Comparison of antibacterial activities of di- and tri-tin(IV) carboxylate complexes
Mohammad Yousefi 1+, Fatemeh Tavakolinia 1 and S.Mehdi Hassanzadeh2
1 Department of Chemistry, Shahr-E-Rey Branch, Islamic Azad University, Tehran, Iran
2 Pasteur Institute of Iran, 69, Pasteur Ave, Tehran, Iran.

Abstract. Two organotin(IV) carboxylates, [Me2Sn(pac)]4 (1), and [Ph3Sn(pac)] (2) (where (pac) is phenyl acetylene carboxylic acid), have been synthesized. Both complexes characterized by FT-IR, 1H NMR, 13C NMR and 119Sn NMR. In addition, the structure of complex 1 was determined by X-Ray crystallography. Moreover, bioassay results showed that these complexes have good antibacterial activities, which among them diorganotin(IV) carboxylate has the higher activity.

Keywords: Organotin(IV) carboxylates, Phenyl acetylene carboxylic acid, Antibacterial.

1. Introduction
Since some organotin(IV) compounds were synthesized, they have attracted more and more attention in their characteristics, such as pharcic value, anti-tumor activity, and biological activity. In general, the biochemical activity of organotin compounds is influenced greatly by the structure of the molecule and the coordination number of the tin atom [1–3]. Among organotin(IV) complexes, organotin (IV) carboxylates show significant antifungal, antibacterial and antitumor activities [4–8] which is essentially related to the number and nature of the organic groups attached to the central Sn atom, however, the role of carboxylate ligand cannot be ignored [5]. Usually triorganotin(IV) compounds display a higher biological activity than their di- and monoorganotin(IV) analogues, which has been related to their ability to bind to proteins [9–11].

Research on new anti-fungal drug candidates is therefore very important since metal-based drugs might represent an alternative therapeutic route. Tin could be a metal of choice, considering that organotin and in particular organotin carboxylate compounds display anti-microbial properties [12,13].

In this article we report the synthesis and spectroscopic characterization of two novel di and triorganotin carboxylates and study their antibacterial activities.

2. Experiment
2.1. Materials and measurements
In our study, triphenyltin(IV) chloride, dimethyltin chloride, and phenyl acetylene carboxylic acid were purchased from Merck and were used without further purification. The melting points were recorded using Branstead-Electro. FT-IR spectra were recorded using Bruker-Tensor 27 with KBr pellets ranging from 4000-400 cm⁻¹. Multinuclear NMR (1H, 13C and 119Sn) spectra were recorded at room temperatures in CDCl₃ on Bruker Advanced DRX-500 MHz.

2.2. Synthesis
2.2.1 Synthesis of tetrakis [ dimethyltin (IV) phenyl acetylene carboxylate](1)
The reaction was carried out by the interaction between of phenyl acetylene carboxylic acid (HL) with dimethyltin dichloride. HL was dissolved in dried methanol. Fresh sodium methoxide was prepared by dissolving equimolar sodium in methanol and adding to the mixture. The resulting mixture was then refluxed with constant stirring for 1 hour under Argon atmosphere at 60°C. A hot methanolic solution of Me₂SnCl₂ was then added to the solution of sodium salt of the ligand in 1:2 molar ratios. The resulting mixture was further refluxed with constant stirring for another 4-5 hour, and then filtered to remove the formed sodium chloride. The product was obtained from the slow evaporation of filtrate. M.p. 200-202 °C. FT-IR (Cm⁻¹): 1634 ν(COC)asym, 1384 ν(COC)sym, 1572 ν(COC)asym, 1215 ν(COC)sym, 2252 ν(C=≡C), 598 ν(Sn-C), 507 ν(Sn-O), 1H-NMR (CDCl₃, ppm): 1.04 (s, CH₃, 3H), 1.14 (s, CH₃, 3H), 7.38-7.62 (m, HAr, 5H). 13C-NMR (CDCl₃, ppm): 5.79 (CH₃), 10.14 (CH₃), 83.20, 84.23 (C=≡C), 120.22 (Cmeta), 128.54 (Cpara), 130.20 (Cortho), 132.95 (Cipso), 158.15 (C=O), ¹¹⁹Sn (CDCl₃, ppm): -180.50, -157.60.

2.2.2 Synthesis of triphenyltin(IV) (phenyl acetylene carboxylate) (2)

Compound 2 was prepared by the interaction between of phenyl acetylene carboxylic acid (HL) with triphenyltin chloride. HL was dissolved in dried methanol. Fresh sodium methoxide was prepared by dissolving equimolar sodium in methanol and adding to the mixture. The resulting mixture was then refluxed with constant stirring for 1 hour under Argon atmosphere at 70°C. A hot methanolic solution of ph₃SnCl was then added to the solution of sodium salt of the ligand in 1:1 molar ratios. The resulting mixture was further refluxed with constant stirring for another 5-6 hour, and then filtered to remove the formed sodium chloride. The product was obtained from the slow evaporation of filtrate. M.p. 166 °C. FT-IR (Cm⁻¹): 1522 ν(COC)asym, 1382 ν(COC)sym, 2214 ν(C=≡C), 533 ν(Sn-C), 454 ν(Sn-O), 1H-NMR (CDCl₃, ppm), 7.29-7.83 (m, HAr, 5H). 13C-NMR (CDCl₃, ppm): 81.46, 86.26 (C=≡C), 120.30-137.48 (8, CAr), 159.81 (C=O), ¹¹⁹Sn (CDCl₃, ppm): -300.05.

2.3. Crystal structure of complex [Me₂Sn(pac)]₄

The molecular structure of complex is shown in Fig.1. whereas the crystal data is listed in Table 1.

![Fig. 1. The molecular structure of complex [Me₂Sn(pac)]₄](image)

<table>
<thead>
<tr>
<th>Empirical formula</th>
<th>C₄₄H₄₄O₁₀Sn₄</th>
</tr>
</thead>
<tbody>
<tr>
<td>Formula weight</td>
<td>1207.55</td>
</tr>
<tr>
<td>Crystal system</td>
<td>Triclinic</td>
</tr>
<tr>
<td>Space group</td>
<td>P</td>
</tr>
<tr>
<td>Crystal size</td>
<td>0.42 * 0.34 * 0.26</td>
</tr>
<tr>
<td>Unit cell dimensions</td>
<td></td>
</tr>
</tbody>
</table>

Table 1. Crystal Data and Structure Refinement parameters for compound [Me₂Sn(pac)]₄

247
a (Å) 7.9751(7)
b (Å) 11.2094(10)
c (Å) 13.6554(12)
α (˚) 85.302(2)
β (˚) 82.003(2)
γ (˚) 70.176(2)
θ range for data collection (˚) 2.41-27.50
V (Å³) 1136.44
Z 4
ρcal (g Cm⁻¹) 1.764
F(000) 588
Temperature (K) 173(2)
Index ranges -10<=h<=10; -12<=k<=14; -17<=l<=13
Unique data [Rint] 5167(0.0678)
Goodness of fit on F² 1.020
Final R indices [I>2σ(I)] R 1=0.0447, wR2=0.1149
R indices (all data) R 1=0.0524, wR2=0.1220

2.4. Antibacterial activity test

For antibacterial study, Agar well diffusion method was used. Duplicates of pure cultures of selected ATCC bacteria (Table 2) on Mueller Hinton agar were prepared for each compound. Solid media were punched to form 7mm diameter wells. Diluted compounds in DMSO at concentrations of 0.1, 1.0, 2.0 and 10 mg/ml and reference drugs at standard concentration all in amount of 100 µl /well were tested against each strain. Imipinem, Clindamycin, Cefixime and Rifampicin as antibacterial reference drugs were used simultaneously. Inhibition zones were measured after the plates were incubated for 3-7 days at 37°C.

Table 2. Antibacterial bioassay results for complexes 1 and 2 (inhibition zone in mm)

<table>
<thead>
<tr>
<th>Bacterium</th>
<th>[Ph₃Sn(pac)]⁺ (2)</th>
<th>[Me₂Sn(pac)]⁺ (1)</th>
<th>Standard drugs³</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>MIC</td>
<td>0.1</td>
<td>1.0</td>
</tr>
<tr>
<td>Escherichia coli</td>
<td>11229</td>
<td>23</td>
<td>28</td>
</tr>
<tr>
<td>Pseudomonas aeruginosa</td>
<td>15442</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Staphylococcus aureus</td>
<td>6538</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Mycobacterium Bovis</td>
<td>35737</td>
<td>28</td>
<td>32</td>
</tr>
</tbody>
</table>

³ Concentration: mg/mL of DMSO. Size of well: 7mm (diameter), dash indicates inactivity.

³ Standard drugs: I: Imipinem, C: Clindamycin, Cx: Cefixime. R: Rifampicin

3. Results and discussion

Reaction of Me₂SnCl₂/Ph₃SnCl with NaL in 1:2/1:1 molar ratio according to Scheme 1 led to formation of complex 1 and complex 2 respectively. However, tetra-nuclear tin complex with four bounded ligand was revealed by solving the crystal structure of compound 1, thus confirming interaction of 1:1 molar ratio of reactants. The white precipitate formed at the end of the reaction is due to the unreacted amount of NaL. Both complexes were white solids, stable in air and soluble in CHCl₃.

The information obtained from crystal data shows tetraneuclear tin carboxylate complex which has two kind of five and six coordinated tin atom with distorted trigonal bipyramidal and octahedral geometry respectively. In this structure two mode of monodentate and triple bridging coordination of carboxylate moiety are observed and in the central part of the structure the Sn₂O₂ cycle is formed. This complex has one of the most interesting structures that has been reported.

4. Antibacterial activity
As indicated in Table 2, both complexes showed antibacterial activity while the ligand was fully inactive. The complex 1 ([Me₂Sn(pac)]₄), in concentrations of 10 mg/ml showed fairly good activity against candidate gram positive and gram-negative bacteria as well as Mycobacterium bovis, comparable with reference drugs while in lower concentration equal to 1.0-2.0 mg/ml its activity was only detected against Pseudomonas and M. bovis. The complex of [Ph₃Sn(pac)] in concentrations higher than 0.1 mg/ml showed good activity against gram positive bacteria and M. bovis, but did not show any activity against gram-negative bacteria even in higher concentrations. These results indicate that in higher concentrations, Complex 1 has wider activity range than complex 2. M. bovis as a bacterium resistance to most of antibiotics showed a good sensitivity to both complexes in ranges used. Minimum inhibitory concentration (MIC) of both complexes are tabulated in Table 2. Achieved antibacterial test results were approximately in agreement with those published in [14]. It has been reported that diorganotin complex indicates more antibacterial activity.

5. Conclusion

The reaction between dimethyltin(IV) dichloride and triphenyltin(IV) chloride with sodium salt of phenyl acetylene carboxylic acid in dried methanol resulted in complexes with stoichiometries [Me₂Sn(pac)]₄ and [Ph₃Sn(pac)], respectively. The presence of bridging and monodentate carboxylate form of pac ligand produced a tetranuclear structure for complex 1 and was confirmed by single crystal X-ray diffraction. No antibacterial effect was observed for the ligand. Complex 1 was found to be more active against different strains of bacteria.

6. Acknowledgment

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7. References