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Dibutyltin perfluoroalkanecarboxylates: synthesis, NMR characterization and in vitro antitumour activity

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Abstract

Three dibutyltin perfluoroalkanecarboxylates have been synthesized, characterized by ^{1}H-, ^{13}C-, ^{19}F- and ^{117}Sn-NMR, Mössbauer, IR and mass spectroscopy. The structure of tetra-*n*-butylbis(trifluoroacetato)distannoxane has been elucidated by X-ray crystallography. The in vitro antitumour activity of the three compounds against seven human tumour cell lines was found to be as high as or even higher than that for reference compounds used clinically. © 2000 Published by Elsevier Science S.A.

Keywords: Dibutyltin perfluoroalkanecarboxylates; NMR; Antitumour activity

1. Introduction

Several organotin fluoro-substituted aromatic carboxylates are very active in vitro against human cancer cell lines [1–6]; Tables 1 and 2 summarize their activities.

Table 1 reveals high antitumour activities [1–4] for a range of di- and triorganotin fluoro-substituted benzoates against two cell lines and Table 2 shows that organotin perfluorophenyl-substituted carboxylates are in general more active than their non-fluorinated analogs against a broader panel of cell lines [5–7]. Data available for organometals with fluorinated organic groups indicated enhanced activity [8]. Hence, we explored the antitumour activity of some aliphatic di-*n*-butyltin perfluoroalkanecarboxylates in order to compare their in vitro antitumour activities with those of di-*n*-butyltin fluorinated aromatic carboxylates. For this purpose, bis(trifluoroacetato-, -pentafluoropropionato- and -heptafluorobutyrato)tetra-*n*-butyldistannoxanes were synthesized and characterized by ^{1}H-, ^{13}C-, ^{19}F- and ^{117}Sn-NMR as well as Mössbauer and electrospray mass spectrometry. Crystallographic data are also presented for the trifluoroacetate compound. The trifluoroacetate is mentioned in an earlier study on a comparative evaluation of its toxic and mutagenic properties [9].

2. Results and discussion

2.1. Synthesis

The different reactions that can in principle be used for the synthesis of the di-*n*-butyltin perfluoroalkanecarboxylates are generally characterized by excellent yields [10–12].

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Table 1
In vitro ID_{50} inhibition doses (in ng ml^{-1}) against the mammary tumour MCF-7 and the colon carcinoma WiDr of di- and tri-organotin fluoro-substituted benzoates [1–4]

Compound	MCF-7	WiDr
$(2\text{-}FC_6H_4CO_2)_2SnBu_2$	74	242
$(3\text{-}FC_6H_4CO_2)_2SnBu_2$	39	271
$(4\text{-}FC_6H_4CO_2)_2SnBu_2$	90	309
$(3\text{-}CF_3C_6H_4CO_2)_2SnBu_2$	102	434
$(2,3\text{-}F_2C_6H_3CO_2)_2SnBu_2$	38	277
$(2,6\text{-}F_2C_6H_3CO_2)_2SnBu_2$	98	326
$(3,5\text{-}F_2C_6H_3CO_2)_2SnBu_2$	52	416
$(3\text{-}FC_6H_4CO_2)_2SnEt_2$	1235	3705
$3\text{-}FC_6H_4CO_2SnPh_3$	11	14
$4\text{-}FC_6H_4CO_2SnPh_3$	15	14
$2,3\text{-}F_2C_6H_3CO_2SnPh_3$	17	14
$3,5\text{-}F_2C_6H_3CO_2SnPh_3$	18	17
$2\text{-}FC_6H_4CO_2SnBu_3$	35	<1
$2,5\text{-}F_2C_6H_3CO_2SnBu_3$	38	26
$2,6\text{-}F_2C_6H_3CO_2SnBu_3$	22	2
$[(2\text{-}FC_6H_4CO_2SnBu_2)_2O]_2$	91	330
$[(4\text{-}FC_6H_4CO_2SnBu_2)_2O]_2$	81	360
$[(2,3\text{-}F_2C_6H_3CO_2SnBu_2)_2O]_2$	13	134
$[(2,5\text{-}F_2C_6H_3CO_2SnBu_2)_2O]_2$	32	353
$[(2,6\text{-}F_2C_6H_3CO_2SnBu_2)_2O]_2$	25	227
$[(3,5\text{-}F_2C_6H_3CO_2SnBu_2)_2O]_2$	43	277

The first step of the one-pot synthesis [10] is the preparation of tetra-*n*-butyldipropoxydistannoxane

$$2Bu_2SnO + 2PrOH \rightarrow (Bu_2SnOPr)_2O + H_2O$$

Usually, the second step is the reaction at room temperature of this distannoxane with a carboxylic acid

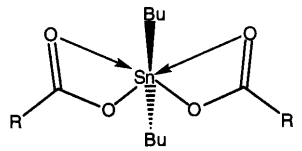

Fig. 1. Structure of the 1/2 compounds of type **a**.

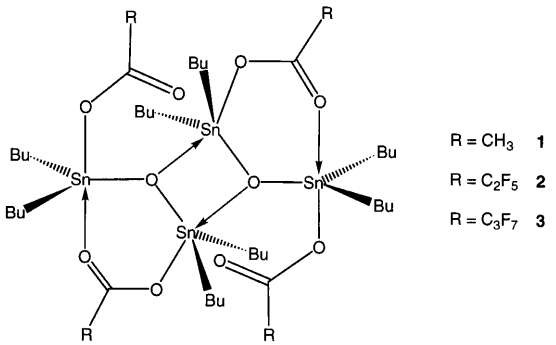

Fig. 2. Structure of the 1/1 compounds of type **b**.

in a tin/acid molar ratio 1/2 or 1/1 providing respectively a di-*n*-butyltin dicarboxylate of type **a** (Fig. 1):

$$(Bu_2SnOPr)_2O + 4RCOOH$$
$$\rightarrow 2Bu_2Sn(OOCR)_2 + 2PrOH + H_2O$$

or a dimeric tetra-*n*-butyldicarboxylatodistannoxane of type **b** (Fig. 2):

$$2(Bu_2SnOPr)_2O + 4RCOOH$$
$$\rightarrow [(Bu_2SnOOCR)_2O]_2 + 4PrOH$$

Table 2
In vitro ID_{50} inhibition doses (ng ml^{-1}) against six human tumour cell lines, two mammary cancers (MCF-7, EVSA-T), a colon carcinoma (WiDr), an ovarian cancer (IGROV), a melanoma (M19 MEL) and a renal cancer (A 498) of di- and triorganotin pentafluorophenyl-substituted carboxylates and their non-fluorinated analogues [5–7], and of some clinically used reference compounds

Compound	MCF-7	EVSA-T	WiDr	IGROV	M19 MEL	A 498
$\{[Bu_2Sn(O_2CC_6F_5)]_2O\}_2$	44	39	214	53	86	76
$\{[Bu_2Sn(O_2CCH_2C_6F_5)]_2O\}_2$	55	43	275	60	114	105
$\{[Bu_2Sn(O_2CCH{=}CHC_6F_5)]_2O\}_2$	32	37	234	41	66	135
$Bu_2Sn(O_2CCH_2C_6F_5)_2$	10	19	145	20	36	51
$Bu_3SnO_2CC_6F_5$	15	<3	20	25	60	50
$Bu_3SnO_2CCH_2C_6F_5$	14	<3	12	12	52	51
$Bu_3SnO_2CCH{=}CHC_6H_5$	13	<3	14	11	45	54
$Bu_3SnO_2CC_6H_5$	130	15	70	100	110	190
$Bu_3SnO_2CCH_2C_6H_5$	42	11	50	50	85	75
$Bu_3SnO_2CCH{=}CHC_6H_5$	23	<3	45	38	47	63
$Ph_3SnO_2CC_6F_5$	45	17	90	44	130	120
$Ph_3SnO_2CCH_2C_6F_5$	14	6	17	20	18	30
$Ph_3SnO_2CCH{=}CHC_6F_5$	20	9	30	34	40	30
$Ph_3SnO_2CC_6H_5$	650	110	500	470	800	950
$Ph_3SnO_2CCH_2C_6H_5$	4	<3	5	5	13	21
$Ph_3SnO_2CCH{=}CHC_6H_5$	12	3	22	16	30	52
Carboplatin	5500	1100	1500	780	5300	3500
Cis-platin	699	422	967	169	558	2253
5-Fluorouracil	750	475	225	297	442	143
Doxorubicine	10	8	11	60	16	90

The compounds reported, tetra-*n*-butylbis(trifluoroacetato)distannoxane (**1**), tetra-*n*-butylbis(pentafluoropropionato)distannoxane (**2**) and tetra-*n*-butylbis(heptafluorobutyrato) distannoxane (**3**) are of type **b**. Surprisingly, they could not be obtained when using a 1/1 molar ratio, but only from 1/2 reaction conditions.

The compounds of type **a** could not be obtained in pure form utilizing this method. Di-*n*-butyltin bis(heptafluorobutyrate) (**3a**) was the only compound of type **a** that could be obtained, however, mixed with its hydrolysis product **3**. Compound **3a** appears indeed very sensitive to moisture, since it is hydrolysed in situ into the corresponding type **b** compound **3**. This is accounted for by the reaction:

$$4R_2Sn(OOCR')_2 + 2H_2O \rightarrow [(R_2SnOOCR')_2O]_2 + 4R'COOH$$

All compounds decompose rapidly if they are not stored in dry media. The literature describes the decomposition of **1** into $(CF_3COO)SnBu_2OSnBu_2(OH)$ [11].

Table 3
^{1}H-NMR data in $CDCl_3$ for compounds **1**–**3**; chemical shift in ppm, $^3J(^1H–^1H)$ homonuclear coupling constants in Hz in parentheses (t = triplet, q = quartet; m = complex pattern)

	1[a]	**2**	**3**
H (α), H (β)	1.56–1.75 m	1.55–1.75 m	1.52–1.74 m
H (γ)	1.39 tq (7.7)	1.38 tq (7.7)	1.35 tq (7.7)
H (δ)	0.93 t (7)	0.92 t (7)	0.89 t (7)
	0.92 t (7)	0.91 t (7)	0.88 t (7)

[a] In agreement with literature data [12].

Table 4
^{13}C-NMR data in $CDCl_3$ for the compounds **1**–**3**; $^nJ(^{13}C–^{117/119}Sn)$ values are given in parentheses; a single value is given when the $^nJ(^{13}C–^{117}Sn)$ and $^nJ(^{13}C–^{119}Sn)$ couplings are unresolved

	1	**2**	**3**
CH_2 (α)	30.1 (627/658)	30.6 (646/672)	30.0 (644/677)
CH_2 (α)	28.6 (596/622)	29.1 (604/631)	28.6 (602/630)
CH_2 (β)	27.8	28.2	27.6
CH_2 (β)	27.4	27.8	27.3
CH_2 (γ)	27.1 (116/121)	27.1 (115/121)	26.6 (116)
CH_2 (γ)	27.1 (136/141)	27.1 (145)	26.5 (142)
CH_3 (δ)	13.9	13.8	13.2

Table 5
^{19}F chemical shifts with respect to $CFCl_3$ and ^{13}C chemical shifts for the perfluoroalkanecarboxylate groups of compounds **1**–**3** in $CDCl_3$

	1	**2**	**3**
CF_3 δ ^{19}F	−77.8	−85.4	−83.5
δ ^{13}C	114.4 (q)	118.7 (qt)	117.6 (qt)
$^1J(^{13}C–^{19}F)$	289	286	288
$^2J(^{13}C–^{19}F)$		35	34
CF_2 (β) δ ^{19}F			−112.0
δ ^{13}C			108.5 (ttq)
$^1J(^{13}C–^{19}F)$			266
$^2J(^{13}C–^{19}F)$			34; 34
CF_2 (α) δ ^{19}F		−122.7	−129.1
δ ^{13}C		107.0 (tq)	108.2 (tt)
$^1J(^{13}C–^{19}F)$		265	266
$^2J(^{13}C–^{19}F)$		39	34
COO δ ^{13}C	160.3 (t)	163.2 (t)	162.4 (t)
$^2J(^{13}C–^{19}F)$	37	27	28

Table 6
^{117}Sn chemical shifts in ppm of compounds **1**–**3** ($CDCl_3$), with unresolved $^2J(^{117}SnO^{119}Sn)$ and $^2J(^{117}SnO^{117}Sn)$ coupling constants

	1	**2**	**3**
$\delta(^{117}Sn)$	−169.0	−175.0	−174.3
	−175.2	−175.9	−175.0
$^2J(^{117}SnO^{119/117}Sn)$	113	122	122

2.2. Characterization

2.2.1. NMR spectroscopy

Compounds **1**–**3** were characterized by ^{1}H-, ^{13}C-, ^{19}F- and ^{117}Sn-NMR in $CDCl_3$ solution. 2D ^{1}H–^{13}C HMBC (heteronuclear multiple bond correlation) [13,14] and HMQC (heteronuclear multiple quantum coherence) NMR spectra [15] were recorded for compound **3** in order to assign the ^{1}H and ^{13}C resonances of the *n*-butyl groups. The basic ^{1}H and ^{13}C-NMR data for the compounds **1** to **3** are given in Tables 3 and 4.

2D ^{13}C–^{19}F HMQC spectroscopy was needed for compound **2** in order to achieve simultaneous assignment of the ^{19}F and ^{13}C resonances of the perfluoroalkanecarboxylate moiety. This was even more necessary because in the ^{1}H decoupled ^{13}C spectrum, the fluorinated carbons give rise to noisy overlapping multiplets which are difficult to unravel. The resulting ^{19}F and ^{13}C assignments are based on the assumption that the $^2J(^{13}C–^{19}F)$ coupling constants are larger than the $^3J(^{13}C–^{19}F)$ ones, as supported by literature data [16]. Subsequently, the $^nJ(^{13}C–^{19}F)$ coupling constants as well as ^{13}C chemical shifts of the fluorinated carbons were assigned from non ^{1}H-decoupled ^{13}C spectra, in order to optimize the dynamic range. Table 5 reports ^{13}C and ^{19}F chemical shifts as well as $^nJ(^{13}C–^{19}F)$ coupling constants for these resonances.

Compound **3a** exhibits a single ^{117}Sn resonance at 167.0 ppm, characteristic for type **a** compounds. For compounds **1**–**3**, two ^{117}Sn resonances are observed (Table 6) and assigned to the endocyclic and exocyclic tin atoms (Fig. 2). These data are in agreement with literature data on type **b** compounds described previously [17–20]. Noticeable, however, is a significant deviation of the ^{117}Sn chemical shifts of compound

Table 7
Mössbauer data of compounds **1–3** (quadrupole splitting QS, isomer shift IS, and line widths Γ_1 and Γ_2) in mm s^{-1} relative to calcium stannate

	QS	IS	Γ_1	Γ_2
1	4.14	1.43	0.92	0.92
	3.37	1.45	0.92	0.92
2	4.20	1.45	1.03	1.03
	3.29	1.42	1.03	1.03
3	3.72	1.45	0.95	0.99

Table 8
Fragment-ions observed in electrospray mass spectra for compounds **1–3**

Fragment	**1**	**2**	**3**
$RCOO(SnBu_2O)_2Bu_2Sn.H_2O^+$		897	
$HOSnBu_2OSnBu_2OSnBu_2^+$	751	751	751
$(RCOO)Bu_2SnOSnBu_2^+$	697	647	
$(HO)Bu_2SnOSnBu_2^+$	501	501	501

Table 9
IR $\nu(COO)_{asym}$ frequencies observed for compounds **1–3** (KBr pellets)

1	**2**	**3**
1660	1656	1663
1694	1695	1701

1 with respect to literature data [12] (-178.6 and -177.5 ppm). These data probably correspond to a decomposition product because, following our experience on the stability of such compounds, the experimental procedures used by the authors [10,12] could lead to such a decomposition.

2.2.2. Mössbauer spectroscopy

The Mössbauer parameters (Table 7) of compounds **1** and **2** reveal two types of tin sites, one with a QS = 3.4 mm s^{-1} and another one with QS = 4.2 mm s^{-1}, characteristic for larger $(alkyl)_2Sn$ bond angles than in an ideal trigonal bipyramid, as effectively observed for **1** in the X-ray structure (see Section 2.2.5).

2.2.3. Electrospray mass spectrometry

The most important fragment ions in the monoisotopic mass spectra (^{12}C, ^{1}H, ^{19}F, ^{16}O, ^{120}Sn) recorded in the cationic mode from water–acetonitrile solutions of compounds **1–3** are described in Table 8.

2.2.4. IR spectroscopy

The two $\nu(COO)$ absorptions observed in the IR spectrum (Table 9) are assigned to monodentate (1694–1701 cm^{-1}) and bidentate perfluorocarboxylates (1656–1663 cm^{-1}), respectively, in agreement with literature data [21].

*2.2.5. X-ray crystal structure of compound **1***

The molecular structure of **1**, $\{[Bu_2Sn(O_2CCF_3)_2]_2O\}_2$ is shown in Fig. 3 and selected interatomic parameters are collected in Table 10. The structure determination is less than optimal owing to significant thermal motion associated with the light atom positions, however, the molecular connectivity is unambiguous. The centrosymmetric structure features a central $Bu_4Sn_2O_2$ core to which are linked two Bu_2Sn entities with the result that the O(1) atom is three coordinate. Links between the endo- and exocyclic tin centres are provided by bridging carboxylate ligands that form slightly asymmetric bond distances: Sn(1)–O(2) 2.373(5) Å and Sn(2)–O(3) 2.233(6) Å. The exocyclic tin atom is also coordinated by the O(4) atom so that Sn(2)–O(4) is 2.200(3) Å. The Sn(2)···O(5) separation of 3.071(4) Å represents a very weak bonding interaction as the close contact approach by the O(5) atom has a stereochemical effect, distorting the coordination geometry about the Sn(2) atom so that the C–Sn(2)–C angle is expanded to 142.1(3)°. A similar intramolecular Sn(1)···O(4) contact of 2.889(3) Å results in a comparable expansion in the C–Sn(1)–C angle, i.e. 143.1(2)°. Each of the independent tin atoms in the structure exists in a distorted trigonal bipyramidal geometry with a C_2O trigonal plane and axial positions occupied by oxygen atoms. The structure reported here for compound **1** resembles closely the predominant motif found for compounds of the general formula $\{[R_2Sn(O_2CR')_2]_2O\}_2$ [22,23].

2.2.6. In vitro antitumour screening

The compounds **1–3** were screened against seven human cancer cell lines, the six lines mentioned in Table 2 and H226, a lung cancer. The screening was performed with aqueous solutions containing 1% of DMSO or ethanol. The ID_{50} values observed are given in Table 11 and compared to those of some clinically used reference compounds [24,25], i.e. doxorubicine (DOX), cis-platin (CPT), 5-fluorouracil (5-FU), methotrexate (MTX) and etoposide (ETO).

The screening results indicate that the compounds **1–3** are more active than cis-platin, 5-fluorouracil and etoposide. They are, however, globally less active than doxorubicine and methotrexate, except for the H226 tumour against which they are strikingly active. Against MCF-7 and WiDr, their in vitro activity is comparable to that of di-*n*-butyltin fluorinated aromatic carboxylates, but lower than those of the tri-*n*-butyl- and triphenyltin ones (see Tables 1 and 2).

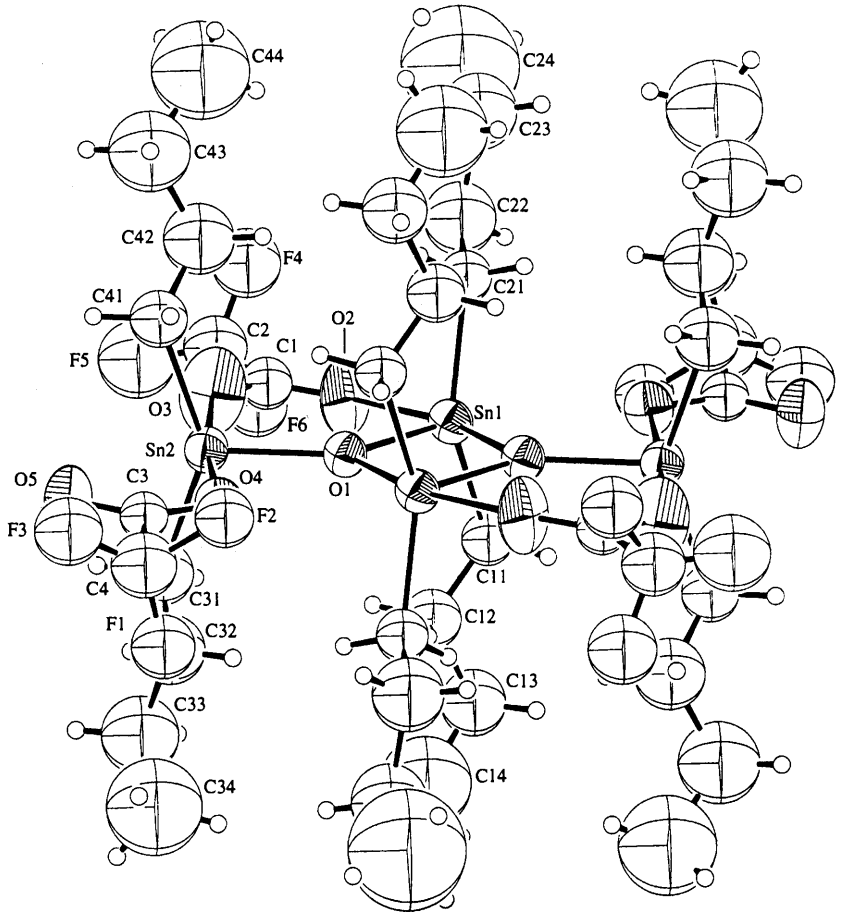

Fig. 3. Molecular structure and crystallographic numbering scheme for compound **1**, $\{[Bu_2Sn(O_2CCF_3)_2]_2O\}_2$.

3. Experimental

3.1. Syntheses

Di-*n*-butyltin oxide is reacted with an excess (4 ml) of propanol in 150 ml of benzene. After 3 h of reflux with elimination (Dean–Stark) of the ternary azeotrope benzene/water/propanol, the reaction mixture is allowed to cool down to room temperature; the appropriate amount of acid is subsequently added slowly and the mixture further stirred for one night. The solvent is evaporated. Purification is achieved by crystallization from a suitable solvent (Table 12) under a dry atmosphere. Compound **3** required successive recrystallizations in undried heptane in order to hydrolyze **3a** completely into **3**. Heating must be avoided in order to prevent decomposition. Anal. Found (calc.): **1**, C 34.12 (33.93); H 4.92 (5.13); F 15.46 (16.10); Sn, 33.56 (33.93); **2**, C 32.82 (32.71); H 4.04 (4.49); F 22.77 (23.51); Sn 29.47 (29.38); **3**, C 31.99 (31.75); H 3.62 (4.00); F 28.36 (29.29); Sn 26.08 (26.15).

Table 10
Selected geometric parameters (Å, °) for compound **1**, $\{[Bu_2Sn(O_2CCF_3)_2]_2O\}_2$

Sn(1)–O(1)	2.058(3)	Sn(1)–$O(1)_i$[a1]	2.170(3)
Sn(1)–O(2)	2.373(5)	Sn(1)–C(11)	2.121(5)
Sn(1)–C(21)	2.104(4)	Sn(2)–O(1)	2.023(3)
Sn(2)–O(3)	2.233(6)	Sn(2)–O(4)	2.200(3)
Sn(2)–C(31)	2.130(5)	Sn(2)–C(41)	2.101(6)
O(1)–Sn(1)–$O(1)_i$	77.8(1)	O(1)–Sn(1)–O(2)	90.3(1)
O(1)–Sn(1)–C(11)	110.2(1)	O(1)–Sn(1)–C(21)	105.7(2)
O(1)I–Sn(1)–O(2)	167.7(1)	O(1)I–Sn(1)–C(11)	98.0(2)
O(1)I–Sn(1)–C(21)	97.7(2)	O(2)–Sn(1)–C(11)	83.0(2)
O(2)–Sn(1)–C(21)	88.5(2)	C(11)–Sn(1)–C(21)	143.1(2)
O(1)–Sn(2)–O(3)	91.9(2)	O(1)–Sn(2)–O(4)	80.8(1)
O(1)–Sn(2)–C(31)	107.9(2)	O(1)–Sn(2)–C(41)	109.6(2)
O(3)–Sn(2)–O(4)	172.7(2)	O(3)–Sn(2)–C(31)	84.7(2)
O(3)–Sn(2)–C(41)	89.0(2)	O(4)–Sn(2)–C(31)	98.3(2)
O(4)–Sn(2)–C(41)	92.5(2)	C(31)–Sn(2)–C(41)	142.1(3)
Sn(1)–O(1)–$Sn(1)_i$	102.2(1)	Sn(1)–O(1)–Sn(2)	134.5(2)
Sn(1)–O(1)–$Sn(2)_i$	123.2(1)	Sn(1)–O(2)–C(1)	135.8(4)
Sn(1)–O(3)–C(1)	139.4(5)	Sn(2)–O(4)–C(3)	114.3(3)

[a] Symmetry operation i: $-x, -y, 1-z$.

Table 11
Inhibition doses ID_{50} in vitro (ng ml^{-1}) of compounds **1**, **2** and **3** against seven human tumour cell lines, two mammary cancers (MCF-7, EVSA-T), a colon carcinoma (WiDr), an ovarian cancer (IGROV), a melanoma (M19 MEL), a renal cancer (A 498) and a non small cell lung cancer (H226)

	MCF-7	EVSA-T	WiDr	IGROV	M19 MEL	A 498	H226
1	57	79	354	113	70	151	147
2	64	93	339	121	101	131	120
3	191	135	340	123	141	177	213
DOX	10	8	11	60	16	90	199
CPT	699	422	967	169	558	2253	3269
5-FU	750	475	225	297	442	143	340
MTX	18	5	<3	7	23	37	2287
ETO	2594	317	150	580	505	1314	3934

Table 12
Reactant amounts, yields, recrystallization solvents and melting points of the diorganotin carboxylates **1**–**3**

Compound synthesized	Amount of acid (g (mmol))	Amount of dibutyltin oxide (g (mmol))	Yield (%)	Recrystallization solvent
1	1.37 (12.0)	1.51 (6.07)	95	hexane
2	1.99 (12.1)	1.51 (6.07)	90	hexane
3	2.80 (12.1)	1.62 (6.51)	72	heptane

3.2. NMR measurements

The ^{19}F-NMR spectra as well as most other 1D spectra were acquired on Bruker AC250 and DRX250 instruments equipped with a Quattro probe tuned to 250.13, 62.93, 89.15, and 235.19 MHz for ^{1}H, ^{13}C, ^{117}Sn, and ^{19}F nuclei, respectively. The ^{19}F detected 2D $^{19}F-^{13}C$ HMQC correlation spectra were acquired on the AC250 spectrometer, as previously [6], without ^{13}C decoupling using the resources of two NMR spectrometers, in a 'master–slave' relationship, as described by Berger [26,27]. ^{19}F acquisition was performed on the AC250 instrument with the ^{1}H coil of the QNP probe being tuned to the ^{19}F resonance frequency, while ^{13}C pulses were generated on the AMX500 instrument under direct control of the AC250 one and sent to the X-coil of the QNP probe. The $^{19}F-^{13}C$ HMQC spectra were acquired in the phase-sensitive mode using TPPI [28], and processed as described elsewhere [6]. All 2D-NMR spectra and some of the 1D spectra were recorded on a Bruker AMX500 spectrometer operating at 500.13, 125.77, and 186.50 MHz for the ^{1}H, ^{13}C, and ^{119}Sn nuclei, respectively. ^{13}C and ^{119}Sn BB proton-decoupled 1D spectra, ^{13}C DEPT spectra as well as the proton-detected 1D and 2D $^{1}H-^{13}C$ HMQC [15] and HMBC [13,14] spectra were acquired using the pulse sequences of the Bruker program library, adapted to include gradient pulses [29,30] as described recently [31]. ^{1}H and ^{13}C chemical shifts were referenced to the standard Me_4Si scale from respectively residual ^{1}H and $^{13}C-^{2}H$ solvent resonances of chloroform ($CHCl_3$, 7.23 and $CDCl_3$, 77.0 ppm for ^{1}H and ^{13}C nuclei, respectively). The ^{119}Sn, ^{117}Sn and ^{19}F reference frequencies were calculated from the absolute references $\Xi(^{119}Sn) = 37.290\ 665$ MHz, $\Xi(^{117}Sn) = 35.632\ 295$ MHz [32,33] and $\Xi(^{19}F) = 94.094\ 003$ MHz [32].

3.3. Mass spectrometry

The electrospray mass spectra were recorded in the cationic mode on a Micromass Quattro II instrument coupled with a Masslynx system (ionization in an electric field of 3.5 kV; source temperature 80°C; source pressure 1 atm; analyser pressure 10^{-5} mbar) [34,35].

3.4. Mössbauer spectroscopy

The Mössbauer spectra were recorded as described previously [36].

3.5. X-ray crystallography

Intensity data for a colourless crystal of **1**, $\{[Bu_2Sn(O_2CCF_3)_2]_2O\}_2$, were collected at room temperature on a Rigaku AFC7R diffractometer employing Mo–K_α radiation ($\lambda = 0.71073$ Å) and the ω:2θ scan technique to $2\theta_{max}$ of 60.0°. The data set was corrected for Lorentz and polarization effects [37] as well as for absorption based on psi-scans. Data that satisfied the $I \geq 3.0\sigma(I)$ criterion of observability were used in the subsequent analysis. Crystal data and refinement details are given in Table 13.

The structure was solved by direct methods [38] and refined by a full-matrix least-squares procedure based

Table 13
Crystallographic data for compound **1**, $\{[Bu_2Sn(O_2CCF_3)_2]_2O\}_2$

Formula	$C_{40}H_{72}F_{12}O_{10}Sn_4$
Formula weight	1415.7
Crystal system	Triclinic
Space group	$P\bar{1}$
Unit cell dimensions	
a (Å)	12.041(2)
b (Å)	14.423(4)
c (Å)	10.182(2)
α (°)	106.98(2)
β (°)	101.87(1)
γ (°)	111.84(2)
V (Å^3)	1468.1(8)
Z	1
Crystal size (mm^3)	$0.2 \times 0.4 \times 0.7$
D_{calc} (g cm^{-3})	1.601
$F(000)$	700
No. of data collected	7140
No. of unique data	6791
No. of reflections with $I \leq 3.0\sigma(I)$	4136
R	0.067
R_w	0.069
Residual ρ_{max} (e Å^{-3})	0.59

on F [37]. The Sn and O atoms were refined with anisotropic displacement parameters, C and F atoms were refined isotropically, and hydrogen atoms were included in the model at their calculated positions (C–H 0.95 Å). The atoms comprising the molecule are subject to high thermal motion. Attempts to collect data at reduced temperatures were unsuccessful as the crystals fragmented, a frequent experience encountered for fluorinated samples of the type reported here. Two positions were resolved for the F atoms comprising each CF_3 group. These were refined with site occupancy factors of 0.6 and 0.4 (primed atoms) determined from the refinement. The carbon atoms were refined so that C–C bond distances were constrained to 1.50 Å. The geometric parameters determined for the light atom positions are thus unreliable, however, the molecular connectivity has been established by this study. The refinement was continued until convergence employing a weighting scheme of the form $1/[\sigma_2(F) + 0.00002|F|_2]$. Selected interatomic parameters are collected in Table 13 and the crystallographic numbering scheme employed is shown in Fig. 3 which was drawn with ORTEP [39] at 25% probability ellipsoids.

3.6. Antitumour screening

The protocol followed for the antitumour screenings has already been reported [24,25].

4. Supplementary material

Crystallographic data for compound **1** have been deposited with the Cambridge Crystallographic Data Centre, CCDC No. 141898. Copies of this information may be obtained free of charge from The Director, CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: +44-1223-336033; e-mail: deposit@ccdc.cam.ac.uk or www: http://www.ccdc.cam.ac.uk).

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