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Synthesis, structures, ^{119}Sn Mössbauer spectroscopic studies and biological activity of some tin(IV) complexes containing pyridyl functionalised selenosemicarbazonato ligands

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ABSTRACT

A series of tin(IV) complexes of the type [Sn(L)ClR$_2$] (R: ^{n}Bu, Me, Cl; L: anionic *N,N,S* or *N,N,Se* donor ligand) containing pyridyl functionalised thio- and selenosemicarbazonates was prepared and fully characterised by spectroscopic methods including ^{119}Sn and ^{77}Se NMR spectroscopy as well as ^{119}Sn Mössbauer spectroscopy. In addition, the solid-state structures of several derivatives were determined by single crystal X-ray diffraction. The *in vitro* cytotoxicity of these compounds was evaluated in three different human tumour cell lines. The IC$_{50}$ values are in the low nM range, the most active compound being a trichlorotin(IV) complex with a selenosemicarbazonato ligand.

1. Introduction

Pyridyl functionalised thiosemicarbazones derived from the condensation of 2-pyridine carboxaldehyde with a thiosemicarbazide have been known for many years. These compounds typically coordinate to a metal centre as monoanionic, tridentate [*N,N,S*]$^-$ ligands. Several reviews summarise the known coordination chemistry with both transition and main group metals of these compounds [1–6]. Interest in this class of compounds has been in part due to their biological activity. In particular, tin(IV) compounds containing thiosemicarbazonato ligands have been investigated for their activity against leukaemia [7–9], as well as their antifungal [10–15] and antibacterial [15] activity. While the anti-tumour activity of organotin compounds has long been recognised [16–20], recent work has also focused on thiosemicarbazonato complexes of tin [10,21]. Such complexes have also been studied by X-ray crystallography, ^{119}Sn Mössbauer spectroscopy and ^{119}Sn NMR spectroscopy [21–28].

Work on the analogous selenium derivates, the selenosemicarbazones, although known for many years has been rather neglected. The organoselenium compounds themselves and some of their metal complexes were investigated for their anti-malaria activity [29–31], however, the coordination chemistry of these [*N,N,Se*]$^-$ ligands is restricted to some older Russian work mainly with Cu and Ni complexes, as well as more recent papers including work from our group [32–49]. Given that there are no reports of tin(IV) complexes containing selenosemicarbazonates combined with the fact that the sulfur counterparts show considerable biological activity, we embarked on an investigation of some tin(IV) compounds containing pyridyl substituted selenosemicarbazonates, the results of which are presented herein.

2. Results and discussion

The thio- and seleno-semicarbazonato tin(IV) complexes **1**–**6** were prepared by reacting the appropriate tin(IV) chlorides with the chalcogenosemicarbazones (**HSe1**, **HSe2** and **HS2**) in the presence of a base. The compounds were obtained as air- and moisture-stable yellow solids in good yields (Scheme 1).

The new complexes were fully characterised by NMR spectroscopy including ^{77}Se and ^{119}Sn as well as ^{119}Sn-Mössbauer spectroscopy. In all cases, the deprotonation of the

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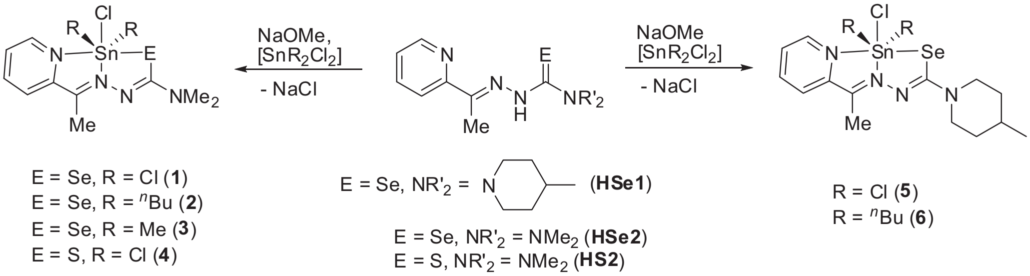

Scheme 1. Synthesis of tin complexes with thio- and selenosemicarbazones.

chalcogenosemicarbazones was apparent from the absence of the signal due to the N–H group in the ^{1}H NMR spectra. Upon coordination to the metal, a significant shift of the ^{13}C NMR signal corresponding to the carbon atom bound to the chalcogen is observed. This can be explained by the change of bond order of the CE unit which changes from a partial double bond in the free ligand to a single bond in the metal complex. The methyl groups bound to the tin atom display the expected tin satellites due to the ^{119}Sn and ^{117}Sn isotopes in the ^{1}H and ^{13}C NMR spectra of complex **3**, with typical coupling constants $J_{\mathrm{H-Sn}}$ and $J_{\mathrm{C-Sn}}$ of *ca.* 90 and 800 Hz, respectively. The spectral pattern of the butyl chains in complexes **2** and **6** are similar to those observed in structurally related butyl tin thiosemicarbazonato complexes [11,21]. Chemical shift data for the ^{119}Sn and ^{77}Se NMR spectra of complexes **1**–**6** are shown in Table 1. The ^{119}Sn NMR resonances of the trichlorotin derivatives (complexes **1**, **4** and **5**) are located at −474 and at *ca.* −560 ppm for the sulfur and selenium compounds, respectively. The difference between the chemical shifts of the S and Se compounds can be explained by the stronger shielding effect of the selenium atom. In the ^{119}Sn or ^{77}Se NMR spectra satellites due to $^1J_{119\mathrm{Sn}-77\mathrm{Se}}$ coupling were sometimes observed. The values of these coupling constants (1044 and 1370 Hz for the dibutyl and trichlorido complexes **2** and **5**, respectively) are consistent with the presence of electronically different ligands at the tin centre. Previously reported values for $^1J_{\mathrm{Sn-Se}}$ coupling in phenylselenido tin(IV) complexes are of similar magnitude [50]. The singlet resonances in the ^{77}Se NMR spectra of the selenium compounds cover a quite wide range (192 to −49 ppm). The data are consistent in that the trichlorotin species show the highest ^{77}Se NMR chemical shifts, while the dibutyltin species show the lowest. Moreover there is a good correlation between NMR and Mössbauer data for all of these compounds.

The proposed structures were confirmed by single crystal X-ray diffraction studies of complexes **1**, **2**, **4** and **5**. The molecular structures are shown in Figs. 1–4; important bond lengths and angles are collected in Table 2.

These complexes represent the first examples of tin(IV) compounds containing organoselenium compounds as ligands. The basic structural unit for all four complexes consists of the deprotonated thio- or selenosemicarbazonato ligand bound to the tin atom through the pyridyl nitrogen atom, the imine nitrogen atom and the chalcogen atom. The distorted octahedral coordination environment about the tin is completed by the chlorido and butyl ligands. In the case of the chlorodibutyl derivative **2**, the two butyl chains are located on one axis. The chlorido ligand occupies the position perpendicular to them, coplanar to the chalcogenosemicarbazonato ligand which is almost planar as can be seen from the torsion angles (Table 2). Compared to the free ligands [51], the C-E distances in the complexes increase only slightly (by 0.02–0.04 Å) while those of the ligand backbone i.e. the (E)C–N(N) and N–N bond lengths do not change significantly. This indicates that the delocalization remains more or less the same upon coordination. The angle about the chalcogen atom is close to 90° in both the sulfur and selenium derivatives. The Sn-chalcogen bond lengths are, as expected, slightly longer in the selenium compounds due to the larger size of Se compared to S. The other bond lengths and angles are also unexceptional and similar to those found in structurally related tin(IV) complexes containing [*S,N,N*]$^-$-tridentate pyridyl substituted thiosemicarbazonato ligands [8,11,21,22,24–26,28,52–55].

Table 1
^{119}Sn and ^{77}Se NMR data for tin complexes **1**–**6**.[a]

Complex	^{119}Sn	^{77}Se	$^1J_{119\mathrm{Sn}-77\mathrm{Se}}$[c]
1	−557[b]	192[b]	–
2	−192	−43	1044
3	−208	−1	–
4	−474	–	–
5	−558	185	1370
6	−193	−49	–

[a] In CD$_2$Cl$_2$.
[b] In DMSO-d6.
[c] Where no data are given, the satellites were not observed.

2.1. ^{119}Sn Mössbauer spectroscopy

The ^{119}Sn Mössbauer spectra of compounds **1**, **2**, **4**, and **5** recorded at 78 K are presented in Fig. 5 together with transmission integral fits. The corresponding fitting parameters are listed in Table 3. The spectra could be well reproduced with single signals which were all subjected to electric quadrupole splitting as expected from the non-cubic site symmetry of the tin atoms. The isomer shifts and the quadrupole splitting parameters nicely reflect the local electronic situation of the tin atoms. Compounds **1**, **4**, and

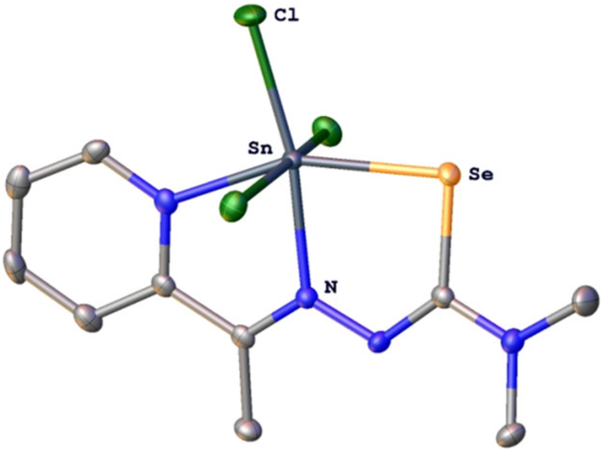

Fig. 1. Molecular structure of complex **1**. Displacement ellipsoids are drawn at a 50% probability level. Hydrogen atoms have been omitted for clarity.

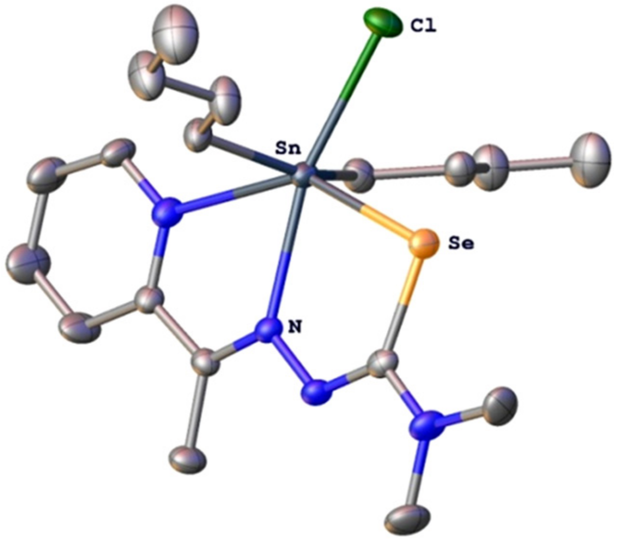

Fig. 2. Molecular structure of complex **2**. Displacement ellipsoids are drawn at a 50% probability level. Hydrogen atoms have been omitted for clarity.

5 have three strongly electronegative chlorido ligands. Among the four compounds we observe the lowest isomer shifts (around 0.6 mm/s) indicating the lowest electron density at the tin nuclei. In compound **2**, two of the three chlorido ligands are substituted by a butyl group, leading to a significant increase of the isomer shift (1.50 mm/s), and consequently also of the local electron density. The substitution of the chlorido ligands by butyl groups leads to a drastic decrease of the local symmetry and thus a strong increase of the quadrupole splitting parameter from only 0.29 mm/s in **5** to 3.33 mm/s in **2**. The course of the isomer shifts nicely scales with the systematics of ^{119}Sn isomer shifts in complex tin chalcogenides given by Lippens [56]. For all four compounds the isomer shifts fall in the range for tetravalent tin. It is also interesting to note that the isomer shift and quadrupole splitting parameters of the selenium compounds reported here are very similar to those reported for structurally analogous sulfur derivates [22,23,25].

2.2. Cytotoxicity studies

The *in vitro* cytotoxicity of complexes **1**, **3**, and **4** as well as that of the selenium ligand **HSe2** were evaluated in three human tumour cell lines. The IC_{50} data of these initial screening experiments are shown in Table 4.

The IC_{50} values of the tin complexes in all three cell lines are significantly lower in comparison to that of the free ligand, suggesting that their activity is due to the presence of the metal. It is also noteworthy, that the IC_{50} values of these compounds (nM range) are two orders of magnitude lower than those of cisplatin. Interestingly, the investigated compounds are more active against cisplatin resistant (DLD-1) than against cisplatin sensitive cell lines (A253 and A549). Structurally related tin(IV) compounds containing benzoylpyridine derived thiosemicarbazone ligands show *in vitro* cytotoxicity in the low nM range [10]. Comparison of the data for the two Se and S analogues (**1** and **4**) shows that the selenium compound seems to be more active than the sulfur complex. As far as we can judge from this initial data of a small set of compounds, we can conclude that the substituents at the metal however, appear to have only a minor influence on the activity of the complexes. Replacement of two chlorido ligands by two methyl groups slightly reduces the activity of the compound in all three cell lines examined, the most active compound being the trichloridotin selenium derivative **1**. Curiously, in a series of related sulfur compounds reported by Beraldo, the diorganotin species was considerably more active than the corresponding trichlorotin compound; this may simply result from a higher toxicity of the organotin species [10]. Although a large number of tin compounds have been screened for their anti-tumour activity over the years, still almost nothing is known about their mode of action. There is experimental evidence, obtained using model compounds in water,

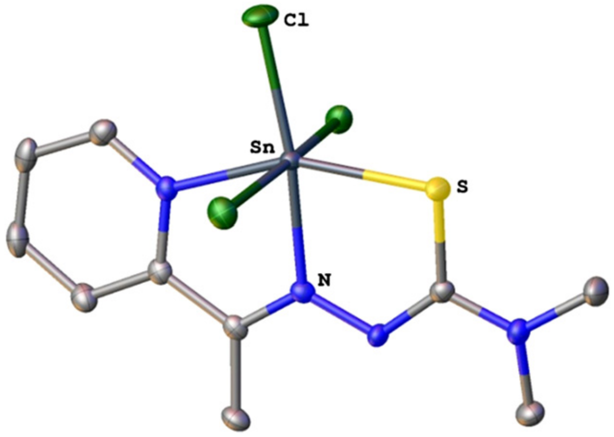

Fig. 3. Molecular structure of complex **4**. Displacement ellipsoids are drawn at a 50% probability level. Hydrogen atoms have been omitted for clarity.

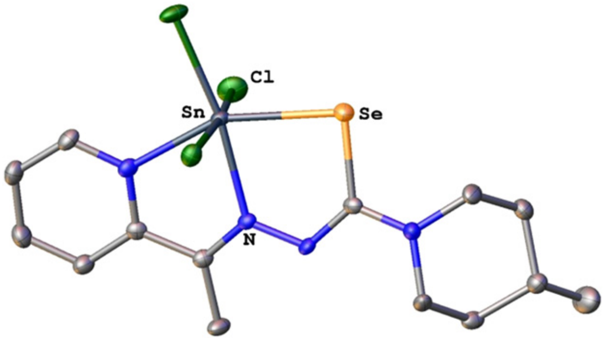

Fig. 4. Molecular structure of complex **5**. Displacement ellipsoids are drawn at a 50% probability level. Hydrogen atoms have been omitted for clarity.

Table 2
Important bond lengths and angles of the tin complexes **1**, **2**, **4** and **5**.

	1	**2**	**4**	**5**
	Bond lengths (Å)			
Sn–Cl	2.5376(3) 2.4724(7) 2.4375(7)	2.6059(7)	2.4249(6) 2.4698(6) 2.3538(7)	2.4341(7) 2.4024(7) 2.3768(7)
Sn–C	–	2.134(3) 2.142(3)	–	–
Sn–E	2.5376(3)	2.5927(3)	2.4331(6)	2.5669(4)
E–C	1.926(2)	1.901(2)	1.757(3)	1.923(3)
(E)C–N(N)	1.328(3)	1.319(3)	1.342(3)	1.315(4)
N–N	1.359(3)	1.375(3)	1.355(3)	1.348(3)
N=C(C)	1.294(3)	1.308(3)	1.301(3)	1.298(3)
(E)C–NR_2	1.343(3)	1.347(3)	1.341(3)	1.340(3)
	Bond angles and torsion angles (°)			
Sn–E–C	90.11(7)	95.78(7)	94.24(8)	91.00(9)
E–C–N(N)	128.05(17)	127.1(2)	128.38(19)	126.76(19)
E–C–N–N	−5.8(3)	−4.13	6.0(3)	−0.9(4)
N(py)–C–C–N	0.2(3)	0.6(3)	−1.6(3)	1.3(4)
E–Sn–N(py)–C(py)	−5.2(3)	−176.0(2)	6.4(1)	−4.9(3)

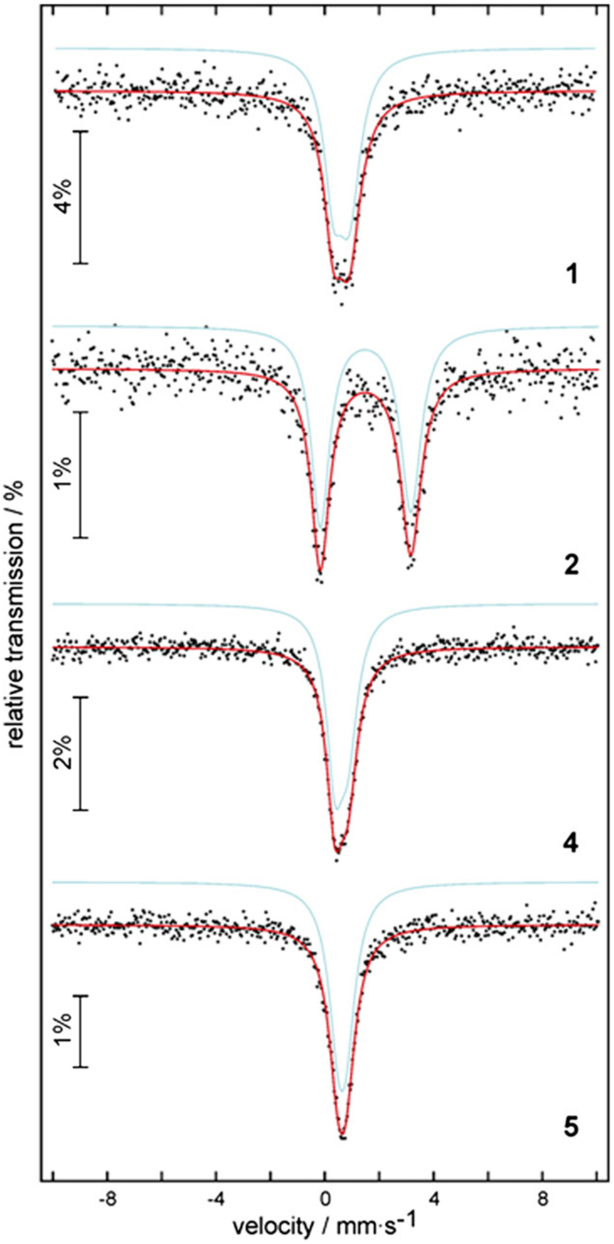

Fig. 5. Experimental and simulated ^{119}Sn Mössbauer spectra of compounds **1**, **2**, **4**, and **5** at 78 K.

that DNA is not a target for tin species [57]. Penninks and Seinen proposed that the anti-tumour activity of organotin compounds arises from their binding to thiol groups in proteins [58]. In order to shed more light on possible modes of action of the substances described herein, further biological studies are currently ongoing in our laboratories.

Table 3
Fitting parameters of ^{119}Sn Mössbauer spectroscopic measurements for compounds **1**, **2**, **4**, and **5** at 78 K. Numbers in parentheses represent the statistical errors in the last digit. δ, isomer shift; Γ, experimental line width; δeq, electric quadrupole splitting.

Sample	δ/mm s^{-1}	ΔE_Q/mm s^{-1}	Γ mm s^{-1}
1	0.60(3)	0.59(2)	0.79(8)
2	1.50(1)	3.33(1)	0.82(3)
4	0.61(2)	0.49(2)	0.75(4)
5	0.64(1)	0.29(2)	0.86(1)

Table 4
IC$_{50}$ values of **HSe2** and the complexes **1**, **3**, and **4**.

	IC$_{50}$ [nM]		
Compound	A253	A549	DLD-1
HSe2	4.54 ± 0.15	4.93 ± 0.14	1.20 ± 0.05
1	2.02 ± 0.38	2.53 ± 0.45	0.50 ± 0.08
3	2.80 ± 0.06	3.04 ± 0.12	0.94 ± 0.05
4	4.84 ± 0.22	5.44 ± 0.32	2.03 ± 0.19
	IC$_{50}$ [μM]		
Cisplatin	0.81 ± 0.02	1.51 ± 0.02	5.14 ± 2.20

3. Experimental

3.1. General

^{1}H, ^{13}C{^{1}H}, ^{31}P{^{1}H}, ^{119}Sn and ^{77}Se NMR spectra were recorded on a Bruker Avance ARX 400 (400 MHz) or a Bruker Avance III 600 (600 MHz) spectrometer. Chemical shifts are quoted relative to external $SiMe_4$ (^{1}H, ^{13}C), H_3PO_4 (^{31}P), $SnMe_4$ (^{119}Sn) and Me_2Se (^{77}Se). Elemental analyses were performed by staff of the microanalytical laboratory of the University of Wuppertal. The pyridyl functionalised thiosemicarbazone **HS2** and selenosemicarbazones **HSe1** and **HSe2** were prepared as described in the literature [29,31]. All other chemicals and solvents (HPLC grade) were sourced commercially and used as received.

3.2. Preparation of the tin thio- and selenosemicarbazonato complexes

A mixture of thio- or selenosemicarbazone and NaOMe (1.1 eq.) in MeOH (20 mL) was heated until a clear solution was obtained. After addition of the tin(IV) chloride (1.0 eq.), the mixture was refluxed for 10–40 min. The yellow solution was evaporated to dryness and the residue was extracted into CH_2Cl_2. The extract was passed through Celite and the filtrate was evaporated to dryness, leaving a yellow residue which was washed with Et_2O and dried in air.

(1) Yield: 170 mg (90%) yellow solid. ^{1}H NMR (400 MHz, CD_2Cl_2): $\delta = 2.80$ (s, 3H, NCC*H*$_3$), 3.42 (s, 6H, NMe_2), 7.81 (ddd, $J = 7.6$, 5.4, 1.1 Hz, 1H, H-5 py), 8.01 (d, $J = 8.1$ Hz, 1H, H-3 py), 8.26 (dt, $J = 7.9$, 1.6 Hz, 1H, H-4 py), 9.19 (ddd, $J = 5.4$, 1.5, 0.6 Hz, 1H, H-6 py) ppm. ^{13}C{^{1}H} NMR (101 MHz, CD_2Cl_2): $\delta = 15.7$ (NC*C*H$_3$), 40.6 (NMe), 42.9 (NMe), 125.2 (C-3 py), 127.5 (C-5 py), 143.1 (Me-*C*-N), 143.4 (C-4 py), 143.5 (C-2 py), 144.9 (C-6 py), 170.8 (C-Se) ppm. ^{119}Sn NMR (224 MHz, DMSO-d6): $\delta = -557$ ppm ^{77}Se NMR (76 MHz, DMSO-d6): $\delta = 192$ ppm. Elemental analysis calcd. (%) for $C_{10}H_{13}N_4Cl_3SeSn$ (493.27 g/mol): C 24.35, H 2.66, N 11.36; found: C 23.45, H 2.67, N 10.68. X-ray quality crystals were obtained by slow evaporation of a CD_2Cl_2 solution of the complex.

(2) Yield: 103 mg (76%) yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 0.72$ (t, $J = 7.2$ Hz, 6H, CH$_2$C*H*$_3$), 1.16 (m, 4H, CH$_2$), 1.26 (m, 2H, CH$_2$), 1.41 (dt, $J = 11.6$, 4.2 Hz, 2H, CH$_2$), 1.73 (m, 2H, CH$_2$), 1.74 (dt, $J = 11.7$, 4.4 Hz, 2H, CH$_2$), 2.66 (s, 3H, NCC*H*$_3$), 3.35 (s, 6H, NMe_2), 7.47 (ddd, $J = 7.5$, 4.9, 0.8 Hz, 1H, H-5 py), 7.79 (d, $J = 8.1$ Hz, 1H, H-3 py), 7.96 (dt, $J = 7.9$, 1.7 Hz, 1H, H-4 py), 8.65 (ddd, $J = 4.8$, 1.5, 0.7 Hz, 1H, H-6 py) ppm. ^{13}C{^{1}H} NMR (101 MHz, CD_2Cl_2): $\delta = 13.9$ (s, $^1J_{13C-Sn} = 10$ Hz, ^{n}Bu-CH$_3$), 17.1 (NCCH$_3$), 26.6 (s, $^2J_{13C-119Sn} = 151$ Hz, $^2J_{13C-117Sn} = 144$ Hz, ^{n}Bu–CH$_2$–β), 28.8 (s, $^3J_{13C-Sn} = 44$ Hz, ^{n}Bu–CH$_2$–γ), 36.9 (s, $^1J_{13C-119Sn} = 759$ Hz, $^1J_{13C-117Sn} = 751$ Hz, ^{n}Bu–CH$_2$–α), 41.4 (br.

s, NMe$_2$), 123.8 (C-3 py), 125.4 (C-5 py), 139.7 (C-4 py), 146.9 (C-6 py), 150.4 (C-2 py), 152.6 (Me-*C*-N), 170.5 (C-Se) ppm. ^{119}Sn NMR (149 MHz, CD_2Cl_2): $\delta = -192$ ppm ^{77}Se NMR (76 MHz, CD_2Cl_2): $\delta = -43$ ($^1J_{77Se-119Sn} = 1044$ Hz, $^1J_{77Se-117Sn} = 1000$ Hz) ppm. Elemental analysis calcd. (%) for $C_{18}H_{31}N_4SeSnCl$ (536.59 g/mol): C 40.29, H 5.82, N 10.44; found: C 39.70, H 5.93, N 10.26. X-ray quality crystals were obtained by slow evaporation of a CD_2Cl_2 solution of the complex.

(3) Yield: 147 mg (95.1%) yellow solid. ^{1}H NMR (400 MHz, CD_2Cl_2): $\delta = 1.04$ (s, 6H, SnMe$_2$, $^2J_{119Sn-1H} = 95.0$ Hz, $^2J_{117Sn-1H} = 90.8$ Hz), 2.68 (s, 3H, NCC*H*$_3$), 3.32 (s, 6H, NMe$_2$), 7.50 (ddd, $J = 7.6$, 4.9, 1.0 Hz, 1H, H-5 py), 7.83 (dt, $J = 8.1$, 0.9 Hz, 1H, H-3 py), 7.98 (dt, $J = 7.9$, 1.7 Hz, 1H, H-4 py), 8.63 (ddd, $J = 4.9$, 1.7, 0.9 Hz, 1H, H-6 py) ppm. $^{13}C\{^1H\}$ NMR (101 MHz, CD_2Cl_2): $\delta = 17.3$ (NCCH$_3$), 19.2 (SnMe$_2$, $^1J_{119Sn-13C} = 826$ Hz, $^1J_{117Sn-13C} = 789$ Hz), 41.2 (NMe$_2$), 124.0 (C-3 py), 125.6 (C-5 py), 139.7 (C-4 py), 146.6 (C-6 py), 149.6 (C-2 py), 152.9 (Me-*C*-N), 169.9 (C-Se) ppm. ^{119}Sn NMR (149 MHz, CD_2Cl_2): $\delta = -208$ ppm ^{77}Se NMR (76 MHz, CD_2Cl_2): $\delta = -1$ ppm. Elemental analysis calcd. (%) for $C_{12}H_{19}N_4ClSeSn$ (452.43 g/mol): C 31.86, H 4.23, N 12.38; found: C 31.19, H 4.10, N 12.05.

(4) Yield: 188 mg (94%) yellow solid. ^{1}H NMR (400 MHz, CD_2Cl_2): $\delta = 2.79$ (s, 3H, NCC*H*$_3$), 3.44 (s, 6H, NMe$_2$), 7.83 (ddd, $J = 7.6$, 5.4, 1.0 Hz, 1H, H-5 py), 8.03 (d, $J = 8.2$ Hz, 1H, H-3 py), 8.30 (dt, $J = 7.9$, 1.5 Hz, 1H, H-4 py), 9.12 (d, $J = 5.1$ Hz, 1H, H-6 py) ppm. $^{13}C\{^1H\}$ NMR (151 MHz, CD_2Cl_2): $\delta = 14.7$ (NC*C*H$_3$), 39.4 (NMe), 41.4 (NMe), 124.7 (C-3 py), 127.1 (C-5 py), 140.8 (Me-*C*-N), 143.3 (C-4 py), 143.6 (C-2 py), 144.7 (C-6 py), 171.8 (C-S) ppm. ^{119}Sn NMR (149 MHz, CD_2Cl_2): $\delta = -474$ ppm. Elemental analysis calcd. (%) for $C_{10}H_{13}N_4Cl_3SSn$ (446.37 g/mol): C 23.79, H 2.60, N 11.01 S 6.35; found: C 23.83, H 2.92, N 11.12 S 5.84. X-ray quality crystals were obtained by slow evaporation of a CD_2Cl_2 solution of the complex.

(5) Yield: 181 mg (78%) orange solid. ^{1}H NMR (600 MHz, CD_2Cl_2): $\delta = 1.05$ (d, $J = 6.4$ Hz, 3H, CHC*H*$_3$), 1.36 (m, 2H, CH$_{ax}$), 1.87 (m, 3H, CH$_{eq}$, C*H*CH$_3$), 2.82 (s, 3H, NCC*H*$_3$), 3.28 (br. s, 2H, NCH$_{ax}$), 4.45 (br. s, 1H, NCH$_{eq}$), 5.04 (br. s, 1H, NCH$_{eq}$), 7.84 (ddd, $J = 7.5$, 5.4, 0.9 Hz, 1H, H-5 py), 8.06 (d, $J = 8.0$ Hz, 1H, H-3 py), 8.31 (dt, $J = 7.9$, 1.5 Hz, 1H, H-4 py), 9.22 (dd, $J = 5.3$, 0.8 Hz, 1H, H-6 py) ppm. $^{13}C\{^1H\}$ NMR (151 MHz, CD_2Cl_2): $\delta = 15.3$ (NCCH$_3$), 21.2 (NCCH$_3$), 31.4 (*C*HCH$_3$), 34.1 (CH$_2$), 48.3 (NCH$_2$), 52.3 (NCH$_2$), 124.7 (C-3 py), 127.0 (C-5 py), 142.5 (Me-*C*-N), 142.9 (C-4 py), 143.1 (C-2 py), 144.3 (C-6 py), 169.1 (C-Se) ppm. ^{119}Sn NMR (149 MHz, CD_2Cl_2): $\delta = -558$ ppm.

^{77}Se NMR (76 MHz, CD_2Cl_2): $\delta = 185$ ($^1J_{77Se-Sn} = 1370$ Hz) ppm. Elemental analysis calcd. (%) for $C_{14}H_{19}N_4Cl_3SeSn{\cdot}0.5CH_2Cl_2$ (589.82 g/mol): C 29.53, H 3.42, N 9.50; found: C 29.55, H 3.52, N 9.94. X-ray quality crystals were obtained by slow evaporation of a CD_2Cl_2 solution of the complex.

(6) Yield: 77 mg (50%) yellow solid. ^{1}H NMR (600 MHz, CD_2Cl_2): $\delta = 0.77$ (t, $J = 7.3$ Hz, 6H, CH$_2$C*H*$_3$), 1.01 (d, $J = 6.2$ Hz, 3H, CHC*H*$_3$), 1.20 (m, 4H, ^{n}Bu–CH$_2$–β), 1.28 (m, 4H, ^{n}Bu–CH$_2$–γ, CH$_{ax}$), 1.42 (dt, $J = 11.7$, 4.5 Hz, 2H, ^{n}Bu–CH$_2$–α), 1.56 (m, 2H, ^{n}Bu–CH$_2$–γ), 1.69 (dt, $J = 11.8$, 4.6 Hz, 2H, ^{n}Bu–CH$_2$–α), 1.77 (m, 3H, CH$_{eq}$, C*H*CH$_3$), 2.70 (s, 3H, NCC*H*$_3$), 3.13 (t, $J = 12.4$ Hz, 2H, NCH$_{ax}$), 4.83 (d, $J = 12.2$ Hz, 2H, NCH$_{eq}$), 7.53 (m, 1H, H-5 py), 7.87 (d, $J = 8.1$ Hz, 1H, H-3 py), 8.03 (dt, $J = 7.9$, 1.6 Hz, 1H, H-4 py), 8.68 (d, $J = 4.2$ Hz, 1H, H-6 py) ppm. $^{13}C\{^1H\}$ NMR (151 MHz, CD_2Cl_2): $\delta = 13.9$ (s, ^{n}Bu-CH$_3$), 17.1 (NC*C*H$_3$), 22.0 (NCCH$_3$), 26.6 (s, $^2J_{13C-119Sn} = 147$ Hz, $^2J_{13C-117Sn} = 141$ Hz, ^{n}Bu–CH$_2$–β), 28.9 (s, $^3J_{13C-Sn} = 43$ Hz, ^{n}Bu–CH$_2$–γ), 32.0 (*C*HCH$_3$), 34.7 (CH$_2$), 36.7 (s, $^1J_{13C-119Sn} = 788$ Hz, $^1J_{13C-117Sn} = 752$ Hz, ^{n}Bu–CH$_2$–α), 50.2 (br. s, NCH$_2$), 123.8 (C-3 py), 125.4 (C-5 py), 139.7 (C-4 py), 147.0 (C-6 py), 150.4 (C-2 py), 152.6 (Me-*C*-N), 169.9 (C-Se) ppm. ^{119}Sn NMR (224 MHz, CD_2Cl_2): $\delta = -193$ ppm ^{77}Se NMR (76 MHz, CD_2Cl_2): $\delta = -49$ ppm. Elemental analysis calcd. (%) for $C_{22}H_{37}N_4ClSeSn$ (590.68 g/mol): C 43.55, H 6.16, N 9.14; found: C 43.58, H 6.29, N 9.24.

3.3. *^{119}Sn Mössbauer spectroscopy*

A $Ca^{119m}SnO_3$ source was available for the ^{119}Sn Mössbauer spectroscopic investigations. The samples were placed within thin-walled plexiglass containers at a thickness of about 10 mg Sn/cm^2. A palladium foil of 0.05 mm thickness was used to reduce the tin K X-rays concurrently emitted by this source. The measurements were conducted in the usual transmission geometry at 78 K.

3.4. *Cytotoxicity studies*

Stock solutions of investigated compounds were prepared in dimethyl sulfoxide (DMSO) at concentrations of 20 mM and afterwards they were diluted with complete nutrient medium (RPMI-1640 with L-glutamine (PAA Labs, Pasching, Austria) containing 10% heat inactivated fetal bovine serum (FBS) (Biochrom AG, Berlin, Germany) and 1% penicillin/streptomycin (100X) (PAA Labs, Pasching, Austria). The cell lines A253 (head and neck tumour), A549 (lung) and DLD-1 (colon) were included in this study. All these cell lines were kindly provided by Dr Thomas Mueller, Department of Hematology/Oncology, Martin Luther University of Halle-Wittenberg, Halle (Saale), Germany. Cultures were maintained as monolayers in RPMI 1640 supplemented with 10% heat inactivated fetal bovine serum and 1% penicillin/streptomycin at 37 °C in a humidified atmosphere with 5% CO$_2$.

The cytotoxic activities of the investigated compounds were evaluated using the sulforhodamine-B (SRB, Sigma–Aldrich) microculture colorimetric assay [59]. Exponentially growing cells were seeded into 96-well plates on day 0 at the appropriate cell densities to prevent confluence of the cells during the period of the experiment. After 24 h, the cells were treated with serial dilutions of the studied compounds for 96 h. Experiments were performed in triplicate on each cell line. The final concentration of DMSO solvent never exceeded 0.5%, which was non-toxic to the cells. The percentages of surviving cells relative to untreated controls were determined 96 h after the beginning of drug exposure. After 96 h treatment, the supernatant medium from the 96 well plates was discarded and the cells were fixed with 10% TCA (trichloroacetic acid). For a thorough fixation, plates were then allowed to stand at 4 °C. After fixation the cells were washed in a strip washer. The washing was carried out four times with water using alternate dispensing and aspiration procedures. The plates were then dyed with 100 μL of 0.4% SRB for about 45 min. After dying the plates were again washed to remove the dye with 1% acetic acid and allowed to air dry overnight. 100 μL of 10 mM Tris base solutions were added to each well of the plate and absorbance was measured at 570 nm using a 96 well plate reader (Tecan Spectra, Crailsheim, Germany). The IC$_{50}$ values, defined as the concentrations of the compound at which 50% cell inhibition were observed, were estimated from the dose–response curves.

3.5. *X-ray diffraction studies*

Diffraction data were collected at 150 K using an Oxford Diffraction Gemini E Ultra diffractometer, equipped with an EOS CCD area detector and a four-circle kappa goniometer. Graphite-monochromated Mo-Kα radiation ($\lambda = 0.71073$ Å) was used. Data

Table 5
Crystallographic and refinement details for the tin compounds **1**, **2**, **4** and **5**.

	1	2	4	5
Empirical formula	$C_{10}H_{13}N_4SnSeCl_3$	$C_{18}H_{31}ClSnN_4Se$	$C_{10}H_{13}N_4SCl_3Sn$	$C_{14}H_{19}N_4SnSeCl_3$
Formula weight	493.24	536.57	446.34	547.33
Crystal system	Monoclinic	Monoclinic	Monoclinic	Monoclinic
Space group	$P2_1/c$	$P2_1/n$	$P2_1/c$	$P2_1/n$
a/Å	13.0083(5)	10.2678(4)	12.9113(7)	9.3898(3)
b/Å	9.5646(3)	17.6592(8)	9.5025(4)	11.3496(4)
c/Å	13.3211(5)	12.8969(7)	13.2860(7)	17.7644(7)
$\beta(^\circ)$	112.851(4)	104.299(5)	112.553(7)	95.950(4)
V/Å^3	1527.33(9)	2266.03(18)	1505.40(14)	1882.96(12)
T/K	150(2)	150(2)	150(2)	150(2)
Z	4	4	4	4
ρ_c/g cm^{-3}	2.15	1.57	1.97	1.93
Crystal size/mm	0.15 × 0.04 × 0.02	0.26 × 0.20 × 0.12	0.07 × 0.06 × 0.05	0.12 × 0.07 × 0.02
μ/mm^{-1}	4.6	2.9	2.4	3.7
θ range (°)	2.72–29.44	2.82–29.46	3.10–29.47	2.92–29.57
Reflections collected	7827	10,459	6592	10,141
Independent reflections	3598	5305	3499	4457
R_{int}	0.0227	0.0239	0.0242	0.0292
$F(000)$	944	1072	872	1064
Data/restraints/parameters	3598/0/175	5305/0/231	3499/0/175	4457/0/210
GOF (F^2)	0.929	0.963	0.934	0.901
R_1, wR_2 [$I > 2\sigma(I)$]	0.0217, 0.0414	0.0258, 0.0565	0.0233, 0.0448	0.0262, 0.0465
R_1, wR_2 (all data)	0.0291, 0.0422	0.0376, 0.0580	0.0308, 0.0460	0.0401, 0.0481
$\Delta\rho_{max,min}$/e Å^{-3}	0.48/−0.51	0.58/−0.69	0.50/−0.44	0.47/−0.72

integration, scaling and empirical absorption correction was carried out using the CrysAlis Pro program package [60]. The structures were solved using Direct Methods or Patterson Methods and refined by Full-Matrix-Least-Squares against F^2. The non-hydrogen atoms were refined anisotropically and hydrogen atoms were placed at idealised positions and refined using the riding model. All calculations were carried out using the program Olex2 [61]. Important crystallographic and refinement parameters are collected in Table 5.

4. Conclusions

We report here the preparation and full spectroscopic and structural characterisation of a family of tin(IV) compounds containing pyridyl substituted, monoanionic thio- or selenosemicarbazonato ligands. Some of these compounds display significant *in vitro* anti-tumour activity in a panel of human tumour cell lines.

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Appendix A. Supplementary material

CCDC 822681–822684; contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

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