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Synthesis, Characterization and Biological Activities of Organotin(IV) Complexes with *l*-Lysine Monohydrate[1]

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Abstract—The new organotin(IV) complexes have been synthesized by the reaction of *l*-lysine monohydrate with CS_2 and R_2SnCl_2/R_3SnCl**.** The organotin(IV) complexes and the ligand have been characterized by elemental analysis, FT-IR and NMR (^1H and ^{13}C) spectrometry. IR data indicated that complexation proceeded –COO and –CSS sites and the ligand acted as a bidentate one. ^1H and ^{13}C NMR data confirmed the tetrahedral structure of the products in solution. Biological activity of the complexes was tested.

Keywords: *l*-Lysine monohydrate, organotin(IV) complexes, IR, NMR, biological activity

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INTRODUCTION

Organotin(IV) complexes are extensively used as catalysts, stabilizers, biocides, antifouling agents and wood preservatives [1]. Methods of synthesis, structural elucidation and biological activity of organotin(IV) derivatives of carboxylic acids have been studied [2, 3]. Increased attention to organotin carboxylates was based on their antitumor activity determined for some of those [4]. Structural diversity of diorganotin and triorganotin esters attracted considerable attention [5, 6]. Metal thiolates attracted considerable attention due to the processes of metals bounding to cysteine in natural systems [7] and some other biology related phenomena [8–10].

In respect to our interest in synthesis, characterization and biological activity of organotin(IV) complexes [11–14], we have synthesized organotin(IV) complexes with *l*-lysine monohydrate and elucidated their structure by FT-IR and ^1H and ^{13}C NMR methods. The products were tested *in vitro* for their antifungal and antibacterial activity.

EXPERIMENTAL

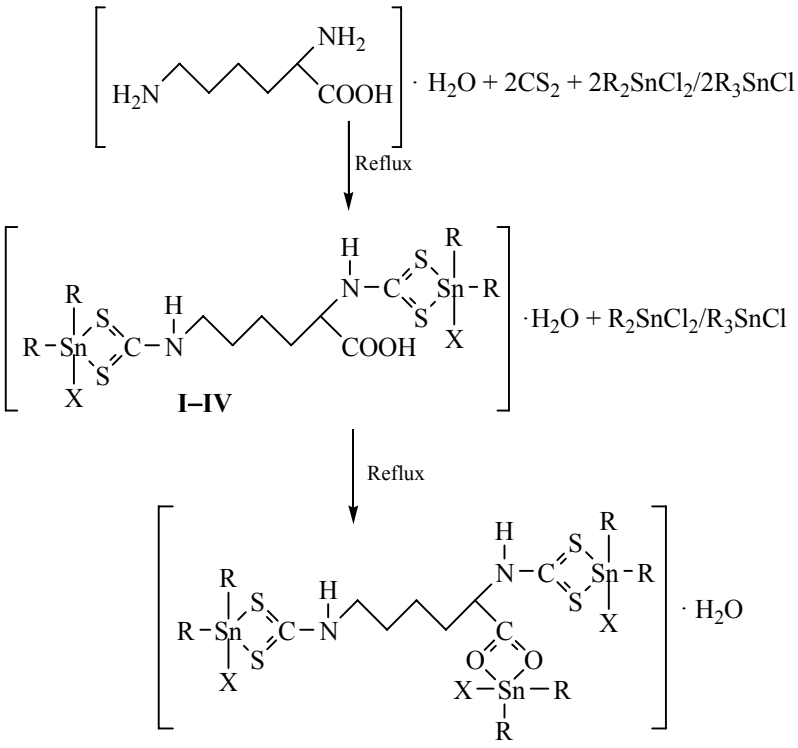
The chemicals were purchased from Merck and used without further purification. Melting points were measured on Stuart SMP3 melting point apparatus. Solvents were dried before use by the conventional methods [15]. Elemental analysis was performed on CHN elemental analyzer 932 Leco, USA. FT-IR spectra were recorded on a 1000 (FT-IR Perkin-Elmer) spectrophotometer in the range of 4000–250 cm^{-1} as KBr/CsBr discs. ^1H and ^{13}C NMR spectra were measured by a Bruker 300 MHz-FT-NMR spectrometer.

Synthesis of organotin(IV) complexes. *l*-Lysine monohydrate (1 mmol) was dissolved in methanol (25 mL) in a 100 mL round bottom flask and carbon sulfide (2 mmol) was added to it drop wise upon stirring. R_2SnCl_2/R_3SnCl (2 mmol) solution in methanol (25 mL) was added drop wise in the above reaction mixture and refluxed for 6–8 h. The solvent was evaporated in vacuum. The solid product was dried in the air and recrystallized from acetone : *n*-hexane (1 : 1).

Thus synthesized solid compound (1 mmol) was dissolved in methanol (40 mL) in a 100 mL two necked round bottom flask and the solution of R_2SnCl_2/R_3SnCl (1 mmol) in methanol (25 mL) was added drop wise to the above reaction mixture upon stirring and refluxed for 6–8 h. The solvent was evaporated slowly at room temperature and the solid product obtained was dried in the air and recrystallized from acetone : *n*-hexane (1 : 1) (Scheme 1).

[1] The text was submitted by the authors in English.

Scheme 1.



X = Cl (diorganotin); R (triorganotin); R = *n*-Bu, Ph.

Antibacterial assay. Pure cultures were maintained on nutrient agar medium in the slants and petri plates. For inoculums preparation 13 g/L of nutrient agar was suspended in distilled water, distributed homogenously and autoclaved. Then 10 μL of pure culture of a bacterial strain was mixed in the medium and shaked for 24 h at 37ºC. The inocula were stored at 4ºC. The inocula with 1×10^8 spores/mL were used for further analysis.

Antimicrobial activity of organotin(IV) complexes was determined by using disc diffusion method [16]. Nutrient agar 28 g/L was suspended in distilled water, mixed well and distributed homogenously. The medium was sterilized by autoclaving at 121ºC for 15 min. Inoculum (100 μL/100 mL) was added to the medium and poured on to sterilized petri plates. Small filter paper discs were laid flat on growth medium containing 100 μL of samples. The petri plates were incubated at 37ºC for 24 h for bacteria growth. The zones of inhibition were measured in millimeters using zone reader [17].

Antifungal assay. Pure culture of the fungi was maintained on sabouraud dextrose agar (SDA) medium in slant and sterilized in hot air oven at 180ºC for 3 h. The culture slants were incubated at 28ºC for 3–4 days for multiplication of fungal strains. The sterilized growth medium was transferred to the sterilized petri plates and incubated at 28ºC for 48 h for fungus growth. Small filter paper discs were laid flat on the growth medium containing 100 μL of samples. The petri plates were again incubated. The zones of inhibition were measured in millimeters using zone reader [18].

RESULTS AND DISCUSSION

The products physical data are presented in Table 1. All complexes were soluble in common organic solvents.

FT-IR spectra. IR spectra of the ligand and organotin(IV) complexes were recorded in the range 4000–250 cm^{-1} (Table 2). The ligand and organotin(IV) complexes demonstrated stretching vibration of lattice water in the range of 3487–3420 cm^{-1}. Deprotonation of the carboxylic acid group was indicated by the absence of the band of the ligand at 2760 cm^{-1} in the spectra of organotin(IV) complexes that confirmed the

Table 1. Physical data of organotin(IV) complexes with *l*-lysine monohydrate

Comp. no.	Formula	Molecular weight	Yield, %	mp, °C	Elemental analysis, %			
					C calculated found	H calculated found	N calculated found	S calculated found
HL	$C_6H_{16}O_3N_2$	164.21	–	224–225	43.88 / 43.90	9.81 / 9.83	17.05 / 17.08	–
I	$C_{24}H_{50}O_3N_2Cl_2S_4Sn_2$	851.25	75	110–111	33.86 / 33.91	5.92 / 5.97	3.29 / 3.23	15.07 / 15.03
II	$C_{32}H_{34}O_3N_2Cl_2S_4Sn_2$	931.21	65	101–102	41.27 / 41.21	3.68 / 3.62	3.01 / 3.05	13.77 / 13.72
III	$C_{32}H_{67}O_3N_2Cl_3S_4Sn_3$	1118.63	78	290–292	34.36 / 34.32	6.04 / 6.01	2.50 / 2.54	11.47 / 11.43
IV	$C_{44}H_{43}O_3N_2Cl_3S_4Sn_3$	1238.57	71	114–115	42.67 / 42.71	3.50 / 3.46	2.26 / 2.20	10.36 / 10.41
V	$C_{32}H_{68}O_3N_2S_4Sn_2$	894.57	69	248–250	42.96 / 42.91	7.66 / 7.62	3.13 / 3.09	14.34 / 14.30
VI	$C_{44}H_{94}O_3N_2S_4Sn_3$	1183.62	74	240–243	44.65 / 44.61	8.00 / 8.05	2.37 / 2.31	10.84 / 10.80
VII	$C_{44}H_{44}O_3N_2S_4Sn_2$	1014.51	70	227–230	52.09 / 52.03	4.37 / 4.33	2.76 / 2.72	12.64 / 12.69
VIII	$C_{62}H_{58}O_3N_2S_4Sn_3$	1366.04	77	198–200	54.61 / 54.65	4.29 / 4.34	2.05 / 2.01	9.41 / 9.36

Table 2. FT-IR data (ν, cm^{-1}) of organotin(IV) complexes with *l*-lysine monohydrate

Comp. no.	ν(H_2O)	ν(NH)	ν(COO)			ν(C=S)	ν(C–S)	ν(Sn–O)	ν(Sn–C)	ν(Sn–S)	ν(Sn–Cl)
			ν_{as}(COO)	ν_s(COO)	Δν						
HL	3420	3323	1582	1348	234	–	–	–	–	–	–
I	3428	3324	1583	1408	175	1010	988	–	562	414	331
II	3430	3326	1575	1428	147	1011	985	–	287	448	330
III	3429	3323	1578	1428	150	1012	985	485	578	444	334
IV	3427	3224	1565	1411	154	1010	987	475	279	445	329
V	3425	3225	1582	1410	172	1011	988	-	550	468	–
VI	3420	3324	1578	1425	153	1016	985	483	572	441	–
VII	3487	3323	1575	1424	151	1015	982	-	290	442	–
VIII	3477	3325	1584	1426	158	1013	980	485	279	421	–

complexation. The strong band of the N–H group at 3323 cm^{-1} in the spectrum of the ligand did not show significant shift upon complexation. The strong asymmetric stretching band (1584–1565 cm^{-1}) and symmetrical stretching band (1428–1408 cm^{-1}) of the carboxylate group supported the structure and bonding of the ligand [19]. The Δ ν values [$\Delta\nu = \nu_{as}(COO) - \nu_s(COO)$] were used to predict the mode of tin–carboxylate interaction. In the synthesized complexes Δν was less than 200 cm^{-1} which confirmed the bidentate nature of the ligand [20]. The stretching vibrations ν(Sn–O) at 485–475 cm^{-1} of the complexes

Table 3. ^{1}H NMR data[a] (δ, ppm) of organotin(IV) complexes with *l*-Lysine monohydrate

Proton no.	Compound								
	HL	**I**	**II**	**III**	**IV**	**V**	**VI**	**VII**	**VIII**
2	1.36 m	1.37 m	1.36 m	1.37 m	1.37 m	1.36 m	1.37 m	1.36 m	1.37 m
3	1.24 m	1.23 m	1.24 m	1.23 m	1.23 m	1.24 m	1.23 m	1.24 m	1.23 m
4	1.42 m	1.42 m	1.41 m	1.42 m	1.42 m	1.42 m	1.41 m	1.41 m	1.41 m
5	2.54 m	2.53 m	2.53 m	2.53 m	2.54 m	2.54 m	2.53 m	2.53 m	2.54 m
–NH	2.1 s	2.1 s	2.1 s	2.1 s	2.1 s	2.1 s	2.1 s	2.1 s	2.1 s
R	–	0.87 t (7.2)	6.52–6.83 m	0.89 t (7.2)	6.56–6.87 m	0.92 t (7.7)	0.96 t (7.7)	6.68–6.95 m	6.60–6.92 m
		1.26–1.34 m	6.12–7.50 m	1.27–1.35 m	6.14–7.53 m	1.63–1.68 m	1.66–1.69 m	6.87–7.38 m	6.86–7.39 m
		1.61–1.87 m	–	1.61–1.86 m	–	1.72–1.77 m	1.71–1.79 m	–	–

[a]

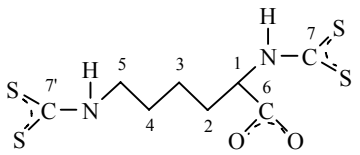


Table 4. ^{13}C NMR data[a,b] (δ, ppm) of organotin(IV) complexes with *l*-lysine monohydrate

Carbon no.	Compound								
	HL	**I**	**II**	**III**	**IV**	**V**	**VI**	**VII**	**VIII**
1	57.3	57.2	57.3	57.2	57.1	57.2	57.1	57.2	57.1
2	24.2	24.2	24.1	24.2	24.2	24.1	24.2	24.1	24.1
3	22.2	22.1	22.2	22.1	22.1	22.2	22.3	22.2	22.1
4	29.2	29.2	29.3	29.2	29.2	29.1	29.2	29.2	29.2
5	44.1	44.2	44.2	44.1	44.3	44.2	44.1	44.2	44.2
6	179.2	–	–	183.9	182.4	–	184.6	–	184.5
7,7'	–	206.9	206.7	206.9	206.8	206.9	206.8	206.9	206.8

[a] **I**: Sn-C_4H_9Cl; (C^{α}) 28.1, (C^{β}) 27.2, (C^{γ}) 26.5, (C^{δ}) 14.1; **II**: Sn-C_6H_5Cl, (C^{a}) 147.3, (C^{b}) 137.8, (C^{g}) 135.6, (C^{d}) 129.6; **III**: Sn-C_4H_9Cl; (C^{α}) 28.8, (C^{β}) 26.80, (C^{γ}) 25.4, (C^{δ}) 14.2; **IV**: Sn-C_6H_5Cl, (C^{a}) 142.1 ^{1}J[638], (C^{b}) 136.0 ^{2}J[47], (C^{g}) 135.9, (C^{d}) 129.2; **V**: Sn-$CH_2CH_2CH_2CH_3$, (C^{a}) 22.6 ^{1}J 578, (C^{b}) 28.7 ^{2}J 34, (C^{g}) 27.6 ^{3}J 87, (C^{d}) 14.2; **VI**: Sn-$CH_2CH_2CH_2CH_3$, (C^{a}) 20.9 ^{1}J[558], (C^{b}) 28.6 ^{2}J[33], (C^{g}) 27.6 ^{3}J[86], (C^{d}) 14.0; **VII**: Sn-C_6H_5, (C^{α}) 137.0, (C^{β}) 129.2, (C^{γ}) 136.2, (C^{δ}) 128.2; **VIII**: Sn-C_6H_5, (C^{α}) 137.2, (C^{β}) 129.8, (C^{γ}) 136.5, (C^{δ}) 128.79.

[b] ^{n}J[^{119}Sn,^{13}C] in Hz are listed in parenthesis.

III, **IV**, **VI,** and **VIII** confirmed the bonding between tin and oxygen [21, 22].

^{1}H NMR spectra. The ^{1}H NMR data of complexes **I–VIII** are presented in Table 3. The number of protons calculated by integration of peaks was found in very close agreement to those theoretically calculated by incremental method [23]. The absence of –OH and –SH signals in the spectra of organotin(IV) complexes indicated the complexation with tin via the COO^{-} and CSS^{-} anion [24, 25].

^{13}C NMR spectra. ^{13}C NMR data are presented in Table 4. The free ligand signal of –COO at 179.2 ppm

Table 5. Antifungal activity (mm) data[a–e] of organotin(IV) complexes with *l*-lysine monohydrate

Complex no.	Fungal inhibition zone, mm			
	A. alternata	*G. lucidum*	*A. niger*	*A. flavus*
HL	19b[c]±1.00	19[c]±1.00	27[c]±0.86	24[b,c]±1.65
I	13[c]±1.00	28[b,c]±1.41	29[b,c]±0.86	21[b,c]±1.00
II	19[b,c]±0.86	26[b,c]±0.86	27[c]±1.00	17[b,c]±1.65
III	25[b,c]±0.86	28[b,c]±0.86	29[b,c]±1.00	15[b,c]±0.86
IV	23[b,c]±0.86	31[a,b]±0.86	31[b,c]±0.86	18[b,c]±0.86
V	21[b,c]±1.00	30[a,b]±0.86	30[b,c]±1.00	23[b,c]±1.41
VI	14[b,c]±0.86	29[b,c]±1.00	27[c]±0.86	25[b]±1.65
VII	21[b,c]±0.86	29[b,c]±1.00	37[a,b]±0.86	36[a,b]±1.65
VIII	27[a,b]±1.00	32[a,b]±1.41	38[a,b]±1.65	38[a]±1.41
Fluconazole	38[a]±0.86	41[a]±0.86	40[a]±1.00	12[c]±0.86

[a] Concentration = 1 mg/mL in DMSO. [b] Standard = Ampicillin. [c] 0 = No activity, 5–10 = activity present, 11–25 = moderate activity, 26–40 = strong activity. [d] Antibacterial values are mean ±S.D of samples analyzed individually in triplicate at $p < 0.1$. [e] Different letters in superscripts indicate significant differences.

was shifted downfield in the spectra of complexes (182.4–184.6 ppm) [26]. Coordination of tin atoms in di- and triorganotin complexes has been related to $^{n}J(^{119}Sn–^{13}C)$ coupling constants. The $^{n}J(^{119}Sn–^{13}C)$ coupling for complexes **IV** and **V** were 638 and 578 Hz respectively and indicated four coordinated geometry [27, 28] of those in the solution.

Antibacterial activity. The newly synthesized organotin(IV) complexes **I–VIII** and the ligand were screened for their *in vitro* antibacterial activity against four bacterial strains two of which were Gram positive (*B. subtilis* and *S. aureus*) and two Gram negative (*P. multocida* and *E. coli*). Ampicillin was used as the positive standard control drug. Antibacterial activity of the newly synthesized compounds was lower than that of the standard drug with few exceptions. The complexes were biologically more active than the free ligand [29].

Antifungal activity. *In vitro* tests for antifungal activity of organotin(IV) complexes and ligand were screened against four fungal strains using disc diffusion method [16] and fluconazole as the standard drug (Table 5). All complexes exhibited significant antifungal activity. Triphenyltin complexes **VII** and **VIII** demonstrated the highest inhibitory effect against all fungal strains [29].

CONCLUSIONS

FT-IR spectra indicated that organotin(IV) moieties reacted via O- and S-donor sites of the ligand in a bidentate manner. NMR data verify the coordination via both $COO^{–}$ and CSS^{-} groups and the complexes exhibited the four coordinated geometry in solutions. The synthesized organotin(IV) complexes demonstrated the certain potential in inhibiting the growth of fungi.

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