APPLIED ORGANOMETALLIC CHEMISTRY
Appl. Organometal. Chem. 2006; **20**: 463–470
Published online 19 June 2006 in Wiley InterScience
(www.interscience.wiley.com) DOI:10.1002/aoc.1083

Synthesis, characterization and *in vitro* cytotoxic effects of new organotin(IV)-2-maleimidopropanoates

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Received 16 February 2006; Revised 28 February 2006; Accepted 28 March 2006

Synthesis, spectral properties and *in vitro* cytotoxic behaviour of five new diorganotin(IV) complexes having general composition R'_2SnR_2 [R′ = 2-maleimidopropanoic acid and R = Me(1), Et(2), *n*-Bu(3), Ph(4), Bz(5)] have been investigated. Various spectroscopic methods like solid-state FT IR, ^{119m}Sn Mössbauer and solution-state multinuclear NMR (^{1}H, ^{13}C and ^{119}Sn) have been employed for structural elucidation. In the solid state, $[R_2Sn(IV)]^{2+}$ moieties interacted with carboxylate group of the ligand in octahedral arrangement, while in the solution state 1–3 showed hyper-coordination and 4 and 5 were tetrahedral. All these results were consistent with elemental analysis and MS data. These complexes were also screened for *in vitro* anti-tumour, anti-leishmanial and anti-fungal activities, and structure–activity relationship have been proposed. Copyright © 2006 John Wiley & Sons, Ltd.

KEYWORDS: 2-maleimidopropanoic acid; diorganotin(IV) esters; anti-tumour, anti-leishmanial; anti-fungal

INTRODUCTION

Organometallics generally and organotin(IV) complexes particularly are a very important class of compounds being actively investigated as possible anti-tumour drugs.[1–4] Although platinum, its complexes and other transition metal complexes exhibit promising anti-tumour activity, most are severely toxic.[5,6] On the other hand, much work is going on to synthesize new metal-based drugs with fewer side-effects.[7–17] Since the introduction of biologically active ligands, complexes like N-protected amino acids that enhance the anti-cancer activity of organotin(IV) have attracted considerable attention.[15–35] In spite of the fact that 2-maleimidopropanoic acid is a bio-active ligand, its diorganotin(IV) complexes have not yet been reported and require detailed investigation. It is interesting to synthesize and examine *in vitro* bio-potential and structure–activity relationships of such complexes.

RESULTS AND DISCUSSION

Compounds **1–6** are non-hygroscopic, stable at room temperature for approximately 10 months, non-crystalline, with good yields (77–88%) and soluble in most organic solvents. The elemental analysis data presented in Table 1 are in good agreement with the calculated percentages of C, H, N and Sn for all the synthesized complexes and the ligand (Scheme 1).

Solid-state FT IR and ^{119m}Sn Mössbauer spectroscopic results

IR data of **1–6** are collected in Table 2. Diagnostically important vibrational bands like $\nu(COO)_{asym}$, $\nu(COO)_{sym}$, $\nu(Sn–C)_{asym}$, $\nu(Sn–C)_{sym}$ and $\nu(Sn–O)$ were assigned in the spectral range 1700–400 cm^{-1}. A broad band at 3500–2500 cm^{-1} for –COOH was observed only in **6**.[36] $\Delta\nu(-COO^-)$ values for **6**, its salt and **1–5** reflected bidentate coordination in *trans*-octahedral arrangement [Fig. 1(a)].[26–30] The C–O–Sn bond was confirmed from the decrease in ν(C–O) by 50 cm^{-1}. ν(Sn–O) vibrational bands were seen in the range of 497–442 cm^{-1} for **1–5** and a sharp peak at 450 cm^{-1} a characteristic of Sn–Ph linkage in **4**.[37] ^{119m}Sn Mössbauer parameters indicated the presence of one hexa-coordinated organotin(IV) moieties (Table 3). The isomer shift (IS) of **1–5** fell in the range 1.07–1.33 mm s^{-1} lower than parent organotin moieties, which can be attributed to rehybridization of Sn(IV) atom to higher coordination in the complexes.[23,30] Sham and Bancroft model yielded C–Sn–C angle for **1–5** > 145°, and $\rho > 2$ supporting an octahedral arrangement, which is in agreement with the structural hypothesis based upon the FT IR study [Fig. 1(a)].[24,38]

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Contract/grant sponsor: Gomal University; Contract/grant number: 717-29/DF/GU.

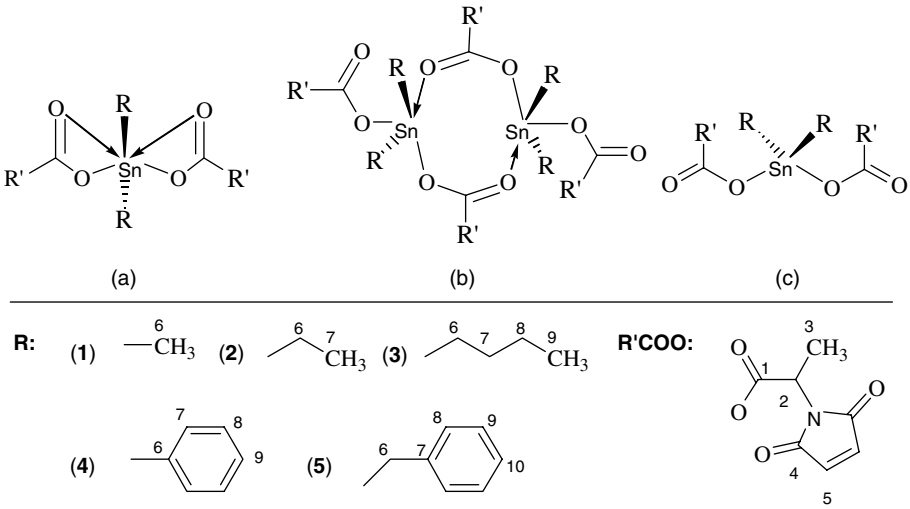
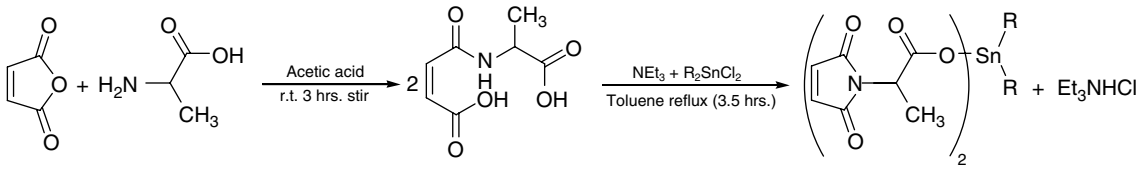


Figure 1. (a) Octahedral geometry; (b) penta-coordination of Sn(IV); (c) tetrahedral geometry and numbering scheme for NMR.



Scheme 1.

Table 1. Physical and analytical data for complexes **1–5** and the ligand **6**

Cpd.	Molecular formula	M.P. (°C)	Yield (%)	Elemental analysis calculated (found)			
				%C	%H	%N	%Sn
1	$C_{16}H_{18}N_2O_8Sn$	158	81	39.62(39.60)	3.74(3.70)	5.78(5.75)	24.47(24.45)
2	$C_{18}H_{22}N_2O_8Sn$	74	77	42.14(42.12)	4.32(4.30)	5.46(5.44)	23.14(23.11)
3	$C_{22}H_{30}N_2O_8Sn$	>350	83	46.42(46.40)	5.31(5.28)	4.92(4.90)	20.86(20.83)
4	$C_{26}H_{22}N_2O_8Sn$	142	86	51.26(51.24)	3.64(3.62)	4.60(4.58)	19.49(19.45)
5	$C_{28}H_{26}N_2O_8Sn$	93	88	52.78(52.75)	4.11(4.09)	4.40(4.38)	18.63(18.60)
6	$C_7H_7NO_4$	118	84	49.71(49.68)	4.17(4.15)	8.28(8.26)	—

Table 2. FT IR Analysis for complexes **1–5** and ligand **6** (cm^{-1})

Compound	$\nu(COO)_{asym}$	$\nu(COO)_{sym}$	$\Delta\nu$	$\nu(Sn-C)_{asym}$	$\nu(Sn-C)_{sym}$	$\nu(O-Sn)$
1	1625	1440	185	513	503	466
2	1643	1480	163	510	502	442
3	1605	1445	160	535	509	497
4	1583	1427	156	555	510	450
5	1591	1433	158	550	508	481
6	1695	1411	284	—	—	—

Solution state ^{1}H-, ^{13}C- and ^{119}Sn-NMR spectroscopic results

^{1}H- and ^{13}C NMR spectra of **1–6** produced close similarity to N-protected amino acids, indicating 1 : 2 (metal-to-ligand) stoichiometry in solution.[26–30] $^1J[^{119}Sn-^{13}C]$, $^2J[^{119}Sn-^1H]$ values for **1** were inserted in Lockhart's equation, and based on the results a distorted octahedral geometry was assigned [Fig. 1(a)].[39] However, ^{119}Sn-NMR spectra of the same complex showed a broad singlet at −152.5 ppm, proving the existence of an equilibrium between penta-

DOI: 10.1002/aoc

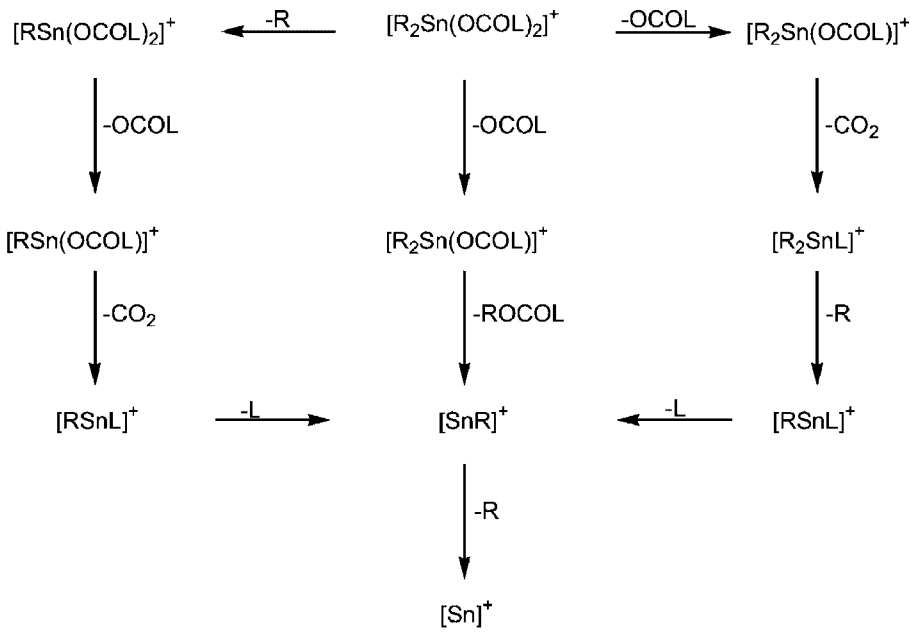


Figure 2. General mass spectral fragmentation pattern for complexes **1–5**.

and hexa-coordinated state at room temperature, thereby describing a skew-trapezoidal geometry.[39,40] ^{1}J, ^{2}J and ^{119}Sn chemical shift (−159.1 and −134.4 ppm) values for **2** and **3** suggested penta coordinated Sn(IV) dimeric complexes, bridged through the C═O group of the ligand [Fig. 1(b)].[40] The trend $[^{1'}J] \gg [^{2'}J] < [^{3'}J]$ and ^{119}Sn chemical shift of **4** and **5** (−71.8 and −13.2 ppm) proved tetra-coordination of Sn(IV) in tetrahedral arrangement [Fig. 1(c)]. The difference in geometry of the complexes in solution can be attributed to the size of the R groups.[26–30,41,42]

MS data

A general fragmentation pattern is given in Fig. 2. In the 70 eV EI mass spectrum, the base peak for **1, 2, 3** and **5** was due to the $[LSnR_2]^+$ fragment at m/z 317, 345, 441, 469 respectively, and to the $[L_2SnR]^+$ fragment at m/z 512 in **4**.[43]

Bioactivity

The complexes and the ligand were tested *in vitro* for their bioavailability, against seven human tumoural cell lines, five leishmanial strains and nine human pathogenic fungi. Table 4 lists the concentration that inhibits 50% of the cell growth (ID_{50}) for 2-maleimidopropanoic acid (**6**) and its tin(IV) complexes (**1–5**) against MCF-7 mammary cancer, EVSA-T mammary cancer, WiDr colon cancer, IGROV ovarian cancer, M19 melanoma, MEL A498 renal cancer and H226 lung cancer of human tumour origin along with the corresponding values of ID_{50} for the clinically used drugs doxorubicin, cisplatin, 5-fluorouracil, methotrexate and etopside for comparison. All the complexes displayed significant activities in comparison

Table 3. ^{119m}Sn Mössbauer spectral data for complexes **1–5** (mm s^{-1})

Compound	QS	IS	Γ_1	Γ_2	ρ = QS/IS
1	3.42	1.21	0.99	0.97	2.82
2	3.55	1.07	0.98	0.89	3.31
3	3.69	1.17	0.92	0.87	3.15
4	3.27	1.31	0.83	0.92	2.49
5	3.63	1.33	0.95	0.90	2.72

Table 4. *In vitro* inhibition doses ID_{50} (ng/ml) of compounds **1–6** against seven tumoural cell lines of human origin

	A498	EVSAT	H226	IGROV	M19	MCF7	WiDr
1	141	265	360	202	107	234	147
2	156	137	133	120	143	89	211
3	178	161	256	87	44	104	111
4	43	62	47	231	38	40	214
5	66	89	140	84	17	36	71
6	235	28	285	169	148	301	283
Do	28	44	68	107	23	35	62
Cp	1432	658	471	478	321	214	105
5-Fu	2214	325	164	205	301	54	82
Mt	3094	210	65	25	212	100	64
Et	514	531	438	328	155	84	103

Cell lines: A498 (renal cancer), EVSA-T (mammary cancer), H226 (lung cancer), IGROV (ovarian cancer), M19 (melanoma), MCF-7 (mammary cancer) and WiDr (colon cancer). *Reference drugs*: Do (doxorubicin), Cp (cisplatin), 5-Fu (5-fluorouracil), Mt (methotrexate) and Et (Etopside).

DOI: 10.1002/aoc

Table 5. *In vitro* effect of **1,2** and **3** (μg/ml) leishmanial strains in promastigote stage

	1		2		3	
Leishmanial strain	IC_{50}	IC_{100}	IC_{50}	IC_{100}	IC_{50}	IC_{100}
L. major	0.42 ± 0.01	0.74 ± 0.01	0.44 ± 0.01	1.08 ± 0.06	0.62 ± 0.01	0.96 ± 0.02
L major (Pak.)	0.40 ± 0.01	0.69 ± 0.02	0.52 ± 0.01	0.86 ± 0.02	0.24 ± 0.01	0.59 ± 0.02
L. tropica	0.56 ± 0.03	0.54 ± 0.02	0.40 ± 0.02	0.98 ± 0.02	0.22 ± 0.01	1.04 ± 0.02
L. mex mex	0.43 ± 0.01	0.66 ± 0.05	0.30 ± 0.01	0.73 ± 0.02	0.31 ± 0.01	1.57 ± 0.02
L. donovani	0.68 ± 0.02	1.12 ± 0.02	0.21 ± 0.01	0.94 ± 0.02	0.42 ± 0.01	0.62 ± 0.02

Table 6. *In vitro* effect of **4**, **5** and **6** (μg/ml) leishmanial strains in promastigote stage

	4		5		6	
Leishmanial strain	IC_{50}	IC_{100}	IC_{50}	IC_{100}	IC_{50}	IC_{100}
L. major	0.21 ± 0.01	0.68 ± 0.02	0.10 ± 0.01	0.88 ± 0.01	1.21 ± 0.01	0.99 ± 0.03
L major (Pak.)	0.10 ± 0.01	0.55 ± 0.02	0.11 ± 0.01	0.85 ± 0.01	0.69 ± 0.01	2.37 ± 0.01
L. tropica	0.32 ± 0.01	0.63 ± 0.02	0.07 ± 0.01	0.64 ± 0.01	0.74 ± 0.02	1.32 ± 0.02
L. mex mex	0.25 ± 0.01	0.64 ± 0.02	0.09 ± 0.01	0.94 ± 0.02	0.68 ± 0.01	1.68 ± 0.02
L. donovani	0.21 ± 0.01	0.94 ± 0.02	0.05 ± 0.01	1.35 ± 0.03	0.98 ± 0.01	3.44 ± 0.06

to the ligand and the reference drugs but **4** and **5** were found to be more potent.

Tables 5 and 6 represent concentrations of compounds **1–6** inducing 50% (IC_{50}) and 100% (IC_{100}) mortality for five leishmanial strains. It is quite evident from the data obtained that the complexes displayed significant activities in comparison to ligand. As shown in Tables 5 and 6, the concentrations of 3.44 μg/ml (**6**) and 1.57 μg/ml (**1–5**) were found to be leishmanicidal for all the leishmanial strains tested, whereas 50% of parasites of all the strains were found to be dead at average values of 1.21 μg/ml (**6**) and 0.94 μg/ml (**1–5**) after 72 h of treatment.

During the *in vitro* anti-fungal activity, promising results were observed. The complexes **1–5** were more effective than the ligand **6** (Tables 7–9). The order of *in vitro* anti-fungal effectiveness is **5** > **4** > **3** > **2** > **1** ≫ **6**. The effect of dose over percentage inhibition was plotted and from that graph; we determined the optimum dose by extrapolating the value up to the extent that further increase in dose does not affect the inhibition. The results so obtained have been displayed in Tables 7–9. The results show a similar trend as their toxicity. It was concluded that the higher the toxicity of a compound is, the lower the optimum dose.

Some workers have suggested that organotin(IV) compounds wield anti-tumour effects through binding to thiol groups of proteins;[44,45] in contrast, but in analogy to the behaviour of several cytotoxic organotin(IV) complexes, these may interact with DNA.[46–48] However, the cause of enhancement in cytotoxicity and the exact mechanism of action of such organotin(IV) complexes is still a question to be answered.

The average ID_{50} values have been plotted vs partition coefficient (Fig. 3) and it is interesting to note that the data

Table 7. *In vitro* anti-fungal effect of compounds **1** and **2** (μg/ml)

	Percentage inhibition (**1**)				Percentage inhibition (**2**)			
Name of fungi	50	25	10	5	50	25	10	5
Alternaria padwicki	58	57	22	12	62	48	19	6
Otryodiplodia theobromae 122	59	31	21	12	55	55	22	15
Colletotrichum mause	41	25	00	13	63	45	23	11
Colletotrichum mause 246	35	31	24	8	78	62	27	14
Colletotrichum mause 273	22	28	00	00	69	44	34	21
Colletotrichum gloeosprioides 282	20	36	7	9	55	43	36	22
Pestalotiposis guepini	47	28	23	14	41	33	18	8
Phytopohothora palmivora	45	27	21	23	54	35	19	3
Phytopohothora palmivora 139	38	32	11	8	63	44	25	13
Optimum dose	600				590			

of complexes **1–5** show that ID_{50} values decrease linearly with the increase in partition coefficient. It is certainly encouraging for us that the major controlling parameter seems to be P_{ow} (partition coefficient in an octanol/water system) or in other words the polarizibility of the R′–Sn bond is induced by R groups. It can be therefore concluded that, in complexes **1–5**, lipophilicity increases with the bulkiness

DOI: 10.1002/aoc

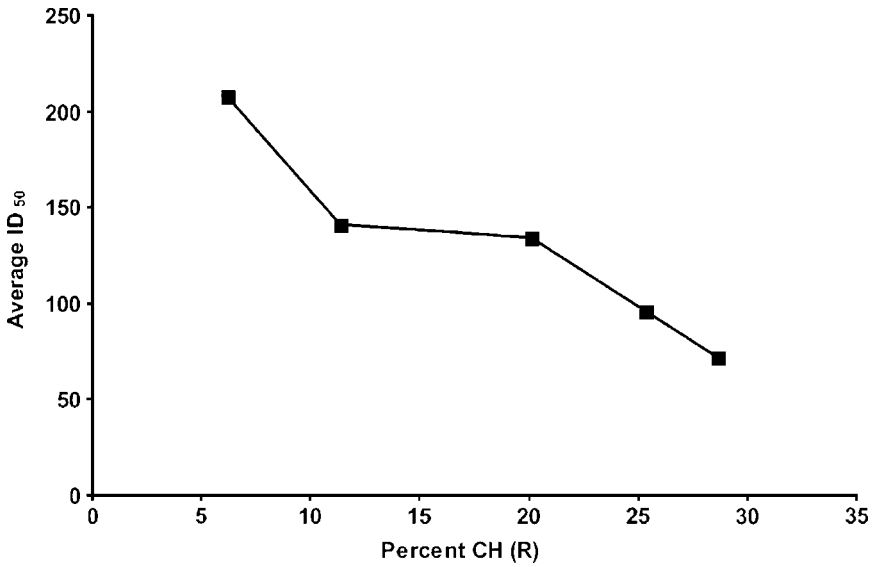


Figure 3. Dependence of *in vitro* anti-tumour ID_{50} on partition coefficients of complexes **1**–**5**.

Table 8. *In vitro* anti-fungal effect of compounds **3** and **4** (μg/ml)

	Percentage inhibition **(3)**				Percentage inhibition **(4)**			
Name of fungi	50	25	10	5	50	25	10	5
Alternaria padwicki	66	46	36	31	78	62	40	17
Otryodiplodia theobromae 122	62	66	44	20	71	55	23	16
Colletotrichum mause	54	63	33	33	88	53	25	00
Colletotrichum mause 246	49	41	47	20	78	45	00	23
Colletotrichum mause 273	63	37	25	21	76	66	36	18
Colletotrichum gloeosporioides 282	42	39	31	14	66	54	29	12
Pestalotiposis guepini	58	43	18	00	56	46	14	3
Phytopohothora palmivora	55	45	34	31	89	98	47	22
Phytopohothora palmivora 139	51	37	37	8	91	87	56	36
Optimum dose	580				540			

Table 9. *In vitro* anti-fungal effect of compounds **5** and **6** (μg/ml)

	Percentage inhibition (**5**)				Percentage inhibition (**6**)			
Name of fungi	50	25	10	5	50	25	10	5
Alternaria padwicki	77	87	49	43	55	00	13	00
Otryodiplodia theobromae 122	82	93	61	54	33	31	14	14
Colletotrichum mause	75	74	60	39	31	8	00	00
Colletotrichum mause 246	65	59	63	43	24	2	00	00
Colletotrichum mause 273	97	38	55	44	22	28	00	22
Colletotrichum gloeosporioides 282	81	84	75	55	21	11	5	31
Pestalotiposis guepini	88	74	47	43	00	10	11	2
Phytopohothora palmivora	91	79	56	39	7	00	00	00
Phytopohothora palmivora 139	82	68	64	44	20	3	00	3
Optimum dose	505				1110			

of R groups, which enhances the partition coefficient, thereby boosting the bioactivity. On the other hand, the use of 2-maleimidopropanoic acid as ligand increases the hydrophillicities of these complexes that might be responsible for such significant results. Moreover, the polarity of Sn–C is also of the same order (Bz > Ph > Bu > Et > Me). The nature of the attached R group, the polar character of the carboxylic group of 2-maleimidopropanoic acid and the partition coefficients are interlinked with each other and toxicity of the complexes. A study is being carried out for the *in vivo* interactions/mechanism of action of these complexes.

EXPERIMENTAL

Materials

2-Aminopropanoic acid, maleic anhydride, triethylamine, dimethyltin(IV) dichloride, dibutyltin(IV) dichloride, diphenyltin(IV) dichloride and diethyltin(IV) dichloride were

DOI: 10.1002/aoc

Sigma or Fluka products of analytical purity used as such, while dibenzyltin(IV) dichloride was prepared according to a reported procedure.[49] Solvents used during this work were dried as reported.[50]

Instrumentation

Elemental analyses (C, H, N) were performed on a Yanaco high-speed CHN analyser; antipyrene was used as a reference, while tin content was estimated according to the reported procedures.[51] Uncorrected melting point was measured on a Reichert Thermovar of F. G. Bode Co. Austria. The FT IR spectra of the pure solid samples were recorded on Bruker FT IR spectrophotometer TENSOR27(ZnSe) using OPUS software covering 5000–400 cm^{-1}. For Mössbauer measurements, the solid samples were maintained in liquid nitrogen at temperature 77.3 K, using a V. G. Micromass 7070 F Cryolid liquid nitrogen cryostat. The multi-channel calibration was performed with an enriched iron foil using a ^{57}Co–Pd source, while the zero point of the Doppler velocity scale was determined through the absorption spectra of $CaSnO_3$ (^{119}Sn = 0.5 mg cm^{-2}). The resulting 5 × 105 count spectra were refined to obtain the isomeric shift, IS (mm s^{-1}), the nuclear quadrupole splitting QS, ρ (mm s^{-1}) and the width at half-height of the resonant peaks, Γ (mm s^{-1}).

^{1}H and ^{13}C NMR spectra ($CDCl_3$) were recorded on a multinuclear Bruker Biospin AMX 300 MHz FT NMR spectrometer using 300 and 75 MHz at room temperature employing TMS as internal reference. ^{119}Sn NMR spectra in $CDCl_3$ were recorded at 186.50 MHz on a Bruker AMX 500 spectrophotometer using external neat $SnMe_4$ (δ^{119}Sn = 0 ppm), while EI mass spectra were recorded using a model MAT 112, double-focusing mass spectrometer (Finnigan).

Methods

Synthesis of 2-maleimidopropanoic acid

Maleic anhydride (10 g, 101.9782 mM) was dissolved in acetic acid (150 ml) and a cold solution of 2-aminopropanoic acid (9.0852 g, 101.9782 mM) in acetic acid (150 ml) was added to it. This mixture was stirred at room temperature for 3 h, resulting in a white precipitate. The white precipitate was washed three times with cold water and recrystallized from water to get maleamic acid of analytical purity. Maleamic acid (5 g, 26.7165 mM) was suspended in dry toluene (350 ml) and triethylamine (7.4806 ml, 53.433 mM) was added to this suspension and refluxed with rigorous stirring for 1.5 h with the concomitant removal of water using a Dean-Stark funnel. The solvent was removed on a rotary evaporator (Büchi) leaving a hygroscopic solid; HCl was added up to pH 2, extracted with ethyl acetate and dried over anhydrous $MgSO_4$. The ethyl acetate fraction was vacuum dried; the solid mass left was recrystallized from hexane.[52]

Synthesis of organotin(IV) complexes of 2-maleimidopropanoic acid

To a reaction flask containing a solution of triethylammonium salt of 2-maleimidopropanoic acid (0.5 g, 2.9563 mM) in dry toluene (75 ml), an appropriate amount of diorganotin(IV) dichloride was added and refluxed for 3.5 h. A turbid solution was filtered off and the filtrate was evaporated on a rotary evaporator. The solid mass was dissolved in a mixture of C_6H_6 and C_6H_{14} (1 : 2) and the compound was re-crystallized.

Partition coefficient

Partition coefficients of the reported complexes were determined in the octanol–water system. Briefly, the complexes were dissolved and diluted to 100 μM in *n*-octanol. Equal volumes of complex solution and water were shaken in vortex for 15 min and after centrifugation (4000 rpm for 15 min) the concentration of complex in the organic layer was analysed by means UV spectroscopy. The partition coefficient (P) is expressed as $P = [\text{Complex}]_o/[\text{Complex}]_w$, where $[\text{Complex}]_o$ and $[\text{Complex}]_w$ represent the total concentrations of the complex in the *n*-octanol and water layers, respectively, and lipophilicity may be defined as its log function (log P).

In vitro anti-tumour activity on human tumoural cell lines

Compounds **1–6** were screened *in vitro* against seven human cancer cell lines, i.e. MCF-7 mammary cancer, EVSA-T mammary cancer, WiDr colon cancer, IGROV ovarian cancer, M19 melanoma, MEL A498 renal cancer and H226 lung cancer, reference drugs used are doxorubicin (Do), cisplatin (Cp), 5-fluorouracil (5-Fu), methotrexate (Mt). The screening was performed with aqueous solutions containing 1% ethanol by a literature procedure.[53]

Anti-leishmanial activity

All the promastigote cultures of both the reference and local Pakistani leishmanial strains were maintained in blood agar-based bi-phasic Evan's modified Tobie's medium supplemented with RPMI-1640 with 25 mM TES at 25 °C. *Leishmanial* strains in promastigote stage that were used include *L. major* (JISH118), *L. major* (MHOM/PK/88/DESTO), *L. tropica* (K27), *L. infantum* (LEM3437), *L. mex mex* (LV4) and *L. donovani* (H43).

Viability test

Parasites in the promastigote stage were transferred from Evan's modified to RPMI-1640 supplemented with 5% fetal bovine serum, 1% sterile human urine and buffered with 25 mM TES, pH 7.2 (complete medium). They were grown in bulk at 25 °C. They were centrifuged at 2500 rpm for 10 min and early log phase promastigotes were collected. The parasites were washed twice with RPMI (without FBS or urine) and re-suspended in the complete medium to achieve a final concentration of 10^6 parasites/ml. In order to get the 100% and IC_{50} mortality concentration, serial dilutions of the test compounds were performed in 96-well microtiter plate. Subsequently, 10^5 promastigotes in 100 μl of culture medium were added to each well and the plate was incubated at 25 °C for 72 h. Negative controls (culture without Test compound)

DOI: 10.1002/aoc

were on the same plate. At the end of the incubation time the plate was shaken mechanically over a plane shaker and parasites were counted by the help of a hemocytometer. Dose-dependent viability curves were obtained.

Anti-fungal activity

The different concentrations (5, 10, 25 and 50 μg/ml) of test compounds **1–6** were used to study the effect on germination of human pathogenic fungi by the hanging drop method;[54,55] the fungi used were *Alternaria padwicki, Botryodiplodia theobromae* 122, *Colletotrichum mause, Colletotrichum mause* 246, *Colletotrichum mause* 273, *Colletotrichum gloeosporioides* 282, *Pestalotiposis guepini, Phytopohothora palmivora* and *Phytopohothora palmivora* 139. The germination of spores was observed under the microscope after 8 h of incubation. The percentage inhibition of spore germination was calculated as:

$$\text{Percentage of inhibition on spore germination} = \frac{\text{No. of ingerminated spores}}{\text{Total no. of spores}} \times 100$$

NMR and MS data

***1**[Me_2SnL_2]*

δ (^{1}H): 2H, 4.63q; 3H, 1.63d; 5H, 7.18s; 6H, 0.58s (85); δ (^{13}C): C1, 178.11; C2, 52.67; C3, 16.87, C4, 169.05; C5, 136.41; C6, 0.07 ($^1J^{119}$Sn-^{13}C: 672); MS (*m*/*z*): $[M]^+$, 485 (7%); $[M-R]^+$, 470 (36%); $[M-2R]^+$, 455 (41%); $[M-2L]^+$, 149 (20%); $[M-L]^+$, 317 (100%); $[Sn]^+$, 119 (46%).

***2**[Et_2SnL_2]*

δ (^{1}H): 2H, 4.83q; 3H, 1.62d; 5H, 7.24s; 6H, 0.93q (100); 7H, 0.81t; δ (^{13}C): C1, 169.63; C2, 52.14; C3, 17.07; C4, 171.32; C5, 138.24; C6, 12.5 ($^1J^{119}$Sn-^{13}C: 684); C7, 6.34 ($^2J^{119}$Sn-^{13}C: 162); MS (*m*/*z*): $[M]^+$, 513 (11%); $[M-R]^+$, 484 (28%); $[M-2R]^+$, 455 (9%); $[M-2L]^+$, 177 (39%); $[M-L]^+$, 345 (100%); $[Sn]^+$, 119 (52%).

***3**[Bu_2SnL_2]*

δ (^{1}H): 2H, 4.72q; 3H, 1.74d; 5H, 7.33s; 6H, 1.11t (107); 7H, 1.72m; 8H, 1.29m; 9H, 0.93m; δ (^{13}C): C1, 170.21; C2, 53.22; C3, 18.09; C4, 171.04; C5, 136.96; C6, 29.4 ($^1J^{119}$Sn-^{13}C: 663); C7, 24.6 ($^2J^{119}$Sn-^{13}C: 124); C8, 23.2 ($^3J^{119}$Sn-^{13}C: 201); C9, 14.6 ($^4J^{119}$Sn-^{13}C: 187); MS (*m*/*z*): $[M]^+$, 569 (9%); $[M-R]^+$, 512 (100%); $[M-2R]^+$, 455 (18%); $[M-2L]^+$, 233 (13%); $[M-L]^+$, 401 (0%); $[Sn]^+$, 119 (11%).

***4**[Ph_2SnL_2]*

δ (^{1}H): 2H, 4.92q; 3H, 1.55d; 5H, 7.41s; 7H, 7.81m; 8H, 7.53m; 9H, 7.44m; δ (^{13}C): C1, 170.84; C2, 54.15; C3, 16.92; C4, 169.94; C5, 140.56; C6, 128.1 ($^1J^{119}$Sn-^{13}C: 648); C7, 134.8 ($^2J^{119}$Sn-^{13}C: 154); C8, 132.3 ($^3J^{119}$Sn-^{13}C: 198); C9, 131.3 ($^4J^{119}$Sn-^{13}C:123); MS (*m*/*z*): $[M]^+$, 609 (18%); $[M-R]^+$, 532 (46%); $[M-2R]^+$, 455 (43%); $[M-2L]^+$, 273 (34%); $[M-L]^+$, 441 (100%); $[Sn]^+$, 119 (26%).

***5**[Bz_2SnL_2]*

δ (^{1}H): 2H, 4.85q; 3H, 1.69d; 5H, 7.37s; 6H, 2.95s (113); 8H, 7.11m; 9H, 7.45m; 10H, 7.22m; δ (^{13}C): C1, 172.01; C2, 53.96; C3, 16.87; C4, 171.35; C5, 138.73; C6, 20.6 ($^1J^{119}$Sn-^{13}C: 629); C7, 142.0 ($^2J^{119}$Sn-^{13}C: 174); C8, 129.3 ($^3J^{119}$Sn-^{13}C: 223); C9, 133.1 ($^4J^{119}$Sn-^{13}C: 231); C10, 128.2; MS (*m*/*z*): $[M]^+$, 637 (22%); $[M-R]^+$, 546 (29%); $[M-2R]^+$, 455 (68%); $[M-2L]^+$, 301 (27%); $[M-L]^+$, 469 (100%); $[Sn]^+$, 119 (0%).

CONCLUSIONS

The solid-state spectral analysis proved hexacoordination of the title complexes. In solution, **1** is skew-trapezoidal, **2** and **3** penta-coordinated and **4** and **5** tetrahedral. Further, complexes **4** and **5**, being highly toxic, are of pharmacological interest for *in vivo* anti-tumour effects.

Acknowledgements

This work was carried out with the financial support of Gomal University, D. I. Khan, Pakistan (research project no. 717-29/DF/GU). The author is grateful to Professor G.J. Peters, Department of Medical Oncology, VU University Medical Center, PO Box. 7057, 1007 MB Amsterdam, The Netherlands, for *in vitro* anti-tumour screenings.

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