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Organotin(IV) complexes with various donor ligands and their cytotoxicity against tumour cell lines. Part(I): R_2SnCl_2 with Schiff bases; unusual C=N bond cleavage of the bases and X-ray structures of the ionic products formed

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Several Schiff bases derived from salicylaldehyde and aminopyridines were found to coordinate with Me_2SnCl_2 in 1:1 or 1:2 (tin:base) molar ratio in diethylether, depending on the nature of the Schiff base used, to form complexes of the general formula $Me_2SnCl_2{\cdot}L$ or $Me_2SnCl_2{\cdot}2L$ respectively. These Schiff bases coordinate with Ph_2SnCl_2 in a similar manner, but if the reaction is carried out in chloroform or if the product formed in ether is dissolved in chloroform then colourless to pale yellow crystals precipitated. The latter were analysed and found to be due to the ionic compounds $[H_2NpyN{-}H^+]_2\ [Ph_2SnCl_4]^{2-}$ which were formed as a result of an unusual cleavage of the C=N bond of the Schiff bases. The Schiff bases, their Me_2SnCl_2 complexes and the ionic compounds were analyzed physicochemically and spectroscopically. The crystal structures of two of the ionic compounds showed that the cation $[H_2NpyN{-}H^+]$ binds with the anion $[Ph_2SnCl_4]^{2-}$ via hydrogen bonds. The Schiff bases, their Me_2SnCl_2 complexes and the ionic compounds were screened against the three tumour cell lines, L_{929}, K_{562} and HeLa, and the results were compared with those of the anticancer drugs, cisplatin, carboplatin and oxaliplatin. Copyright © 2003 John Wiley & Sons, Ltd.

KEYWORDS: Organotin(IV); Schiff bases; complexes; ionic products; X-ray structures; cytotoxicity

INTRODUCTION

Free Schiff-bases of *N*-hydroxy-*N*′-aminoguanidines have been found to act as antiviral, antibacterial and anticancer agents.[1] They have been found to coordinate with diorganotin(IV) dichloride in a chelate fashion to give complexes with hexa-coordinate tin.[2] Organotin(IV) complexes of several donor ligands, including biologically active ligands, have been covered by at least two review articles.[3,4] In our previous communication, we described our findings on diorganotin(IV) complexes of some Schiff-bases and their antibacterial activity.[5] Very recently, we reported full data of the diorganotin(IV) complexes of some Schiff bases (i.e. $R_2SnCl_2{\cdot}L$, where R = Me, Bu, Ph and L = Schiff base derivatives) and their lymphocyte proliferation activity.[6] Several articles have also been reported on the chemistry and X-ray structures of ionic compounds containing the diphenyl tetrachlorostannate anion, i.e. $[Ph_2SnCl_4]^{2-}$. They have the general formula $[LH^+]_2[Ph_2SnCl_4]^{2-}$, where L = *N*-(4-hydroxybenzalidene)-*p*-methoxyaniline,[7] 6-methylpyridine-2-carboxaldehyde phenylhydrazone,[8] 8-methoxyquinoline,[9] 8-methylaminoquinoline[10] and thiamine.[11] The present work describes the reaction of Me_2SnCl_2 and Ph_2SnCl_2, in various

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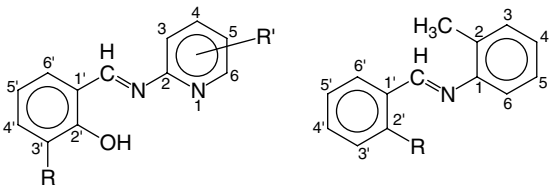
molar ratios, with some Schiff bases (Fig. 1) in diethylether or chloroform. It also describes the formation of the ionic compounds $[H_2Npy(R)N{-}H^+]_2[Ph_2SnCl_4]^{2-}$, where R = H, (2-aminopyridine); 3-Me, (2-amino-3-methylpyridine) and 4-Me, (2-amino-4-methylpyridine) formed from the unusual cleavage of C=N bonds of the Schiff bases (containing a pyridine nucleus) upon their reactions with Ph_2SnCl_2 only (Fig. 2). Further, the work describes the X-ray crystal structures of both ionic compounds (R = 3-Me and 4-Me). It also describes the biological evaluation of the Schiff bases, their Me_2SnCl_2 complexes and the ionic products against some tumour cells.

EXPERIMENTAL

General

^1H, ^{13}C and ^{119}Sn NMR spectra, mass spectra and CHN elemental analyses were performed at Anorganische Chemie Institute, Martin-Luther-Universität, Halle Wittenberg, Germany. IR spectra were recorded on a Nicolet (Impact 400) FTIR spectrometer in the range 4000–400 cm^{-1} using KBr discs.



L1, R=R'=H
L2, R=H, R'=3-CH_3
L3, R=H, R'=4-CH_3
L4, R=OCH_3, R'=H
L5, R=OCH_3, R'=3-CH_3

L6, R=H
L7, R=OH

Figure 1. The Schiff bases used in this study.

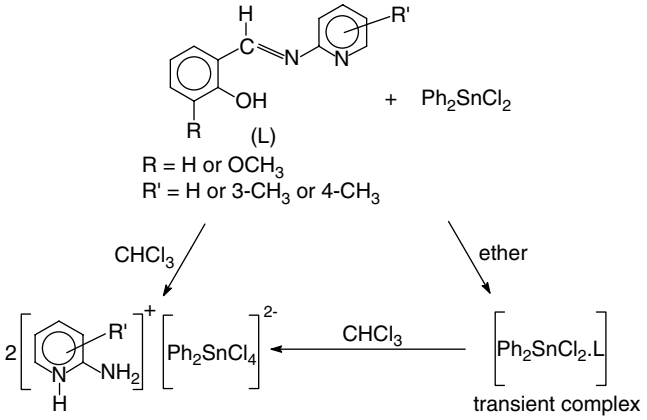


Figure 2. Reaction routes leading to the formation of the ionic compounds.

Starting materials

The diorganotin dichloride compounds, Me_2SnCl_2 and Ph_2SnCl_2, were commercial products (Fluka and Merck) and were crystallized from *n*-hexane or diethylether before use. The Schiff bases (Fig. 1) were prepared as described elsewhere.[12]

Preparation of $Me_2SnCl_2{\cdot}L$ or $Me_2SnCl_2{\cdot}2L$ complexes (1–5)

The compound Me_2SnCl_2 (0.22 g, 1 mmol) was dissolved in diethylether (10 ml), and a solution of an excess of Schiff base in diethylether was added. An immediate precipitate of the product was observed. This was filtered off, washed several times with diethylether to remove the excess Schiff base and dried in vacuum for several hours. The Schiff bases L1, L2 and L3 formed 1:2 complexes, i.e. $Me_2SnCl_2{\cdot}2L$, and L4 and L5 formed 1:1 complexes, i.e. $Me_2SnCl_2{\cdot}L$.

$[H_2Npynh]_2[Ph_2SnCl_4]$ compounds (6–8)

The compound Ph_2SnCl_2 (0.344 g, 0.1 mmol) was dissolved in chloroform, and a solution of an equimolar quantity, or even excess, of the Schiff bases (L1–L5) was added. The mixture was stirred for a few minutes. The transparent coloured solution was reduced in volume and diethylether was added to the point of turbidity. Upon leaving the mixture aside, colourless to pale yellow crystals deposited. The crystals were collected by filtration, washed with a small amount of chloroform, diethylether and dried in vacuum for several hours.

Crystal structure determinations

Diffraction data for both compounds were collected using a Bruker APEX diffractometer[13,14] with the sample at 100 K. Empirical absorption corrections were applied to the data.[15] The structures were refined on F^2. Details of the structures are given in Table 1. The dianions of both compounds sit on crystallographic centres of symmetry. The asymmetric unit of compound **7** was found to contain two cations and two half dianions. The asymmetric unit of compound **8** was found to contain one cation and one half dianion. The programs used include SMART, SAINT, SADABS, and SHELXTL.

Biological methods and tumour cell lines

The human myleogenous leukaemia cell lines K_{562}, Cervix cell lines (HeLa) and murine L_{929} fibrosarcoma were used in this study. Approximately 3×10^6 cells of each of these cell lines were plated in plastic culture flasks in RPMI 1640 medium supplemented with 10% foetal calf serum (Gibco/BRL, Grand Island, NY) and incubated at 37 °C in an atmosphere of 5% CO_2 and 95% air. The Schiff bases (L1–L5), their Me_2SnCl_2 complexes (**1**–**5**) and the ionic compounds (**6**–**8**) were dissolved in 10% dimethylsulphoxide (DMSO)

Table 1. Crystal data for compounds **7** and **8**

	Compound **7**	Compound **8**
Molecular formula	$C_{24}H_{28}Cl_4N_4Sn$	$C_{24}H_{28}Cl_4N_4Sn$
Molecular weight	632.99	632.99
Crystal system	Triclinic	Monoclinic
Space group	$P\bar{1}$	$P2_1/n$
Cell parameters (Å, °)	$a = 8.3766(3)$, $\alpha = 87.021(2)$ $b = 11.5768(4)$, $\beta = 83.787(2)$ $c = 13.4167(4)$, $\gamma = 85.174(2)$	$a = 10.9602(4)$ $b = 8.6129(3)$, $\beta = 93.743(2)$ $c = 13.7976(5)$
Volume (Å^3)	1287.64(7)	1299.70(8)
Z	2	2
Unique data, R_{int}	7477, 0.0137	3904, 0.0184
θ_{max} (°)	30.51	30.52
R (obsd data)	0.022	0.022
wR (all data)	0.0593	0.0571
S	1.00	1.08
Obsd data, $I > 2\sigma(I)$	7089	3599
ρ_{max} e$^-$ Å^{-3}	0.71	0.82
CCDC no.	203033	203034

and further diluted in the medium. The three reference standards of cisplatin, carboplatin and oxaliplatin were used for comparison. For determination of relative growth inhibition, the compounds and the reference standards were added to cells in the logarithmic phase of growth. Cytotoxicity tests were conducted in quadruplicate. Cells were exposed to the compounds and the drugs (reference standards) for 72 h prior to addition of MTT, a vital dye, according to the method of Mossmann.[16] The resulting products were dissolved in DMSO and the absorbance of the samples was read at 570 mm on a microplate reader.

RESULTS AND DISCUSSION

In a previous article, we reported the synthesis of 1:1 (tin compound : Schiff-base) molar ratio complexes, i.e. R_2SnCl_2·L, where R = Me, Bu, Ph and L = Schiff base derivatives, in diethylether.[2] In the present work we found that the tin compound Me_2SnCl_2 reacted with Schiff bases (Fig. 1) either in 1:1 or 1:2 (tin compound : Schiff base) ratio, depending on the nature of the Schiff base used. The Schiff bases L1–L3 formed complexes of the type Me_2SnCl_2·2L (**1–3**) with Me_2SnCl_2, whereas the Schiff bases L4 and L5 formed complexes of the type Me_2SnCl_2·L (**4** and **5**). This is clear from the CHN elemental analyses and the ^{1}H NMR spectral data of the complexes. The physical properties of the Me_2SnCl_2·Schiff-base complexes are listed in Table 2 and the ^{1}H and ^{13}C NMR spectral data of the Schiff bases and their Me_2SnCl_2 complexes are listed in Tables 3 and 4.

IR and NMR studies

The IR spectral data of the products clearly revealed that complexation of Me_2SnCl_2 with the Schiff bases had taken place as shown by the change in the ν(C═N)$_{im}$ and ν(C═N)$_{Py}$ values. Since the Schiff bases L1–L5 used in this study (Fig. 1) contained two different aromatic nuclei, i.e. the pyridyl and the aryl moieties, the COSY H–H and H–C NMR couplings of these Schiff bases were examined. The ^{1}H and ^{13}C NMR spectral data of the Schiff bases were assigned and are listed in Tables 3 and 4, together with those of their Me_2SnCl_2 complexes. For Me_2SnCl_2·Schiff-base complexes (**1–5**), the ratio of the integrals of the signals from methyl and the N═CH protons of the Schiff bases to those from the protons of the methyl groups on tin provides, in addition to elemental analysis, a reliable measure of the number of coordinated Schiff bases. From Tables 3 and 4, no remarkable differences between the chemical shifts of the protons and carbon atoms of the free Schiff bases were observed on going to their Me_2SnCl_2 complexes. On the other hand, both

Table 2. Physical properties of Me_2SnCl_2·Schiff-base complexes and the ionic compounds

			Analysis (%) Found (Calc.)			Selected IR bands (cm^{-1})[b]	
Compound[a]	M.p. (°C)	Formula	C	H	N	ν(C═N)$_{im}$ (Δ)	ν(C═N)$_{Py}$ (Δ)
1 Me_2SnCl_2·2L1	132–135	$C_{26}H_{26}N_4O_2Cl_2Sn$	50.4 (50.7)	4.4 (4.2)	9.1 (9.1)	1629 s (6)	1567 m (−2)
2 Me_2SnCl_2·2L2	71–74	$C_{28}H_{30}N_4O_2Cl_2Sn$	52.6 (52.2)	5.0 (4.7)	8.9 (8.7)	1615 s,sh (−5)	1555 s (−23)
3 Me_2SnCl_2·2L3	98–102	$C_{28}H_{30}N_4O_2Cl_2Sn$	52.3 (52.2)	4.8 (4.7)	8.6 (8.7)	1631 s,sh (41)	1536 m (−14)
4 Me_2SnCl_2·L4	99–100	$C_{15}H_{18}N_2O_2Cl_2Sn$	40.3 (40.2)	4.3 (4.0)	6.3 (6.3)	1630 s,sh (11)	1560 m (−15)
5 Me_2SnCl_2·L5	83–86	$C_{16}H_{20}N_2O_2Cl_2Sn$	41.7 (41.6)	4.6 (4.3)	6.1 (6.1)	1650 s,sh (30)	1570 m (−10)
6 $[H_2NpyNH]_2[Ph_2SnCl_4]$[c]	146–150	$C_{22}H_{26}N_4Cl_4Sn$	44.0 (43.7)	3.9 (4.0)	8.9 (9.3)	—	1662 s
7 $[H_2Npy(3\text{-}Me)NH]_2[Ph_2SnCl_4]$[c]	156–160	$C_{24}H_{28}N_4Cl_4Sn$	45.1 (45.5)	4.4 (4.4)	8.7 (8.9)	—	1649 s
8 $[H_2Npy(4\text{-}Me)NH]_2[Ph_2SnCl_4]$[c]	150–156	$C_{24}H_{28}N_4Cl_4Sn$	45.5 (45.5)	4.5 (4.4)	8.6 (8.9)	–	1654 s

[a] Free Schiff bases L1–L7 have molecular weights of 198, 212, 212, 228, 242, 195 and 211 respectively (from mass spectra). Complexes **1–5** are yellow to orange and compounds **6–8** are colourless to pale yellow.
[b] For IR bands: s, strong; m, medium and sh, shoulder. $\nu(\Delta) = \nu_{complex} - \nu_{Schiff\ base}$
[c] Compounds **6**, **7** and **8** are with the cations 2-aminopyridinium, 2-amino-3-methylpyridinium and 2-amino-4-methylpyridinium respectively. Their other IR bands are: ν(NH), 3590; ν(NH$_2$), 3400 and 3300 cm^{-1}.

Table 3. ^{1}H and ^{119}Sn NMR data (δ[a] ppm and J Hz) of Schiff bases and their Me_2SnCl_2 complexes

Compound	$\delta^{119}Sn$	δ(Me–Sn)/ $^{2}J(^{119}Sn–CH)$	δ(HC=N)	δ(OH)	δ(Me/OMe)	δ(Ph/Py)[c]
L1			9.4 s	13.4 s	_	6.9–8.5 m
1	—[b]	1.25/72.2	9.4 s	13.5 s	_	6.9–8.5 m
L2			9.4 s	13.7 s	2.4 s	6.9–8.3 m
2	96.6	1.25/71.0	9.4 s	13.7 s	2.4 s	6.9–8.3 m
L3			9.4 s	13.5 s	2.4 s	6.9–8.4 m
3	37.5	1.25/77.0	9.3 s	13.5 s	2.4 s	6.9–8.4 m
L4			9.5 s	14.2 s	3.9 s	6.9–8.5 m
4	−33.7	1.25/75.3	9.4 s	14.3 s	3.9 s	6.7–8.5 m
L5			9.5 s	14.2 s	2.5 s/4.0 s	6.9–8.4 m
5	66.2	1.25/73.4	9.4 s	14.4 s	2.5 s/4.0 s	6.8–8.3 m
6[d]	−212.6					6.6–8.8 m
7[d]	−212.8				2.2 s	6.7–7.8 m
8[d]	−212.8				2.3 s	6.5–7.9 m
L6			8.5 s	—	2.6 s	7.1–8.0 sm
L7			8.6 s	13.5 s	2.4 s	7.0–7.4 sm

[a] Downfield from internal tetramethylsilane (TMS) using $CDCl_3$ as solvent.
[b] Not recorded.
[c] Assignments are for total protons of the phenyl and pyridine nuclei due to a very close chemical shift of each independent proton to the other.
[d] The assignments of both NH and NH_2 appeared as broad signals and centred at *ca* 6.5 ppm and 5.5 ppm respectively.

Table 4. ^{13}C NMR data,[a] δ (ppm) and J (Hz) of free Schiff bases and complexes **1**–**5**[b]

Compound	$\delta(CH_3)$/ $J(^{119}Sn–^{13}C)$	δ(C1)	δ(C2)	δ(C3)	δ(C4)	δ(C5)	δ(C6)	δ(C1′)	δ(C2′)	δ(C3′)	δ(C4′)	δ(C5′)	δ(C6′)	δ(CH)	δ(*R*)	δ(R′)
L1			157.5	120.3	138.3	122.4	148.8	118.9	161.8	119.1	133.4	133.7	117.2	164.6	—	—
1	8.2[c]		156.9	120.1	138.4	122.5	148.8	118.7	162.4	119.0	133.5	134.1	117.4	164.3	—	—
L2			155.8	128.5	139.4	122.6	146.3	119.2	162.0	119.1	133.4	133.7	117.2	163.9	—	17.6
2	7.6[c]		155.5	128.3	139.3	122.5	146.1	119.1	162.0	119.0	133.3	133.7	117.1	163.7	—	17.7
L3			157.4	123.4	149.6	121.0	148.4	116.9	161.8	117.0	133.2	133.5	117.1	164.4	—	20.7
3	9.5[c]		157.4	124.2	150.6	121.2	149.0	118.1	163.5	119.3	134.2	134.9	119.5	164.7	—	21.6
L4			157.3	118.8	138.8	122.8	149.1	120.8	152.8	148.6	123.0	125.0	115.3	164.8	56.3	—
4	13.0/660.5		161.4	117.8	139.7	118.6	149.5	116.9	152.2	150.3	123.9	126.7	117.3	161.6	56.3	—
L5			155.3	128.9	140.0	119.0	146.3	118.3	153.3	148.8	122.9	124.8	115.0	163.4	56.1	17.8
5	8.6[c]		155.5	128.6	140.2	118.7	146.8	119.0	154.7	149.3	123.3	125.6	115.8	163.5	56.6	18.1
L6		150.9	131.7	117.5	125.5	126.6	131.0	136.0	130.1	128.5	128.7	128.5	130.1	159.1	—	17.7
L7		147.2	132.1	117.5	126.6	126.8	132.8	119.1	161.0	118.8	130.5	132.0	117.0	161.9	—	18.2

[a] Downfield from internal TMS, using $CDCl_3$ as solvent. For atoms numbering see Fig. 1.
[b] The ionic compounds **6**, **7** and **8** are not soluble enough in $CDCl_3$ in order to obtain ^{13}C NMR spectra.
[c] Tin satellites obscured by noise.

the chemical shift (δ ppm) and the $^{119}Sn–CH$ and $^{119}Sn–^{13}C$ coupling constants (J Hz) for the Me_2SnCl_2 compound were noticeably affected on donor coordination, particularly the J value, which goes to a higher value upon coordination. Thus, the $^{2}J(^{119}Sn–CH)$ coupling constants of Me_2SnCl_2·Schiff-base complexes (**1**–**5**) were observed between 71 and 77 Hz in $CDCl_3$, the $^{2}J(^{119}Sn–CH)$ of the free Me_2SnCl_2 is 70 Hz, which is confidently assigned to a complex formation. Further, clear observation of complex formation comes from the ^{13}C NMR data; the $\delta^{13}C$ and $J(^{119}Sn–^{13}C)$ values of Me_2SnCl_2 are 6.7 ppm and 481 Hz respectively in $CDCl_3$,[17,18] and these values increased drastically to 13 ppm and 660 Hz respectively upon coordination with the Schiff base, e.g. with L4 to form the complex Me_2SnCl_2·L4 (**4**; Table 4).

The ^{119}Sn NMR data of Me_2SnCl_2·Schiff-base complexes were also recorded and the data are listed in Table 3. The

chemical shifts of the complexes vary from −33.7 to 96.6 Hz. The δ ^{119}Sn for the free Me_2SnCl_2 was reported to be 141.2 Hz (in CCl_4).[19,20]

The matter is different with Ph_2SnCl_2 in its reaction with the Schiff bases L1–L5, in which the reaction takes a different course. When the reaction was carried out in diethylether, the product thus formed, i.e. Ph_2SnCl_2·Schiff base, can be isolated and treated as for Me_2SnCl_2·Schiff-base complexes.[2] If the product Ph_2SnCl_2·Schiff base, however, is dissolved in chloroform or the reaction between Ph_2SnCl_2 and the Schiff bases is carried out in chloroform from the start, colourless to pale yellow crystals deposited. The analyses of these crystals, including the X-ray diffraction (*vide infra*), showed that they are ionic compounds of the type $[H_2NpyN{-}H^+]_2[Ph_2SnCl_4]^{2-}$ (Fig. 2). All the ligands L1–L4 with Ph_2SnCl_2 gave the same ionic compound as a result of C═N cleavage of the Schiff bases. Ligands L1 and L4 shared the same cation, i.e. 2-aminopyridinium, ligands L2 and L5 shared the same cation, i.e. 2-amino-3-methylpyridinium, and ligand L3 gave the cation 2-amino-4-methylpyridinium. The physical properties of the three compounds **6**–**8** are listed in Table 2.

The IR spectral data of the ionic compounds showed absorption bands at *ca* 3590 cm^{-1} as strong and sharp bands, probably due to ν(N–H) of the pyridinium ion; bands at *ca* 3350 and 3300 cm^{-1} are due to $\nu(NH_2)$ and a strong and sharp shoulder band at *ca* 1650 cm^{-1} is probably due to ν(C═N) of the pyridinium ion. The ^{1}H and ^{13}C NMR of the ionic compounds showed signals due to the pyridinium ion as well as due to the Ph_2SnCl_4 anion (Table 3), but, owing to their low solubility in $CDCl_3$, no proper ^{13}C NMR spectrum could be obtained. The ^{119}Sn NMR spectra of the three ionic compounds almost certainly shared one signal, appearing at a chemical shift of *ca*-212 ppm.

In an attempt to check whether there is any role for the pyridine site of the Schiff bases L1–L5 on formation of the ionic compounds, we prepared two more Schiff bases without pyridine, i.e. L6 and L7 (Fig. 1), and had them analysed. Upon treating both Schiff bases L6 and L7 with Ph_2SnCl_2 in 1:1 or 1:2 (tin:Schiff base) molar ratio in diethylether or chloroform, a coloured complex of Ph_2SnCl_2·Schiff base was formed. The latter, however, when analysed, did not give the ionic compound formed through C═N bond cleavage. This means that the pyridine site of the Schiff base is necessary in order for the C═N bond to be cleaved. Also, the presence of chloroform as a source of chlorine is crucial for the ionic compounds to be formed.

For the mechanism of the ionic compounds formation, we believed at first that it might be possible that some hydrogen chloride was present in the chloroform used, and this in turn was involved in the C═N bond cleavage. Therefore, we treated chloroform with sodium carbonate for a few days to remove any hydrogen chloride from the solvent. Again, the reaction of Ph_2SnCl_2 with the Schiff bases L1–L5 gave the ionic compounds when the reactions are carried out in chloroform or when the reactions are carried out in diethylether and the products dissolved in chloroform. Further studies on the mechanisms of formation of the ionic compounds are in progress in our laboratories.

Crystal structure of compounds 7 and 8

Compounds **7** and **8** crystallized as well-shaped colourless crystals. The molecular structures of both compounds are shown in Figures 3 and 4. Selected bond lengths and angles are listed in Tables 5 and 6. For both compounds **7** and **8**, the crystallographic asymmetric unit contains one cation and one half of one dianion. The dianion sits on a crystallographic centre of symmetry. The geometry around the tin in both compounds is octahedral, as expected for $(Ph_2SnCl_4)^{2-}$. The four chlorine atoms occupy the square planar corners with the two axial phenyl groups in trans relationship to each other. The bond lengths between tin and the chlorine atoms in both compounds are very similar (Table 5). Lengths and angles between atoms in the pyridinium ion of both compounds (Table 5) are similar to within statistical error.

Hydrogen bonding between the hydrogen atoms of the pyridinium ion and the amino group with chlorine atoms of the dianion Ph_2SnCl_4 are described in Table 6. With few exceptions, the hydrogen bond lengths in both compounds **7** and **8** are almost similar. The larger hydrogen bond angle of N(7D)–H(7DA)···Cl(2B) is shown in compound **7** and 166°.

Additional material (available from the Cambridge Crystallographic Data Centre) includes thermal parameters,

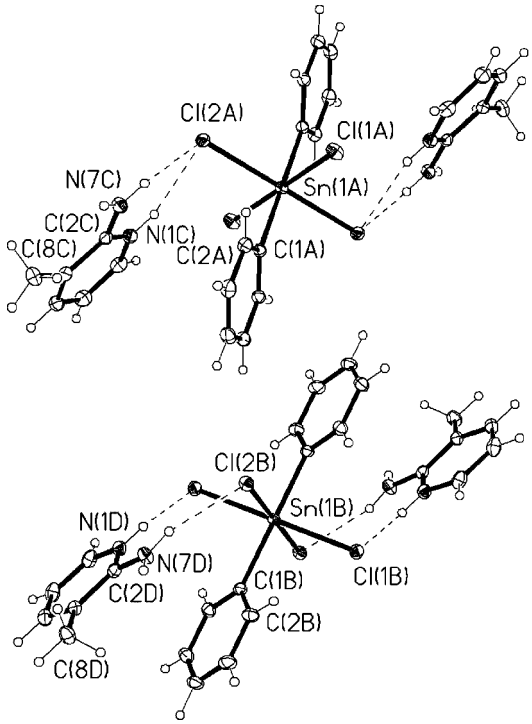


Figure 3. Structure of $[H_2Npy(3\text{-}Me)NH]_2[Ph_2SnCl_4]$ (**7**) with atomic numbering scheme. The displacement ellipsoids are drawn at the 50% probability level.

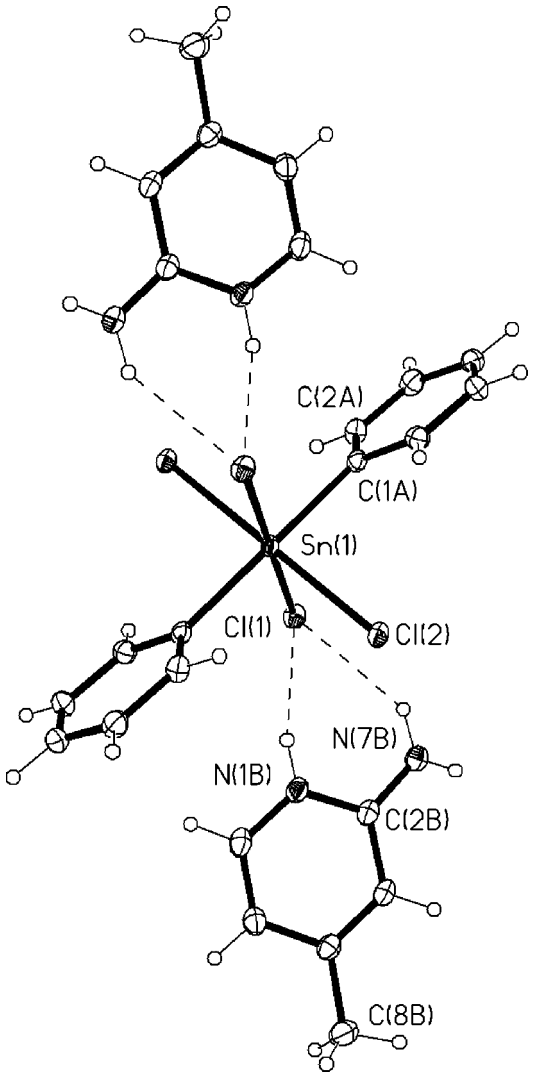


Figure 4. Structure of $[H_2Npy(4\text{-}Me)NH]_2[Ph_2SnCl_4]$ (**8**) with atomic numbering scheme. The displacement ellipsoids are drawn at the 50% probability level.

the remaining atomic coordinates, and the remaining bond lengths and angles of both compounds as supplementary publications CCDC-203 033 (**7**) and CCDC-203 034 (**8**). Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: +44-1223-336 033; e-mail: deposit@ccdc.cam.ac.uk).

Cytotoxicity evaluation

The free Schiff bases (L1–L5), their Me_2SnCl_2 complexes (**1**–**5**) and the ionic compounds (**6**–**8**) were examined for their cytotoxic activity against the three tumour cell lines L_{929}, K_{562} and HeLa and the results are summarized in Table 7, together with those of the reference standards (the known anti-cancer drugs, cisplatin, carboplatin and oxaliplatin) for comparison.

It is clear from Table 7 that the free Schiff bases (L1–L5) and their Me_2SnCl_2 complexes (**1**–**5**) have no cytotoxic activity against any of the three tumour cell lines used (their IC_{50} values ranged between 32 and >50 μg ml^{-1} and between 17 and >50 μg ml^{-1} respectively). The most cytotoxically active compounds among all the compounds studied were the ionic compounds (**6**–**8**), whose IC_{50} values ranged between 0.2 and 4.7 μg ml^{-1}. The cytotoxicity results of the ionic compounds are much better than those of the reference standards, cisplatin (IC_{50} ranged between 2.8 and 28.3 μg ml^{-1}) and carboplatin (IC_{50} ranged between 12.2 and >50 μg ml^{-1}) and even better than that of oxaliplatin against the HeLa cell line (IC_{50} = 33.2 μg ml^{-1}). Further, the IC_{50} values of the ionic compounds **6**–**8** against the K_{562} cell line, i.e. 0.2–0.3 μg ml^{-1}, are very similar to that of oxaliplatin (IC_{50} = 0.3 μg ml^{-1}) against the same cell line.

Table 5. Selected bond distances (Å) and bond angles (°) with ESDS in parentheses for compounds **7** and **8**[a]

	Compound **7**	Compound **7**	Compound **8**
Dianion on $\overline{1}$	(A)	(B)	
Sn–Cl(1)	2.5762(3)	2.5757(3)	2.5761(3)
Sn–Cl(2)	2.6025(3)	2.5934(3)	2.5696(3)
Sn–C(1)	2.1404(13)	2.1400(13)	2.1486(13)
Cl(1)–Sn–Cl(2)	91.438(11)	91.225(11)	88.286(10)
Cl(1)–Sn–C(1)	91.24(4)	89.56(4)	90.31(3)
Cl(2)–Sn–C(1)	89.11(4)	90.52(4)	90.43(3)
Cation	(C)	(D)	(B)
N(1)–C(2)	1.3501(18)	1.3452(18)	1.3538(17)
N(1)–C(6)	1.3598(19)	1.3452(18)	1.3615(19)
C(2)–N(7)	1.3447(18)	1.3404(18)	1.3315(18)
C(2)–N(1)–C(6)	123.55(13)	123.62(13)	122.72(13)
N(1)–C(2)–N(7)	118.14(12)	118.97(13)	118.36(13)
N(1)–C(2)–C(3)	118.60(13)	118.63(13)	123.53(12)

[a] Labels (A), (B), (C) and (D) indicate bonded ionic groups.

Table 6. Hydrogen bonds (Å) for the ionic compounds **7** and **8**

D–H···A	D–H	H···A	D···A	D–H···A
Compound **7**				
N(1C)–H(1C)···Cl(2A)	0.88	2.43	3.2568(13)	157
N(7C)–H(7CA)···Cl(2A)	0.88	2.56	3.3501(13)	150
N(7C)–H(7CB)···Cl(1A)[a]	0.88	2.62	3.3450(13)	140
N(1D)–H(1D)···Cl(1B)[b]	0.88	2.34	3.1131(12)	147
N(7D)–H(7DA)···Cl(2B)	0.88	2.41	3.2690(12)	166
N(7D)–H(7DB)···Cl(2B)[c]	0.88	2.58	3.3311(13)	144
Compound **8**				
N(1B)–H(1B)···Cl(1)	0.88	2.57	3.3168(13)	144
N(7B)–H(7A)···Cl(1)	0.90	2.58	3.3359(13)	142
N(7B)–H(7B)···Cl(2)[d]	0.81	2.56	3.3214(12)	155

Symmetry transformation used to generate equivalent atoms: [a] $1-x, -y, -z$; [b] $-x, 1-y, 1-z$; [c] $1-x, 1-y, 1-z$; [d] $3/2-x, 1/2+y, 3/2-z$.

Table 7. Cytotoxic activity of Schiff bases, their Me_2SnCl_2 complexes and ionic compounds against tumour cell lines

Compound	IC_{50} (μg ml^{-1})		
	L_{929}	K_{562}	HeLa
L1	>50	>50	41.0
L2	>50	>50	40.7
L3	>50	>50	41.7
L4	34.9	34.5	32.3
L5	>50	>50	40.7
1	>50	22.7	42.3
2	42.2	18.4	37.0
3	>50	22.4	38.8
4	34.0	17.1	32.5
5	33.3	17.8	34.7
6	0.6	0.2	4.7
7	0.6	0.2	3.7
8	1.0	0.3	4.3
Cisplatin	2.8	4.9	28.3
Carboplatin	>50	12.2	38.7
Oxaliplatin	0.3	0.3	33.2

In conclusion, the present results exhibited by the ionic compounds **6**–**8** against the three cell lines used in the present study are very promising when compared with those of the reference standards. However, it is premature to comment on these preliminary results, as further studies using more cell lines are required to confirm the activity of these ionic compounds.

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