Synthesis and crystal structure of the one-dimensional chain triphenyltin compound bridged by 5-chloro-6-hydroxynicotinic acid

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Abstract. Reaction of 5-chloro-6-hydroxynicotinic acid with \( \text{Ph}_3\text{SnCl} \) and sodium ethoxide in 1:1:1 stoichiometry yielded triphenyltin compound. This compound has been characterized by single crystal X-ray diffraction, elemental analysis, IR and \( ^1\text{H} \) NMR spectroscopy. In the molecular structure of the title compound, the tin atoms are five-coordinated in a distorted trigonal bipyramidal geometry. The resulting structure is 1D linear polymer through an interaction between the O atoms of phenolic hydroxide and tin atoms of an adjacent molecule. The compound exhibit high antitumor activity.

1. Introduction

Organotin compounds are widely used as fungicides, biocides and in industry as homogeneous catalysts[1-3]. Recently, pharmaceutical properties of organotin esters of carboxylic acids have been investigated for their antitumour activity[4-7]. Many triphenyltin compounds with ketocarboxylic and hydroxyarylcarboxylic acids and many other N and O containing derivatives of carboxylic acids display high antitumor activities. However triphenyltin ester 5-chloro-6-hydroxynicotinic acid were not investigated. In order to continue exploring relationships between the biological activity and structure, We choose another ligand: 5-chloro-6-hydroxynicotinic acid. This carboxylic acid is interesting because of its potential multidentate coordinate possibilities[8].

2. Experimental

2.1. Materials and measurements

Triphenyltin chloride and 5-Cl-6-OH-C\(_2\)H\(_5\)NCO\(_2\)H were purchased from Aldrich. Analytical grade solvents were dried before use. The melting points were obtained with Kofler micromelting point apparatus and are uncorrected. Infrared-spectra (KBr pellets) were recorded on a Nicolet-460 spectrophotometer. \(^1\text{H} \) NMR spectra were taken on a Varian Mercury Plus 400 spectrometer. The chemical shifts were given in ppm in CDCl\(_3\) solvent. Carbon, hydrogen and nitrogen analyses were performed on a PE-2400II apparatus.

2.2. Synthesis of the title compound

The reaction was carried out under \( \text{N}_2 \) by use of standard Schlenk techniques. The 5-Cl-6-OH-C\(_2\)H\(_5\)NCO\(_2\)H (0.521 g, 3 mmol) was added to the solution of dry C\(_2\)H\(_5\)OH (50mL) together with C\(_2\)H\(_5\)ONa (0.214 g, 3 mmol), and the mixture was stirred for 0.5 h. \( \text{Ph}_3\text{SnCl} \) (1.165 g, 3 mmol) was...
then added to the mixture, and the reaction was allowed to continue for 16 h at 45°C. After cooling
down to 20°C and then filtered. The filtrate was gradually removed by evaporation under vacuum until
solid product was obtained. Colorless block-like crystal was recrystallized from 1-propanol alcohol.
Yield 68 %, m.p. 216-217°C. ¹H NMR (CDCl₃, 400 MHz): δ 8.88(1H, d, 2-pyridine-H), 7.99(1H, d, 4-
pyridine-H), 6.78-7.37(15H, m, Ph-H), 0.91-3.51(7H, m, CH₃CH₂CH₃). IR (KBr)(cm⁻¹): vₛ(CO), 1643; vₐ(COO), 1355; v(Sn-CN), 569; v(Sn-O), 458. Anal. Caled for C₂₇H₂₅ClNO₅Sn: C 55.75, H 4.33, N 2.41. found: C 57.77, H 4.36, N 2.42.

2.3. Determination of the crystal structure
A single crystal having approximate dimensions of 0.23mm × 0.16mm × 0.12mm was mounted in a
glass capillary. All measurements were made on a Bruker Smart-II diffractometer equipped with a
graphite-monochromated Mo-Kα (λ=0.71073 Å) radiation at 298(2) K by using the φ-ω scan technique.
For crystal of the compound, a total of 6290 reflections were collected in the range of
1.96<θ<25.01° and 3672 (Rint=0.0269) were independent. The structure was solved by direct methods
and difference Fourier map with SHELX/L-97 program[9], and refined by full-matrix least-squares
methods on F². All non-hydrogen atoms were refined anisotropically, and the hydrogen atoms were
located at the calculated positions and refined isotropically. Crystallographic data are listed in Table 1.
The selected bond lengths and angles for compound 1 are given in Table 2.

| Molecular formula | C₂₇H₂₅ClNO₅Sn | Z   | 4 |
|-------------------|----------------|-----|---|
| Formula weight    | 581.62         |     |   |
| Crystal system    | Monoclinic     |     |   |
| Space group       | Cc             |     |   |
| a/Å               | 16.436(6)      |     |   |
| b/Å               | 14.562(5)      |     |   |
| c/Å               | 11.466(4)      |     |   |
| β (°)             | 115.181(4)     |     |   |
| V (Å³)            | 2483.9(15)     |     |   |

| Bond lengths [Å]  | Bond angles [°] |
|-------------------|-----------------|
| Sn1-C19           | 2.103(6)        | C19-Sn1-C7      | 116.8(3) |
| Sn1-C7            | 2.130(4)        | C19-Sn1-C13     | 122.3(4) |
| Sn1-C13           | 2.133(9)        | C7-Sn1-C13      | 116.8(4) |
| Sn1-O1            | 2.138(6)        | C19-Sn1-O1      | 104.6(3) |
| Sn1-O3#1          | 2.662(8)        | C7-Sn1-O1       | 89.4(3)  |
| O1-C1             | 1.298(5)        | C13-Sn1-O1      | 95.7(3)  |
| O2-C1             | 1.231(9)        | C19-Sn1-O3#1    | 83.9(3)  |
| C1-C3             | 1.449(11)       | C7-Sn1-O3#1     | 81.9(3)  |
| C2-C3             | 1.378(11)       | C13-Sn1-O3#1    | 83.9(3)  |
| O3-C6             | 1.230(9)        | O1-Sn1-O3#1     | 169.9(2) |

Symmetry transformations used to generate equivalent atoms:
#1: x-1/2, y+1/2, z.

3. Results and discussion

3.1. IR Spectra
The assignment of IR bands of the title compound has been determined by comparison with the other
two compounds: 5-Cl-6-OH-C₆H₃NCO₂H and Ph₃SnCl. The broad absorption at 3000-2500 cm⁻¹ in
free acid due to –OH group, which is absent from the spectra of the coordination of carboxylate group, showing the deprotonation of the -COOH group during the reactions. Asymmetric stretching vibration peak of carboxyl ($v_{as}$($COO$)) is located at 1643 cm$^{-1}$ and the corresponding symmetric one ($v_s$($COO$)) at 1355 cm$^{-1}$. The magnitude of $\Delta v [v_{as}(COO) - v_s(COO)]$ is above 288 cm$^{-1}$, thus indicate that the carboxylate ligand function as monodentate ligand under the conditions employed[10]. The bonds at 458 cm$^{-1}$ and 569 cm$^{-1}$ can be assigned to $v$ (Sn-O) and $v$(Sn-C) vibration, respectively.

3.2. $^1$HNMR Spectra
The chemical shifts of the $^1$H of pyridine ring exhibit signals at region 7.99-8.88 ppm as multiplet, which are considerably shifted towards higher frequencies with respect to that corresponding free carboxylate group[11]. The $^1$H NMR spectra of the compound show that the chemical shifts of the protons on the phenyl group exhibit signals at 6.78-7.37 ppm as multiplet.

3.3. CrystalStructure
The molecular structure and One-dimensional chain structure are illustrated in Figure 1 and Figure 2, respectively.

![Figure 1](image1.png)

**Figure 1.** Molecular structural unit of the compound (probability of ellipsoid is 30%, hydrogen atoms have been omitted for clarity).

![Figure 2](image2.png)

**Figure 2.** One-dimensional chain structure of the compound.

As can be seen from Figures 1 and 2, the crystal structure of the compound possess unequivocally polymeric structure, but these structures are differ from compounds [[PhCH$_2$]$\text{SnO}_2$]$\text{CCH}_3$][12] and [Ph$_3$Sn(OCOC$_5$H$_4$NO)$_n$]*3(CHC$_2$Cl)$_2$][13]. Each tin atom is five-coordinated with three phenyl carbon atoms and two oxygen atoms one from carboxylate and other from the phenolic hydroxide.

The intramolecular Sn1-O1 bond length of 2.138(6) Å is longer than $^\circ$C$_3$H$_5$SnCl$_3$(C$_{10}$H$_7$N$_2$O$_2$S)(2.053 nm)[14], but is shorter than those of [Ph$_3$Sn(OCOC$_5$H$_4$NO)$_n$]$_n$(0.2174 Å)[15]. The Sn1-O3#1 bond length is 2.662(8) Å, longer than the sum of the covalent radii of Sn and O (2.07 Å), but well within the sum of the Van der waals’ radii for Sn and O of 2.80 Å, so it should be considered as a bonding interaction. The angles of C13-Sn1-O1 95.7(3)$^\circ$, C19-Sn1-O1 104.6(3)$^\circ$, are greater than 90$^\circ$;but the angles of C19-Sn1-O3#1 83.9(3)$^\circ$, C7-Sn1-O3#1 81.9(3)$^\circ$ and C13-Sn1-O3#1 83.9(3)$^\circ$ are deviate from 90$^\circ$, So on the side of the Sn-O bond of the phenyl groups are moved away from carboxylate group. The sum of the C19-Sn1-C7 116.8(3)$^\circ$, C19-Sn1-C13 122.3(4)$^\circ$ and C7-Sn1-
C13 116.8(4)° bond angles is 355.9°, which shows that the atoms of Sn1, C7, C13 and C19 are not co-planar. The angle of O1-Sn1-O3#1 [169.9(2)°], deviate from the linear angle, for which the coordination at the tin atom is in a distorted trigonal bipyramidal polyhedron.

3.4. Antitumor activity

The antitumor activity was in vitro according to the SRB methods[16]. The compound was tested in vitro against to human hepatocellular carcinoma (SMMC-7721) and mouse pmh adenomaly (P388), which displayed quite high activity with inhibition value IC_{50} being 24, 43 ng/mL, respectively. In vitro biological assays suggest that the compound is still rather active against selected tumor cell lines, and the compound exhibit cytotoxic effects against the two cell lines varying in the order SMMC-7721 > P388. The compound displayed the high in vitro antitumor activities, which were more active than clinically widely used cisplatin did.

In summary, a one-dimensional linear polymer has been obtained by the reaction of chlorotriphenyltin with 5-chloro-6-hydroxynicotinic acid. The compound exhibit high antitumor activity. The synthesis of the compound confirms that it is crucial to choose an appropriate carboxylate ligand for the formation of one-dimensional linear polymers. Further studies on antitumor activity of the compound are under way.

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