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Formation, Structure and *In Vitro* Antitumour Activity of a Novel Binuclear Organotin Complex

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Abstract: A 1:1 reaction of triphenyltin chloride with potassium N-[(3,5-dibromo-2-hydroxyl-phenyl)methylene]valinate in benzene led to the formation of a novel mixed organotin dinuclear complex, (HL)$SnPh_3$•Ph_2SnL [L=2-O-3,5-$Br_2C_6H_3CH$=NCH(*i*-Pr)COO], by means of a facile phenyl-tin bond cleavage process. In the complex, there are two distinct types of carboxylate moieties and a *trans*-O_2SnC_2N and a *trans*-O_2SnC_3 in distorted trigonal bipyramidal geometries were bridged by a carboxylate group. *In vitro* antitumor activity of the complex against three human tumour cell lines (HeLa, CoLo205 and MCF-7) was found to be much higher than *cis*-platin used in clinic.

Keywords: Binuclear tin complex, organotin carboxylate, antitumor activity, crystal structure.

In recent years, triorganotin carboxylates ($R'CO_2SnR_3$) have received considerable attention because of their structural diversity[1] and biological properties, particularly anti-tumour activity[2]. In carboxylate ligand, the carboxylate oxygen atoms and the potential donor atoms (N, O, *etc*.) in R′ group can be available for coordination to tin atom. The N-[(2-hydroxyaryl)alkylidene]-α-amino acid represent an interesting class of such ligands[3-5]. Baul *et al.*[3] synthesized several triorganotin esters of N-[(2-hydroxy-aryl)alkylidene]glycine, (2-HOArCH=NCH_2COO)SnR_3, (where R = Me, Bu, Ph) by the reaction of triorganotin chloride with potassium N-[(2-hydroxyaryl)alkylidene]glycinate. The reaction of triphenyltin chloride with potassium N-[(3,5-dibromo-2-hydroxyphenyl)-

Scheme 1 Formation of complex **2**

$$Ph_3SnCl + HLK \xrightarrow{-KCl} \underset{\mathbf{1}}{[(HL)SnPh_3]} \xrightarrow{-PhH}$$

$$[Ph_2SnL] \xrightarrow[\mathbf{1}]{[(HL)SnPh_3]} (HL)SnPh_3 \bullet Ph_2SnL$$

3 **2**

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methylene]valinate (HLK) in benzene under reflux yielded a novel mixed organotin binuclear complex, (HL)$SnPh_3$•Ph_2SnL (**2**), which was characterized by elemental analysis, IR, NMR (^1H, ^{13}C and ^{119}Sn) spectra and X-ray diffraction[6].

The formation of **2** was suggested in **Scheme 1**. The reaction of triphenyltin chloride with the ligand afforded triphenyltin ester **1**, and then elimination of a PhH from **1** by the cleavage of Sn–C and H–O bonds resulted the corresponding diphenyltin complex, Ph_2SnL **3**, finally, the reaction of **3** with **1** gave a novel organotin binuclear complex **2**. The Sn–Ph bond cleavage of organotin with a carboxylic acid to form an organotin carboxylate was reported[7,8], but the formation of organotin phenoxide by cleaving the Sn-Ph bond with phenol is uncommon. The facile Sn–C bond cleavage occurred as a result of the special electronic and steric requirements of the N-[(3,5-dibromo-2-hydroxylphenyl) methylene]valinate unit by contrast with (2-$HOC_6H_4CH=NCH_2COO)SnPh_3$[3].

The compound **2** was a binuclear complex formed by carboxyl group bridging a triphenyltin carboxylate **1** and a diphenyltin carboxylate **3** (**Figure 1**). Each of the two tin atoms, Sn1 and Sn2, possessed five-coordination geometry in distorted trigonal bipyramidal arrangement. The Sn1 atom lay in the ligand plane and formed five-membered and six-membered chlate ring with the ligand. The two phenyl groups and the imino N1 atom occupied the equatorial positions of the trigonal bipyramid and the axial positions were taken up by a phenoxide O1 and a carboxylate oxygen O2 atom (O1–Sn1–O2 156.92(16)°). The trigonal plane of Sn2 atom was defined by the three phenyl groups. The axial position was occupied by the carbonyl oxygen O3 atom of bridging carboxylate group and the carboxylate group oxygen O4 atom of the other ligand (O3–Sn2–O4 178.35(16)°). An intramolecular O–H···N hydrogen bond was found between the uncoordinated imino N2 and the phenolic hydroxy group.

The presence of bidentate bridging carboxylate residues in organotin carboxylate structures was well established[1], however, two different diorganotin carboxylate and triorganotin carboxlate were linked *via* a bridging carboxyl group to produce a binuclear tin complex is rare. To the best of our knowledge the formation of such a novel ditin structure starting from a triorganotin precursor has no report in organotin carboxylate chemistry.

The spectral data (IR, ^1H and ^{13}C NMR) of **2** agreed with its structure completely. The complex displayed two ^{119}Sn resonances at -96.1 and -333.4 ppm in $CDCl_3$ solution, which fell well within the range of four-coordinate and five-coordinate tin centers, respectively[3,4].

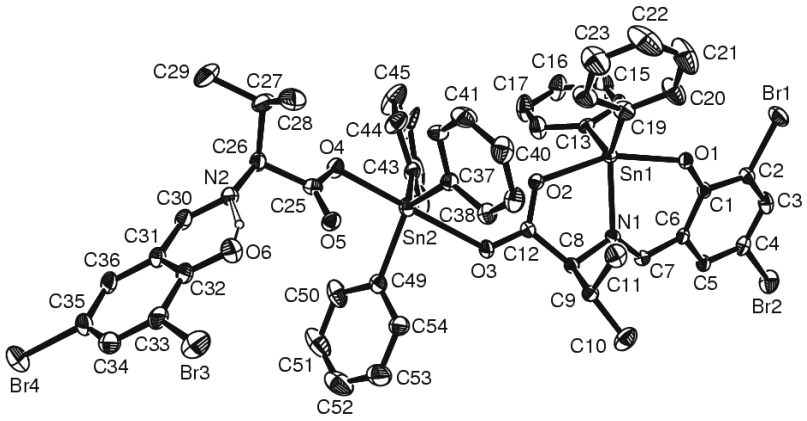
The results of *in vitro* antitumour assay against three human tumour cell lines of **2** were shown in **Table 1**. The compound belonged to the very efficient cytostatic agents and its *in vitro* antitumour activities were more active than that of *cis*-platin used in clinic.

Table 1 *In vitro* antitumour activity (IC_{50}, μmol L^{-1}) of **2** and *cis*-platin

Compound	HeLa	CoLo205	MCF-7
2	0.096±0.035	0.288±0.027	0.209±0.070

cis-platin	4.81±1.10	13.94±0.47	18.73±0.60

Figure 1 Molecular structure of complex **2**



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6. **2** is a yellow crystal with m.p.172-173 °C and yield is 63%. Intensity data of the complex were collected at 295 K on a Bruker Smart Apex CCD diffractometer. The crystal parameters were as follows: $C_{54}H_{48}Br_4N_2O_6Sn_2$, Mr = 1377.96, orthorhombic, space group $P2_12_12_1$, a = 11.7776(9), b =18.0548(14), c = 26.039(2) Å, V = 5537.0(8) Å^3, Z = 4, μ = 3.836 mm^{-1}, R_1 = 0.0515, wR_2 = 0.0942. Flack x is 0.001(8). The elemental analysis, IR, NMR (^{1}H and ^{13}C) spectra and the final coordinates, bond lengths and angles of **2** have been deposited in the editorial office of CCL.
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