Structure, Properties and Cytostatic Activity of Triorganotin (Aminoaryl)carboxylates

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The properties of vinyltin and phenyltin complexes $[Sn(CH=CH_2)_3\{\mu\text{-}OOCC_6H_3(NH_2)_2\text{-}3,4\}]_n$ (**1**), $[Sn(C_6H_5)_3\{OOCC_6H_3(NH_2)_2\text{-}3,4\}]$ (**2**), $[Sn(C_6H_5)_3\{OOC\text{-}2\text{-}C_6H_4N{=}NC_6H_4N(CH_3)_2\text{-}4\}]$ (**3**) and $[Sn(CH=CH_2)_3\{OOC\text{-}2\text{-}C_6H_4N{=}NC_6H_4N(CH_3)_2\text{-}4\}]$ (**4**) have been investigated. The structures of complexes **1**, **2**, and **3**, have been determined by X-ray crystallography. Compound **1** is a distorted trigonal-bipyramidal complex and compounds **2** and **3** adopt a distorted tetrahedral structure. Complex **1** is a single-strand polymer with a bridging 3,4-diaminobenzoato ligand coordinating via the O(1) atom of the carboxylato group and the nitrogen atom of the *para*-amino group. The oxygen and nitrogen atoms occupy the axial coordination sites. The Sn(1)–N(2A) bond is weak. In complexes **2** and **3** the carboxylato ligands are strongly coordinated to the central atom via one oxygen atom, and the Sn(1)–O(2) distances are considerably longer. Weak interactions of the central atom with the amino group in complex **1**, and with the O(2) atoms in complexes **2** and **3**, as well as the hydrogen bonds, stabilize the crystal structure. The complexes are effective cytostatic agents.

Introduction

Coordination and organometallic compounds belong to the very important group of antitumor agents.[1,2] Many platinum complexes and other transition metal compounds, as well as organometallic compounds of the main group metals show high cytostatic activity. A number of organotin compounds have been shown to be active against various types of cancers. A series of organotin dipeptide compounds and a number of diorganotin halides containing amino ligands $[SnR_2X_2L_2]$ have displayed modest antitumor activity.[3,4] Many di-*n*-butyl-, tri-*n*-butyl-, and triphenyltin hydroxycarboxylates, oxycarboxylates, and fluorocarboxylates display interesting antitumor activities.[5−15] However, only few tin carboxylates with amino groups have been investigated. These complexes comprise pyridinocarboxylato and aminosalicylato organotin compounds.[5] Here, we report on the synthesis, properties, structure, and in vitro cytostatic activity of trivinyltin and triphenyltin complexes with 3,4-diaminobenzoate and 2-[4-(dimethylamino)phenylazo]benzoate.

Results and Discussion

The complexes $[Sn(CH=CH_2)_3\{\mu\text{-}OOCC_6H_3(NH_2)_2\text{-}3,4\}]_n$ (**1**), $[Sn(C_6H_5)_3\{OOCC_6H_3(NH_2)_2\text{-}3,4\}]$ (**2**), $[Sn(C_6H_5)_3\{OOC\text{-}2\text{-}C_6H_4N{=}NC_6H_4N(CH_3)_2\text{-}4\}]$ (**3**) and $[Sn(CH=CH_2)_3\{OOC\text{-}2\text{-}C_6H_4N{=}NC_6H_4N(CH_3)_2\text{-}4\}]$ (**4**) are soluble in ethanol, methanol, acetone, chloroform, dichloromethane, and in other polar organic solvents, and are slightly soluble in aqueous ethanol (50%). The vinyl complexes **1** and **4** have been obtained by the reactions of $SnO(CH=CH_2)_2$ and the appropriate acid in ethanol, while complexes **2** and **3** have been prepared by the reactions of $SnO(C_6H_5)_2$ or $\{Sn(C_6H_5)_3\}_2O$ with the acids. Thus, in the reactions of $SnO(CH=CH_2)_2$ and $SnO(C_6H_5)_2$ with the acids, the vinyl or phenyl groups are transferred. Other products obtained were SnO(R)(OOCR′), $Sn(OH)_2R(OOCR')$ and similar monoorganotin(IV) compounds, however, these compounds were not pure enough.

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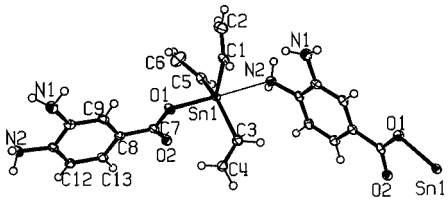


Figure 1. $[Sn(CH{=}CH_2)_3\{\mu\text{-}OOCC_6H_3(NH_2)_2\text{-}3,4\}]_n$

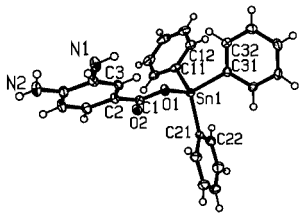


Figure 2. $[Sn(C_6H_5)_3\{OOCC_6H_3(NH_2)_2\text{-}3,4\}]$

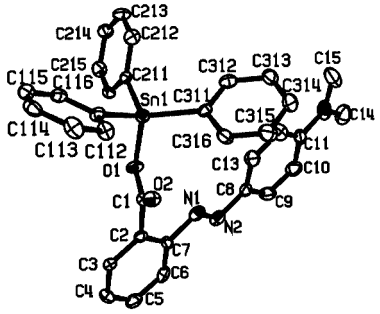


Figure 3. $[Sn(C_6H_5)_3\{OOC\text{-}2\text{-}C_6H_4N{=}NO_6H_4N(CH_3)_2\text{-}4\}]$

Table 1. Bond lengths [Å] and angles [°] for complex **1**

Sn(1)−C(3)	2.118(3)	C(3)−Sn(1)−C(1)	113.18(12)
Sn(1)−C(5)	2.120(3)	C(5)−Sn(1)−C(1)	112.63(12)
Sn(1)−C(1)	2.135(3)	C(3)−Sn(1)−O(1)	96.01(10)
Sn(1)−O(1)	2.1353(19)	C(5)−Sn(1)−O(1)	98.73(10)
Sn(1)−O(2)	2.955(3)	C(1)−Sn(1)−O(1)	92.61(10)
Sn(1)−N(2i)	2.685(3)	C(3)−Sn(1)−N(2i)	84.69(10)
O(1)−C(7)	1.310(3)	C(5)−Sn(1)−N(2i)	80.05(10)
O(2)−C(7)	1.240(4)	C(1)−Sn(1)−N(2i)	88.04(10)
C(3)−Sn(1)−C(5)	130.87(12)	O(1)−Sn(1)−N(2i)	178.76(7)

Table 2. Bond lengths [Å] and angles [°] for complex **2**

Sn(1)−O(1)	2.069(2)	O(1)−Sn(1)−C(11)	112.05(12)
Sn(1)−C(11)	2.121(3)	O(1)−Sn(1)−C(21)	109.64(12)
Sn(1)−C(21)	2.128(3)	C(11)−Sn(1)−C(21)	119.14(13)
Sn(1)−C(31)	2.146(3)	O(1)−Sn(1)−C(31)	95.72(11)
Sn(1)−O(2)	2.680(3)	C(11)−Sn(1)−C(31)	108.51(13)
O(1)−C(1)	1.320(4)	C(21)−Sn(1)−C(31)	109.21(13)
O(2)−C(1)	1.241(4)	O(2)−Sn(1)−C(31)	149.18(13)

The structures of complexes **1**, **2** and **3** are shown in Figures 1, 2, and 3, and selected bond lengths and angles are given in Tables 1, 2, and 3, the lengths and angles of the hydrogen bonds in the solid compounds in Tables 4, 5, and 6, and the crystallographic data in Table 8. Compound $[Sn(CH{=}CH_2)_3\{OOCC_6H_3(NH_2)_2\text{-}3,4\}]$ (**1**) is a distorted trigonal-bipyramidal complex, it consists of three vinyl ligands and a bridging 3,4-diaminobenzoato ligand, which is coordinated via one oxygen atom and the nitrogen atom of the *para*-amino group. The monodentate coordination of the carboxylate group is reflected in the short Sn(1)−O(1) bond [2.1353(19) Å] and the different C(7)−(O1) and C(7)−O(2) distances of 1.310(3) and 1.240(4) Å, respectively. The Sn−O(2) bond [2.955(3) Å] is much longer than the Sn−O(1) bond [2.1353(19) Å], thus the interaction of the O(2) atom with the central atom is very weak. The fifth

Table 3. Bond lengths [Å] and angles [°] for complex **3**

Sn(1)−O(1)	2.054(2)	O(1)−Sn(1)−C(311)	108.23(12)
Sn(1)−O(2)	2.827(2)	O(1)−Sn(1)−C(111)	109.32(12)
Sn(1)−C(311)	2.117(4)	C(311)−Sn(1)−C(111)	118.20(15)
Sn(1)−C(111)	2.121(4)	O(1)−Sn(1)−C(211)	95.81(12)
Sn(1)−C(211)	2.126(4)	C(311)−Sn(1)−C(211)	112.61(14)
O(1)−C(1)	1.314(4)	C(111)−Sn(1)−C(211)	110.29(14)
O(2)−C(1)	1.219(4)	C(1)−O(1)−Sn(1)	110.1(2)

Table 4. Lengths [Å] and angles [°] of the hydrogen bonds in solid compound **1**

D−H···A[a]	D−H	H···A	D···A	D−H···A
N(2)−H(4N)···O(2)^{i}	0.90(4)	2.06(4)	2.956(3)	170(3)
N(2)−H(3N)···C(2)^{ii}	0.84(3)	3.08(3)	3.712(4)	134(3)
N(1)−H(1N)···X1A (C1/C2)^{iii}	0.88(4)	2.63	3.50	170
N(1)−H(2N)···X1B (C3/C4)^{iv}	0.89(4)	2.94	3.53	125

[a] Symmetry transformations used to generate equivalent atoms: i: $-x + 1/2, y - 1/2, -z + 1/2$; ii: $-x, y - 1, -z + 1/2$; iii: $x, -y, z - 1/2$; iv: $-x, y, -z + 1/2$.

Table 5. Lengths [Å] and angles [°] of the hydrogen bonds in solid compound **2**

D−H···A[a]	D−H	H···A	D···A	D−H···A
N(1)−H(2N)···N(2)^{ii}	0.87	2.40	3.181(5)	150.5
N(2)−H(3N)···O(2)^{iii}	0.92	2.08	2.979(4)	165.7

[a] Symmetry transformations used to generate equivalent atoms: i: $-x, -y - 1, -z$; ii: $-x, -y, -z$; iii: $-x, y - 1/2, -z + 1/2$.

Table 6. Lengths [Å] and angles [°] of weak C−H···π hydrogen bonds in solid complex **3**

C−H···Ph[a]	H···Ph	Offset	C−H···Ph
C(13)−H(13)···Ph5	3.07	0.91	134
C(3)−H(3)···Ph4^{i}	2.54	0	155
C(213)−H(213)···Ph3^{ii}	3.07	1.04	144
C(315)−H(315)···Ph1^{iii}	2.63	0.32	168

[a] Ph1 is defined by C(2), C(3), C(4), C(5), C(6), and C(7) atoms; Ph3 by C(111), C(112), ..., C(116) atoms; Ph4 by C(211), C(212), ..., C(216) atoms; Ph5 by C(311), C(312), ..., C(316) atoms. Symmetry code superscript: (none) x, y, z; (i) $x + 1, y, z$; (ii) $x - 1, y, z$; (iii) $x, y - 1, z$.

coordination site is occupied by the N(2A) atom of a neighboring molecule (Figure 1). Thus, complex **1** is a single-strand polymer in the solid state. The Sn(1)−N(2A) distance is 2.685(3) Å and the O(1)−Sn(1)−N(2A) angle is 178.76(7)°. The angles C(1)−Sn(1)−C(3) [113.18(12)°] and C(1)−Sn(1)−C(5) [112.63(12)°] are considerably smaller, and the C(3)−Sn(1)−C(5) angle [130.87(12)°] is substantially larger than those expected for a regular trigonal bipyramid. A relatively strong Sn(1)−N(2A) bonding interaction is important for the stabilization of the crystal structure of complex **1**. The crystal structure is also stabilized by the relatively strong hydrogen bond N(2)−H(4N)···O(2)(i) and the weaker hydrogen bonds N(2)−H(3N)···C(2)(ii), N(1)−H(1N)···X1A(C1/C2)(iii), and N(1)−H(2N)···X1B-(C3/C4)(iv) (Table 4). In complex **2**, the central atom has a distorted tetrahedral geometry, with the Sn(1)−O(1) bond length of 2.069(2) Å, the Sn(1)−C bond lengths of 2.121(3)−2.146(3) Å, and the considerably longer Sn(1)−O(2) distance of 2.680(3) Å. The C(11)−Sn(1)−C(31) and C(21)−Sn(1)−C(31) angles are 108.51(13) and 109.21(13)°, respectively, and the C(11)−Sn(1)−C(21) angle is 119.14(13)°. The interaction of the oxygen atom O(2) with the central atom Sn(1) is relatively strong in comparison with analogous interactions in complex **1**. The O(2)−Sn(1)−C(31) angle is 149.18(13)°, while the O(2)−Sn(1)−C(11) and O(2)−Sn(1)−C(21) angles are 84.67(13) and 86.38(13)°, respectively. The structure of complex **2** is similar to that of $[Sn(C_6H_5)_3(OOCC_6H_5)]$, in which the O(2)−Sn distance is 2.674(3) Å.[7,16] The crystal structure of the complex **2** is stabilized not only by the Sn(1)−O(2) interaction, but also by intermolecular hydrogen bonds, namely, N(1)−H(2N)···N(2)(ii) and N(2)−H(3N)···O(2)(iii) (Table 5). Complex **3** has a molecular structure similar to that of compound **2**, with the Sn(1)−O(1) bond length of 2.054(2) Å, Sn(1)−C bond lengths of 2.117(4)−2.126(4) Å and Sn(1)−O(2) bond length of 2.827(3) Å. Thus, in this compound the interaction between the Sn(1) and O(2) atoms is weaker than in complex **2**. However, the crystal structure of compound **3** is also stabilized by weak C−H···Ph intermolecular and intramolecular hydrogen bonds (Table 6), as well as by intermolecular stacking interactions between parallel C(2)−C(7) and C(8)(i)−C(13)(i) phenyl rings of the two neighboring molecules. The distance between these rings is 2.49 Å and the offset is 1.42 Å. There are three intermolecular and one intramolecular C(13)−H(13)···Ph5 (C311,C312, ..., C316 ring) hydrogen bonds (Table 6). Two bonds with short distances between the hydrogen donor atom and the phenyl centroid (Ph1 and Ph4) have a short offset, which is defined as the distance from the ring centroid to the projection of the H-atom position on the plane of the ring.[17] These bonds are also more linear than long hydrogen bonds. Intermolecular hydrogen bonds link all the molecules located along the [100] and [010] directions in the crystal. Short lattice vectors ***a*** and ***b***, relative to ***c***, suggest that analyzed weak hydrogen bonds control the growth of the crystals. The same was observed earlier in the case of other compounds.[18]

Infrared spectra of all investigated complexes are consistent with X-ray data for compounds **1**, **2**, and **3**. The presence of $\nu_{as}(COO)$ and $\nu_s(COO)$ in the ranges 1600−1614 cm^{-1}, and 1334−1368 cm^{-1}, respectively, and therefore the large $\Delta\nu = \nu^{as}_{COO} - \nu^{s}_{COO}$ values are consistent with the presence of the asymmetrically coordinated carboxylato group in complexes **1**, **2**, **3**, and **4**. The ν(SnC) bands for the vinyl compounds (**1** and **4**) are observed in the range 496−542 cm^{-1}, and are similar to the values in other vinyl−Sn^{IV} compounds.[19] The substituent-sensitive r-modes for the phenyl groups were observed at 620 cm^{-1} and 588 cm^{-1} for complex **2**, and 636 cm^{-1}, 610 cm^{-1}, and 590 cm^{-1} for compound **3**, and the y-modes at 452 cm^{-1} and 442 cm^{-1} for **2**, and 457 cm^{-1} and 444 cm^{-1} for **3**. These values agree well with the data for $Sn(C_6H_5)_4$.[19]

The ^1H chemical shift ranges for the trivinyl, triphenyl moieties and the carboxylato ligands were deduced from resonance intensities and $^nJ(^1H\text{-}^1H)$ coupling constants. Both chemical shifts and coupling constants for complexes **1**−**4** agree well with the data found for $[Sn(C_6H_5)_3(OOCC_6H_5)]$,[7] $[Sn(C_6H_5)_3(OOCC_6H_4NH_2)]$, and other triphenyltin(IV) compounds,[20,21] $[Sn(CH{=}CH_2)_2X_2]$ and $[Sn(CH{=}CH_2)_3X]$,[22−24] and with the spectra of 3,4-diaminobenzoic and 2-[(4-dimethylamino)phenylazo]benzoic acid and their metal salts. The first-order spectra of the vinyl ligands of the $[Sn(CH{=}CH_2)_3(OOCR)]$ complexes **1** and **4** consist of three quadruplets with $^{119/117}Sn$ satellites. The chemical shifts of H^7, H^8, and H^9 and the $^3J(H^7H^9)$, $^3J(H^7H^8)$, and $^2J(H^8H^9)$ coupling constants in chloroform solution are slightly higher than those found for $[Sn(CH{=}CH_2)_3X]$ (X = Cl, Br, I). It has been found that the ^1H chemical shifts and the $^nJ(^1H\text{-}^1H)$ coupling constants of the vinyltin halides depend on the electronegativity of the halide.[22] Thus, deshielding of H^1, H^2, and H^3 and a slight increase in the $^nJ(^1H\text{-}^1H)$ coupling constants are caused by the higher electronegativity of the RCOO ligand in comparison with that of the ligands Cl, Br, and I. The chemical shift differences $[\delta(H^7) - \delta(H^8)]$ for complexes **1** and **4** are also greater because of the higher electronegativity of the carboxylato ligand. These differences increase in more polar solvents. They are equal to δ = 0.24 ppm in $CDCl_3$ and 0.36 ppm in $(CD_3)_2CO$ and $(CD_3)_2SO$. The ^{119}Sn chemical shifts are higher for four-coordinate compounds than for the five-coordinate complexes. The values of $\delta(^{119}Sn)$ in the latter are shifted upfield over a wide range.[20−22,24] The ^{119}Sn chemical shifts for compounds **1** and **4** in acetone are δ = −167.9 and −168.9 ppm, respectively. They are lower than the chemical shift for $Sn(CH{=}CH_2)_4$ (δ = −157.4 ppm),[24] and greater than for $[Sn(CH{=}CH_2)_2(OOCPh)_2]$ in $CDCl_3$ (δ = −317.7 ppm).[23] The value of the $^1J(^{119/117}Sn\text{-}^{13}C^7)$ coupling constant for complex **4** in chloroform is 600.2/574.9 Hz and is similar to that found for complex $[Sn(CH{=}CH_2)_3Cl]$ in $CDCl_3$ (594.7/568.2 Hz). Thus, the ^1H, ^{13}C, and ^{119}Sn NMR spectra indicate that complexes **1** and **4** in chloroform solution are tetrahedral molecules, and that the coordination of acetone, methanol or dimethyl sulfoxide with tin compounds is rather weak. The formation of weak adducts of complexes **2** and **3** with

polar solvents is also confirmed by the ^{13}C and ^{119}Sn NMR spectra. The $^{1}J(^{119}Sn\text{-}^{13}C)$ coupling constants for tetrahedral $SnPh_3X$ (X = Cl, RCOO, etc.) complexes in chloroform solution are in the range 550−650 Hz, while for five-coordinate complexes, they are often in the range 770−850 Hz. The $^{2}J(^{119}Sn\text{-}^{13}C)$ coupling constants do not depend on the coordination number of tin and have values of 47.6−50.0 Hz, and the $^{3}J(^{119}Sn\text{-}^{13}C)$ and $^{4}J(^{119}Sn\text{-}^{13}C)$ coupling constants are slightly greater for five-coordinate compounds than for four-coordinate complexes and are in the range 63−73 Hz and 12.7−14.6 Hz, respectively.[20−22,24] Small differences between five-coordinate and four-coordinate triphenyltin(IV) compounds were found in the values of the chemical shifts $\delta(^{13}C^{i})$ of the carbon atoms in the *ipso*-positions of the phenyl groups. The values of the $\delta(^{13}C^{i})$ for the five-coordinate complexes are shifted downfield from those of four-coordinate tin compounds by several ppm.[20] The ^{13}C chemical shifts and $^{n}J(^{119}Sn\text{-}^{13}C)$ coupling constants for complexes **2** and **3** in chloroform are in the range characteristic of tetrahedral triphenyltin compounds since $\delta(^{13}C^{i})$ = 138.88 ppm and $^{1}J(^{119/117}Sn\text{-}^{13}C^{i})$ = 651.0/621.8 Hz for the *ipso*-carbon atoms of complex **2**, and $\delta(^{13}C^{i})$ = 138.48 ppm and $^{1}J(^{119/117}Sn\text{-}^{13}C^{i})$ = 644.6/618.5 Hz for those of compound **3**. The chemical shift $\delta(^{13}C^{i})$ is slightly higher in more polar solvents, thus for complex **2** in $(CD_3)_2CO$ a value of δ = 140.69 ppm is observed and for compound **3** in CD_3OD, a value of δ = 140.12 ppm is observed. The values of $\delta(^{119}Sn)$ in $CDCl_3$ for **2** and **3** are δ = −118.9 and −108.6 ppm, and are similar to those found for complexes $[SnPh_3(OOCC_6H_4NH_2\text{-}4)]$ and $[SnPh_3(OOCC_6H_4NH_2\text{-}2)]$ (δ = −122.6 and −116.8 ppm).[20] The $\delta(^{119}Sn)$ values for complex **2** in acetone (δ = −123.1 ppm) is ca. 4 ppm greater than that in chloroform. These data also confirm the formation of weak adducts of compounds **2** and **3** with polar solvents.

The molecular and electronic structures of a single molecule of $[Sn(CH{=}CH_2)_3(OOCC_6H_3(NH_2)_2\text{-}3,4)]$ with C_1 symmetry has been studied by both semiempirical and nonempirical ab initio methods. The quantum chemical calculations were performed using the PM3 of the MOPAC2000 package,[25] and the GAUSSIAN-98 computer program.[26]

The geometry optimization in the first case was performed at the PM3 level and in the second case within the 3-21G basis set and MP2 formalism. The evaluated Sn−O1 bond length with PM3 is found to be 2.019 Å and the Sn···O2 distance 2.685 Å. The respective ab initio results are 2.071 Å and 2.609 Å, whereas the relevant crystallographic values are 2.1353(19) Å and 2.955(2) Å, respectively. This discrepancy results from the formation of the weak Sn(1)−N(2A) bond and the distorted trigonal-bipyramidal coordination of the tin atom in the solid state. In complex **2**, in which the Sn−N bond in the solid state is not formed, the Sn(1)−O(1) bond [2.069(2) Å] and the Sn(1)−O(2) bond [2.680(3) Å] are very similar to those calculated with semiempirical and ab initio methods. Thus, these methods can most likely be applied for the calculations of the interactions of Sn^{IV} compounds with nucleotides and other molecules important for the explanation of the biological activity of tin compounds. The theoretical dipole moment is 1.543 D, the ionization energy is 8.572 eV, and the heat of formations is estimated to be 9.98 kJ/mol.

Complexes **1**, **2**, **3**, and **4** belong to the efficient cytostatic agents (Table 7). Compound **2** is very active against HCV29T cells (ID_{50} = 0.0072 μmol/dm^3). The activity of the compounds against the HCV29T cell line decreases in the order **2** > **1** > **3** > **4**. It is worth noting that the complexes are also very active in ethanol solution. Cytostatic activity of complexes **1** and **2** against the A549 and CACO-2 lines is relatively high, although lower than that against HCV29T cells. Thus, these compounds are promising cytostatic agents against some tumor lines in vitro.

Conclusion

Investigations of the structures of the complexes $[Sn(CH{=}CH_2)_3\{\mu\text{-}OOCC_6H_3(NH_2)_2\text{-}3,4\}]_n$ (**1**), $[Sn(C_6H_5)_3\{OOCC_6H_3(NH_2)_2\text{-}3,4\}]$ (**2**), and $[Sn(C_6H_5)_3\{OOC\text{-}2\text{-}C_6H_4N{=}NC_6H_4N(CH_3)_2\text{-}4\}]$ (**3**) reveal that the coordination of the central atom in complex **1** is distorted trigonal-bipyramidal, and in complexes **2** and **3** distorted tetrahedral. Complex **1** is a regular single-strand polymer. The vinyl

Table 7. Inhibition doses ID_{50} of complexes **1**−**4**

Compound	Cancer HCV29T		A549		CACO	
	ID_{50} [μmol/dm^3]	Solvent	ID_{50} [μmol/dm^3]	Solvent	ID_{50} [μmol/dm^3]	Solvent
1	1.36	MeOH	20.0	EtOH	12.0	EtOH
2	0.0072	MeOH	0.90	EtOH	i.	EtOH
	0.058	EtOH				
3	3.40	DMSO	n. d.[a]		n. d.	
	0.53	EtOH				
4	7.05	DMSO	n. d.		n. d.	
	1.28	EtOH				
$HOOCC_6H_4N{=}NC_6H_4NMe_2\text{-}4$	20.16	DMSO	i.	H_2O	i.	EtOH
	84.29	EtOH				
$HOOCC_6H_3(NH_2)_2\text{-}3,4$	i.	EtOH	i.	EtOH	i.	H_2O

[a] n.d.: activity was not determined; i.: inactive.

ligands are coordinated in the equatorial positions and the bridging 3,4-diaminobenzoato ligands occupy the axial coordination sites, and form a strong Sn−O bond and a weak Sn−N bond with the *para*-amino group, the Sn(1)−O(1) and Sn(1)−N(2A) distances are 2.1353(19) and 2.685(3) Å, respectively. In complexes **2** and **3**, the carboxylato ligand is strongly coordinated to the central atom via one oxygen atom and the Sn(1)−O(2) distances are considerably longer. However, these weak interactions, as well as the N−H···O, N−H···C, N−H···N hydrogen bonds, and in the case of complex **3** the C−H···Ph hydrogen bonds, stabilize the crystal structure of these complexes. The crystal structure of complex **3** is additionally stabilized by the intermolecular stacking interaction between parallel C(2)−C(7) and C(8)(i)−C(13)(i) phenyl rings of the 2-[4-(dimethylamino)-phenylazo]benzoato ligand of two neighboring molecules. The IR and NMR spectra reveal that the structure of complex **4** is analogous to that of the complexes **2** and **3**. The molecular and electronic structure of a single molecule of complex **1** [$Sn(CH=CH_2)_3(OOCC_6H_3(NH_2)_2$-3,4)], calculated both with semiempirical and ab initio methods, reveal that coordination about the tin atom is similar to that in complex **2**. Thus, the relatively long Sn(1)−O(1) bond in complex **1**, relative to that in compounds **2** and **3**, results from the weak interaction between the Sn atom and the N atom of the *para*-amino group of the 3,4-diaminobenzoato ligand. The complexes are effective cytostatic agents against HCV29T, A549 and CACO-2 tumor lines.

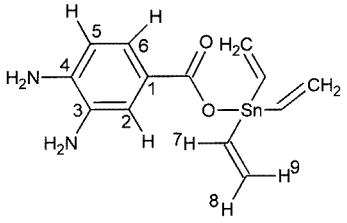
Experimental Section

Materials and Methods

Compounds: 3,4-diaminobezoic acid was obtained from Aldrich, 2-[4-(dimethylamino)phenylazo]benzoic acid from POCH (Poland), diphenyltin dichloride and divinyltin dichloride from Strem and used without further purification. Diphenyltin oxide, triphenyltin oxide, and divinyltin oxide were prepared from diphenyltin dichloride, triphenyltin chloride, and divinyltin dichloride with sodium hydroxide in aqueous ethanol solution. Syntheses were carried out under nitrogen. Infrared spectra (KBr pellets) were recorded with a Bruker IFS 113v, and ^{1}H NMR spectra were recorded with a Bruker AMX 300 and a Bruker Avance 500. C,H,N analyses were performed with a Perkin−Elmer 2400 CHN analyzer, and Sn was determined using ICP-AES with an ARL 3410.

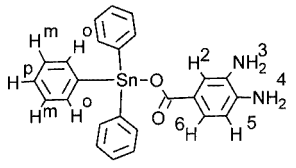
Synthesis of Complexes

$[Sn(CH=CH_2)_3\{OOCC_6H_3(NH_2)_2$-3,4$\}]$ (1): A suspension of $Sn(CH=CH_2)_2O$ (0.75 g, 3.95 mmol) and $HOOCC_6H_3(NH_2)_2$ (0.60 g, 3.95 mmol) in ethanol (10 mL) was refluxed with stirring for 5 h. The dark-brown solid was filtered and the filtrate was concentrated to dryness. The dry residue was extracted with chloroform. The light beige solid was filtered. The filtrate was concentrated and the obtained solid was crystallized from hot toluene. The light brown product $[Sn(CH=CH_2)_3\{OOCC_6H_3(NH_2)_2$-3,4$\}]$ (**1**) was filtered and washed with cold toluene. Yield 0.32 g (46%). $C_{13}H_{16}N_2O_2Sn$ (350.95): C 44.49, H 4.59, N 7.98, Sn 33.82; found: C 44.06, H 4.50, N 7.65, Sn 33.43. Single crystals were grown by concentration of a toluene solution of the compound. IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3412 s (ν_{NH2}), 3348 s (ν_{NH2}), 3048 w (ν_{CH}), 2984 w (ν_{CH}), 2940 w (ν_{CH}), 1614 vs (ν_{COO}), 1599 s ($\nu_{C=C}$), 1590 s, 1584 s, 1570 s, 1556 vs (ν_{COO}), 1520 s, 1442 m, 1396 s, 1362 vs (ν_{COO}), 1332 vs(ν_{COO}),1304 vs, 1248 vs, 1152 m, 1096 w, 1004 s, 956 s, 904 w, 820 m, 784 s, 648 m, 588 m, 542 m (ν_{SnC}), 498 m (ν_{SnC}), 451 m, 389 m. ^{1}H NMR ($CDCl_3$, ppm): δ = 7.50 [dd, $^3J(H^5H^6)$ = 8.1, $^4J(H^2H^6)$ = 1.8 Hz, H^6], 7.43 (d, H^2), 6.65 [d, H^5], 6.59 [dd, $^3J(H^7H^8)$ = 13.5, $^3J(H^7H^9)$ = 20.4, $^2J(^{119/117}SnH^7)$ = 125.9/120.4 Hz, H^7], 6.32 [dd, $^2J(H^8H^9)$ = 2.6, $^3J(^{119/117}SnH^8)$ = 236.2/226.0 Hz, H^8], 5.96 [dd, $^3J(^{119/117}SnH^9)$ = 115.9/110.9 Hz, H^9], 3.47, 3.69 (2s, H^3, H^4). ^{1}H NMR [$(CD_3)_2CO$, ppm]: δ = 7.60 [dd, $^3J(H^5H^6)$ = 8.3, $^4J(H^2H^6)$ = 1.9 Hz, H^6], 7.20 (d, H^2), 6.74 (d, H^5), 6.62 [dd, $^3J(H^7H^8)$ = 13.6, $^3J(H^7H^9)$ = 20.4, $^2J(^{119/117}SnH^7)$ = 129.0/122.9 Hz, H^7], 6.26 [dd, $^2J(H^8H^9)$ = 2.9, $^3J(^{119/117}SnH^8)$ = 239.5/228.2 Hz, H^8], 6.01 [dd, $^3J(^{119/117}SnH^9)$ = 114.9/109.9 Hz, H^9], 3.47, 3.69 (H^3, H^4). ^{119}Sn NMR [$(CD_3)_2CO$, ppm]: δ = −167.9.

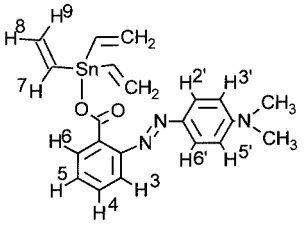


$[Sn(C_6H_5)_3\{OOCC_6H_3(NH_2)_2$-3,4$\}]\cdot 0.5C_6H_5CH_3$ (2). Method a: A mixture of $Sn(C_6H_5)_2O$ (0.58 g, 2.01 mmol) and $HOOCC_6H_3(NH_2)_2$ (0.31 g, 2.03 mmol) in toluene/ethanol (3:1) (10 mL) was refluxed with stirring for 4 h. The light brown solid was filtered. The yellow filtrate was slowly concentrated giving yellow crystals of complex **2**. The solid was washed with cold ethanol and dried in vacuo. Yield 0.32 g (56%). $C_{28,5}H_{26}N_2O_2Sn$ (547.24): C 62.55, H 4.79, N 5.12, Sn 21.69; found C 62.50, H 4.85, N 5.40, Sn 22.02. Single crystals for X-ray investigations were prepared by slow concentration of a toluene/ethanol solution of the complex. **Method b:** A mixture of $\{Sn(C_6H_5)_3\}_2O$ (0.716 g, 1.0 mmol) and $HOOCC_6H_3(NH_2)_2$ (0.31 g, 2.03 mmol) in ethanol (15 mL) was refluxed with stirring for 0.3 h. The red-brown solution was filtered. The filtrate was concentrated, giving a yellow polycrystalline precipitate of complex **2**. The solid was recrystallized from toluene and washed with cold ethanol and dried in vacuo. Yield 0.652 g (65%). IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3408 s (ν_{NH2}), 3320 s (ν_{NH2}), 3295 w (ν_{NH2}), 3250 w (ν_{NH2}), 3200 w (ν_{NH2}), 3075 w (ν_{CH}), 3070 w (ν_{CH}), 3064 w (ν_{CH}), 1632 s (δ_{NH2}), 1600 vs (ν_{COO}), 1572 vs, (ν_{COO}), 1518 s, 1480 s, 1446 w 1430 vs, 1368 vs (ν_{COO}), 1334 vs (ν_{COO}),1300 vs, 1246 vs, 1192 w, 1152 s, 1112 w, 1076 s, 1060 w, 1024 w, 956 vw, 898 w, 836 m, 778 s, 732 vs, 700 vs, 658 s, 620 w (r-mode SnC), 588 w (r-mode SnC), 512 m, 468 w, 452 m (y-mode SnC), 442 s (y-mode SnC), 402 m. $C_{28,5}H_{26}N_2O_2Sn$ (547.24): C 62.55, H 4.79, N 5.12, Sn 21.69; found C 62.40, H 4.65, N 5.30, Sn 21.92. ^{1}H NMR ($CDCl_3$, ppm): δ = 7.78−7.84 [m, $^3J(^1H$-$^{119/117}Sn)$ = 63.6 Hz, H^o], 7.60 [dd, $^3J(H^5H^6)$ = 8.1, $^4J(H^2H^6)$ = 1.8 Hz, H^6], 7.50 (d, H^2), 7.43−7.49 (m, $H^{m,p}$), 7.29 [H^m(toluene)], 7.19 [$H^{o,p}$(toluene)], 6.63 (d, H^5), 3.38, 3.69 (2s, $H^{3,4}$), 2.37 [s, CH_3(toluene)]. ^{13}C NMR ($CDCl_3$, ppm): δ = 173.34 (COO), 140.39 (C^4) 138.88 , [$^1J(^{13}C$-$^{119/117}Sn)$ = 651.0/621.8 Hz, C^i], 136.88 [$^2J(^{13}C$-$^{119/117}Sn)$ = 48.0 Hz, C^o], 133.20 (C^3), 129.93 [$^4J(^{13}C$-$^{119/117}Sn)$ = 13.0 Hz, C^p], 128.78 [$^3J(^{13}C$-$^{119/117}Sn)$ = 62.7 Hz, C^m], 124.49 (C^6), 120.91 (C^1), 119.46 (C^2), 114.73 (C^5); toluene: 137.82 (C^i), 128.99 (C^o), 128.19 (C^m), 125.26 (C^p), 21.41 (CH_3). ^{13}C NMR [$(CD_3)_2CO$, ppm]: δ = 172.14 (COO), 141.79 (C^4), 140.69 (C^i), 137.65 [$^2J(^{13}C$-$^{119/117}Sn)$ = 47.5 Hz, C^o], 134.61 (C^3), 130.61 [$^4J(^{13}C$-$^{119/117}Sn)$ = 13.2 Hz, C^p], 129.50 [$^3J(^{13}C$-$^{119/117}Sn)$ = 64.4 Hz,C^m], 123.57 (C^6), 119.71 (C^1),

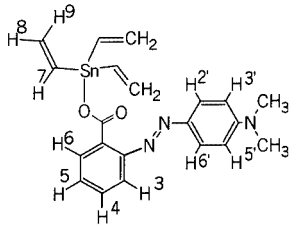
118.43 (C^2), 114.24 (C^5); toluene: 129.73 (C^o), 129.01 (C^m) 126.09 (C^p), 21.43 (CH_3). ^{119}Sn NMR ($CDCl_3$, ppm): δ = −118.9, [$(CD_3)_2CO$, ppm]: δ = −123.1.



[$Sn(C_6H_5)_3${OOC-2-C_6H_4N=$NC_6H_4N(CH_3)_2$-4}] (3). Method a: A mixture of $Sn(C_6H_5)_2O$ (0.58 g, 2.01 mmol) and 2-[4-(dimethylamino)phenylazo]benzoic acid [$HOOCC_6H_4N$=$NC_6H_4N(CH_3)_2$-4] (0.58 g, 2.01 mmol) in ethanol (15 mL) was refluxed with stirring for 4 h. The red solid was filtered. The red filtrate was slowly concentrated, giving red crystals of complex **3**. The solid was washed with cold hexane and dried in vacuo. Yield 0.32 g (50%). $C_{33}H_{29}N_3O_2Sn$ [$Sn(C_6H_5)_3${OOC-2-C_6H_4N=$NC_6H_4N(CH_3)_2$-4}] (618.33): C 64.10, H 4.73, N 6.80, Sn 19.20; found C 64.80, H 4.95, N 7.15, Sn 18.85. **Method b:** A mixture of $\{Sn(C_6H_5)_3\}_2O$ (0.716 g, 1.0 mmol) and) and 2-[(4-dimethylamino)phenylazo]benzoic acid [$HOOCC_6H_4N$=$NC_6H_4N(CH_3)_2$-4] (0.54 g, 2.01 mmol) in ethanol (15 mL) was refluxed with stirring for 0.3 h. The red solution was filtered. The red filtrate was slowly concentrated, giving a red product. The solid was washed with cold hexane and dried in vacuo. Yield 0.841 g (68%). $C_{33}H_{29}N_3O_2Sn$ [$Sn(C_6H_5)_3${OOC−2-C_6H_4N=$NC_6H_4N(CH_3)_2$-4}] (618.33): C 64.10, H 4.73, N 6.80, Sn 19.20; found C 64.40, H 4.85, N 7.04, Sn 18.94. IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3068 w (ν_{CH}), 3048 w, 3020 vw, 1640 m, 1600 vs (ν^{as}_{COOH}), 1560 w, 1520 s, 1480 m, 1442 w, 1432 m, 1416 w, 1406 m, 1366 vs (ν^{s}_{COOH}), 1340 s (ν^{s}_{COOH}), 1312 m, 1276 w, 1250 w, 1232 w, 1190 vw, 1144 vs, 1088 w, 1076 w, 1020 vw, 996 wm, 944 m, 860,w, 820 ms, 784 w, 760 m, 746 w, 736 s, 726 s, 696 s, 676 w 636 w (r-mode SnC), 610 vw (r-mode SnC), 590 vw (r-mode SnC), 570 vw, 546 m, 510 wvw, 494 vw, 464 w, 457 m (y-mode SnC), 444 m (y-mode SnC), 390 w. ^1H NMR (CD_3OD, ppm): δ = 7.78−7.86 [m, $^3J(^1H$-$^{119/117}Sn)$ = 63 Hz, H^o], 7.62 [d, $^3J(H^{2'}H^{3'})$ = 9.1 Hz, $H^{2'}$ + $H^{6'}$], 7.48−7.59 (m, H^3 + H^6), 7.30−7.46 (m, H^4 + H^5 + H^m + H^p), 6.71 [d, $^3J(H^{5'}H^{6'})$ = 9.1 Hz, $H^{3'}$ + $H^{5'}$], 3.08 (s, CH_3). ^{13}C NMR ($CDCl_3$, ppm): δ = 174.47 (COO), 152.88 (C^2), 152.43 ($C^{4'}$), 143.89 ($C^{1'}$), 138.48 [$^1J(^{13}C$-$^{119/117}Sn)$ = 644.6/618.5 Hz, C^i], 136.99 [$^2J(^{13}C$-$^{119/117}Sn)$ = 48.0 Hz, C^o], 131.50 (C^1, C^4), 130.31 (C^6), 129.91 [$^4J(^{13}C$-$^{119/117}Sn)$ = 13.0 Hz, C^p], 128.76 [$^3J(^{13}C$-$^{119/117}Sn)$ = 63.5 Hz, C^m], 128.06 (C^5), 125.48 ($C^{2'}$, $C^{6'}$), 118.36 (C^3), 111.36 ($C^{3'}$, $C^{5'}$), 40.25 (NCH_3). ^{13}C NMR (CD_3OD, ppm): δ = 173.25 (COO), 154.45 (C^2), 152.54 ($C^{4'}$), 144.76 ($C^{1'}$), 140.12 (C^i), 137.76 [$^2J(^{13}C$-$^{119/117}Sn)$ = 48.1 Hz, C^o], 132.57 (C^1), 131.62 (C^4), 130.36 (C^p), 130.05 (C^6), 129.58 (C^m), 129.11 (C^5), 126.62 ($C^{2'}$, $C^{6'}$), 118.23 (C^3), 112.63 ($C^{3'}$, $C^{5'}$), 40.45 (NCH_3). ^{119}Sn NMR ($CDCl_3$, ppm): δ = −108.6.



[$Sn(CH$=$CH_2)_3${OOC-2-C_6H_4N=$NC_6H_4N(CH_3)_2$-4}] (4): A mixture of $Sn(CH$=$CH_2)_2O$ (0,38 g, 2.0 mmol) and 2-[4-(dimethylamino)phenylazo]benzoic acid $HOOCC_6H_4N$=$NC_6H_4N(CH_3)_2$-4 (0.54 g, 2.0 mmol) in ethanol (15 mL) was refluxed with stirring for 4 h. The red solid was filtered. The red filtrate was concentrated, giving a red solid that was crystallized from a hot dioxane/toluene mixture (1:4, v/v). Red needles of complex **4** were separated and washed with diethyl ether and dried in vacuo. Yield 0.22 g (47%). $C_{21}H_{23}N_3O_2Sn$ [$Sn(CH$=$CH_2)_3${OOC-2-C_6H_4N=$NC_6H_4N(CH_3)_2$-4}] (468.15): C 53.88, H 4.95, N 8.98, Sn 25.36; found C 53.40, H 4.65, N 9.05, Sn 24.69. IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3070 vw (ν_{CH}), 3065 vw (ν_{CH}), 3040 vw (ν_{CH}), 2980 w (ν_{CH}), 2936 w (ν_{CH}), 2860 vw (ν_{CH}), 2800 vw (ν_{CH}), 1602 vs (ν^{as}_{COO}), 1560 ms, 1546 ms, 1526 s, 1482 m 1465 w, 1452 vw, 1442 wm, 1420 ms, 1400 s, 1366 vs (ν^{s}_{COO}), 1338 w, 1312 s,1276 ms, 1248 w, 1230 m1196 vw, 1148 vs, 1112 ms, 1092 m, 1060 w, 1040 vw, 998 m, 944 ms, 880 vw, 860 vw, 830 w, 820 s, 790 vw, 766 ms, 747 vw, 730 w, 688 w672 wm, 636 wm, 618 vw, 580 w, 544 s, 520 wm (ν_{SnC}), 496 m (ν_{SnC}), 426 vw, 416 w, 390 w, 385 w. ^1H NMR ($CDCl_3$, ppm): δ = 7.81 [d, $^3J(H^{2'}H^{3'})$ = 8.9 Hz, $H^{2'}$ + $H^{6'}$], 7.27−7.67 (m, H^3 + H^4 + H^5 + H^6), 6.73 (d, $H^{3'}$ + $H^{5'}$), 6.56 [dd, $^3J(H^7H^8)$ = 13.5, $^3J(H^7H^9)$ = 20.2, $^2J(^{119/117}SnH^7)$ = 128.2/125.6 Hz, H^7], 6.32 [dd, $^2J(H^8H^9)$ = 2.5, $^3J(^{119/117}SnH^8)$ = 236.6/225.2 Hz, H^8], 5.95 [dd, $^3J(^{119/117}SnH^9)$ = 114.2/109.2 Hz, H^9], 3.14 (s, CH_3). ^1H NMR [$(CD_3)_2CO$, ppm]: δ = 7.83 [d, $^3J(H^{2'}H^{3'})$ = 8.9 Hz, $H^{2'}$ + $H^{6'}$], 7.35−7.65 (m, H^3 + H^4 + H^5 + H^6), 6.83 (d, $H^{3'}$ + $H^{5'}$), 6.59 [dd, $^3J(H^7H^8)$ = 13.6, $^3J(H^7H^9)$ = 20.4 Hz, H^7], 6.23 [dd, $^2J(H^8H^9)$ = 3.0 Hz, H^8], 5.99 (dd, H^9), 3.11 (s, CH_3). ^1H NMR [$(CD_3)_2SO$, ppm]: δ = 7.73 [d, $^3J(H^{2'}H^{3'})$ = 8.9 Hz,$H^{2'}$ + $H^{6'}$], 7.33−7.50 (m, H^3 + H^4 + H^5 + H^6), 6.79 (d, $H^{3'}$ + $H^{5'}$), 6.50 [dd, $^3J(H^7H^8)$ = 13.3, $^3J(H^7H^9)$ = 20.2, $^2J(^{119/117}SnH^7)$ = 132.1/127.4 Hz, H^7], 6.14 [dd, $^2J(H^8H^9)$ = 3.1 Hz, $^3J(^{119/117}SnH^8)$ = 244.5/234.2 Hz, H^8], 5.92 [dd, $^3J(^{119/117}SnH^9)$ = 122.2/116.0 Hz, H^9], 3.05 (s, CH_3). ^{13}C NMR ($CDCl_3$, ppm): δ = 173.53 (COO), 152.38 (C^2), 151.28 ($C^{4'}$), 143.95 ($C^{1'}$), 137.79 (C^8), 135.95 [$^1J(^{13}C$-$^{119/117}Sn)$ = 600.2/574.9 Hz, C^7], 133.58 (C^1), 130.62 (C^4), 129.22 (C^6), 128.26 (C^5), 125.60 ($C^{2'}$, $C^{6'}$), 116.68 (C^3), 111.26 ($C^{3'}$, $C^{5'}$), 40.29 (NCH_3). ^{119}Sn NMR [$(CD_3)_2CO$, ppm]: δ = −168.9.



X-ray Crystallographic Study: All measurements were performed at low temperature using an Oxford Cryosystem device with a Kuma KM4CCD κ-axis diffractometer with graphite-monochromated Mo-K_α radiation (Table 8). The crystal was positioned at 65 mm from the CCD camera. 612 frames were measured at 0.75Θ intervals with a counting time of 20 s. Accurate cell parameters were determined and refined by least-squares fit of the strongest reflections. The data were corrected for Lorentz and polarization effects. No absorption correction was applied. Data reduction and analysis were carried out with the Oxford Diffraction, Poland (formerly Kuma Diffraction Wrocław, Poland), programs. The structure was solved by direct methods (program SHELXS-97[27]) and refined by the full-matrix least-squares method on all F^2 data using the SHELXL-97[28] programs. Non-hydrogen atoms were refined with anisotropic vibrational parameters; hydrogen atoms were included from the geometry of the molecules and Δρ maps and were refined with isotropic vibrational parameters. CCDC-176692, -176693, and -176694 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge at www.ccdc.cam.ac.uk/conts/retrieving.html or from the Cambridge

Table 8. Crystal data and structure refinement for complexes [Sn(CH=CH$_2$)$_3${OOCC$_6$H$_3$(NH$_2$)$_2$-3,4}] (**1**), [Sn(C$_6$H$_5$)$_3${OOCC$_6$H$_3$(NH$_2$)$_2$-3,4}]·0.5C$_6$H$_5$CH$_3$ (**2**·0.5C$_6$H$_5$CH$_3$), and [Sn(C$_6$H$_5$)$_3${OOC-2-C$_6$H$_4$N=NC$_6$H$_4$N(CH3)$_2$-4}] (**3**)

	1	**2**·0.5C$_6$H$_5$CH$_3$	**3**
Empirical formula	$C_{13}H_{16}N_2O_2Sn$	$C_{25}H_{22}N_2O_2Sn{\cdot}0.5C_6H_5CH_3$	$C_{33}H_{29}N_3O_2Sn$
Formula mass	350.97	547.20	618.28
T [K]	100(2)	100(2)	100(2)
λ [Å]	0.71073	0.71073	0.71073
Crystal system	monoclinic	monoclinic	triclinic
Space group	$C2/c$	$P2_1/c$	$P\bar{1}$
a [Å]	20.137(3)	15.4320(19)	7.958(2)
b [Å]	8.0714(15)	9.3788(12)	8.719(2)
c [Å]	19.020(3)	17.510(2)	21.162(4)
α [°]	90	90	88.20(3)
β [°]	117.04(3)	102.291(10)	87.58(3)
γ [°]	90	90	76.72(3)
V [Å^3]	2753.4(8)	2476.3(5)	1427.4(6)
Z	8	4	2
$D_{calcd.}$ [Mg·m^{-3}]	1.693	1.468	1.438
μ [mm^{-1}]	1.852	1.059	0.929
F(000)	1392	1108	628
Crystal size [mm]	0.15 × 0.15 × 0.12	0.14 × 0.12 × 0.08	0.15 × 0.10 × 0.10
Diffractometer	Kuma KM4CCD	Kuma KM4CCD	Kuma KM4CCD
θ range [°]	3.31−28.42	3.47−28.41	3.21−28.44
Ranges of h,k,l	−26/26, −10/6, −25/25	−19/20, −12/12, −23/14	−10/6, −11/11, −28/28
Reflections collected	8935	15971	9924
Independent reflections (R_{int})	3151(0.0436)	5788(0.0268)	6270(0.0584)
Data/parameters	3151/227	5788/355	6270/469
GOF(F^2)	1.079	1.078	0.910
Final R_1/wR_2 ind.($I > 2\sigma_I$)	0.0313/0.0777	0.0389/0.0981	0.0453/0.0568
Largest difference peak/hole [e· Å^{-3}]	1.568/−1.412	1.982/−1.852	0.616/−0.585

Crystallographic Data Centre, 12, Union Road, Cambridge CB2 1EZ, UK [Fax: (internat.) + 44-1223/336-033; E-mail: deposit@ccdc.cam.ac.uk].

Cytostatic Activity in vitro: Human cell lines HCV29T, A549 (lung adenocarcinoma) and CACO-2 were used for the proliferation assay. The experiments were repeated in triplicate for each tested Sn compound concentration. Statistical significance was tested using Student's t-test ($p < 0.05$ was considered statistically significant). The in vitro tests against all cell lines were performed as described previously.[29−31] The results of cytotoxic activity in vitro were expressed as ID_{50} − the dose of compound that inhibits proliferation rate of the tumor cells by 50% as compared with untreated control cells.

Acknowledgments

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[1] E. Wong, C. M. Giandomenico, *Chem. Rev.* **1999**, *99*, 2451.
[2] M. J. Clarke, F. Zhu, D. R. Frasca, *Chem. Rev.* **1999**, *99*, 2511.
[3] F. Huber, R. Barbieri, in: *Metal Complexes in Cancer Chemotherapy* (Ed.: B. Keppler), VCH, Weiheim, New York, **1993**, p. 351.
[4] M. Nath, S. Pokharia, R. Yadav, *Coord. Chem. Rev.* **2001**, *215*, 99.
[5] M. Gielen, *Coord. Chem. Rev.* **1996**, *151*, 41.
[6] M. Gielen, M. Biesemans, D. de Vos, R. Willem, *J. Inorg. Biochem.* **2000**, *79*, 139, and references therein.
[7] R. Willem, A. Bouhdid, B. Mahieu, L. Ghys, M. Biesemans, E. R. T. Tieking, D. de Vos, M. Gielen, *J. Organomet. Chem.* **1997**, *531*, 151.
[8] M. Gielen, A. Bouhdid, F. Kayser, M. Biesemans, D. de Vos, B. Mahieu, R. Willem, *Appl. Organomet. Chem.* **1995**, *9*, 251.
[9] J. Tao, W. Xiao, Q. Yang, *J. Organomet. Chem.* **1997**, *531*, 223.
[10] J. J. Bonire, S. P. Fricker, *J. Inorg. Biochem.* **2001**, *83*, 217.
[11] D. de Vos, R. Willem, M. Gielen, K. E. van Wingerden, K. Nooter, *Met.-Based Drugs* **1998**, *5*, 179.
[12] M. Kemmer, M. Gielen, M. Biesemans, D. de Vos, R. Willem, *Met.-Based Drugs* **1998**, *5*, 189.
[13] J. Li, Y. Ma, R. Liu, J. Li, *Appl. Organomet. Chem.* **2001**, *15*, 227.
[14] E. R. T. Tiekink, M. Gielen, A. Bouhdid, R. Willem, V. I. Bregadze, L. V. Ermanson, S. A. Glazun, *Met.-Based Drugs* **1997**, *4*, 75.
[15] M. Gielen, K. Handlir, M. Hollein, D. de Vos, *Met.-Based Drugs* **2000**, *7*, 233.
[16] E. R. T. Tiekink, *Appl. Organomet. Chem.* **1991**, *5*, 1.
[17] Z. Ciunik, G. R. Desiraju, *Chem. Commun.* **2001**, 703−704].
[18] Z. Ciunik, S. Jarosz, *J. Mol. Struct.* **1998**, *442*, 115.
[19] E. Maslowsky, *Vibrational Spectra of Organometallic Compounds*, J. Wiley, New York, **1977**.
[20] J. Holeček, M. Nádvornik, K. Handliř, A. Lyčka, *J. Organomet. Chem.* **1983**, *241*, 177.
[21] A. Lyčka, J. Holeček, M. Nádvornik, K. Handliř, *J. Organomet. Chem.* **1985**, *280*, 323.
[22] E. Vincent, L. Verdonck, l. Naessens, G. P. van der Kelen, *J. Organomet. Chem.* **1984**, *277*, 235.
[23] J. Holeček, K. Handliř, M. Nádvornik, S. M. Teleb, A. Lyčka, *J. Organomet. Chem.* **1988**, *339*, 61.
[24] B. Wrackmeyer, *Annu. Rep. NMR Spectrosc.* **1999**, *38*, 203.
[25] *MOPAC2000*, Version 1.06, Fujitsu Limited, **1999**.
[26] M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, V. G. Zakrzewski, J. A. Montgomery, Jr., R. E. Stratmann, J. C. Burant, S. Dapprich, J. M. Millam, A. D. Daniels, K. N. Kudin, M. C. Strain, O. Farkas, J.

Tomasi, V. Barone, M. Cossi, R. Cammi, B. Mennucci, C. Pomelli, C. Adamo, S. Clifford, J. Ochterski, G. A. Petersson, P. Y. Ayala, Q. Cui, K. Morokuma, D. K. Malick, A. D. Rabuck, K. Raghavachari, J. B. Foresman, J. Cioslowski, J. V. Ortiz, A. G. Baboul, B. B. Stefanov, G. Liu, A. Liashenko, P. Piskorz, I. Komaromi, R. Gompers, R. L. Martin, D. J. Fox, T. Keith, M. A. Al-Laham, C. Y. Peng, A. Nanayakkara, M. Challacombe, P. M. W. Gill, B. Johnson, W. Chen, M. W. Wong, J. L. Andres, C. Gonzales, M. Head-Gordon, E. S. Replogle, J. A. Pople, *Gaussian 98, Revision A.9*, Gaussian, Inc., Pittsburgh, PA, **1998**.

[27] G. M. Sheldrick, *SHELXS-97, Program for solution of crystal structures*, University of Göttingen, **1997**.

[28] G. M. Sheldrick, *SHELXL-97, Program for crystal structure refinement*, University of Göttingen, **1997**.

[29] F. P. Pruchnik, D. Duś, *J. Inorg. Biochem.* **1996**, *61*, 55.

[30] F. P. Pruchnik, R. Starosta, Z. Ciunik, A. Opolski, J. Wietrzyk, E. Wojdat, D. Duś, *Can. J. Chem.* **2001**, *79*, 868.

[31] F. P. Pruchnik, M. Bańbuła, Z. Ciunik, H. Chojnacki, B. Skop, M. Latocha, T. Wilczok, *J. Inorg. Biochem.* **2002**, *90*, 149.

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