Synthesis and Characterization of Organotin(IV) Complexes Derived of 3-(Dimethylamino)benzoic Acid: Cytotoxic Assay on Human Liver Carcinoma Cells (HepG2)

Yip-Foo Win, Siang-Guan Teoh, Tengku-Sifizul Tengku-Muhammad, Yasodha Sivasothy and Sie-Tiong Ha

Department of Chemical Science, Faculty of Science, University Tunku Abdul Rahman, Perak Campus, Jalan University, Bandar Barat, 31900 Kampar, Perak, Malaysia
School of Chemical Sciences, University Sains Malaysia, 11800 Minden Penang, Pulau Pinang, Malaysia
Department of Biological Sciences, University Malaysia Terengganu, 21030 Kuala Terengganu, Malaysia
Department of Chemistry, Faculty of Science, University Malaya, 50603, Kuala Lumpur, Malaysia

Abstract: Problem statement: Many studies have been carried out on organotin(IV) complexes derivative of carboxylate anions. However, the synthesis and characterization as well as the cytotoxic assay of organotin(IV) carboxylate derived of 3-(dimethylamino)benzoic acid have not been studied.

Approach: Organotin(IV) carboxylate complexes derivative of 3-(dimethylamino)benzoic acid, 3-[N(CH3)2]C6H4COOH have been successfully synthesized. Two types of diorganotin(IV) complexes, [3-[N(CH3)2]C6H4COO(R)2Sn]2O (R = methyl 1, butyl 3) and [3-[N(CH3)2]C6H4COO]2(C4H9)2Sn, 2 (monomer) as well as 3-[N(CH3)2]C6H4COO(C6H5)3Sn, 4 were successfully synthesized and obtained in solid state. The acid and complexes 1-4 obtained were characterized quantitatively using C, H, N and Sn elemental analysis as well as spectroscopic methods such as infrared (FTIR) and nuclear magnetic resonance (1H, 13C, 1H-13C HMQC and 119Sn NMR). In addition, complexes 1-4 obtained were screened for their cytotoxicity activity against HepG2 cells line.

Results: Infrared spectroscopy showed that the coordination took place via oxygen atoms from the carboxylate anions. This indicated that the carboxylate anion acts as monodentate ligand in complexes 2 and 4. However, for distannoxane dimer (complexes 1 and 3), the carboxylate anions are found to exhibit monodentate and bidentate manner. In 119Sn NMR solution study, the tin atoms of complexes 1-3 were five-coordinated and four-coordinated in complex 4. From the 119Sn NMR, the tin atom of complex 2 was five-coordinated, this might be upon dilution, the crystal lattice were broken up resulting the carboxylate anions assembly self-arrangement. Hence, one of the carboxylate anions was located close to the tin atoms and exhibited bidentate chelation while the other carboxylate anion exhibited monodentate chelation in complex 2. Conclusion: Pure complexes 1-4 have been successfully obtained and complex 4 possessed promising biological screening activity compared to the parent acid and complexes 1-3.

Key words: Organotin(IV) carboxylate, preparation, biological activity

INTRODUCTION

Organotin(IV) complexes are extensively studied due to the applications in industrial as well as biocidal properties (Molloy et al., 1984; Willem et al., 1997; Gielen et al., 2000). Numerous studies on organotin(IV) complexes have been carried out in order to study its biological properties against bacterial, fungus and cancer cells line (Teoh et al., 1997; Novelli et al., 1999; Gielen et al., 2000; Crouse et al., 2004). Moreover, the biological activity of organotin(IV) carboxylate complexes are greatly influenced by the structure of the molecule as well as the coordination number of the tin moiety (Parulekar et al., 1990). The search for...
organometallic compounds as a new alternative drug in combating human cancers has been initiated due to certain side-effects of cis-platin and carboplatin as antitumour drugs (Khan et al., 2000). Hence, organotin(IV) compounds with general formula \( R_2SnX_2 \), \( R_2SnL_n \), or \( R_2SnL_2 \) (R = alkyl, aryl or phenyl, X = halogen, L = coordinated ligands and n = 1 or 2) belong to the largest group including organotin(IV) carboxylate complexes selected for the anti cancer screening (Gielens et al., 2000; Ronconi et al., 2002; Pruchnik et al., 2003). In fact, organotin(IV) complexes are extensively studied due to its coordination geometries as well as structural diversity (monomer, dimeric, hexameric and oligomeric) (Zhang et al., 2005; Win et al., 2007a; 2008a; Amini et al., 2009). As part of our interest and research on organotin(IV) work, we have synthesized and characterized organotin(IV) complexes derived of 3-(dimethylamino)benzoic acid. In addition, the cytotoxic assay of the complexes obtained was screened against human liver carcinoma cells, HepG2 and the results are reported herein.

**MATERIALS AND METHODS**

**General and instrumental:** Triphenyltin(IV) hydroxide, \( Ph_3SnOH \) was purchased from Aldrich Chemical. Dibutyltin(IV) oxide, \( Bu_2SnO \), dimethyltin(IV) dichloride, \( Me_2SnCl_2 \) and 3-(dimethylamino)benzoic acid, \( 3-[N(CH_3)2]C_6H_4COOH \) were obtained from Fluka Chemika. All reagents and solvents were purchased commercially and used without any further purification. Infrared spectra were recorded using a Perkin-Elmer System 2000 FTIR Spectrophotometer as a KBr disc in the frequency range of 4000-400 cm\(^{-1}\). The spectra for \( ^1H \) and \( ^119Sn \) NMR were recorded on a Bruker AC-P 400 MHz FTNMR Spectrometer and \( ^13C \) NMR was recorded on a Bruker AC-P 300MHz FTNMR Spectrometer using deuterated CDC\(_13\) as the solvent and tetramethylsilane, TMS as the internal standard. Elemental C, H and N analyses were carried out on a Perkin-Elmer 2400 CHN Elemental Analyzer. Tin was determined gravimetrically by igniting a known quantity of each complex to SnO\(_2\). The melting points were determined in an open capillary and were uncorrected.

**In vitro cytotoxic assay:** The in vitro cytotoxic assay was carried out on human liver carcinoma cells line, HepG2. The cells were maintained in Eagle’s Minimum Essential Medium (MEM) supplemented with 2 mM of L-glutamine, 1 mM of sodium pyruvate, 0.1 mM of non-essential amino acid, 1.5 μg mL\(^{-1}\) sodium bicarbonate, 100 IU mL\(^{-1}\) penicillin and 100 μg mL\(^{-1}\) streptomycin. The cytotoxicity assay was determined using the microtitration 3-(4, 5-dimethylthiazol-2-yl)-2, 5-diphenyltetrazolium bromide (MTT) assay (Mosmann, 1983). The assay of each concentration for each compound was performed in triplicate. The fraction of surviving cells was measured relative to the untreated cell population by measuring the absorbance values at 570 nm with reference at 630 nm using an ELISA microplate reader (Bio Tek EL 340, USA). Cytotoxicity was expressed as fifty percent cytotoxic dose (IC\(_{50}\)), i.e., the concentration causing 50% inhibition of cell growth with reference to the control (untreated cells). The IC\(_{50}\) and the S.E.M. (standard error of the mean) were determined using Probit Analysis (SPSS, version 12.0.1).

**Preparation of sodium salt and dimethyltin(IV) oxide, \( Me_3SnO \):** The sodium salt of the acid was obtained by heating under reflux a 1:1 molar mixture of sodium hydroxide, \( NaOH (0.12 \ g, 3 \ mmole) \) and 3-(dimethylamino)benzoic acid, \( 3-[N(CH_3)2]C_6H_4COOH (0.50 \ g, 3 \ mmole) \) in ethanol (50 mL) for two hours. After a few days, white precipitates were obtained. Dimethyltin(IV) dichloride, \( Me_2SnCl_2 \) was dissolve in distilled water and stirred overnight which later gave colorless solution. Ammonia solution (60%) was added into the colorless solution and finally fine white precipitates were obtained, filtered and dried in oven (60°C) for a day.

**Preparation of complexes:**

\[
\text{Bis}[3-(\text{dimethylamino})\text{benzoato}]\text{tetramethyldistannoxane(IV) dimer, } [\{3-[N(CH_3)2]C_6H_4COO(CH_3)2Sn\}2]2 (1)
\]

Complex 1 was obtained by heating under reflux a 1:2 molar mixture of dimethyltin(IV) oxide (0.49 g, 3 mmole) and 3-(dimethylamino)benzoic acid (0.99 g, 6 mmole) in methanol (50 mL) for two hours. A clear brown transparent solution was isolated by filtration and kept in a bottle. After few days, brown solids (0.59 g, 61.3% yield) were collected.

\[
\text{Bis}[3-(\text{dimethylamino})\text{benzoato}]\text{dibutyltin(IV), } \\
\{3-[N(CH_3)2]C_6H_4COO\}2(C_4H_9)2Sn (2)
\]

This complex was obtained by heating under reflux a 1:2 molar mixture of dibutyltin(IV)oxide, (0.75 g, 3 mmole) and 3-(dimethylamino)benzoic acid, (0.99 g, 6 mmole) in acetonitrile (60 mL) for four hours. A clear brown solution was separated by filtration and kept in a...
bottle. After two weeks, some brown crystals (1.31 g, 74.0% yield) were collected.

Bis[3-(dimethylamino)benzoato]tetrabutyldistannoxane (IV) dimer, [{3-[N(CH3)2]C6H4COO(C4H9)2Sn]2O}2 (3)

This title complex was prepared by similar method to those described for complex 1, except substituting with Bu2SnO and the reaction was heating under reflux for three hours. After five days, brown crystals (2.14 g, 66.1% yield) were collected.

3-(dimethylamino)benzoatotriphenyltin(IV), 3-[N(CH3)2]C6H4COO(C6H5)3Sn (4)

Complex 4 was prepared by heating under reflux a 1:1 molar mixture of triphenyltin(IV) hydroxide (1.10 g, 3 mmole) and 3-(dimethylamino)benzoic acid (0.50 g, 3 mmole) in acetonitrile (50 mL) for two hours. Clear brown solution was isolated by filtration and kept in a bottle. After eight days, brown crystals (1.01 g, 65.7% yield) were collected.

RESULTS

Physical and elemental analysis: An outline of the proposed structure for complexes 1-4 are depicted in Fig. 1. The melting points and elemental analytical data of complexes 1-4 are given in Table 1.

Structural and cytotoxic assay: The characteristic infrared absorption frequencies (cm−1) and assignments of important absorption bands of the acid, sodium salt and complexes 1-4 are listed in Table 2. The 1H NMR spectral data of complexes 1-4 are summarized in Table 3, 13C and 119Sn NMR data are listed in Table 4. From the spectroscopy methods, the structure of complexes 1-4 are characterized and the cytotoxic activity of complexes 1-4 are given in Table 5.

| Complexes | Melting points | C    | H    | N    | Sn   |
|-----------|----------------|------|------|------|------|
| 1         | 246.3-247.8    | 41.11 (41.17) | 5.02 (5.03) | 4.23 (4.36) | 36.50 (36.98) |
| 2         | 113.3-114.1    | 55.63 (55.64) | 6.77 (6.82) | 4.90 (4.99) | 20.75 (21.15) |
| 3         | 137.3-138.2    | 50.62 (50.40) | 6.52 (6.97) | 3.44 (3.46) | 23.53 (29.30) |
| 4         | 140.2-141.5    | 63.05 (63.07) | 4.91 (4.90) | 2.67 (2.72) | 23.00 (23.08) |

Calculated value are given in parentheses.

![Fig. 1: The proposed structure for complexes 1-4](image-url)
### Table 2: Important infrared data of acid, salt and complexes 1-4

| Complexes | ν(OH) | ν(COO)as | ν(COO)s | Δν | ν(Sn-O) | ν(O-Sn-O)/ν(Sn-O-Sn) | ν(Sn-C) |
|-----------|-------|---------|---------|----|---------|----------------------|---------|
| Acid      | 2885-2544 | 1677 | 1360 | 317 | -       | -                    | -       |
| Salt      | -     | 1569 | 1387 | 2182 | -       | -                    | -       |
| 1         | -     | 1597 | 1333 | 264  | 426     | 658                  | 575     |
| 2         | -     | 1608 | 1360 | 248  | 459     | 679                  | 551     |
| 3         | -     | 1595 | 1330 | 265  | 420     | 635                  | 572     |
| 4         | -     | 1625 | 1322 | 303  | 445     | -                    | -       |

Δν = ν(COO)as − ν(COO)s.

### Table 3: ¹H NMR data of acid and complexes 1-4

| Compounds | Benzene | Amino-N(CH₃)₂ | Sn-R (R = Me, Bu and Ph) |
|-----------|---------|---------------|-------------------------|
| Acid      | 7.00 (d, 9.3 Hz, 1H) H4 | 3.03 (s, 6H) Hy | -                       |
| 1         | 7.35 (t, 8.1 Hz, 1H) H5 | 0.97 (s, 12H) Ha | 1.06 (s, 12H) Ha |
| 2         | 6.94 (dd, 2.4 Hz, 7.9 Hz, 2H) H4 | 0.88 (t, 7.3 Hz, 6H) Hd | 1.14-1.44 *(m, 4H) Hc |
| 3         | 7.34 (t, 1.8 Hz, 2H) H5 | 1.32-1.45 *(m, 16H) Hc | 1.49-1.53 *(m, 16H) Hc |
| 4         | 6.87 (dd, 2.7 Hz, 8.3 Hz, 1H) H4 | 2.95 (s, 6H) Hy | 7.42-7.49 *(m, 9H) Hm & Hp |

s: Singlet; d: Doublet; t: Triplet; dd: Doublet of doublet; m: Multiplet; o: Ortho; m: Meta; p: Para; Coupling constant: Hz, *: overlap

### Table 4: ¹¹⁹Sn and ¹³C NMR data of complexes 1-4

| Compounds | ¹¹⁹Sn | Benzene | Amino N(CH₃)₂ | Sn-R (R = Me, Bu and Ph) | ¹³C/¹¹⁹Sn (n = 1, 2, 3 and 4) | COO |
|-----------|-------|---------|---------------|-------------------------|------------------------------|-----|
| Acid      | -     | 173.29 | 40.97 (Cy)    | -                       | -                            |     |
| 1         | -178.82 | 114.11 (C2), 118.06 (C4), 130.76 (C5), 130.46 (C6), 150.87 (C3) | 40.89 (Cy) | 7.40 *(J = 779.3 Hz) (Ca) | 173.8    |
| 2         | -156.4 | 113.70 (C2), 116.30 (C4), 130.76 (C5), 130.46 (C6), 150.87 (C3) | 41.02 (Cy) | 9.40 *(J = 795.3 Hz) (Ca) | 26.82 (C2), 27.11 (C3) |
| 3         | -195.35 | 114.42 (C2), 117.40 (C4), 130.76 (C5), 130.46 (C6), 150.87 (C3) | 41.09 (Cy) | 13.98 (Cd), 25.85 (Cb) | 13.98 (Cd), 25.85 (Cb) |
| 4         | -114.19 | 119.02 (C6), 129.36 (C5), 130.76 (C5), 130.46 (C6), 150.87 (C3) | 41.09 (Cy) | 14.04 (Cd), 26.82 (C2), 27.11 (C3) | 26.84 (C2), 27.26 (C2), 27.96 (Cb), 28.24 (C2), 29.06 (Ca), 30.99 (Ca) |

Chemical shift (ppm)

![Diagram](image-url)
Table 5: Cytotoxicity assays, IC₅₀ of acid and complexes 1-4

| Complexes     | IC₅₀ (µg mL⁻¹)       |
|---------------|----------------------|
| Acid          | Inactive (start at 1.0) |
| 1             | 0.60±0.033           |
| 3             | 0.54±0.027           |
| 4             | 0.15±0.010           |
| Vincristine sulphate | 0.042±0.013      |

IC₅₀ (µg mL⁻¹): The concentration that yields 50% inhibition of the cell compared with untreated control. The cytotoxicity values are expressed as mean ± S.E.M. from the triplicate. Reference drug = Vincristine sulphate.

**DISCUSSION**

In this study, complexes 1-4 derived of 3-[N(CH₃)₂]C₆H₄COOH have been obtained in solid state. Complexes 2 and 4 were obtained as single brown crystals and the X-ray crystal structure of both complexes have been reported (Win et al., 2007b; 2008b). Elemental analysis C, H, N and Sn data obtained were in agreement with the predicted formula derived of 3-[N(CH₃)₂]C₆H₄COOH. Complexes 1-4 gave a sharp melting points which indicate the isolation of fairly pure complexes.

The ν(O-H) bands which appeared in the range 2885-2544 cm⁻¹ for the acid, were absent in the infrared spectra of salt and complexes 1-4 also showed the deprotonation and coordination of the carboxylate anion. The infrared spectra of complexes 1-4 revealed that the ν(COO)ₙ was shifted to a lower wave length number compared to the parent acid which signify that the coordination took place via the oxygen atoms of the carboxylate anion. Complexes 1-4 showed the ν(COO)ₙ and ν(COO)ₙ⁻ are in the range of 1605-1579 and 1394-1347 cm⁻¹ respectively.

The magnitude of Δν = [ν(COO)ₙ⁻-ν(COO)ₙ] is a useful indicator in the correlation of the coordination modes of the carboxylate anion to the tin atoms. Sandhu and Verma (1987) have shown that the Δν value of complexes greater by 65-90 cm⁻¹ than in their sodium salts indicates either asymmetric or monodentate bonding of the carboxylate group to tin(IV) atom. Complex 2 was isolated as a monomer type and its Δν value indicated that the carboxylate anions were bonded to tin atom moiety in a monodentate mode. Two Δν values for the organodistannoxane dimer type complexes indicate that the carboxylate anions were coordinated to the tin atom moiety in either a monodentate or bidentate manner (Win et al., 2008a). For complex 1, the first Δν value (264 cm⁻¹) was larger than the Δν value of the sodium salt while the second Δν value (176 cm⁻¹) was comparable to the sodium salt (182 cm⁻¹). Hence a pair of carboxylate anions bonded to tin atom in monodentate manner and another pair of carboxylate anions bonded to tin atom in bidentate manner respectively resulting the tin atoms in complex 1 exhibited distorted trigonal bipyramid geometry. Complex 3 was also isolated as bulky organodistannoxane dimer types and were found to be similar to complex 1. Moreover, for complexes derived from triphenyltin(IV) carboxylate, Δν below 200 cm⁻¹ would be expected for bridging or chelating carboxylates, but greater than 200 cm⁻¹ for the monodentate bonding carboxylate anions (Yeap and Teoh, 2003). Hence, carboxylate anion in complex 4 would be expected to bond to the tin atom in monodentate manner since the Δν above 200 cm⁻¹.

Further evidence for the coordination to Sn via O atoms was revealed by the presence of the Sn-O stretching bands in the spectra of complexes 1-4 in the region of 459-420 cm⁻¹. The presence of a medium absorption band at 679-635 cm⁻¹ in the infrared spectra of complex 1-3 was ascribed to ν(Sn-O-Sn)/ν(O-Sn-O) which further supported the coordination of the oxygen atoms to the tin atom moiety (Gielen et al., 1989; Win et al., 2008a). Generally, ν(Sn-O-Sn) band was fit in the assignation of additional Sn-O bonding in organodistannoxane dimer type since the centrosymmetry of the complexes were occupied by Sn₂O₂ (complexes 1 and 3).

The ¹H NMR spectra of complexes 1-4 revealed similarities to their parent acid, 3-(dimethylamino)benzoic acid. The ¹H NMR spectrum of 3-(dimethylamino)benzoic acid exhibited three sets of signals at downfield region [7.00 ppm, 7.35 ppm and 7.54 ppm] with integration values of 1:1:2 which was also observed in the ¹H NMR spectra of complexes 1-4 arising from the aromatic protons of the benzene ring. The upfield regions of the ¹H NMR spectra of the complexes 1-3 showed the signal of the methyl and butyl protons in the range of 0.97-1.11 and 0.88-1.78 ppm respectively. Complexes 2 and 3 consisted of dibutyl groups (monomer and distannoxane dimer types) and found in the upfield region in the NMR spectra. Theoretically, the butyl groups should exhibit four signals corresponding to the protons of butyl groups, with multiplicities of triplet, sextet, quintet and triplet with integration values of 3:2:2:2, respectively. However, these complexes only exhibited three sets of signals in the range of 0.81-0.93 ppm (CH₃, triplet or multiplet), 1.32-1.45 ppm (CH₂, multiplet) and 1.69-1.84 ppm (CH₃, multiplet) respectively, due to the methylene protons having very similar environment causing their signals to overlap with each other in the ¹H NMR spectra (Danish et al.,...
The formation of the complexes were evident from the $\delta$(COO) value in the $^{13}$C NMR spectra. All the complexes exhibited a $\delta$(COO) signal in the range of 173.80-177.25 ppm. The $^{13}$C NMR spectra of complexes 1-4 showed that the chemical shift of the $\delta$(COO) signal in each complex was shifted downfield compared to that of their parent acids (173.29 ppm), indicating the participation of the carboxylate anions in the coordination to the tin(IV) atom (Win et al., 2007b; 2008a). The occurrence of six resonances in the range of 114.11-150.90 ppm and a single resonance in the range of 40.89-41.09 ppm in the $^{13}$C NMR spectra of the complexes and acid defined as benzene and -methylamino carbons signals respectively. Complex 1 (organodistannoxane dimer type) exhibited two sharp signals at 7.40 and 9.40 ppm indicating the presence of the methyl groups in the SnMe$_2$ moiety with $^3$(119Sn) values are summarized in Table 4. For triphenyltin(IV) NMR solution study, the tin atom of complex 1 showed that the chemical shift of the $\delta$(119Sn)(ipso) at 139.01 ppm indicative of a four-coordinated Sn atom (Holecek et al., 1983a; 1983b). From the $^{119}$Sn NMR solution study, the tin atom of complex 2 was five-coordinated (predominantly). Moreover, based on the infrared spectroscopy and single crystal X-ray structure determination, complex 2 was pure and the tin atom was four-coordinated and existed in a distorted tetrahedral geometry (Win et al., 2007b). This might be upon dilution, the crystal lattice were broken up resulting the carboxylate anions assembly self-arrangement (in dynamic state). Hence, one of the carboxylate anions was located close to the tin atoms and exhibited bidentate chelation while the other carboxylate anion exhibited monodentate chelation resulting five-coordinated tin atom in complex 2.

The IC$_{50}$ values for the acid and complexes 1-4 are given in Table 5. From the data in Table 5, it was found that 3-(dimethylamino)benzoic acid and complex 1 are inactive against HepG2 cells compared to complexes 2-4. Complex 4 showed a significant cytotoxic activity with a lower IC$_{50}$ value of 0.153 $\mu$g mL$^{-1}$ compared to complexes 2 (0.602 $\mu$g mL$^{-1}$) and 3 (0.541 $\mu$g mL$^{-1}$). This was due to complex 4 was derived from triphenyltin(IV) (triorganotin) which is more active compared to the diorganotin(IV) derivatives (complexes 1-3). In addition, complex 4 existed as monomer and the tin moiety was four-coordinated with distorted tetrahedral geometry consequently enhanced the cytotoxic activity (Ashfaq et al., 2004). Hence the biological activities of organotin(IV) obtained in this present study could be arranged as: Triorganotin(IV) > diorganotin(IV).

**CONCLUSION**

Complexes 1-4 derivative of 3-(dimethylamino)benzoic acid have been successfully synthesized and characterized. Elemental analysis C, H,
N and Sn data obtained were in agreement with the predicted formula. Results of the infrared and NMR spectroscopy on the acid and complexes showed that the coordination took place via oxygen atoms from the carboxylate group. As a result, in solid and liquid state, the tin atoms of complexes 1 and 3 are five-coordinated whereas four-coordinated in complex 4. With the exceptional case, the tin atom in complex 2 is four-coordinated in solid state and exhibited five-coordinated in solution which may be attributed from the dynamic stage and self-rearrangement of one carboxylate anion. Based on the cytotoxic activity, complex 4 showed significant cytotoxic activity compared to complexes 1-3 but lower compared to reference drug and believed to possess a significant role in the medicinal area in the future.

ACKNOWLEDGEMENT

We would like to thank University Tunku Abdul Rahman and University Sains Malaysia and for financial support and technical assistance.

REFERENCES

Amini, M.M., A. Azadmeher, V. Alijani, H.R. Khavazi and T. Hajiaashrafi et al., 2009. Di- and triorganotin(IV) carboxylates derived from triorganotin(IV) iodide with mixed organic groups on tin: Cyclic, hexameric triorganotin(IV) carboxylates. Inorganica Chim. Acta, 362: 355-360. DOI: 10.1016/j.ica.2008.04.009

Ashfaq, M., M.I. Khan, M.K. Baloch and A. Malik, 2004. Biologically potent organotin(IV) complexes of 2-maleimidoacetic acid. J. Organomet. Chem., 689: 238-245. DOI: 10.1016/j.jorganchem.2003.10.007

Baul, T.S.B., S. Dhar, S.M. Pyke, E.R.T. Tiekink and E. Rivarola et al., 2001. Synthesis and characterization of triorganotin(IV) complexes of 5-[(E)-2-(aryl)-1-diazenyl]-2-hydroxybenzoic acids. Crystal and molecular structures of a series of triphenyltin 5-[(E)-2-(aryl)-1-diazenyl]-2-hydroxybenzoates (aryl= phenyl, 2-methylphenyl, 3-methylphenyl and 4-methoxyphenyl). J. Organomet. Chem., 633: 7-17. DOI: 10.1016/S0022-328X(01)01024-5

Careri, M., A. Mangia, G. Predieri and C. Vignali, 1989. The 1H, 13C and 119Sn NMR spectra of heptacoordinated diorganotin(IV) complexes. J. Organomet. Chem., 375: 39-44. DOI: 10.1016/0022-328X (89)85081-8

Crouse, K.A., K.B. Chew, M.T.H. Tarafder, A. Kasbollah and A.M. Ali et al., 2004. Synthesis, characterization and bio-activity of S-2-picolylidithiocarbamate (S2PDTc), some of its Schiff bases and their Ni(II) complexes and X-ray structure of S-2-picolyl-b-N-(2-acetylpyrrole) diithiocarbamate. Polyhedron, 23: 161-168. DOI: 10.1016/j.poly.2003.09.025

Danish, M., H.G. Alt, A. Badshah, S. Ali, M. Mazhar and N. Islam, 1995. Organotin esters of 3-(2-furanyl)-2-propenoic acid: Their characterization and biological activity. J. Organomet. Chem., 486: 51-56. DOI: 10.1016/0022-328X(94)05050-L

Gielen, M., M. Melotte, G. Atassi and R. Willem, 1989. Synthesis, characterization and antitumour activity of 7,7-di-n-butyl-5,9-dioxo-7-stanna spiro[3,5]nonane, di-n-butyltin(IV) analog of “paraplatin” and of a series of di-n-butyltin(IV) derivatives of mono-and disubstituted malonic acids. Tetrahedron, 45: 1219-1229. DOI: 10.101016/0040-4020(89)80030-4

Gielen, M., M. Biesemans, d. Vos and R. Willem, 2000. Synthesis, characterization and in vitro antitumor activity of di- and triorganotin derivatives of polyoxa- and biologically relevant carboxylic acids. J. Inorg. Biochem., 79: 139-145. DOI: 10.101016/S0162-0134(99)00161-0

Gomez, E., R. Flores, G. Huerta, C. Alvarez-Toledano and R.A. Toscano et al., 2003. Dimethyltin(IV) 2,6-disubstituted pyridine complexes J. Organomet. Chem., 672: 115-122. DOI: 10.1016/S0022-328X (03)00150-5

Holecek, J., K. Handlir, M. Nádvornik and A. Lycka, 1983a. 11C and 119Sn NMR study of some triphenyltin(IV) carboxylates J. Organomet. Chem., 258: 147-153. DOI: 10.1016/S0022-328X (00)99251-9

Holecek, J., M. Nadvornik, K. Handlir and A. Lycka, 1983b. 13C and 119Sn NMR study of some four- and five-coordinate triphenyltin(IV) compounds. J. Organomet. Chem., 241: 177-184. DOI: 10.1016/S0022-328X (00)99251-9

Holecek, J., M. Nadvornik, K. Handlir and A. Lycka, 1986. 11C and 119Sn NMR spectra of di-n-butyltin (IV) compounds. J. Organomet. Chem., 315: 299-308. DOI: 10.101016/0022-328X (86)80450-8

Khan, S.R.A., S. Huang, S. Shamsuddin, S. Inutsuka and K.H. Whitmire et al., 2000. Synthesis, characterization and cytotoxicity of new platinum(IV) axial carboxylate complexes: crystal structure of potential antitumor agent [PtIV(trans-1R, 2R-diaminocyclohexane)trans(acetate)2Cl2]. Bioorg. Med. Chem., 8: 515-521. DOI: 10.101016/S0968-0896(99)00313-2
Lockhart, T.P. and W.F. Manders, 1986. Structure determination by NMR spectroscopy dependence of $[J(119\text{Sn}, 1^\text{H})]$ and the Me-Sn-Me angle in methyltin(IV) compounds. J. Inorg. Chem., 25: 892-895. DOI: 10.1021/ic00227a002

Molloy, K.C., T.G. Purcell, K. Quill and I.W. Nowell, 1984. Organotin biocides: I. The structure of triphenyltin acetate. J. Organomet. Chem., 25: 892-895. DOI: 10.1016/0022-328X (84)80194-1

Mosmann, T., 1983. Rapid colometric assay for cellular growth and survival: Application on to proliferation and cytotoxicity assays. J. Immunol. Methods, 65: 55-63. DOI: 10.1016/0022-1759(83)90303-4

Nath, M., Sulaxna, X. Song and G. Eng, 2006. Organotin(IV) triazolates: Synthesis and their spectral characterization. J. Organomet. Chem., 691: 1649-1657. DOI: 10.1016/j.jorganchem.2005.11.047

Novelli, F., M. Recine, F. Sparatore and C. Juliano, 1999. Triorganotin compounds as antimicrobial agents. IL Farmaco, 54: 237-241. DOI: 10.1016/S0014-827X(99)00020-8

Parulekar, C.S., V.K. Jain, T. Kesavadas and E.R.T. Tiekink, 1990. Structure chemistry of organotin carboxylates IV*. Synthesis and spectroscopic properties of diorganotin(IV) complexes with o-anisic acid. The crystal and molecular structure of [nBu$_2$Sn(2-MeOC$_6$H$_4$COO)]$_2$O$_2$. J. Organomet. Chem., 387: 163-173. DOI: 10.1016/0022-328X(90)80021-Q

Pruchnik, F.P., M. Bańbula, Z. Ciunik, M. Latocha and B. Skop et al., 2003. Structure, properties and cytostatic activity of tributyltin aminoxyacarboxylates. Inorganica Chimica Acta, 356: 62-68. DOI: 10.1016/S0020-1693(03)00475-4

Ronconi, L., C. Marzano, U. Russo, S. Sitran and R. Graziani et al., 2002. Synthesis, characterization and in vitro cytotoxicity of new organotin(IV) derivatives of N-methylglycine. J. Inorg. Biochem., 91: 413-420. DOI: 10.1016/S1074-5645(02)00465-8

Sandhu, G.K. and S.P. Verma, 1987. Triorganotin(IV) derivatives of five membered heterocyclic 2-carboxylic acids. Polyhedron, 6: 587-592. DOI: 10.1016/S0277-5387(00)81029-3

Sau, A.C. and R.R. Holmes, 1981. Characterization of phenyl-substituted pentacoordinated compounds of main group elements by $^1$H NMR. J. Organomet. Chem., 217:157-167. DOI: 10.1016/S0222-328X (00)85776-9

Teoh, S.G., E.S. Looi, S.B. Teo and S.W. Ng, 1996b. Synthesis and crystal structure of the tetrabutylbis(thiophene glycolxylato)distannoxane dimer, $\left\{\left[(C$_6$H$_5$)$_2$SnO$_2$CC(O)C$_6$H$_3$S\right]_2\right\}$. J. Organomet. Chem. 509: 57-61. DOI: 10.1016/0022-328X(95)05795-Q

Teoh, S.G., S.H. Ang, S.B. Teo, H.K. Fun and K.L. Khew et al., 1997. Synthesis, crystal structure and biological activity of bis(acetonethiosemicarbazone-S)dichlorodihydrin(IV). J. Chem. Soc., Dalton Trans., 4: 465-468. DOI: 10.1039/a605679b

Willem, R., A. Bouhid, B. Mahieu, L. Ghys and M. Biesmans et al., 1997. Synthesis, characterization and in vitro antitumour activity of triphenyl- and tri-n-butyltin benzoates, phenyacetates and cinnamates. J. Organomet. Chem., 531:151-158. DOI: 10.1016/S0022-238X (96)06686-7

Win, Y.F., S.G. Teoh, J.B.J. Teh, H.K. Fun and L. Zakaria, 2007a. [4-(diethylamino)benzoato-kO]triphényltin(IV). Acta Cryst., 63: m323-m325. DOI: 10.1107/S1600536806055905

Win, Y.F., S.G. Teoh, P. Ibrahim, S.L. Ng and H.K. Fun, 2007b. Dibutylbis[3-(dimethylamino)benzoato]tin(IV). Acta Cryst., 63: 667-669. DOI: 10.1107/S1600536807004540

Win, Y.F., S.G. Teoh, E.K. Lim, S.L. Ng and H.K. Fun, 2008a. Synthesis, characterization and crystal structure of the bis(2,4-dinitrobenzoato)tetramethyltin(IV) dimer. J. Chem. Crystallogr., 38: 345-350. DOI: 10.1007/s10870-008-9315-0

Win, Y.F., S.G. Teoh, R.K. Ha and H.K. Fun, 2008b. [3-(dimethylamino)benzoato]triphényltin(IV). Acta Cryst., 64: 1530-1531. DOI: 10.1107/S1600536808036337

Yeap, L.L. and S.G. Teoh, 2003. Synthesis, spectral characterization and x-ray crystal structure of some triphenyltin(IV) carboxylate compounds. J. Coord. Chem., 56: 701-708. DOI: 10.1080/0095897031000113968

Zhang, R., J. Sun and C. Ma, 2005. Structural chemistry of mononuclear, tetracnuclear and hexanuclear organoptin(IV) carboxylates from the reaction of di-n-butyltin oxide or diphenyltin oxide with rhodanine-N-acetic acid. J. Organomet. Chem., 690: 4366-4372. DOI: 10.1016/j.jorganchem.2005.07.005