table 1). It is suggested that the anti-microbial activity of the complexes is due to either by killing the microbes or inhibiting their multiplication by blocking their active sites [42].

The anti-inflammatory activity data (percent inhibition) of the triorganotin(IV) derivatives of the ligand studied are given in Table 2. The results obtained (Fig. 1) (Table 2), indicate the order of the anti-inflammatory activity of *n*-R_3Sn(IV) derivatives as: *n*-Ph_3SnL > *n*-Bz_3SnL > Bu_3SnL > Et_3SnL > Me_3SnL. Among the tri-alkylltin(IV) derivatives triphenyltin complex showed promising activity as compared to others.

Moreover, the results of anti-inflammatory activity of the triorganotin(IV) derivatives of the ligand investigated are comparable with the previously reported [43–45]. The detail consideration of the activity and the structure of the complexes conclude that

- the anti-inflammatory activity is a function of both number and nature of organic group(s) attached;
- availability of coordination positions at tin;
- occurrence of stable ligand–Sn bonds viz., Sn–O bonds; and
- among the studied tin(IV) complexes highest activity is exhibited by Ph_3Sn(IV) derivatives.

Further to it one can presume that the lower activity of trialkyltin complexes except for triphenyltin(IV) is probably due to formation of most stable bond upon complexation than the latter one. The higher activity of triphenyltin(IV) complex is also probably due to less number of coordination sites/bonds, which facilitate the easier formation of Ph_3Sn^{2+}(IV) moiety as a part of inhibition. It may be due to stronger interactions in trialkyltin(IV) complexes except triphenyltin(IV) complex in which there are weaker interactions of ligand with tin, thereby, regulating the formation of R_2Sn^{2+}(IV) moiety.

ALD50 values of the investigated triorganotin(IV) derivatives are greater than 500 mg kg^{-1} (the maximum dose tested), whereas for the ligand is <400 mg kg−1 indicating that the bigger biomolecules lower the toxicities but increase the activities of the resulting organotin(IV) complexes.

The results of cytostatic activity are summarized in Table 3. IC50 values of the compounds are expressed in μM, together with that of *cis*-$[PtCl_2(NH_3)_2]$ for comparison. All complexes show significant cytostatic activity. In particular, tributyltin complex is more active than the *cis*-$[PtCl_2(NH_3)_2]$.

Table 2
ALD50 (in mg kg^{-1}), anti-inflammatory activity for R_3SnL

Compound	ALD50 (mg kg^{-1})	Anti-inflammatory activity (percent inhibition) 50 mg kg^{-1}
HL	<300	20.5
Me_3SnL	<400	21.5
Et_3SnL	<400	23.3
Bu_3SnL	<400	26.7
Ph_3SnL	<500	34.5
Bz_3SnL	>400	29.3
Standard drug (phenyl butazone)	–	38.4

Table 3
Cytostatic activity for R_3SnL

Compound	IC50 (μg ml^{-1} medium)	IC50 (μM)
HL	0.08	0.10
Me_3SnL	0.10	0.25
Et_3SnL	0.22	0.19
Bu_3SnL	2.20	2.95
Ph_3SnL	0.36	0.66
Bz_3SnL	0.40	0.28
Standard drug *cis*-$[PtCl_2(NH_3)]$	0.11	0.37

Acknowledgments

One of the authors, Dr. Amin Badshah, is highly thankful to Professor B. Wrackmeyer (University of Bayreuth Germany) for spectral studies. HEJ Institute of Chemistry and University of Karachi (Pakistan) are highly acknowledged for the determination of some of the bioactivities. Associate Professor A. Christofides (University of Thessalonki, Greece) is highly obliged for providing useful research material. Mr. Isfahan Tauseef, Department of Microbiology, Hazara University, Mansehra is highly acknowledged for useful discussion.

References

[1] A.G. Davies, Organotin Chemistry, VCH, Weinheim, Germany, 2004.
[2] M. Gielen, J. Braz. Chem. Soc. 14 (2003) 1.
[3] P.J. Smith, A.J. Crow, R. Hill, Publication no. 559, International Tin Research Institute, London, 1979.
[4] C.J. Evans, R.J. Hill, Oil Color Chem. Assoc. 64 (1981) 215.
[5] S.R. Collinson, D.E. Fenton, Coord. Chem. Rev. 148 (1996) 19.
[6] R. Sylvain, J.L. Bernier, M.J. Waring, J. Org. Chem. 61 (1996) 2326.
[7] S.M. Santanu, B. Subbrangsu, J. Chem. Soc., Chem. Commun. (1995) 2489.
[8] D.J. Gravert, J.H. Griffin, J. Org. Chem. 58 (1993) 820.
[9] W. Rehman, M.K. Baloch, A. Badshah, S. Ali, J. Chin. Chem. Soc. 52 (2005) 231.
[10] W. Rehman, A. Badshah, M.K. Baloch, S. Ali, G. Hameed, K.M. Khan, J. Chin. Chem. Soc. 51 (2004) 929.
[11] W. Rehman, M.K. Baloch, B. Muhammad, A. Badshah, K.M. Khan, Chin. Sci. Bull. 49 (2004) 119.
[12] W. Rehman, M.K. Baloch, A. Badshah, Saqib Ali, 65, Spectrochim. Acta A (2006) 689.
[13] W. Rehman, M.K. Baloch, A. Badshah, J. Braz. Chem. Soc. 16 (2005) 827.
[14] W. Rehman, M.K. Baloch, A. Badshah, Saqib Ali, Russ. J Coord. Chem 31 (2005) 856.
[15] W. Rehman, M.K. Baloch, A. Badshah Russ, J. Inorg. Chem. 52 (2007) 140.
[16] K. Sisido, Y. Takeda, Z. Kingawa, J. Am. Chem. Soc. 83 (1961) 538.
[17] D.D. Perrin, W.L.F. Armengo, Purification of Laboratory Chemicals, Pergamon, Oxford, 1988.
[18] A. Rahman, M.I. Choudhary, W.J. Thomsen, Bioassay Techniques for Drug Development, Harwood Academic Publishers, The Netherlands, 2001, p. 16.
[19] C.A. Winter, E.A. Fisley, G.W. Nuss, Proc. Soc. Exp. Biol. NY 111 (1962) 544.
[20] Q.E. Smith, Pharmacological-screening Test Progress in Medicinal Chemistry I, Butterworths, London, 1960.
[21] C. Rossi, A. Ambrogi, G. Grandolini, V. Scarcia, A. Furlani, J. Pharm. Sci. 75 (1986) 784.
[22] P. Skehan, R. Storeng, D. Scudiero, A. Monks, J. Mcmahon, D. Vistica, J.T. Warren, H. Bokesch, S. Kenny, M.R. Boyd, J. Natl. Cancer Inst. 82 (1990) 1107.
[23] C.L. Ma, Q. Jiang, R.F. Zhang, Can. J. Chem. 81 (2003) 825.
[24] C.L. Ma, Q. Jiang, R.F. Zhang, Appl. Organomet. Chem. 17 (2003) 623.
[25] J.J. Bonire, S.P. Fricker, J. Inorg. Biochem. 83 (2001) 217.
[26] S.G. Teoh, S.H. Ang, J.-P. Declercq, Polyhedron 16 (1997) 3729.
[27] M. Nath, S. Pokharia, X. Song, G. Eng, M. Gielen, M. Kemmer, M. Biesemans, R. Willem, D. de Vos, Appl. Organomet. Chem. 17 (2003) 305.
[28] R. Zhang, G. Tian, C. Ma, J. Organomet. Chem. 690 (2005) 4049.
[29] T.P. Lockhart, W.F. Manders, Inorg. Chem. 25 (1986) 892.
[30] H.D. Yin, Q.B. Wang, S.C. Xue, J. Organomet. Chem. 690 (2005) 831.
[31] J. Holeĉek, A. Lycka, Inorg. Chim. Acta 118 (1986) L15.
[32] J. Holeĉek, M. Nadvornik, K. Handlir, A. Lycka, J. Organomet. Chem. 241 (1983) 177.
[33] M. Nadvornik, J. Holeĉek, K. Handlir, A. Lycka, J. Organomet. Chem. 275 (1984) 43.
[34] A. Lycka, J. Holeĉek, M. Nadvornik, K. Handlir, J. Organomet. Chem 280 (1985) 323.
[35] J. Holeĉek, M. Nadvornik, K. Handlir, A. Lycka, J. Organomet. Chem. 258 (1983) 2903.
[36] R. Barbieri, F. Huber, L. Pellerito, G. Ruisi, A. Silvestri, ^{119}Sn Mössbauer studies on tin compounds, in: P.J. Smith (Ed.), Chemistry of Tin, Blackie Academic and Professional, London, 1998, p. 496.
[37] N. Sari, S. Arslan, E. Logoglu, I. Sakiyan, J. Sci. 16 (2003) 283.
[38] M.B. Ferrari, S. Capacchi, G. Pelosi, G. Reffo, P. Tarasconi, R. Albertini, S. Pinelli, P. Lunghi, Helicin. Inorg. Chim. Acta 286 (1999) 134.
[39] A.S.A. Zidan, Phosphorus Sulfur Silicon Relat. Elem. 178 (2003) 567.
[40] A. Chaudhary, R.V. Singh, Phosphorus Sulfur Silicon Relat. Elem. 178 (2003) 603.
[41] A.P. Mishra, J. Ind. Chem. Soc. 76 (1999) 35.
[42] M. Nath, S. Pokharia, X. Song, G. Eng, M. Gielen, M. Kemmer, M. Biesemans, R. Willem, D. De Vos, Appl. Organomet. Chem. 17 (2003) 305.
[43] M. Nath, S. Pokharia, G. Eng, X. Song, A. Kumar, J. Organomet. Chem. 669 (2003) 109.
[44] M. Nath, S. Pokharia, G. Eng, X. Song, A. Kumar, M. Gielen, R. Willem, M. Biesemans, Appl. Organomet. Chem. 18 (2004) 460.
[45] M. Nath, R. Yadav, G. Eng, T.-T. Nguyen, A. Kumar, J. Organomet. Chem. 577 (1999) 1.