Synthesis, structure elucidation and antimicrobial activity of triorganotin(IV) derivatives of N-laurylsacosine sodium salt

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Abstract

*Trimethyl(IV) **1**, tributyl(IV) **2** and triphenyltin(IV) **3** derivatives of sodium N-laurylsacosinate **L-salt**, were synthesized by refluxing triorganotin(IV) chlorides with N-laurylsacosine sodium salt in dry toluene for 7-8 hours in good yield. Synthesized compounds were structurally elucidated by CHNS elemental analyzer, FTIR, ^{1}H and ^{13}C NMR spectroscopy. FTIR results showed that compounds exhibited a Penta coordinated solid state geometry. ^{13}C NMR spectrum of **1** showed that it was dissociated in solution to adopt a 4-coordinated geometry. Antibacterial activity of the compound **1-3** was investigated against four different strains of bacteria. The results obtained showed that compounds exhibit moderate to good antibacterial activities.*

Keywords: *Triorganotin(IV), N-laurylsacosinate, Geometry, Antibacterial*

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Introduction

Organotin(IV) complexes with various donor ligands have been subject of concern for many years (Shahzadi et al., 2008; Talal et al., 2003; Singh, 1998). Interest in organotin complexes provoked from their widespread applications in biological and non-biological systems (Mahmood et al., 1992; Mahmoud et al., 1992) (Gielen et al., 2008).Currently many organotin(IV) compounds have also been tested for their anticancer activities due to their apoptotic inducing nature (de Vos et al., 1998; Tabassum&Pattinari, 2006]. They also possess exiting structural possibilities and crystal chemistry[Baul et al., 2007]. Ligand attached to tin center has marked influence on their applications and crystal chemistry. So judicious choice of the ligand can aid in development of desired organotin(IV) derivatives. N-acyl sarcosines and the sarcosinates (their salts), are mild and biodegradable, anionic surfactants which are formed from amino acid sarcosine N-methyl glycine and fatty acids. They display a maximum surface activity at slight acidic pH. This pH range is most friendly with human skin. Under optimal conditions, they can attain a low surface tension upto 21 dynes per centimeter, and can reduce the skin permeation and metal corrosion by strongly absorbing by head group interaction on proteinaceous faces, while to metals and ceramics developing a hydrophobic protecting film (Deberry et al., 1984). N-Laurylsarcosine sodium salt has both the hydrophobic and hydrophilic parts. It can interact with Sn(IV) center thus developing a system with membrane specific properties. Interaction of surfactants with organotin(IV) carboxylates is already reported in literature, where they found applications in drug delivery system, in cleaning environment by eradicating soil or water contamination etc (Ali &Badawi, 2008;Shah et al., 2015; Mathurasa et al., 2012). In view of the multidimensional applications of organotin(IV) carboxylates in general and surfactant based organotins in particular, we synthesized three new organotin(IV) derivatives of N-laurylsarcosine sodium salt. The synthesized compounds are further subjected to antibacterial screening as well.

Materials and Methods

Materials

Analytical grade chemicals were used in the experimental work. Triorganotin(IV) chlorides were bought from Fluka and Sigma Aldrich chemical company and used without further purification. All the solvents used in the synthetic work were distilled or dried before use by standard reported procedures (Armarego& Chai, 2003).

Physical measurements

Melting points of compounds were taken in capillary tube in a Gallenkamp (UK) electrothermal melting point apparatus. Elemental composition was determined by thermoscientific flash 2000 CHNS elemental analyser. FTIR spectra were taken on Thermo-Nicolet-6700 FTIR spectrophotometer. ^{1}H and ^{13}C NMR spectra were taken in deuterated chloroform on Bruker -300 MHz FT-NMR spectrometer. Chemical shift values are provided in ppm and the coupling constants are expressed in Hertz (Hz). Signal multiplicities are provided in ^{1}H NMR as, s= singlet, d= doublet, t= triplet, and m= multiplet.

Synthesis

L-salt was purchased and used directly. Triorganotin(IV) complexing were then synthesized by refluxing L-salt in appropriate molar ratios for 6-7 hrs in dry toluene.

Antimicrobial Studies

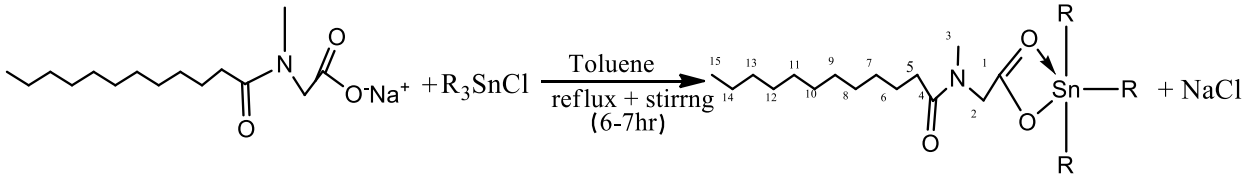
Antibacterial Assay

Triorganotin(IV) derivatives **1, 2** and **3** of sodium N-lauroylsarcosinate were tested against four different strains of bacteria; two gram negative strains which were *Escherichia coli* and *Klebsiella pneumoniae*, and two Gram positive strains which were *Bacilus subtulis* and *Staphylococcus aureus* by standard agar well diffusion protocol (Rahman et al., 2001). *Cefixime* was the standard drug used. 1 ml of broth culture having 10^4 - 10^6 colony forming units (CFU) per mL was added in 100 mL of nutrient agar medium at about 318K, shaked and mixed well and then transferred to a 14 cm sterilized petri plate. The media was kept for some time to solidify, and then by using sterilized metallic borer, 6 mm wells were dug into it. Then solutions of the test samples (100 μL) in DMSO at concentration of 1 mg/mL was added to the different wells. *Cefixime*(standard antibacterial drug) and DMSO of 1 mg/mL concentration served correspondingly as a positive and negative control. The plates were aerobically incubated for 24 hr at 310K. The activity was measured by calculating the diameter of the zone evincing complete inhibition in mm. The growth inhibition was measured with reference to *Cefixime*.

Results and Discussion

General method for the synthesis of compounds 1-3

Triorganotin(IV) complexes **1**, **2**and **3** of **L-salt** were synthesized by refluxing the sodium salts, with trimethyl-, tributyl- and triphenyltin(IV) chlorides respectively in distilled toluene for 6 to 7 hr. Mixture was then filtered to remove NaCl formed as by-product, and isolation of product was achieved by removing toluene in rotary evaporator. The isolated product was recrystallized in mixture of chloroform and n-hexane in 3:1.



R= CH_3**1**, *n*-C_4H_9 **2**, C_6H_5 **3**

Scheme 1 Synthetic scheme of compound **1**, **2** and **3** along with atomic numbering scheme

Physical data of the L-salt and compounds **1-3** is shown in table 1.

Table 1 Physical data of L-salt and synthesized compounds

Compound	Molecular formula	Yield	m.p (°C)	Solubility	Elemental analysis (%) Found (calculated values)		
					C	H	N
L-salt	$C_{15}H_{30}NNaO$	-	320 Decompose	Distilled water	-	-	-
1	$C_{18}H_{39}NO_2Sn$	82%	Liquid	$CHCl_3$	51.45 (51.23)	9.35 (9.44)	3.33 (3.98)
2	$C_{27}H_{57}NO_2Sn$	78%	65-68	$CHCl_3$	59.34 (59.14)	10.51 (10.80)	2.56 (2.53)
3	$C_{33}H_{45}NO_2Sn$	76.5%	118-120	$CHCl_3$	65.36 (64.71)	7.48 (7.68)	2.31 (2.60)

FTIR spectroscopy

FTIR spectroscopic analysis of the ligand salt and synthesized compounds **1**, **2** and **3** provides valuable information about product formation. Results are provided in table 2. Appearance of new signals for Sn-C and Sn-O in compounds **1-3**, which were absent in **L-salt** put forward the product formation (Shaheen et al., 2017). Difference between symmetric and asymmetric COO stretching vibrations provides information about the binding mode of the ligand to the tin center. $\Delta\upsilon$ value below 200 cm^{-1} is an indicative of bidentate or bridging mode of coordination, while the value above 200 cm^{-1} confirms a monodentate coordination mode (Win et al., 2010). It is in accordance with earlier reports that an increase in coordination number from 4-6 results in decrease in $\nu(COO_{asym})^{-1}$ and an increase in $\nu(COO_{sym})$ frequencies (Sirajuddin et al., 2014). It is inferred from IR data that, all the three synthesized compounds exhibited a 5-coordinated solid state geometry. Proposed structures of the compounds **1-3** are provided in Fig. 2.

Table 2 IR data of compounds **1-3**

Compound	Sn-C	Sn-O	vas $(COO)^{-1}$	ν_s (COO)	Δν
L-salt	-	-	1637	1392	245
1	557	439	1564	1407	157
2	572	439	1571	1404	167
3	282	440	1561	1418	143

Multinuclear NMR spectroscopy

^1H and ^{13}C NMR spectroscopic investigation of the compounds **1-3** were carried out in deuterated chloroform and results are compiled respectively in table 3 and 4. ^1H NMR spectra gave a very complex signal pattern because all groups differ very slightly in their chemical environment. Most of these signals overlapped and combined to provide broad signals. Signals were assigned to alkyl or aryl units attached to the tin atom by comparing with literature value (Shahid et al., 2003; Shahid et al., 2003). The $^2J(^{119}Sn, ^1H)$ values obtained for **1** was 57.4 Hz, which corresponds to 4- coordinated geometry around tin with angle value of 110.4° (Win et al., 2010).

The ^{13}C NMR data of compounds show that the C-1, appears between 172.3 to 173.6 ppm, which is in same region as obtained for already reported analogous compounds [Camacho et al., 2013). Another interpretatively important feature in structure assignment is the appearance of ipso carbon signal near 138 ppm which is due to tetrahedral geometry of the compound in solution (Willem et al., 1996).

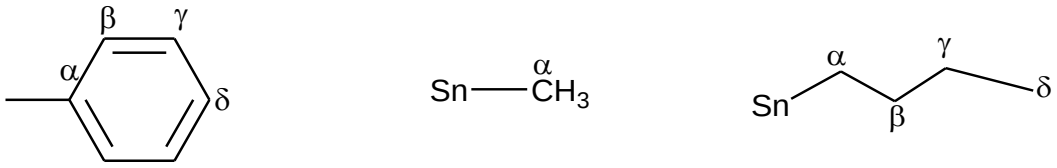
Table 3 ^{1}H-NMR data of triorganotin(IV) derivatives of the N-laurylsarcosine sodium salt (L-salt)

Proton	Chemical Shifts (ppm)		
	1	**2**	**3**
H_3	3.41(s)	3.03 (s)	3.35 (s)
H_2	3.71(s)	3.97(s)	3.82(s)
$H_{5\text{-}15}$	1.28-1.40 (bs)	1.24-1.34(bs)	1.26-1.38 (bs)
α	0.43 (s, [57.4], θ= 110.4 °)	0.82-0.93 (m)	-
β			7.36-7.52 (m)
γ			
δ			

*Chemical shift (δ) in ppm. ^{n}J [^{119}Sn, ^{1}H] and ^{3}J(^{1}H, ^{1}H) in Hz are documented respectively in square brackets and parenthesis.
ǂ Multiplicity is provided as s = singlet, m = multiplet, bs = broad signal.
ǂǂSee scheme 2 for α, β, γ and δ.

Table 4 ^{13}C-NMR data of triorganotin(IV) derivatives of the N-Laurylsarcosine sodium salt (L-salt)

Carbon	Chemical Shifts (ppm)		
	1	**2**	**3**
C-1	172.3	173.6	172.5
C-3	50.7	49.6	50.3
C-2	53.4	52.3	52.7
C-4	169.1	170.6	169.0
$C_{5\text{-}15}$	15.1,16.5, 18.4, 21.3, 27.2, 29.8, 31.3, 33.9, 35.6, 38.4, 43.1	15.3, 16.1, 18.6, 21.5, 27.8, 29.4, 31.7, 33.2, 35.6, 38.2, 43.3	15.2, 16.4, 18.2, 21.3, 27.4, 29.5, 30.4, 31.5, 33.7, 38.5, 43.2
α	3.05 (s)	13.5	137.8
β		13.9	130.4
γ		18.5	131.3
δ		21.4	129.5



Scheme 2 Labelling of alkyl and phenyl carbons attached to the tin atom in **1-3**

*Chemical shift (δ) in ppm. ^{n}J [^{119}Sn, ^{13}C] in Hz are listed in square brackets.
ǂǂSee scheme 2 for α, β, γ and δ

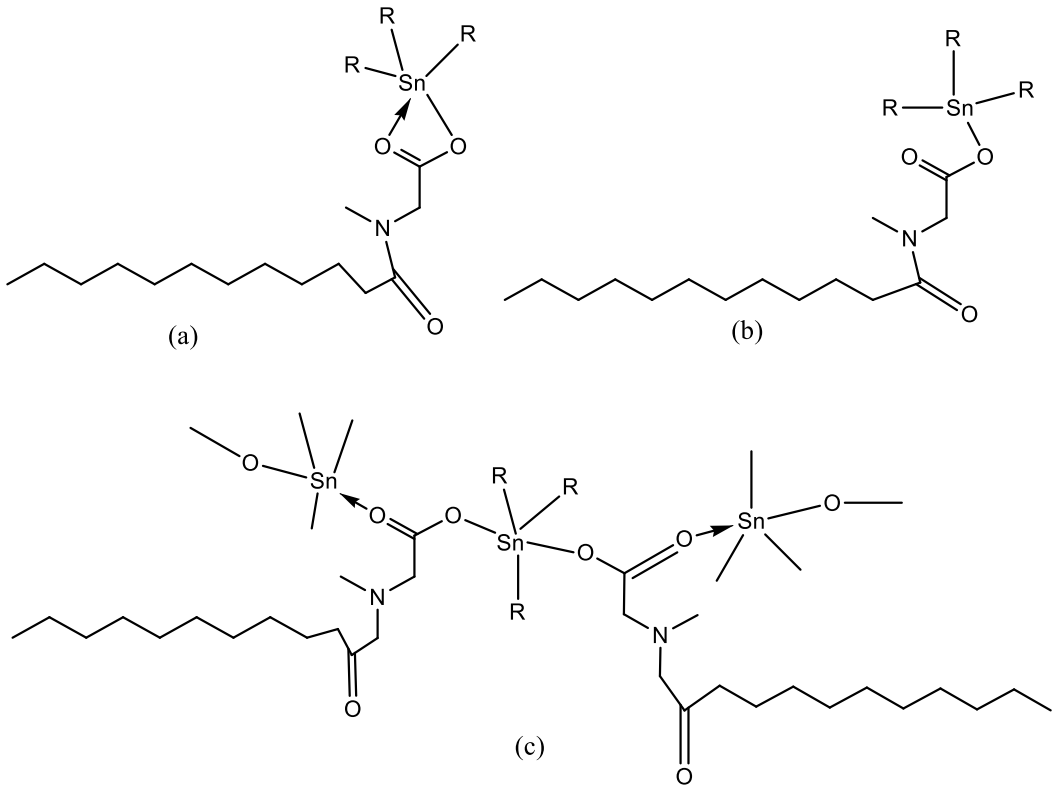


Fig. 2 Proposed structures of **1-3** in solid (a and c) and in solution state (a-c)

Antimicrobial Activities

Antibacterial Activity

Antibacterial activities of compounds **1-3** were carried out by the agar well diffusion method against two gram positive (*Escherichia coli* and *Klebsiella Pneumoniae*) and two gram negative bacteria (*Bacillus Subtilis* and *Staphylococcus aureus*). The results are presented in table 5. Graphical representation is shown in Fig. 3. The inhibition zone is a standard to check the significance of compound's activity. Generally, inhibition zones below 11-14 are considered insignificant, and above 20 mm are considered to be significant, however below 18-20mm is said to be good (Sirajuddin et al., 2012). Among three organotin(IV) compounds synthesized, tributyl and triphenyl derivatives were more active than corresponding methyl derivative which may be possibly due to the ligand in addition to organic groups attached to the tin center. Furthermore, it is well recognized that, with the increase in chain length, the lipophilicity of compounds also increases which enhances biological activities (Fargasova 1998). Generally the methyl compounds are less toxic (Gadd et al., 1990).

Table 5 Antibacterial activities of organotin(IV) derivatives of N-laurylsarcosin sodium salt

Compound	Average inhibition zone in mm			
	Klebsiella pneumonia **(700603)**	***Escherichia coli*** **(8739)**	***Staphylococcus aureus*** **(25923)**	***Bacillus subtilis*** **(6633)**
1	25	23	23	26
2	27	25	27	28
3	29	31	28	25
[a]***Cefixime***	40	40	40	30

[a]reference drug used

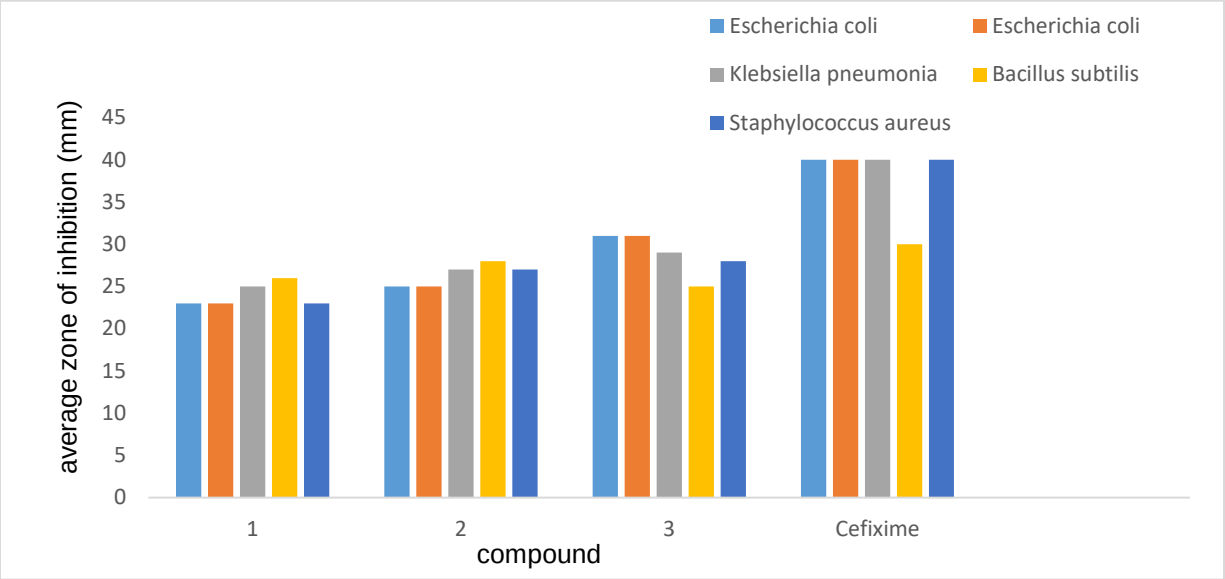


Fig. 3 Graphical representation of antibacterial activity of compounds 1-3 and *cefexime*

Conclusions

Three organotin(IV) complexes derived from N-laurylsarcosine sodium salt were efficiently synthesized and characterized spectrophotometrically. All three compounds possessed five coordinated geometry in solid state as referred by IR spectra. Compound **1** possessed tetrahedral geometry in solution state as evident from ^{1}H and ^{13}C-NMR spectra. Antibacterial screening showed that the complexes showed good activity. Compound **3** showed maximum activity, but none of the complexes was more active than reference drug used. These compounds can further be investigated for DNA binding studies.

Author(s) Contribution Statement

Farzana Shaheen performed synthetic part, while Naseer Ali Shah measured antibacterial activity of synthesized compounds.

Conflict of interest. The article is an original work and has not been submitted anywhere else. The authors declare no conflict of interest.

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