DI-n-BUTYL-, TRI-n-BUTYL- AND TRIPHENYLTIN STEROIDCARBOXYLATES: SYNTHESIS, NMR CHARACTERIZATION AND *IN VITRO* ANTITUMOUR ACTIVITY

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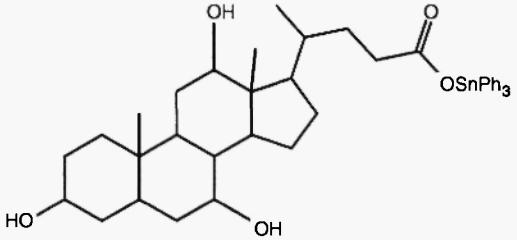
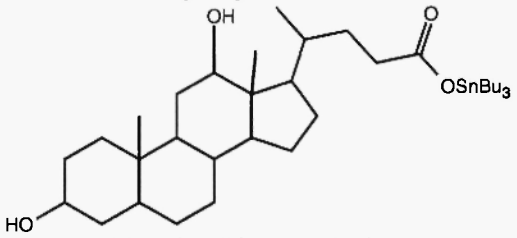
Abstract
A series of tri- and diorganotin steroidcarboxylates were synthesized and characterized by 1D and 2D ^{1}H, ^{13}C, ^{117}Sn and ^{1}H-^{13}C HMQC and HMBC NMR spectroscopy as well as by ^{119}Sn MAS NMR. The *in vitro* antitumour activities of the di-n-butyltin compound **1** against seven human tumour cell lines, MCF-7 and EVSA-T, two breast cancers, WiDr, a colon cancer, IGROV, an ovarian cancer, M19 MEL, a melanoma, A498, a renal cancer, and H226, a non small cell lung cancer lie between those of 5-fluorouracil and doxorubicin. The activities of the triorganotin compounds **6**, **7**, **9** and **11** are comparable to those of methotrexate or doxorubicin.

Introduction

Steroid-based organotin compounds, in which the tin atom is linked to a steroid moiety through a carbon-tin bond[1], show anti-tumour activity. Likewise, when the steroid contains an Sn-O bond as in the two organotin steroidcarboxylates, triphenyltin cholate and tri-n-butyltin deoxycholate, of which the structure is shown in figure 1, antitumour activity against some cancer models[2,3] was also observed.



Triphenyltin cholate



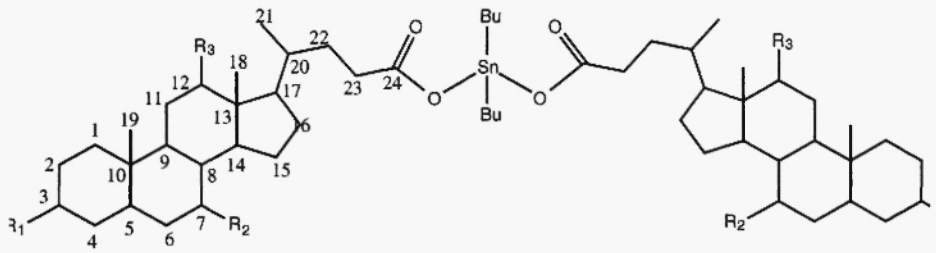
Tri-n-butyltin deoxycholate

Figure 1: Structures of triphenyltin cholate and tri-n-butyltin deoxycholate

Triphenyltin cholate is characterized by a T/C value of 350% against adenocarcinoma in A/KI mice and by an inhibition index ED_{50} of 0.22 µg/ml against the human KB tumour, and of 0.18 µg/ml against mouse P-388 leukemia[3]. For tri-n-butyltin deoxycholate, T/C = 168%[3] is the most relevant of the reported values in addition to ED_{50} values of 0.25 and 0.26µg/ml against the human KB tumour and P-388, respectively[3].
With the purpose of screening such compounds on a wider panel of tumour cells, the present report presents the synthesis, characterization and anti-tumour activity of a series of novel di- and triorganotin steroidcarboxylates.

Results and discussion

Five diorganotin and eight triorganotin steroidcarboxylates were synthesized. Their structures are shown in figure 2a and 2b. The triorganotin steroidcarboxylates **6**, **7**, **9** and **11** and the di-n-butyltin bis steroidcarboxylate **1** were screened against seven human tumour cell lines. They were all prepared from the corresponding steroidcarboxylic acid and tri-n-butyltin acetate, triphenyltin hydroxide or di-n-butyltin oxide, as for previous organotin carboxylates exhibiting *in vitro* antitumour activities[4].



$R_1 = R_3 = OH$ and $R_2 = H$
3α, 12α - deoxycholate **1**

$R_1 = OH$ and $R_2 = R_3 = H$
3α - lithoxycholate **2**

$R_1 = R_2 = OH$ and $R_3 = H$
3α, 7α - chenodeoxycholate **3**

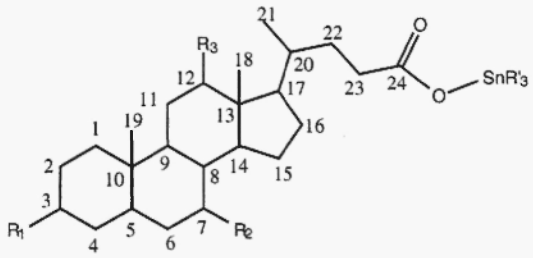
$R_1 = R_2 = R_3 = O$
dehydroxycholate **4**

$R_1 = R_2 = OH$ and $R_3 = H$
3α, 7β - ursodeoxycholate **5**

Figure 2a: Structure of the diorganotin steroidcarboxylates synthesized

They were characterized by Mössbauer spectroscopy, ^1H, ^{13}C and ^{117}Sn NMR. The ^1H and ^{13}C chemical shifts of the organic moiety have been fully assigned by ^1H-^{13}C HMQC and HMBC spectroscopy as described elsewhere[5].
The ^1H NMR spectra display complex overlapping patterns from which $^nJ(^1H$-$^1H)$ coupling constants and multiplicities cannot be determined straightforwardly except for the triplet of the terminal methyl group of the butyltin moieties. Accordingly,only ^1H chemical shifts determined from ^1H-^{13}C HMQC and HMBC spectra are given as ^1H resonance characteristics for the organotin steroidcarboxylates (see experimental section). The ^1H resonances have been assigned in ^1H-^{13}C HMQC spectra from the ^{13}C resonances of carbon atoms to which the hydrogen atoms are bound; the ^{13}C resonances were assigned from a combination of ^{13}C DEPT and 2D 1H-^{13}C HMBC spectra, allowing to reconstitute the carbon skeleton, starting from the unambiguous ^{13}C resonance of the carbonyl group. The ^{13}C resonances of the n-butyl and phenyl groups are easily identified from their $^nJ(^{13}C$-$^{119/117}Sn)$ coupling satellites, using the well known ranking $|^1J| >> |^3J| > |^2J|$[6]. Noticeable is also the difference of ca. 10 ppm for the C-17 carbon depending on whether $R_3 = H$ ($\delta^{13}C \approx 56$ ppm) or contains an oxygen atom ($\delta^{13}C \approx 46$ ppm).
The solution ^{117}Sn NMR parameters, as well as the $^1J(^{13}C$-$^{119/117}Sn)$ coupling constants conform to previous data for dibutyltin dicarboxylates[7] and triorganotin carboxylates[8] which are all monomeric in solution, the tin configuration being trapezoidal bipyramidal in the former, distorted tetrahedral in the latter.
All compounds failed to provide single crystals appropriate for X-ray diffraction analysis. In order to get indirect information as to possible coordination differences in solution and solid states, MAS ^{119}Sn NMR spectra were recorded on compounds **1** - **4**, **6**, **7** and **11**. All these spectra exhibit ill defined anisotropy patterns with low signal-to-noise ratio, due to broad resonances, and required therefore acquisitions of typically 24 hours per spectrum. Isotropic ^{119}Sn chemical shift values are found in the experimental section. The

dibutyltin carboxylates **1**, **3** and **4** reveal a solid state isotropic ^{119}Sn chemical shift close to the solution value, with however, for the latter two compounds, an additional resonance at lower frequency. This suggests essentially an amorphous arrangement of monomeric units, part of which is involved in coordination expansion by a weak contact, probably from a carboxylic oxygen, increasing in strength in the order **1** ≈ **3** > **4**. Another explanation might be a shortening of one or two of the long Sn-O coordination bonds.



$R_1 = R_3 =$ OH and $R_2 =$ H 3α, 12α- deoxycholate	$R' = C_6H_5$	**6**
$R_1 =$ OH and $R_2 = R_3 =$ H 3α- lithoxycholate	$R' = C_6H_5$ $R' = C_4H_9$	**7** **11**
$R_1 = R_2 =$ OH and $R_3 =$ H 3α, 7α- chenodeoxycholate	$R' = C_6H_5$ $R' = C_4H_9$	**8** **12**
$R_1 = R_2 = R_3 =$ O dehydroxycholate	$R' = C_6H_5$ $R' = C_4H_9$	**9** **13**
$R_1 = R_2 =$ OH and $R_3 =$ H 3α, 7β - ursodeoxycholate	$R' = C_6H_5$	**10**

Figure 2b: Structure of the triorganotin steroidcarboxylates synthesized

By contrast, the dibutyltin carboxylate **2** reveals two species with ^{119}Sn resonances to high and low frequency with respect to the solution resonance. While the latter can be explained by a higher coordination than in solution or by a shortening of one or two of the long Sn-O coordination bonds, the former can be understood only if it is assumed that some of the carboxylate functions are bound in a monodentate mode rather than in the unsymmetric bidentate mode characteristic for the trapezoidal bipyramidal arrangement in solution[7].
The triphenyltin carboxylates **6** and **7** exist as amorphous mixtures of four-coordinate tin atoms evidenced by isotropic chemical shifts similar to the solution values and tin atoms with five-coordinate configurations, as assessed by lower frequency chemical shifts and Mössbauer QS parameters[9]. Similar considerations hold for the tributyltin carboxylate **11**.

Compounds	MCF-7	EVSA-T	WiDr	IGROV	M19 MEL	A498	H226
1	74	66	382	134	161	195	396
6	18	<3	15	17	32	53	53
7	11	<3	22	16	22	11	58
9	16	<3	15	<3	51	138	76
11	16	<3	19	18	51	65	61
Carboplatin	10500	4500	3500	2400	5500	18000	25000
Cisplatin	699	422	967	169	558	2253	3269
5-Fluorouracil	750	475	225	297	442	143	340
Methotrexate	18	5	<3	7	23	37	2287
Doxorubicin	10	8	11	60	16	90	199

Table 1. In vitro antitumour activities (ng/mL) of compounds **1**, **6**, **7**, **9** *and* **11**, *together with those of some reference compounds used clinically, against several tumoural cell lines.*

The results of the *in vitro* screening of these compounds, as compared to some reference compounds[10] used clinically (carboplatin, cis-platin, 5-fluorouracil, methotrexate and doxorubicin), against seven human tumour cell lines, MCF-7 and EVSA-T, two breast cancers, WiDr, a colon cancer, IGROV, an ovarian cancer, M19 MEL, a melanoma, A498, a renal cancer, and H226, a non small cell lung cancer, are given in Table 1.
The *in vitro* antitumour activities of the di-n-butyltin compound **1** lie between those characterizing 5-fluorouracil and doxorubicin. The activities of the triorganotin compounds **6**, **7**, **9** and **11** are comparable to those of methotrexate or doxorubicin against all tumour cell lines, except EVSA-T against which they are significantly more active.

Experimental part

Characterization methods
Mössbauer data: QS: quadrupole splitting; IS: isomer shift; Γ_1 and Γ_2: line widths, all in mm/s.
NMR data: the NMR spectra were recorded from $CDCl_3$ solutions on a Bruker AC250 spectrometer, using a QNP probe tuned at 250.13, 62.93 and 89.15 MHz for ^1H, ^{13}C and ^{117}Sn nuclei, respectively. ^{117}Sn rather than ^{119}Sn NMR was used to overcome local radiofrequency interferences. ^1H and ^{13}C resonances were referenced to the solvent peak at 7.24 and 77.0 ppm respectively, while $\Xi(^{117}Sn) = 35.632295$[11] was used for the ^{117}Sn resonances. The ^1H-^{13}C HMQC and HMBC 2D spectra were recorded on an AMX500 Bruker instrument, as described elsewhere [5a]. t = triplet. $^nJ(^1H$-$^1H)$ coupling constants are given in Hz between parentheses. $^nJ(^{13}C$-$^{119/117}Sn)$ coupling constants are indicated explicitely.
Solid-state NMR: the ^{119}Sn MAS NMR experiments were performed with a MSL 300 Bruker solid-state spectrometer equipped with a 7.05 T (111.909 MHz for ^{119}Sn) wide-bore magnet and a MAS broad-band probe. Samples were filled into double bearing 4mm ZrO_2 cyclindrical rotors. All ^{119}Sn MAS spectra were obtained with the standard Bruker QUADCYCL pulse sequence, followed by Fourier transformation with an exponential line broadning of about 500 Hz. The pulse angle was about 30 deg. and the recycling delay was 10 s. Spinning rates used for MAS ranged from 10 to 15 KHz. For each sample, two experiments with different spinning rates were performed to locate unambiguously the isotropic chemical shifts. The chemical shifts are referenced against $Sn(CH_3)_4$ using solid tetracyclohexyltin as a secondary external reference (= - 97.35 ppm).

Synthesis and characterization
Compound **1**, $(C_{23}H_{39}O_2CO_2)_2Sn(CH_2CH_2CH_2CH_3)_2$
Recrystallized from dichloromethane/petroleum ether, mp: 103-104 °C, yield: 84%
Mössbauer parameters (in mm/s): QS: 3.33, IS: 1.35, Γ_1 & Γ_2: 1.22 & 1.20
^1H NMR ($CDCl_3$): H-1: 0.94, 1.70; H-2: 1.32, 1.64; H-3: 3.92; H-4: 1.48, 1.75; H-5: 1.36
H-6: 1.10, 1.39; H-7: 1.25, 1.42; H-8: 1.38; H-9: 1.77; H-11: 1.45, 1.52; H-12: 3.55; H-14: 1.52; H-15: 1.53; H-16: 1.10, 1.39; H-17: 1.66; H-18: 0.66; H-19: 0.90; H-20: 1.34; H-21: 0.97; H-22: 1.33, 1.79; H-23: 2.17, 2.29; H-α: 1.61; H-β: 1.60; H-γ: 1.32; H-δ: 0.88 t (7)
^{13}C NMR ($CDCl_3$): C-1: 35.4; C-2: 30.5; C-3: 71.8; C-4: 36.5; C-5: 42.1; C-6: 27.5; C-7: 27.2; C-8: 36.1; C-9: 33.7; C-10: 34.1; C-11: 28.7; C-12: 73.1; C-13: 46.6; C-14: 48.3; C-15: 23.7; C-16: 26.2; C-17: 47.5; C-18: 12.7; C-19: 23.2; C-20: 35.3; C-21: 17.3; C-22: 31.6; C-23: 31.3; C-24: 184.6; C-α-Sn: 24.9 [$^1J(^{13}C$-$^{119/117}Sn)$ = 585/560]; C-β: 26.7 [$^2J(^{13}C$-$^{119/117}Sn) \approx 32$]; C-γ: 26.3 [$^3J(^{13}C$-$^{119/117}Sn) \approx 100$]; C-δ: 13.5
^{117}Sn NMR ($CDCl_3$): -149.5; ^{119}Sn NMR MAS: -170

Compound **2**, $(C_{23}H_{39}OCO_2)_2Sn(CH_2CH_2CH_2CH_3)_2$
Recrystallized from dichloromethane/petroleum ether, mp: 93-95 °C, yield: 80%
Mössbauer parameters (in mm/s): QS: 3.32, IS: 1.29, Γ_1 & Γ_2: 1.15 & 0.82
^1H NMR ($CDCl_3$): H-1: 0.93, 1.75; H-2: 1.30, 1.62; H-3: 3.57; H-4: 1.47, 1.71; H-5: 1.34
H-6: 1.23, 1.78; H-7: 1.25, 1.40; H-8: 1.34; H-9: 1.35; H-11: 1.13, 1.35; H-12: 1.11, 1.91; H-14: 1.00; H-15: 1.03, 1.54; H-16: 1.23, 1.82; H-17: 1.05; H-18: 0.63; H-19: 0.88; H-20: 1.41; H-21: 0.89; H-22: 1.28, 1.80; H-23: 2.20, 2.37; H-α: 1.60; H-β: 1.60; H-γ: 1.34; H-δ: 0.88 t (7)
^{13}C NMR ($CDCl_3$): C-1: 35.4; C-2: 30.5; C-3: 71.8; C-4: 36.4; C-5: 42.1; C-6: 27.2; C-7: 26.4; C-8: 35.9; C-9: 40.5; C-10: 34.6; C-11: 20.8; C-12: 40.2; C-13: 42.8; C-14: 56.5; C-15: 24.2; C-16: 28.2; C-17: 56.1; C-18: 12.0; C-19: 23.4; C-20: 35.5; C-21: 18.2; C-22: 31.5; C-23: 31.2; C-24: 183.6; C-α-Sn: 24.9 [$^1J(^{13}C$-$^{119/117}Sn)$ = 586/564]; C-β: 26.6 [$^2J(^{13}C$-$^{119/117}Sn) \approx 36$]; C-γ: 26.3 [$^3J(^{13}C$-$^{119/117}Sn) \approx 98$]; C-δ: 13.5
^{117}Sn NMR ($CDCl_3$): -149.9; ^{119}Sn NMR MAS: -80; -290

Compound **3**, $(C_{23}H_{39}O_2CO_2)_2Sn(CH_2CH_2CH_2CH_3)_2$
Recrystallized from acetone/petroleum ether, mp: 105-107 °C, yield: 81%
Mössbauer parameters (in mm/s): QS: 3.36, IS: 1.38, Γ_1 & Γ_2: 1.05 & 0.98
^{1}H NMR ($CDCl_3$): H-1: 0.98, 1.78; H-2: 1.30, 1.63; H-3: 3.40; H-4: 1.67, 2.17; H-5: 1.34
H-6: 1.48, 1.92; H-7: 3.80; H-8: 1.43; H-9: 1.78; H-11: 1.24, 1.45; H-12: 1.13, 1.93; H-14: 1.37; H-15: 1.07, 1.62; H-16: 1.29, 1.89; H-17: 1.11; H-18: 0.62; H-19: 0.88; H-20: 1.38; H-21: 0.91; H-22: 1.29, 1.82; H-23: 2.22, 2.38; H-α: 1.60; H-β: 1.60; H-γ: 1.33; H-δ: 0.88 t (7)
^{13}C NMR ($CDCl_3$): C-1: 35.4; C-2: 30.7; C-3: 72.0; C-4: 39.9; C-5: 41.6; C-6: 34.7; C-7: 68.5; C-8: 39.5; C-9: 32.9; C-10: 35.1; C-11: 20.6; C-12: 39.7; C-13: 42.7; C-14: 50.5; C-15: 23.7; C-16: 28.2; C-17: 56.0; C-18: 11.8; C-19: 22.8; C-20: 35.6; C-21: 18.3; C-22: 31.7; C-23: 31.3; C-24: 184.3; C-α-Sn: 24.9 [$^1J(^{13}C\text{-}^{119/117}Sn)$ = 582/561]; C-β: 26.7 [$^2J(^{13}C\text{-}^{119/117}Sn)$ ≈34]; C-γ: 26.3 [$^3J(^{13}C\text{-}^{119/117}Sn)$ ≈ 95]; C-δ: 13.5
^{117}Sn NMR ($CDCl_3$): -148.8; ^{119}Sn NMR MAS: -177; -205

Compound **4**, $(C_{23}H_{39}O_3CO_2)_2Sn(CH_2CH_2CH_2CH_3)_2$
Recrystallized from ethanol/chloroform, mp: 176-178 °C, yield: 78%
Mössbauer parameters (in mm/s): QS: 3.29, IS: 1.37, Γ_1 & Γ_2: 1.00 & 1.01
^{1}H NMR ($CDCl_3$): H-1: 1.56, 1.91; H-2: 2.14, 2.24; H-4: 2.05, 2.17; H-5: 2.27
H-6: 1.96, 2.87; H-8: 2.84; H-9: 2.28; H-11: 2.08, 2.80; H-14: 1.79; H-15: 1.20, 2.25; H-16: 1.25, 1.98; H-17: 1.98; H-18: 1.01; H-19: 1.35; H-20: 1.24; H-21: 0.80; H-22: 1.38, 1.81; H-23: 2.25, 2.35; H-α: 1.59; H-β: 1.59; H-γ: 1.31; H-δ: 0.88 (7)
^{13}C NMR ($CDCl_3$): C-1: 35.2; C-2: 36.4; C-3: 208.8; C-4: 44.9; C-5: 46.8; C-6: 42.7
C-7: 208.5; C-8: 49.0; C-9: 45.5; C-10: 36.0; C-11: 38.6; C-12: 211.7; C-13: 56.9;
C-14: 51.7; C-15: 25.1; C-16: 27.6; C-17: 45.7; C-18: 11.8; C-19: 21.8; C-20: 35.8;
C-21: 18.6; C-22: 31.1; C-23: 31.5; C-24: 184.4; C-α-Sn: 24.8 [$^1J(^{13}C\text{-}^{119/117}Sn)$ = 585/560]; C-β: 26.6 [$^2J(^{13}C\text{-}^{119/117}Sn)$ ≈ 35]; C-γ: 26.2 [$^3J(^{13}C\text{-}^{119/117}Sn)$ = 97/93]; C-δ: 13.5
^{117}Sn NMR ($CDCl_3$): -149.2; ^{119}Sn NMR MAS: -140; -220

Compound **5**, $(C_{23}H_{39}O_2CO_2)_2Sn(CH_2CH_2CH_2CH_3)_2$
Recrystallized from cyclohexane, mp: 109-111 °C, yield: 70%
Mössbauer parameters (in mm/s): QS: 3.35, IS: 1.37, Γ_1 & Γ_2: 1.16 & 1.02
^{1}H NMR ($CDCl_3$): H-1: 0.97, 1.74; H-2: 1.21, 1.60; H-3: 3.54; H-4: 1.45, 1.63; H-5: 1.44
H-6: 1.55, 1.74; H-7: 3.51; H-8: 1.36; H-9: 1.39; H-11: 1.21, 1.38; H-12: 1.10, 1.95; H-14: 1.18; H-15: 1.41, 1.76; H-16: 1.28, 1.84; H-17: 1.02; H-18: 0.65; H-19: 0.89; H-20: 1.36; H-21: 0.87; H-22: 1.30, 1.78; H-23: 2.22, 2.36; H-α: 1.58; H-β: 1.58; H-γ: 1.31; H-δ: 0.88 t (7)
^{13}C NMR ($CDCl_3$): C-1: 35.0; C-2: 30.3; C-3: 71.3; C-4: 37.3; C-5: 42.5; C-6: 37.0; C-7: 71.3; C-8: 43.8; C-9: 39.3; C-10: 34.1; C-11: 21.2; C-12: 40.2; C-13: 43.8; C-14: 55.8; C-15: 26.9; C-16: 28.7; C-17: 55.0; C-18: 12.2; C-19: 23.4; C-20: 35.5; C-21: 18.4; C-22: 31.7; C-23: 31.3; C-24: 184.6; C-α-Sn: 24.9 [$^1J(^{13}C\text{-}^{119/117}Sn)$ = 583/560]; C-β: 26.7 [$^2J(^{13}C\text{-}^{119/117}Sn)$ ≈37]; C-γ: 26.4 [$^3J(^{13}C\text{-}^{119/117}Sn)$ ≈ 100]; C-δ: 13.6
^{117}Sn NMR ($CDCl_3$): -149.5

Compound **6**, $(C_{23}H_{39}O_2CO_2)Sn(C_6H_5)_3$
Recrystallized from acetone/petroleum ether, mp: 91-92°C, yield: 95%
Mössbauer parameters (in mm/s): QS: 3.14, IS: 1.25, Γ_1 & Γ_2: 1.10 & 1.01
^{1}H NMR ($CDCl_3$): H-1: 0.95, 1.72; H-2: 1.36, 1.64; H-3: 3.58; H-4: 1.49, 1.76; H-5: 1.37
H-6: 1.22, 1.82; H-7: 1.26, 1.41; H-8: 1.36; H-9: 1.77; H-11: 1.47; H-12: 3.91; H-14: 1.51; H-15: 1.52; H-16: 1.10, 1.38; H-17: 1.64; H-18: 0.57; H-19: 0.88; H-20: 1.34; H-21: 0.92; H-22: 1.33, 1.85; H-23: 2.31, 2.48; *H-o*: 7.73 [$^3J(^1H\text{-}^{119/117}Sn)$ ≈ 59]; *H-m & H-p* 7.44
^{13}C NMR ($CDCl_3$): C-1: 35.3; C-2: 30.5; C-3: 71.8; C-4: 36.5; C-5: 42.2; C-6: 27.6; C-7: 27.2; C-8: 36.1; C-9: 33.6; C-10: 34.2; C-11: 28.6; C-12: 73.2; C-13: 46.5; C-14: 48.2; C-15: 23.8; C-16: 26.2; C-17: 47.4; C-18: 12.7; C-19: 23.2; C-20: 35.1; C-21: 17.4; C-22: 31.8; C-23: 31.3; C-24: 181.4; C-*i*: 138.5 [$^1J(^{13}C\text{-}^{119/117}Sn)$ = 648/618]; C-*o*: 137.0 [$^2J(^{13}C\text{-}^{119/117}Sn)$ ≈ 48]; C-*m*: 128.9 [$^3J(^{13}C\text{-}^{119/117}Sn)$ = 64/61]; C-*p*: 130.1 [$^4J(^{13}C\text{-}^{119/117}Sn)$ ≈ 13]
^{117}Sn NMR ($CDCl_3$): -116.9; ^{119}Sn NMR MAS: -121; -300

Compound **7**, $(C_{23}H_{39}OCO_2)Sn(C_6H_5)_3$
Recrystallized from ethyl acetate/petroleum ether, mp: 78-79°C, yield: 90%
Mössbauer parameters (in mm/s): QS: 3.27, IS: 1.28, Γ_1 & Γ_2: 1.08 & 0.98
^{1}H NMR ($CDCl_3$): H-1: 0.95, 1.78; H-2: 1.30, 1.68; H-3: 3.60; H-4: 1.50, 1.74; H-5: 1.37
H-6: 1.23, 1.86; H-7: 1.05, 1.38; H-8: 1.36; H-9: 1.38; H-11: 1.14, 1.36; H-12: 1.13, 1.92; H-14: 1.00; H-15: 0.93, 1.53; H-16: 1.16, 1.86; H-17: 1.07; H-18: 0.57; H-19: 0.93; H-20: 1.35; H-21: 0.90; H-22: 1.32, 1.85; H-23: 2.30, 2.48; *H-o*: 7.72 [$^3J(^1H\text{-}^{119/117}Sn) \approx 58$]; *H-m*: & *H-p*: 7.45
^{13}C NMR ($CDCl_3$): C-1: 35.4; C-2: 30.6; C-3: 71.9; C-4: 36.5; C-5: 42.1; C-6: 27.2; C-7: 26.4; C-8: 35.9; C-9: 40.4; C-10: 34.6; C-11: 20.8; C-12: 40.2; C-13: 42.7; C-14: 56.5; C-15: 24.2; C-16: 28.3; C-17: 56.0; C-18: 12.0; C-19: 23.4; C-20: 35.5; C-21: 18.3; C-22: 31.8; C-23: 31.2; C-24: 181.5; C-*i*: 138.5 [$^1J(^{13}C\text{-}^{119/117}Sn) = 648/621$]; C-*o*: 137.0 [$^2J(^{13}C\text{-}^{119/117}Sn) \approx 48$]; C-*m*: 128.9 [$^3J(^{13}C\text{-}^{119/117}Sn) \approx 63$]; C-*p*: 130.1 [$^4J(^{13}C\text{-}^{119/117}Sn) \approx 13$]
^{117}Sn NMR ($CDCl_3$): -116.8; ^{119}Sn NMR MAS: -114; -281

Compound **8**, $(C_{23}H_{39}O_2CO_2)Sn(C_6H_5)_3$
Recrystallized from ethanol, mp: 121-123, yield: 88%
Mössbauer parameters (in mm/s): QS: 3.38, IS: 1.32, Γ_1 & Γ_2: 0.98 & 0.90
^{1}H NMR ($CDCl_3$): H-1: 0.95, 1.82; H-2: 1.28, 1.64; H-3: 3.44; H-4: 1.64, 2.20; H-5: 1.36
H-6: 1.51, 2.15; H-7: 3.81; H-8: 1.45; H-9: 1.83; H-11: 1.24, 1.47; H-12: 1.15, 1.93; H-14: 1.33; H-15: 1.06, 1.60; H-16: 1.25, 1.88; H-17: 1.11; H-18: 0.56; H-19: 0.88; H-20: 1.40; H-21: 0.90; H-22: 1.31, 1.92; H-23: 2.34, 2.44; *H-o*: 7.75 [$^3J(^1H\text{-}^{119/117}Sn) \approx 59$]; *H-m*: & *H-p*: 7.47
^{13}C NMR ($CDCl_3$): C-1: 35.5; C-2: 30.8; C-3: 72.0; C-4: 39.9; C-5: 41.6; C-6: 34.7; C-7: 68.5; C-8: 39.5; C-9: 32.9; C-10: 35.1; C-11: 20.7; C-12: 39.7; C-13: 42.7; C-14: 50.5; C-15: 23.7; C-16: 28.2; C-17: 56.0; C-18: 11.8; C-19: 22.9; C-20: 35.5; C-21: 18.4; C-22: 31.9; C-23: 31.2; C-24: 181.3; C-*i*: 138.6 [$^1J(^{13}C\text{-}^{119/117}Sn) = 648/621$]; C-*o*: 136.9 [$^2J(^{13}C\text{-}^{119/117}Sn) \approx 48$]; C-*m*: 128.9 [$^3J(^{13}C\text{-}^{119/117}Sn) \approx 63$]; C-*p*: 130.1
^{117}Sn NMR ($CDCl_3$): -116.8

Compound **9**, $(C_{23}H_{39}O_3CO_2)Sn(C_6H_5)_3$
Recrystallized from chloroform/petroleum ether, mp: 180-182°C, yield: 95%
Mössbauer parameters (in mm/s): QS: 3.22, IS: 1.28, Γ_1 & Γ_2: 1.01 & 0.96
^{1}H NMR ($CDCl_3$): H-1: 1.61, 1.94; H-2: 2.17, 2.25; H-4: 2.06, 2.22; H-5: 2.30; H-6: 2.83, 2,90; H-8: 2.82; H-9: 2.30; H-11: 2.09, 2.79; H-14: 1.79; H-15: 1.15, 2.25; H-16: 1.21, 1.99; H-17: 1.99; H-18: 0.92; H-19: 1.37; H-20: 1.37; H-21: 0.81; H-22: 1.36, 1.86; H-23: 2.36, 2.48; *H-o*: 7.71 [$^3J(^1H\text{-}^{119/117}Sn) \approx 59$]; *H-m*: & *H-p*: 7.42
^{13}C NMR ($CDCl_3$): C-1: 35.4; C-2: 36.4; C-3: 208.8; C-4: 42.8; C-5: 46.8; C-6: 45.0
C-7: 208.5; C-8: 49.0; C-9: 45.6; C-10: 36.0; C-11: 38.6; C-12: 211.7; C-13: 56.9;
C-14: 51.8; C-15: 25.1; C-16: 27.6; C-17: 45.8; C-18: 11.7; C-19: 21.9; C-20: 35.6;
C-21: 18.6; C-22: 31.4; C-23: 31.5; C-24: 181.1; C-*i*: 138.6 [$^1J(^{13}C\text{-}^{119/117}Sn) = 650/622$]
C-*o*: 136.9 [$^2J(^{13}C\text{-}^{119/117}Sn) \approx 48$]; C-*m*: 128.9 [$^3J(^{13}C\text{-}^{119/117}Sn) = 64/61$]; C-*p*: 130.1
[$^4J(^{13}C\text{-}^{119/117}Sn) \approx 13$]
^{117}Sn NMR ($CDCl_3$): -117.4

Compound **10**, $(C_{23}H_{39}O_2CO_2)Sn(C_6H_5)_3$
Recrystallized from chloroform/ethanol, mp: 118-120 °C, yield: 75%
Mössbauer parameters (in mm/s): QS: 3.33, IS: 1.27, Γ_1 & Γ_2: 0.88 & 0.96
^{1}H NMR ($CDCl_3$): H-1: 0.98, 1.75; H-2: 1.23, 1.62; H-3: 3.56; H-4: 1.45, 1.77; H-5: 1.45
H-6: 1,56, 1.60; H-7: 3.56; H-8: 1.36; H-9: 1.39; H-11: 1.19, 1.39; H-12: 1.08, 1.93; H-14: 1.15; H-15: 1.35, 1.76; H-16: 1.21, 1.85; H-17: 1.03; H-18: 0.53; H-19: 0.91; H-20: 1.35; H-21: 0.87; H-22: 1.32, 1.82; H-23: 2.32, 2.44; *H-o*: 7.70 [$^3J(^1H\text{-}^{119/117}Sn) \approx 59$]; *H-m*: & *H-p*: 7.40
^{13}C NMR ($CDCl_3$): C-1: 35.0; C-2: 30.4; C-3: 71.4; C-4: 37.4; C-5: 42.5; C-6: 36.9; C-7: 71.4; C-8: 43.8; C-9: 39.2; C-10: 34.1; C-11: 21.2; C-12: 40.2; C-13: 43.8; C-14: 55.8; C-15: 26.9; C-16: 28.7; C-17: 55.0; C-18: 12.1; C-19: 23.4; C-20: 35.3; C-21: 18.4; C-22: 31.9; C-23: 31.2; C-24: 181.3; C-*i*: 138.5 [$^1J(^{13}C\text{-}^{119/117}Sn) = 650/619$]; C-*o*: 136.9 [$^2J(^{13}C\text{-}^{119/117}Sn) \approx 48$]; C-*m*: 128.9 [$^3J(^{13}C\text{-}^{119/117}Sn) \approx 63$]; C-*p*: 130.1
^{117}Sn NMR ($CDCl_3$): -116.7

Compound **11**, $(C_{23}H_{39}OCO_2)Sn(CH_2CH_2CH_2CH_3)_3$
Recrystallized from ethyl acetate/petroleum ether, mp: 45-46°C, yield: 86%
Mössbauer parameters (in mm/s): QS: 3.47, IS: 1.40, Γ_1 & Γ_2 : 1.32 & 1.37
^{1}H RMN ($CDCl_3$): H-1: 0.96, 1.77; H-2: 1.30, 1.63; H-3: 3.58; H-4: 1.47, 1.74; H-5: 1.35
H-6: 1.24, 1.86; H-7: 1.05, 1.39; H-8: 1.36; H-9: 1.36; H-11: 1.14, 1.39; H-12: 1.11, 1.92; H-14: 1.03; H-15: 1.03, 1.56; H-16: 1.23, 1.82; H-17: 1.06; H-18: 0.63; H-19: 0.91; H-20: 1.40; H-21: 0.91; H-22: 1.27, 1.76; H-23: 2.18, 2.31; H-α: 1.24; H-β: 1.55; H-γ: 1.31; H-δ: 0.91, t (7)
^{13}C NMR ($CDCl_3$): C-1: 35.4; C-2: 30.6; C-3: 71.8; C-4: 36.5; C-5: 42.2; C-6: 27.2; C-7: 26.4; C-8: 35.9; C-9: 40.5; C-10: 34.6; C-11: 20.8; C-12: 40.2; C-13: 42.7; C-14: 56.5; C-15: 24.2; C-16: 28.2; C-17: 56.2; C-18: 12.0; C-19: 23.4; C-20: 35.5; C-21: 18.3; C-22: 31.9; C-23: 31.9; C-24: 179.8; C-α-Sn: 16.4 [$^1J(^{13}C\text{-}^{119/117}Sn)$ = 360/344]; C-β: 27.8 [$^2J(^{13}C/^{119/117}Sn) \approx 20$]; C-γ: 27.0; [$^3J(^{13}C\text{-}^{119/117}Sn)$ = 66/63]; C-δ: 13.6
^{117}Sn NMR ($CDCl_3$): 101.6; ^{119}Sn NMR MAS: 89; -42

Compound **12**, $(C_{23}H_{39}O_2CO_2)Sn(CH_2CH_2CH_2CH_3)_3$
Recrystallized from hexane, mp: 46-48 °C, yield: 75%
Mössbauer parameters (in mm/s): QS: 3.36, IS: 1.37, Γ_1 & Γ_2: 1.31 & 1.47
^{1}H NMR ($CDCl_3$): H-1: 0.95, 1.79; H-2: 1.31, 1.65; H-3: 3.41; H-4: 1.68, 2.18; H-5: 1.35
H-6: 1.48, 1.94; H-7: 3.80; H-8: 1.46; H-9: 1.79; H-11: 1.25, 1.45; H-12: 1.15, 1.94; H-14: 1.36; H-15: 1.07, 1.60; H-16: 1.31, 1.88; H-17: 1.13; H-18: 0.63; H-19: 0.87; H-20: 1.39; H-21: 0.90; H-22: 1.26, 1.75; H-23: 2.18, 2.32; H-α: 1.21; H-β: 1.57; H-γ: 1.31; H-δ: 0.87, t (7)
^{13}C NMR ($CDCl_3$): C-1: 35.4; C-2: 30.7; C-3: 72.0; C-4: 39.9; C-5: 41.6; C-6: 34.7; C-7: 68.5; C-8: 39.5; C-9: 32.9; C-10: 35.1; C-11: 20.6; C-12: 39.7; C-13: 42.7; C-14: 50.5; C-15: 23.7; C-16: 28.2; C-17: 56.1; C-18: 11.8; C-19: 22.8; C-20: 35.6; C-21: 18.3; C-22: 31.8; C-23: 31.8; C-24: 179.7; C-α-Sn: 16.4 [$^1J(^{13}C\text{-}^{119/117}Sn)$ = 359/344]; C-β: 27.9 [$^2J(^{13}C\text{-}^{119/117}Sn) \approx 20$]; C-γ: 27.0 [$^3J(^{13}C\text{-}^{119/117}Sn) \approx 65$]; C-δ: 13.6
^{117}Sn NMR ($CDCl_3$): 102.0

Compound **13**, $(C_{23}H_{39}O_3CO_2)Sn(CH_2CH_2CH_2CH_3)_3$
Recrystallized from dichloromethane/ethanol, mp: 194-195°C, yield: 75%
Mössbauer parameters (in mm/s): QS: 2.65, IS: 1.36, Γ_1 & Γ_2: 1.11 & 0.82
^{1}H NMR ($CDCl_3$): H-1: 1.56, 1.90; H-2: 2.15, 2.23; H-4: 2.05, 2.16; H-5: 2.30
H-6: 1.97, 2.85; H-8: 2.83; H-9: 2.28; H-11: 2.07, 2.80; H-14: 1.78; H-15: 1.19, 2.24; H-16: 1.27, 1.98; H-17: 1.99; H-18: 1.03; H-19: 1.34; H-20: 1.22; H-21: 0.82; H-22: 1.31, 1.78; H-23: 2.18, 2.34; H-α: 1.20; H-β: 1.54; H-γ: 1.27; H-δ: 0.87, t (7)
^{13}C NMR ($CDCl_3$): C-1: 35.3; C-2: 36.5; C-3: 209.1; C-4: 42.8; C-5: 46.9; C-6: 45,0
C-7: 208.8; C-8: 49.0; C-9: 45.5; C-10: 36.0; C-11: 38.7; C-12: 211.8; C-13: 56.9;
C-14: 51.9; C-15: 25.2; C-16: 27.7; C-17: 45.8; C-18: 11.8; C-19: 21.9; C-20: 35.7;
C-21: 18.7; C-22: 31.4; C-23: 32.3; C-24: 179.6; C-α-Sn: 24.8 [$^1J(^{13}C\text{-}^{119/117}Sn)$ = 360/343]; C-β: 26.6 [$^2J(^{13}C\text{-}^{119/117}Sn) \approx 20$]; C-γ: 26.2 [$^3J(^{13}C\text{-}^{119/117}Sn)$ = 66/63]; C-δ: 13.5
^{117}Sn NMR ($CDCl_3$): 103.4

Antitumour screening
The protocol followed for these screenings has already been reported[10].

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