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Synthesis, characterization and *in vitro* antitumour properties of complexes of bis(alkoxycarbonylmethyl)tin dibromides with bidentate nitrogen ligands

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The synthesis and characterization of 10 new bis(alkoxycarbonylmethyl)tin dibromides and of 14 of their complexes with bidentate nitrogen ligands (bipyridyl, 1,10-phenanthroline and 5-nitro-1,10-phenanthroline) are described. Their proton NMR spectra are discussed. Their *in vitro* antitumour activity against two human cancer cell lines, MCF-7 and WiDr, is low compared to antitumour drugs used clinically.

Keywords: Organotin, nitrogen ligands, synthesis, antitumour activity, NMR

INTRODUCTION

Since Crowe reported that diorganotin dichloride complexes have some interesting antitumour properties,[1–4] a wide interest has developed in this field.[5–10] We report here the synthesis, characterization and antitumour properties of some bis(alkoxycarbonylmethyl)tin dibromides and of their complexes with the bidentate nitrogen ligands bipyridyl, 1,10-phenanthroline and 5-nitro-1,10-phenanthroline.

EXPERIMENTAL

Instruments

Elemental analyses: Perkin-Elmer 2400
Conductivity: Shanghai Analysis Instrument, Factory No. 2, DDS-11A
FT-IR spectrometer: Nicolet 5-DX
UV spectrometer: Beckman DU-78
NMR spectrometer: Bruker AM-270

Syntheses

Synthesis of alkyl bromoacetates or alkyl α-bromopropionates

Method 1

Bromoacetic acid (1.0 mol), alcohol (1.1 mol), benzene (70 cm^3) and $H_3PO_{40}W_{12}.xH_2O$ (0.4 g) were put into a 250 cm^3 round-bottom flask connected with a Dean–Stark condenser and refluxed for 3–4 h until 15–18 cm^3 water was collected. The crude solution was separated, washed with water, twice with a saturated sodium bicarbonate solution and finally again with water, and dried over magnesium sulphate and sodium sulphate (1:1), filtered, and distilled under normal pressure or under vacuum.

Method 2

Alcohol or phenol (0.5 mol), bromoacetyl bromide (0.5 mol) and benzene (70 cm^3) were put into a 250 cm^3 round-bottom flask, equipped with a condenser connected through an outlet glass pipe to a gas trap containing pyridine in order to complete the absorption of HBr gas. The flask was heated to reflux until no more HBr gas was formed. The purification was performed as in Method 1.

Method 3

The reaction was carried out in a Soxhlet apparatus, using a 1:1 mixture of magnesium sulphate and sodium sulphate in the filter bag as drying agent, from 1.0 mol bromoacetic acid, 1.1 mol alcohol, 0.4 g $H_3PO_{40}W_{12}.xH_2O$ and 100 cm^3 benzene. The reaction mixture was heated to 130–

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Table 1 Yields, boiling points, refractive indexes and IR stretching frequencies ν(CO) for a series of alkyl bromocetates or alkyl α-bromopropionates

Product	Method[a]	Yield (%)	B.p. (°C)	n_D^{20}	ν(CO) (cm^{-1})
$BrCH_2COOCH_2CH_3$	3	50	168–170 (lit.[b] 168–169[16])	1.4516	
$BrCH_2COO(CH_2)_3CH_3$	1	90	194–196 (lit.[b] 196)	1.4567	1743
$BrCH_2COOCH_2CH(CH_3)_2$	1	88	186–187 (lit.[b] 188)	1.4530	1738
$BrCH_2COOC(CH_3)_3$	2	52	167–168	1.4246[d] (lit. 1.4162[d])	1733
$BrCH_2COO(CH_2)_4CH_3$	1	70	214	1.4580	1740
$BrCH_2COO(CH_2)_2CH(CH_3)_2$	1	81	208–210 (lit[b] 207)	1.4559	1740
$BrCH_2COOCH(CH_2CH_2CH_3)CH_3$	1	82	198–200	1.4523	1737
$BrCH_2COOC(CH_3)_2(CH_2CH_3)$	2	57	84–86/16 torr	1.4515 (lit. 1.4486)	1740
$BrCH_2COO(CH_2)_6CH_3$	1	86	108–109/4 torr	1.4568	1738
$BrCH_2COO\text{-cyclo-}C_6H_{11}$	1	79	102/6 torr	1.4891[d]	1734
$BrCH_2COOCH_2C_6H_5$	1	85	127.5–129.5/5 torr	1.5466 (lit. 1.5412)	1740
$BrCH_2COOC_6H_5$	2	71	108–110/6 torr[c] (lit[b] 140/20 torr)		1758
$CH_3CHBrCOO(CH_2)_3CH_3$	1	84	199–200	1.4529	1740
$CH_3CHBrCOOCH_2CH(CH_3)_2$	1	72	80–81/14 torr	1.4481	1740
$CH_3CHBrCOO(CH_2)_4CH_3$	1	77	100–101/9 torr	1.4534	1740
$CH_3CHBrCOO(CH_2)_2CH(CH_3)_2$	1	78	100–101/15 torr	1.4517	1740

[a] See Experimental section. [b] Ref. 11. [c] M.p. 32–33 °C (lit[11], 32 °C) [d] n_D^{25}.

140 °C in an oil bath for 6 h. The drying agent was washed with benzene and the solution obtained was combined with the other benzene solution. The purification was identical to that used in Method 1.

Synthesis of bis(alkoxycarbonylmethyl)tin(IV) dibromide

Tin powder (99.5%, 200 mesh; 0.5 mol), alkyl bromoacetate (0.11 mol), magnesium powder (0.2 g) and benzene (20 cm^3) (dried over sodium) were put in a 150 cm^3 Erlenmeyer flask equipped with a condenser. The flask was heated to reflux for 0.5 h with stirring until the tin powder had disappeared. A yellow solid appeared on cooling that was filtered and recrystallized from benzene.

Synthesis of complexes of bis(alkoxycarbonylmethyl)tin(IV) dibromides with bipyridyl, 1,10-phenanthroline and 5-nitro-1,10-phenanthroline

A solution of 4 mmol bis(alkoxycarbonylmethyl)tin dibromide in 20 cm^3 benzene was

Table 2 Yields and melting points of a series of bis(alkoxycarbonylmethyl)tin(IV) dibromides (**1**–**10**), and the molar conductivities Λ of their 10^{-5} M acetone solutions

Compd no.	Bis(alkoxycarbonylmethyl)tin(IV) dibromide	Yield (%)	M.p. (°C)	$\Lambda \times 10^3$ (cm^2 ohm^{-1} mol^{-1})
1	$[CH_3CH_2OOCCH_2]_2SnBr_2$	50	140–142	7.08
2	$[CH_3(CH_2)_3OOCCH_2]_2SnBr_2$	78	122–123	6.23
3	$[(CH_3)_2CHCH_2OOCCH_2]_2SnBr_2$	72	155–156	6.33
4	$[CH_3(CH_2)_4OOCCH_2]_2SnBr_2$	63	116–117	3.87
5	$[(CH_3)_2CH(CH_2)_2OOCCH_2]_2SnBr_2$	61	136–137	7.49
6	$[(CH_3CH_2CH_2)(CH_3)CHOOCCH_2]_2SnBr_2$	97	122–123	2.26
7	$[C_6H_5OOCCH_2]_2SnBr_2$	63	196 (dec.)	1.05
8	$[\text{cyclo-}C_6H_{11}OOCCH_2]_2SnBr_2$	93	203–204	3.72
9	$[C_6H_5H_2OOCCH_2]_2SnBr_2$	50	117–118	9.29
10	$[CH_3(CH_2)_6OOCCH_2]_2SnBr_2$	67	114–116	5.23

Table 3 IR (cm^{-1}) and UV (nm) data of a series of bis(alkoxycarbonylmethyl)tin(IV) dibromides (**1–10**)

Compd no.	ν(C=O) (cm^{-1})	ν(C—O—C) (cm^{-1})	ν(Sn—C) (cm^{-1})			λ_{max} (nm)	
1	1648	1281	522	231		265	
2	1646	1286	487	231		267	
3	1647	1291	484	231		265	
4	1645	1291	490	232		264	
5	1648	1291	525	224	257	263	
6	1648	1291	489	231		266	
7	1687	1248	502	230		266	
8	1640	1287	500	230		265	269
9	1651	1286	478	228		265	
10	1646	1294	494	227		265	269

added to a solution of 4 mmol of the ligand in 20 cm^3 benzene. The mixture was warmed with stirring for 4 h. The solid that appeared upon cooling was filtered and recrystallized from the appropriate solvent ($CHCl_3/CCl_4$, 1:1, for compounds **11–15**, benzene for compounds **16–18** and chloroform for compounds **19–24**).

In vitro tests

Drug activity was determined using an automated *in vitro* technique.[14,16] In summary, human tumour cells were plated in the wells of 96-well flat-bottom microtitre plates (Falcon, type 3070). The plates were incubated for two days at 37 °C (5% CO_2) to allow the cells to adhere and resume exponential growth prior to the addition of the drugs. After two days, 50 µl of the highest drug concentrations were added to the wells of column 12 and from there serially diluted three-fold to row 1 by serial transfer of 50 µl using an eight-channel micropipette. The final volume of row 1 was adjusted to 100 µl. No additions were made to the wells of rows A and B, which served as controls. All drugs were tested in duplicate.

The plates were further incubated for five days 37°C (5% CO_2). On day 7, the cultures were terminated by the addition of 100 µl saline containing 0.002% (w/v) propidium iodide, 0.3% drawing ink and 0.5% Triton X-100. The plates were kept overnight at 4 °C before reading.

Table 4 Yields, melting points of a series of complexes of bis(alkoxycarbonylmethyl)tin(IV) dibromides with bidentate nitrogen ligands (**11–24**) and the molar conductivities Λ of their 10^{-5}M acetone solutions

Compd no.	$(ROOCCH_2)_2SnBr_2 . L^a$	Yield (%)	M.p. (°C)	$\Lambda \times 10^3$ ($cm^2 ohm^{-1} mol^{-1}$)
11	$[CH_3(CH_2)_3OOCCH_2]_2SnBr_2$. Bipy	100	162–163	1.31
12	$[(CH_3)_2CHCH_2OOCCH_2]_2SnBr_2$. Bipy	100	173–174	1.21
13	$[CH_3(CH_2)_4OOCCH_2]_2SnBr_2$. Bipy	100	141–142	1.25
14	$[(CH_3)_2CH(CH_2)_2OOCCH_2]_2SnBr_2$. Bipy	99	144–145	1.72
15	$[(CH_3CH_2CH_2)(CH_3)CHOOCCH_2]_2SnBr_2$. Bipy	99	161–162	1.63
16	$[CH_3(CH_2)_3OOCCH_2]_2SnBr_2$. O_2N-Phen	83	108–109	1.87
17	$[CH_3(CH_2)_4OOCCH_2]_2SnBr_2$. O_2N-Phen	97	112–114	1.01
18	$[(CH_3)_2CH(CH_2)_2OOCCH_2]_2SnBr_2$. O_2N-Phen	99	148–149	1.38
19	$[(CH_3CH_2CH_2)(CH_3)CHOOCCH_2]_2SnBr_2$. O_2N-Phen	92	154–155	3.62
20	$[CH_3(CH_2)_3OOCCH_2]_2SnBr_2$. Phen	84	145–147	1.44
21	$[(CH_3)_2CHCH_2OOCCH_2]_2SnBr_2$. Phen	100	155–157	1.02
22	$[CH_3(CH_2)_4OOCCH_2]_2SnBr_2$. Phen	98	118–119	2.61
23	$[(CH_3)_2CH(CH_2)_2OOCCH_2]_2SnBr_2$. Phen	96	128–130	1.17
24	$[(CH_3CH_2CH_2)(CH_3)CHOOCCH_2]_2SnBr_2$. Phen	99	160(dec.)	1.35

[a] Bipy, bipyridyl, Phen, 1,10-phenanthroline, O_2N-Phen, 5 nitro-1,10-phenanthroline.

Table 5 IR and UV data of a series of complexes of bis(alkoxycarbonylmethyl)tin(IV) dibromides with bidentate nitrogen ligands (**11–24**)

Compd no.	$\nu(C{=}O)$ (cm^{-1})	$\nu(C{=}N)$ (cm^{-1})	$\nu(C{-}O{-}C)$ (cm^{-1})	$\nu(Sn{-}C)$ (cm^{-1})	λ_{max} (nm)			
Bipy					235	281		
11	1705	1441	1246	417	232	265	301	312
12	1693	1443	1254	419	232	265	301	311
13	1695	1443	1254	419	232	266		312
14	1702	1444	1250	419	232	266	301	312
15	1691	1437	1257	417	231	267	301	312
O_2N-Phen					232	265		
16	1686	1521	1250	421	232	273		
17	1696	1523	1256	423	232	273		
18	1683	1522	1257	421	232	272		
19	1696	1522	1250	421	231	267	275	312
Phen					231		274	323
20	1705	1473	1248	420	232		275	296
21	1694	1471	1259	417	232		275	295
22	1695	1468	1250	420	232	266	278	296
23	1693	1468	1250	420	232		275	296
24	1688	1464	1256	418	230	266	277	

Fluorescence intensity was measured by a photomultiplier. Dose–response curves were obtained and ID_{50} values were calculated.

RESULTS AND DISCUSSION

Synthesis and physical properties of alkyl bromoacetates and alkyl α-bromopropionates

We synthesized a series of alkyl bromoacetates and alkyl α-bromopropionates by using a novel catalyst, a heteropolyacid, 12-tungstophosphoric acid $H_3PO_{40}W_{12}.xH_2O$, allowing us to increase the yields up to 70–90%. Table 1 gives the yields, boiling points, refractive indices and IR data [ν(CO)] for the prepared alkyl bromoacetates or alkyl α-bromopropionates.

Synthesis and physical properties of bis(alkoxycarbonylmethyl)tin(IV) dibromides

Gilman[12] allowed tin powder to react with ethyl bromoacetate, which gave bis(ethoxycarbonylmethyl)tin dibromide with only 15% yield. Bogatiskii[13] modified this synthesis by using 15-crown-5 as a catalyst, and thus increased the yield up to 51%. We used magnesium as a catalyst, and benzene as a solvent. With this procedure, tin powder reacted with alkyl bromoacetates with yields of 50–97%. Table 2 gives the yields, melting points and conductivities of the diorganotin(IV) dibromides prepared from these alkyl α-bromoacetates.

Satisfactory C, H, Br and Sn elemental analyses have been obtained for compounds **1–10**; these data are available from the authors (H.P.) on request.

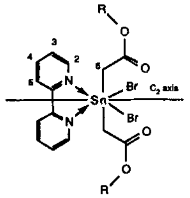
The IR and UV data of the bis(alkoxycarbonylmethyl)tin(IV) dibromides **1–10** are given in Table 3.

Synthesis and physical properties of complexes of bis(alkoxycarbonylmethyl)tin(IV) dibromides with bidentate nitrogen ligands

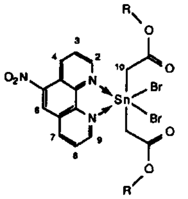
The bis(alkoxycarbonylmethyl)tin(IV) dibromides **1–10** have been complexed with bipyridyl, 1,10-phenanthroline and 5-nitro-1,10-phenanthroline. The yields, melting points and conductivities of these chelates are given in Table 4. Satisfactory C, H, N, Br and Sn elemental analyses that have been obtained for compounds **11–24** are available from the authors (H.P.) on request.

The IR and UV data of these complexes of bis(alkoxycarbonylmethyl)tin(IV) dibromides with bidentate nitrogen ligands (**11–24**) are given in Table 5.

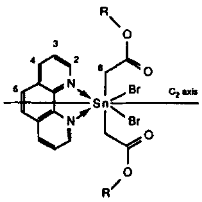
Table 6a ^{1}H NMR spectra of $CDCl_3$ solutions of complexes of the type $[CH_3(CH_2)_nCH_2OOCCH_2]_2SnBr_2.L$ (with $n = 1$ or 2 and L = bipyridyl, 5-nitro-phenanthroline or phenanthroline)



Compd no.	CH_3 (t)	$(CH_2)n$ (m)	CH_2—O (t)	CH_2—Sn (s, H-6)	Bipyridyl protons (d, H-2)	(d, H-5)	(ddd, H-4)	(ddd, H-3)
11	0.82	1.14–1.31	3.20	2.80ᵃ	9.64	8.32	8.27	7.80
[*J*]	[7]		[7]		[5]	[8]	[8; 7; 1.5]	[7; 5; 1.5]
13	0.83	1.11–1.32	3.19	2.82ᵃ	9.67	8.38	8.31	7.82
[*J*]	[7]		[7]		[5]	[8]	[8; 7;1]	[7; 5; 1]



Compd. no.	CH_3 (t)	$(CH_2)n$ (m)	CH_2—O (t)	CH_2—Sn (s, H-10)	5-Nitrophenanthroline protons (dd)	(dd)	(dd)	(s, H-6)	(dd)	(dd)	(dd)
16	0.79	1.07–1.14	3.04	2.86ᵃ	10.04	10.01	9.52	9.86	8.99	8.29	8.28
[*J*]	[7]		[6]		[5; 1.5]	[5; 1.5]	[8; 1.5]		[8; 1.5]	[8; 5]	[8; 5]
17	0.82	1.00–1.20	3.03	2.86ᵃ	10.04	10.02	9.52	9.05	9.00	8.29	8.28
[*J*]	[7]		[6]		[5; 1.5]	[5; 1.5]	[8; 1]		[8; 1]	[8; 5]	[8; 5]



Compd. no.	CH_3 (t)	$(CH_2)n$ (m)	CH_2—O (t)	CH_2—Sn (s, H-6)	Phenanthroline protons (dd, H-2)	(dd, H-4)	(s, H-5)	(dd, H-3)
20	0.73	0.95–1.05	2.92	2.89ᵃ	9.89	8.84	8.23	8.14
[*J*]	[7]		[7]		[5; 1.5]	[8; 1.5]		[8; 5]
22	0.79	0.87–1.13	2.90	2.89ᵃ	9.86	8.81	8.20	8.11
[*J*]	[7]		[7]		[5; 1]	[8; 1]		[8; 5]

Abbreviations: d, doublet; m, complex pattern; s, singlet; t, triplet.
[a] $^2J(^{119/117}Sn—H) = 165/158$ Hz.

Table 6b ^{1}H NMR spectra of complexes of the type $[(CH_3)_2CH(CH_2)_nCH_2OOCCH_2]_2SnBr_2.L$ (with $n=0$ or 1 and L = bipyridyl, 5-nitro-phenanthroline or phenanthroline)

Compd. no.	CH_3 (d)	CH (pn)	CH_2 (pqua)	CH_2—O	CH_2—Sn (s, H-6)	Bipyridyl protons			
						(d, H-2)	(d, H-5)	(ddd, H-4)	(ddd, H-3)
12	0.77	1.62		d:2.98	2.82[a]	9.62	8.35	8.31	7.79
[*J*]	[7]	[7]		[7]		[5]	[8]	[8; 7; 1.5]	[7; 5; 1.5]
14	0.78	1.47	1.18	t:3.24	2.81[a]	9.62	8.46	8.35	bt:7.82
[*J*]	[7]	[7]	[7]	[7]		[5]	[8]	[8; 7; 1]	[7; 5; 1]

Compd no.	CH_3 (d)	CH (pn)	CH_2 (pqua)	CH_2O (t)	CH_2Sn (s, H-10)	5-Nitrophenanthroline protons						
						(dd)	(dd)	(dd)	(s, H-6)	(dd)	(dd)	(dd)
18	0.745	1.415	1.043	3.081	2.848[a]	10.044	10.018	9.511	9.045	8.981	8.285	8.278
[*J*]	[7]	[7]	[7]	[7]		[8.5; 1.5]	[8.5; 1.5]	[8.5; 1.5]		[8.5; 1.5]	[8; 5]	[8; 5]

Compd. no.	CH_3 (d)	CH (pn)	CH_2 (pqua)	CH_2—O	CH_2—Sn (s, H-6)	Phenanthroline protons			
						(dd, H-2)	(dd, H-4)	(s, H-5)	(dd, H-3)
21	0.621	1.326		d:2.726	2.901[a]	9.859	8.823	8.207	8.109
[*J*]	[7]	[7]		[7]		[5; 1]	[8; 1]		[8; 5]
23	0.733	1.318	0.882	t:2.949	2.872a	9.890	8.794	8.195	8.119
[*J*]	[7]	[7]	[7]	[7]		[5; 1.5]	[8; 1.5]		[8; 5]

Abbreviations: d, doublet; ḿ, complex pattern; pn, pseudo-nonet, i.e. degenerated septet of doublets; Pqua, pseudo-quartet, i.e. degenerated triplet of doublets; qua, quartet; s, singlet; t, triplet.

[a] $^{2}J(^{119/117}\text{Sn—H}) = 165/158$ Hz.

Proton NMR spectra of complexes of bis(alkoxycarbonylmethyl)tin(IV) dibromides with bidentate nitrogen ligands

The proton NMR spectra of compounds **11–24** are described in Tables 6a, 6b and 6c.

The signal of the bipyridyl proton in complexes **11–13** (see Table 6a), and likewise that in compounds **12–14** (see Table 6b), appearing as a broad doublet at the lowest field, is proton 2, *ortho* to the ring nitrogen;[14] it is broad because of a small unresolved *para* coupling, probably of the order of magnitude of 0.5 Hz; it is coupled ($J = 5$ Hz) with the aromatic proton 3 appearing at the highest field of the aromatic ones; proton 5 appears as another broad doublet and is coupled ($J = 8$ Hz) with the fourth aromatic proton. Assuming a coupling constant of 7 Hz between the two protons displaying triplets ($J = 5$ or 8 Hz, *vide supra*) of doublets ($J = 1.5$ Hz, *meta* coupling) provides a fitted spectrum almost identical to the experimental one.

Analogously, the signals of the phenanthroline protons of compounds **20** and **22** (see Table 6a), and compounds **21**, **23** and **24** (see Tables 6b and 6c) can easily be assigned from the observed patterns, chemical shifts and coupling constants: the singlet is assigned to proton 5; the doublet of doublets appearing at high field, being characterized by two large coupling constants (8 and 5 Hz), is therefore proton 3; the doublet of doublets at low field (5 and 1.5 Hz) is assigned to proton 2 because it is *ortho* to nitrogen;[9] proton 4 is then the doublet of doublets (8 and 1.5 Hz) lying between the other two.

The proton NMR spectra of the 5-nitrophenanthroline complexes is of course more complicated because of the disappearance of the *C*2 axis present in phenanthroline which causes all the protons to become different. However, it is quite clear that the singlet appearing around 9 ppm can be assigned to H-6; the signals appearing as two doublets ($J = 5$ Hz) of doublets ($J = 1$ Hz, *meta* coupling)) at low field (*ca* 10 ppm) are due to H-2 and H-9 (*ortho* to the ring nitrogen); the two doublets ($J = 8$ Hz) of doublets ($J = 5$ Hz) at high field (*ca* 8.3 ppm) are therefore assigned to H-3 and H-8; these two last protons are respectively coupled ($J = 8$ Hz) with H-4 and

Table 6c ^1H NMR spectra of acetone (**19**) and chloroform (**24**) solutions of complexes of the type $[(CH_3CH_2CH_2)(CH_3)CHOOCCH_2]_2SnBr_2 . L$ (with L = 5 nitrophenanthroline or phenanthroline)

Compd	CH_3	CH_2CH_2	CH_3	CH—O	CH_ASn	CH_B Sn	5-Nitrophenanthroline protons						
no.	(obsc)	(m)	(d)	(pse)	(AB system)		(bd)	(bd)	(bd)	(s, H-6)	(d)	(dd)	(dd)
19	0.77	1.0–1.2	0.77	3.89	2.70	2.69	9.94	9.93	9.45	9.11	9.09	8.28	8.25
[*J*]	[obsc]		[6]	[6]	[10]	[10]	[5]	[5]	[8]		[8]	[8; 5]	[8; 5]

Cpd	CH_3	CH_2CH_2	CH_3	CH—O	CH_ASn	CH_BSn	Phenanthroline protons			
	(d)	(m)	(d)	(pse)	(AB system)		dd, H-2	dd, H-4	s, H-5	dd, H-3
24	0.75	1.0–1.1	0.68	3.88	2.84	2.82	9.90	8.78	8.18	8.09
[*J*]	[6]		[6]	[6]	[10]	[10]	[5; 1.5]	[8; 1.5]		[8; 5]

Abbreviations: d, doublet; m, complex pattern; obsc; obscured by overlappings; s, singlet; pse, pseudo-sextet, i.e. degenerated quartet of triplets, t, triplet.

[a] $^2J(^{119/117}Sn—H) = 165/158$ Hz.

H-7 appearing as doublets ($J = 8$ Hz) of doublets (1 Hz, *meta* coupling) at *ca* 9 and 9.5 ppm.

The CH_2 group linked to tin clearly appears as an AB system for compounds **19** and **24**. This is due to the fact that, for these two compounds, the carbon atom of the alkyl chain linked to the oxygen is an asymmetric carbon atom making the protons of each methylene group of these molecules pairwise diasteretopic. For compound **24**, four lines are clearly seen from which the chemical shifts of the A and B protons can be calculated (see Table 6c). For compound **19**, the two central lines of the AB pattern are not resolved. However, from the relative intensities of the side and central lines and from the chemical shift difference between the side lines, a value of 0.01 ppm could be calculated as the chemical shift difference between the unresolved central lines.

In vitro antitumour properties of compounds 11–14, 16 and 18–24

The ID_{50} values of compounds **11–14**, **16** and **18–24** tested against two human tumour cell lines, MCF-7 (mammary tumour) and WiDr (colon carcinoma) using an *in vitro* propidium iodide staining technique[14] are given in Table 7.

These data clearly show that the organotin compounds reported in Table 7 are less active *in vitro* than *cis*-platin, *cis*-$PtCl_2(NH_3)_2$, against the two tested tumours, in which they differ considerably from other diorganotin compounds which were found much more active than *cis*-platin[14, 15]

Table 7 ID_{50} values of compounds **11–14**, **16** and **18–24** tested against two human tumour cell lines, MCF-7 and WiDr

Compound no.	ID_{50} values (ng cm^{-3}) MCF-7	WiDr
11	20 000	20 000
12	14 600	16 300
13	20 000	12 700
14	>20 000	>20 000
16	1330	1040
18	1520	1260
19	1500	1200
20	2070	1090
21	1470	1040
22	1240	950
23	2520	1090
24	1940	980
cis-$PtCl_2(NH_3)_2$	850	624

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