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Synthesis of novel bioactive phthalimido-4-methyl pentanoateorganotin(IV) esters with spectroscopic investigation

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Abstract

The synthesis of monomer, dimer, tricyclohexyl- and triphenyl-tin(IV) complexes with phthalimido-4-methyl pentanoic acid (PMPA) are described and characterized by FT IR, CHN analyzer, ^{1}H, ^{13}C ^{119}Sn NMR and ^{119m}Sn Mössbauer spectroscopic techniques. In vitro ED_{50}, anti-tumor (phytotoxic), anti-yeast, blood pressure and heart rate effect, and bactericidal, fungicidal as well as analgesic bioassays of complexes are also be carried out. The ligand (PMPA) shows excellent analgesic activity while the dimer exhibit strong biocidal and excellent anti-tumor behavior besides of tri-organotin(IV) complexes.

Keywords: Phthalimido-4-methylpentanoic acid; Triphenyltin chloride; Tricyclohexyltin chloride; Dibutyltin oxide

1. Introduction

The di and triorganotin(IV) esters of *N*-benzoylglycine have been found to be active in anti-tumor tests against leukaemia P-388 cells line [1]. Organotin(IV) complexes of amino acids and their organic derivatives containing the carboxylic oxygen and tin(IV) bond display significant anti-tumor activity and promising potential in many other fields like, pesticidal, bactericidal, fungicidal, anti-fouling, wood preservation, polymer and paint industries as well as biomedical fields, etc. [1–8]. The structural chemistry of di- as well as tri-organotin(IV) complexes of carboxylic moieties as amino acids and N-protected amino acids with a coordination number higher than four has significant potential which have been cited in the literature pertaining the bioactivity as anti-tumor agents [5–11]. Literature divulges that the metal complexes were found to be more potentiated than the parent drugs while the organotin(IV) esters are exhibited themselves more promising in character [2,3]. The derivatives of amino acids are used as an antioxidant and have shown to have potential in increasing immune response to the flu and salmonella. They enhance cellular and hormonal immunity; help to transport oxygen into cells as well prevent lactic acid. The supplements are used for improvement of behavior, speech and frustration in children with in 24 h [5,6]. The choice of ligand (PMPA) is made keeping in view of muscle growth, faster recuperation, and improved performance. The L-leucine is vital for nitrogen retention in body, and is direct precursor to building muscle tissue and increasing lean body mass. This is an extension of our previous work as well as reported by others on bioactivity and structural chemistry of organotin(IV) complexes [3,4,7–9,11–15]. We also report here the ED_{50} (effective dose), anti-tumor (phytotoxic), anti-yeast, effect on blood pressure and heart rate, bactericidal, fungicidal as well as analgesic tests besides of the spectral characterization of the title novel compounds. The complexation of (PMPA) with tin(IV) metal yield products of exceedingly improved character as powerful biocides.

2. Results and discussion

2.1. Synthesis

The phthalimido-4-methylpentanoic acid (ligand) was synthesized by fusing of phthalic anhydride and 2-amino-

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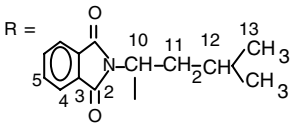
4-methylpentanoic acid in an oil bath at 185 °C. The di-*n*-butyltin(IV)-di(phthalimido-4-methylpentanoate)tin(IV) and bis[di-*n*-butyl(phthalimido-4-methylpentanoate)tin(IV)] ox ide were synthesized in 2:1 and 1:1 ratio with ligand and di-*n*-butyltin(IV) oxide, respectively.

$$C_8H_4O_3 + NH_2CH \cdot R \cdot COOH \rightarrow C_8H_4O_2 \cdot NCH \cdot R \cdot COOH + H_2O \quad (1)$$

$R = [CH_2C_6H_5]$

$$Bu_2SnO + 2RCOOH \rightarrow Bu_2Sn(OOCR)_2 + 2H_2O \quad (2)$$

$$4Bu_2SnO + 4RCOOH \rightarrow [\{Bu_2Sn(OOCR)\}_2O]_2 + 4H_2O \quad (3)$$



Equimolar of triphenyltin(IV) chloride or tricyclohexyltin (IV) chloride and phthalimido-4-methyl pentanoate sodium were refluxed for 4–5 h in chloroform to prepare triorganotin(IV)phthalimido-4-methylpentanoate esters. The sodium salt of ligand was prepared by shaking of ethanolic solution of NaOH and ligand(PMPA) in equimolar ratio.

$$RCOOH + NaOH \rightarrow RCOONa + H_2O \quad (4)$$

$$R'_3SnCl + RCOONa \rightarrow R'_3SnOOCR + NaCl \quad (5)$$

(where: R'_3 = phenyl or cyclohexyl)

2.2. Spectral studies of mono- and dimer complexes

The OH broad band for ligand disappeared in the complexes. Both asymmetric and symmetric stretching of the phthalimido (C_2O_2N) and of the carbonyl (CO) groups and the stretching for Sn–C and Sn–O were exhibited as reported in the literature [16–23]. The asymmetric and symmetric stretching values of CO groups of monomeric as well in dimeric type esters were raised and lowered than the ligand's values and $\Delta\nu$ values of compounds were higher than the $\Delta\nu$ of ligand. The monomeric and dimeric esters showed bidentate symmetric bonding with tin(IV) atom, which suggested the octahedral geometry for monomeric type and hexa coordinate bonding of carboxylate to the tin atoms, which are easily be indicated by ranking of asymmetric and symmetric stretching of CO group of complexes and of ligand [$\nu_{asym(comp.)} > \nu_{asym(ligand)}, \nu_{sym(comp.)} < \nu_{sym(ligand)}, \Delta\nu_{(compound)} > \Delta\nu_{(ligand)}$]. The butyl protons in mono- and dimeric types were resolved on a proper position as multiplet at room temperature indicating fluxional behavior [24–26]. The monodentate coordination of carboxylic function to tin(IV) atom and in its correspond, two triplets for the methyl protons of butyl tin in the dimer compound were reported by Gielen in 1997 and Camacho et al. in 1999 [14] at very low temperature and high resolution NMR 500 MHz, which is due to non-equivalent environment of methyl protons bonded to endo and exo cyclic tin(IV) atoms. The ^{13}C NMR signals were properly resolved, and showed single signal for each methylene carbon in butyl group around the tin atom in monomer and a pair of signals around exo and endo cyclic tin(IV) were observed in dimer ester. The coupling satellite $^nJ(^{13}C–^{119}Sn)$ at high resolution NMR for the both monomer and dimer compound with well known ranking $[^1J] \gg [^3J] > [^2J]$ was reported in the literature[14,27,28]. The ^{119}Sn chemical shift at −144.13 ppm of monomeric type reveals coordination from carboxylic oxygen to tin center, which suggests the bidentate mode in equatorial positions with two adjacent short and two longer Sn–O bonds (Fig. 1). The ^{119}Sn NMR spectrum of dimer type showed two signals at low and high resonance. The exo tin(IV) atom may be bonded in monodentate mode with carboxylic oxygen of ligand. However, the endo cyclic tin(IV) atom may be bonded in bidentate mode with oxygen of carboxylic groups ligand. This mode of coordination with exo cyclic tin atoms results in penta coordination, trigonal bi-pyramidal geometry [25]. Such behavior of tetraorganotin(IV) compounds were reported by Pervez et al. [6,17,18,21] as centro-symmetric skew trapezoidal bi-pyramidal geometry for the endo-cyclic tin status while the exo-cyclic tin status are in distorted trigonal bi-pyramidal geometry. The ^{119m}Sn Mössbauer spectra displayed quadrupole splitting values over the range of 3.41 mm s^{-1}, which is greater than the 2.1 mm s^{-1} value reported in the literature [9,16,29] for a *trans* octahedral geometry around tin atom of monomer diorganotin dicarboxylate complexes Similarly, Gielen et al. [15] reported *trans* octahedral geometry of monomer type compounds (Fig. 1).

The large quadrupole splitting value (QS = 3.65 mm s^{-1}) of ^{119m}Sn Mössbauer for dimer type compound recommended a penta coordinate environment, which strongly suggested the tetrabutyl bis(phthalimido-4-methylpentanoato) distannoxane dimer type (Fig. 2). The %CHN verified the monomeric and dimeric composition of compounds **1** and **2** is 2.3.

Spectral studies tri-organotin(IV) complexes. The IR behavior of carbonyl (CO) found same as reported in the literature [9,29]. The asymmetric and symmetric stretching of compounds **3** and **4** were raised and lowered than the values of sodium salt while $\Delta\nu$ in the complexes was also larger than the $\Delta\nu$ in sodium salt of ligand, which indicated unidentate or weak bidentate bonding to tin(IV) [30,31], which may easily be identified by given stretching ranks of CO groups between complexes and salt [$\nu_{asym(comp.)} > \nu_{asym(salt)}, \nu_{sym(comp.)} < \nu_{sym(salt)}, \Delta\nu_{(compound)} > \Delta\nu_{(salt)}$]. The ^1H, ^{13}C and ^{119}Sn NMR spectra of the triorganotin(IV)phthalimido-4-methylpentanoate esters were re-

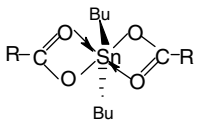


Fig. 1. *Trans* octahedral geometry.

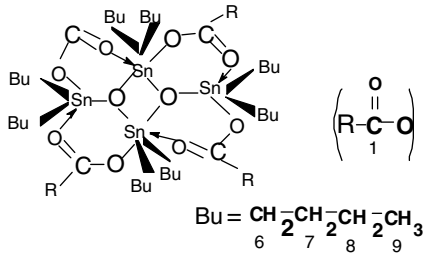


Fig. 2. Dimeric geometry.

corded. The expected shifting was assigned by their multiplicity and intensity pattern. Based on the literature, [3,8] it is suggested that the complexes have tetrahedral geometry. The ^{119}Sn NMR signals were seen over the range of −121.17 ppm for triphenyl and 74.43 ppm for the tri-cyclohexyl moieties bonded to Sn(IV). It recommended a penta coordinate environment around tin(IV) atom, which suggested that the triphenyltin(IV) ester leaded to a polymeric trigonal bi-pyramidal in the solid and a tetrahedral geometry in an inert solvent while tricyclohexyltin(IV) compound exhibited tetrahedral geometry in the solid as well as in solution [31]. Based on evidences, their structures are displayed in Figs. 3 and 4.

The ^{119m}Sn Mössbauer spectra of triphenyl- and tricyclohexyl-tin(IV) phthalimido-4-methylpentanoate have quadrupole splitting values of 3.42 and 2.73 mm s^{-1}, respectively. According to a literature [3,19,29,30] the compounds with 3.59–3.70 mm s^{-1} QS values have a five-coordinate chain structure and the complexes with 3.39 mm s^{-1} QS value displayed a tetrahedral in solid and trigonal bi-pyramidal geometry with a bridging carboxyl group in an inert solvent, where $\delta = \mathrm{QS/IS}$ also supports the same geometry [9,30].

2.3. Biological activities

The ligand and the compounds **1** and **2** at the doses of 10, 20 and 40 mg/kg body weight showed no effect on blood pressure and heart rate of animal as well as no activity was found towards the yeasts. The compounds **5** (ligand), **1** and **2** exhibited an excellent analgesic activity. The results can be viewed in Tables 1, 2.

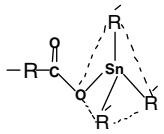


Fig. 3. Tetrahedral geometry.

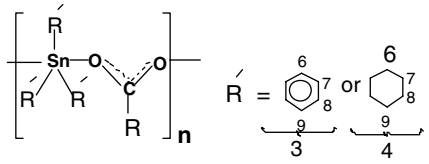


Fig. 4. Polymeric trigonal bi-pyramidal geometry.

Table 1
Anti-yeast bioassay

Name of yeast*	Activities					
	1	**2**	**3**	**4**	**5**	Streptonigrin
(m). RS 322Y (RAD52)	–	–	+++	+++	++	+++++
(w). LF 15 (RAD$_+$)						

Key. *, *Saccharomyces cerevisiae*; ++++, very high activity; +++, high; ++, optimum.

Table 2
Analgesic activity on albino mice

Dosage (mg/kg)	No. of writhes	% Inhibition by compounds			
		1	**2**	**5**	Aspirin[b]
Control[a]	48	–	–		–
10	–	5(2)	7(3)	20(10)	–
50	–	55(26)	57(27)	54(26)	–
100	–	64(31)	63(30)	70(34)	–
150	–	–	–		67

Note. Writhes remained are given in parentheses
[a] Acetic acid.
[b] Standard drug.

The compounds **3** and **4** showed the highest toxicity against brine shrimp larvae and in vitro phytotoxic antitumor activity against Lemna acquinoctialis welv (Tables 3, 4) [32–36]. Both the di- and tri-organotin complexes (**1**–**4**) exhibited bactericidal and fungicidal properties (Tables 5, 6). Triorganotin(IV) class is significantly active than other classes since having a greater partition coefficient value [18]. It may also be considered the presence of lone pair on oxygen of carbonyl of ligand is not involved in coordination process, which may play a key role to increase the toxicity. Such trend was not observed in mono and dimer types since the lone pair may actually be bounded through a weak/strong bidentate bonding. Moreover, toxicity is also confined with an attached "R" group to tin(IV) atom. In the R_3SnL unit, the function of L (ligand) plays a key role in transporting the active site of organotin(IV) moiety, which is released on hydrolysis [1,35,36]. Among such compounds, the carboxylate derivatives are used as anticancer and anti-tumor agents in vivo as well as in vitro fungicides or bactericides [37,38]. The biocide activity of triorganotin(IV) motifs is enhanced on account of their geometry in solution. The tetrahedral structure in solution is more active than other forms. It is also reported in the literature [39–41] that the

Table 3
Brine shrimp bioassay

Compounds	% Deaths at doses			ED_{50} μg/ml	Results
	1000 μg/ml	100 μg/ml	10 μg/ml		
1	35	12	9	∞	–
2	30	10	10	∞	–
3	100	100	80	3.85	++++
4	100	95	90	0.0085	++++

Key. ++++, more significant; –, no activity.

Table 4
Invitro phytotoxic (anti-tumor) bioassay of Lemna acquinoctialis welv

Compounds	Dose (μg/ml)	No. of fronds		% Growth regulation	F1 50[a] (μg/ml)
		Experimental	Control		
1	500	00	11	100	0.0000
	50	00	9	100	0.125
	5	8	9	20	
2	500	00	11	100	0.0000
	50	00	9	100	0.125
	5	8	10	20	
3	500	00	11	100	0.0000
	50	00	11	100	0.125
	5	00	11	100	
4	500	00	11	100	0.0000
	50	00	11	100	0.125
	5	00	11	100	

[a] Concentration used to inhibit and promote 50% of frond proliferation. Reference inhibitor: Praqual 100%.

four-coordinated species has stronger tendency to increase the coordination numbers by O, S, or N donor groups while the five-coordinate species do not undergo further coordination which play no long-term role in vivo chemistry of organotin(IV) esters.

3. Experimental

3.1. Materials

Phthalic anhydride, 2-amino-4-methylpentanoic acid, dibutyltin(IV) oxide, tri- phenyltin(IV) chloride and tricyclohexyltin(IV) chloride were commercially available from Merck Chemicals Co. Ltd. and were used without further purification. The ligand was prepared according to a reported procedure [21]. All the complexes were prepared according to reported procedures [8,9]. They were soluble in chloroform and ethanol (on heating) and insoluble in methanol and water.

Table 5
Bactericidal bioassay

Name of bacteria (human pathogens)	Activity[a] of compounds			
	1	**2**	**3**	**4**
Bacillus cereus	++++	++++	++++	++++
Cornye bacterium diphtheriae	++++	++++	+++++	+++++
Escherichia coli ETEC.	++	++	++++	++++
Klebsiella pneumoniae	++	++	++++	++++
Salmonella typhi	+	+	++++	++++
Staphylococcus aureus	+++	+++	++++	++++
Shigella boydii	−	−	−	−
Pseudomons aeroginosa	−	−	−	−
Proteus mirabillis	−	−	−	−
Streptococcus pyogenes	+++	+++	++++	++++

Reference drug: Amoxicillin (H_2O), Ampicillin (H_2O), Cephlaxin Na. Incubation period: 8 h, 37 °C; colony forming unit = 10^4–10^6; size of well = 5 mm radius.
[a] ++++, highest; +++, high; ++, optimum; + and −, no activity.

Table 6
Fungicidal bioassay

Name of fungi	Activity[a] of compounds			
	1	**2**	**3**	**4**
Aspergillus flame (human pathogens)[b]	−	−	++++	++++
Trichophyton schoenlem	++	++	++++	++++
Pseudallescheria boydii	++	++	++++	++++
Candida albicans	+	+	++++	++++
Aspergillus niger[c]	+	+	++++	++++
Animal pathogens[b]				
Microsporum canis	−	−	−	−
Trichophyton mantagrophytes	+++	+++	++++	++++
Trichophyton rubrum	−	−	−	−
Trichophyton	+++	+++	++++	++++
Plant pathogens[d]				
Fusanum oxysponumvarlycopersici	++++	++++	++++	++++
Fusanum solanivarlycopersici	++++	++++	++++	++++
Macrophormina phaseolina	++++	++++	++++	++++
Rhizoctonia solani	−	−	−	−

Incubation time = 7 h, 27 °C. Reference Drug: [b]Miconazole, Ketoconazole; [c]Amphotenicin-B, Flycytosine; [d]Benlate, Nabam.
[a] ++++, highest; +++, high; ++, optimum; + and −, no activity.

3.2. Physical measurements

The melting points of all compounds were measured on a Reichert thermovar of F.G. Bode Co. Austria. The Perkin–Elmer FTIR-1605 was used with KBr disc for IR analysis. Elemental analyses were carried out on a Yanaco MT-3 high-speed CHN analyzer with an antipyrene reference compound. The ^1H, ^{13}C and ^{119}Sn NMR spectra were recorded on a multinuclear FT NMR 200 MHz of JEOL using TMS at room temperature. Some of the ^{13}C spectra were measured on a Bruker AM 270 instrument at 50 MHz with ^{13}C probe. The ^{119}Sn NMR spectra were obtained on a Bruker WM 500 instrument at 93.1 MHz. The ^{119m}Sn Mössbauer spectra were recorded on a V.G.Micromass 7070 F instrument at a temperature of 200 °C. The ED_{50} of the complexes was determined against a brine shrimp hatching method while bactericidal and fungicidal activity was measured by agar-well diffusion and agar-tube dilution methods [25,26] In vitro phytotoxic anti-tumor activity tests (potato disc assay) were carried out using 10 plants of Lemna acquinoctialis welv for the purpose [24,25]. The anti-yeast bioassay of ligand and the organotin compounds against mutant (*Saccharomyces cerevisiae*, Rs 322Y RAD52) and wild types strains (*S. cerevisiae* LF15RAD$^+$) was determined. Streptonigrin was used as a standard drug. Effect of compounds on blood pressure and heart rate were checked using Sprague Dawely wistars rats. SathamP_{23} coupled with 79-Polygraph was used for the purpose and normal response was found against acetylcholine and noradrenaline (hypertensive) as standard drugs. Albino mice were under the experiments for an analgesic activity test and number of writhing response for each mouse was recorded using aspirin as a standard. Acetic acid was used for writhing response. Intraperitoneal rout was used for dose administration [39,40].

3.3. Synthesis and characterization

3.3.1. Compound **1**

{$C_6H_4(CO)_2N\{CHCH_2CH(CH_3)_2\}COO\}_2SnBu_2$

Re-crystallized from chloroform, m.p.: 204 °C, yield 81%, solubility: soluble in chloroform, soluble in ethanol on heating, slightly soluble in methanol and insoluble in water, when fourfold of water was added its alcoholic solution remained clear.

CHN analysis (%) antipyrene: C, 57.25 (57.37); N, 3.75 (3.74); H, 5.21 (5.11); the calculated values are in the parentheses.

FT IR analysis (cm^{-1}): C_2O_2N (phthalimido): 1775_{asym} sp, 1721_{sym} s.sp; CO(carbonyl): 1639_{asym} sp, 1383_{sym} sb; Δv: 256; Sn–C: 545 w.sp; Sn–O: 486 sp.

^{119m}Sn Mössbauer data (mm s^{-1}): QS: 3.41; IS: 1.35; G1: 1.18; G2: 1.17; δ = QS/IS: 2.53.

^{1}H NMR ($CDCl_3$): H-4, 7.83 d (8); H-5, 7.59 d (8); H-6, 1.64 t (7); H-7, 1.52–1.61 m; H-8, 1.33–1.10 m; H-9, 0.91; H-10, 4.74 dd (6,6,5); H-11, 2.35 t (~7); H-12, 1.81–1.85 m; H-13, 0.78 d (8).

^{13}C NMR ($CDCl_3$): C-1, 176.3; C-2, 166.8; C-3, 132.5; C-4, 123.2; C-5, 133.7; C-6, 27.3; C-7, 27.7; C-8, 23.1; C-9, 13.4; C-10, 52.5; C-11, 38.1; C-12, 27.9; C-13, 21.2.

^{119}Sn NMR $(CH_3)_4$Sn: −144.13.

3.3.2. Compound **2**

[$C_6H_4(CO)_2N\{CHCH_2CH(CH_3)_2COOSnBu_2\}_2O]_2$

Re-crystallized from chloroform, m.p.: 212 °C, yield: 89%, solubility: soluble in $CHCl_3$, soluble in ethanol on heating, slightly soluble in methanol and insoluble in water.

CHN analysis (%) antipyrene: C, 52.55 (52.72); N, 2.79 (2.81); H, 6.23 (6.24).

FT IR analysis (cm^{-1}): C_2O_2N (phthalimido): 1774_{asym} sp, 1720_{sym} s.sp; CO(carbonyl): 1640_{asym} sp, 1385_{sym} sb; Δv: 255; Sn–C: 545 w.sp; Sn–O: 487 sp.

^{119m}Sn Mössbauer data (mm s^{-1}): QS, 3.65; IS, 1.32; G1, 0.84; G2, 0.82; δ = QS/IS: 2.77.

^{1}H NMR ($CDCl_3$): H-4, 7.80 d (8); H-5, 7.71 d (8); H-6, 1.50 t (7); H-7, 1.44–1.48 m; H-8, 1.20–1.25 m; H-9, 0.94; H-10, 4.82 dd (5,5,4); H-11, 2.39 t (~7); H-12, 1.85–1.89 m; H-13, 0.69–0.74 m.

^{13}C NMR ($CDCl_3$): C-1, 175.7; C-2, 167.6; C-3, 133.4; C-4, 123.9; C-5, 134.0; C-6, 27.1/ 28.5; C-7, 26.6/ 26.8; C-8, 23.02/24.2; C-9, 13.1; C-10, 52.3; C-11, 37.8; C-12, 26.9; C-13, 21.1.

^{119}Sn NMR $(CH_3)_4$Sn: −199.50, −208.51.

3.3.3. Compound **3**

[$(C_6H_5)_3SnOOCCHCH_2CH(CH_3)_2N(CO)_2C_6H_4$]

Solidified from *n*-hexane, m.p.: 145–147 °C, yield: 89%, solubility: soluble in chloroform, soluble in ethanol on heating, slightly soluble in methanol and insoluble in water. When sevenfold of water was added its alcoholic solution remained clear.

CHN analysis (%) antipyrene: C, 62.95 (62.98); N, 4.72 (4.79); H, 2.25 (2.30).

FT IR analysis (cm^{-1}): C_2O_2N (phthalimido): 1772_{asym} sp, 1715_{sym} s.sp; CO (carbonyl): 1670_{asym} s, 1387_{sym} s; Δv: 283; Sn–C: 541 sp; Sn–O: 513 w.

^{119m}Sn Mössbauer data (mm s^{-1}): QS, 3.42; IS, 1.6; G1, 0.84; G2, 0.81; δ = QS/IS: 2.14.

^{1}H NMR ($CDCl_3$): H-4, 7.73 d (8); H-5, 7.53 d (8); H-7, 7.31–7.34 m; H-8/9, 7.48–7.52 m; H-10, 5.02 dd (4, 4, 3); H-11, 2.42–2.02 m; H-12, 1.42–1.28 m; H-13, 0.99 d (8).

^{13}C NMR ($CDCl_3$): C-1, 172.3; C-2, 167.8; C-3, 131.1; C-4, 123.3; C-5, 133.8; C-6, 135.0; C-7, 124.0; C-8, 129.1; C-9, 133.8; C-10, 51.7; C-11, 38.3; C-12, 25.6; C-13, 21.3.

^{119}Sn NMR $(CH_3)_4$Sn: −121.17.

3.3.4. Compound **4**

[$(C_6H_{11})_3SnOOCCHCH_2CH(CH_3)_2N(CO)_2C_6H_4$]

Solidified from *n*-hexane, m.p.: 145–147 °C, yield: 89%, solubility: soluble in chloroform, soluble in ethanol on heating, slightly soluble in methanol but insoluble in water. When sixfold water was added its alcoholic solution remained clear.

CHN analysis (%): C, 61.09 (61.16); N, 7.50 (7.54); H, 2.19 (2.22).

FT IR analysis (cm^{-1}): C_2O_2N (phthalimido): 1772_{asym} sp, 1702_{sym} sb; CO(carbonyl): 1665_{asym} s.sp, 1387_{sym} s.sp; Δv: 278; Sn–C: 543 sp; Sn–O: 513 w.

^{119m}Sn Mössbauer data (mm s^{-1}): QS, 2.73; IS, 1.45; G1, 0.98; G2, 1; δ = QS/IS: 1.88.

^{1}H NMR ($CDCl_3$): H-4, 7.74 d (8); H-5, 7.55 d (8); H-6, 1.47; H-7-9, 1.44–1.52 m; H-10, 3.96 d (8.5); H-11, 2.89; H-12, 2.87–1.88 m; H-13, 0.85 d (8).

^{13}C NMR ($CDCl_3$): C-1, 178.3; C-2, 167.5; C-3, 132.8; C-4, 123.6; C-5, 133.4; C-6, 35.3; C-7, 31.07; C-8, 29.1; C-9, 28.4; C-10, 60.5; C-11, 27.7; C-12, 28.9; C-13, 22.6.

119Sn NMR $(CH_3)_4$Sn: 74.43.

3.3.5. Compound **5** ligand:

[$C_6H_4(CO)_2N\{CH\cdot CH_2CH(CH_3)_2\}COOH$]

Re-crystallized from 10% ethanol, m.p.: 118 °C, yield 94%, solubility: soluble in ethanol and methanol, insoluble in chloroform and water.

CHN analysis (%) antipyrene: C, 57.33 (57.37); N, 3.72 (3.74); H, 5.10 (5.11).

FT IR analysis (cm^{-1}): OH (acidic) 3435–3243 b, C_2O_2N (phthalimido): 1785_{asym} m.b, 1713_{sym} s.b; CO (carbonyl): 1639_{asym} m.b, 1393_{sym} s.sp; Δv: 222.

3.3.6. Compound **6** sodium salt of ligand:

[$C_6H_4(CO)_2N\{CH\cdot CH_2CH(CH_3)_2\}COONa$]

Re-crystallized from water, m.p.: >300 °C, yield 96%, solubility: soluble in water slightly soluble in ethanol and methanol and insoluble in chloroform.

CHN analysis (%) antipyrene: C, 53.34 (53.36); N, 4.92 (4.94); H, 4.93 (4.94).

FT IR analysis (cm^{-1}): OH (acidic) band disappeared, C_2O_2N (phthalimido): 1774_{asym} s.sp, 1728_{sym} s.sp; CO-(carbonyl): 1587_{asym}, 1431_{sym} s.sp; Δv: 156. (s = strong, sp = sharp, b = broad, w = weak).

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