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配合物二乙基锡 *N*-[(2-氧苯基)亚甲基]甘氨酸酯的合成、结构表征和生物活性

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摘要: 合成了 5 个新的二乙基锡 *N*-[(2-氧苯基)亚甲基]甘氨酸酯$(CH_3CH_2)_2Sn$(2-O-3-X-5-$YC_6H_2CH=NCH_2COO$)(X,Y=H,H,**1**;H,Cl,**2**;H,Br,**3**;Cl,Cl,**4**;Br,Br,**5**),利用元素分析、IR、^1H 和 ^{119}Sn NMR 表征了其结构。通过 X-射线单晶衍射测定了 **1** 和 **4** 的晶体结构。化合物 **1** 的晶体属单斜晶系,$P2_1$ 空间群; 化合物 **4** 的晶体属三斜晶系,$P\bar{1}$ 空间群。2 个化合物均为由羧基桥联形成的$[Sn_3O_6C_3]$十二元大环三聚体结构,锡原子的配位构型为六配位$[SnC_2NO_3]$畸变八面体。生物活性测试结果表明,化合物 **5** 对 3 种人癌细胞 HeLa、CoLo205 和 MCF-7 及大肠杆菌均有抑制活性。

关键词: 有机锡羧酸酯; 甘氨酸; 体外抗癌活性; 晶体结构
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Synthesis, Structural Characterization and Biological Activity of the Complex Diethyltin *N*-[(2-oxyphenyl)methylene]glycinates

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Abstract: Five new diethyltin *N*-[(2-oxyphenyl)methylene]glycinates, $(CH_3CH_2)_2Sn$(2-O-3-X-5-$YC_6H_2CH=NCH_2COO$) (X, Y=H, H, **1**; H, Cl, **2**; H, Br, **3**; Cl, Cl, **4**; Br, Br, **5**), have been prepared and characterized by elemental analysis, IR, ^1H and ^{119}Sn NMR spectra. The crystal structures of **1** and **4** have been determined. The crystal for **1** belongs to monoclinic space group $P2_1$, and the crystal for **4** belongs to triclinic space group $P\bar{1}$. The two compounds have a 12-membered macrocyclic structure with a trimeric $[Sn_3O_6C_3]$ core. Each tin atom is six-coordinated in distorted $[SnC_2NO_3]$ octahedron geometry. Bioassay results show that the compound **5** has *in vitro* anti-tumor activity against three human tumour cell lines, HeLa, CoLo205 and MCF-7 and anti-bacterial activity against *E. coli*. CCDC: 729956, **1**; 729957, **4**.

Key words: organotin carboxylate; glycine; *in vitro* antitumor activity; crystal structure

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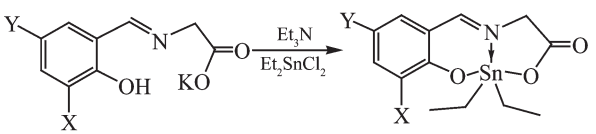
0 Introduction

In recent years, organotin carboxylates have received considerable attention due to their structural diversity[1~3] and biological properties, particularly anti-tumour activities[4~7]. In general, the organotin moiety, the ligand (carboxylic acid) and the number of tin atom appear to play an important role in anti-tumor activity[4,6]. To design and synthesize new organotin carboxylates by changing ligands and organotin substrates has been encouraged. The *N*-salicylidene-amino acid are very versatile ligands creating the possibility of a variety of coordination modes because of the type and position of the donor atoms that allow tin atoms to be linked together. Some diorganotin complexes of *N*-salicylidene-amino acid have been reported by several groups[8~11]. The structural studies have shown that these diorganotin complexes generally have the isolated monomeric structures with the tin atom in a distorted trigonal bipyramid and the carboxylate moiety in unidentate mode[8~11]. In order to continue to expand the chemistry and therapeutic potential of the diorganotin complexes of the ligands and develop a correlation between structure and cytotoxic activity, more recently, we have reported the synthesis and *in vitro* antitumor activity of some diorganotin complexes with *N*-salicylidene-α-amino acid[12~14]. As a continuation of our work, here we selected *N*-salicylideneglycine as a ligand and diethyltin chloride as a substrate, synthesized five new diethyltin complexes, $(CH_3CH_2)_2Sn$(2-O-3-X-5-$YC_6H_2CH{=}NCH_2COO$) (X, Y=H, H, **1**; H, Cl, **2**; H, Br, **3**; Cl, Cl, **4**; Br, Br, **5**) (Scheme 1), and determined the *in vitro* anti-tumor and anti-bacterial activities of **5**.



X, Y=H, H, **1**; H, Cl, **2**; H, Br, **3**; Cl, Cl, **4**; Br, Br, **5**

Scheme 1

1 Experimental

1.1 Materials and physical measurements

All chemicals were of reagent grade and used as received. Elemental analyses were determined using a Perkin Elmer 2400 Series II elemental analyzer. The melting points were measured on a WRS-1A digital melting point apparatus. IR spectra were recorded on a Nicolet 470 FTIR spectrophotometer using KBr discs in the range 4 000~400 cm^{-1}. NMR spectral data were collected using a Bruker Avance DPX300 NMR spectrometer with $CDCl_3$ as solvent and TMS as internal standard for ^1H NMR and using $SnMe_4$ as external reference for ^{119}Sn NMR. A2277 Thermal Activity Monitor was used to determine the power-time curves of bacterial growth at 310 K.

1.2 Synthesis of the title complexes 1~5

Potassium hydroxide (0.112 g, 2 mmol) and glycine (0.151 g, 2 mmol) were added in 60 mL 95% ethanol. The mixed solution was stirred untill the solid disappeared, and then an ethanol solution (20 mL) of salicylaldehyde or substituted salicylaldehyde (2 mmol) was added dropwise. The yellow color solution formed was continued to stir for 30 min. at room temperature. An ethanol solution (20 mL) of diethyltin dichloride (0.496 g, 2 mmol) and Et_3N (0.202 g, 2 mmol) was added to the yellow mixture. The reaction mixture was refluxed for 2 h. After removal of the solvent, the residues were dissolved using 15 mL dichloromethane and filtered. A yellow crystal was obtained by addition of light petroleum ether (15 mL) into the filtrate and slow evaporation at room temperature.

Diethyltin *N*-[(2-oxyphenyl)methylene]glycinate (**1**): Yield 74%, m.p. 192.8~193.4℃. Anal. calcd for $C_{13}H_{17}NO_3Sn$(%): C 44.11, H 4.84, N 3.96; found(%): C 44.00, H 4.61, N 3.92. IR (KBr) ν: 1 621 (C=N), 1 580 [$(COO)_{as}$], 1 399 [$(COO)_s$], 1 300 (Ph-O), 535 (Sn-O) cm^{-1}. ^1H NMR δ: 1.28 (t, J=7.8 Hz, J_{Sn-H}=130.4 Hz, 6H, $2CH_3$), 1.53 (q, J=7.8 Hz, J_{Sn-H}=62.2 Hz, 4H, $2CH_2$), 4.30 (s, J_{Sn-H}=18.2 Hz, 2H, CH_2N), 6.74 (t, J=8.0 Hz, 1H), 6.81 (d, J=8.0 Hz, 1H), 7.15 (d, J=8.0 Hz, 1H), 7.44 (t, J=8.0 Hz, 1H) (Ar-H), 8.40 (s, J_{Sn-H}=45.0 Hz, 1H, N=CH). ^{119}Sn NMR δ: −189.2

Diethyltin *N*-[(3-chloro-2-oxyphenyl)methylene] glycinate (**2**): Yield 72%, m.p. 218.2~219.3 ℃. Anal. calcd for $C_{13}H_{16}ClNO_3Sn$ (%): C 40.20, H 4.15, N 3.61; found(%): C 44.23, H 4.01, N 3.60%. IR (KBr) ν: 1 630

(C=N), 1 586 [$(COO)_{as}$], 1 396 [$(COO)_s$], 1 302 (Ph-O), 548 (Sn-O) cm^{-1}. ^1H NMR δ: 1.28 (t, J=8.0 Hz, J_{Sn-H}=129.8 Hz, 6H, $2CH_3$), 1.54 (q, J=8.0 Hz, J_{Sn-H}=68.4 Hz, 4H, $2CH_2$), 4.35 (s, J_{Sn-H}=17.5 Hz, 2H, CH_2N), 6.77 (d, J=9.2 Hz, 1H), 7.13 (d, J=2.4 Hz, 1H), 7.36 (dd, J=9.2, 2.4 Hz, 1H) (Ar-H), 8.34 (s, J_{Sn-H}=41.0 Hz, 1H, N=CH). ^{119}Sn NMR δ: −191.4

Diethyltin *N*-[(3-bromo-2-oxyphenyl)methylene]glycinate (**3**): Yield 72%, m.p. 226.0~227.0 ℃. Anal. calcd for $C_{13}H_{16}BrNO_3Sn$ (%): C 36.07, H 3.73, N 3.24; found (%): C 35.98, H 3.69, N 3.20. IR (KBr) ν: 1 629 (C=N), 1 588 [$(COO)_{as}$], 1 394 [$(COO)_s$], 1 301 (Ph-O), 550 (Sn-O) cm^{-1}. ^1H NMR δ: 1.21 (t, J=8.0 Hz, J_{Sn-H}=132.8 Hz, 6H, $2CH_3$), 1.49 (q, J=8.0 Hz, 4H, $2CH_2$), 4.27 (s, J_{Sn-H}=16.4 Hz, 2H, CH_2N)), 6.64 (d, J=9.2 Hz, 1H), 7.20 (s, 1H), 7.39 (d, J=9.2 Hz, 1H) (Ar-H), 8.23 (s, J_{Sn-H}=44.8 Hz, 1H, N=CH). ^{119}Sn NMR δ: −192.1.

Diethyltin *N*-[(3,5-dichloro-2-oxyphenyl)methylene]glycinate (**4**): Yield 59%, m.p. 191.9~192.5 ℃. Anal. calcd for $C_{13}H_{15}Cl_2NO_3Sn$ (%): C 36.92, H 3.58, N 3.31; found (%): C 37.00, H 3.49, N 3.29. IR (KBr) ν: 1 626 (C=N), 1 586 [$(COO)_{as}$], 1 404 [$(COO)_s$], 1 298 (Ph-O), 547 (Sn-O) cm^{-1}. ^1H NMR δ: 1.28 (t, J=8.0 Hz, J_{Sn-H}=128.6 Hz, 6H, $2CH_3$), 1.54 (q, J=8.0 Hz, 4H, $2CH_2$), 4.37 (s, J_{Sn-H}=17.7 Hz, 2H, CH_2N)), 7.05 (d, J=2.4 Hz, 1H), 7.67 (d, J=2.4 Hz, 1H) (Ar-H), 8.30 (s, J_{Sn-H}=40.2 Hz, 1H, N=CH). ^{119}Sn NMR δ: −192.8

Diethyltin *N*-[(3,5-dibromo-2-oxyphenyl)methylene]glycinate (**5**): Yield 57%, m.p. 119.9~121.0 ℃. Anal. calcd for $C_{13}H_{15}Br_2NO_3Sn$(%): C 30.51, H 2.95, N 2.74; found (%): C 30.65, H 2.69, N 2.82. IR (KBr) ν: 1 620 (C=N), 1 583 [$(COO)_{as}$], 1 398 [$(COO)_s$], 1 294 (ph-O), 543 (Sn-O) cm^{-1}. ^1H NMR δ: 1.25 (t, J=7.8 Hz, J_{Sn-H}=132.0 Hz, 6H, $2CH_3$), 1.51 (q, J=7.8 Hz, 4H, $2CH_2$), 4.43 (s, J_{Sn-H}=16.8 Hz, 2H, CH_2N), 7.37 (d, J=2.7 Hz, 1H), 7.96 (d, J=2.7 Hz, 1H) (Ar-H), 8.36 (s, J_{Sn-H}=44.2 Hz, 1H, N=CH). ^{119}Sn NMR δ: −194.0.

1.3 X-ray crystal structure determination

Intensity data for compounds **1** and **4** were measured at 295(2) K on a Bruker Smart Apex CCD diffractometer with graphite monochromatized Mo $K\alpha$ radiation (0.071 073 nm) using the φ and ω scan technique. Empirical corrections for absorption effects were made using the SADABS program. The structures were solved by direct-methods and refined by a full-matrix least squares procedure based on F^2 using SHELX-97. The non-hydrogen atoms were refined anisotropically and hydrogen atoms were placed at calculated positions and refined in the riding model approximation. Crystallographic parameters and refinements are listed in Table 1.

CCDC: 729956, **1**; 729957, **4**.

Table 1　Crystallographic data and structure refinement parameters for 1 and 4

Compound	**1**	**4**
Empirical formula	$C_{39}H_{51}N_3O_9Sn_3$	$C_{39}H_{45}Cl_6N_3O_9Sn_3$
Formula weight	1 061.90	1 268.55
Crystal system	Monoclinic	Triclinic
Space group	$P2_1$	$P\bar{1}$
a / nm	1.744 0(2)	1.419 7(7)
b / nm	1.424 59(19)	1.673 6(9)
c / nm	1.7497(2)	2.2814(12)
α / (°)		98.830(8)
β / (°)	95.179(2)	92.978(8)
γ / (°)		114.244(7)
Volume / nm^3	4.329 4(9)	4.844(4)
Z	4	4
D_c / ($g\cdot cm^{-3}$)	1.629	1.74
μ / mm^{-1}	1.77	1.918
F(000)	2 112	2 496
Crystal size / mm	0.20×0.10×0.10	0.25×0.09×0.03

Continued Table 1

Reflections collected / unique (R_{int})	34 201/17 007 (0.024 8)	38 010/18 800 (0.046 2)
Reflections with $I>2\sigma(I)$	15 502	12 459
Flack parameter	−0.005(14)	
GOF on F^2	1	0.995
R, wR [$I>2\sigma(I)$]	0.037, 0.075	0.050, 0.089
R, wR (all data)	0.041, 0.077	0.084, 0.101
$\Delta\rho_{min}$, $\Delta\rho_{max}$ / (e·nm^{-3})	−309, 793	−1 053, 755

1.4 Determination of biological activity

The *in vitro* anti-bacterial and anti-tumor activities of **5** were determined by microcalorimetric method [15] and the MTT assay according to the literature[12]. The dose causing 50% inhibition of cell growth (IC_{50}) was calculated by NDST software as previously described[16].

2 Results and discussion

Diethyltin dichlo ride reacted with potassium *N*-(salicylidene)glycinate *in situ* formed by condensation of salicylaldehyde and glycine in the presence of KOH, to afford compounds **1**~**5**, respectively (Scheme 1). The complexes are yellow crystalline solids that are soluble in common organic solvents such as benzene, chloroform, methanol, ethanol and acetone, but insoluble in water and in saturated aliphatic hydrocarbons.

2.1 Crystal structures of compounds 1 and 4

The molecular structures of **1** and **4** are shown in Figs.1 and 2, respectively. The compounds **1** and **4** both crystallize with two independent molecules (molecule A and molecule B) in the crystallographic asymmetric unit that do not differ from each other significantly. The structures of **1** and **4** were described by the molecule A. The selected bond lengths and angels of **1** (molecule A) and **4** (molecule A) are given in Tables 2 and 3.

The compound **1** crystallizes in monoclinic space group $P2_1$. Three carbons (C2, C4 and C17) in ethyl groups are disordered over two positions with site occupancy factors of 0.839(13) and 0.161(13), 0.833(15) and 0.167(15), and 0.583(11) and 0.417(11), respectively. Three monomers of **1** self-assemble through the bidenate bridging coordination of carboxylate group to tin atoms to form a 12-membered macrocyclic structure with a trimeric [$Sn_3O_6C_3$] core (Fig.1). The carboxylate bridges two Sn atoms in a highly symmetric fashion (the

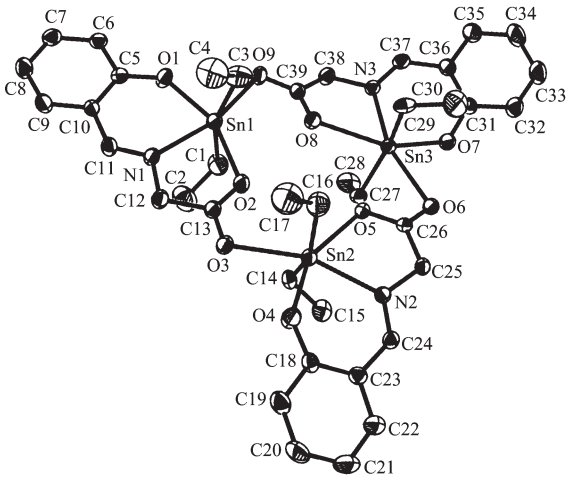


Fig.1 Molecular structure of complex **1**

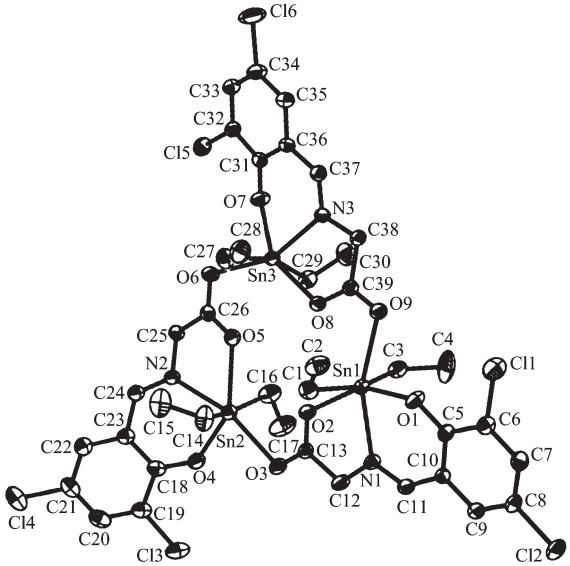


Fig.2 Molecular structure of complex **4**

average difference between two Sn-O bonds is 0.003 2 nm.) and the C-O distances within each carboxylate moiety do not differ significantly (the average difference between two C-O bonds is 0.001 5 nm.), indicating substantial delocalization of the CO_2 π-electron density. The Sn-O bonds in the 12-membered macrocycle range

Table 2　Selected bond lengths (nm) and angles (°) for 1

Sn(1)-O(1)	0.209 3(4)	Sn(2)-O(4)	0.207 1(4)	Sn(3)-O(7)	0.209 5(4)
Sn(1)-C(1)	0.210 7(7)	Sn(2)-C(16)	0.209 9(7)	Sn(3)-C(29)	0.210 8(5)
Sn(1)-C(3)	0.210 0(8)	Sn(2)-C(14)	0.212 6(5)	Sn(3)-C(27)	0.212 7(5)
Sn(1)-N(1)	0.227 4(4)	Sn(2)-N(2)	0.227 6(4)	Sn(3)-N(3)	0.230 5(4)
Sn(1)-O(2)	0.231 6(4)	Sn(2)-O(3)	0.236 6(4)	Sn(3)-O(6)	0.236 4(4)
Sn(1)-O(9)	0.237 7(4)	Sn(2)-O(5)	0.238 6(3)	Sn(3)-O(8)	0.240 0(3)
O(2)-C(13)	0.125 5(6)	O(5)-C(26)	0.126 6(6)	O(8)-C(39)	0.126 2(6)
O(3)-C(13)	0.124 2(6)	O(6)-C(26)	0.124 7(6)	O(9)-C(39)	0.123 8(6)
O(1)-Sn(1)-C(3)	96.8(3)	O(4)-Sn(2)-C(16)	98.1(3)	O(7)-Sn(3)-C(29)	101.3(2)
O(1)-Sn(1)-C(1)	98.2(3)	O(4)-Sn(2)-C(14)	102.8(2)	O(7)-Sn(3)-C(27)	96.9(2)
C(3)-Sn(1)-C(1)	158.2(3)	C(16)-Sn(2)-C(14)	154.5(3)	C(29)-Sn(3)-C(27)	159.2(2)
O(1)-Sn(1)-N(1)	82.19(15)	O(4)-Sn(2)-N(2)	81.77(15)	O(7)-Sn(3)-N(3)	79.53(15)
C(3)-Sn(1)-N(1)	101.8(3)	C(16)-Sn(2)-N(2)	102.0(2)	C(29)-Sn(3)-N(3)	95.0(2)
C(1)-Sn(1)-N(1)	95.9(2)	C(14)-Sn(2)-N(2)	95.43(18)	C(27)-Sn(3)-N(3)	97.94(19)
O(1)-Sn(1)-O(2)	153.45(14)	O(4)-Sn(2)-O(5)	153.06(14)	O(7)-Sn(3)-O(8)	149.16(14)
O(1)-Sn(1)-O(9)	81.14(14)	O(4)-Sn(2)-O(3)	78.42(14)	O(7)-Sn(3)-O(6)	80.42(14)
C(3)-Sn(1)-O(2)	86.6(3)	C(16)-Sn(2)-O(3)	84.7(2)	C(29)-Sn(3)-O(6)	86.98(18)
C(1)-Sn(1)-O(2)	87.1(3)	C(14)-Sn(2)-O(3)	85.19(18)	C(27)-Sn(3)-O(6)	86.44(17)
C(3)-Sn(1)-O(9)	83.9(3)	C(16)-Sn(2)-O(5)	86.6(3)	C(29)-Sn(3)-O(8)	83.7(2)
C(1)-Sn(1)-O(9)	82.7(2)	C(14)-Sn(2)-O(5)	81.48(18)	C(27)-Sn(3)-O(8)	85.62(19)
N(1)-Sn(1)-O(2)	71.36(14)	N(2)-Sn(2)-O(3)	71.32(13)	N(3)-Sn(3)-O(8)	69.69(13)
N(1)-Sn(1)-O(9)	162.90(14)	N(2)-Sn(2)-O(5)	159.80(14)	N(3)-Sn(3)-O(6)	159.85(13)
O(2)-Sn(1)-O(9)	125.40(13)	O(3)-Sn(2)-O(5)	128.51(12)	O(6)-Sn(3)-O(8)	130.40(12)

Table 3　Selected bond lengths (nm) and angles (°) of 4

Sn(1)-O(1)	0.208 2(4)	Sn(2)-C(14)	0.210 4(6)	Sn(3)-O(7)	0.209 5(4)
Sn(1)-C(1)	0.211 1(6)	Sn(2)-O(4)	0.211 7(4)	Sn(3)-C(27)	0.211 1(6)
Sn(1)-C(3)	0.211 6(6)	Sn(2)-C(16)	0.215 0(7)	Sn(3)-C(29)	0.211 8(6)
Sn(1)-N(1)	0.232 6(5)	Sn(2)-N(2)	0.231 1(5)	Sn(3)-N(3)	0.232 0(5)
Sn(1)-O(2)	0.238 7(4)	Sn(2)-O(3)	0.234 7(4)	Sn(3)-O(8)	0.233 1(4)
Sn(1)-O(9)	0.238 9(4)	Sn(2)-O(5)	0.242 4(4)	Sn(3)-O(6)	0.244 0(4)
O(2)-C(13)	0.124 7(6)	O(5)-C(26)	0.127 9(6)	O(8)-C(39)	0.127 1(6)
O(3)-C(13)	0.126 0(6)	O(6)-C(26)	0.125 1(7)	O(9)-C(39)	0.123 9(6)
O(1)-Sn(1)-C(1)	95.6(2)	C(14)-Sn(2)-O(4)	100.0(3)	O(7)-Sn(3)-C(27)	100.6(2)
O(1)-Sn(1)-C(3)	100.1(2)	C(14)-Sn(2)-C(16)	158.1(3)	O(7)-Sn(3)-C(29)	93.6(2)
C(1)-Sn(1)-C(3)	161.8(2)	O(4)-Sn(2)-C(16)	100.8(2)	C(27)-Sn(3)-C(29)	159.9(3)
O(1)-Sn(1)-N(1)	80.51(16)	C(14)-Sn(2)-N(2)	95.2(2)	O(7)-Sn(3)-N(3)	79.30(16)
C(1)-Sn(1)-N(1)	100.0(2)	O(4)-Sn(2)-N(2)	78.87(16)	C(27)-Sn(3)-N(3)	94.1(2)
C(3)-Sn(1)-N(1)	91.6(2)	C(16)-Sn(2)-N(2)	95.4(2)	C(29)-Sn(3)-N(3)	102.6(2)
O(1)-Sn(1)-O(2)	150.26(14)	O(4)-Sn(2)-O(5)	147.78(14)	O(7)-Sn(3)-O(8)	149.04(15)
C(1)-Sn(1)-O(2)	84.6(2)	C(14)-Sn(2)-O(3)	88.4(2)	C(27)-Sn(3)-O(8)	89.5(2)
C(3)-Sn(1)-O(2)	86.2(2)	C(16)-Sn(2)-O(3)	87.3(2)	C(29)-Sn(3)-O(8)	85.5(2)
N(1)-Sn(1)-O(2)	70.24(15)	N(2)-Sn(2)-O(5)	68.91(15)	N(3)-Sn(3)-O(8)	70.77(15)
O(1)-Sn(1)-O(9)	80.09(15)	O(4)-Sn(2)-O(3)	83.41(15)	O(7)-Sn(3)-O(6)	79.22(15)

Continued Table 3

C(1)-Sn(1)-O(9)	90.2(2)	C(14)-Sn(2)-O(5)	83.7(3)	C(27)-Sn(3)-O(6)	82.2(2)
C(3)-Sn(1)-O(9)	83.6(2)	C(16)-Sn(2)-O(5)	82.3(2)	C(29)-Sn(3)-O(6)	86.5(2)
N(1)-Sn(1)-O(9)	158.85(15)	N(2)-Sn(2)-O(3)	162.27(15)	N(3)-Sn(3)-O(6)	157.15(15)
O(2)-Sn(1)-O(9)	129.63(13)	O(3)-Sn(2)-O(5)	128.80(13)	O(8)-Sn(3)-O(6)	131.44(14)

from 0.231 6(4) and 0.240 0(3) nm, which are comparable to those found in cyclic trimeric organotin carboxylates such as $[Bu_2Sn(2,5\text{-pdc})(DMSO)]_3$[3], $[Bu_2Sn(pca)Cl]_3$[17], $[Bu_2Sn(2\text{-}OC_6H_4CH{=}NCH_2COO)]_3$[10,11]. The three tin atoms and the six oxygen atoms in the macrocycle almost lie in a plane with the maximal deviation of 0.009 7 nm (O8) from the mean plane defined by these Sn and O atoms. The dimension of the cavity in this planar cyclic derivative can be evaluated by the distance of Sn…Sn (0.510 3~0.527 6 nm) and the transannular O…O distance (O2…O5, O5…O8 and O8…O2) (0.340 1~0.340 7 nm).

The six atoms around each tin atom are respectively from two carbons of ethyl groups, an imine N atom, a phenolic O and a carboxylic O of the ligand and the carbonyl O of carboxylate from an adjacent ligand. Tin atom forms a five- and a six-membered chelate ring with the ligand. Thus, the coordination geometry about each Sn atom is a distorted octahedron with the average bond angles C-Sn-C, O-Sn-O and N-Sn-O being 157.3(3)°, 151.89(14)° and 160.85(14)°, respectively. Distortions from the ideal geometry may be rationalized partly by the restricted bite angles (O(1)-Sn(1)-N(1), 82.19(15)° and N(1)-Sn(1)-O(2), 71.36(14)°) of the tridentate ligand. The average Sn-N distance in **1** [0.228 5(4) nm] lies in the normal range of 0.227 to 0.258 nm [17] and is slightly shorter than that reported in $[Bu_2Sn(2\text{-}OC_6H_4CH{=}NCH_2COO)]_3$ (0.228 1(6) nm)[10] and $[Bu_2Sn(2\text{-}OC6H_4CH(CH_3){=}NCH_2COO)]_3$ (0.231 9(2) nm)[11]. The Sn-C lengths are in a narrow range from 0.209 9(7) to 0.212 7(5) nm, typical of organotin compounds.

The compound **4** crystallizes in triclinic space group $P\bar{1}$. The carbon C15 of an ethyl group is disordered over two positions with site occupancy factors of 0.651(11) and 0.349(11). Compound **4** is also a cyclic trinuclear complex with a molecular structure similar to that of 1 (Fig.2). The only difference between the structure of **1** and that of **4** is the presence of two additional chlorine atoms on the ligands of the latter compound. Otherwise, the coordination geometry about each Sn atom in **4** is the same as in **1** and all geometric parameters are close to those in **1**.

2.2 Spectroscopic analysis

The infrared spectra of all these complexes don′t show a strong band at ~3 400 cm^{-1} assigned to ν(OH), indicting the deprotonation of the phenolic oxygen of the ligand upon complexation with tin atom[9,18]. This is further confirmed by the appearance of a sharp band at ~550 cm^{-1} assignable to the Sn-O stretching vibration[18]. The ν(C=N) appears as a strong band at 1 620~1 630 cm^{-1} and the strong absorptions at ~1 585 cm^{-1} and ~1 400 cm^{-1} are assigned to $\nu_{as}(CO_2)$ and $\nu_s(CO_2)$, respectively. In these complexes, the difference between the $\nu_{as}(CO_2)$ and $\nu_s(CO_2)$ bands, $\Delta\nu(CO_2)$ (181~194 cm^{-1}), is below 200 cm^{-1}, indicating that the carboxylate group is bidentate coordination to tin in the solid state[19], which is consistent with the above X-ray structure.

The ^{1}H NMR spectra of the complexes show that the signal assigned to azomethine proton N=CH and methylene proton CH_2N= appear at δ ~8.30 and ~4.30, respectively. The appearance of spin-spin coupling between the N=CH proton and tin nucleus ($^3J_{Sn\text{-}H}$=40~45 Hz) and CH_2N= proton and tin nucleus ($^3J_{Sn\text{-}H}$=16~18 Hz) further confirms the presence of N→Sn in all cases. The ^{119}Sn chemical shifts primarily depend on the coordination number and the nature of the donor atom directly bonded to the central tin atom. The ^{119}Sn chemical shifts of **1** ~**5** occur between δ −189.2 to −194.0, which fall well within the range proposed for penta-coordinate tin centres[20]. Thus, in $CDCl_3$ solution carbonyl O of carboxylate in these complexes is not coordinated to tin atom of adjacent molecule and all complexes are monomeric with pentacoordinated tin atoms.

2.3 Biological activity

In order to evaluate the biological activity of these diethyltin derivatives, we selected **5** as sample and test its activity against *E. coli* and three human tumor cell lines, HeLa (cervix tumor cell), CoLo 205 (colon carcinoma cell) and MCF-7 (mammary tumor cell). The minimum inhibitory concentration (MIC) of 5 against *E. coli* (9.26 μg·mL^{-1}) and the IC_{50} against HeLa, CoLo205 and MCF-7 (7.22 ±0.42, 15.21 ±2.23 and 10.28±1.29 μg·mL^{-1}, respectively.) indicate that **5** is active against *E. coli* and the three tumor cells, but its activity is lower than that of the reference drug ampicillin sodium (MIC 3.10 μg·mL^{-1}) and *cis*-platin (IC_{50} 1.97±0.36, 4.12±0.12 and 5.60±0.51 μg·mL^{-1}, respectively.). In comparison with our previous results, compound **5** is also less active than the dibutyltin analogues, such as Bu_2Sn [2-O-3,5-$Br_2C_6H_4$CH=NCH(*i*-Pr)COO] (IC_{50} 0.32±0.05, 1.35±0.15 and 0.43± 0.08 μg·mL^{-1}, respectively) [14], which is in accord with earlier reports[4,6]. Thus, the alkyls bond to tin play an important role in anti-tumor activity of organotin carboxylates.

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