Journal of Organometallic Chemistry 694 (2009) 3768–3774

Contents lists available at ScienceDirect

Journal of Organometallic Chemistry

journal homepage: www.elsevier.com/locate/jorganchem

Synthesis, crystal structure and in vitro antitumor activity of carboxylate bridged dinuclear organotin(IV) complexes

Zafar A. Siddiqi *, M. Shahid, Sarvendra Kumar, Mohd Khalid, Shabana Noor

Bio-inorganic Research Group, Division of Inorganic Chemistry, Department of Chemistry, Aligarh Muslim University, Aligarh, 202002, India

ARTICLE INFO

Article history:
Received 4 May 2009
Received in revised form 13 July 2009
Accepted 16 July 2009
Available online 19 July 2009

Keywords:
Dinuclear organotin(IV) complexes
^{119}Sn-NMR
^{119}Sn-Mössbauer
Crystal structure
Cytotoxicity

ABSTRACT

Two novel dinuclear organotin(IV) complexes [n-Bu_2Sn(imda)(H_2O)]$_2$·Bipy (**1**) and [n-Bu_2Sn(imda)(H_2O)]$_2$·Phen (**2**) [H_2imda = iminodiacetic acid, Bipy = 2,2′-bipyridine and Phen = 1,10-phenanthroline] were synthesised and characterized employing IR, ^{1}H, ^{13}C, ^{119}Sn NMR, and ^{119}Sn Mössbauer spectroscopic and elemental analyses. Single crystal X-ray crystallography of **1** has confirmed that it is a binuclear Sn(IV) species formed via carboxylate bridges where each metal adopted a seven coordinate distorted pentagonal bipyramidal geometry. The iminodiacetate dianion (imda^{2-}) acts as a potential tridentate [N,O,O] carboxylate bridging ligand. The packing revealed that the additional α-diimine (Bipy or Phen) does not coordinate to metal ion. However, its presence in the crystal lattice as spacer helps for the formation of a supramolecular framework by bringing the two binuclear species close enough through extensive H-bonding. The in vitro cytotoxicity of compounds **1** and **2** indicate better results than cisplatin against three tumor cell lines investigated.

1. Introduction

The importance of metal-based drugs in treatment of various diseases was pioneered from the successful results by cisplatin [1]. Since then a number of other metal complexes have been investigated and organotin complexes received special interest [2]. Polynuclear organotin(IV) complexes [3] were found to give satisfactory results among the various Sn(IV) compounds screened for such investigations. Metal-directed self-assembly of metal organic frameworks (MOFs) or organometallic derivatives having various intriguing topologies have also been extensively studied [4,5]. An important objective in this regard is the synthesis of new highly water soluble polymetallic complexes which may be useful for testing the distinctive biological reactivity patterns. In recent years, diorganotin (IV) carboxylates have attracted the attention because of their biochemical and commercial applications [6]. In general, the biochemical activity of organotin compounds is influenced by the structure of the resulting complex molecules, henceforth, the coordination number around the tin metal [7–9]. This recognition of relations between the structure and the biological properties [10] becomes more pronounced for those organotin(IV) compounds which contain functionalized carboxylate moieties. Crystallographic data have also revealed that such complexes adopt structures which are dependent on both the nature of the alkyl (or aryl) substituents bound to the tin atom and the type of carboxylate derived ligands [11,12]. Moreover, the complexes containing two butyl groups at the tin(IV) center possessed the highest biological activity [3]. The effort to correlate the biological activities of the metal complexes with the coordinating behavior of the ligand moieties specially those containing functionalized dicarboxylate analogous with [N,O,O] biting centers is scarce. Mononuclear as well as dinuclear organotin(IV) derivatives containing pyridine-2,6-dicarboxylate complexes [13–15], some of which exhibit in vitro antitumor activities, are known. However, the polynuclear diorganotin(IV) complexes with hepta coordinated {Sn} metal of an analogous functionalized dicarboxylate moeity such as iminodiacetate dianion (imda^{2-}), have not been tested for biocidal as well as antitumor activities in vitro. Iminodiacetic acid is a potential tridentate [N,O,O] chelating agent [16] forming transition metal complexes whose X-ray crystallographic studies indicate the presence of metal–organic framework through H-bonding and π–π interactions. These complexes exhibit antimicrobial and superoxide dismutase (SOD) activities. This contemplated us to carry out the synthesis of a few diorganotin(IV) complexes incorporating iminodiacetate (imda^{2-}) dianion with a view to investigate if these complexes may be exploited as candidates for antitumor activities. Here-in, we report the complexes [n-Bu_2Sn(imda)(H_2O)]$_2$·Bipy (**1**) and [n-Bu_2Sn(imda)(H_2O)]$_2$·Phen (**2**) characterized by IR, ^{1}H, ^{13}C, ^{119}Sn NMR and ^{119}Sn Mössbauer spectral data. The single crystal X-ray crystallographic data are also presented for the compound (**1**).

* Corresponding author. Tel.: +91 9411803461.
E-mail address: zafarasiddiqi@yahoo.co.in (Z.A. Siddiqi).

0022-328X/$ - see front matter © 2009 Elsevier B.V. All rights reserved.
doi:10.1016/j.jorganchem.2009.07.030

2. Experimental

2.1. Materials and measurements

Iminodiacetic acid (Merck), di-n-butyltin diacetate (Aldrich) and 2,2′-bipyridine or 1,10-phenanthroline (Merck) were used as received. The solvents used in the reactions were of AR grade and dried using standard literature procedures. IR spectra were recorded on a Perkin–Elmer spectrum GX automatic recording spectrophotometer as KBr disc. ^{1}H and ^{13}C NMR spectra of the complexes were recorded on a Brucker DPX-400 spectrometer operating at 400 and 100.6 MHz, respectively, and with TMS as internal reference in $CDCl_3$. ^{119}Sn NMR spectra were collected at a spectrometer frequency of 186.4 MHz on a Varian UNITY 500 with a 10 mm broad band probe. All samples were prepared in $CDCl_3$ solution and chemical shift values were referenced externally with Me_4Sn. Elemental analyses were performed on a PE-2400-II elemental analyzer. The ^{119}Sn Mössbauer spectrum of the complex **1** in the solid state was recorded using a Model MS-900 (Ranger Scientific Co., Burleson, TX) spectrometer in the acceleration mode with moving source geometry. A $Ca^{119}SnO_3$ source was used and the spectrum was measured at 80 K using a liquid-nitrogen cryostat. The velocity was calibrated at ambient temperature using a composition of $BaSnO_3$ and tin foil (splitting 2.52 mm s^{-1}). Tumor inhibiting effect of compounds **1** and **2** was tested in vitro by using the murine leukemia cell line P388 and human leukemia cell line HL-60 with the method of MTT. The human Lung Epithelial Cell line A-549 was tested with the method of SRB.

2.2. Synthesis of the complexes [n-$Bu_2Sn(imda)(H_2O)]_2$·Bipy (**1**) and [n-$Bu_2Sn(imda)(H_2O)]_2$·Phen (**2**)

Di-n-butyltin diacetate (1.75 g, 5 mmol) in 15 ml ethanol was added dropwise to a magnetically stirred aqueous solution (20 ml) of iminodiacetic acid (0.67 g, 5 mmol) in presence of 2,2′-bipyridine (0.3 g, 2.5 mmol) or 1,10-phenanthroline (0.45 g, 2.5 mmol) at room temperature. The stirring was continued overnight and the solution was refluxed for 6 h. On cooling, colorless crystals of **1** and **2** were obtained in solution. However, only the crystals of **1** were single and suitable for X-ray crystallography.

2.2.1. Compound (**1**)

yield 64%, m.p.: 218 °C. Anal. Calc. for $C_{34}H_{54}N_4O_{10}Sn_2$: C, 44.57; H, 5.94; N, 6.12; Sn, 25.91. Found: C, 44.24; H, 5.99; N, 6.11; Sn, 25.86%. IR (KBr, cm^{-1}): υ_{as}(COO), 1668; υ_{s}(COO), 1382; υ(CH_3), 3086, 2928; υ(CH_2), 2958, 2876; υ(C=O), 1772, 1705; υ(Ar), 1616, 1605, 1510, 1460; υ(Sn–O–Sn), 685; υ(Sn–C), 531; υ(Sn–O), 459; υ(Sn–N), 466. ^{1}H NMR ($CDCl_3$, ppm): δ 0.89 (t, CH_3), 1.92 (t, αCH_2), 1.71–1.84 (m, βCH_2), 1.32 (h, γCH_2), 3.91 (s, $-CH_2-CO$), 2.35 (q, –NH–), 7.23–8.48 (m, Ar), 3.42 (s, H_2O). ^{13}C NMR ($CDCl_3$, ppm): δ 26.5 {αCH_2, 962 Hz, $^{1}J(^{119}Sn-^{13}C_{\alpha})$}, 26.3 ($\beta CH_2$), 26.2 ($\gamma CH_2$), 13.3 ($CH_3$), 165 (COO), 56.4 ($-CH_2-NH-$), 125.6–147.1 (m, Ar). ^{119}Sn NMR ($CDCl_3$, ppm): δ −521.

2.2.2. Compound (**2**)

yield 64%, m.p.: 218 °C. Anal. Calc. for $C_{36}H_{54}N_4O_{10}Sn_2$: C, 45.99; H, 5.79; N, 5.96; Sn, 25.25. Found: C, 45.93; H, 5.75; N, 5.91; Sn, 25.21%. IR (KBr, cm^{-1}): υ_{as}(COO), 1662; υ_{s}(COO), 1384; υ(CH_3), 3083, 2926; υ(CH_2), 2953, 2874; υ(C=O), 1773, 1707; υ(Ar), 1613, 1606, 1508, 1463; υ(Sn–O–Sn), 682; υ(Sn–C), 533; υ(Sn–O), 456; υ(Sn–N), 465. ^{1}H NMR ($CDCl_3$, ppm): δ 0.87 (t, CH_3), 1.90 (t, αCH_2), 1.76–1.82 (m, βCH_2), 1.36 (h, γCH_2), 3.93 (s, $-CH_2-CO$), 2.34 (q, –NH–), 7.31–8.43 (m, Ar), 3.40 (s, H_2O). ^{13}C NMR ($CDCl_3$, ppm): δ 26.7 (αCH_2), 26.1 {βCH_2, 44.56 Hz, $^{2}J(^{119}Sn-^{13}C_{\beta})$}; 26.3 {$\gamma CH_2$, 117.53 Hz, $^{3}J(^{119}Sn-^{13}C_{\gamma})$}, 13.5 ($CH_3$), 167 (COO), 56.1 ($-CH_2-NH-$), 125.2–146.8 (m, Ar). ^{119}Sn NMR ($CDCl_3$, ppm): δ −532.

2.2.3. Spectra of free ligands

H_2imda: IR (KBr, cm^{-1}): υ(COOH), 3322; υ(C=O), 1775, 1707; ^{1}H NMR (D_2O, ppm): δ 3.91 (s, $-CH_2-CO$), 2.35 (q, –NH–); ^{13}C NMR (D_2O, ppm): δ 171 (COOH), 57.2 ($-CH_2-NH-$).

Phen/Bipy: IR (KBr, cm^{-1}): υ(Ar), 1628, 1608, 1510, 1464; ^{1}H NMR (CD_3OD, ppm): δ 7.20–8.51 (m, Ar); ^{13}C NMR (CD_3OD, ppm): δ 124–148 (m, Ar).

2.3. Crystal structure determination of (**1**)

A single crystal of the compound **1** was mounted on a glass capillary and data were collected using graphite-monochromated Mo $K\alpha$ radiation (λ = 0.71073 Å) on Bruker SMART APEX CCD diffractometer at 293 K. The data integration and reduction were processed with SAINT [17] software. An empirical absorption correction was applied to the collected reflections with SADABS using XPREP [17]. All the structures were solved by the direct method using SIR-97 [18] and were refined on F^2 by the full-matrix least-squares technique using the SHELXL-97 [18] program package. Crystal parameters and refinement results are presented in Table 1.

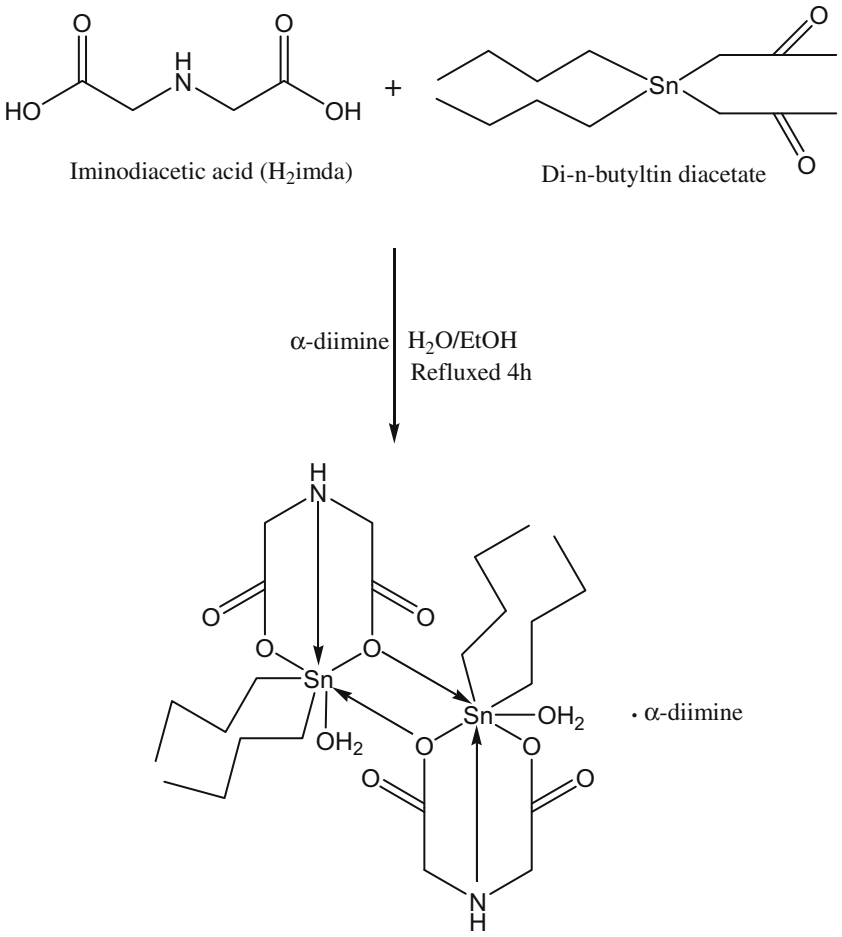
3. Results and discussion

3.1. Synthesis

Iminodiacetic acid (H_2imda) reacts with di-n-butyltin diacetate in presence of an α-diimine viz. 2,2′-bipyridine (Bipy) or 1,10-phenanthroline (Phen), to yield a dinuclear compounds **1** or **2**. The synthetic route for the compounds is shown in Scheme 1. The analytical data are consistent with the stoichiometry [n-$Bu_2Sn(imda)(H_2O)]_2$·Bipy (**1**) or [n-$Bu_2Sn(imda)(H_2O)]_2$·Phen (**2**). The compounds were soluble in water and usual organic solvents. Suitable crystals of the compound **1** were obtained on slow evaporation of the mother liquor. The compounds were characterized

Table 1
Crystal data with refinement parameters for complex (**1**).

Empirical formula	$C_{34}H_{54}N_4O_{10}Sn_2$
Formula weight	918.31
Wavelength (Å)	0.71073
Crystal system	triclinic
Space group	$P\bar{1}$
Unit cell dimension	
a (Å)	7.955 (5)
b (Å)	19.819 (5)
c (Å)	25.413 (5)
α (°)	85.264 (5)
β (°)	89.974 (5)
γ (°)	89.898 (5)
Z	4
Absorption coefficient (mm^{-1})	
Crystal size (mm)	0.24 × 0.22 × 0.18
θ Range for data collection (°)	1.0–28.4
Index ranges	$-10 \leqslant h \leqslant 7$, $-26 \leqslant k \leqslant 26$ $-33 \leqslant l \leqslant 33$
Reflections collected	18 920
Unique reflections (R_{int})	12 349 (0.035)
Refinement method	Full matrix least square on F^2
Data/restrainst/parameters	12 349/0/902
Goodness of fit on F^2	1.118
Final R indices [$I > 2\sigma(I)$]	R_1 = 0.0847, wR_2 = 0.2208
R indices (all data)	R_1 = 0.1314, wR_2 = 0.3158



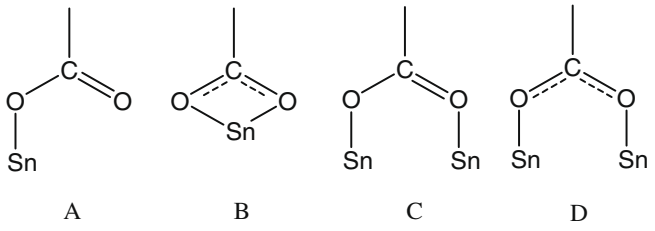
Scheme 1. Synthetic procedure for the complexes **1** and **2**.

by various spectroscopic techniques and single crystal X-ray diffraction of **1**.

3.2. Spectroscopic studies

3.2.1. FT-IR spectra

The coordination sites of the ligands were determined by means of FT-IR spectroscopy. The stretching frequencies of interest are those characteristic of the carboxylic acid function, υ(Sn–C), υ(Sn–O) and υ(Sn–O–Sn) bonds frequencies. The free iminodiacetic acid (H_2imda) shows broad band due to O–H stretching frequencies of COOH group in the 3500–3050 cm^{-1} region which was absent in the spectrum of the complexes, indicating that the ligand binds Sn metal in the anionic ($imda^{2-}$) form. The carboxylate group in $imda^{2-}$ may exhibit a range of different coordination mode as presented in Scheme 2. When the COO^- group coordinates as a monodentate ligand (structure A), the difference between the wavenumbers of the asymmetric and symmetric carboxylate stretching vibration frequencies, $\Delta\nu = (\nu_{as}COO^- - \nu_{sym}COO^-)$, is in the range 250–300 cm^{-1} [19]. For the symmetric bidentate coordination (structure B), $\Delta\nu$ is considerably smaller compared to that of the ionic carboxylate compounds [20]. The magnitude of $\Delta\nu$ for asymmetric bidentate coordination modes as depicted in structures C and D, is also very large but smaller compared to that of the monodentate (structure A) mode of coordination. It is therefore concluded that iminodiacetate anion ($imda^{2-}$) coordinates preferably in a monodentate manner. A medium intensity band near 685 cm^{-1} in the spectra of the complexes **1** and **2** is characteristic of the υ(Sn–O–Sn) bond stretching vibration suggesting formation of an Sn–O–Sn bridged structure for the complexes. The absorption bands characteristic of Sn–C, Sn–O and Sn–N, bonds stretching vibrations were also observed at appropriate positions. The X-ray crystallographic data for the complex **1** have confirmed a carboxylate bridged structure.



Scheme 2. Important coordination modes of $-COO^-$ group.

3.2.2. NMR spectroscopy

The ^{1}H NMR spectrum of the complexes did not show the resonance signal of the O–H proton for the H_2imda expected at 13.12 ppm. However, the spectra contained resonance signals characteristic of $-CH_3$, α-CH_2, β-CH_2 and γ-CH_2 protons of the n-butyl substituents at Sn atom as the multiplets in the appropriate intensity ratio. The multiplet appearing in the range 7.22–8.50 ppm is characteristic of the aromatic protons of Phen/Bipy

moeity. The broad multiplet in the spectra is probably due to iminic proton. The broadening of the signal is characteristic of nuclear quadrupole relaxation effect of nitrogen ($I = 1$) [21]. The additional broad strong singlet at ~3.40 ppm is probably due to the coordinated water in the complex moeity.

The ^{13}C NMR spectra of the compounds contained resonance signals characteristic of the skeletal carbons of the ligand moeity, n-butyl substituents bound to {Sn} atom as well as that of the aromatic carbons of the bipyridine or phenanthroline moeity present in the complexes **1** or **2**. The spectra of the compounds showed a significant downfield shift of carbon resonances, compared with the free ligand. This shift is a consequence of an electron density transfer form ligand to the acceptor. The $^{119}Sn–^{13}C$ resonance couplings were also observed as satellites i.e. $^{1}J(^{119}Sn–^{13}C_{\alpha})$ at 972 Hz for compound **1**; $^{2}J(^{119}Sn–^{13}C_{\beta})$ and $^{3}J(^{119}Sn–^{13}C_{\gamma})$ at 44.56 and 117.53 Hz, respectively for compound **2**. The complementary information for complexes is given by the value of the coupling constants. The Lockhart and Manders equation [22] which correlates the C–Sn–C bond angle with the coupling constant $^{1}J(^{119}Sn–^{13}C_{\alpha})$ is given below

$$\theta = 0.0877^{1}J(^{119}Sn—^{13}C_{\alpha}) + 76.7543$$

The magnitude of θ calculated from this expression (162°) for compound **1** is comparable to that obtained ($\theta = 163.6°$) from the X-ray crystallographic data. This indicates that the two butyl groups are in axial positions (Fig. 1a).

^{119}Sn NMR spectra of the complexes **1** and **2** exhibited sharp resonance signals at −521 and −532 ppm, respectively, consistent with the hepta coordination of {Sn} atom [23].

3.2.3. Mössbauer spectroscopy

While IR spectroscopic data provide ample informations regarding the coordination sites and their probable binding with metals, they give no indication about the molecular structures. This latter question is resolved usually from the X-ray crystallographic data and if possible by recording ^{119}Sn-Mössbauer spectra of the organotin(IV) complex. Complex **1** gave beautiful single crystals suitable for X-ray diffraction study. We have performed ^{119}Sn-Mössbauer spectral investigations for this complex (**1**) in order to compare the probable informations given by these two techniques. The compound **1** showed a doublet with the experimental Mossbauer parameters, $\delta = 1.45$, $|\Delta| = 4.16$ and $\Gamma_1 = 0.87$ mms^{-1} determined by computer evaluation [24]. These values are characteristic for the {Sn} atom of the organotin(IV) moeity within the complex. A successful correlation has been reported between the quadrupole splitting $|\Delta|$ and the structure of differently coordinated Sn(IV), using either a simple point charge model [24] or a more elaborate hybridization treatment [25]. The observed $|\Delta|$ value obtained by means of the pqs concept considering a monodentate coordination mode of the –COO$^-$, indicated that the Sn(IV) could be present in octahedral (O_h) or pentagonal bipyramidal (pbp) environment. Linear oligomerization (as also indicated from the X-ray data) through the monodentate –COO$^-$ groups may result in carboxylate bridges between the two tin centers. The observed $|\Delta|$ value indicate configuration where the n-butyl groups are located invariably in axial position. The hepta coordination to form the most probable pbp geometry is achieved via additional coordination from the iminic nitrogen of the imda^{2-} and H_2O. For Sn(IV) complexes containing a n-Bu_2Sn(IV) moeity, the magnitude of quadrupole splitting $|\Delta|$ is also related with the parameter [R] and angle θ, which is given [24] by

$$|\Delta| = -4[R][1 - (3/4)\sin^2\theta]^{1/2} \quad (1)$$

where [R] denotes the pqs value of substituent (i.e. butyl group), and θ is the C–Sn–C angle. On inserting the value $|\Delta| = 4.16$ mms^{-1} and $\theta = 163.6$ for complex **1** (X-ray data) in Eq. (1), we get [R] = −1.07 mms^{-1}. This value of [R] agrees well within 1% error with that reported i.e. [R] = −1.09 mms^{-1} for heptacoordinated Sn(IV) complexes [26]. The present Mössbauer data are consistent

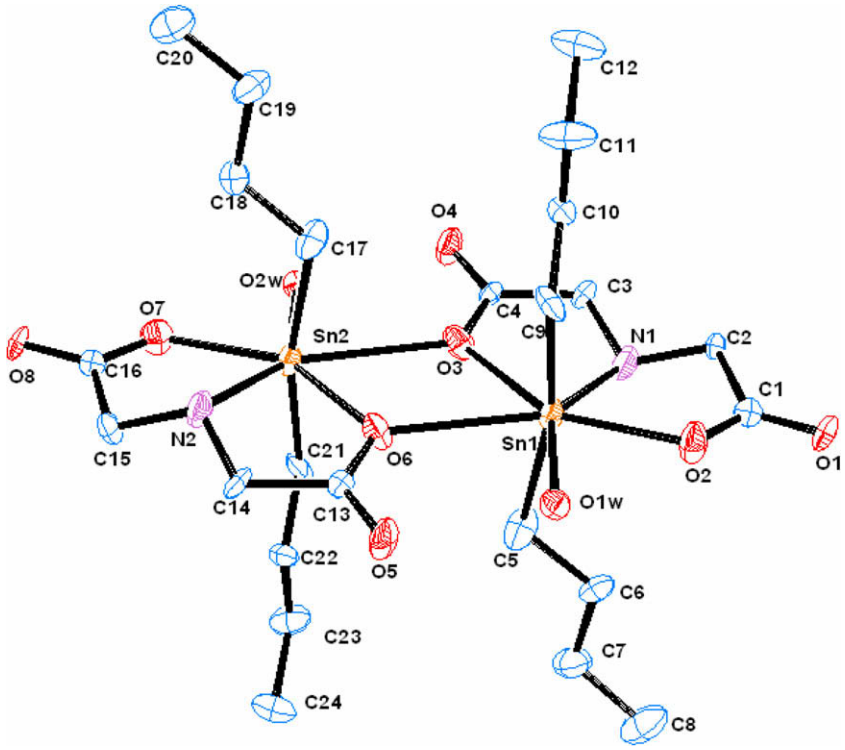


Fig. 1a. ORTEP view of the moeity [n-Bu_2Sn(imda)(H_2O)]$_2$ drawn at 50% probability of the thermal ellipsoids (H-atoms have been omitted for clarity).

Table 2
Selected bond lengths (Å) and angles (°) for [n-$Bu_2Sn(imda)(H_2O)]_2$·Bipy (**1**).

Bond lengths			
Sn1–C5	2.118(11)	Sn2–C17	2.113(11)
Sn1–C9	2.128(10)	Sn2–C21	2.132(10)
Sn1–O2	2.233(7)	Sn2–O7	2.208(8)
Sn1–N1	2.310(9)	Sn2–O2W	2.309(7)
Sn1–O1W	2.324(7)	Sn2–N2	2.321(10)
Sn1–O3	2.330(7)	Sn2–O6	2.338(7)
Sn1–O6	2.767(7)	Sn2–O3	2.752(7)
Bond angles			
C5–Sn1–C9	163.6(4)	C17–Sn2–C21	163.9(4)
C5–Sn1–O2	97.2(4)	C17–Sn2–O7	97.2(4)
C9–Sn1–O2	93.4(4)	C21–Sn2–O7	93.0(3)
C5–Sn1–N1	91.9(4)	C17–Sn2–O2W	84.8(3)
O2–Sn1–N1	103.3(4)	C21–Sn2–O2W	85.8(3)
O2–Sn1–N1	71.8(3)	O7–Sn2–O2W	74.8(3)
C5–Sn1–O1W	85.3(4)	C17–Sn2–N2	91.4(4)
C9–Sn1–O1W	85.4(3)	C21–Sn2–N2	103.6(4)
O2–Sn1–O1W	75.2(3)	O7–Sn2–N2	72.0(3)
N1–Sn1–O1W	146.3(3)	O2W–Sn2–N2	145.8(3)
C5–Sn1–O3	88.6(4)	C17–Sn2–O6	89.7(3)
C9–Sn1–O3	90.5(4)	C21–Sn2–O6	89.9(3)
O2–Sn1–O3	142.5(3)	O7–Sn2–O6	142.4(3)
N1–Sn1–O3	71.0(3)	O2W–Sn2–O6	142.8(2)
O1W–Sn1–O3	142.2(2)	N2–Sn2–O6	70.9(3)

with a seven coordinate distorted pentagonal bipyramidal (pbp) geometry of the complex.

3.3. Single crystal X-ray crystallographic studies

The single crystal X-ray data for the complex **1** have been summarized in Tables 1 and 2. The ORTEP views of the moiety [n-$Bu_2Sn(imda)(H_2O)]_2$ and [n-$Bu_2Sn(imda)(H_2O)]_2$·Bipy are shown in Figs. 1a and b, respectively. The molecular unit is apparently a dimers, held together via two carboxylate bridges with d(Sn–O–Sn) = 5.0935 ± 0.023 Å. Additional coordination from H_2O to the metal atom results in a seven coordinate, distorted pentagonal bipyramidal (pbp) geometry around each tin metal (Fig. 1a). The H_2O oxygen (O1W), $imda^{2-}$ oxygens (O2, O3) along with nitrogen (N1) and the bridging oxygen (O6) form the equatorial plane [Sn–O = 2.324(7), 2.330(7), 2.233(7), 2.767(7) and Sn–N = 2.310(9) Å]. The observed C–Sn–C bond angle [163.6°(4)] indicates that the two butyl groups are attached to each {Sn} atom at the axial positions [Sn–C = 2.118(11) and 2.128(10) Å]. The Sn···Sn distance within the dimeric moiety is 4.242 ± 0.002 Å, which is comparable to that reported for an analogous dimeric complex [Bu_2Sn(pyridine-2,6-dicarboxylate)$(H_2O)]_2$ [27]. The neighboring [n-$Bu_2Sn(imda)(H_2O)]_2$ dimers are further attached to each other by weak H-bonding through Bipy nitrogen atoms as well as the intermolecular H-bonding (Fig. 1b). It appears from the packing diagram (Fig. 2) that the 2,2′-bipyridine is present in the crystal lattice and acts as a spacer in the formation of supramolecular framework to stabilize the crystal lattice (Table 3).

3.4. In vitro antitumor activity

In order to compare the cytotoxicity of the compounds presented in this paper, the preliminary in vitro cell tests were performed on tumor cells whose detailed experimental procedures are available in the literature [28]. The growth inhibitory effects on the murine leukemia cell line (P388) and human leukemia cell line (HL-60) were measured by the microculture tetrazolium [3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide, MTT] assay [29]. The growth inhibition for the human non-small-cell lung cancer cell line (A-549) was analyzed employing the sulforhodamine B (SRB) assay [30]. The results of the in vitro cytotoxic effects of the compounds **1** and **2** (Table 4) against the three tumor cell lines (P388, HL-60 and A-549) were compared using cisplatin as a reference (control). The inhibitory effect of the compounds **1** and **2** was relatively higher than that exhibited by cisplatin against the three tumor cell lines for the experimental concentration range (10^{-4}–10^{-7} M) suggesting that the present compounds can be used as potent antitumor agents. The observed higher activities of the test compounds in reference to that of the cisplatin can reasonably be correlated [31] in terms of a structural effect i.e. a long chain of the dinuclear (Sn–Sn) units stabilized or controlled via an

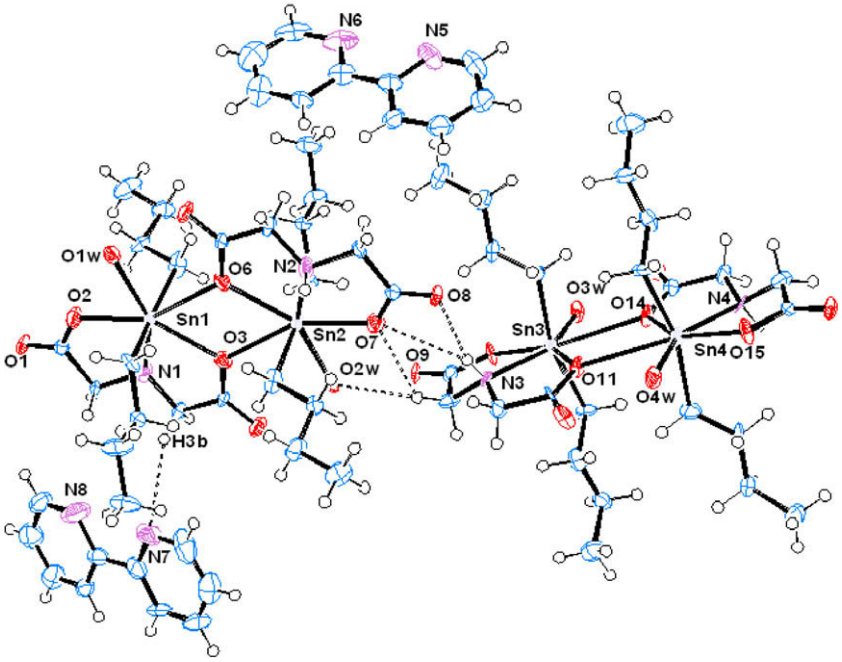


Fig. 1b. ORTEP view of [n-$Bu_2Sn(imda)(H_2O)]_2$·Bipy (**1**) showing H-bonding interactions between adjacent units.

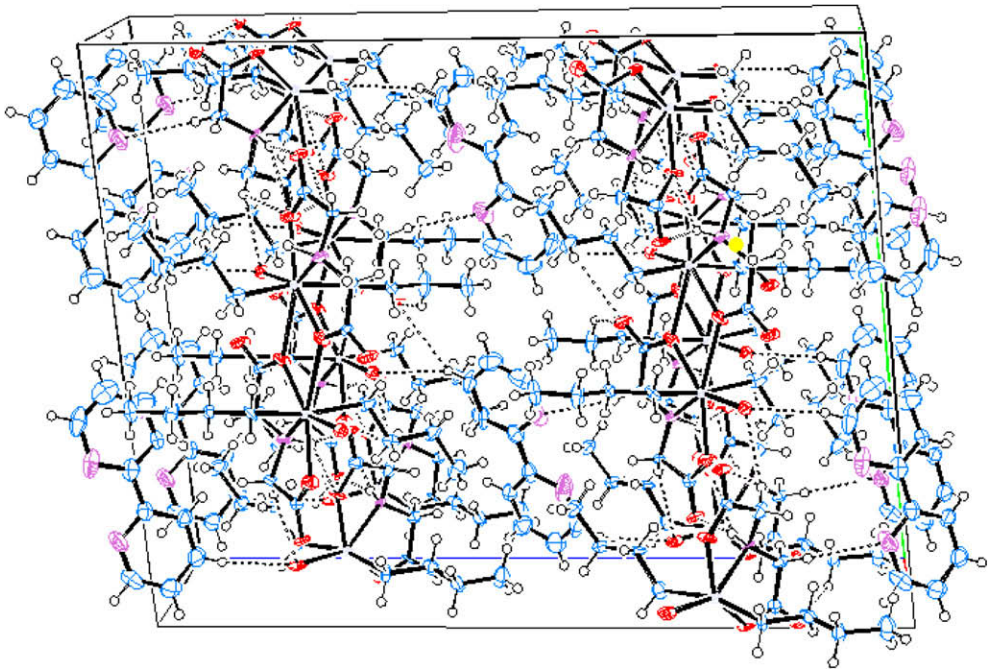


Fig. 2. Packing diagram of the complex **1**.

Table 3
Hydrogen-bond geometry (Å, °).

D–H···*A*	*D*–H	H···*A*	*D*···*A*	*D*–H···*A*
N4–H01···O1^{i}	0.80(9)	2.22(9)	2.973(10)	157(9)
N4–H01···O2^{i}	0.80(9)	2.61(10)	3.308(10)	146(8)
N3–H02···O8	0.78(9)	2.23(9)	2.972(10)	159(9)
N3–H02···O7	0.78(9)	2.66(10)	3.343(11)	149(8)
N2–H03···O9^{ii}	1.08(9)	1.91(9)	2.922(11)	155(7)
N2–H03···O10^{ii}	1.08(9)	2.43(9)	3.307(11)	138(6)
N1–H04···O16^{iii}	1.21(9)	1.90(8)	2.935(11)	140(6)
N1–H04···O15^{iii}	1.21(9)	2.28(9)	3.297(11)	139(6)

Symmetry codes: (i) $x+1, y-1, z$; (ii) $x-1, y, z$; (iii) $x, y+1, z$.

Table 4
Inhibitory effect of the compounds on tumor cells of P388 (MTT), HL-60 (MTT) and A-549 (SRB).

Cell line	Concentration	Inhibitory rate (%)		
	(mol/l)	Compound **1**	Compound **2**	Cisplatin
P388	10^{-4}	100	100	84
	10^{-5}	100	100	48.4
	10^{-6}	100	100	23
	10^{-7}	19.5	62.6	18.5
HL-60	10^{-4}	100	100	100
	10^{-5}	98.9	98.6	100
	10^{-6}	97.1	92.8	48.9
	10^{-7}	90.3	29.1	19.2
A-549	10^{-4}	100	100	36.8
	10^{-5}	72.0	74.7	15.1
	10^{-6}	61.7	40.2	12.5
	10^{-7}	34.9	23.8	17.4

extensive H-bonding and the presence of additional spacers like Bipy or Phen in the molecular unit (Fig. 1b). A few organotin derivatives specially those containing a long chain alkyl substituent on {Sn} atom preferably n-butyl group are reported [32] to exhibit remarkable cytotoxic effects. The additional contribution from n-butyl group bonded to {Sn} atom in the present compounds towards the cytotoxic effects may not be ruled out.

The data in Table 4 indicate that compounds **1** and **2** at 10^{-4} M concentration are highly effective against all the cell lines examined. They retained high inhibition rates of 100% against P388 tumor cell line even for the concentration range 10^{-5}–10^{-6} M but were relatively less active towards HL-60 and A-549. However, they were observed not much effective against all the three tumor cell lines at 10^{-7} M concentration.

4. Conclusion

Iminodiacetic acid reacts with di-n-butyltin diacetate in presence of an α-diimine viz. 2,2′-bipyridine or 1,10-phenanthroline taken in 2:2:1 mole ratio in aqueous ethanol resulting in complexes with stoichiomoetries [n-Bu_2Sn(imda)(H_2O)]$_2$·Bipy and [n-Bu_2Sn(imda)(H_2O)]$_2$·Phen. The FT-IR, ^{1}H, ^{13}C and ^{119}Sn NMR as well as ^{119}Sn Mössbauer spectroscopic data on the complexes revealed that the ligand imda^{2-} binds the metal as dianionic ligand behaving as tridentate [N,O,O] chelating agent such that the metal adopts a hepta coordinate distorted pentagonal bipyramidal (pbp) geometry. The presence of carboxylate bridging from imda^{2-} produced a dinuclear structure of the complex as confirmed from the single crystal X-ray diffraction data. The α-diimine chelator, which does not directly bind the {Sn} atom is rather present in the crystal lattice acting as a spacer between the adjacent dinuclear units involving weak H-bonding interactions to form a supramolecular framework. Apart from this special structural feature, the present compounds deserve attention as they are rare examples of hepta coordinated organotin derivatives. The cytotoxicity tests of the compounds show that these compounds can be used as potent antitumor drugs.

Acknowledgements

The authors are thankful to the Chairman, Department of Chemistry, AMU, Aligarh, India for providing necessary research facilities and UGC, New Delhi for the financial assistance. We gratefully acknowledge Dr. D. Das, UGC-DAE Consortium for Scientific Research, Kolkata for ^{119}Sn Mössbauer spectral studies.

Appendix A. Supplementary material

CCDC 728949 contains the supplementary crystallographic data for compound **1**. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.jorganchem.2009.07.030.

References

[1] (a) G. Ciarimboli, T. Ludwig, D. Lang, H. Pavenstadt, H. Koepsell, H.-J. Piechota, J. Haier, U. Jaehde, J. Zisowsky, E. Schlatter, Am. J. Pathol. 167 (2005) 1477–1484;
(b) S. Terstriep, A. Grothey, Expert Rev. Anticancer Ther. 6 (2006) 921–930;
(c) A. Gelasco, S.J. Lippard, Top. Biol. Inorg. Chem. 1 (1999) 1–43;
(d) E.R. Jamieson, S.J. Lippard, Chem. Rev. 99 (1999) 2467–2498.

[2] V. Narayanan, M. Nasr, K.D. Paull, in: M. Gielen (Ed.), Tin-based Antitumour Drugs, vol. 1, Springer, Berlin, 1990, pp. 201–216.

[3] (a) F. Caruso, M. Giomini, A.M. Giuliani, E. Rivarola, J. Organomet. Chem. 466 (1994) 69–75;
(b) M. Gielen, Appl. Organomet. Chem. 16 (2002) 481–494;
(c) M. Gielen, H. Dalil, L. Ghys, B. Boduszek, E.R.T. Tiekink, J.C. Martins, M. Biesemans, R. Willem, Organometallics 17 (1998) 4259–4262.

[4] (a) D.L. Caulder, K.N. Raymond, Acc. Chem. Res. 32 (1999) 975–982;
(b) P.J. Langley, J. Hulliger, Chem. Soc. Rev. 28 (1999) 279–291;
(c) M. Fujita, Struct. Bond. 96 (2000) 177–201;
(d) R.W. Saalfrank, E. Uller, B. Demleitner, I. Bernt, Struct. Bond. 96 (2000) 149–175;
(e) G.F. Swiegers, T.J. Malefetse, Chem. Rev. 100 (2000) 3483–3538;
(f) B.J. Holliday, C.A. Mirkin, Angew. Chem., Int. Ed. 40 (2001) 2022–2043.

[5] (a) O.M. Yaghi, H. Li, C. Davis, D. Richardson, T.L. Groy, Acc. Chem. Res. 31 (1998) 474–484;
(b) G. Ferey, Chem. Mater. 13 (2001) 3084–3098;
(c) R. García-Zarracino, J. Ramos-Quiñoes, H. Höpfl, Inorg. Chem. 42 (2003) 3835–3845.

[6] (a) C.J. Evans, S. Karpel, J. Organomet. Chem. 16 (1985);
(b) S.P. Narula, S.K. Bhardwaj, H.K. Sharma, G. Mairesse, P. Barbier, G. Nowogrocki, J. Chem. Soc., Dalton Trans. (1988) 1719–1723;
(c) I. Haiduc, C. Silvetru, Coord. Chem. Rev. 99 (1990) 253–296.

[7] K.C. Molloy, T.G. Purcell, E. Hahn, H. Schumann, J.J. Zuckerman, Organometallics 5 (1986) 85–89.

[8] (a) R.R. Holmes, Acc. Chem. Res. 22 (1989) 190–197;
(b) J. Otera, T. Yano, R. Owawara, Organometallics 5 (1986) 1167–1170.

[9] S.R. Collinson, D.E. Fenton, Coord. Chem. Rev. 148 (1996) 19–40.

[10] (a) T.P. Lockhart, J.C. Calabrese, F. Davidson, Organometallics 6 (1987) 2479–2483;
(b) Y. Maeda, R. Okawara, J. Organomet. Chem. 10 (1967) 247–256;
(c) T.N. Mitchell, J. Organomet. Chem. 59 (1973) 189–197;
(d) S.G. Teoh, S.H. Ang, E.S. Looi, C.A. Keok, S.B. Teo, J.P. Declercq, J. Organomet. Chem. 523 (1996) 75–78.

[11] (a) E.R.T. Tiekink, Appl. Organomet. Chem. 5 (1991) 1–23;
(b) E.R.T. Tiekink, Trends in Organometallic Chemistry, vol. 1, Council of Scientific Research Integration, Trivandrum, India, 1994. p. 71.

[12] C.S. Parulekar, V.K. Jain, T.K. Das, A.R. Gupta, B.F. Hoskins, E.R.T. Tiekink, J. Organomet. Chem. 372 (1989) 193–199.

[13] S.W. Ng, V.G. Kumar Das, J. Holecek, A. Lycka, M. Gielen, M.G.B. Drew, Appl. Organomet. Chem. 11 (1997) 39–45.

[14] M. Gielen, T. Joosen, T. Mancilla, K. Jurkschat, R. Willem, C. Roobol, J. Bernheim, G. Atassi, F. Huber, E. Hoffman, H. Preut, B. Mahieu, Main Group Met. Chem. 10 (1987) 147–167.

[15] R. Willem, M. Biesemans, M. Boûalam, A. Delmotte, A. El Khloufi, M. Gielen, Appl. Organomet. Chem. 7 (1993) 311–317.

[16] Z.A. Siddiqi, M. Shahid, M. Khalid, S. Kumar, Eur. J. Med. Chem. 44 (2009) 2517–2522.

[17] (a) SAINT+, 6.02 ed., Bruker AXS, Madison, WI, 1999.;
(b) G.M. Sheldrick, SADABS, Empirical Absorption Correction Program; University of Göttingen, Göttingen, Germany, 1997.;
(c) XPREP, 5.1 ed., Siemens Industrial Automation Inc., Madison, WI, 1995.

[18] (a) A. Altomare, M.C. Burla, M. Camalli, G.L. Cascarano, C. Giacovazzo, A. Guagliardi, A.G.G. Moliterni, G. Polidori, R.J. Spagna, Appl. Crystallogr. 32 (1999) 115–119;
(b) G.M. Sheldrick, SHELXL-97, Program for Crystal Structure Refinement, University of Göttingen, Göttingen, Germany, 1997.

[19] G.B. Deacon, R.J. Philips, Coord. Chem. Rev. 33 (1980) 227–250.

[20] K. Nakamoto, Infrared and Raman Spectra of Inorganic and Coordination Compounds, Wiley-Interscience, New York, 1986.

[21] R.S. Drago, Physical Methods for Chemists, Saunders College Publishing, New York, 1992.

[22] T.P. Lockhart, W.F. Manders, Inorg. Chem. 25 (1986) 892–895.

[23] J. Otere, A. Kusaba, T. Hinoishi, Y. Kawasaki, J. Organomet. Chem. 228 (1982) 223–228.

[24] R.V. Parish, Structure and bonding in tin compounds, in: G.J. Long (Ed.), Mössbauer Spectroscopy Applied to Inorganic Chemistry, Plenum Press, New York and London, 1984.

[25] M.G. Clark, A.G. Maddock, R.H. Platt, J. Chem. Soc., Dalton Trans. (1972) 281–290.

[26] C. Pelizzi, G. Pelizzi, P. Tarasconi, Polyhedron 2 (1983) 145–147.

[27] A. Szorcsik, L. Nagy, J. Sletten, G. Szalontai, E. Kamu, T. Fiore, L. Pellerito, E. Kálmán, J. Organomet. Chem. 689 (2004) 1145–1154.

[28] J.Y. Zhang, X.Y. Wang, C. Tu, J. Lin, J. Ding, L.P. Lin, Z.M. Wang, C. He, C.H. Yan, X.Z. You, Z.J. Guo, J. Med. Chem. 46 (2003) 3502–3507.

[29] (a) M.C. Alley, D.A. Scudiero, A. Monks, M.L. Hursay, M.J. Czerwinski, D. Fine, B.J. Abbott, J.G. Mayo, R.H. Shoemaker, M.R. Boyd, Cancer Res. 48 (1988) 589–601;
(b) J.J. Bonire, S.P. Fricker, J. Inorg. Biochem. 83 (2001) 217–221.

[30] (a) P. Skehan, R. Storeng, D. Scudiero, A. Monks, J. McMahon, D. Vistica, J.T. Warren, H. Bokesch, S. Kenney, M.R. Boyd, J. Natl. Cancer Inst. 82 (1990) 1107–1112;
(b) A. Opolski, J. Kuduk-Jaworska, J. Wietrzyk, E. Wojdat, K. Waszkiewicz, A. Romaniewska, C. Radzikowski, Anti-Cancer Drugs 11 (2000) 363–368.

[31] X. Shang, J. Cui, J. Wu, A.J.L. Pombeiro, Q. Li, J. Inorg. Biochem. 102 (2008) 901–909.

[32] M. Gielen, M. Biesemans, R. Willem, Appl. Organomet. Chem. 19 (2005) 440–450.