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ORIGINAL ARTICLE

Biological Potential of Homo- and Heteronuclear Complexes of Iminodiacetic Acid

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ABSTRACT

Background: Natural ligands containing the carboxylate group have been broadly utilized in many coordination complexes because of their simple manufacturing strategies, magnificent chelation properties, and biological potential. The carboxylate ligands may bind to the metal atoms in a variety of coordination modes which include monodentate/bidentate/chelating modes and may result in the formation of homo- and heterobimetallic complexes.

Objective: Current research is focused on synthesis, characterization, antibacterial and anti-inflammatory studies of homo- and heteronuclear complexes with iminodiacetic acid (NA_2L).

Methodology: Four homo-bimetallic $Me_3SnLSnPh_3$ (1), $Me_3SnLSn(Cl)Ph_2$ (2), $Ph_3SnLSn(Cl)Me_2$ (3) and $Bu_3SnLSn(Cl)Me_2$ (4) products having different organotin moieties were successfully synthesized by refluxing NA_2L in toluene firstly with Me_3SnCl/Bu_3SnCl/Ph_3SnCl and then with Ph_3SnCl/Ph_2SnCl_2/Me_2SnCl_2. Refluxing NA_2L with tributyltin(IV) chloride in 1:2 molar ratio for 3 hours and subsequent reaction with equimolar MCl_2 produced the heterobimetallic products of the general formula $Bu_3SnLMLSnBu_3$ where M (a transition metal) = Zn, Cu, Mn and Cd for compounds 5-8, respectively. The products were characterized by elemental analysis (CHN), FTIR, and ^{1}HNMR spectroscopy.

Result: The carboxylate donor sites of NA_2L ligand act with organotin(IV) moieties in an iso-bidentate fashion. In solid state, the central tin atom exhibits a trigonal bipyramidal configuration and hetero metal atoms (Zn, Cu, Mn, Cd) has square planer geometry. ^{1}H NMR spectroscopy verified the ligand-metal coordination. The coordination products 2 and 5 have shown the highest biofilm inhibitions against *Escherichia coli* and *Staphylococcus aureus*, respectively. Complex 3 is inactive against both strains of bacteria. The anti-inflammatory activities of the synthesized products were lowered in the following descending order: 3>4>1>2>5.

Conclusion: We have successfully synthesized four homo-binuclear complexes i.e., $Me_3SnLSnPh_3$ (1), $Me_3SnLSn(Cl)Ph_2$ (2), $Ph_3SnLSn(Cl)Me_2$ (3) and $Bu_3SnLSn(Cl)Me_2$ (4) and four heterobimetallic products of the general formula $Bu_3SnLMLSnBu_3$ where M = Zn, Cu, Mn and Cd for compounds 5-8, respectively. Their structural features were verified by elemental analysis, FTIR, and ^{1}HNMR spectroscopy. They have generally shown good antibacterial and anti-inflammatory potential.

Keywords
Homobimetallic (Sn, Sn), Heterobimetallic (Sn & Zn/Cu/Mn/Cd), Iminodiacetic Acid, Antibacterial, Anti-Inflammatory.

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INTRODUCTION

Organotin (IV) products are comprised of at least one C-Sn bond and exist as mono-/di-/tri-/tetra-organotins, depending upon the number of alkyl/aryl groups bonded to tin. The anion in these compounds is commonly a thiolate, carboxylate, chloride, fluoride, oxide, hydroxide[1]. Recently, organotin(IV) aldehydes have also been reported by using 4-(dimethylamino) benzaldehyde as the ligand precursor[2]. Organotin(IV) compounds of numerous oxygen, sulfur and nitrogen donor ligands have been widely reported for their diverse applications in industrial, agricultural, and medicinal field[3]. Organotin compounds are commonly prepared on industrial scale by alkylation of $SnCl_4$ with organo-magnesium or -aluminum compounds[4]. Organotin(IV) compounds find applications as ion carriers in electrochemical membrane design[5], miticides, biocides, wood preservatives[6], PVC stabilizers[7], photo-stabilizers of PVC[8] and as catalysts for transesterification/esterification[9] and biodiesel formation[10]. They also display anti-inflammatory, antimicrobial, antituberculosis[11], anticancer[12], lipoxygenase inhibitors, radical scavengers and reducing agents[13].

Carboxylate ligands have been broadly utilized to synthesize coordination complexes because they show broad chelation with various metals[14,15]. Coordination of metals with carboxylate moieties provides various coordination modes which may be mono dentate, bidentate or chelate in symmetric/asymmetric forms[16]. The bimetallic compounds may show the two-fold chelating impact of a ligand and moreover, the existence of multiple metal atoms may lead to an enhanced activity[17]. The existence of both metal centers in close proximity resembles with the active sites of many metalloenzymes and thus helps to investigate the metal–enzyme and metal–proteins interactions[18]. Therefore, there is a growing trend towards the synthesis of homo- and heterobimetallic complexes[19,20]. Heterobimetallic products find applications in photochemical molecular devices and as light sensitive probes in biological systems[21]. The heterobimetallic compounds having simultaneously electron-deficient and electron-rich transition metal centers may perform their functions in a cooperative way resulting in their increased reactivities[22].

In continuous to our previous studies on organotin complexes[2,23], current studies were performed on the synthesis and characterization (elemental analysis, FTIR, ^{1}H NMR) of homo- (Sn, Sn) and heterobimetallic (Sn & Cu/Zn/Cd/Mn) complexes of iminodiacetic acid (NA_2L). The synthesized products were also tested for their antibacterial and anti-inflammatory potential. No studies were reported earlier on the antibacterial and anti-inflammatory potential of homonuclear (Sn & Sn) and heteronuclear (Sn & Zn/Cu/Mn/Cd) complexes of NA_2L.

MATERIALS AND METHODS

Pyrex origin glassware was used during the synthesis of coordination products 1-8. Organotin chloride precursors including triphenyltin (IV) chloride (Ph_3SnCl), tri-*n*-butyltin (IV) chloride (Bu_3SnCl), trimethyltin (IV) chloride (Me_3SnCl), diphenyltin (IV) chloride (Ph_2SnCl_2) and dimethyltin (IV) chloride (Me_2SnCl_2) were purchased from Sigma Aldrich-USA. Analytical grade transition metal chlorides MCl_2 (M = Cu, Zn, Mn, Cd) (analytical grade) and organic solvents (methanol, ethanol, DMSO and chloroform) were used. The ligand precursor i.e., iminodiacetic acid was procured from Merck, Germany.

FTIR spectroscopy was performed by Carry-630 FTIR spectrometer in the range of 450 to 4000 cm^{-1}. ^{1}HNMR spectroscopy of the free ligand (Na_2L) and coordination products (2 & 3) was performed in deuterated water and DMSO, respectively by Bruker ARC 300 MHz-FT-NMR spectrometer. The synthesized compounds were investigated for their anti-biofilm potential against two bacterial strains namely *S. aureus* (Gram-positive) and *E. coli* (Gram-negative) by a microtiter plate technique reported earlier[24] whereas ciprofloxacin was used as the reference drug. We used a microplate reader (BioTek, USA) to find the OD of each well at 630nm[24]. Anti-inflammatory activities were performed by a reported procedure by using diclofenac and DMSO as positive and negative controls, respectively[25]. The %age inhibition of precipitation (stabilization of the protein) was found as compared to the standard control drug (diclofenac) by the following equation:

$$\frac{\text{Absorbance of control minus Absorbance of treated}}{\text{Absorbance of control}} \times 100$$

Synthesis of Homo-Bimetallic Complexes 1-4

2mmoles of iminiodiacetic acid (NA_2L) were dissolved in 30ml toluene in a two-necked round bottom flask (250ml) by magnetic stirring at room temperature. Then 2mmoles of an organotin chloride (R_3SnCl where R = Me, *n*-Bu, Ph) were added and the flask's contents were refluxed for 3 hours. Subsequently, another organotin chloride (e.g., $Ph_3SnCl/Ph_2SnCl_2/Me_2SnCl_2$) containing different organotin moiety, was added in equimolar amount and the flask contents were refluxed for 2 hours. Then, the reaction mixture was stayed for overnight. It was finally filtered through a filter paper to separate out the residue of a homo-bimetallic product (1-4) which was dried in air. The synthetic routes for complexes 1-2 and 3-4 are displayed in Figure **1** and **2**, respectively.

Synthesis of Hetero-Bimetallic Complexes 5-8

2mmoles of ligand iminiodiacetic acid (NA_2L) was dissolved in 30ml toluene by stirring in a two-necked round bottom flask (250ml) and then 2mmoles of Bu_3SnCl were added. Subsequently, the flask's contents were refluxed for 3 hours followed by the addition of 1mmole of a metal chloride (MCl_2 where M = Zn, Cu, Mn, Cd). Then, the reaction mixture was refluxed for 2 hours and stayed for overnight. It was finally filtered by a filter paper and residue was air dried to produce the hetero-bimetallic products 5-8 (Figure **3**).

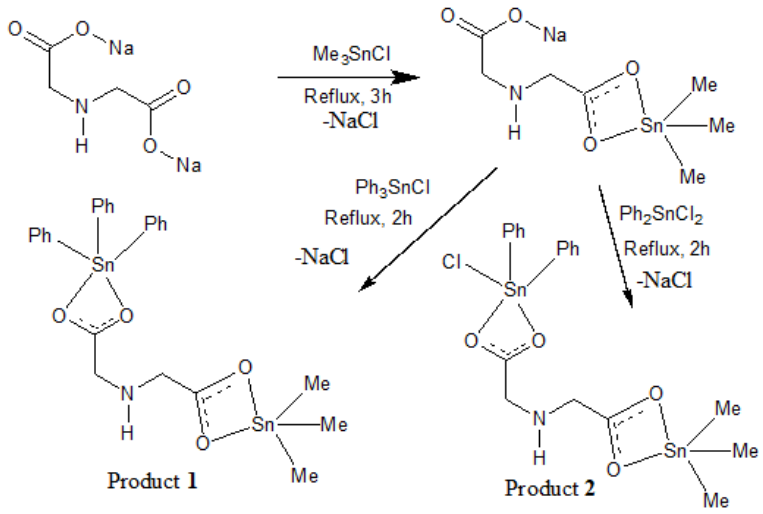


Figure 1. Reactions involved in the syntheses of homo-bimetallic complexes **1-2**.

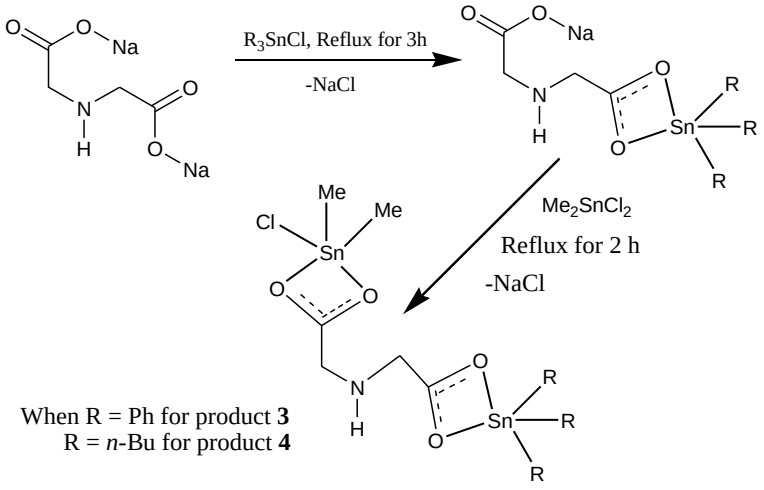


Figure 2. Reactions involved in the syntheses of homo-bimetallic complexes **3-4**.

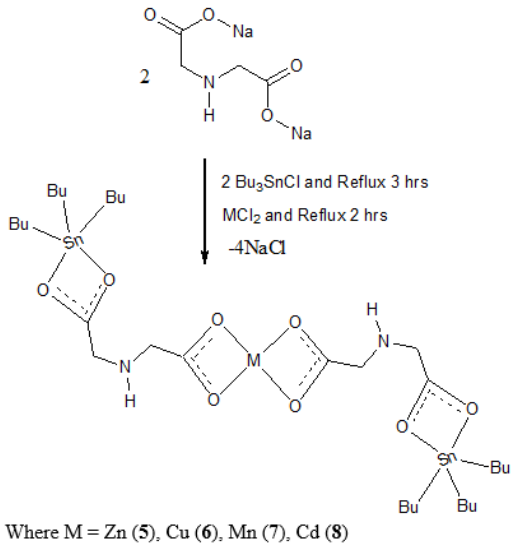


Figure 3. Summary of reactions involved in the syntheses of hetero-bimetallic complexes **5-8**.

Biofilm Inhibition Assessment

The synthesized coordination products 1-5 were investigated for their antibacterial potential by biofilm inhibition method reported earlier[24]. We have used a microplate reader to find the optical density of each well at 630 nm. Following formula was applied to find the percentage of bacterial growth inhibition:

$$\text{Inhibition \%} = \frac{100 - (OD630_{sample} \times 100)}{OD630_{control}}$$

Anti-Inflammatory Potential

Anti-inflammatory potential of the synthesized compounds 1-5 was evaluated by a reported procedure [25]. Following equation was used to find the degree of inhibition of denaturation or precipitation of each product:

$$\frac{\text{Absorbance of control minus Absorbance of treated}}{\text{Absorbance of control}} \times 100$$

The products having anti-inflammatory activities greater than 20% can be considered as having anti-inflammatory potential and could find importance in the development of drugs[25].

RESULTS AND DISCUSSION

Homo-bimetallic products having the formulas of $Me_3SnLSnPh_3$ (1), $Me_3SnLSn(Cl)Ph_2$ (2), $Ph_3SnLSn(Cl)Me_2$ (3) and $Bu_3SnLSn(Cl)Me_2$ (4) were produced by refluxing Na_2L firstly with one organotin chloride ($Me_3SnCl/Bu_3SnCl/Ph_3SnCl$) for 3 hours and then with another organotin chloride ($Ph_3SnCl/Ph_2SnCl_2/Me_2SnCl_2$) for 2 hours in toluene. The heterobimetallic products 5-8 of the general formula $Bu_3SnLMLSnBu_3$ were produced by refluxing Na_2L (2mmoles) with Bu_3SnCl (2mmoles) in toluene for 3 hours and then with MCl_2 (1mmole. where M = Zn, Cu, Mn and Cd) for 2 hours.

The products were analyzed by elemental (CHN) analysis, FTIR, and ^{1}HNMR spectroscopy. All the synthesized products were whitish except the hetero-bimetallic complex 6 which was blue-colored. They had sharp melting points and were well-stable in air. They had shown good solubility in common organic solvents (Table **1**).

Elemental analysis data demonstrated that the observed percentages of elements (C, H and N) are very closer to those theoretically calculated for all the products 1-8. The physical data of the synthesized products are summarized in Table **1.**

FTIR Spectroscopy

Fourier transform infrared (FTIR) spectroscopy can be used to find the functional groups of compounds. The free ligand (Na_2L) and the homo-/heteronuclear products (1-8) were subjected to FTIR spectroscopic analysis and the obtained data are displayed in the Table **2**. Two representative spectra of products 2 and 8 are shown in Figures **S1** and **S2**, respectively of the Supplementary Information.

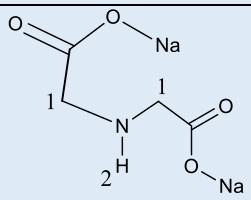
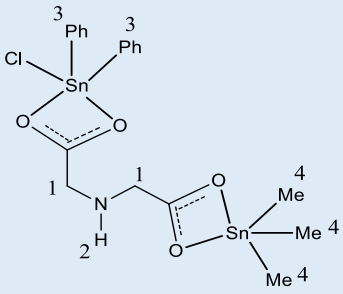
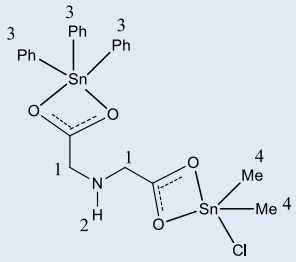
Table 1. Physical Data of Homo and Hetero-Bimetallic Complexes.

Comp. No.	Mol. Formula	Mol. wt (g/mol)	Yield %	M.P (°C)	Solubility	Elemental Data (CHN)					
						C% Calc.	C% Obs.	H% Calc.	H% Obs.	N% Calc.	N% Obs.
1	$C_{25}H_{29}O_4Sn_2N$	644.42	82	355	DMSO	46.55	46.10	4.50	4.12	2.17	2.03
2	$C_{19}H_{24}ClNO_4Sn_2$	603.27	81	315	DMSO	28.78	27.89	4.96	4.28	12.16	11.98
3	$C_{24}H_{26}O_4Sn_2NCl$	664.92	70	303	DMSO	43.31	42.96	4.36	4.21	2.10	1.98
4	$C_{18}H_{38}O_4Sn_2NCl$	584.75	80	317	DMSO	36.93	35.21	6.69	5.84	2.39	2.00
5	$C_{32}H_{64}O_8Sn_2N_2Zn$	0.75	82	309	DMSO, MeOH, EtOH	42.34	41.22	7.11	6.91	3.09	2.97
6	$C_{32}O_8H_{64}Sn_2N_2Cu$	0.67	72	312	DMSO, MeOH, EtOH	42.43	41.89	7.12	6.95	3.09	2.88
7	$C_{32}H_{64}O_8Sn_2N_2Mn$	0.53	75	307	MeOH, EtOH	42.84	42.21	7.19	6.96	3.12	2.85
8	$C_{32}H_{64}O_8Sn_2N_2Cd$	0.67	81	302	$CHCl_3$, MeOH, EtOH	40.26	39.88	6.76	6.23	2.93	2.68

Table 2. FTIR Data of Complexes 1-8.

Comp No.	υ COO (cm^{-1})			υSn-C (cm^{-1})	υSn-O (cm^{-1})	υM-O (cm^{-1})
	Sym	Asym	Δυ			
Na_2L	1576s	1412s	164	-	-	-
1	1621m	1480w	141	528s	422s	-
2	1633m	1431m	202	566s	454s	-
3	1633m	1432w	201	535s	428w	-
4	1637w	1493w	144	523m	489w	-
5	1653w	1458m	195	504w	465m	620s
6	1636m	1423w	213	522w	421w	696s
7	1585m	1428m	157	552w	443m	638s
8	1621w	1479w	142	551 w	473m	692s

Table 3. ^{1}HNMR Data (ppm) of Free Ligand (Na_2L) and Homo-Bimetallic Products 2 and 3.

	Proton No.	Proton Nature	Chemical Shift
	1	CH_2 protons	3.03-3.06 ppm (multiplet)
	2	NH protons	4.70 ppm (singlet)
	1	CH_2 protons	6.12-6.15 ppm (multiplet)
	2	NH proton	5.70 ppm (singlet)
	3	Phenyl protons	7.10–7.51 ppm multiplet (7.51ppm ortho, 7.12 ppm meta and 7.10 ppm para)
	4	CH_3 protons	1.62 ppm (multiplet)
	1	CH_2 protons	2.50 ppm (singlet)
	2	NH proton	-
	3	Phenyl protons	7..39-7.89 ppm (multiplet) with 7.89 ppm for ortho while 7.39-7.43 ppm for meta and para positions
	4	CH_3 protons	3.39 ppm (singlet)

The mono-/bidentate coordination linkage of the carboxylate ligand for the tin metal was estimated from $\Delta\upsilon = \upsilon COO_{(asym)} - \upsilon COO_{(sym)}$[26] whose value is changed depending upon the coordination number around tin (IV)[27] or other metal atom (Zn, Cu, Mn, Cd). A smaller Δυ value reflects the more symmetric binding of carboxylate groups with a metal and vice versa[28]. The Δυ value of the synthesized products 1-8 were ranged from 141 to 213 cm^{-1} (Table **2**), which indicated the chelating (in 2,3,5-7) and iso-bidentate (in 1,4 and 8) binding modes of carboxylate ligand for its binding to a metal[28,29]. The iso-bidentate (bridging) coordination modes are common in organotin carboxylates[30] where each of the carboxylate oxygen is simultaneously bonded to the same metal center, with one M-O bond comparatively longer as compared to the other. The results thus demonstrate that there is a trigonal bipyramidal geometry of tin in complexes 1-8 while a square planner geometry around the other metal atom (Zn, Cu, Mn, Cd) was shown in heterobimetallic complexes 5-8.

Other bands of special interest are Sn-O, M-O and Sn-C vibrations. The FTIR spectroscopy displayed Sn-C and Sn-O vibrations at 504-566 and 421-489cm^{-1}, respectively[31]. M-O band was appeared at 620-696cm^{-1} [32] in heterobimetallic products 5-8.

^{1}HNMR Spectroscopy

^{1}HNMR spectra of the ligand precursor (Na_2L) and coordination products (2 & 3) were recorded in deuterated water and DMSO, respectively. The observed chemical shifts (ppm) are shown in Table **3** whereas the ^{1}HNMR spectra of 2 & 3 are shown in Figures **S3** and **S4** of the Supplementary Information.

The free ligand (Na_2L) displayed a multiplet at 3.03-3.06 ppm for the methylenic protons and a singlet at 4.70 ppm for -NH protons[33] (Table **3**). The ^{1}H NMR spectrum of product 2 (homo-bimetallic) displayed the proton signals of ligand skeleton (L) as well as those of trimethyltin (IV) and diphenyltin (IV) moieties (Table **3** and Figure **S3**). The chemical shifts at 6.12-6.15 and 5.67-5.70 ppm were assigned to the CH_2 and NH protons, respectively as a

multiplet[34]. The tin-bonded methyl protons were appeared at 1.62 ppm as a multiplet. The phenyl group bonded to tin were displayed as a multiplet at 7.10-7.51 ppm which contained the ortho signals at 7.51 ppm, meta signals at 7.12 ppm and para signals at 7.10 ppm[35]. The ^{1}HNMR data thus completely verify the homobimetallic complexation in product 2, with incorporation of two different organotin (IV) moieties (trimethyltin (IV) and diphenyltin (IV)).

The ^{1}HNMR spectrum of complex 3 also verified the homobimetallic complexation with incorporation of two different organotin (IV) moieties (trimethyltin(IV) and diphenyltin(IV)) (Table **3** and Figure **S4**). The methyl (CH_3) protons attached to tin were appeared at 3.39 ppm as a singlet. The phenyltin (IV) moiety displayed its proton signals at 7.39-7.89 ppm as a multiplet; the ortho protons had shown downfield shift (7.89 ppm) as compared to meta and para protons (7.39-7.43 ppm)[36]. The methylene (CH_2) protons of the coordinated ligand (iminodiacetate ion) were appeared at 2.50 ppm as a multiplet[33]. The ^{1}HNMR spectrum of product 3 did not display any peak for -NH protons because they might be displaced by the deuterium from source solvent (deuterated DMSO).

Table 4. Biofilm Inhibition (%) Data of Complexes 1-5.

	Biofilm Inhibition (%)	
Sample Code	**Escherichia Coli**	**Staphylococcus Aureus**
1	48	68
2	58	73
3	0	0
4	57	63
5	0	76
Ciprofloxacin	67	69

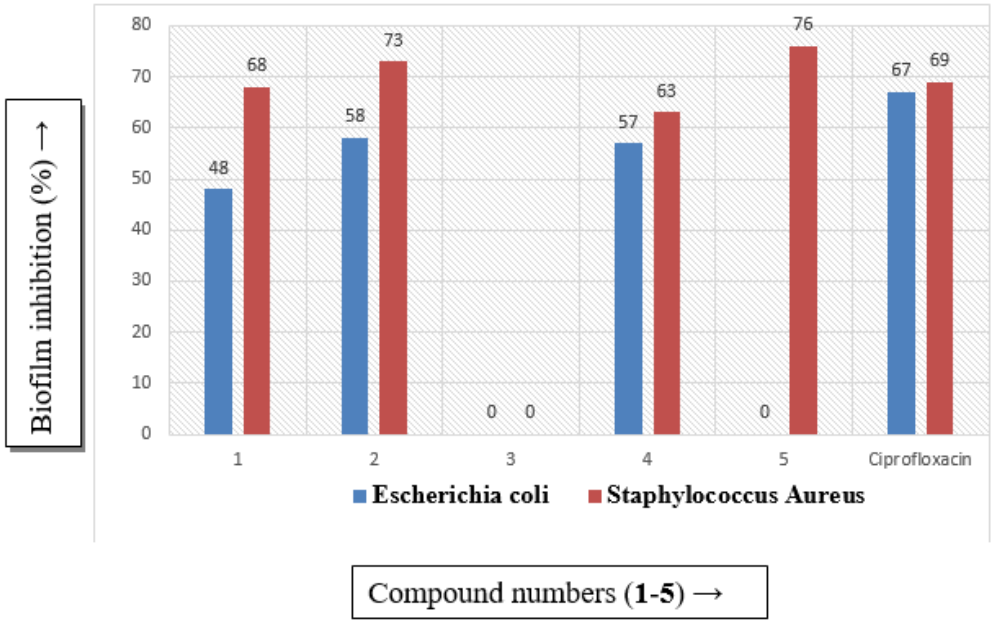


Figure 4. Graphical representation of biofilm inhibition data of complex 1-5.

Antibacterial Activity

The biofilm inhibition method[24] was used to test the antimicrobial efficacy of the coordinated products 1-5. The synthesized complexes were tested against the bacterial strains of *S. aureus* (G-positive) and *E. coli* (G-negative). We employed 1 mg/ml concentration of a sample in DMSO for each test. Ciprofloxacin was used as a reference drug. The obtained data are displayed in Table **4** and graphically compared in Figure **4**.

It was found that biofilm inhibition depends upon the nature of the coordinated metal (tin alone or in the presence of Zn) and substitution pattern at tin[28]. All the products 1-5 have shown less activity (0-58%) against *E. coli* as compared to ciprofloxacin (67%). However, coordination products 2 and 5 have shown 73% and 76%, respectively biofilm inhibition against *S. aureus*, which was even superior as compared to that (69%) of the standard drug (ciprofloxacin). The homo-bimetallic product 2 displayed higher activity (58%) against *E. coli* whereas the heterobimetallic complex 5 has shown highest potential against *S. aureus* as compared to all the other complexes. Complex 3 was found inactive against both the tested strains of bacteria (*E. coli* and *S. aureus*). The results of complex 5 are interesting since it is inactive against *E. coli* but at the same time, it showed highest inhibition (76%) as compared to all the complexes against *S. aureus*; it was even higher as compared to that of the reference drug.

A general comparison between observed activities (Table **4** and Figure **4**) clarifies that all the coordination products have shown higher antibacterial potential against *S. aureus* (Gram-positive bacteria) as compared to *E. coli* (Gram-negative bacteria). It is due to the difference in thickness of layers surrounding the plasma membrane of bacteria[37]. The surrounding layers of Gram-negative bacteria are thicker as compared to those of Gram-positive bacteria so Gram-negative bacteria (*Escherichia coli*) are comparatively more drug resistant while Gram-positive bacteria (*Staphylococcus aureus*) are generally more sensitive to drugs.

Anti-Inflammatory Activity

The coordinated products 1-5 were tested for their anti-inflammatory activities by a reported procedure[25]. Diclofenac and DMSO were employed as positive and negative controls, respectively. A recommended concentration of 1mg/1ml in DMSO was used for each test[38]. The obtained data are summarized in Table **5** and they are graphically compared in Figure **5**.

Among all the tested complexes, the coordination product 3 has displayed the highest anti-inflammatory activity (84.51%) while the second highest activity (83.22%) was shown by complex 4. The compound 5 has displayed the lowest (54.83%) anti-inflammatory activity. So, it can easily be concluded that the synthesized organotin (IV) products 1-5 may find potential applications as anti-inflammatory agents. Overall, the anti-inflammatory activities of the synthesized products were decreased in the following order: 3>4>1>2>5.

Table 5. Anti-Inflammatory Activity Data (%) of Complex 1-5.

Comp. Code	Absorbance	Negative Control (DMSO)	Positive Control (Diclofenac)	Anti-Inflammatory Activity (%)
1	0.032	0.155	0.042	79.35
2	0.044	0.155	0.042	71.61
3	0.024	0.155	0.042	84.51
4	0.026	0.155	0.042	83.22
5	0.07	0.155	0.042	54.83

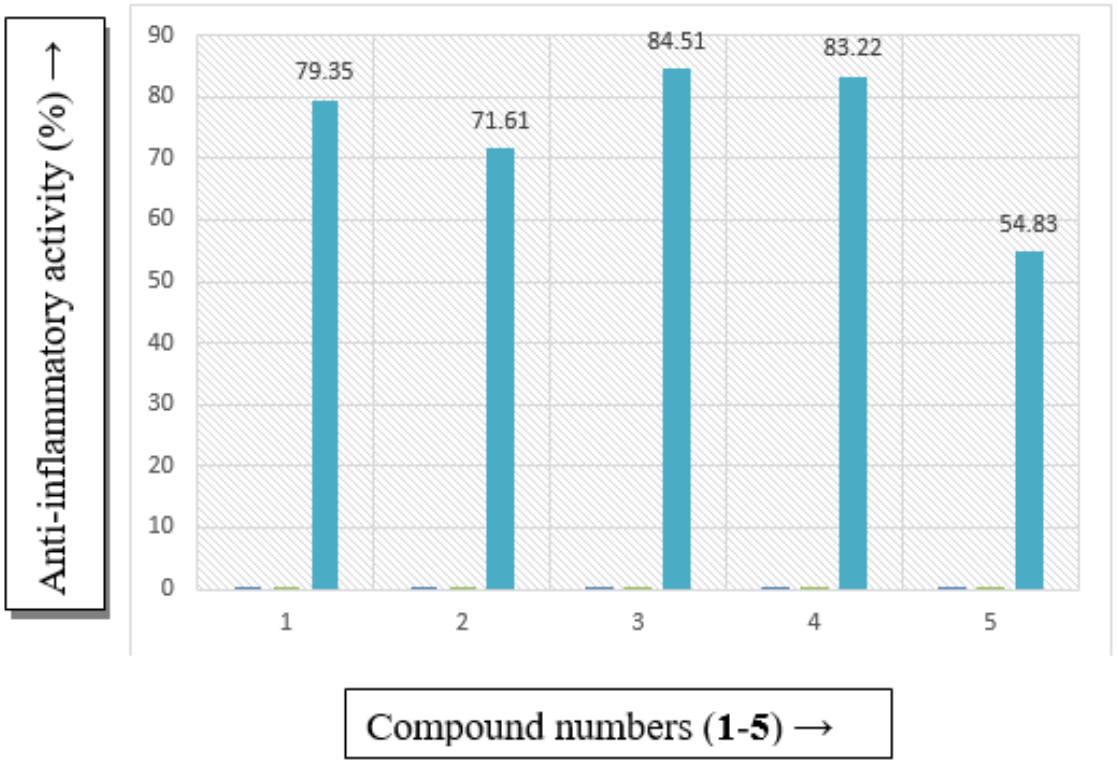


Figure 5. Graphical representation of anti-inflammatory activity data of complex 1-5.

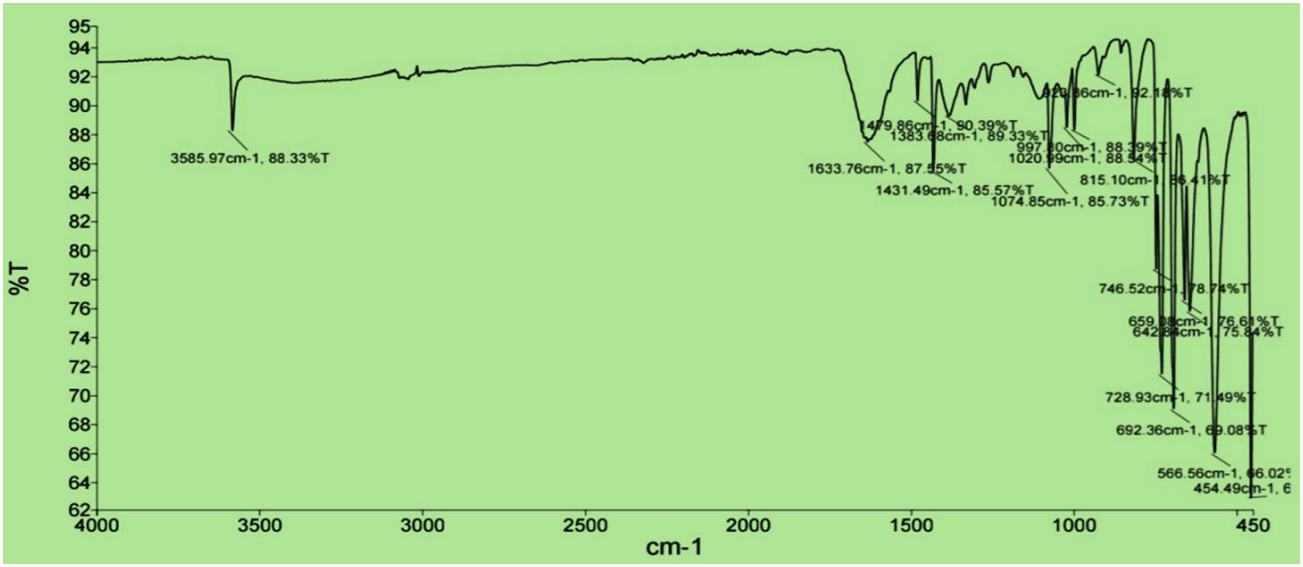


Figure S1. FTIR spectrum of complex 2.

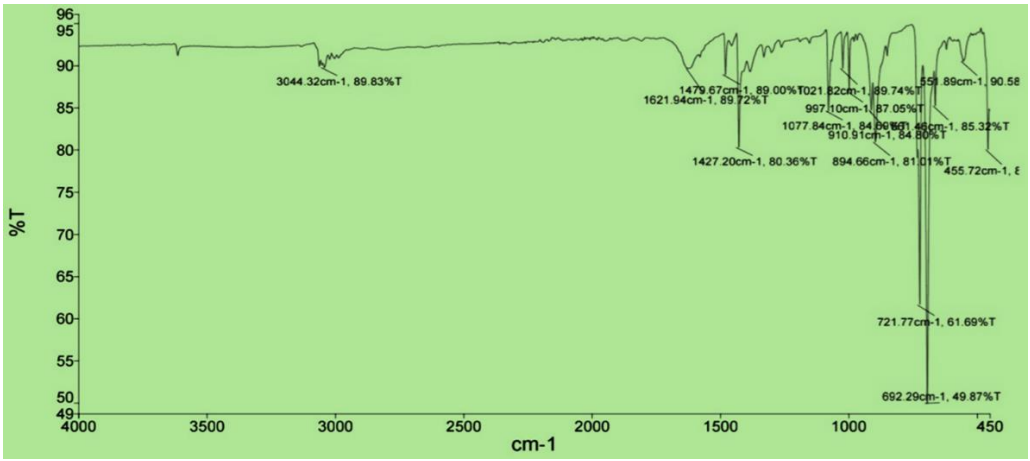


Figure S2. FTIR spectrum of complex 8.

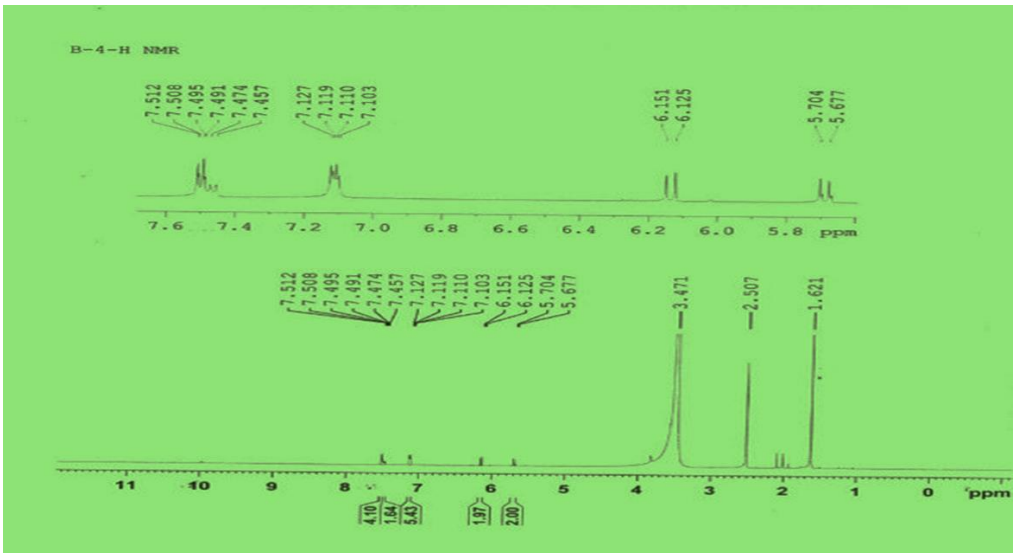


Figure S3. [1]HNMR of homo-bimetallic complex 2.

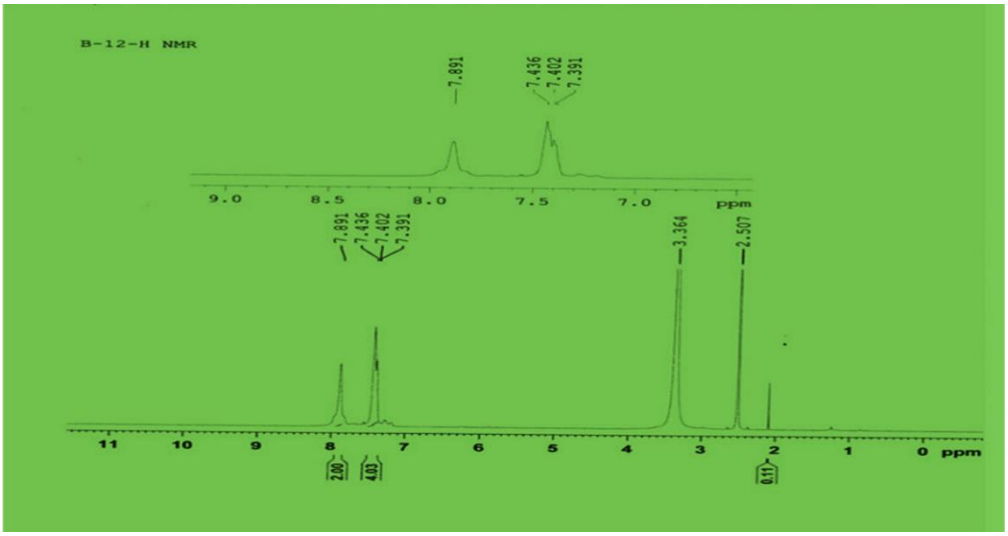


Figure S4. [1]HNMR of homo-bimetallic complex 3.

CONCLUSION

Four homo-bimetallic $Me_3SnLSnPh_3$ (1), $Me_3SnLSn(Cl)Ph_2$ (2), $Ph_3SnLSn(Cl)Me_2$ (3) and $Bu_3SnLSn(Cl)Me_2$ (4) products having different organotin moieties were successfully synthesized by refluxing iminodiacetic acid (NA_2L) firstly with $Me_3SnCl/Bu_3SnCl/Ph_3SnCl$ and then with $Ph_3SnCl/Ph_2SnCl_2/Me_2SnCl_2$ in ethanol. The refluxing of NA_2L with tributyltin (IV) chloride and subsequent reaction with MCl_2 produced the heterobimetallic products of the general formula $Bu_3SnLMLSnBu_3$ where M = Zn, Cu, Mn and Cd for compounds 5-8, respectively. The obtained products were analyzed by elemental analysis, FTIR, and ^{1}HNMR spectroscopy. The coordination products 1-8 had shown melting point higher than 300°C and were stable in air at normal temperature. All complexes were whitish in color except complex 6 which was blue in color. The carboxylate donor sites of the ligand act in an iso-bidentate fashion in 1, 4 and 8 and in a chelating mode in products 2, 3 and 5-7). The central tin atom displays a trigonal bipyramidal configuration in the solid state whereas transition metal atoms (Zn, Cu, Mn, Cd) had shown a square planer geometry. ^{1}HNMR spectroscopic data were in good agreement with the proposed structures of coordination products 2 and 3. Antibacterial activity evaluation by biofilm inhibition method has shown that the tested coordination products possess higher activity against *S. aureus* (Gram-positive bacteria) as compared to *E. coli* (Gram-negative bacteria). The newly synthesized products 2 and 5 have shown 73% and 76%, respectively biofilm inhibition against *S. aureus*, which was even higher as compared to ciprofloxacin (69%). Complexes 3 and 5 displayed the highest (84.51%) and lowest (54.83%) anti-inflammatory activities, respectively. Overall, the anti-inflammatory potential of the synthesized products was lowered in the following order: 3>4>1>2>5.

CONFLICT OF INTEREST

None.

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REFERENCES

1. Abd Aziz NA, Awang N, Chan KM, Kamaludin NF, Mohamad Anuar NN. Organotin (IV) dithiocarbamate compounds as anticancer agents: A review of syntheses and cytotoxicity studies. Molecules. 2023; 28(15): 5841.
2. Iftikhar S, Hussain S, Murtaza S, Ali D, Yousuf S, Ali MA, *et al*. Synthetic route for O, S-coordinated organotin (IV) aldehydes: Spectroscopic, computational, XRD, and antibacterial studies. Appl Organomet Chem. 2024; 38(8): e7581.
3. Barbosa ASL, de Siqueira Guedes J, da Silva DR, Meneghetti SMP, Meneghetti MR, da Silva AE, *et al*. Synthesis and evaluation of the antibiotic and adjuvant antibiotic potential of organotin (IV) derivatives. J Inorgan Biochem. 2018; 180: 80-88.
4. Ghazi D, Rasheed Z, Yousif E. Review of organotin compounds: chemistry and applications. Development. 2018; 3(4).
5. Martynov LY, Sergeeva AS, Sakharov KA, Shkinev VM, Yashtulov NA, Zaitsev NK. Voltammetric determination of phosphates using ion-selective electrode based on organotin ionophore. Microchem J. 2023; 191: 108877.
6. Hadi AG, Baqir SJ, Ahmed DS, El-Hiti GA, Hashim H, Ahmed A, *et al*. Substituted organotin complexes of 4-methoxybenzoic acid for reduction of poly (vinyl chloride) photodegradation. Polymers. 2021; 13(22): 3946.
7. Fawzi S, Yousif E, Zainulabdeen K, Bufaroosha M, Ahmed D. Highly effective photostabilization of polyvinyl chloride films using omeprazole-tin additive complexes. J Umm Al-Qura Uni Appl Sci. 2025: 1-25.
8. Arraq RR, Hadi AG, Ahmed DS, El-Hiti GA, Kariuki BM, Husain AA, *et al*. Enhancement of photostabilization of poly (vinyl chloride) in the presence of tin–cephalexin complexes. Polymers. 2023; 15(3): 550.
9. da Silva EPS, de Melo LN, Bortoluzzi JH, Meneghetti SMP. Synthesis of glycerol levulinates in the presence of Sn (IV) catalysts: Evaluation of the catalyst nature and reactional parameters. Catal Today. 2025; 448: 115165.
10. Zubair M, Sirajuddin M, Haider A, Hussain I, Tahir MN, Ali S. Organotin (IV) complexes as catalyst for biodiesel formation: synthesis, structural elucidation and computational studies. Appl. Organomet Chem. 2020; 34(1): e5305.
11. Boora A, Devi J, Kumar B, Taxak B. Organotin (IV) complexes of tridentate (ONO) hydrazone ligands: synthesis, spectral characterization, antituberculosis, antimicrobial, anti-inflammatory, molecular docking and cytotoxicity studies. BioMetals. 2025; 38(1): 153-171.

12. Akim AM, Ken TW, Sung YY, Muhammad TST. Cytotoxic effect and apoptotic induction of tricyclohexyltin p-methoxycinnamate on HT-29 colorectal cancer cells: Implications for anticancer therapeutics. J Adv Pharm Technol Res. 2025; 16(1): 1-5.
13. Antonenko TA, Gracheva YA, Shpakovsky DB, Vorobyev MA, Mazur DM, Tafeenko VA, *et al*. Biological activity of novel organotin compounds with a schiff base containing an antioxidant fragment. Int J Mol Sci. 2023; 24(3): 2024.
14. Hussain S, Ali S, Shahzadi S, Rizzoli C. Polymeric three-dimensional crystal structure of a tributyltin (IV) derivative with acetylene dicarboxylic acid. Phosphorus, Sulfur, and Silicon and the Related Elements. 2013; 188(6): 812-818.
15. Hussain S, Ali S, Shahzadi S, Tahir MN, Shahid M. Synthesis, characterization, biological activities, crystal structure and DNA binding of organotin (IV) 5-chlorosalicylates. J Coord Chem. 2015; 68(14): 2369-2387.
16. Hussain S, Ali S, Shahzadi S, Riaz M, Nazir K, Arshad MN, *et al*. Synthesis, structural and biological studies of organotin (IV) complexes with N-(Dithiocarboxy) sarcosine. Arabian J Sci Eng. 2020; 45: 4785-4795.
17. Becker S. Understanding cooperativity in homo-and heterometallic complexes: from basic concepts to design. Chem Plus Chem. 2024; 89(6): e202300619.
18. Kositzki R. Metal centers in hydrogenases, bimetallic oxidases, and model complexes studied by advanced x-ray spectroscopy techniques and quantum chemistry. 2020.
19. Fatima J, Hussain S, Ali S, Shahzadi S, Ramzan S, Shahid M. Organo Sn (IV) and Pd (II) complexes with various oxygen and sulphur donor ligands: Synthesis, spectroscopy and biological activity. Russ J Gen Chem. 2016; 86: 2914-2923.
20. Mariam S, Hussain S, Ali S, Shahzadi S, Ramzan S, Shahid M. Homobimetallic (Sn, Sn) complexes with [2-Dithiocarboxy (methyl) amino] acetic acid: synthesis, characterization and biological studies. Iranian J Sci Technol Trans A Sci. 2018; 42: 1277-1284.
21. Sinhababu S, Mankad NP. Diverse thermal and photochemical reactivity of an Al–Fe bonded heterobimetallic complex. Organometallics. 2022; 41(15): 1917-1921.
22. Lachguar A, Pichugov AV, Neumann T, Dubrawski Z, Camp C. Cooperative activation of carbon–hydrogen bonds by heterobimetallic systems. Dalton Trans. 2024; 53(4): 1393-1409.
23. Hussain S, Kanwal F, Tariq M, Parveen B, Rauf A, Rasool L, *et al*. Synthetic, structural, and biological studies of organotin (IV) derivatives of 6-amino-2-(methyleneamino) hexanoic acid. J Coord Chem. 2024; 77(1-2): 203-218.
24. Anjum F, Bukhari SA, Shahid M, Bokhari TH, Talpur MMA. Exploration of nutraceutical potential of herbal oil formulated from parasitic plant. Afr J Tradit Complement Altern Med. 2014; 11(1): 78-86.
25. Williams L, O'connar A, Latore L, Dennis O, Ringer S, Whittaker J, *et al*. The in vitro anti-denaturation effects induced by natural products and non-steroidal compounds in heat treated (immunogenic) bovine serum albumin is proposed as a screening assay for the detection of anti-inflammatory compounds, without the use of animals, in the early stages of the drug discovery process. West Indian Med J. 2008; 57(4).
26. Hanifa B, Sirajuddin M, Tiekink ER, Khan I, Kubicki M, Bari A. Designing, physiochemical confirmation, evaluation of biological and in-silico potential of Triorganotin (IV) complexes. J Mol Struct. 2022; 1260: 132814.
27. Hussain S, Ali S, Shahzadi S, Sharma SK, Qanungo K, Shahid M. Synthesis, characterization, semiempirical and biological activities of organotin (IV) carboxylates with 4-piperidinecarboxylic acid. Bioinorg Chem Appl. 2014; 2014: 959203.
28. Hussain S, Ali S, Shahzadi S, Tahir MN, Shahid M, Munawar KS, *et al*. Synthesis, spectroscopy, single crystal XRD and biological studies of multinuclear organotin dicarboxylates. Polyhedron. 2016; 117: 64-72.
29. Shahzadi S, Ali S. Structural chemistry of organotin (IV) complexes. J Iranian Chem Soc. 2008; 5: 16-28.
30. Vasquez-Ríos MG, Rojas-León In, Montes-Tolentino P, Hernández-Ahuactzi InF, Höpfl H. Pyridinedicarboxylic acids as versatile building blocks for coordination-driven self-assembly: Solvent-induced macrocycle and coordination polymer formation upon combination of 2, 5-pyridinedicarboxylate with diorganotin moieties. Crystal Growth & Design. 2018; 18(11): 7132-7149.
31. Rocha C, De Morais B, Rodrigues B, Donnici C, De Lima G, Ardisson J, *et al*. Spectroscopic and X-ray structural characterization of new polymeric organotin (IV) carboxylates and their in vitro antifungal activities: Part II. Appl Organomet Chem. 2017; 31(7): e3645.
32. Zhuiykov S. In situ FTIR study of oxygen adsorption on nanostructured RuO 2 thin-film electrode. Ionics. 2009; 15: 507-512.
33. Pavia D, Lampman G, Kriz G, Vyvyan J. Introduction to spectroscopy 4th edition. Cram Learning Syst. 2012: 15-85.
34. Said MA, Hughes DL, Rezki N, Aouad MR, Lücke C, Frey W, *et al*. Rare open zinc cluster of a novel multidentate Schiff base containing 1, 2, 3-triazole derivative: Stepwise synthesis, characterization, XRD,

HSA,% Vbur, τ and CV studies. Inorg Chim Acta. 2025: 122569.

35. Krivdin LB. Liquid-phase NMR of humic and fulvic acids. Magn Reson Chem 2025; 63(2): 128-150.
36. Hussain S, Ali S, Shahzadi S, Sharma SK, Qanungo K, Bukhari IH. Homobimetallic complexes containing Sn (IV) with acetylene dicarboxylic acid: their syntheses and structural interpretation by spectroscopic, semi-empirical, and DFT techniques. J Coord Chem. 2012; 65(2): 278-285.
37. Parveen B, Bukhari IH, Shahzadi S, Ali S, Hussain S, Ali KG, *et al*. Synthesis and spectroscopic characterization of mononuclear/binuclear organotin (IV) complexes with 1H-1, 2, 4-triazole-3-thiol: Comparative studies of their antibacterial/antifungal potencies. J Serb Chem Soc. 2015; 80(6): 755-766.
38. Amin MM, Ali S, Shahzadi S, Sharma SK, Qanungo K. Di-and triorganotin (IV) complexes of 2-aminobenzoic acid with and without triphenylphosphine: synthesis, spectroscopy, semi-empirical study, and antimicrobial activities. J Coord Chem. 2011; 64(2): 337-350.