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Synthesis, Characterization and *in-vitro* Antitumour Activity of Dibutyltin Carboxylates Involving the Perfluorophenyl Moiety: Crystal Structure of the Dimeric Bis[(4-fluoro- and Pentafluoro-benzoato)di-n-butyltin] Oxides

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Crystal structure determinations of $\{[(F_5C_6COO)Bu_2Sn]_2O\}_2$ and $\{[(4\text{-}F\text{-}C_6H_4COO)\text{-}Bu_2Sn]_2O\}_2$ show that the structures are similar and feature central $Bu_4Sn_2O_2$ units with two Bu_2Sn groups connected by bridging oxygen atoms. Each pair of exo- and endo-cyclic tin atoms is linked by an almost symmetrically bridging carboxylate group, with the two remaining groups attached to the exocyclic tin atom only. Crystals of $\{[(F_5C_6COO)Bu_2Sn]_2O\}_2$ are triclinic, space group $P\bar{1}$, with unit cell dimensions $a=12.425(3)$ Å, $b=13.090(5)$ Å, $c=11.697(3)$ Å, $\alpha=95.31(3)°$, $\beta=93.28(2)°$, $\gamma=113.01(2)°$, $V=1734(1)$ Å^3, $Z=1$. Crystals of $\{[(4\text{-}F\text{-}C_6H_4COO)Bu_2Sn]_2O\}_2$ are also triclinic, space group $P\bar{1}$, $a=12.599(6)$ Å, $b=25.359(4)$ Å, $c=11.480(4)$ Å, $\alpha=91.44(3)°$, $\beta=114.77(3)°$, $\gamma=97.43(3)°$, $V=3289(2)$ Å^3, $Z=2$. The structures were refined to final $R=0.046$, $R_w=0.046$ for 4312 reflections with $I\geq 3.0\,\sigma(I)$ for $\{[(F_5C_6COO)Bu_2Sn]_2O\}_2$ and $R=0.061$, $R_w=0.068$ for 4112 reflections with $I\geq 3.0\,\sigma(I)$ for $\{[(4\text{-}F\text{-}C_6H_4COO)Bu_2Sn]_2O\}_2$.

Keywords: organotin; carboxylate; crystal structure; distannoxane; antitumour

INTRODUCTION

The substitution of hydrogen by fluorine influences markedly the biological activity of organic molecules.[1] Although the van der Waals radii of fluorine (1.35 Å) and hydrogen (1.20 Å) are comparable, because of the strength of the C–F bond the fluorine substituent is very resistant to metabolic transformations. The much higher electronegativity of fluorine also strongly affects the electronic-density distribution in the molecule.

We have already synthesized a series of organotin carboxylates containing mono- or polyfluorophenyl groups,[2–6] and their antitumour activity was screened against two human tumour cell lines, MCF-7, a mammary tumour, and WiDr, a colon carcinoma (see Table 1).

The di-n-butyltin monofluorobenzoates[2] are characterized by ID_{50} values roughly half those of etoposide.

The 2,3-difluorobenzoates are more active than the 4-monofluorobenzoates, which shows that the activity is enhanced when the number of fluorine atoms on the benzoate moiety is increased. The $\{[(2,3\text{-}F_2C_6H_2CO_2)Bu_2Sn]_2O\}_2$ compound provides, against MCF-7 (a mammary tumour), an ID_{50} value comparable with that of mitomycin C. The ID_{50} value of the corresponding 2,3,6-trifluorobenzoate is of the same order of magnitude while that of the 2,3,4,5-tetrafluorobenzoate is lower. Against WiDr (a colon carcinoma), all fluorobenzoates exhibit comparable activities, except again $\{[(2,3\text{-}F_2C_6H_2CO_2)Bu_2Sn]_2O\}_2$ which is significantly more active. The di-n-butyltin fluorocinnamate and fluorophenylacetate are comparably active, while di-n-butyltin tetrafluorophthalate is characterized by quite a low ID_{50} value against WiDr.

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Table 1 Overview of ID_{50} values *in vitro* of condensation compounds of dibutyltin oxide with fluorine-containing carboxylic acids against MCF-7 (a mammary tumour) and WiDr (a colon carcinoma)

Compound	ID_{50} value (ng ml^{-1})		
	Against MCF-7	Against WiDr	Ref.
$\{[(4\text{-F-}C_6H_4CO_2)Bu_2Sn]_2O\}_2$	81	360	2
$(4\text{-F-}C_6H_4CO_2)_2SnBu_2$	90	309	2
$\{[(2,3\text{-}F_2\text{-}C_6H_3CO_2)Bu_2Sn]_2O\}_2$	9	120	3
$(2,3\text{-}F_2\text{-}C_6H_3CO_2)_2SnBu_2$	23	283	3
$\{[(2,3,6\text{-}F_3\text{-}C_6H_2CO_2)Bu_2Sn]_2O\}_2$	13	200	4
$\{[(2,3,4,5\text{-}F_4\text{-}C_6HCO_2)Bu_2Sn]_2O\}_2$	35	250	4
$\{[(2\text{-F-}C_6H_4CH{=}CHCO_2)Bu_2Sn]_2O\}_2$	28	368	5
$\{[(4\text{-F-}C_6H_4CH_2CO_2)Bu_2Sn]_2O\}_2$	38	268	5
$1,2\text{-}F_4C_6(CO_2)_2SnBu_2$	51	68	6
Etoposide	187	624	7
Mitomycin C	3	17	7

As a continuation of our study on organotin compounds of fluorinated aromatic carboxylic acids, we report here the synthesis, characterization and *in vitro* antitumour activity of three di-n-butyltin carboxylates involving the pentafluorophenyl moiety. The crystal structure of one of them, $\{[(F_5C_6CO_2)Bu_2Sn]_2O\}_2$, was determined by X-ray diffraction, as was that of a previously synthesized compound $\{[(4\text{-F-}C_6H_4COO)Bu_2Sn]_2O\}_2$.[2] Results of antitumour screenings on the latter compound are presented also.

RESULTS AND DISCUSSION

Syntheses

The new diorganotin carboxylates containing the perfluorophenyl moiety are $\{[(F_5C_6CO_2)Bu_2Sn]_2O\}_2$ (**1**), $\{[(F_5C_6CH{=}CHCO_2)Bu_2Sn]_2O\}_2$ (**2**), as obtained from a 1:1 condensation, and $(F_5C_6CH_2CO_2)_2SnBu_2$ (**3**), as obtained from a 2:1 condensation of the appropriate carboxylic acid with dibutyltin(IV) oxide. Attempts to prepare the 2:1 complexes from perfluorobenzoic and perfluorocinnamic acids failed and resulted in the 1:1 dimers, compounds **1** and **2**, respectively, and unreacted acid. A reasonable explanation of this is an increased sensitivity of the 2:1 complex to hydrolysis by water generated by the condensation, as a consequence of the strong electron-withdrawing nature of the pentafluorophenyl group. Thus the 1:1 complex can be generated from the 2:1 one by simple hydrolysis, according to

$$2(R'COO)_2SnR_2 + H_2O \rightarrow (R'COO)R_2Sn{-}O{-}SnR_2(OOCR') + 2R'COOH$$

followed by dimerization of the above distannoxane to the usual dimeric 1:1 complexes.

We obtained crystals of **1** which enabled us to determine its structure by X-ray diffraction. In order to examine the influence of the substitution of the monofluorophenyl for the pentafluorophenyl ring on the structural features of the dimeric distannoxane core, we determined likewise the structure of $\{[(4\text{-F-}C_6H_4CO_2)Bu_2Sn]_2O\}_2$ (**4**).[2]

The ^1H, ^{13}C and ^{119}Sn NMR spectra of compounds **1** and **2** displayed the usual duplicate resonances for the different types of atoms, characteristic of the dimeric dicarboxylatotetraorganodistannoxanes, $\{[(R'COO)R_2Sn]_2O\}_2$.[2] For compound **3**, ^1H resonance integration and the presence of single resonances for each type of atom in the ^{13}C NMR spectrum are in agreement with the usual monomeric, distorted trapezoidal bipyramidal structure of diorganotin dicarboxylates.[2]

Crystal and molecular structures of $\{[(F_5C_6COO)Bu_2Sn]_2O\}_2$ and $\{[(4\text{-F-}C_6H_4COO)Bu_2Sn]_2O\}_2$

The crystal structures of $\{[(F_5C_6COO)Bu_2Sn]_2O\}_2$, compound **1**, and $\{[(4\text{-F-}C_6H_4COO)Bu_2Sn]_2O\}_2$, compound **4**, reveal that both compounds adopt

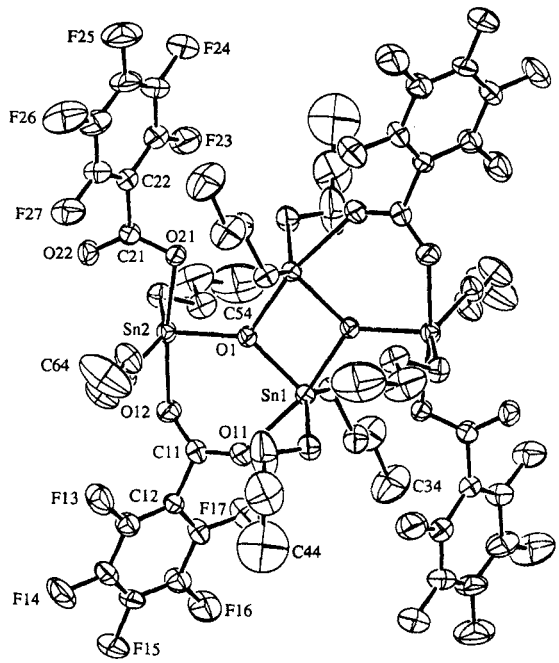

Figure 1 Molecular structure and crystallographic numbering scheme for $\{[(F_5C_6COO)Bu_2Sn]_2O\}_2$.

essentially similar structures in the solid state. The molecular structure of $\{[(F_5C_6COO)Bu_2Sn]_2O\}_2$ is shown in Fig. 1 and selected interatomic parameters are collected in Table 2 for both compounds.

The structure is centrosymmetric about a $Bu_4Sn_2O_2$ core. Attached to each bridging oxygen atom is an exocyclic Bu_2Sn unit leading to a three-coordinate O(1) atom. Further connections between the tin atoms arise as a result of bridging carboxylate ligands which form almost equal Sn–O bond distances to the endo- and exo-cyclic tin atoms, i.e. 2.296(5) and 2.265(5) Å. The remaining independent carboxylate ligand coordinates in the monodentate mode to the exocyclic tin atom exclusively with Sn(2)–O(21) 2.198(4) Å. This configuration leads to two five-coordinate tin centres, each existing in a distorted trigonal bipyramidal geometry. Distortions from ideal geometries may be traced, in part, to the presence of close intramolecular Sn···O interactions. Thus, the centrosymmetrically related O(21) atom forms a contact of 2.869(4) Å with the Sn(1) atom which has the effect of opening up the C(31)–Sn(1)–C(41) angle to 140.1(3)°. Similarly, an interaction of 2.829(5) Å between the Sn(2) and O(22) atoms results in the expansion of the C(51)–Sn(2)–C(61) angle to 144.9(3)°. Whereas the intramolecular Sn···O contacts are well within the van der Waals distances for these atoms, the relatively large separations and the minor perturbations from the ideal trigonal bipyramidal geometries indicate that these interactions must be considered weak. The dihedral angles of 118.8° and 62.0° between the O(11)–C(11)–O(12)/C(12)–C(17) and O(21)–C(21)–O(22)/C(22)–C(27) planes, respectively, indicate little conjugation between the carboxylate and C_6F_5 groups. Other parameters associated with the carboxylate residues are as expected. In the lattice there is a close intermolecular contact between each Sn(2) atom and a centrosymmetrically related O(22′) atom, i.e. a non-coordinating atom, of 3.204(5) Å (symmetry operation: $-x$, $-y$, $-z$). This loose association between Sn(2) and O(22) atoms leads to chains of weakly connected dimers of distannoxanes running parallel to the *c*-axis, as shown in Fig. 2. Similar chains, involving the equivalent Sn and O atoms, are observed in the crystal lattice of $\{[(MeCOO)Me_2Sn]_2O\}_2$;[8] however, in this structure the intermolecular contacts were significantly closer at 2.56(1) Å. A further difference arises between the two structures as a result of the presence of three bidentate, bridging carboxylate ligands rather than two as in the present determination. The intermolecular Sn(2)···O(22′) interactions notwithstanding, the molecular structure for $\{[(F_5C_6COO)Bu_2Sn]_2O\}_2$ conforms with the common structural motif found for compounds with the general formula $\{[(R'COO)R_2Sn]_2O\}_2$.[9,10]

The structure of $\{[(4\text{-}F\text{-}C_6H_4COO)Bu_2Sn]_2O\}_2$, shown in Fig. 3, is essentially the same as described above for the perfluoro derivative: the notable difference is that in the structure of **4** there is no crystallographically imposed symmetry in the molecule; this is the first such example among systems that use this structural motif.[9,10] Nevertheless, the mode of attachment of the carboxylate ligands and the tin atom geometries are unremarkable. The intramolecular Sn(1)···O(21′) and Sn(1′)···O(21) interactions are 2.79(1) Å and 2.78(1) Å, respectively, and the Sn(2)···O(22) and Sn(2′)···O(22′) contacts are 2.76(1) Å and 2.81(2) Å, respectively. These contacts are consistently shorter than the corresponding contacts in the structure of $\{[(F_5C_6COO)Bu_2Sn]_2O\}_2$ and probably reflect the greater inductive effect of the C_6F_5 group, which renders the $C_6F_5CO_2^-$ ligand a less effective donor. This conclusion is further supported by the observation that the Sn–O(carboxylate) bond dis-

tances in $\{[(4\text{-F-}C_6H_4COO)Bu_2Sn]_2O\}_2$ are shorter than or at most equal to, within experimental error, the corresponding separations in $\{[(C_6F_5COO)Bu_2Sn]_2O\}_2$ (Table 2). It is also notable in this context that the dihedral angles between the O(11)–C(11)–O(12), O(21)–C(21)–

Table 2 Selected interatomic parameters (Å, deg) for $\{[(F_5C_6COO)Bu_2Sn]_2O\}_2$ and $\{[(4\text{-F-}C_6H_4COO)Bu_2Sn]_2O\}_2$

		$\{[(4\text{-F-}C_6H_4COO)Bu_2Sn]_2O\}_2$	
Compound	$\{[(F_5C_6COO)Bu_2Sn]_2O\}_2$	Unprimed	Primed
Bond lengths (Å)			
Sn(1)–O(1)	2.024(4)	2.035(9)	2.025(9)
Sn(1)–O(1′)	2.130(4)	2.118(9)	2.128(9)
Sn(1)–O(11)	2.296(5)	2.22(1)	2.26(1)
Sn(1)–C(31)	2.090(8)	2.14(2)	2.15(3)
Sn(1)–C(41)	2.110(8)	2.09(2)	2.12(2)
Sn(2)–O(1)	2.034(4)	2.013(9)	2.022(8)
Sn(2)–O(12)	2.265(5)	2.20(1)	2.27(1)
Sn(2)–O(21)	2.198(4)	2.14(1)	2.18(1)
Sn(2)–C(51)	2.112(8)	2.14(3)	2.12(2)
Sn(2)–C(61)	2.077(9)	2.21(3)	2.11(2)
O(11)–C(11)	1.205(8)	1.22(2)	1.19(2)
O(12)–C(11)	1.221(8)	1.20(2)	1.23(2)
O(21)–C(21)	1.252(8)	1.23(2)	1.26(2)
O(22)–C(21)	1.207(8)	1.23(2)	1.24(2)
C(11)–C(12)	1.49(1)	1.49(2)	1.46(2)
C(21)–C(22)	1.50(1)	1.48(2)	1.49(2)
Angles (deg)			
O(1)–Sn(1)–O(1′)	77.5(2)	75.8(3)	75.8(3)
O(1)–Sn(1)–O(11)	90.2(2)	92.7(4)	92.6(4)
O(1)–Sn(1)–C(31)	106.5(2)	108.9(5)	111.0(8)
O(1)–Sn(1)–C(41)	111.8(3)	109.4(5)	109.8(5)
O(1′)–Sn(1)–O(11)	167.1(2)	168.5(4)	168.1(4)
O(1′)–Sn(1)–C(31)	101.5(2)	96.6(5)	106.3(8)
O(1′)–Sn(1)–C(41)	97.3(3)	97.6(5)	97.3(5)
O(11)–Sn(1)–C(31)	85.6(3)	87.4(5)	80.2(8)
O(11)–Sn(1)–C(41)	83.6(3)	85.7(6)	83.9(5)
C(31)–Sn(1)–C(41)	140.1(3)	141.3(6)	136.6(9)
O(1)–Sn(2)–O(12)	92.4(2)	90.0(4)	90.5(4)
O(1)–Sn(2)–O(21)	80.6(2)	80.3(4)	80.0(4)
O(1)–Sn(2)–C(51)	108.5(3)	110.5(8)	107.1(6)
O(1)–Sn(2)–C(61)	105.8(3)	107.5(7)	109.0(5)
O(12)–Sn(2)–O(21)	172.4(2)	170.2(4)	170.1(4)
O(12)–Sn(2)–C(51)	85.0(3)	83.9(9)	89.3(6)
O(12)–Sn(2)–C(61)	86.1(3)	88.5(9)	85.5(6)
O(21)–Sn(2)–C(51)	94.5(3)	98.5(9)	96.0(6)
O(21)–Sn(2)–C(61)	98.5(3)	95.4(8)	95.1(6)
C(51)–Sn(2)–C(61)	144.9(3)	141(1)	143.6(7)
Sn(1)–O(1)–Sn(1′)	102.5(2)	103.7(4)	104.3(4)
Sn(1)–O(1)–Sn(2)	134.5(2)	134.4(5)	133.8(5)
Sn(1′)–O(1)–Sn(2)	122.9(2)	121.6(4)	121.9(4)
Sn(1)–O(11)–C(11)	136.8(6)	136(1)	134(1)
Sn(2)–O(12)–C(11)	132.4(5)	143(1)	137(1)
Sn(2)–O(21)–C(21)	107.4(4)	108(1)	107(1)
O(11)–C(11)–O(12)	126.1(8)	123(2)	125(2)
O(21)–C(21)–O(22)	125.1(7)	124(2)	120(2)

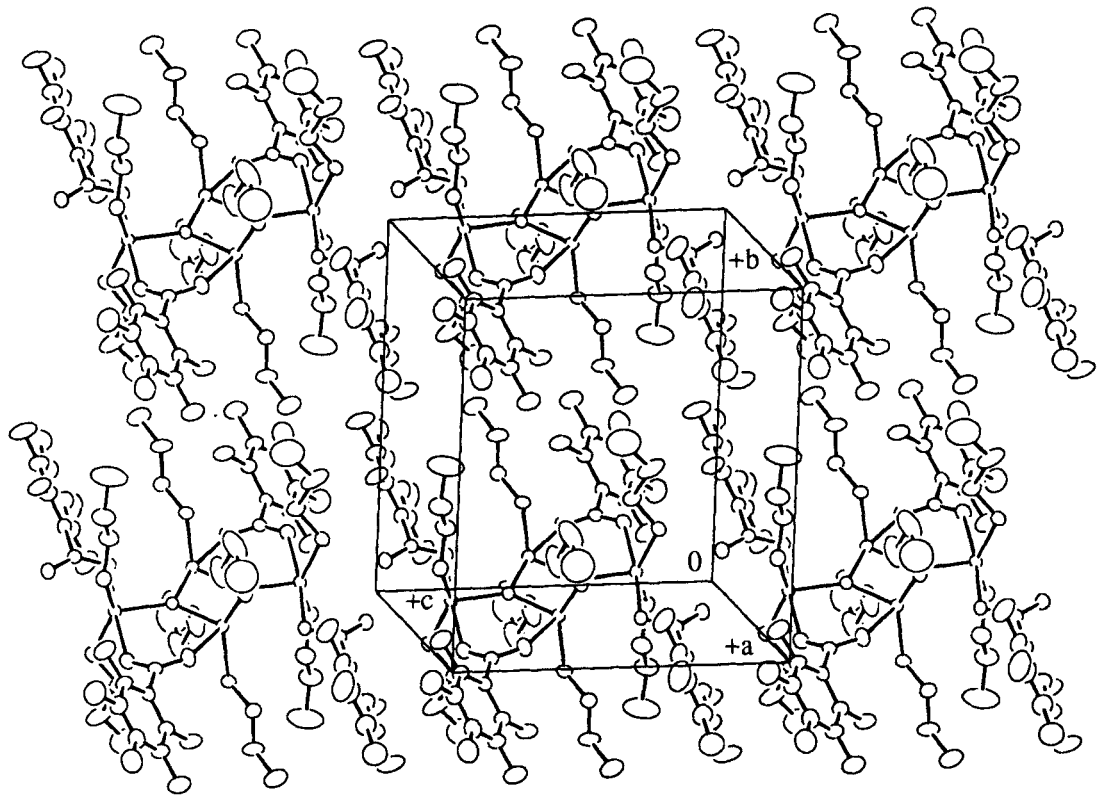

Figure 2 Unit cell contents for $\{[(F_5C_6COO)Bu_2Sn]_2O\}_2$.

O(22), O(11′)–C(11′)–O(12′) and O(21′)–C(21′)–O(22′) planes and their respective C_6H_4F substituents are 176.3°, 2.1°, 175.6° and 9.0°, respectively in contrast to those observed in the perfluoro derivative. In the lattice of $\{[(4\text{-}F\text{-}C_6H_4COO)Bu_2Sn]_2O\}_2$ there are no significant intermolecular interactions.

In-vitro antitumour activities

The ID_{50} values obtained for compounds **1–3** are described in Table 3. The activity of $\{[(F_5C_6CH_2CO_2)Bu_2Sn]_2O\}_2$, compound **5**, characterized elsewhere,[11] is likewise given, for comparison.

As far as the cell lines MCF-7 and WiDr are concerned, compounds **1**, **2** and **5** have activities comparable with those of the tri- and tetrafluorobenzoates as well as the monofluorophenylacetates and -cinnamates of Table 1. Compound **3** exhibits a higher activity, comparable with that of the 2,3-difluorobenzoate of Table 1. The activities of compounds **1**, **2**, **3** and **5** against the cell lines EVSAT (a breast cancer) and IGROV (an ovarian cancer) parallel those against the MCF-7 cells. Against M19 MEL (a melanoma) and A498 (a renal cancer), compound **3** remains most active, while compounds **5** and **2** are least active against M19 MEL and A498, respectively.

EXPERIMENTAL

Syntheses and purifications

The compounds **1**, $\{[(F_5C_6CO_2)Bu_2Sn]_2O\}_2$, and **2**, $\{(F_5C_6CH{=}CHCO_2)Bu_2Sn]_2O\}_2$, were synthesized from the corresponding organic acid and di-n-butyltin oxide in a 1:1 molar ratio, and for $(F_5C_6CH_2CO_2)_2SnBu_2$, **3**, a 2:1 molar ratio was used, by the following procedure. The appropriate acid was dissolved in a 4:1 mixture of toluene and ethanol, and di-n-butyltin oxide is added. The reacting mixture was refluxed for 4–6 h. The ternary azeotrope, water/ethanol/toluene, and subsequently the binary azeotrope ethanol/toluene, were distilled off with a Dean–Stark funnel to 50% of the initial volume. The solvent

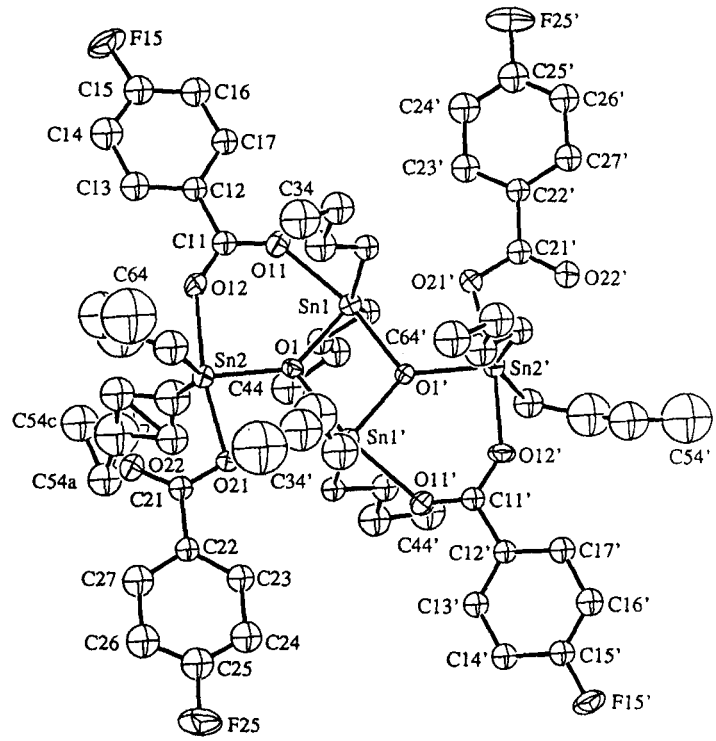

Figure 3 Molecular structure and crystallographic numbering scheme for $\{[(4\text{-F-}C_6H_4COO)Bu_2Sn]_2O\}_2$; for clarity only one position of each of the disordered atoms is represented (see Experimental section).

was evaporated under reduced pressure. The solid or oil obtained was purified by crystallization from the appropriate solvent.

X-ray crystallography for $\{[(F_5C_6COO)Bu_2Sn]_2O\}_2$ and $\{[(4\text{-F-}C_6H_4COO)Bu_2Sn]_2O\}_2$

Intensity data for the colourless crystals were measured at room temperature on a Rigaku AFC6R diffractometer fitted with MoKα radiation (graphite monochromator, $\lambda = 0.71073$ Å) using the $\omega:2\theta$ scan technique in each case. No decomposition of the crystals occurred during their respective data collections and each data set was corrected for Lorentz and polarization effects,[12] and for absorption employing an empirical procedure.[13] Crystal data are summarized in Table 4.

The structures were solved by direct methods[14,15] and each refined by a full-matrix least-squares procedure based on F.[12] For

Table 3 *In vitro* antitumour activities of **1–3**, **5**, and some reference compounds used clinically

Compound	MCF-7	EVSAT	WiDr	IGROV	M19 MEL	A498
1	44	39	214	53	86	76
2	32	37	234	41	66	135
3	10	19	145	20	36	51
5	55	43	275	60	114	105
Carboplatin	5500	1100	1500	780	5300	3500
Cisplatin	800	1200	650	79	530	1200
5-Fluorouracil	210	650	260	280	160	80
Methotrexate	150	170	140	240	190	100
Doxorubicin	8	6	20	28	5	5

Table 4 Crystallographic data for $\{[(F_5C_6COO)Bu_2Sn]_2O\}_2$ and $\{[(4\text{-}F\text{-}C_6H_4COO)Bu_2Sn]_2O\}_2$

Compound	$\{[(F_5C_6COO)Bu_2Sn]_2O\}_2$	$\{[(4\text{-}F\text{-}C_6H_4COO)Bu_2Sn]_2O\}_2$
Formula	$C_{60}H_{72}F_{20}O_{10}Sn_4$	$C_{60}H_{88}F_4O_{10}Sn_4$
Mol. wt	1808.0	1520.1
Crystal system	Triclinic	Triclinic
Space group	$P\bar{1}$	$P\bar{1}$
a, Å	12.425(3)	12.599(6)
b, Å	13.090(5)	25.359(4)
c, Å	11.697(3)	11.480(4)
α, deg	95.31(3)	91.44(3)
β, deg	93.28(2)	114.77(3)
γ, deg	113.01(2)	97.43(3)
V, Å^3	1734(1)	3289(2)
Z	1	2
D_c (g cm^{-3})	1.731	1.535
$F(000)$	892	1528
Crystal size, mm	0.08 × 0.16 × 0.24	0.08 × 0.08 × 0.40
μ, cm^{-1}	15.29	15.63
Transmission factors	0.894–1.184	0.998–1.060
No. of data collected	6751	14 450
θ_{max}, deg	25.0	27.5
No. of unique data	6390	13 768
No. of unique reflections used with $I \geq 3.0\,\sigma(I)$	4312	4112
R	0.046	0.061
R_w	0.046	0.068
Residual ρ_{max}, e Å^{-3}	0.74	0.77

$\{[(F_5C_6COO)Bu_2Sn]_2O\}_2$ the non-hydrogen atoms were refined with anisotropic thermal parameters [except for the C(44) atom] and carbon-bound hydrogen atoms were included in the model at their calculated positions. For the refinement of $\{[(4\text{-}F\text{-}C_6H_4COO)Bu_2Sn]_2O\}_2$, only the Sn, F and O atoms were refined anisotropically, owing to high thermal motion. Further, the C(51)–C(54) butyl group was found to be disordered. The disorder was modelled so that there were two equivalent sites for C(52), each with 50% occupancy, and three sites for C(54), each with 33.3% occupancy; hydrogen atoms were not included for this group owing to the disorder, but were included for the other carbon atoms. The refinements were continued until convergence; final refinement details are collected in Table 4. Final fractional atomic coordinates for the non-hydrogen atoms are listed in Tables 5 and 6 and the numbering schemes employed are shown in Figs 1 and 2, which were drawn with ORTEP.[16] Data manipulations were performed with the teXsan program[12] installed on an Iris Indigo workstation. Other crystallographic details, comprising thermal parameters, H-atom parameters, all bond distances and angles, and tables of observed and calculated structure factors are available on request (E.R.T.T.).

NMR experiments

All NMR spectra were recorded for $CDCl_3$ solutions on a Bruker AC250 instrument, using a QNP probe tuned at 250.13, 62.93, 93.28 and 235.36 MHz for ^1H, ^{13}C, ^{119}Sn and ^{19}F nuclei, respectively. ^1H and ^{13}C resonances were referenced to internal TMS using the solvent peak at 7.24 and 77.0 ppm, while the absolute reference $\Xi(^{119}Sn) = 37.290665$[17] was used for the ^{119}Sn resonances. ^{19}F resonances are referenced to $CFCl_3$ in $CDCl_3$.

Chemical shifts are given in ppm and coupling constants in Hz. The following abbreviations are used: d, doublet; t, triplet; q, quartet; s, singlet; b, broad; nv, non-visible; m, complex pattern.

The ^{19}F spectral patterns were simulated using the PANIC software of Bruker and NMR″II from Calleo Software.

^{13}C multiplets refer to $^nJ(^{13}C–^{19}F)$ couplings. $^nJ(^{13}C–Sn)$ refer to unresolved pairs of coupling

constants $^{n}J(^{13}C-^{119}Sn)^{n}J(^{13}C-^{117}Sn)$. $^{2}J(^{119}Sn-O-Sn)$ refers to unresolved $^{2}J(^{119}Sn-O-^{119}Sn)$ and $^{2}J(^{119}Sn-O-^{117}Sn)$ couplings between two heterotopic tin atoms connected by an oxygen bridge.

Table 5 Fractional atomic coordinates for $\{[(F_5C_6COO)Bu_2Sn]_2O\}_2$

Atom	*x*	*y*	*z*
Sn(1)	0.08848(5)	−0.06108(4)	−0.52683(4)
Sn(2)	0.02345(5)	−0.02647(4)	−0.22059(4)
F(13)	0.3575(6)	−0.0562(5)	−0.1158(5)
F(14)	0.5167(6)	−0.1333(6)	−0.0544(5)
F(15)	0.5142(6)	−0.3186(6)	−0.1706(5)
F(16)	0.3598(6)	−0.4205(5)	−0.3511(6)
F(17)	0.2047(5)	−0.3398(4)	−0.4173(5)
F(23)	−0.3363(6)	0.0268(6)	−0.2186(6)
F(24)	−0.4627(7)	0.1475(8)	−0.1963(6)
F(25)	−0.3669(7)	0.3523(7)	−0.0718(7)
F(26)	−0.1492(7)	0.4289(6)	0.0283(8)
F(27)	−0.0230(6)	0.3070(5)	0.0041(5)
O(1)	0.0169(4)	−0.0122(4)	−0.3923(3)
O(11)	0.1976(5)	−0.1181(5)	−0.4026(4)
O(12)	0.1227(5)	−0.1390(5)	−0.2397(5)
O(21)	−0.0807(4)	0.0758(4)	−0.2264(4)
O(22)	−0.0656(5)	0.0675(5)	−0.0410(4)
C(11)	0.1917(8)	−0.1459(6)	−0.3070(6)
C(12)	0.2766(7)	−0.1943(7)	−0.2695(6)
C(13)	0.3553(9)	−0.1464(8)	−0.1778(8)
C(14)	0.4384(9)	−0.1858(9)	−0.1438(8)
C(15)	0.4375(9)	−0.2765(10)	−0.2007(9)
C(16)	0.3603(9)	−0.3292(8)	−0.2915(9)
C(17)	0.2786(8)	−0.2879(7)	−0.3256(7)
C(21)	−0.1004(7)	0.0972(6)	−0.1251(6)
C(22)	−0.1739(8)	0.1643(8)	−0.1097(6)
C(23)	−0.2860(10)	0.1267(10)	−0.1591(8)
C(24)	−0.3526(11)	0.1881(14)	−0.1481(10)
C(25)	−0.3075(14)	0.2871(14)	−0.0872(12)
C(26)	−0.1960(13)	0.3307(10)	−0.0331(11)
C(27)	−0.1315(9)	0.2644(9)	−0.0481(9)
C(31)	−0.0129(7)	−0.2315(6)	−0.5745(6)
C(32)	0.0457(9)	−0.2982(8)	−0.6365(7)
C(33)	−0.0284(12)	−0.4177(9)	−0.6593(10)
C(34)	0.0327(15)	−0.4839(11)	−0.7149(12)
C(41)	0.2537(7)	0.0624(8)	−0.5501(7)
C(42)	0.3190(13)	0.1368(15)	−0.4581(11)
C(43)	0.4431(16)	0.2341(16)	−0.4708(14)
C(44)	0.5166(28)	0.1675(25)	−0.4772(25)
C(51)	−0.1197(7)	−0.1730(7)	−0.1930(6)
C(52)	−0.1569(9)	−0.2658(8)	−0.2833(8)
C(53)	−0.2528(14)	−0.3654(12)	−0.2532(15)
C(54)	−0.3023(16)	−0.4489(17)	−0.3489(21)
C(61)	0.1825(8)	0.0976(8)	−0.1474(6)
C(62)	0.2046(9)	0.2128(9)	−0.1534(8)
C(63)	0.3219(10)	0.2958(10)	0.1080(10)
C(64)	0.3433(14)	0.4100(13)	−0.1143(17)

Table 6 Fractional atomic coordinates for $\{[(4\text{-}F\text{-}C_6H_4COO)Bu_2Sn]_2O\}_2$

Atom	*x*	*y*	*z*
Sn(1)	0.4337(1)	0.22755(4)	0.4013(1)
Sn(1′)	0.6511(1)	0.24573(4)	0.3140(1)
Sn(2)	0.6007(1)	0.36508(4)	0.4495(1)
Sn(2′)	0.4731(1)	0.11022(4)	0.2467(1)
F(15)	0.0889(12)	0.4124(5)	0.7037(15)
F(15′)	0.9825(9)	0.0666(4)	−0.0200(11)
F(25)	1.1662(13)	0.4066(6)	0.2559(17)
F(25′)	−0.1009(12)	0.0576(6)	0.4272(14)
O(1)	0.5544(8)	0.2867(4)	0.3912(9)
O(1′)	0.5218(8)	0.1885(3)	0.3110(10)
O(11)	0.3663(11)	0.2829(4)	0.4979(12)
O(11′)	0.7330(11)	0.1868(5)	0.2386(13)
O(12)	0.4573(14)	0.3611(5)	0.5128(19)
O(12′)	0.6020(10)	0.1172(4)	0.1553(11)
O(21)	0.7315(9)	0.3454(4)	0.3820(11)
O(21′)	0.3537(9)	0.1185(4)	0.3364(11)
O(22)	0.7721(11)	0.4398(5)	0.4313(14)
O(22′)	0.3009(10)	0.0362(4)	0.2534(12)
C(11)	0.3804(17)	0.3311(7)	0.5224(18)
C(11′)	0.6963(17)	0.1448(7)	0.1754(17)
C(12)	0.3018(15)	0.3503(7)	0.5759(16)
C(12′)	0.7713(14)	0.1232(6)	0.1244(16)
C(13)	0.3115(17)	0.4047(8)	0.5956(19)
C(13′)	0.8790(16)	0.1507(6)	0.1492(16)
C(14)	0.2348(22)	0.4235(9)	0.6450(22)
C(14′)	0.9527(15)	0.1315(7)	0.1022(17)
C(15)	0.1546(20)	0.3897(9)	0.6573(21)
C(15′)	0.9122(17)	0.0849(7)	0.0253(17)
C(16)	0.1447(18)	0.3378(8)	0.6395(20)
C(16′)	0.8067(18)	0.0586(7)	−0.0040(18)
C(17)	0.2172(16)	0.3179(7)	0.5935(17)
C(17′)	0.7333(15)	0.0770(7)	0.0460(17)
C(21)	0.7905(17)	0.3986(7)	0.3924(17)
C(21′)	0.2862(17)	0.0742(7)	0.3121(18)
C(22)	0.8878(15)	0.3999(6)	0.3520(16)
C(22′)	0.1844(15)	0.0685(6)	0.3471(16)
C(23)	0.9191(17)	0.3556(7)	0.3111(18)
C(23′)	0.1742(18)	0.1096(7)	0.4170(19)
C(24)	1.0120(21)	0.3568(9)	0.2756(21)
C(24′)	0.0735(21)	0.1045(8)	0.4443(21)
C(25)	1.0697(23)	0.4033(10)	0.2828(23)
C(25′)	−0.0041(21)	0.0605(9)	0.4023(22)
C(26′)	0.0048(18)	0.0210(8)	0.3325(20)
C(27)	0.9536(21)	0.4477(8)	0.3564(21)
C(27′)	0.1025(17)	0.0240(7)	0.3007(18)
C(31)	0.2706(15)	0.2245(6)	0.2340(17)
C(31′)	0.6094(26)	0.2720(11)	0.1249(28)
C(32)	0.2527(20)	0.2731(8)	0.1737(22)
C(32′)	0.5341(35)	0.2965(15)	0.0914(42)
C(33)	0.1366(21)	0.2665(9)	0.0468(24)
C(33′)	0.5123(33)	0.3241(14)	−0.0552(40)
C(34)	0.1365(26)	0.3093(12)	−0.0262(30)
C(34′)	0.5485(48)	0.3642(21)	−0.0608(54)

Table 6 *Continued*

Atom	x	y	z
C(41)	0.5064(15)	0.1957(6)	0.5789(16)
C(41′)	0.8053(14)	0.2473(6)	0.4878(15)
C(42)	0.6022(15)	0.2323(6)	0.6847(18)
C(42′)	0.8141(16)	0.1933(7)	0.5418(18)
C(43)	0.6632(18)	0.2068(8)	0.8104(21)
C(43′)	0.9178(20)	0.1935(8)	0.6671(22)
C(44)	0.7670(20)	0.2450(9)	0.9038(22)
C(44′)	0.9141(21)	0.1388(9)	0.7159(24)
C(51)	0.7133(27)	0.3770(11)	0.6516(28)
C(51′)	0.5875(17)	0.0674(8)	0.3917(19)
C(52a)	0.8011(48)	0.3770(18)	0.6840(51)[a]
C(52b)	0.7346(48)	0.4231(20)	0.7125(53)[a]
C(52′)	0.5950(32)	0.0134(15)	0.3735(39)
C(53)	0.8543(42)	0.4142(18)	0.8413(44)
C(53′)	0.5611(28)	−0.0125(13)	0.2574(32)
C(54a)	0.9601(69)	0.4230(27)	0.9002(73)[b]
C(54b)	0.8641(78)	0.3936(34)	0.9196(88)[b]
C(54c)	0.8609(81)	0.4420(34)	0.9068(95)[b]
C(54′)	0.5505(38)	−0.0669(18)	0.2615(43)
C(61)	0.4956(23)	0.4087(10)	0.2869(26)
C(61′)	0.3401(16)	0.1025(7)	0.0561(18)
C(62)	0.4883(40)	0.4514(18)	0.3274(50)
C(62′)	0.3535(20)	0.1468(9)	−0.0209(24)
C(63)	0.4114(38)	0.4806(16)	0.1888(45)
C(63′)	0.2502(22)	0.1424(9)	−0.1564(25)
C(64)	0.3695(47)	0.4662(22)	0.0723(55)
C(64′)	0.2661(22)	0.1913(10)	−0.2263(26)

[a] Each atom has 50% site occupancy. [b] Each atom has 33% site occupancy.

Mössbauer spectra

Mössbauer spectra were obtained as described previously.[18]

The following abbreviations are used: QS, quadrupole splitting; IS, isomer shift; Γ_1 and Γ_2, line widths. All of these parameters are in mm s^{-1}.

Characterization

$\{(F_5C_6CO_2SnBu_2)_2O\}_2$, compound 1
Recrystallized from ethanol/petroleum ether; m.p. 151–153 °C, yield 94%.

Mössbauer: QS 3.68; IS 1.42; Γ_1 and Γ_2 1.10 and 0.98.

^{1}H NMR: α and β-CH_2: m, 1.46–1.78; γ-CH_2: tq, 1.34 [7, 7] and tq, 1.51 [7, 7]; CH_3: t, 0.87 [7] and *t*, 0.89 [7].

^{13}C NMR: C-1: tt, 111.8 [19, 2]; C-2 and C-6: bd, 141.8 [253]; C-3 and C-5: bd, 137.8 [248]; C-4: bd, 144.2 [264]; CO: 164.4; α-C: bs, 28.7 [^1J(^{13}C–Sn), nv] and bs, 29.8 [^1J(^{13}*C*–Sn), nv]; β-C: 27.0 [^2J(^{13}C–Sn), 35] and 27.3 [^2J(^{13}C–Sn)35]; γ-C: 26.6 [^3J(^{13}C–Sn): 121] and 26.7 [^3J(^{13}C–Sn): 123]; CH_3: 13.2 and 13.3.

^{19}F NMR: F-2 and F-6: dddd, −141.4 [^nJ(^{19}F–^{19}F), 21, 3, 2, −8]; F-3 and F-5: dddd, −161.2 [^nJ(^{19}F–^{19}F), 21, 21, 3, −8]; F-4: bt, −152.1 [^3J(^{19}*F*–^{19}*F*), 21].

^{119}Sn NMR: −189.5, −190.6 [^2J(^{119}Sn–O–Sn): 126].

$\{(F_5C_6CH{=}CHCO_2SnBu_2)_2O\}_2$, compound 2
Recrystallized from ethanol/petroleum ether; m.p. 110–112 °C, yield 93%.

Mössbauer: QS 3.53; IS 1.34; Γ_1 and Γ_2 0.98 and 0.99.

^{1}H NMR: α-CH: d, 6.70 [16]; β-CH: d, 7.52 [16]; α- and β-CH_2: m, 1.64–1.75; γ-CH_2: tq, 1.37 [7, 7] and tq, 1.43 [7, 7]; CH_3: t, 0.86 [7] and t, 0.89 [7].

^{13}C NMR: C-1: tt, 110.4 [14, 2]; C-2 and C-6: bd, 145.5 [254]; C-3 and C-5: bd, 137.5 [249]; C-4: bd, 137.9 [249]; α-CH: 130.0; β-CH: 126.9; CO: 171.4; α-CH_2: bs, 29.7 [^1J(^{13}C–Sn), nv] and bs, 29.7 [^1J(^{13}C–Sn), nv]; β-CH_2: 27.4 [^2J(^{13}C–Sn), 36] and 27.7 [^2J(^{13}C–Sn), 36]; γ-CH_2: 26.6 [^3J(^{13}C–Sn), 121] and 26.8 [^3J(^{13}C–Sn), 125]; CH_3: 13.2 and 13.3.

^{19}F NMR: F-2 and F-6: dddd, −140.4 [^nJ(^{19}F–^{19}F), 21, 3, 1, −8]; F-3 and F-5: dddd, −162.7 [21, 21, 3, −8]; F-4: bt, −152.9 [21].

^{119}Sn NMR: −206.6, −215.5 [^2J(^{119}Sn–O–Sn), 113].

$\{(F_5C_6CH_2CO_2)_2SnBu_2\}$, compound 3
Recrystallized from ethanol/hexane; m.p. 125–126 °C; yield 90%.

Mössbauer: QS 3.85; IS 1.51; Γ_1 and Γ_2 0.99 and 0.89.

^{1}H NMR: CH_2CO: s, 3.70; α- and β-CH_2: m, 1.58–1.72; γ-CH_2: tq, 1.34 [7, 7]; CH_3: t, 0.88 [7].

^{13}C NMR: C-1: tt, 108.7 [18, 2]; C-2 and C-6: bd, 145.3 [248]; C-3 and C-5: bd, 137.5 [253]; C-4: bd,

140.6 [253]; $\underline{C}H_2CO$: 27.7; CO: 178.1; α-C: 25.6 [$^1J(^{13}C-^{119/117}Sn)$, 561/536]; β-C: 26.4 [$^2J(^{13}C-Sn)$, 35]; γ-C: 26.2 [$^3J(^{13}C-Sn)$, 95]; CH_3: 13.3.

^{19}F NMR: F-2 and F-6: dddd, −143.1 [$^nJ(^{19}F-^{19}F)$: 21, 3, 1, −8]; F-3 and F-5; dddd, −162.9 [21, 21, 3, −8]; F-4: t, −156.1 [21].

^{119}Sn NMR: −131.3.

Antitumour assays

The *in-vitro* tests were performed as described previously.[19]

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