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Synthesis, structural characterization and antimicrobial activity of mixed aryl–alkyl diorganotin(IV) compounds with quinoline-2-carboxylate (L^-): $\{RR'SnLCl\}_n$ and $RR'SnL_2$

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A series of unsymmetrical diorganotin derivatives of quinoline-2-carboxylic acid (LH), namely polymeric $\{MePhSnClL\}_n$ (1) and $\{EtPhSnClL\}_n$ (2), and mononuclear $MePhSnL_2$ (3) and $EtPhSnL_2$ (4), was synthesized by the reaction of LH with the $MePhSnCl_2$, $EtPhSnCl_2$, MePhSnO, and EtPhSnO precursors, respectively. The compounds were characterized by elemental analysis and infrared spectroscopy, as well as by ^{1}H, ^{13}C and ^{119}Sn NMR. The molecular structures of representative compounds 2 and 4 were determined by single-crystal X-ray crystallography. This study showed that polymeric 2 adopts a distorted octahedral geometry as the carboxylate ligand N,O chelates an Sn atom and at the same time bridges a neighbouring Sn atom via the second O atom, with the remaining sites being occupied by the Cl and two C atoms; the O atoms are *trans* to each other. The result of the μ_2-bridging mode of L^- is the formation of a supramolecular helical chain. Compound 4 adopts a skew-trapezoidal bipyramidal geometry with the organo groups lying over the plane of the two N,O-chelating carboxylate ligands and being directed over the weaker Sn-N bonds. The *in vitro* antimicrobial activities of 1–4 against a Gram-positive bacteria strain (*Bacillus subtilis*), a Gram-negative bacteria strain (*Escherichia coli*) and against *Candida albicans* were studied and compared with the antimicrobial activities of Ph_2SnL_2 and Me_2SnL_2, and with the antimicrobial standards gentamicin, tetracycline, ampicillin and penicillin. All organotin compounds displayed remarkable antibacterial activities that were comparable to those of the standard drugs, in particular against *B. subtilis*, where the activity was correlated with the number of Cl substituents. Copyright © 2012 John Wiley & Sons, Ltd.

Keywords: organotin(IV); quinoline-2-carboxylic acid; crystal structure; NMR structure; antimicrobial activity

Introduction

Diorganotin carboxylates have been subject of extensive investigations owing to their biological activity, including their potential antineoplastic and anti-tuberculosis activities.[1–6] In the context of anti-cancer activity, a particular motivation for their study stems from the known side effects exhibited by the widely used anti-tumour drugs cisplatin and carboplatin, which has stimulated the search for organometallic compounds as alternative drugs for combating human cancer.[7–10] The significant biological activities of organotin compounds in general and organotin carboxylates in particular, i.e. *in vitro* antifungal, antibacterial, antiviral, pesticidal and antitumour activities, have been attributed to the number and nature of the organic groups attached to the central tin atoms.[4,5] However, the role of carboxylate ligand should not be discounted.[11] For instance, a number of biological activities such as anti-inflammatory, anti-allergic,[12] antibacterial,[13] antimalarial,[14] anti-parasitic,[15] anti-proliferative,[16] and anti-cancer[17] have been observed for quinoline-containing compounds. Recent studies on organotin(IV) derivatives containing carboxylate ligands with additional donor atoms such as nitrogen and sulphur have revealed new structural motifs which can lead to compounds with enhanced biological activities;[18] accordingly, a number of such organotin(IV) carboxylates have been reported.[19–21] Among the many carboxylic acids available, quinoline-2-carboxylic acid (HL) is particularly interesting due to its inherent steric bulk, which is capable of controlling the coordination geometry of tin regardless of the nature of the R groups bonded to tin.[18–21] To investigate the role of tin-bound organic groups upon biological activity of organotin compounds, in this work a series of unsymmetric diorganotin derivatives of L^- have been prepared. As the accumulated evidence shows that the activities of mixed organotin systems are significantly different from those of the symmetrical systems,[22] the investigation of organotin compounds with an asymmetric tin centre will reveal valuable insight into the biological activity of organotin (IV) compounds. Herein, the synthesis, characterization and

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molecular structures of four new unsymmetrical diorganotin(IV) compounds derived from quinoline-2-carboxylic acid, some known symmetric derivatives, and their *in vitro* antimicrobial activity against a Gram-positive bacteria strain (*Bacillus subtilis*), a Gram-negative bacteria strain (*Escherichia coli*) and *Candida albicans* are reported. Dialkyltin(IV), diaryltin(IV) and alkylaryltin (IV) compounds of quinoline-2-carboxylic acid were prepared employing methods reported in previous studies by reaction of diorganotin(IV) dichloride with sodium quinoline-2-carboxylate or condensation of diorganotin(IV) oxide with HL.[18–21] The specific motivation of the study was to evaluate the influence of the tin-bound organic groups and also role of mixed tin-bound alkyl/aryl groups on their antibacterial activity.

Experimental

Materials

Triphenyltin(IV) chloride, methyl bromide, ethyl bromide, sodium, quinoline-2-carboxylic acid (HL) and magnesium were purchased from Merck and used without further purification. All solvents were dried and distilled under a nitrogen atmosphere prior to use. Methyltriphenyltin(IV) was prepared using a conventional Grignard synthesis with triphenyltin(IV) chloride and methyl magnesium bromide, and purified by recrystallization from methanol (m.p. 47 °C; yield 75%).[23] Ethyltriphenyltin(IV) was prepared similarly from triphenyltin(IV) chloride and ethyl magnesium bromide, and purified by recrystallization form ethanol at room temperature (m.p: 55 °C, yield 72%).[24]

Physical Measurements

Melting points were obtained with an Electrothermal 9200 melting point apparatus and are not corrected. Infrared spectra in the range 4000–400 cm^{-1} were recorded on a Shimadzu 470 FT-IR spectrophotometer using KBr pellets. ^{1}H, ^{13}C and ^{119}Sn NMR spectra were recorded at room temperature in $CDCl_3$ solution on a Bruker AVANCE 300-MHz instrument operating at 300.3, 75.4 and 111.9 MHz, respectively. The NMR spectra are referenced to Me_4Si (^{1}H and ^{13}C) or Me_4Sn (^{119}Sn) as internal standards.

X-Ray Crystallography

Intensity data were measured at 100 K on an Agilent Technologies SuperNova Dual CCD with an Atlas detector fitted with Mo $K\alpha$ radiation so that $\theta_{max} = 27.6°$. Data processing and absorption correction were accomplished with CrysAlis PRO.[25] The structures were solved by direct methods with SHELXS-97[26] and refinement (anisotropic displacement parameters, hydrogen atoms in the riding model approximation and a weighting scheme of the form $w = 1/[\sigma^2(F_o^2) + (aP)^2 + bP]$ for $P = (F_o^2 + 2F_c^2)/3$) was on F^2 by means of SHELXL-97.[26] Crystallographic data and final refinement details are given in Table 1. Figures 1(a) and 2 were drawn with ORTEP-3[27] at the 50% probability level and the remaining crystallographic figures were drawn with DIAMOND using arbitrary spheres.[28] Data manipulation and interpretation were with WinGX[29] and PLATON.[30]

Synthesis of Compounds

*Synthesis of catena-poly[[chlorido(methyl)phenyltin(IV)]-μ-quinoline-2-carboxylato-κ³ N,O:O′], {MePhSnLCl}$_n$ (**1**) and catena-poly[[chlorido(ethyl) phenyltin(IV)]-μ-quinoline-2-carboxylato-κ³ N,O:O′], {EtPhSnLCl}$_n$ (**2**)*

Table 1. Crystal data and refinement details for **2** and **4**

Crystal data	**2**	**4**
Empirical formula	$C_{18}H_{16}ClNO_2Sn$	$C_{28}H_{22}N_2O_4Sn$
Formula weight	432.46	569.17
Crystal colour	Colourless	Colourless
Crystal dimensions (mm)	0.20 × 0.25 × 0.30	0.25 × 0.30 × 0.35
Crystal system	Monoclinic	Monoclinic
Space group	$P2_1/n$	$P2_1/n$
a (Å)	11.0263(3)	9.9932(3)
b (Å)	12.4110(3)	16.2070(4)
c (Å)	12.4432(4)	15.0750(5)
β (deg.)	91.448(3)	105.410(3)
V Å^3	1702.28(8)	2353.77(12)
Z	4	4
D_x (g cm^{-3})	1.687	1.606
F (000)	856	1144
μ(Mo $K\alpha$) (mm^{-1})	1.666	1.124
Reflections collected	12244	24877
R_{int}	0.032	0.045
Unique reflections	3919	5442
Obs. reflections [$I > 2\sigma(I)$]	3405	4563
R [obs. reflns]	0.025	0.029
a, b, in weighting scheme	0.025, 1.251	0.041, 1.663
wR (all data)	0.032	0.079
CCDC deposit no.	856935	856936

Methylphenyltin(IV) dichloride and ethylphenyltin(IV) dichloride were prepared by hydrochlorination of methyltriphenyltin(IV) and ethyltriphenyltin(IV), respectively, according to the literature synthesis[31] of mixed organotin compounds of the type $(C_6H_5)RSnCl_2$. For the preparation of **1**, a solution of $MePhSnCl_2$ (0.28 g, 1 mmol) in methanol (5 ml) was added to a solution of sodium quinoline-2-carboxylate (0.20 g, 1 mmol) also in methanol (5 ml) at room temperature with vigorous stirring. After 2 h, sodium chloride was removed by filtration and the solid was crystallized (yield 75%; m.p. 185–186 °C). Anal. Calcd for $C_{17}H_{14}ClNO_2Sn$: C, 48.80; H, 3.37; N, 3.35%. Found C, 48.12; H, 3.78; N, 3.23%. IR (KBr, cm^{-1}): ν_{as}(OCO), 1674; ν_s(OCO), 1322; ν(Sn-C), 550; ν(Sn-N), 482; ν(Sn-O), 445. ^{1}H NMR ($CDCl_3$, ppm; the atom numbering for the ^{1}H and ^{13}C NMR spectra for quinoline-2-carboxylato ligand in **1–4** is shown in Scheme 1): 1.29 (3 H, s, Sn-CH_3, $^{2}J^{117/119}$Sn-H = 78 Hz), 7.33–7.37 (3 H, m, $H_{m,p}$-C_6H_5), 7.58 (2 H, d, H_o-C_6H_5, ^{3}JH-H = 6.0 Hz), 7.81–7.87 (3 H, m, H5–7), 8.12 (1 H, d, H8, ^{3}JH-H = 7.0 Hz), 8.61 (1 H, d, H3, ^{3}JH-H = 7.0 Hz), 8.67 (1 H, d, H2, ^{3}JH-H = 7.0 Hz). ^{13}C NMR (DMSO-d_6, ppm): 165.0 (COO), 147.9 (C_6H_5, C_{ipso}, $^{1}J^{117/119}$Sn-^{13}C = 622 Hz), 135.2 (C^6H_5, C_o, $^{2}J^{117/119}$Sn-^{13}C = 48 Hz), 128.7 (C_6H_5, C_p), 125.4 (C_6H_5, C_m, $^{3}J^{117/119}$Sn-^{13}C = 65 Hz), 142.6 (C1), 142.2 (C9), 132.8 (C2), 130.8 (C8), 130.4, 130.0 (C4), 129.2 (C6), 125.3, 121.3, 9.6 (Sn-CH_3, $^{1}J^{117/119}$Sn-^{13}C = 632 Hz). ^{119}Sn NMR (DMSO-d_6, ppm): −312.4.

EtPhSnClL (**2**) was prepared similarly from $EtPhSnCl_2$ and sodium quinoline-2-carboxylate, and was recrystallized from methanol (yield 71%; m.p. 190–191 °C). Anal. Calcd for $C_{18}H_{16}ClNO_2Sn$: C, 49.99; H, 3.73; N, 3.24%. Found C, 50.22; H, 3.28; N, 3.48%. IR (KBr, cm^{-1}): ν_{as}(OCO) 1642; ν_s(OCO) 1334; ν(Sn-C) 595; ν(Sn-N) 523; ν(Sn-O) 456. ^{1}H NMR ($CDCl_3$, ppm): 1.00 (3 H, t, $SnCH_2\underline{CH_3}$, ^{3}JH-H = 7.8 Hz, $^{3}J^{117/119}$Sn-H = 195 Hz), 1.59 (2 H, q, $SnCH_2$, ^{3}JH-H = 7.8 Hz, $^{2}J^{117/119}$Sn-H = 98 Hz), 7.30–7.34 (3 H, m, $H_{m,p}$-C_6H_5), 7.58 (2 H, d, H_o-C_6H_5, ^{3}JH-H = 6.0 Hz),

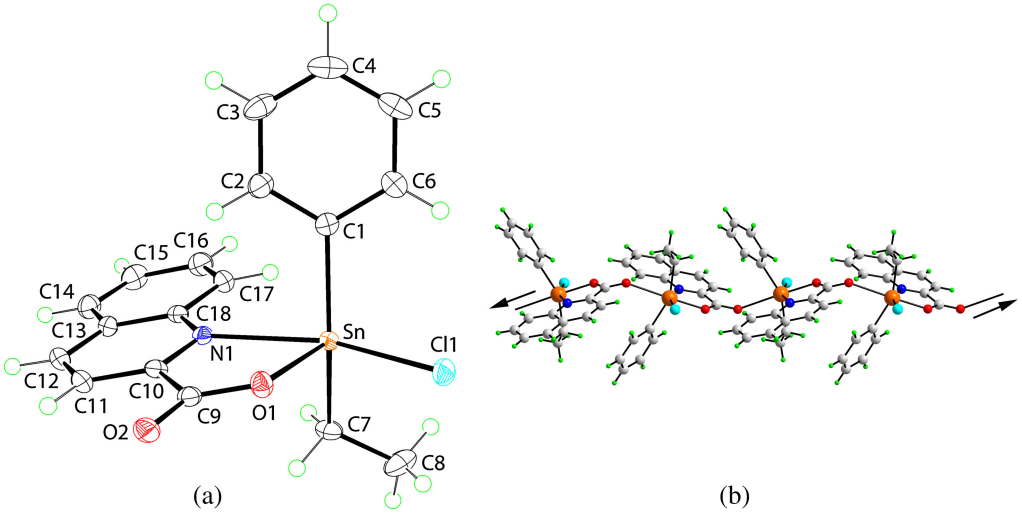


Figure 1. (a) The asymmetric unit in polymeric $\{PhEtSnLCl\}_n$ (**2**) showing the atom labelling scheme and displacement ellipsoids drawn at 50% probability level, and (b) helical supramolecular chain along [010] mediated by intermolecular Sn–O2 interactions. Selected geometric parameters: Sn–Cl1 2.4387(6), Sn–O1 2.1136(16), Sn–N1 2.4311(19), Sn–$O2^i$ 2.6255(16) Å; O1–Sn–$O2^i$ 177.40(6), C1–Sn–C7 152.59(9)°. Symmetry operation i: 3/2 − x, −1/2 + y, 3/2 − z

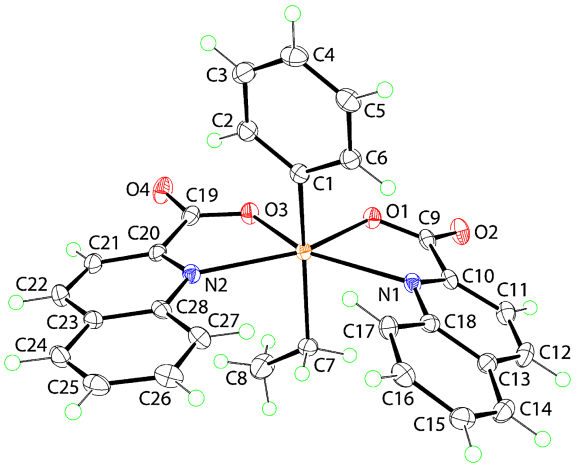
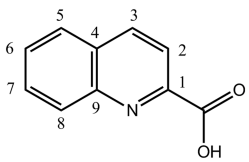


Figure 2. Molecular structure of $PhEtSnL_2$ (**4**) showing the atom labelling scheme and displacement ellipsoids drawn at 50% probability level. Selected geometric parameters: Sn–O1 2.1023(16), Sn–N1 2.532(2), Sn–O3 2.0929(17), Sn–N2 2.473(2) Å; O1–Sn–O3 80.61(7), N1–Sn–N2 137.21(7), C1–Sn–C7 152.33(10)°



Scheme 1. The atom numbering for quinoline-2-carboxylic acid

7.78–7.83 (3 H, m, H5–7), 8.10 (1 H, d, H8, ^3J H-H = 7.0 Hz), 8.64 (1 H, d, H3, ^3J H-H = 7.0 Hz), 8.69 (1 H, d, H2, ^3J H-H = 7.0 Hz). ^{13}C NMR ($CDCl_3$, ppm): 164.5 (COO), 148.2 (C_6H_5, C_{ipso}, $^1J^{117/119}$Sn-^{13}C = 775 Hz), 135.4 (C^6H_5, C_o, $^2J^{117/119}$Sn-^{13}C = 46 Hz), 128.6 (C_6H_5, C_p), 125.5 (C_6H_5, C_m, $^3J^{117/119}$Sn-^{13}C = 65 Hz), 142.9 (C1), 142.2 (C9), 132.7 (C2), 130.7 (C8), 130.3, 129.9 (C4), 129.2 (C6), 125.1, 121.5, 22.1 (CH_2), 9.6 (CH_3). ^{119}Sn NMR ($CDCl_3$, ppm): −158.4 and ^{119}Sn NMR (DMSO-d_6, ppm): −319.8.

*Synthesis of methyl(phenyl)bis(quinoline-2-carboxylato-κ^2 N,O)tin(IV) (MePhSnL$_2$) (**3**) and ethyl(phenyl)bis(quinoline-2-carboxylato-κ^2 N,O)tin(IV) (EtPhSnL$_2$) (**4**)*

Methylphenytinoxide(IV) (MePhSnO) and ethylphenytinoxide(IV) (EtPhSnO) were prepared by reacting methylphenyltin(IV) dichloride and ethylphenyltin(IV) dichloride with sodium hydroxide, respectively. The resulting white precipitate was removed by filtration and washed copiously with water and dried at room temperature. For the preparation of **3**, a mixture of methylphenyltin oxide (0.21 g, 1 mmol) and quinoline-2-carboxylic acid (0.40 g, 2 mmol) in toluene (25 ml) was refluxed and the water that was produced during the reaction was removed azeotropically by a Dean–Stark trap. After 8 h, toluene was removed under reduced pressure and the white solid was recrystallized from methanol (yield 82%; m.p. 140 °C dec.). Anal. Calcd for $C_{27}H_{20}N_2O_4Sn$: C, 58.42; H, 3.63; N, 5.05%. Found: C, 57.84; H, 4.32; N, 4.98%. IR (KBr, cm^{-1}): ν_{as}(OCO) 1674; ν_s(OCO) 1329; ν(Sn-C) 545; ν(Sn-N) 501; ν(Sn-O) 455. ^{1}H NMR (DMSO-d_6, ppm): δ 1.01 (3 H, s, $SnCH_3$, $^2J^{117/119}$Sn-H = 87 Hz), 7.18–7.23 (3 H, m, $H_{m,p}$-C_6H_5), 7.58 (2 H, d, H_o-C_6H_5, ^3J H-H = 6.0 Hz), 7.78–7.83 (6 H, m, H5–7), 8.01 (2 H, d, H8, ^3J H-H = 7.0 Hz), 8.68 (2 H, d, H3, ^3J H-H = 7.0 Hz), 8.74 (2 H, d, H2, ^3J H-H = 7.0 Hz), ^{119}Sn NMR (DMSO-d_6, ppm): −362.3.

$EtPhSnL_2$ (**4**) was prepared similarly but from ethylphenyltin(IV) oxide and quinoline-2-carboxylic acid, and crystallized from ethanol (yield 75%; m.p. 245–246 °C). Anal. Calcd for $C_{28}H_{22}N_2O_4Sn$: C, 59.09; H, 3.90; N, 4.92%. Found; C, 59.22; H, 3.55; N, 5.15%. IR (KBr, cm^{-1}): ν_{as}(OCO) 1678; νs(OCO) 1324; ν(Sn-C) 522; ν(Sn-N) 498; ν(Sn-O) 452. ^{1}H NMR (DMSO, ppm): 1.16 (3 H, t, $SnCH_2\underline{CH}_3$, ^3J H-H = 7.8 Hz, $^3J^{117/119}$Sn-H = 171 Hz), 1.85 (2 H, q, $\underline{CH}_2$, ^3J H-H = 7.8 Hz, $^2J^{117/119}$Sn-H = 108 Hz), 7.13–7.17 (3 H, m, $H_{m,p}$-C_6H_5), 7.66 (2 H, d, H_o-C_6H_5, ^3J H-H = 6.0 Hz), 7.22–7.83 (6 H, m, H5–7), 8.00 (2 H, d, H8, ^3J H-H = 7.0 Hz), 8.46 (2 H, d, H3, ^3J H-H = 7.0 Hz), 8.52 (2 H, d, H2, ^3J H-H = 7.0 Hz). ^{13}C NMR (DMSO, ppm): 165.0 (COO), 146.7 (C_6H_5, C_{ipso}, $^1J^{117/119}$Sn-^{13}C = 785 Hz), 137.9 (C_6H_5, C_o, $^2J^{117/119}$Sn-^{13}C = 48 Hz), 129.6 (C_6H_5, C_p), 124.6 (C_6H_5, C_m, $^3J^{117/119}$Sn-^{13}C = 68 Hz), 141.8 (C1), 141.7 (C9), 132.1 (C2), 131.8 (C8), 131.6, 127.5 (C5), 126.7, 124.4, 119.4, 21.0 (CH_2, $^1J^{117/119}$Sn-^{13}C = 768 Hz), 7.3 (CH^3). ^{119}Sn NMR ($CDCl_3$, ppm): −309.7 and ^{119}Sn NMR (DMSO-d_6, ppm): −367.1.

*Synthesis of dimethyl-bis(quinoline-2-carboxylato-κ^2 N,O)tin(IV) Me_2SnL_2 (**5**) and diphenyl-bis(quinoline-2-carboxylato-κ^2 N,O)tin(IV) Ph_2SnL_2 (**6**)*

Dimethyltin(IV) and diphenyltin(IV) compounds of quinoline-2-carboxylate, **5** and **6**, known materials (m.p. 268–269 °C cf. lit.[21] 268–270 °C and 218–219 °C cf. lit.[18] 217–219 °C, respectively), were prepared similarly from the reaction of freshly prepared Me_2SnO and Ph_2SnO with quinoline-2-carboxylic acid in toluene and their purity confirmed by ^{1}H NMR analysis.

Antimicrobial Activity

The anti-microbial activity of the synthesized diorganotin(IV) compounds was evaluated by the disc diffusion method against *Bacillus subtilis* (ATCC 9372, Gram-positive), *Escherichia coli* (ATCC 9763, Gram-negative) and *Candida albicans* (ATCC 1023) with the determination of inhibition zones.[32]

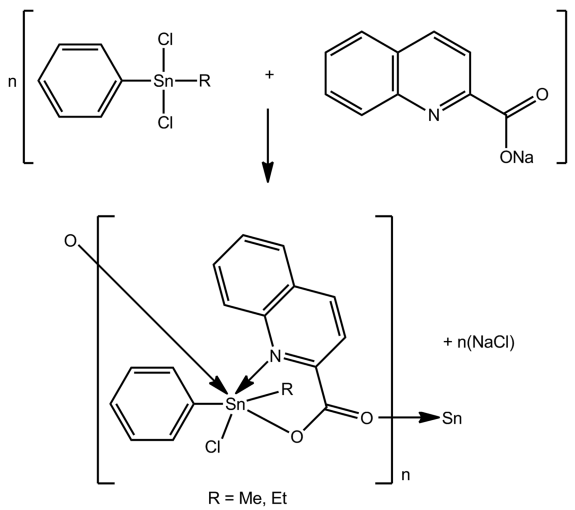
A stock solution of each synthesized compound (1 mg ml^{-1}) in DMSO was prepared and used in all evaluations. In a typical test, a 10 µl solution of each trial organotin compound was poured into a disc prior to placement in bacterial lawns. The control antibiotic discs were gentamicin (10 µg), tetracycline (30 µg), ampicillin (10 µg) and penicillin (10 µg). The plates were incubated at 37 °C for 24 h, after which the diameters of inhibition zones (mm) were measured. The tests were performed in triplicate and the results were averaged.

Results and Discussion

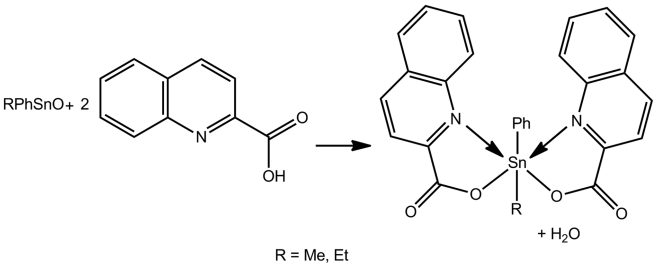
The reaction of each of $MePhSnCl_2$ and $EtPhSnCl_2$ with sodium quinoline-2-carboxylate in a 1:1 molar ratio led to the formation of compounds **1** and **2**, respectively (Scheme 2).

The reaction of each of MePhSnO and EtPhSnO with quinoline-2-carboxylic acid in a 1:2 molar ratio in boiling toluene with removal of formed water in a Dean–Stark trap afforded compounds **3** and **4**, respectively (Scheme 3).

The compounds were characterized by elemental analysis, IR spectroscopy, as well as ^{1}H, ^{13}C and ^{119}Sn NMR. The molecular structures of representative compounds **2** and **4** were also verified by single-crystal X-ray analyses.



Scheme 2. Reaction of $MePhSnCl_2$ and $EtPhSnCl_2$ with sodium quinoline-2-carboxylate



Scheme 3. Reaction of RPhSnO with quinoline-2-carboxylic acid

Infrared Spectroscopy

In each of the IR spectra of polymeric $\{MePhSnLCl\}_n$ (**1**) and $\{EtPhSnClCl\}_n$ (**2**), and monomeric $MePhSnL_2$ (**3**) and $EtPhSnL_2$ (**4**), the absence of a broad band in the range 2500–3400 cm^{-1} and the presence of Sn-O vibrations in the range 450–500 cm^{-1} clearly indicate that deprotonation of the quinoline-2-carboxylic acid has taken place, resulting in coordination to tin. The infrared spectra of **1–4** exhibit u_{asym}(OCO) and u_{sym}(OCO) stretching vibrations in the ranges 1642–1678 and 1322–1334 cm^{-1}, respectively. The red shifts of these bands with respect to the free acid also serve to confirm the formation of **1–4**. The magnitude of Δu (= $u_{asym} - u_{sym}$) has been previously employed to determine the specific type of carboxylate binding present.[33] For all four compounds, the Δu values indicate monodentate coordination modes for the carboxylate ligands. In comparison with the free ligand, the new bands in the 482–524 cm^{-1} region were assigned to Sn-N vibrations, which prove coordination of nitrogen to tin. The presence of a single Sn-C stretching vibration at 550, 595, 545 and 522 cm^{-1} in the infrared spectra of **1–4**, respectively, indicates that the C–Sn–C bond angles approach linearity, conclusions confirmed by single-crystal structure determinations on **2** and **4**.

NMR Spectroscopy

For the determination of structural features of the prepared compounds in solution, attempts were made to record ^{1}H, ^{13}C and ^{119}Sn NMR spectra of **1–4**. However, the poor solubility of **3**, even in DMSO-d_6 solution, precluded the recording of ^{13}C and ^{119}Sn NMR spectra. In the ^{1}H NMR spectrum of **1**, recorded in the non-coordinating solvent $CDCl_3$, the $^2J^{117/119}$Sn-C-^{1}H coupling constant of 78 Hz is consistent with trigonal bipyramidal geometry about the tin atom and indicates that the observed polymeric solid-state structure (see below) is not maintained in solution. Based on the magnitude[34] of $^2J^{119/117}$Sn-C-^{1}H for **1** in $CDCl_3$ solution, the C–Sn–C angle is estimated to be 128.4°. The ^{13}C NMR spectra of **1**, **2** and **4** showed the expected aliphatic and/or aromatic signals. Similar behaviour was reported for **5** in an earlier report.[21] The slight downfield shifts of all carbon resonances compared with the free acid in their ^{13}C NMR spectra is attributed to the coordination of quinoline-2-carboxylate ligand to tin and formation of Sn-N bonds.

Table 2 summarizes the ^{119}Sn NMR data, when obtained, for **1–4** along with those for **5** and **6**, two known derivatives,[18,21] in coordinating (DMSO-d_6) and non-coordinating ($CDCl_3$) solvents. As mentioned earlier, insufficient solubility of **1** and **3** precluded the measurement of chemical shifts in $CDCl_3$, but for **2** and **4** ^{119}Sn data were accessible in both solvents. The significant up-field shift in the ^{119}Sn resonance of **2** in DMSO-d_6

Table 2. ^{119}Sn NMR data (δ, ppm) for **1–6**, recorded in $CDCl_3$ and DMSO-d_6 solution

Compound	$CDCl_3$	DMSO-d_6
$\{MePhSnLCl\}_n$ (**1**)	—[a]	−312.4
$\{EtPhSnLCl\}_n$ (**2**)	−158.4	−319.8
$MePhSnL_2$ (**3**)	—[a]	−362.3
$EtPhSnL_2$ (**4**)	−309.7	−367.1
Me_2SnL_2 (**5**)	a[21]	−260.8[21]
Ph_2SnL_2 (**6**)	−312.0[18]	—[b]

[a]Not measured due to poor solubility.
[b]Not determined.

solution in comparison with that in $CDCl_3$ solution is consistent with dissociation of the six-coordinate solid-state structure (see below) in $CDCl_3$ solution, leading to a low coordination number (five), and coordination of DMSO in DMSO-d_6 solution, leading to a higher (six) coordination number. Interestingly, no significant solvent dependence was found in the chemical shifts observed for **4**, an observation that indicates that the six-coordinate solid-state structure (see below) remains intact in solution. Further, the values of ^{119}Sn chemical shifts for **1** and **2** in DMSO-d_6 solution, when compared to the value observed for six-coordinate **4**, lends support to the notion of coordination by DMSO and formation of six-coordinate coordination geometries for **1** and **2** in DMSO-d_6 solution. While the molecular structures of **3** and **4** are similar to that of **5**,[21] the ^{119}Sn chemical shift of the latter is shifted about 100 ppm down-field when measured in the same solvent (Table 2). This large shift is attributed to the presence of tin-bound phenyl groups in **3** and **4**, which are absent in **5**.

Crystal Structures

*Molecular structure of $\{EtPhSnLCl\}_n$ (**2**)*

The asymmetric unit of **2** is shown in Fig. 1(a) and salient bond lengths and angles are listed in the figure caption. The tin atom in **2** is N,O-chelated by the quinoline-2-carboxylate anion, with the second O atom bridging a neighbouring Sn, resulting in a supramolecular chain with a helical topology (see Fig. 1b). The coordination geometry is distorted octahedral based on a C_2ClNO_2 donor set with the O atoms *trans* to each other, subtending an angle of 177.40(6)° at the tin atom. A similar coordination geometry and polymeric structure were observed previously in the crystal structure of the dimethyltin analogue, $\{Me_2SnLCl\}_n$.[35]

*Molecular structure of $EtPhSnL_2$ (**4**)*

The molecular structure of **4** is illustrated in Fig. 2 and selected bond lengths and angles are given in the figure caption. The tin atom in **4** is N,O-chelated by two quinoline-2-carboxylate ligands and the six-coordinate coordination geometry is completed by the two C atoms derived from the tin-bound substituents. The resultant $C_2N_2O_2$ donor set defines a skewed trapezoidal bipyramidal geometry, with the Sn-C bonds lying over the weaker Sn-N bonds; the C1–Sn–C7 bond angle is 152.33(10)°. The structural motif is consistent with literature precedents.[18,21,36]

*Crystal packing patterns in $\{EtPhSnLCl\}_n$ (**2**) and $EtPhSnL_2$ (**4**)*

In **2**, the supramolecular chains aligned along the *b*-axis assemble along the *a*-axis by weak C14-H14···Cl1 interactions of 3.10 Å [symmetry operation $1+x, y, z$]. The connections between the layers in the *ab*-plane are of the type C-H···Cl and C-H···π [C5–H5...Cl1^{i} = 2.79 Å, C5...Cl1i = 3.655(3) Å, and angle at H5 = 151° for symmetry operation i: 2-x, 1-y, 1-z. C4–H4...Cg(C13-C18)^{ii} = 2.77 Å, C41...Cg(C53-C58)^{ii} = 3.643(3) Å, and angle at H4 = 153° for symmetry operation ii: 1-x, 1-y, 1-z] (see Fig. 3). In **4**, supramolecular layers mediated by C-H···O interactions formed in the *ab*-plane [C21–H21...O2^{i} = 2.56 Å, C21...O2^{i} = 3.274(4) Å, and angle at H21 = 132°. C22–H22...O1^{i} = 2.45 Å, C22...O1^{i} = 3.363(3) Å, and angle at H22 = 161°. C24–H24...O4^{i} = 2.43 Å, C24...O4^{i} = 3.226(3) Å, and angle at H24 = 141°. Symmetry operation i: 3/2-x, -1/2 + y, 3/2-z] (Fig. 4a), and these stack along the *c*-axis with no specific intermolecular interactions between the layers (see Fig. 4b). A comparison of Figs 3 and 4(b) reveals a remarkable similarity in the global crystal packing despite the different chemical compositions and modes of supramolecular association operating in their crystal structures.

Antimicrobial Activity

The organotin(IV) derivatives of N,O donor ligands are of considerable interest as they have been suggested to possess mild to good biological activities.[6] The antimicrobial activities of **1–6**, together with those of $MePhSnCl_2$ and $EtPhSnCl_2$ and several standard antibiotics were evaluated against *B. subtilis* (Gram-positive), *E. coli* (Gram-negative) and *C, albicans* using the disc diffusion technique; results are listed in Table 3. The first key observation is that the diorganotin compounds displayed remarkable activity against all three bacteria. In particular, **1–6** as well as the chloride precursor molecules, $MePhSnCl_2$ and $EtPhSnCl_2$, proved as effective as the known antibiotics against *B. subtilis*. Of the organotin compounds, the chloride species were the most active, followed by the monochlorides **1** and **2**, with hexa-coordinated **3** and **4** the least potent. The greater antibacterial activities against *B. subtilis* can be attributed to the presence of chloride atom and enhanced Lewis acidity this imparts to the tin centres. It is notable that there is no measurable difference in antibacterial activity between pairs of related compounds (Table 3). It is also of interest that the organotin compounds with the same tin-bound substituents, i.e. Me_2SnL_2 (**5**) and Ph_2SnL_2 (**6**), have slightly reduced antibacterial activity compared to their unsymmetrical analogues. Such behaviour has been reported earlier in antibacterial trials of mixed aryl–alkyl organotin compounds.[38] Additional work is required for deeper understanding of this phenomenon.

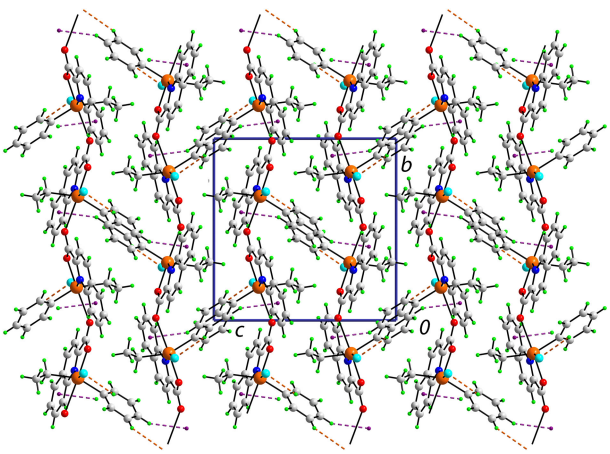


Figure 3. A view of the crystal packing in $\{PhEtSnLCl\}_n$ (**2**) shown in projection down the *a*-axis. The C-H···Cl and C-H...π interactions are shown as orange and purple dashed lines, respectively

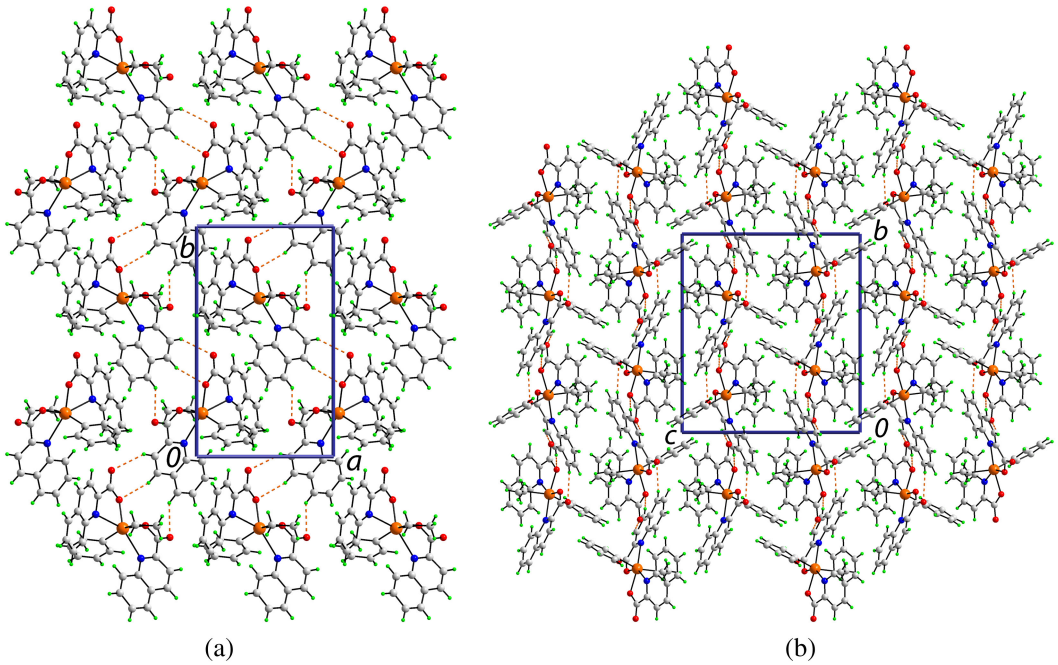


Figure 4. Crystal packing in $PhEtSnL_2$ (**4**): (a) a view of the supramolecular layer in the *ab*-plane mediated by C-H···O interactions (orange dashed lines), and (b) a view of the unit cell contents shown in projection down the *a*-axis

Table 3. Antibacterial activity of the diorganotin (IV) compounds and standard anti-microbial agents

Compound (10 μl)	*Bacillus subtilis*	*Escherichia coli*	*Candida albicans*
$\{MePhSnLCl\}_n$ (**1**)	22	19	16
$\{EtPhSnLCl\}_2$ (**2**)	22	25	22
$MePhSnL_2$ (**3**)	19	10	14
$EtPhSnL_2$ (**4**)	19	24	18
Me_2SnL_2 (**5**)	18	0	12
Ph_2SnL_2 (**6**)	16	10	10
$MePhSnCl_2$	25	17	—
$EtPhSnCl_2$	25	17	—
Ampicillin	23	27	32
Penicillin	20	22	—
Gentamicin	20	25	24
Tetracycline	20	30	32

The antibacterial activities against *E. coli* and *C. albicans* exhibited by the organotin compounds are quite different from that against *B. subtilis*. As indicated in Table 3, the activities of compounds **2** and **4**, with tin-bound ethyl groups, against *E. coli* are higher than their methyl counterparts, **1** and **3**. This difference is associated with the organic group attached to the tin and may be due to the difference in the structure of the cell walls,[11,38] where the more hydrophobic nature of ethyl group allows favourable interaction with the lipopolysaccharides of the outer lipid membrane.

The antimicrobial activities against *C. albicans* and, uniformly, the organotin compounds were less active than the antibiotic standards. Nevertheless, the beneficial influence of a tin-bound ethyl substituent was again demonstrated (Table 3).

Conclusions

This work described the synthesis of unsymmetric diorganotin(IV) compounds with quinoline-2-carboxylate and their full characterization, including by X-ray crystallography. The $\{RR'SnLCl\}_n$ compounds adopt polymeric structures as the quinoline-2-carboxylate ligand is tridentate and bridging. Monomeric, six-coordinate structures are found in the $RR'SnL_2$ compounds. Antibacterial assays prove the remarkable activity of the organotin compounds against the Gram-positive bacterium *B. subtilis*, with enhanced potency correlated with the number of chloride substituents/Lewis acidity of the tin centre. In trials against Gram-negative *E. coli* and *C. albicans*, evidence was provided to indicate a benefit of having unsymmetric diorganotin compounds and, especially, those with tin-bound ethyl groups.

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References

[1] M. Gielen, *Appl. Organomet. Chem.* **2002**, *16*, 481.
[2] M. Gielen, M. Biesemans, D. de Vos, R. Willem, *J. Inorg. Biochem.* **2000**, *79*, 139.
[3] 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.* **1987**, *10*, 147.
[4] A. G. Davies, M. Gielen, K. H. Pannell, E. R. T. Tiekink (Eds), *Tin Chemistry: Fundamentals, Frontiers, and Applications*, Wiley, New York, **2008**.

[5] M. Gielen, E. R. T. Tiekinkin in *Metallotherapeutic Drugs and Metal-Based Diagnostic Agents* (Eds.: M. Gielen, E. R. T. Tiekink), Wiley, Chichester, **2005**, pp. 421.
[6] M. Nath, P. K. Saini, *Dalton Trans.* **2011**, *40*, 7077.
[7] Y. F. Win, S. G. Teoh, T. S. Tengku-Muhammad, Y. Sivasothy, S. T. Ha, *Am. J. Appl. Sci.* **2010**, *7*, 301.
[8] I. C. Mendes, J. P. Moreira, J. D. Ardisson, R. G. dos Santos, P. R. da Silva, I. Carcia, A. Castineiras, H. Beraldo, *Eur. J. Med. Chem.* **2008**, *43*, 1454.
[9] J. S. Casas, M. C. Rodriguez-Argüelles, U. Russo, A. Sanchez, J. Sordo, A. Vazquez-Lopez, S. Pinelli, P. Lunghi, A. Bonati, R. Albertini, *J. Inorg. Biochem.* **1998**, *69*, 283.
[10] J. S. Casas, A. Castineiras, M. C. Rodriguez-Argüelles, A. Sanchez, J. Sordo, A. Vazquez-Lopez, S. Pinelli, P. Lunghi, P. Ciancianaini, A. Bonati, P. Dall'Aglio, R. Albertini, *J. Inorg. Biochem.* **1999**, *76*, 277.
[11] B. Ruan, Y. Tan, R. Hu, H. Zhou, J. Wu, J. Yang, *Inorg. Chim. Acta* **2011**, *365*, 473.
[12] H. Cairns, D. Cox, K. J. Gould, A. H. Ingall, J. L. Suschitzky, *J. Med. Chem.* **1985**, *28*, 1832.
[13] A. Mohammed, N. Abdel-Hamid, F. Maher, A. Farghaly, *Czech. Chem. Commun.* **1992**, *57*, 1547.
[14] R. Jain, S. Jain, R. C. Gupta, N. Anand, G. P. Dutta, S. K. Pur, *Indian J. Chem.* **1994**, *33B*, 251.
[15] A. H. Abadi, R. Brun, *Arzneimforsch. Drug Res.* **2003**, *53*, 655.
[16] M. Croisy-Delcey, A. Coroisy, D. Carrez, C. Huel, A. Chiaroni, P. Ducrot, E. Bisagni, L. Jin, G. Leclercq, *Bioorg. Med. Chem.* **2000**, *8*, 2629.
[17] A. Dlugosz, D. Dus, *Farmaco* **1996**, *51*, 367.
[18] H. D. Yin, Q. B. Wang, S. Xue, *J. Organomet. Chem.* **2005**, *690*, 3111.
[19] C. S. Parulekar, V. K. Jain, T. K. Das, A. R. Gupta, B. F. Hoskins, E. R. T. Tiekink, *J. Organomet. Chem.* **1989**, *372*, 193.
[20] H. D. Yin, C. H. Wang, C. L. Ma, H. X. Fang, *Chin. J. Chem.* **2003**, *22*, 452.
[21] D. Dakternieks, A. Duthie, D. R. Smyth, C. P. D. Stapleton, E. R. T. Tiekink, *Organometallics* **2003**, *22*, 4599.
[22] V. G. Kumar Das, A. J. Kuthubutheen, S. Balabaskaran, S. W. Ng, *Main Group Met. Chem.* **1989**, *12*, 389.
[23] P. J. Smith, *J. Organomet. Chem. Libr.* **1981**, *12*, 97.
[24] M. Lesbre, R. Buisson, J. G. A. Luijten, G. J. M. van der Kerk, *Recl. Trav. Chim. Pays-Bas* **1955**, *74*, 1056.
[25] Agilent Technologies, CrysAlis PRO, Agilent Technologies, Yarnton, UK, **2010**.
[26] G. M. Sheldrick, *Acta Cryst.* **2008**, *A64*, 112.
[27] L. J. Farrugia, *J. Appl. Cryst.* **1997**, *30*, 565.
[28] K. Brandenburg, DIAMOND, Crystal Impact GbR, Bonn, **2006**.
[29] L. J. Farrugia, *J. Appl. Crystallogr.* **1999**, *32*, 837.
[30] A. L. Spek, *J. Appl. Crystallogr.* **2003**, *36*, 7.
[31] M. Gielen, I. Vander Eynde, *J. Organomet. Chem.* **1981**, *217*, 205.
[32] National Committee for Clinical Laboratory Standard, Performance standard for antimicrobial susceptibility testing (9th Int. Suppl.), NCCLS, Wayne, PA, **1999**, M100-S9.
[33] X. N. Fang, X. Q. Song, Q. L. Xie, *J. Organomet. Chem.* **2001**, *619*, 43.
[34] T. P. Lockart, W. F. Manders, *Inorg. Chem.* **1986**, *25*, 892.
[35] I. W. Nowell, J. S. Brooks, G. Beech, R. Hill, *J. Organomet. Chem.* **1983**, *244*, 119.
[36] E. R. T. Tiekink, *Appl. Organomet. Chem.* **1991**, *5*, 1.
[37] R. N. Kapoor, P. Apodaca, M. Montes, D. G. Gomez, K. H. Pannell, *Appl. Organomet. Chem.* **2005**, *19*, 518.
[38] W. Rehman, M. K. Baloch, A. Badshah, *Eur. J. Med. Chem.* **2008**, *43*, 2380.