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Di-n-butyltin and diethyltin monofluorobenzoates: synthesis, spectroscopic characterization and *in vitro* antitumor activity

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The di-n-butyltin(IV) and diethyltin(IV) fluorobenzoates $[FC_6H_4COO]_2SnR_2$ and $(FC_6H_4COOR_2Sn)_2O$ have been synthesized and characterized spectroscopically. Their *in vitro* antitumor activity against two human tumor cell lines, MCF-7, a mammary tumor, and WiDr, a colon carcinoma, as well as against the NCI cell panel, is satisfactory.

Keywords: Organotin, synthesis, Mössbauer, ^1H NMR, ^{13}C NMR, antitumor activity

INTRODUCTION

Di-n-butyltin 2,5-bis(trifluoromethyl)benzoate exhibits rather promising *in vitro* antitumor activities since its ID_{50} values against two human tumor cell lines, MCF-7 and WiDr, were found to be respectively 48 and 176 ng cm^{-3}.[1] These results are significantly better than the values of 850 and 624 ng cm^{-3} found for *cis*-platin.[2] We prepared some di-n-butyl- and diethyl-tin monofluorobenzoates in order to compare their activities with those of the bis(trifluoromethyl)benzoates. They were characterized by ^1H, ^{13}C, ^{119}Sn and ^{19}F NMR, as well as by Mössbauer and mass spectrometry. The compounds prepared are either diorganotin bis(monofluorobenzoate)s (Type **a** compounds) or bis[diorgano(monofluorobenzato)tin] oxides (Type **b** compounds).

RESULTS AND DISCUSSION

Synthesis

The compounds prepared are $(XC_6H_4COO)_2SnR_2$ (Fig. 1; Type **a**) and $\{[(XC_6H_4COO)R_2Sn]_2O\}_2$ (Fig. 2; Type **b**), with

1a and **1b**: X = 2-F, R = n-C_4H_9
2a and **2b**: X = 3-F, R = n-C_4H_9
3a and **3b**: X = 4-F, R = n-C_4H_9
4a and **4b**: X = 2-F, R = C_2H_5
5a and **5b**: X = 3-F, R = C_2H_5
6a and **6b**: X = 4-F, R = C_2H_5

They were obtained by the condensation of the appropriate diorganotin oxide and monofluorobenzoic acid, in the molar ratios 1:2 and 1:1 for compounds of Type **a** and **b**, respectively, according to a previously reported procedure.[3]

Spectroscopic data

The ^1H NMR spectra of compounds of Type **a** exhibit a single triplet resonance for the methyl groups of the diethyltin or dibutyltin moieties. In contrast, compounds of Type **b** display two trip-

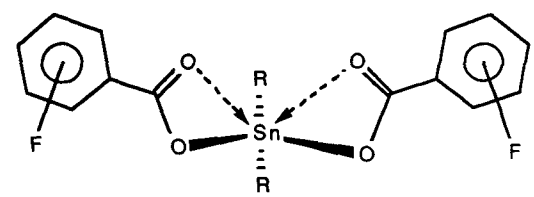

Figure 1 Structure proposed for the diorganotin bis(fluorobenzoate)s, compounds of Type **a** (R = Et, n-Bu).

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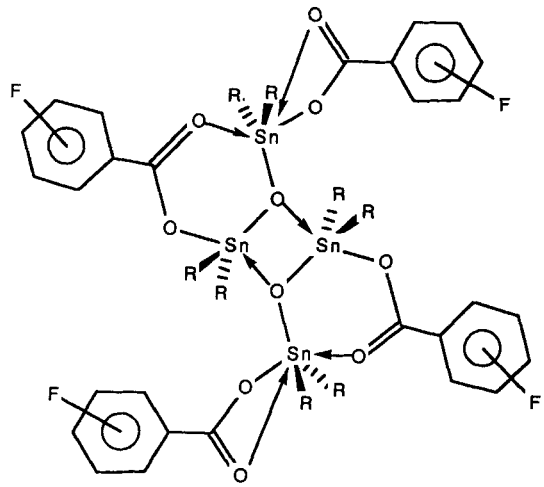

Figure 2 Structure proposed for bis[diorgano(fluorobenzoato))tin] oxides, compounds of Type **b** (R = Et, n-Bu).

lets with identical intensities. The ^{13}C NMR spectra also show pairs of resonances for the butyl, viz. the ethyl carbon atoms of compounds **b**, in contrast with the single signals for those of compounds **a**. Accordingly, the ^{119}Sn NMR spectra (see Table 1) also show the same dichotomy, a single resonance for the Type **a** diorganotin dibenzoates and two of identical intensities for the Type **b** bis(benzoatodiorganotin) oxides. The latter exhibit characteristic $^{2}J(^{119}Sn–O–^{117/119}Sn)$ coupling satellites.

The structure proposed from these data for compounds of Type **a**, displayed in Fig. 1, is in agreement with the previous observation[4] of a strongly distorted square bipyramid, with apical organic groups bound to tin and equatorial bidentate carboxylate groups with unequal carboxylate oxygen–tin bonds.[4]

The structure proposed for compounds of Type **b** is a dimeric one (see Fig. 2), as found for bis(5-methoxysalicylatodi-n-butyltin) oxide.[3] One set of resonances is associated with the organotin moieties involved in the dioxadistannetane ring, the second set with the terminal diorganotin moieties. This suggests that the dimeric structures found previously in the solid state[3] are retained in deuteriochloroform ($CDCl_3$) solution.

Mössbauer spectrometry does not distinguish the two different types of tin atoms typical to the compounds of Type **b**. This is not unexpected since Mössbauer spectroscopy has a rather small isomer shift scale and is therefore less sensitive to small variations in tin environments, as already reported earlier.[1,3,4]

Analogously, the ^{19}F NMR spectra (see Table 1) do not discriminate between the two unequivalent monofluorobenzoate groups in compounds of Type **b**. This is again understandable since the fluorine atom lies quite far away from the tin atoms and is therefore quite insensitive to the tin atom heterotopicity.

The aromatic ^{19}F chemical shift increments, deduced from the ^{19}F NMR spectra after comparison with the ^{19}F chemical shift of fluorobenzene, are given in Table 2. These increments are in general independent to within 0.2 ppm of the R groups on the tin atom, but are more sensitive to the compound type, **a**, or **b**, especially in *ortho* and *para* positions.

In vitro antitumor activity

The results of the *in vitro* tests against the two human tumor cell lines MCF-7 and WiDr, performed with a selection of these compounds, are given as ID_{50} values in Table 3. Data on some

Table 1 ^{119}Sn (chemical shifts versus tetramethyltin, external reference) and ^{19}F (chemical shifts versus $CFCl_3$) NMR parameters for solutions of compounds **1–6** in $CDCl_3$

	1a	**2a**	**3a**	**1b**	**2b**	**3b**	**4a**	**5a**	**6a**	**4b**	**5b**	**6b**
R =	C_4H_9	C_4H_9	C_4H_9	C_4H_9	C_4H_9	C_4H_9	C_2H_5	C_2H_5	C_2H_5	C_2H_5	C_2H_5	C_2H_5
X =	2-F	3-F	4-F	2-F	3-F	4-F	2-F	3-F	4-F	2-F	3-F	4-F
^{119}Sn NMR	−140.4	−144.3	−148.8	−210.4	−213.0	−212.4	−145.7	−149.4	−153.3	−211.5	−213.8	−213.9
				−211.7	−215.9	−215.1				−213.5	−214.4	−214.1
$[^{2}J(SnOSn)]^{a}$				[121]	[113]	[127]				[126]	—[c]	[128]
^{19}F NMR	−109.3	−112.9	−105.9	−110.5	−113.3	−107.2	−109.3	−112.7	−105.7	−110.3	−113.1	−107.7
Undecoupled	ddd	ddd	bs	bs	bs	bs	ddd	ddd	tt	bs	bs	bs
$^{n}J(FH)^{b}$	10; 8; 5	9; 9; 5					10; 7; 5	9; 9; 6	8; 5			

[a] $^{2}J(SnOSn)$, unresolved $^{2}J(^{119}Sn–O–^{119}Sn)$ and $^{2}J(^{119}Sn–O–^{117}Sn)$ satellites. [b] $^{n}J(FH)$, $^{n}J(^{19}F–^{1}H)$ ($n = 3$ or 4). [c] Unresolved because of overlappings and signal broadness.

Table 2 Aromatic ^{19}F chemical shift increments[a] induced in *ortho*, *meta* and *para* positions to the CO_2SnR_2L[b] and CO_2SnR_2L complex substituents in compounds of Type **a** and **b** respectively

	Type **a** CO_2SnR_2L		Type **b** CO_2SnR_2L complex	
Isomer	n-Bu	Et	n-Bu	Et
ortho	+4.0	+4.0	+2.9	+3.0
meta	+0.5	+0.6	0	+0.2
para	+7.5	+7.6	+6.1	+5.7

[a] The increments were deduced from the ^{19}F NMR spectrum of fluorobenzene as reference [$\delta(^{19}F) = -113.3$; tt, 9; 6]. [b] L, fluorobenzoate.

compounds currently used clinically as antitumor agents are given for comparison.[2]

Table 3 clearly shows that all compounds, except **5b**, are more active *in vitro* than cis-platin and etoposide against both tumor cell lines. Their activity is comparable with that of doxorubucin against MCF-7; however, they are less active than mitomycin C.

There is no significant difference between the activities of compounds of Types **a** and **b** with the same ligand (**1a** and **1b** on the one hand, **3a** and **3b** on the other). Compounds **2a**, **4a**, **4b**, **5b**, **6a** and **6b** were tested *in vitro* by the National Cancer Institute (NCI), Bethesda, Maryland, USA, for cytotoxic activity against a panel of about 60 human tumor cells lines. Except **2a**, only diethyltin compounds were selected by the NCI, probably because earlier *in vivo* tests on P388 leukemia established diethyltin compounds to be more active than di-n-butyltin ones. However, more recent *in vitro* results[5] showed the di-n-butyltin compounds to be more active than the diethyltin ones against MCF-7 and WiDr cell lines so compound **2a** was tested. The results obtained are summarized in Table 4. The detailed parameter significance was presented previously.[6]

Table 3 ID_{50} values (ng cm^{-3}) of compounds **1a**, **2a**, **3a**, **1b**, **3b** and **5b** tested against two human tumor cell lines, MCF-7 and WiDr

Compound	MCF-7	WiDr
1a	74	242
2a	39	271
3a	90	309
1b	91	330
3b	81	360
5b	496	3431
'*Cis*-platin'[2]	850	624
Doxorubicin[2]	63	31
Etoposide[2]	187	624
Mitomycin C[2]	3	17

From the experimental data collected from each cell line grouped in subpanels (e.g. leukemia), the principal response parameters, GI50, TGI and LC50, are calculated by the NCI following a procedure described in Ref. 6 and represent sensitivities of the cell lines to the test agent. They are interpolated values representing the concentrations at which the percentage growth (PG) is +50, 0 and −50.[6] Δ(Range) expresses the difference between the lowest and highest dose needed for each.

D_{GI50}, D_{TGI} and D_{LC50} subpanel selectivities, with, between parentheses, the log concentration at which they occur, are also calculated by the NCI following a procedure described in Ref. 6. Computer simulations performed by the NCI suggest that a value of D_{GI50}, D_{TGI} and $D_{LC50} \geq 50$ represents a statistically significant sensitivity.[7] The highest of the three values D_{GI50}, D_{TGI} and D_{LC50} determines whether the subpanel-cytoxic selectivity occurs most markedly at the GI50, the TGI, or the LC50 level.

The value of D_H calculated by the NCI following a procedure described in Ref. 6 provides a more general measure of selective effects and assigns relative scores of subpanel selectivity to the compounds. Similarly the MGD_H value reflects the subpanel selectivity. Computer simulations performed by the NCI suggest values of D_H and $MGD_H \geq 75$ to represent statistically significant selectivities.[7]

All compounds exhibit some interesting features. Compound **2a** exhibits D_H and MGD_H parameters exceeding by a large amount the threshold of statistically significant selectivity. The sensitivity is significant at the level of +50 % growth only, the other values reflecting low sensitivity. In contrast, compounds **4a**, **6a**, **5b** and **6b** exhibit only borderline or no noticeable selectivities. However, compounds **4a** and **6a** display borderline (**4a**) to significant (**6a**) sensitivities at the levels of 0 % and −50 % growth, with the optimal response parameters being TGI and LC50 respectively. Compound **4b** provided results comparable with **4a**. Differences between **6a** and **6b** are hardly more marked, suggesting no clear activity difference between Type **a** and Type **b** compounds to exist.

Table 4 NCI *in vitro* screening data for some diorganotin monofluorobenzoates[a]

Compd	NSC no. R, X Molar ratio	MG–MID response parameter			Selectivity analysis Δ(Range)			Response parameter	Subpanel sensitivity	D_{GI50} D_{TGI} D_{LC50}	D_H MGD_H
		Log GI50	Log TGI	Log LC50	GI50	TGI	LC50				
2a	643839 n-Bu, *m*-F 1:2	−6.07	−5.64	−5.12	0.66 (1.19)	0.67 (1.29)	0.69 (1.82)	GI50	REN	59 (−6) 21 (−6) 24 (−5)	85 (−6) 84
4a	643838 Et, *o*-F 1:2	−4.54	−4.27	−4.11	1.29 (1.82)	1.18 (1.45)	0.96 (1.07)	TGI	LNS	33 (−4) 50 (−4) 49 (−4)	78 (−5) 49
	643838 Et, *o*-F 1:2	−4.52	−4.31	−4.16	0.52 (1.04)	0.32 (0.63)	0.13 (0.29)			43 (−4) 34 (−4) 49 (−4)	74 (−5) 57
4b	643849 Et, *o*-F 1:1	−4.67	−4.35	−4.14	1.20 (1.87)	1.21 (1.56)	1.11 (1.25)			18 (−5) 28 (−4) 49 (−4)	78 (−5) 43
5b	643850 Et, *m*-F 1:1	−4.67	−4.36	−4.17	1.21 (1.88)	1.21 (1.58)	1.11 (1.28)	LC50	LNS	18 (−5) 34 (−4) 47 (−4)	67 (−5) 44
6a	643840 Et, *p*-F 1:2	−4.56	−4.28	−4.10	1.21 (1.77)	1.07 (1.35)	0.57 (1.67)	LC50	LNS	23 (−4) 52 (−4) 60 (−6)	64 (−4) 59
6b	643851 Et, *p*-F 1:1	−4.31	−4.11	−4.04	1.21 (1.52)	0.80 (0.91)	0.40 (0.44)	GI50	LNS	40 (−4) 27 (−4) 36 (−4)	76 (−5) 40

[a] Units of GI50, TGI and LC50 are molar. [b] Tumor cell line subpanels are identified as follows: LNS = non-small cell lung; REN = kidney. [c] Both sets of data for **4a** were under the same experimental conditions.

EXPERIMENTAL

Instruments

The Mössbauer spectra were recorded as described previously.[3]

The ^{1}H and ^{13}C NMR spectra were recorded on a Bruker AM 270 instrument at 270.13 and 67.93 MHz respectively. The ^{119}Sn NMR spectra were obtained on a Bruker WM 500 instrument at 186.5 MHz. The ^{19}F NMR spectra were recorded on a Bruker AC250 instrument at 235.36 MHz. The FAB mass spectra were recorded on a V.G. Micromass 7070 F instrument (source temperature: 200 °C).

Syntheses

Compounds of Type **a** were typically prepared as follows. Di-n-butyltin oxide (1.00 g; 4.0 mmol) or diethyltin oxide (0.86 g; 4.0 mmol) was added to 1.26 g (8.0 mmol) of the appropriate monofluorobenzoic acid dissolved in 150 cm^3 of toluene and 50 cm^3 of ethanol. The mixture was refluxed for 6 h and the ternary azeotrope water/ethanol/toluene was distilled off with a Dean–Stark funnel. Half of the remaining solution was evaporated under vacuum. The oily compound obtained was crystallized from ethanol.

The synthesis of compounds of Type **b** occurred similarly but only half the amount of monofluorobenzoic acid was used, i.e. 0.63 g (4.0 mmol). The crystallization solvents are given below for each compound.

In vitro tests

Drug activity was determined using an automated *in vitro* technique as described previously.[2,8] The NCI test protocols have been described elsewhere.[6,7]

Spectroscopic characterization

Details are given below for each compound, using the following conventions.

Abbreviations: b, broad; d, doublet; q, quartet; t, triplet; nr, non-resolved; nv, non-visible; m, complex pattern; ^{n}J(Sn–C), unresolved $^{n}J(^{119}Sn–^{13}C)$ and $^{n}J(^{117}Sn–^{13}C)$; ^{2}J(SnOSn), unre-

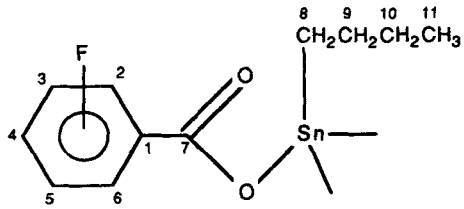

Figure 3 Labelling of compounds **1–3** (R = n-Bu).

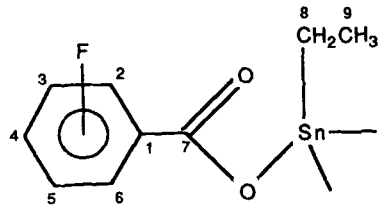

Figure 4 Labelling of compounds **4–6** (R = Et).

solved $^2J(^{119}Sn–O–^{119}Sn)$ and $^2J(^{117}Sn–O–^{119}Sn)$. Coupling constants in Hz; chemical shifts in ppm with respect to TMS and $CDCl_3$ taken to be 0.0 and 77.0 ppm for ^1H and ^{13}C spectra respectively, with tetramethyltin in $CDCl_3$ (*ca* 40 %) as external reference for ^{119}Sn spectra and with $CFCl_3$ (*ca* 10 %) as external reference for ^{19}F spectra. All spectra were recorded in $CDCl_3$. $^1H–^{19}F$ couplings are given in **bold**. Carbon atoms are labelled in Figs 3 and 4.

Compound 1a (X = 2-F; R = n-Bu)
Yield 72 %; m.p. 82–83 °C.
Mössbauer: QS 3.29; IS 1.39; Γ_1 0.84, Γ_2 0.87 mm s^{-1}.
^1H NMR: H-3 7.16 (dd, **10**, 8); H-4 7.50–7.57 (bm); H-5 7.21 (dd, 8, 8); H-6 8.08 (ddd, **8**, 8, 2); H-8 and H-9 1.72–1.88 (m); H-10 1.41 (tq, 7, 7); H-11 0.88 (t, 7).
^{13}C NMR: C-1 119.0 [d, $^2J(^{19}F–^{13}C) = 9$] (*calcd: 117.7*); C-2 163.0 [d, $^1J(^{19}F–^{13}C) = 261$] (*164.8*); C-3 117.3 [d, $^2J(^{19}F–^{13}C) = 22$] (*115.6*); C-4 135.1 [d, $^3J(^{19}F–^{13}C) = 9$] (*135.0*); C-5 124.2 [d, $^4J(^{19}F–^{13}C) = 3$] (*124.0*); C-6 133.5 (*131.4*); C-7 174.0; C-8 25.8 [$^1J(^{119/117}Sn–^{13}C) = 583/552$]; C-9 26.9 [$^2J$(Sn–C) = 33]; C-10 26.5 [^3J(Sn–C) = 99]; C-11 13.7.
Mass spectrometry: $(FC_6H_4COO)_2SnBu^+$ 8 %; $(FC_6H_4COO)SnBu_2^+$ 100; $(FC_6H_4COO)Sn^+$ 85; $FC_6H_4Sn^+$ 31; $BuSn^+$ 31 %.

Compound 2a (X = 3-F; R = n-Bu)
Yield 96 %; m.p. 55–57 °C.
Mössbauer: QS 3.90; IS 1.53; Γ_1 0.86, Γ_2 0.85 mm s^{-1}.
^1H NMR: H-2 7.82 (ddd, **9**, 3, 1); H-4 7.29 (dddd, **8**, 8, 3, 1); H-5 7.44 (ddd, 8, 8, **5**); H-6 7.93 (ddd, 8, 1, 1); H-8 and H-9 1.68–1.85 (m); H-10 1.40 (tq, 7, 7); H-11 0.88 (t, 7).
^{13}C NMR: C-1 133.0 [d, $^3J(^{19}F–^{13}C) = 7$] (*calcd: 132.0*); C-2 117.9 [d, $^2J(^{19}F–^{13}C) = 23$] (*117.1*); C-3 163.3 [$^1J(^{19}F–^{13}C) = 247$] (*163.3*); C-4 120.8 [d, $^2J(^{19}F–^{13}C) = 21$] (*120.7*); C-5 130.6 [d, $^3J(^{19}F–^{13}C) = 8$] (*129.9*); C-6 126.8 [d, $^4J(^{19}F–^{13}C) = 3$] (*125.5*); C-7 175.2; C-8 26.1 [$^1J(^{119/117}Sn–^{13}C) = 573/551$]; C-9 27.1 [$^2J$(Sn–C) = 35]; C-10 26.8 [^3J(Sn–C) = 98]; C-11 13.9.
Mass spectrometry: $(FC_6H_4COO)_2SnBu^+$ 16; $(FC_6H_4COO)SnBu_2^+$ 100; $FC_6H_4COOSn^+$ 78; $FC_6H_4Sn^+$ 10; $BuSn^+$ 17 %.

Compound 3a (X = 4-F; R = n-Bu)
Yield 90 %; m.p. 69–70 °C.
Mössbauer: QS 3.40; IS 1.40; Γ_1 0.93, Γ_2 0.88 mm s^{-1}.
^1H NMR: H-2 and H-6 8.15 (dd, 9, **5**); H-3 and H-5 7.12 (dd, **9**, 9); H-8 and H-9: 1.66–1.83 (m); H-10 1.40 (tq, 7, 7); H-11 0.88 (t, 7).
^{13}C NMR: C-1 127.0 (*calcd: 126.1*); C-2 and C-6 133.6 [d, $^3J(^{19}F–^{13}C) = 9$] (*131.4*); C-3 and C-5 115.9 [d, $^2J(^{19}F–^{13}C) = 22$] (*115.6*); C-4 166.5 [d, $^1J(^{19}F–^{13}C) = 254$] (*168.4*); C-7 175.5; C-8 26.0 [^1J(Sn–^{13}C) = 580]; C-9 27.5 [^2J(Sn–C) = 33]; C-10 26.8 [^3J(Sn-C) = 99] C-11 13.9.
Mass spectrometry: $(FC_6H_4COO)_2SnBu^+$ 7; $(FC_6H_4COO)SnBu_2^+$ 100; $FC_6H_4COOSn^+$ 15; $BuSn^+$ 17 %.

Compound 1b (X = 2-F; R = n-Bu)
Yield 81 %; recrystallized from petroleum ether, m.p. 100–102 °C.
Mössbauer: QS 3.44; IS 1.33; Γ_1 0.87, Γ_2 0.89 mm s^{-1}.
^1H NMR: H-3 7.13 (dd, **11**, 8); H-4 7.45–7.49 (m); H-5 7.20 (dd, 8, 8); H-6 7.86–7.90 (bm); H-8 and H-9 1.58–1.76 (m); H-10 1.25 (tq, 7, 7) and 1.36 (tq, 7, 7); H-11 0.77 (t, 7) and 0.86 (t, 7).
^{13}C NMR: C-1 122.8 (*calcd: 117.7*); C-2 162.2 [d, $^1J(^{19}F–^{13}C) = 257$] (*164.8*); C-3 117.1 [d, $^2J(^{19}F–^{13}C) = 23$] (*115.6*); C-4 133.5 [d, $^3J(^{19}F–^{13}C) = 8$] (*135.0*); C-5 124.1 (*124.0*); C-6 132.6 (*131.4*); C-7 170.7; C-8 28.8 [$^1J(^{119/117}Sn–^{13}C) = 704/672$] and 30.3 [$^1J(^{119/117}Sn–^{13}C) = 750/719$]; C-9 28.0 [$^2J$(Sn–C) = 29] and 28.3 [$^2J$(Sn–C) = 38]; C-10 27.1 [^3J(Sn–C) ≈ 125]; C-11 13.8 and 13.9.
Mass spectrometry: $(FC_6H_4COO)SnBu_2^+$ 100; $FC_6H_4COOSn^+$ 58; $FC_6H_4Sn^+$ 57; $BuSn^+$ 3 %.

Compound 2b (X = 3-F; R = n-Bu)
Yield 74 %; recrystallized from ethanol, m.p. 78–80 °C.
Mössbauer: QS 3.48; IS 1.34; Γ_1 1.02, Γ_2 1.06 mm s^{-1}.
^{1}H NMR: H-2 7.69 (d, **8**, 2); H-4 7.26 (ddd, **8**, 8, 2); H-5 7.44 (ddd, 8, 8, **6**); H-6 7.82 (d, 8); H-8 and H-9 1.59–1.81 (m); H-10 1.26 (tq, 7, 7) and 1.38 (tq, 7, 7); H-11 0.77 (t, 7) and 0.86 (t, 7).
^{13}C NMR: C-1 135.4 (*calcd: 132.0*); C-2 116.2 [d, $^2J(^{19}F-^{13}C) = 22$] (*117.1*); C-3 162.2 [d, $^1J(^{19}F-^{13}C) = 247$] (*163.3*); C-4 118.7 [d, $^2J(^{19}F-^{13}C) = 21$] (*120.7*); C-5 129.3 [d, $^3J(^{19}F-^{13}C) = 7$] (*129.9*); C-6 125.1 (*125.5*); C-7 171.1; C-8 28.0 [$^1J(^{119/117}Sn-^{13}C) = 712/685$] and 29.9 [$^1J(Sn-C) \approx 706$, b, nr]; C-9 27.0 [$^2J(Sn-C) = 34$] and 27.3 [$^2J(Sn-C) = 37$]; C-10 26.3 [$^3J(Sn-C) \approx 125$]; C-11 13.0 and 13.1.
Mass spectrometry: $(FC_6H_4COO)SnBu_2^+$ 100; $FC_6H_4COOSn^+$ 22; $FC_6H_4Sn^+$ 6; $BuSn^+$ 14 %.

Compound 3b (X = 4-F; R = n-Bu)
Yield 82 %; recrystallized from petroleum ether, m.p. 133–134 °C.
Mössbauer: QS 3.42; IS 1.32; Γ_1 0.94, Γ_2 0.93 mm s^{-1}.
^{1}H NMR: H-2 and H-6 8.03 (bs); H-3 and H-5 7.14 (dd, **8**, 8); H-8 and H-9 1.61–1.75 (m); H-10 1.31 (tq, 7, 7) and 1.36 (tq, 7, 7); H-11 0.78 (t, 7) and 0.85 (t, 7).
^{13}C NMR: C-1 129.1 (*calcd: 126.1*); C-2 and C-6 132.1 [d, $^2J(^{19}F-^{13}C) = 8$] (*131.4*); C-3 and C-5 115.9 [d, $^2J(^{19}F-^{13}C) = 22$] (*115.6*); C-4 165.2 [d, $^1J(^{19}F-^{13}C) = 252$] (*168.4*); C-7 171.8; C-8 27.8 [$^1J(^{119/117}Sn-^{13}C) = 739/707$] and 28.2 [$^1J(^{119/117}Sn-^{13}C) = 718/687$]; C-9 28.0 [$^2J(Sn-C) = 38$] and 27.7 [$^2J(Sn-C) = 32$]; C-10 26.6 [$^3J(Sn-C) = 131$] and 26.6 [$^3J(Sn-C) \approx 124$]; C-11 13.5 and 13.4.
Mass spectrometry: $(FC_6H_4COO)_2SnBu_2^+$ 100; $FC_6H_4COOSn^+$ 15; $FC_6H_4Sn^+$ 5; $BuSn^+$ 10 %.

Compound 4a (X = 2-F; R = Et)
Yield 93 %; m.p. 112–114 °C.
Mössbauer: QS 3.87; IS 1.53; Γ_1 0.87, Γ_2 0.88 mm s^{-1}.
^{1}H NMR: H-3 7.15 (ddd, **10**, 8, 1); H-4 7.49–7.57 (m); H-5 7.21 (ddd, 8, 8, 1); H-6 8.08 (ddd, **8**, 8, 1); H-8 1.83 [q, 8; $^2J(^{119/117}Sn-^1H) = 70/67$]; H-9 1.38 [t, 8; $^3J(^{119/117}Sn-^1H) = 144/138$].
^{13}C NMR: C-1 119.1 [d, $^2J(^{19}F-^{13}C) = 9$] (*calcd: 117.7*); C-2 163.3 [d, $^1J(^{19}F-^{13}C) = 260$] (*164.8*); C-3 117.6 [d, $^2J(^{19}F-^{13}C) = 22$] (*115.6*); C-4 135.5 [d, $^3J(^{19}F-^{13}C) = 9$] (*135.0*); C-5 124.4 [d, $^4J(^{19}F-^{13}C) = 3$] (*124.0*); C-6 133.8 (*131.4*); C-7 174.3; C-8 18.4 [$^1J(^{119/117}Sn-^{13}C) = 599/573$]; C-9 9.4 [$^2J(Sn-C) = 44$].
Mass spectrometry: $(FC_6H_4COO)_2SnEt^+$ 3 %; $(FC_6H_4COO)SnEt_2^+$ 100; $(FC_6H_4COO)Sn^+$ 61; $FC_6H_4Sn^+$ 37; $MeCOOOSn^+$ 7; EtSn 2 %.

Compound 5a (X = 3-F; R = Et)
Yield 93 %; m.p. 83–85 °C.
Mössbauer: QS 3.75; IS 1.53; Γ_1 0.79, Γ_2 0.88 mm s^{-1}.
^{1}H NMR: H-2 7.82 (ddd, **8**, 1, 1); H-4 7.28 (dddd, **8**, 8, 2, 1); H-5 7.43 (ddd, 8, 8, **6**); H-6 7.93 (d, 8); H-8 1.81 [q, 8; $^2J(^{119/117}Sn-^1H) = 69/67$]; H-9 1.36 [t, 8; $^3J(^{119/117}Sn-^1H) = 144/138$].
^{13}C NMR: C-1 132.7 [d, $^3J(^{19}F-^{13}C) = 7$] (*calcd: 132.0*); C-2 117.8 [d, $^2J(^{19}F-^{13}C) = 23$] (*117.1*); C-3 163.1 [d, $^1J(^{19}F-^{13}C) = 247$] (*163.3*); C-4 120.7 [d, $^2J(^{19}F-^{13}C) = 21$] (*120.7*); C-5 130.4 [d, $^3J(^{19}F-^{13}C) = 7$] (*129.9*); C-6 126.6 (*125.5*); C-7 175.1; C-8: 18.4 [$^1J(^{119/117}Sn-^{13}C) = 596/570$]; C-9 9.4 [$^2J(Sn-C) = 43$].
Mass spectrometry: $(FC_6H_4COO)_2SnEt^+$ 5; $(FC_6H_4COO)SnEt_2^+$ 100; $FC_6H_4COOSn^+$ 53; $FC_6H_4Sn^+$ 18; $MeCOOSn^+$ 20; $EtSn^+$ 7%.

Compound 6a (X = 4-F; R = Et)
Yield 95 %; m.p. 90–92 °C.
Mössbauer: QS 3.83; IS 1.49; Γ_1 0.89, Γ_2 0.88 mm s^{-1}.
^{1}H NMR: H-2 and H-6 8.14 (dd, 9, **6**); H-3 and H-5 7.10 (dd, **9**, 9); H-8 1.78 [q, 8; $^2J(Sn-H) = 68$]; H-9 1.34 [t, 8; $^3J(^{119/117}Sn-^1H) = 144/137$].
^{13}C NMR: C-1 126.8 (*calcd: 126.1*); C-2 and C-6 133.6 [d, $^3J(^{19}F-^{13}C) = 9$] (*131.4*); C-3 and C-5 115.9 [d, $^2J(^{19}F-^{13}C) = 22$] (*115.6*); C-4 166.5 [d, $^1J(^{19}F-^{13}C) = 255$] (*168.4*); C-7 175.6; C-8 18.3 [$^1J(^{119/117}Sn-^{13}C) = 603/577$]; C-9 9.4 [$^2J(Sn-C) = 43$].
Mass spectrometry: $(FC_6H_4COO)_2SnEt^+$ 6 %; $(FC_6H_4COO)SnEt_2^+$ 100; $(FC_6H_4COO)Sn^+$ 71; $FC_6H_4Sn^+$ 23; $MeCOOSn^+$ 3; $EtSn^+$ 2 %.

Compound 4b (X = 2-F; R = Et)
Yield 84 %; recrystallized from petroleum ether, m.p. 215–216 °C.
Mössbauer: QS 3.50; IS 1.33; Γ_1 0.87, Γ_2 0.89 mm s^{-1}.
^{1}H NMR: H-3 7.40 (dd, **11**, 8); H-4 7.48 (dddd, 8, 8, **6**, 2); H-5 7.21 (ddd, 8, 8, 1); H-6 7.95 (ddd, **8**, 8, 2); H-8 1.59 [q, 8; $^2J(Sn-H) = 67$] and 1.66 (q, 8); H-9 1.34 [*t*, 8, $^3J(^{119/117}Sn-^1H) = 148/142$] and 1.41 [t, 8, $^3J(^{119/117}Sn-^1H) = 145/139$].

^{13}C NMR: C-1 122.6 (*calcd: 117.7*); C-2 162.7 [d, $^{1}J(^{19}F-^{13}C) = 257$] (*164.8*); C-3 117.5 [d, $^{2}J(^{19}F-^{13}C) = 23$] (*115.6*); C-4 134.0 [d, $^{3}J(^{19}F-^{13}C) = 9$] (*135.0*); C-5 124.4 [d, $^{4}J(^{19}F-^{13}C) = 3$] (*124.0*); C-6 133.2 (*131.4*); C-7 171.1; C-8 21.2 [$^{1}J(^{119/117}Sn-^{13}C) = 739/708$] and 23.3 [$^{1}J(^{119/117}Sn-^{13}C) \sim 758$, b]; C-9 10.1 [$^{2}J(Sn-C) = 29$] and 11.3 [$^{2}J(Sn-C) = 33$].
Mass spectrometry: $(FC_6H_4COO)_2SnEt_2OSnEt_2^+$ 100; $(FC_6H_4COO)SnEt_2^+$ 32; $(FC_6H_4COO)Sn^+$ 24; $MeCOOSnEt_2^+$ 16; $MeCOOSn^+$ 51; $EtSn^+$ 5 %.

Compound 5b (X = 3-F; R = Et)
Yield 95 %; recrystallized from petroleum ether, m.p. 206–209 °C.
Mössbauer: QS 3.46; IS 1.34; Γ_1 0.79, Γ_2 0.87 mm s^{-1}.
^{1}H NMR: H-2 7.72 (d, 9); H-4 7.26 (dddd, **8**, 8, 2, 1); H-5 7.45 (ddd, 8, 8, **6**); H-6 7.85 (d, 7); H-8 1.60 (q, 8) and 1.69 [q, 8, $^{2}J(Sn-C) = 58$]; H-9 1.36 [t, 8, $^{3}J(^{119/117}Sn-^{1}H) = 146/140$] and 1.41 [t, 8, $^{3}J(^{119/117}Sn-^{1}H) = 149/143$].
^{13}C NMR: C-1 136.1 (*calcd: 132.0*); C-2 117.2 [d, $^{2}J(^{19}F-^{13}C) = 23$] (*117.1*); C-3 163.2 [d, $^{1}J(^{19}F-^{13}C) = 247$] (*163.3*); C-4 119.7 [d, $^{2}J(^{19}F-^{13}C) = 20$] (*120.7*); C-5 130.3 [d, $^{3}J(^{19}F-^{13}C) = 7$] (*129.9*); C-6 126.1 (*125.5*); C-7 172.2; C-8 21.2 and 23.7 [$^{1}J(Sn-C) = nv$]; C-9 10.3 [$^{2}J(Sn-C) = 37$] and 10.6 [$^{2}J(Sn-C) = 44$].
Mass spectrometry: $(FC_6H_4COO)SnEt_2OSnEt_2^+$ 87; $(FC_6H_4COO)SnEt_2OSn^+$ 90; $(FC_6H_4COO)_2SnEt^+$ 7; $(FC_6H_4COO)_2SnMe^+$ 44; $(FC_6H_4COO)SnEt_2^+$ 100; $(FC_6H_4COO)Sn^+$ 21; $MeCOOSnEt_2^+$ 11; $MeCOOSn^+$ 28; $EtSn^+$ 14 %.

Compound 6b (x = 4-F; R = Et)
Yield 74 %; recrystallized from petroleum ether, m.p. 247–248 °C.
Mössbauer: QS 3.49; IS 1.33; Γ_1 0.86, Γ_2 0.87 mm s^{-1}.
^{1}H NMR: H-2 and H-6 8.06 (dd, 9, **6**); H-3 and H-5 7.14 (dd, **9**, 9); H-8 1.58 [q, 8, $^{2}J(Sn-H) = nv$] and 1.67 [q, 8, $^{2}J(Sn-H) = 66$]; H-9 1.36 [t, 8, $^{3}J(^{119/117}Sn-^{1}H) = 148/143$] and 1.39 [t, 8, $^{3}J(^{119/117}Sn-^{1}H) = 146/140$].
^{13}C NMR: C-1 129.8 (*calcd: 126.1*); C-2 and C-6 132.7 [d, $^{3}J(^{19}F-^{13}C) = 9$] (*131.4*); C-3 and C-5 115.7 [d, $^{2}J(^{19}F-^{13}C) = 22$] (*115.6*); C-4 165.9 [d, $^{1}J(^{19}F-^{13}C) = 253$] (*168.4*); C-7 172.4; C-8 21.2 [$^{1}J(^{119/117}Sn-^{13}C) = 748/714$] and 23.3 [$^{1}J(Sn-C) = 750$]; C-9 9.3 [$^{2}J(Sn-C) = 38$] and 9.9 [$^{2}J(Sn-C) = 44$].
Mass spectrometry: $(FC_6H_4COO)SnEt_2OSnEt_2^+$ 63; $(FC_6H_4COO)SnEt_2^+$ 48; $(FC_6H_4COO)Sn^+$ 36; $MeCOOSnEt_2^+$ 39; $MeCOOSn^+$ 100; $SnOH^+$ 18 %.

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