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Synthesis, characterization and *in vitro* antitumour activity of di-n-butyltin(IV) derivatives of some aromatic carboxylic acids, including aspirin

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Eleven di-n-butyltin(IV) derivatives of the type (a) $(C_4H_9)_2(XYC_6H_3COO)_2Sn$ or (b) $\{[(C_4H_9)_2(XYC_6H_3COO)Sn]_2O\}_2$ (X, Y = H, 2-OH, compound 1a; H, 2-OCH$_3$, compounds 2a and 2b; H, 2-OCOCH$_3$, 3a; 2-OH, 3-OCH$_3$, 4a; 2-OH, 3-CH$_3$, 5a; H, 3-OCH$_3$, 6a and 6b; H, 3-N(CH$_3$)$_2$, 7a; H, 2-(CF$_3$), 5-(CF$_3$), 8a and 3-OCH$_3$, 4-OH, 9a) have been prepared and characterized by ^{1}H, ^{13}C and ^{119}Sn NMR, Mössbauer and mass spectroscopy. The *in vitro* antitumour activity of these compounds against MCF-7 human tumour cells was higher than that of *cis*-platin, but only three compounds, 4a, 8a and 9a, scored better than *cis*-platin against the WiDr cell line.

Keywords: Organotin, NMR, anti-tumour, Mössbauer, mass spectrum, carboxylate

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INTRODUCTION

The reactions of aromatic carboxylic acids ArCOOH with dibutyltin oxide, in molar ratios 2:1 and 1:1, yield respectively $Bu_2(ArCOO)_2Sn$ (e.g. Refs 1,2) and $\{[Bu_2(ArCOO)Sn]_2O\}_2$ (e.g. Refs 3–6). Several such compounds exhibited a promising *in vitro* antitumour activity[1-6] against human cancer cell lines.[7] Therefore we prepared and characterized compounds of these types derived from other substituted aromatic carboxylic acids [including acetylsalicylic acid (aspirin)] and di-n-butylin oxide. they were submitted to *in vitro* antitumour screening tests on the human tumoral cell lines MCF-7 and WiDr.

EXPERIMENTAL

Syntheses

Compounds **1–9** were synthesized as analogous organotin derivatives of substituted salicylic acids or benzoates[1-7]. The synthetic procedure used for compounds of series **a** was that described below for compound **1a** (except for compound **3a**); compound **6b** was prepared as compound **2b**.

Compound **1a** was prepared by refluxing for 5 h a suspension of 0.01 mol of diorganotin oxide in a solution of 0.02 mol of salicylic acid in a mixture of 200 cm^3 of benzene and 50 cm^3 ethanol. The azeotrope generated was distilled off with a Dean–Stark apparatus and the solvent evaporated under vacuum. The oil obtained was recrystallized from petroleum ether. For compound **2a**, the oil obtained crystallized in the refrigerator. the solid was washed several times with petroleum ether and recrystallized from hexane/CH_2Cl_2 (80:20). For compound **2b**, synthesized from 0.02 mol of diorganotin oxide in a solution of 0.02 mol of 2-methoxybenzoic acid in benzene, the oil obtained crystallized after addition of some petroleum ether. The solid was recrystallized from hexane/DMF (80:20).

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Estimation of ID_{50} values

Drug activity was determined using an automated *in vitro* technique described previously[8]. The organotin compound was dissolved in DMSO and this solution was poured onto an amount of water such that the final mixture contained less than 0.3% DMSO. A concentration of 0.3% DMSO is not toxic for MCF-7 cells, but causes a slight inhibition in the growth of WiDr cells. Lower concentrations of DMSO are not toxic.

Equipment

The Mössbauer spectra were recorded in the constant-acceleration mode on a home-made (INAN, Université Catholique de Louvain) instrument, designed and built by the Institut voor Kern- en Stralingsfysika (IKS), Leuven, with a $Ca^{119m}SnO_3$ source from Amersham, UK. The probe was maintained at a temperature between 90 and 100 K, the source at room temperature. The digital data were treated with a least-squares iterative program deconvoluting the spectrum as a sum of lorentzians. The mass spectra were recorded on an AEI MS 902S instrument coupled to a NOVA computer. Samples were introduced via the direct insertion probe.

The ^{1}H NMR spectra were recorded at 270.13 MHz on a Bruker AM 270 instrument operating in the FT mode, equipped with an Aspect 2000 computer; the solution ^{13}C NMR spectra were taken at 62.97 MHz on a Bruker SF 250 instrument equipped with an Aspect 3000 computer. The ^{119}Sn NMR spectra were recorded at 186.5 MHz on a Bruker AM 500 instrument equipped with an Aspect 3000 computer.

RESULTS

Syntheses

Eleven compounds were synthesized from di-n-butyltin oxide and the suitable substituted aromatic carboxylic acid XYC_6H_3COOH either in a 2:1 molar ratio (series **a**), yielding $Bu_2(XYC_6H_3COO)_2Sn$, or in a 1:1 molar ratio (series **b**), yielding $Bu_2(XYC_6H_3COO)Sn]_2O\}_2$. A complete list with the substituents X,Y used is given in Table 1 together with the yields, the TLC R_f values (elution with cyclohexane/dioxane, 99:1) and the melting points. The recrystallization solvent of each compound is also stated.

The syntheses, which are easy, were conducted with yields of at least 65% and, in general, of more than 80%. The synthesis of compound **3a**, the 2:1 adduct obtained from acetylsalicylic acid (aspirin) and dibutyltin oxide, had to be performed in dry benzene. Indeed, in a mixture of benzene/ethanol, the di-n-butyltin(IV) derivative of salicylic acid,[9] compound **1a**, was obtained instead of the desired compound **3a**. Hydrolysis of compound **3a** by water generated during the synthesis and/or present in ethanol explains this unexpected result since it was checked that acetylsalicylic acid does not hydrolyse in an ethanol/benzene mixture. When both reagents are reacted in molar ratio 1:1 in benzene/ethanol, a 2:2 hydrolysed condensation product, $[HO—C_6H_4—COO(C_4H_9)_2Sn]_2O$, compound **1b**, is obtained. A mixture of compound **3a** and of the non-hydrolysed 2:2 adduct $[CH_3COO—C_6H_4—COO(C_4H_9)_2Sn]_2O$ was obtained when the reaction was performed in dry benzene with equal amounts of both reagents.

Besides compound **9a**, 20% of a 2:2 condensation derivative $[4—HO—3—OCH_3—C_6H_3—COO(C_4H_9)_2Sn]_2O$ was obtained as a by product that could not be separated from **9a**.

Molar mass determinations

Cryoscopy in benzene provided a molar mass of 1750 for compound **2b** (calculated for $[CH_3OC_6H_4COO(CH_3CH_2CH_2CH_2)_2Sn]_2O$: 744) and of 1520 for compound **6b** (calculated for $[(CH_3)_2NC_6H_4COO(CH_3CH_2CH_2CH_2)_2Sn]_2O$:810) suggesting that both are dimeric in that solvent as they are in $CDCl_3$ (see NMR results) and in the solid state.[5] The experimental molar mass of compound **6b** in DMSO obtained by the same cryoscopic technique was found to be 780, indicating that in this solvent no dimerization occurs.

Mössbauer data

The Mössbauer parameters of compounds **1a–9a** and **2b**, **6b** are given in Table 2.

^{1}H NMR data

The ^{1}H NMR spectral data of the compounds are summarized in Table 3.

The signals observed for the aromatic protons of compound **1a** were very easily assigned from the signal (a doublet of doublets) at lowest field

Table 1 Yields, R_f value (TLC; elution with cyclohexane/dioxane, 99:1), and melting points obtained for compounds **1a–9a**, **2b** and **6b**

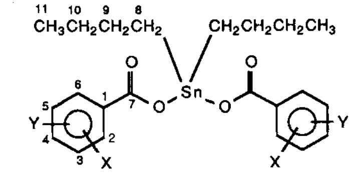
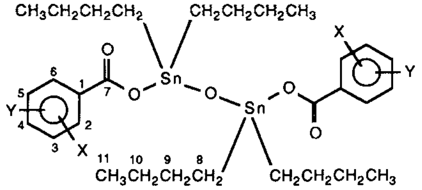
Compd no.	X	Y	Yield (%)	R_f	Recrystallization solvent	Melting point (°C)
Series **a**						
						
1a	H	2-OH	84	0.79	Petrol. ether[a]	74–75
2a	H	2-OCH_3	92	0.81	Hexane/CH_2Cl_2	70–72
3a	H	2-$OCOCH_3$	93	Hydrolyses	Oil: does not recrystallize	
4a	2-OH	3-OCH_3	90	0.79	Petrol. ether/EtOH	108–110
5a	2-OH	3-CH_3	78	0.81	Hexane/EtOH	121–122
6a	H	3-OCH_3	82	0.78	EtOH	62–62
7a	H	3-$N(CH_3)_2$	85	0.76	Hexane	104–105
8a	2-CF_3	5-$(CF_3)_2$	82	0.69	Petrol. ether/CH_2Cl_2	48–50
9a	3-OCH_3	4-OH	65	0.81	CH_2Cl_2	78–80
Series **b**						
						
2b	H	2-OCH_3	78	0.80	Hexane/DMF	91–94
6b	H	3-OCH_3	76	0.64	Hexane/EtOH	85–88

Table 2 Mössbauer parameters (quadrupole splitting QS, isomer shift IS, and linewidths Γ_1 and Γ_2 in mm s^{-1}) for compounds **1a–9a**, **2b** and **6b**

Compd no.	QS	IS	Γ_1	Γ_2
1a	3.69	1.51	0.87	0.91
2a	3.41	1.32	1.08	1.05
3a	3.69	1.50	1.15	1.01
4a	3.59	1.48	0.92	0.94
5a	3.79	1.53	0.85	0.89
6a	3.14	1.28	1.08	1.07
7a	3.27	1.37	0.95	0.99
8a	3.91	1.60	0.87	0.90
9a	3.37	1.36	1.11	1.02
2b	3.29	1.39	1.09	1.19
6b	3.73	1.49	0.90	0.91

(8.017 ppm) that is attributed to proton 6 because of its position *ortho* to the carboxyl group[1,2,7]. The other doublet of doublets at 6.998 ppm is therefore assigned to proton 3; irradiation of the doublet of doublets of doublets at 7.483 ppm changes the latter doublet of doublets into a broad singlet, meaning that the multiplet at 7.483 ppm originates from proton 4. Simultaneously, the doublet of doublets of proton 6 becomes a doublet as expected. the other doublet of doublets of doublets at 6.924 ppm, originating henceforth from proton 5, reduces to a doublet of doublets, as expected.

The same multiplet patterns are also observed for compounds **2a**, **2b** and **3a**, with roughly analogous chemical shifts.

The spectra of compounds **4a** and **5a** are very similar to those of comparable compounds[7], which made the resonance assignment straightforward.

Table 3 ^{1}H chemical shifts in ppm with respect to tetramethylsilane as internal standard, and multiplicities (coupling constants in Hz) obtained for $CDCl_3$ solutions of compounds **1a–9a** and of **2b** and **6b**.

Compd no.	H(2)	H(3)	H(4)	H(5)	H(6)	H(8)	H(9)	H(10)	H(11)	X	Y
1a	—	6.998	7.483	6.924	8.017	1.85	1.74	1.410	0.898	—	10.6
	—	dd(8, 1)	ddd(8,8,2)	ddd(8,8,1)	dd(8,2)	m	tt(7,7)	tq(7,7)	t(7)	—	bs
2a	—	6.978	7.488	6.993	8.027	1.74–1.83		1.414	0.887	—	3.927
	—	d(8)	ddd(8,8,2)	dd(8,8)	dd(8,2)	m		tq(7,7)	t(7)	—	s
2b	—	6.914	7.373	6.943	7.591	1.47–1.80		1.21–1.45	0.815	—	3.835(s)
	—	d(8)	ddd(8,8,2)	dd(8,8)	dd(8,2)	m		m	0.856	—	3.880(s)
									t(7); t(7)		
3a	—	7.118	7.325	7.577	8.104	1.66–1.90		1.409	0.910	—	2.360
	—	d(8)	ddd(8,8,2)	ddd(8,8,1)	dd(8,2)	m		tq(7,7)	t(7)	—	s
4a	—	—	7.084	6.875	7.609	1.8–2.0	1.6–1.8	1.405	0.893	10.86	3.923
	—	—	dd(8,1)	dd(8,8)	dd(8,1)	m	m	tq(7,7)	t(7)	bs	s
5a	—	—	7.350	6.827	7.867	1.85	1.73	1.404	0.896	10.88	2.284
	—	—	dd(8,1)	dd(8,8)	dd(8,1)	m	m	tq(7,7)	t(7)	s	s
6a	7.5–7.7	—	7.137	7.372	7.759	1.5–2.1		1.413	0.890	—	3.879
	bs	—	dd(8,2)	dd(8,8)	d(8)	m		tq(7,7)	t(7)	—	s
6b	7.5	—	7.104	7.380	7.626	1.5–2.0		1.249	0.772	—	3.800
	bs	—	dd(8,3)	dd(8,8)	d(8)	m		1.371	0.856	—	s
								tq; tq(7,7)	t; t(7)		
7a	7.51–7.54	—	6.92–6.96	7.332	7.51–7.54	1.6–1.9		1.415	0.897	—	3.025
	m	—	m	dd(8,8)	m	m		tq(7,7)	t(7)	—	s
8a	—	8.214	7.942[a]	7.896[a]	—	1.988	1.850	1.491	0.963	—	—
	—	s	d(9)	d(9)	—	t(7)	tt(7,7)	tq(7,7)	t(7)	—	—
9a	7.637	—	—	6.975	7.764	1.5–1.9		1.395	0.877	3.952	6.2
	d:2	—	—	d(8)	dd(8,2)	m		tq(7,7)	t(7)	s	bs

Abbreviations: b, broad; d, Doublet; m, complex pattern; s, singlet; t, triplet; q, quartet.

[a] Values may be interchanged.

The protons 2 and 6 of compounds **6a**, **6b** and **7a** are expected to be the less shielded ones appearing around 7.5 ppm. Indeed, they display similar chemical shifts. Except in compound **7a** where they display isochronous complex patterns, they are assigned according to their low field pattern, singlet for proton 2, doublet for proton 6. Proton 5 is the one displaying the doublet of doublets with identical coupling splittings (8 Hz), the assignment of proton 4 then being evident.

Compound **8a** is easily assigned, though not unambiguously for protons 4 and 5. For compound **9a** the aromatic proton assignment is evident from the multiplet patterns.

^{13}C NMR data

The ^{13}C NMR data of compounds **1–9** are summarized in table 4.

The assignment of the signals of the ^{13}C spectra were based on the distortionless enhancement by polarization transfer (DEPT) spectra, the comparison of the experimental chemical shifts with those calculated using the incremental values[5, 8, 10] and on the data given in refs 1, 2 and 7.

^{119}Sn NMR data

The ^{119}Sn NMR data are given in Table 5. Clearly, compounds of series **a** exhibit a single signal whereas those of type **b** exhibit two. Compounds **2b** and **6b** exhibit $^{2}J(^{119/117}Sn–O–^{119}Sn)$ coupling satellites of 111 and 121 Hz respectively.

Mass spectra

The mass spectra of compounds **1–9** are given in table 6. The molecular ion is never observed but the fragment-ions found are in agreement with the expected structure of the compounds.

DISCUSSION

All compounds display Mössbauer quadrupole splitting values in agreement with a *trans*-octahedral (compounds **a**) or a trigonal bipyramidal (compounds **b**) geometry at the tin atom.

All compounds of series **a** obtained from the condensation of Bu_2SnO with the ligand in 1:2

Table 4 ^{13}C NMR data (chemical shifts in ppm with respect to tetramethylsilane as internal standard, coupling constants in Hz) obtained for $CDCl_3$ solutions of compounds **1a** to **9a**, **2b** and **6b**[a]

Compd no.	C(1)	C(2)	C(3)	C(4)	C(5)	C(6)	C(7)	C(8)	C(9)	C(10)	C(11)	X	Y
1a	112.7	161.8	117.5	136.2	119.2	131.8	177.8	26.3	26.6	26.3	13.4	—	—
Calcd	*117.4*	*157.3*	*115.4*	*134.4*	*120.8*	*131.8*		^1J565/540	^2J54	^3J97			
2a	119.7	159.7	112.0	133.8	120.1	132.9	175.5	26.2	26.7	26.3	13.5	56.0	—
Calcd	*115.8*	*161.8*	*113.8*	*134.0*	*120.5*	*131.4*		^1J592/566	^2J38	^3J94			
2b	125.0	157.8	111.6	131.5	120.0	130.4	173.0	26.8; 27.0; 27.2; 27.5			13.6	55.5	—
3a	123.2	151.0	123.4	134.0	125.7	132.5	173.8	25.4	26.4	26.2	13.4	21.0	169.6
Calcd	*123.1*	*152.8*	*121.1*	*133.4*	*125.0*	*130.8*		^1J574/550	^2J32	^3J122			
4a	112.0	148.5	152.0	117.2	118.6	122.7	177.6	26.2	26.6	26.4	13.4	56.2	—
Calcd	*118.4*	*142.9*	*146.8*	*120.0*	*121.8*	*124.1*		^1J566/542	^2J35	^3J94			
5a	113.0	161.0	127.3	137.6	119.4	130.0	178.8	27.0	27.4	27.3	14.0	16.4	—
Calcd	*117.3*	*158.0*	*124.6*	*135.1*	*120.7*	*128.7*		^1J588/556	^2J35	^3J95			
6a	131.7	114.8	158.8	120.4	129.7	123.4	176.2	25.7	26.9	26.5	13.7	55.7	—
Calcd	*131.2*	*116.0*	*159.6*	*118.6*	*129.2*	*122.7*		^1J587/562	^2J33	^3J100			
6b	135.0	115.2	160.0	118.7	129.5	122.7	173.2	27.1[b]	27.1[b]	27.8[b]	13.8	55.7	—
								28.2[b]	28.9[b]	30.4[b]	13.7		
7a	131.0	114.6	150.0	117.6	129.6	119.2	177.0	25.8	27.2	26.8	14.0	40.9	—
Calcd	*131.1*	*115.0*	*150.7*	*117.6*	*129.1*	*118.9*		^1J596/570	^2J36	^3J99			
8a	133.3	134.8	128.3[b]	128.7[b]	133.3	128.4[b]	175.2	26.6	27.3	27.1	14.0	123.7	124.0
		^2J(C–F)32			^2J(C–F)34			^1J549	^2J33	^3J97		^1J(C–F)273	^1J(C–F)274
Calcd	*127.3*	*136.2*	*125.3*	*130.1*	*134.0*	*127.5*							
9a	121.7	114.9	151.4	146.4	112.8	125.7	176.0	26.4	26.8	25.4	13.6	56.2	
Calcd	*123.8*	*117.4*	*146.8*	*145.5*	*116.4*	*124.1*		^1J600	^2J37	^3J110			

[a] Values in *italics* are calculated using the increment values for aromatic ^{13}C chemical shifts.[5,10] [b] Assignment interchangeable; $^xJ = {}^xJ(^{119/117}$Sn–^{13}C) (increment $COOSnBu_2L$:[8] *ipso* 1.7; *ortho* 1.9; *meta* −0.3; *para* 4.5).

molar ratio are characterized by a single signal in their ^{119}Sn NMR spectrum and by one triplet for the methyl groups of the dibutyltin moiety. ^{1}H integration data indicate a Bu:L ratio of 1:1 (Bu_2Sn:L = 1:2). These data are in agreement with a structure containing an octahedral tin atom, similar to that in the solid state[1,2] for diorganotin dicarboxylates (see Fig. 1).

The six-coordination of tin is confirmed by the $^1J(^{119/117}$Sn–^{13}C) coupling splittings[5] and by the Mössbauer data.

For compounds of series **b** obtained from a condensation in 1:1 molar ratio, the two tin signals and two methyl triplets observed can be explained by the fact that these bis(carboxylatodi-n-butyltin) oxides, which are dimeric in chloroform and benzene, as evidenced by cryoscopy, and in the solid state[5], contain two different types of tin atoms: two involved in a distannadioxetane ring and two which are not (see Fig. 2).

The observed ^2J(Sn–O–Sn) coupling satellites support this structure. Mössbauer spectroscopy, however, does not distinguish two different types of tin atoms in these series **b** compounds.

The ^{119}Sn signal observed for compound **6a** appears at higher field because of the complexation of tin by DMSO.

In vitro antitumour tests

The results of the *in vitro* antitumour tests performed with compounds **1–9** are summarized in Table 7. They are compared with the screening results from other di-n-butyltin(IV) compounds[9–11] and from some reference compounds used clinically.

Table 5 ^{119}Sn NMR data (chemical shifts in ppm with respect to tetramethyltin as external standard) obtained for $CDCl_3$ solutions (in DMSO-d_6 for compound **6a**) of compounds **1a–9a**, **2b** and **6b**

Compd no.	**1a**	**2a**	**2b**	**3a**	**4a**	**5a**	**6a**	**6b**	**7a**	**8a**	**9a**
δ(ppm)	−123.0	−150.5	−203.8 −203.3	−142.0	−121.0	−126.0	−308.5	−217.7 −211.8	−155.6	−125.0	−157.4

Table 6 Monoisotopic FAB mass spectra of compounds **1a–9a**, **2b** and **6b**

	1a[a]	**2a**[b]	**2b**[c]	**3a**[d]	**4a**[e]	**5a**[f]	**6a**[g]	**6b**[h]	**7a**[i]	**8a**[j]	**9a**
$ArCOOSnBu_2OSnBu_2^+$	—	5	78	—	—	—	2	30	—	—	—
$ArCOOSnBu_2OSn^+$	—	4	45	—	—	—	2	20	—	—	—
$ArCOOSnBu_2O^+$	—	—	39	—	—	—	—	75	—	—	—
$ArCOOSnBu_2^+$	100	100	100	40	100	100	26	25	55	100	96
$ArCOSnBu_2^+$	—	—	—	—	3	6	—	—	—	—	—
$ArCOOSnBuH^+$	—	16	7	—	—	1	1	—	—	—	—
$ArCOOSn^+$	33	6	2	—	4	15	100	100	100	—	100
$ArSn^+$	13	7	2	—	1	6	90	20	41	—	34
$BuSn(OH)_2^+$	—	—	—	—	13	—	—	—	—	—	8
$BuSnH_2^+$	2	—	—	—	—	—	—	—	—	—	—
$BuSn^+$	11	—	—	—	3	5	20	40	80	16	6
$SnOH^+$	12	—	—	—	2	—	—	—	—	6	—
SnH^+	23	—	—	—	1	4	6	20	14	10	4
$Sn^{\cdot +}$	4	—	—	—	1	7	4	25	63	12	2

[a] **1a**: Fragment-ions have also been observed at $m/z = 269$ (6%), 327 (7%), 427 (7%) and 487 (4%).

[b] **2a**: Fragment-ions have also been observed at $m/z = 209$ (30%) and 403 (3%).

[c] **2b**: Fragment-ions have also been observed at $m/z = 257$ (15%), 443 (4%), 463 (3%) and 557 (4%).

[d] **3a**: Fragment-ions have also been observed that correspond formally to hydrolysis fragments of compound **3a**, i.e. of fragments observed for compound **1a**, i.e. at $m/z = 371$ (100%), 257 (5%) and 213 (4%).

[e] **4a**: Fragment-ions have also been observed at $m/z = 327$ (6%), 329 (7%), 443 (3%) and 557 (3%).

[f] **5a**: Fragment-ions are also present at $m/z = 209$, 293, 501 and 557 as traces.

[g] **6a**: A fragment-ion has also been observed at $m/z = 403$ (5%).

[h] **6b**: Fragment-ions have also been observed at $m/z = 293$ (12%), 403 (30%) and 557 (11%).

[i] **7a**: Fragment-ions have also been observed at $m/z = 293$ (25%) and 557 (4%).

[j] **8a**: Fragment-ions have also been observed at $m/z = 387$ (3%) and 407 (2%).

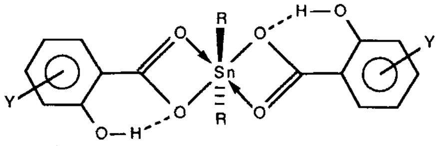


Figure 1 General structure type of compounds of series **a**.

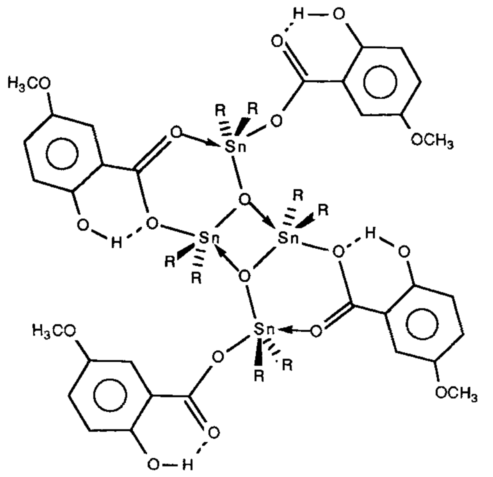


Figure 2 General structure type of bis(5-methoxy-salicylatodi-n-butyltin) oxide determined by X-ray diffraction[5] and proposed for compounds of series **b** in solution.

Table 7 ID_{50} values (ng cm^{-3}) of organotin derivatives tested against two human tumour cell lines, MCF-7 (mammary tumour) and WiDr (colon carcinoma), and of some reference compounds[12]

Compd no. or formula	MCF-7	WiDr
1a	541	2974
2a	356	2665
2b	156	1661
3a	283	2495
4a	105	474
5a	646	3787
7a	174	1959
8a	48	176
9a	44	82
cyclo-$C_4H_6(COO)_2SnBu_2$[9]	42	121
cyclo-$C_3H_4(COO)_2SnBu_2$[9]	60	302
$C_6H_5CH(COO)_2SnBu_2$[9]	42	283
$\{[(CH_3CH(OH)COO)Bu_2Sn]_2O\}_2$[5, 11]	60	248
$\{[(C_6H_5CH(OH)COO)Bu_2Sn]_2O\}_2$[5, 11]	54	210
$H_2NCOCH_2N(CH_2COO)_2SnBu_2$[12]	76	349
$HOCH_2CH_2N(CH_2COO)_2SnBu_2$[12]	52	277
Cis-platin[8]	850	624
Doxorubicin[8]	63	31
Etoposide[8]	187	624
Mitomycin C[8]	3	17

Table 7 clearly shows that compounds **9a**, **8a** and, to a lesser extent, **4a** are more active *in vitro* than *cis*-platin and etoposide against MCF-7 (mammary tumour) and WiDr (colon carcinoma), remaining however significantly less active than doxorubicin and mitomycin C, especially against WiDr. Table 7 also indicates that compound **9a** scores as well as a series of organotin derivatives of dicarboxylic acids[9, 12] and hydroxyacids[11] in the case of the MCF-7 cells, and significantly better against WiDr cells. However, the other organotin compounds described in this paper are less active than *cis*-platin. In particular, the 2:1 adduct of aspirin and dibutyltin oxide, compound **3a**, does not exhibit any activity worth outlining.

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