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Di-*n*-butyltin aminoarylcarboxylates: structure, properties and *in vitro* antitumor activity

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The properties and structures of the tetranuclear dibutyltin complexes $[Sn_4(\mu_3\text{-}O)_2(C_4H_9\text{-}n)_8\{OOCC_6H_3(NH_2)_2\text{-}3,4\}_4]$ (1), $[Sn_4(\mu_3\text{-}O)_2(C_4H_9\text{-}n)_8\{OOCC_6H_3(NH_2)_2\text{-}3,5\}_4]$ (2), $[Sn_4(\mu_3\text{-}O)_2(C_4H_9\text{-}n)_8\{OOC\text{-}2\text{-}C_6H_4N{=}NC_6H_4N(CH_3)_2\text{-}4\}_4]$ (3) are described. Complex 3 adopts a structure with a tetranuclear $Sn_4(\mu_3\text{-}O)_2$ core. All tin atoms are five-coordinate and form bonds with three oxygen atoms and two butyl ligands. Two carboxylates are bridging and two are terminal ligands. IR and NMR spectra indicate that the same structure is adopted by complexes 1 and 2. The molecular and electronic structures of complex 1 of C_i symmetry have been studied using the semi-empirical PM3 formalism. The calculated structure and bond distances agree with X-ray data. All complexes are effective antitumor agents.

KEYWORDS: organotin complexes; antitumor agents; crystal structure

INTRODUCTION

Coordination and organometallic compounds comprise an important class of antitumor agents. Platinum complexes show significant activity against several human cancers: testicular, ovarian, bladder, head and neck, lung (small cell and non-small cell), cervical, breast, sarcomas and brain.[1] However, the severe side-effects of cisplatin and other platinum complexes (nephrotoxicity, neurotoxicity, etc.) prompted a search for new drugs with high activity and decreased side-effects.[2–4] A number of organotin compounds have been shown to be active against various types of cancer. A number of organotin dipeptide compounds have displayed modest antitumor activity.[2–4] A number of compounds [$SnR_2X_2L_2$; R = organic group, X = halide or pseudohalide, L_2 = a nitrogen ligand (py) or a bidentate nitrogen ligand (bpy, phen, en, etc.)] have been tested and they have also shown modest antitumor activity.[2–4] Many di-*n*-butyl, tri-*n*-butyl and triphenyltin carboxylates display interesting antitumor activities.[5–12] However, the solubility of diorgano- and triorgano-tin carboxylates in water and water–ethanol is poor. Therefore, many organotin compounds with carboxylato ligands containing polar substituents, mainly hydroxo and oxo groups, have been prepared and studied.[5–12] However, only a few tin carboxylates with amino groups have been investigated. These complexes comprise pyridinocarboxylato and aminosalicylato diorganotin compounds,[5] which are also effective antitumor agents. Recently, organotin compounds with mepirizol (an anti-inflamatory agent),[13] cyclic amide-acid,[14] derivatives of dodecaborane-carboxylates[15] and cysteaminates[16] have been studied and their antitumor activities determined. Here, we report the synthesis, properties, structure and *in vitro* antitumor activity of dibutyltin complexes with 3,4-diaminobenzoate, 3,5-diaminobenzoate, and 2-[4-(dimethylamino)phenylazo]-benzoate.

EXPERIMENTAL

Materials and measurements

The compounds 3,4-diaminobenzoic acid and 3,5-diaminobenzoic acid were obtained from Aldrich, 2-[4-(dimethylamino)phenylazo]benzoic acid was from POCH (Poland) and di-*n*-butyltin oxide was from Strem and were used

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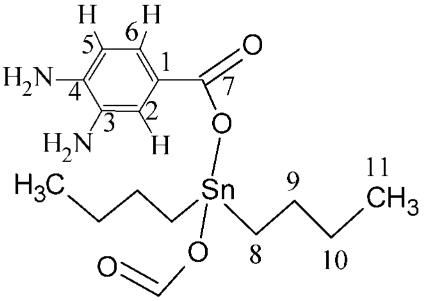
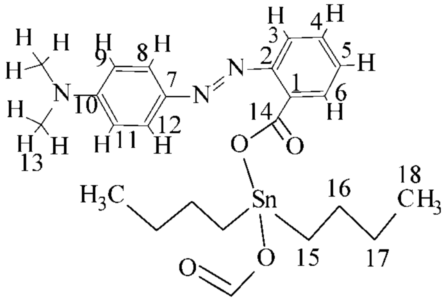


Scheme 1. Labeling of compounds **1** and **2**.



Scheme 2. Labeling of compound **3**.

without further purification. Syntheses were carried out in a nitrogen atmosphere. Infrared spectra (KBr pellets) were recorded on a Bruker IFS 113v and ^{1}H spectra were taken on Bruker AMX 300 and Avance 500 spectrometers. The percentage of tin was determined using an inductively coupled plasma-atomic emission spectroscopy method on an ARL 3410.

Syntheses

$[Sn_4(\mu_3\text{-}O)_2(C_4H_9\text{-n})_8\{OOCC_6H_3(NH_2)_2\text{-}3,4\}_4]$ (**1**)

A suspension of $Sn(C_4H_9\text{-}n)_2O$ (2.4894 g, 10^{-2} mol) and $HOOCC_6H_3(NH_2)_2$ (1.5215 g, 10^{-2} mol) in ethanol (25 cm^3) was refluxed with stirring for 1 h. The orange–red solution was filtered and the filtrate was evaporated to one-third of the initial volume. The solution was cooled to 0 °C and the yellow–orange product was washed with diethyl ether and dried in vacuo. Yield: 2.274 g, 58%. Anal. Found: C, 45.77; H, 6.35; N, 6.98; Sn, 30.63. Calc. for $C_{60}H_{100}N_8O_{10}Sn_4$: C, 45.95; H, 6.43; N, 7.14, Sn 30.28%.

IR (KBr, cm^{-1}): 3360 vs (ν_{NH}), 3260 (ν_{NH}), 2956 vs (ν^{as}_{CH}), 2924 s (ν^{as}_{CH}), 2868 m (ν^{s}_{CH}), 1624 vs (ν^{as}_{COO}), 1596 vs (ν^{as}_{COO}), 1570 vs (ν^{as}_{COO}), 1550 vs (ν^{as}_{COO}), 1530 vs, 1520 vs, 1460 m, 1440 s, 1390 vs (ν^{s}_{COO}), 1360 vs (ν^{s}_{COO}), 1338 vs (ν^{s}_{COO}), 1302 vs, 1244 s, 1150 s, 1080 m, 1018 w, 950 w, 884 m, 865 w, 824 m, 782 s, 675 m, 640 s, 632 s, 620 s, 550 w, 510 w, 440 m, 400 m, 382 w.

^{1}H NMR ($CDCl_3$), δ, ppm: H^2, 7.45 (s); H^6, 7.41 (d, $^3J(H^5H^6) = 7.8$ Hz); H^5, 6.68 (d); H^3, H^4, 3.80 (s), 3.58 (s), 3.37 (s); H^8, H^9, 1.53–1.74 (m); H^{10}, 1.22–1.38 (m); H^{11}, 0.75–0.86 (m). **^{13}C NMR** ($CDCl_3$), δ, ppm: C^1, 123.98; C^2, 118.94; C^3, 133.80; C^4, 140.07; C^5, 114.91; C^6, 123.36; C^7, 173.39; C^8, 29.44 ($^1J(^{119/117}Sn\text{–}^{13}C) = 735.3/701.7$ Hz), 27.76 ($^1J(^{119/117}Sn\text{–}^{13}C) = 685.6/657.6$ Hz); C^9, 28.19, 27.81; C^{10}, 27.27, 27.19; C^{11}, 13.79. **^{119}Sn NMR** ($CDCl_3$), δ, ppm: −189.5, −215.6. See Scheme 1 for atom labeling.

The complexes with 3,5-diaminobenzoate, and 2-[4-(dimethylamino)phenylazo]benzoate were prepared analogously.

$[Sn_4(\mu_3\text{-}O)_2(C_4H_9\text{-n})_8\{OOCC_6H_3(NH_2)_2\text{-}3,5\}_4]$ (**2**)

Yield: 3.39 g, 87%. Anal. Found: C, 45.72; H, 6.28; N, 7.05, Sn 29.88. Calc. for $C_{60}H_{100}N_8O_{10}Sn_4$: C, 45.95; H, 6.43; N, 7.14, Sn 30.28%.

IR (KBr, cm^{-1}): 3352 s (ν_{NH}), 3224 m (ν_{NH}), 3050 vw (ν^{Ar}_{CH}), 2956 vs (ν^{as}_{CH}), 2928 vs (ν^{as}_{CH}), 2868 s (ν^{s}_{CH}), 1620 vs (ν^{as}_{COO}), 1588 vs (ν^{as}_{COO}), 1552 vs (ν^{as}_{COO}), 1464 m, 1412 vs (ν^{s}_{COO}), 1376 vs (ν^{s}_{COO}), 1338 m, 1306 s, 1188 s, 1160 m, 1080 m, 1002 m, 992 m, 872 m, 852 m, 784 s, 678 s, 636 s, 592 s, 496 m, 428 m.

^{1}H NMR ($CDCl_3$), δ, ppm: H^2_t, 6.86 (s); H^2_b, H^6_b, 6.74 (d, $^4J(H^2H^4) = 1.6$ Hz); H^6_t, 6.70 (s); H^4_t, 6.19 (s); H^4_b, 6.17 (s); H^3_t, H^5_t, 3.73 (s); H^3_b, H^5_b, 3.66 (s); H^8, H^9, 1.52–1.75 (m); H^{10}, 1.25–1.41 (m); H^{11}, 0.77–0.92(m); (t: terminal carboxylato ligand; b: bridging carboxylato ligand). **^{1}H NMR [$(CD_3)_2SO$]**, δ, ppm: H^2, H^6, 6.41 (d, $^4J(H^2H^4) = 1.6$ Hz); H^4, 5.99 (s); H^3, H^5, 4.90 (s); H^8, 1.53–1.80 (m); H^9, H^{10}, 1.20–1.50 (m); H^{11}, 0.72–0.92(m). **^{13}C NMR ($CDCl_3$)**, δ, ppm: C^1, 135.36; C^2, C^6, 107.28; C^3, C^5, 148.10; C^4, 104.90; C^7, 173.27; C^8, 29.73 ($^1J(^{119/117}Sn\text{–}^{13}C) = 718.6/686.8$ Hz), 27.92 ($^1J(^{119/117}Sn\text{–}^{13}C) = 683.6/649.4$ Hz); C^9, 28.21, 27.80; C^{10}, 27.27, 27.18; C^{11}, 13.78. **^{119}Sn NMR** ($CDCl_3$), δ, ppm: −191.4, −215.0. See Scheme 1 for atom labeling.

$[Sn_4(\mu\text{-}O)_2(C_4H_9\text{-n})_8\{OOC\text{-}2\text{-}C_6H_4N{=}NC_6H_4N(CH_3)_2\text{-}4\}_4]$ (**3**)

Yield: 3.717 g, 73%. Anal. Found: C, 53.94; H, 6.00; N, 8.11. Calc. for $C_{92}H_{128}N_{12}O_{10}Sn_4$: C, 54.25; H, 6.33; N, 8.25%.

IR (KBr, cm^{-1}): 3058 vw (ν_{CH}), 2952 s (ν_{CH}), 2932 s (ν_{CH}), 2868 w (ν_{CH}), 1636 s (ν^{as}_{COO}), 1602 vs (ν^{as}_{COO}), 1558 s (ν^{as}_{COO}), 1520 m, 1444 w, 1418 m (ν^{s}_{COO}), 1404 s (ν^{s}_{COO}), 1366 vs (ν^{s}_{COO}), 1344 s (ν^{s}_{COO}), 1312 m, 1252 m, 1230 w, 1144 vs, 1088 m, 948 m, 820 s, 760 m, 670 w, 634 m, 544 m, 518 w, 488 w, 400 w.

^{1}H NMR ($CDCl_3$) (243 K), δ, ppm: H^8, H^{12}, 7.86 (d, $^3J(H^8H^9) = 7.3$ Hz); H^6, 7.53, (d, $^3J(H^5H^6) = 7.9$ Hz); H^3, 7.50 (d, $^3J(H^3H^4) = 7.4$ Hz); H^4, 7.40 (t, $^3J(H^3H^4) = {}^3J(H^4H^5) = 7.3$ Hz); H^5, 7.28 (t); H^9, H^{11}, 6.66 (d); H^{13} 3.0 (s); H^{15} and H^{16}, 1.37–1.72 (m); H^{17}, 1.22 (tq, $^3J(H^{16}H^{17}) = {}^3J(H^{17}H^{18}) = 7.2$ Hz) and 1.06 (tq); H^{18}, 0.75 (t) and 0.66 (t). **^{13}C NMR ($CDCl_3$)** (243 K), δ, ppm: C^1, 127.7; C^2, 152.0; C^3, 116.3; C^4, 130.12; C^5, 128.4; C^6, 134.0; C^7, 143.3; C^8 and C^{12}, 125.2; C^9 and C^{11}, 110.87; C^{13}, 40.3; C^{14}, 173.9; C^{15}, 27.98 ($^1J(^{119/117}Sn\text{–}^{13}C) = 701.5/667.3$ Hz), 27.23 ($^1J(^{119/117}Sn\text{–}^{13}C) =$

690.1/657.6 Hz); C^{16}, 27.21, 27.07; C^{17}, 26.80, 26.75; C^{18}, 13.76, 13.71. **^{119}Sn NMR (CDCl$_3$)**, δ, ppm: −198.3, −203.2. See Scheme 2 for atom labeling.

X-ray crystallographic measurements

All measurements of crystals were performed at low temperature using an Oxford Cryosystem device on a Kuma KM4CCD κ-axis diffractometer with graphite-monochromated Mo Kα radiation. The crystal was positioned at 65 mm from the KM4CCD camera. 612 frames were measured at 0.75° intervals with a counting time of 30 s. Accurate cell parameters were determined and refined by least-squares fit of 3500 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 SHELXS97,[17] and refined by the full-matrix least-squares method on all F^2 data using the SHELXL97 programs.[18] Non-hydrogen atoms were refined with anisotropic thermal parameters; hydrogen atoms were included from the geometry of molecules and $\Delta\rho$ maps but were not refined. The $\Delta\rho$ maps revealed two conformations of the symmetry-independent n-butyl chains. The disorder was taken into account during refinement of the structure. Parameters of all disordered carbon atoms were refined including their occupancy factors (OF). The C(4) atom (OF = 0.57) and the C(4A) were refined with anisotropic displacement parameters. The C(5), C(6), C(7), and C(8) atoms (OF = 0.91), and C(14), C(15), and C(16) atoms (OF = 0.82) were refined with anisotropic displacement parameters, but minor components were refined isotropically.

Crystallographic data for the structure of compound **3** reported in this paper have been deposited at the Cambridge Crystallographic Data Centre and allocated the deposition number CCDC 167023. Copies of this information may be obtained free of charge from the Director, CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: +44-1223-336033; e-mail: deposit@ccdc.cam.ac.uk; or web: http://www.ccdc.cam.ac.uk).

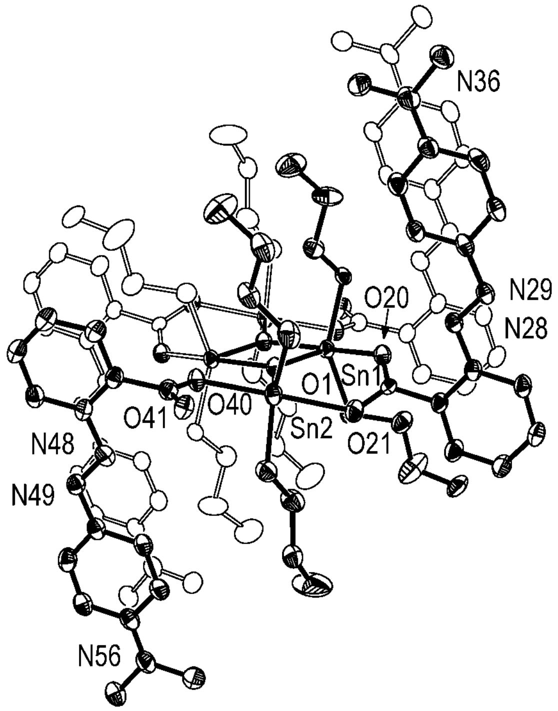


Figure 1. The molecular structure of complex **3**.

Computational details

The molecular and electronic structures of the complex [Sn$_4$(μ-O)$_2$(C$_4$H$_9$-n)$_8${OOCC$_6$H$_3$(NH$_2$)$_2$-3,4}$_4$] (see Fig. 2) of C_i symmetry have been studied with semi-empirical methods using the PM3 MOPAC2000.[19] The numerical calculations were performed, in part, in the Wrocław Networking and Supercomputing Center.

Cytotoxic activity *in vitro*

The human cell lines A549 (lung adenocarcinoma) and HSMC (vascular human smooth muscle cells) were used for the proliferation assay. The cells were seeded at a density of 5×10^3 cells/well on the 96-well microplate. The A549 tumor cells were grown in RPMI-1640 medium with 10% fetal bovine serum (FBS) supplemented with 1% antibiotic–antimycotic solution at 37 °C, in 5% CO$_2$ in air. Vascular smooth muscle cells were cultured in DMEM with 10% FBS and 1% antibiotic–antimycotic solution. The next day the media were removed and replaced with fresh media (RPMI or DMEM, as appropriate) and cells were incubated for a further 24 h. Then the cells were incubated by the addition of 200 μl/well media with 5% FBS and organotin complexes **1, 2** and **3** at a final concentration of 10^{-5}–10^{-7} M. The stock solutions of the organometallic compounds of tin at a concentration of 10^{-4} M were prepared in 70% ethanol. The control cells culture was performed in standard media enriched with adequate dilution of 70% ethanol.

After 72 h, at the end of the experiment the culture media were aspirated and the wells were washed with phosphate-buffered saline (PBS). The cells were the basic material for an estimation of the proliferation according to the CyQUANT Cell Proliferation Assay Kit (Molecular Probe) procedure. The assay was based on dye fluorescence enhancement upon binding to cellular nucleic acids. The fluorescence was measured using a WALLAC 1420 VICTPOR$^{2™}$ (Perkin Elmer) multilabel plate counter with filters for 480 nm excitation and 535 nm emission. The analyses were repeated in triplicate for each tin compound concentration tested. Statistical significance was tested using Student's t-test ($p < 0.05$ was considered statistically significant). The results of cytotoxic activity *in vitro* were expressed as ID$_{50}$ (the dose

Table 1. Crystal data and structure refinement for $[Sn_4(\mu_3\text{-}O)_2(C_4H_9\text{-}n)_8\{OOCC_6H_4N{=}NC_6H_4N(CH_3)_2\text{-}4\}_4]$ (**3**)

Empirical formula	$C_{92}H_{128}N_{12}O_{10}Sn_4$
Formula weight	2036.82
T/K	100 (2)
λ/Å	0.710 73
Crystal system	Monoclinic
Space group	$P2_1/n$
a/Å	17.002 (3)
b/Å	14.714 (3)
c/Å	20.095 (4)
β/°	100.652 (15)
V/Å^3	4940.5 (15)
Z	2
D_c/Mg m^{-3}	1.369
μ/mm^{-1}	1.058
F (000)	2088
Crystal size/mm^3	0.16 × 0.12 × 0.10
Diffractometer	Kuma KM4CCD
θ range for data collection/°	3.4–28.6
Ranges of h, k, l	$-22 \rightarrow 22$, $-19 \rightarrow 19$, $-26 \rightarrow 26$
Reflections collected	61 004
Independent reflections (R_{int})	11 858 (0.0690)
Data/parameters	11 858/580
Goodness-of-fit (F^2)	1.174
Final R_1/wR_2 indices ($I > 2\sigma_I$)	0.081/0.215
Largest diff. peak/hole/e$^-$ Å^{-3}	2.773/−1.420

Table 2. Selected bond distances and angles for $[Sn_4(\mu_3\text{-}O)_2(C_4H_9\text{-}n)_8\{OOCC_6H_4N{=}NC_6H_4N(CH_3)_2\text{-}4\}_4]$ (**3**)

Bond distances (Å)		Bond angles (°)	
Sn (1)−O (1)	2.055 (4)	O (1)−Sn (1)−C (1)	103.3 (2)
Sn (1)−C (1)	2.126 (6)	O (1)−Sn (1)−C (5)	111.5 (2)
Sn (1)−C (5)	2.148 (6)	C (1)−Sn (1)−C (5)	144.1 (3)
Sn (1)−O (1a)	2.165 (4)	O (1)−Sn (1)−O (1a)	75.71 (17)
Sn (1)−O (20)	2.308 (4)	C (1)−Sn (1)−O (1a)	100.4 (2)
Sn (2)−O (1)	2.031 (4)	C (5)−Sn (1)−O (1a)	96.1 (2)
Sn (2)−C (9)	2.105 (7)	O (1)−Sn (1)−O (20)	88.59 (15)
Sn (2)−C (13)	2.142 (7)	C (1)−Sn (1)−O (20)	88.9 (2)
Sn (2)−O (40)	2.180 (4)	C (5)−Sn (1)−O (20)	83.9 (2)
Sn (2)−O (21)	2.252 (4)	O (1a)−Sn (1)−O (20)	163.17 (16)
O (1)−Sn (1a)	2.165 (4)	O (1)−Sn (2)−C (9)	116.9 (2)
C (1)−C (2)	1.534 (9)	O (1)−Sn (2)−C (13)	108.1 (3)
C (2)−C (3)	1.526 (11)	C (9)−Sn (2)−C (13)	134.6 (3)
C (3)−C (4)	1.390 (14)	O (1)−Sn (2)−O (40)	77.88 (16)
C (5)−C (6)	1.562 (9)	C (9)−Sn (2)−O (40)	96.1 (2)
C (6)−C (7)	1.510 (11)	C (13)−Sn (2)−O (40)	99.3 (2)
C (7)−C (8)	1.538 (14)	O (1)−Sn (2)−O (21)	90.83 (16)
C (9)−C (10)	1.497 (10)	C (9)−Sn (2)−O (21)	83.7 (2)
C (10)−C (11)	1.553 (10)	C (13)−Sn (2)−O (21)	89.6 (2)
C (11)−C (12)	1.483 (12)	O (40)−Sn (2)−O (21)	167.30 (17)
O (20)−C (21)	1.258 (7)	Sn (2)−O (1)−Sn (1)	134.18 (19)
O (21)−C (21)	1.254 (7)	Sn (2)−O (1)−Sn (1a)	121.33 (19)
C (21)−C (22)	1.492 (7)	Sn (1)−O (1)−Sn (1a)	104.29 (17)

of compound that inhibits proliferation rate of the tumor cells by 50% compared with control untreated cells). The *in vitro* tests against HCV29T cell line were performed as described previously.[20,21]

RESULTS AND DISCUSSION

The X-ray crystallography study revealed that compounds **1** and **3** have structure characteristic for compounds of the general formula $[Sn_4(\mu_3\text{-}O)_2R_8(OOCR')_4]$.[22] Crystallographic data for **3** are given in Table 1, and Table 2 contains selected bond lengths and angles. The ORTEP view of **3** is depicted in Fig. 1.

The structure is built up around a planar centrosymmetric Sn_2O_2 fragment. Tin atoms in complex **3** have a distorted trigonal bipyramidal coordination. The endocyclic tin atoms of the Sn_2O_2 unit are connected to the bridging μ$_3$-O atoms, the bridging carboxylato ligand and to the two *n*-butyl ligands. The oxo ligand and the oxygen atom of the carboxylato group occupy trans coordination sites. The exocyclic tin atoms are bound with μ$_3$-O ligands, two oxygen atoms of bridging and terminal carboxylato ligands and two *n*-butyl groups. The $Sn_4(\mu_3\text{-}O)_2$ unit is nearly planar. This is confirmed by the torsional angles Sn2−O1−Sn1−O1a and Sn2−O1−Sn1a−O1a, which are 174.6(4)° and −175.6(4)° respectively. The intramolecular Sn1−O40 ($1-x$, $-y$, $-z$) (2.745(4) Å) and Sn2−O41 (2.946(4) Å) distances are too long to assume a significant bonding interaction between these atoms; however, they can play an important role in stabilization of the structure of this complex. The intermolecular Sn−O distances are very long because of the bulkiness of the *n*-butyl ligands and substituents connected with carboxylato groups. The structure of complex **1** with 3,4-diaminobenzoate is analogous; however, the quality of single crystals was not good enough to obtain interatomic distances of the desired accuracy. The crystals of this compound are triclinic, and the space group is $P\bar{1}$. Two symmetry-independent centrosymmetric molecules are in the unit cell. The bond distances in complex **1** are similar to those in complex **3**.

The IR spectra of all complexes investigated are consistent with the X-ray data for compounds **1** and **3**. The presence of $\nu_{as}(COO)$ above 1600 cm^{-1} and large $\Delta\nu = \nu^{as}_{COO} - \nu^{s}_{COO}$ values are consistent with the presence in complexes **1, 2** and **3** of both bridging and monodentate carboxylato ligands. Thus, IR spectra indicate that complex **2** has the same type of structure as compounds **1** and **3**. The relatively low frequencies of the ν(N−H) stretching vibration con-

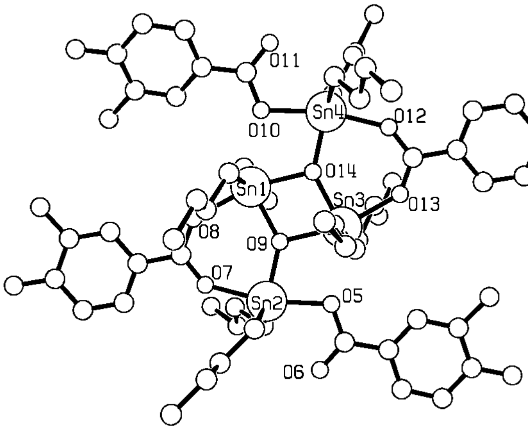


Figure 2. Molecular structure of complex **1** after its geometry optimization at the PM3 level.

firm the formation of N—H···N and N—H···O hydrogen bonds.

The ^{1}H chemical shift ranges of the butyl and carboxylato ligands were deduced from resonance intensities and $^nJ(^1H–^1H)$ coupling constants. The chemical shifts and the coupling constants for complexes **1–3** both agree well with the data found for the 3,4-diaminobenzoic, 3,5-diaminobenzoic and 2-(4-dimethylaminophenylazo) benzoic acids and their metal salts and with spectra of other tetranuclear complexes $[Sn_4(\mu_3\text{-}O)_2R_8(OOCR')_4]$.[23–26] The ^{1}H chemical shifts of the 3,4-diaminobenzoato and 3,5-diaminobenzoato ligands are similar to those of the 3,4-diaminobenzoic and 3,5-diaminobenzoic acids; however, the signals of the *ortho* protons to the carboxylato and diazo groups in complex **3** (H^3 and H^6 in Scheme 2) are shifted to higher fields by *ca* 0.8 ppm and 0.4 ppm respectively, in comparison with 2-(4-dimethylaminophenylazo)benzoic acid. The same tetranuclear structure of the complexes **1, 2** and **3** was also confirmed by ^{13}C and ^{119}Sn NMR. In the spectra of all complexes, pairs of signals for C^{15}, C^{16} and C^{17} atoms of butyl groups have been observed. In the case of complex **3** the two signals were also found for methyl groups of the butyl ligands (C^{18} atoms). The $^1J(^{119}Sn–^{13}C)$ coupling constants assume values in the range 701.5–735.5 Hz for carbon atoms with ^{13}C NMR signals at higher chemical shifts (27.98–29.73 ppm) and 686.8–701.7 Hz in the case of atoms showing signals at lower chemical shifts (27.23–27.92 ppm). The $^1J(^{117}Sn–^{13}C)$ coupling constants agree well with values calculated from the gyromagnetic ratios of the ^{119}Sn and ^{117}Sn atoms. The values of the coupling constants are similar to those found for other $[Sn_4(\mu_3\text{-}O)_2Bu_8(OOCR)_4]$. The same dichotomy was observed in the case of the ^{119}Sn NMR spectra. Two signals with the same intensities and chemical shifts typical for tetranuclear tin complexes have been observed.[23–26] The chemical shifts are equal to −189.5 and −215.6 ppm, −191.4 and −215.0 ppm and −198.3 and −203.2 ppm for complexes **1, 2** and **3** respectively.

Table 3. *In vitro* antitumor activities of complexes **1**, **2** and **3** against A549 and HCV29T cancers

Compound	ID$_{50}$/μM A549	ID$_{50}$/μM HCV29T
1	5	0.02
2	0.5	0.02
3	2	0.005
(SP-4-2)-$[PtCl_2(NH_3)_2]$		2.4

The molecular and electronic structures of the complex $[Sn_4(\mu\text{-}O)_2(C_4H_9\text{-}n)_8\{OOCC_6H_3(NH_2)_2\text{-}3,4\}_4]$ (Fig. 2) of C_i symmetry has been studied using semi-empirical methods. The PM3 MOPAC2000 package was used in our calculations.[19] The geometry optimization was performed at the PM3 level with a basis set of 428 molecular orbitals. The HOMO and LUMO energies are −8.513 eV and −0.833 eV respectively. The evaluated PM3 Sn1—O10, Sn1—O10a, Sn1—O4, Sn2—O10, Sn2—O1 and Sn2—O3 interatomic distances are 2.040 Å, 2.105 Å, 2.188 Å, 2.013 Å, 2.136 Å and 2.122 Å, whereas the relevant experimental values are 2.042 Å, 2.169 Å, 2.276 Å, 2.022 Å, 2.170 Å and 2.195 Å respectively. The calculated molecular structure is very similar to that determined crystallographically. The ionization energy is equal to 8.543 eV and the heat of formation was estimated to be −2032.86 kJ mol^{-1}. The results indicate that the used method can probably be applied for calculation of the interaction of these compounds with nucleotides and oligonucleotides to understand better the cytostatic activity of polynuclear organotin compounds.

Complexes **1, 2** and **3** are efficient cytostatic agents (Table 3). Their cytostatic activity is higher than or comparable with that of cisplatin. Compound **2** is more active against the A549 line than complexes **1** and **3**; however, the activity of all complexes against HCV29T is much higher. Compound **3** is exceptionally active. These compounds are promising antitumor agents because they are soluble in ethanol and aqueous ethanol, contrary to most other organotin carboxylates.

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