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Structure and *in vitro* antifungal activity of [2,6-bis(dimethylaminomethyl)phenyl]diphenyltin(IV) compounds

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A set of seven [2,6-bis(dimethylaminomethyl)phenyl]diphenyltin(IV) ($\{[(CH_3)_2NCH_2]_2(C_6H_3)\}(C_6H_5)_2Sn^+X^-$) ionic organotin(IV) compounds (X = Br, NO_3, CN, SCN, SeCN, BF_4 and PF_6) has been prepared and characterized by electrospray ionization mass spectrometry, ^{1}H NMR spectroscopy in $CDCl_3$, ^{119}Sn NMR in $CDCl_3$ and DMSO-d_6 solution, as well as by ^{13}C and ^{119}Sn CP/MAS NMR spectroscopy and X-ray diffraction techniques in the solid state. The *in vitro* antifungal activity of these water-soluble ionic organotin(IV) compounds was compared with starting compounds and the antifungal drugs currently in clinical use.

KEYWORDS: water-soluble organotin(IV) compounds; N, C, N-ligand; NMR spectroscopy; CP/MAS NMR spectroscopy; X-ray diffraction; ESI mass spectrometry; *in vitro* antifungal screening

INTRODUCTION

The organometallic derivatives of the ligand C_6H_3-2,6-$(CH_2NMe_2)_2$— have interesting structures[1] and very good catalytic properties (Ni,[2] Pd,[3] and Pt[4]). These types of compound are also well known for their coordination ability, due to one or two nitrogen donor centres. The organotin(IV) compounds have been studied extensively and screened *in vitro* and *in vivo* for antitumour activity, usually against P388 lymphocytic leukaemia.[5] Recently, considerable attention has been paid to triorganotin(IV) derivatives having high *in vitro* antifungal activities against some medically important fungi.[6] The low aqueous solubility of organotin compounds is a limiting factor in the further research of their use in medicine.[7]

We have previously reported on the evaluation of intramolecular interactions[8,9] using NMR parameters. On the basis of our previous experience, we have prepared a set of seven 2,6-(*N,N*-dimethylaminomethylphenyl)diphenyltin derivatives (Fig. 1) that are soluble in water as a result of their ionic structures. These compounds have been tested *in vitro* against medically important fungi.

EXPERIMENTAL

General comments

All solvents were obtained from commercial sources. The synthesis of **1** was carried out under an argon atmosphere using standard Schlenk-tube techniques. All solvents for this synthesis were dried and purified by standard procedures. The other reactions were performed in air and with commercially available solvents, without drying and further purification. In the cases of reactions leading to compounds

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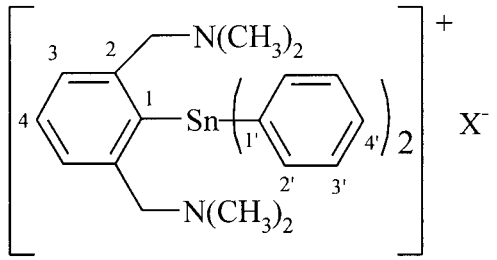

X = **1** Br, **2** NO_3, **3** SCN, **4** BF_4, **5** SeCN, **6** CN, **7** PF_6

Figure 1. Structural and numbering scheme of compounds studied.

2–6 the reaction flasks were protected from light by aluminium foil. The relevant physico-chemical parameters for compounds **1–7** are given in Table 1 and the ^{1}H NMR parameters are listed in Table 2.

Synthesis

*[2,6-Bis(dimethylaminomethyl)phenyl]diphenyltin bromide (**1**)*

Compound **1** was prepared according to the literature.[9] Yield: 5.36 g (70%). ^{119}Sn NMR ($CDCl_3$, 300 K): $\delta = -69.5$ ppm, ^{119}Sn NMR (DMSO-d_6, 300 K): −66.7 ppm. ^{13}C CP/MAS NMR δ 64.3 (CH_2), δ 46.9 (CH_3), δ 127.3 (Ar), δ 127.7 (Ar), δ 131.9 (Ar), δ 133.4 (Ar), δ 135.2 (Ar), δ 135.7 (Ar), δ 139.1 (Ar), δ 144.7 (Ar). ^{119}Sn CP/MAS NMR $\delta(^{119}Sn)_{iso} = -71.6$ ppm (centre of gravity of three-line pattern).

Syntheses of compounds **2–6**

Compounds **2–6** were obtained according to the general procedure described below. To a stirred suspension of **1** (0.5 g; 0.92 mmol) in benzene (100 ml) at room temperature was added an equimolar ratio of an aqueous (200 ml) solution (suspension) of the appropriate silver(I) compound. The mixture was stirred for several days at room temperature. The aqueous phase was separated and washed (3 × 50 ml) with chloroform. The chloroform layer was dried by Na_2SO_4 and evaporated *in vacuo*, and the resulting white crystals were washed with hexane, filtered off and dried *in vacuo*.

For **2** (**nitrate**): $AgNO_3$ (0.156 g; 0.92 mmol); yield: 0.32 g (66%).

For **3** (**thiocyanate**): AgSCN 0.152 g (0.92 mmol); yield: 0.37 g (77%); ^{13}C CP/MAS NMR δ 63.7 (CH_2), δ 46.0 (CH_3), δ 127.2 (Ar or SCN), δ 130.3 (Ar or SCN), δ 130.5 (Ar or SCN), δ 132.5 (Ar or SCN), δ 133.4 (Ar or SCN), δ 134.6 (Ar or SCN), δ 137.8 (Ar or SCN), δ 139.1 (Ar or SCN), δ 143.2 (Ar or SCN);

Table 2. Parameters of ^{1}H NMR spectra for **1–7** in $CDCl_3$ (300 K)

	$\delta(^1H)$ (ppm)			
Compound[a]	NCH_2	$N(CH_3)_2$	H(2′)[b]	H(3, 3′, 4 and 4′)[c]
1	4.01	2.26	7.65 (68.8)	7.61–7.55
1[d]	4.07	2.14	7.75 (68.6)	7.65–7.58
2	4.03	2.23	7.67 (64.8)	7.63–7.56
3	3.89	2.17	7.65 (73.0)	7.62–7.55
4	3.98	2.21	7.64 (64.8)	7.62–7.54
5	4.02	2.24	7.67 (68.4)	7.62–7.55
6	3.99	2.24	7.73 (72.0)	7.69–7.63
7	3.97	2.21	7.63 (72.1)	7.63–7.58

[a] See Fig. 1.
[b] $^3J(^{119}Sn,^1H)$/H(3) in parentheses.
[c] Complex multiplet of signals.
[d] DMSO-d^6.

Table 1. Physico-chemical parameters for **1–7**

	Found (Calc.) (%)			MW	M.p.	Negative ion ESI-MS,	
Compound[a]	C	H	N	(g mol^{-1})	(°C)	*m/z* [exp./theor. (%)]	Λ_M[b] (S cm^{2}mol^{-1})
1	52.79 (52.98)	5.16 (5.37)	5.26 (5.15)	544.1	197–203	79 [99/100], 81 [100/97]	159.7
2	54.69 (54.78)	5.62 (5.55)	8.05 (7.99)	526.2	238–245	62 [100/100]	96.6
3	57.61 (57.49)	5.66 (5.60)	8.15 (8.05)	522.2	172–177	58 [100/100], 59 [2/2], 60 [4/4]	93.0
4	52.23 (52.32)	5.22 (5.30)	5.15 (5.08)	551.0	205–210	86 [26/25], 87 [100/100]	99.0
5	52.85 (52.76)	5.26 (5.14)	7.47 (7.38)	569.2	155[c]	102 [12/18], 103 [9/15], 104 [35/48], 106 [100/100], 108 [20/18]	45.5
6	61.34 (61.25)	5.86 (5.96)	8.45 (8.57)	490.2	100–105	26 [100/100]	77.3
7	47.35 (47.32)	4.83 (4.80)	4.56 (4.60)	609.2	195–200	145 [100/100]	136.1

[a] See Fig. 1.
[b] 1×10^{-3} M solution studied compounds in CH_3CN.
[c] Decomposition.

^{119}Sn CP/MAS NMR $\delta(^{119}Sn)_{iso} = -70.7$ ppm (centre of gravity of three-line pattern).

For **4** (**tetrafluoroborate**): $AgBF_4$ 0.179 g (0.92 mmol); yield: 0.39 g (76%). ^{13}C CP/MAS NMR δ 63.2 (CH_2), δ 45.1 (CH_3), δ 126.4 (Ar), δ 130.4 (Ar), δ 130.8 (Ar), δ 131.0 (Ar), δ 132.2 (Ar), δ 135.3 (Ar), δ 137.8 (Ar), δ 143.7 (Ar); ^{119}Sn CP/MAS NMR $\delta(^{119}Sn)_{iso} = -71.5$ ppm (centre of gravity of three-line pattern).

For **5 (selenocyanate)**: AgSeCN 0.195 g (0.92 mmol); yield: 0.26 g (50%).

For **6 (cyanide)**: AgCN 0.123 g (0.92 mmol); yield: 0.28 g (62%).

*[2,6-Bis(dimethylaminomethyl)phenyl]diphenyltin hexafluorophosphate (**7**)*

KPF_6 (0.169 g; 0.92 mmol) was added to a solution of **1** (0.5 g; 0.92 mmol) in dichloromethane (200 ml). This suspension was stirred for 24 h at room temperature, and the mixture was filtered; the dichloromethane solution was evaporated *in vacuo* and the residue was crystallized from a chloroform–pentane mixture (2:1), to give compound **7** as a pure white solid. Yield: 0.31 g (55%); ^{13}C CP/MAS NMR δ 62.8 (CH_2), δ 45.1 (CH_3), δ 125.7 (Ar), δ 130.7 (Ar), δ 134.2 (Ar), δ 135.4 (Ar), δ 137.4 (Ar), δ 139.2 (Ar), δ 143.7 (Ar), δ 144.8 (Ar); ^{119}Sn CP/MAS NMR $\delta(^{119}Sn)_{iso} = -73.9$ ppm (centre of gravity of three-line pattern).

NMR measurements

The solution-state ^{1}H NMR and ^{119}Sn NMR spectra were acquired at 360.13 MHz and 134.28 MHz respectively on a Bruker AMX 360 NMR spectrometer, using a 5 mm tuneable broad-band probe at 300 K. The measurable solutions were obtained by dissolving approximately 10 mg of each compound in 0.5 ml of the deuterio-solvent. Appropriate chemical shifts were calibrated using the peak of internal HDMSO ($\delta = 0.05$) or the residual peak of DMSO ($\delta = 2.50$) and the ^{119}Sn on external tetramethylstannane ($\delta = 0.00$ ppm).

The solid-state ^{13}C NMR and ^{119}Sn NMR spectra of the studied compounds were acquired at 50.32 MHz and 74.63 MHz respectively on a Bruker DSX 200 spectrometer equipped with a double-bearing CP/MAS probe at room temperature. The compounds were packed in standard 4 mm or 7 mm ZrO_2 rotor takes. The ^{13}C and ^{119}Sn Hartmann–Hahn cross-polarization match was set with adamantane and tetracyclohexyltin respectively, using a ^{1}H 90° pulse of 4 μs. Contact time was set to 1–2 ms. Recycle delay was 10 s. In the case of ^{119}Sn CP/MAS NMR experiments, at least two spinning frequencies (4.5–9 kHz) were used to identify the isotropic chemical shift. The number of scans varied between 200 and 22 000 to achieve acceptable signal-to noise ratios. The ^{13}C and ^{119}Sn chemical shifts were calibrated indirectly by external glycine (carbonyl signal $\delta = 176.03$ ppm) and tetracyclohexyltin ($\delta = -97.35$ ppm) respectively.

Mass spectrometry

Electrospray ionization (ESI) mass spectra were measured on an ion trap analyser (Esquire 3000; Bruker Daltonics, Bremen, Germany) and a quadrupole analyser (Platform; Micromass, UK). The samples were dissolved in acetonitrile and analysed by direct infusion at a flow rate 1 μl min^{-1}. Mass spectra were recorded in the range *m/z* 15–600, in both negative-ion and positive-ion modes.

X-ray crystallography

Colourless crystals of compounds **3** and **4** were obtained by vapour diffusion of hexane into *ca* 3% dichloromethane solutions of appropriate compounds, mounted on a glass fibre with epoxy cement and measured at low temperature. The crystallographic details are summarized in Table 3. Both structures were solved by a direct method (SIR92) and refined by a full-matrix least-squares procedure based on F^2 (SHELXL97). The absorptions were corrected by a multi-scan method (SORTAV[10]). Hydrogen atoms were calculated in theoretical positions, arising during refinement on the respective pivot atom. Some of the anionic parts of the structures are disordered, with the BF_4^- moiety in two positions, and the SCN^- in four positions, which causes large residual peaks in the vicinity of the SCN^- ion on the final difference map. However, the tin-complex moieties are ordered in **3** and **4**; therefore, the resulting structure determinations are suitable to supply the main geometric features.

A full list of crystallographic data and parameters including fractional coordinates is deposited at the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, UK [fax: + 44(1223) 336033; e-mail: deposit@ccdc.cam.ac.uk]. Deposition numbers are given in Table 3.

In vitro antifungal screening

The *in vitro* testing was carried out using a modified microdilution broth of the M27-A guidelines. Quality-control strains (*Candida albicans* ATCC 90028, *Candida parapsilosis* ATCC 22019, *Candida krusei* ATCC 6258) and amphotericin B, fluconazole (Pfizer), ketoconazole (Janssen–Cilag, Beerse) as a reference drug were involved. All fungal strains were passaged on Sabouraud dextrose agar at 35 °C prior to being tested.

The minimum inhibitory concentration (MIC) was determined by the following method; DMSO served as a diluent for all compounds tested. DMSO did not exceed a final concentration of 2%. RPMI 1640 (Sevapharma, Prague) medium supplemented with L-glutamine and buffered with 0.165 M morpholinepropanesulfonic acid (Serva) to pH 7.0 (using 10 M NaOH) was used as a test medium. Each well of the microdilution tray was filled with 200 μl of the RPMI 1640 medium with a diluted compound tested and then inoculated with 10 μl of suspension of a given fungal strain in sterile water. Fungal inoculum was prepared to give a

Table 3. Crystal data and structure refinement details for **3** and **4**

Compound/parameter	**3**	**4**
Formula	$C_{25}H_{29}N_3SSn$	$C_{24}H_{31}BrN_2OBF_4Sn$
Crystal system	Monoclinic	Monoclinic
Space group	*C*2/*c*	*C*2/*c*
Formula weight	522.26	569.01
Crystal size (mm^3)	0.35 × 0.35 × 0.3	0.32 × 0.25 × 0.25
a (Å)	13.8530(3)	14.0990(2)
b (Å)	20.9900(5)	19.8680(3)
c (Å)	10.3310(3)	10.8010(2)
β (°)	126.172(2)	125.3051(8)
V (Å^3)	2425.0(1)	2469.12(7)
Z	4	4
D_{calcd} (g cm^{-3})	1.431	1.531
θ_{max}	27.5	27.5
μ(Mo Kα) (cm^{-1})	11.56	10.84
Temperature (K)	190(2)	150(2)
Trans. factors	0.609, 0.712	0.729, 0.766
F(000)	1064	1152
Reflns measured	16335	19653
Reflns unique, R_{int}	2785, 0.035	2831,0.025
Reflns with $I \geq 2.0\sigma(I)$	2713	2731
$R(F)$, $R_w(F)$[a]	0.046, 0.127	0.020, 0.050
Goodness-of-fit (GOF)	1.17	1.12
w_1; w_2[b]	0.0637, 14.162	0.0234, 2.273
$\Delta\rho$ (e^- Å^{-3})	2.78; −2.35	0.35; −0.55
CCDC deposition number	171585	171586
Diffractometer	Nonius Kappa CCD area detector	
Programs used	SORTAV, SIR92, SHELXL97, PLATON	

[a] Definitions: $R(F) = \sum \|\|F_o\| - \|F_c\|\| / \sum |F_o|$ for $I \geq 2.0\sigma(I)$, $wR_2 = \{\sum [w(F_o^2 - F_c^2)^2] / \sum w(F_o^2)^2\}^{1/2}$, for all reflections, GOF = $\{\sum [w(F_o^2 - F_c^2)^2] / (N_{reflns} - N_{params})\}^{1/2}$.

[b] Weighting scheme: $w = [\sigma^2(F_o^2) + (w_1P) + w_2P]^{-1}$, $P = [\max(F_o^2,0) + 2F_c^2]/3$.

final size of $5 \times 10^3 \pm 0.2$ CFU ml^{-1}. The trays were incubated at 35 °C and the MICs read after 24 and 48 h. Owing to slow growth, the *Trichophyton mentagrophytes* strain was read at 72 and 120 h. The MICs were determined visually and defined as 80% inhibition of the growth of control.

RESULTS AND DISCUSSION

Identification and preparation of compounds studied

The compounds **1–7** are relatively soluble (*ca* 200 mg/100 ml) in water and were prepared by addition of appropriate silver(I) (for **2–6**) compounds into a suspension of compound **1** in a heterogenous mixture water–benzene, and than extracted from water with chloroform. Compound **7** was prepared by reaction of KPF_6 with **1** in dichloromethane. Compound **1** was prepared following the literature method.[9]

All compounds studied were of satisfactory elemental analysis (Table 1). In accordance with the proposed structures, one set of signals was observed in each ^1H NMR and ^{13}C CP/MAS NMR spectrum. Only one isotropic signal was found in all ^{119}Sn CP/MAS NMR spectra measured. The major identification of the prepared compounds was made by ESI mass spectrometry (MS).

MS

The structures and the purity of the compounds studied were confirmed by ESI-MS; the cationic part of the molecule was analysed in positive-ion mode using full scan mass spectra and MS/MS analysis of the precursor ion at *m/z* 465, where as the anions were studied in negative-ion mode.

The cationic part ($C_{24}H_{29}N_2Sn$) of compounds **1–7** with the characteristic tin isotopes was measured in positive-ion mode (theoretical relative abundances in parentheses): *m/z* 461, 23.9% (40.8%); *m/z* 462, 21.7% (32.7%); *m/z* 463, 59.5% (74.9%); *m/z* 464, 34.4% (43.6%); *m/z* 465, 100% (100%); *m/z* 466, 24.5% (26.4%); *m/z* 467, 13.3% (16.4%); *m/z* 468, 3.7% (3.8%); *m/z* 469, 17.0% (16.6%) and *m/z* 470, 4.3% (4.5%). The ion *m/z* 465 was further analysed by MS/MS analysis with the ion trap analyser under the following conditions: isolation width *m/z* 8; collision amplitude, 0.8 V; ion source temperature, 300 °C; flow rate and nitrogen-pressure, 4 l min^{-1} and 7 psi respectively. MS/MS spectra of the product ion *m/z* 465 yielded the following fragment ions with suggested interpretation (all tin-containing fragment ions show the characteristic isotopic pattern) and relative abundances in parentheses; 'cation' corresponds to $C_{24}H_{29}N_2Sn$: *m/z* 465 (85%), $[cation]^+$; *m/z* 420 (11%), $[cation - CH_3NHCH_3]^+$; *m/z* 387 (20%), $[cation - C_6H_6]^+$; *m/z* 344 (100%), $[cation - C_6H_6 - CH_3N{=}CH_2]^+$; *m/z* 299 (38%), $[cation - C_6H_6 - CH_3NHCH_3 - CH_3N{=}CH_2]^+$; *m/z* 267 (8%), $[cation - C_6H_6 - Sn]^+$; *m/z* 224 (12%), $[cation - C_6H_6 - Sn - CH_3N{=}CH_2]^+$; *m/z* 181 (9%), $[cation - C_6H_6 - Sn - 2 \times CH_3N{=}CH_2]^+$; *m/z* 166 (3%), $[cation - C_6H_6 - Sn\ CH_3N{=}CH_2\ -(CH_3)_2NCH_2]^+$. The different anions (X) of the compounds studied were characterized in the negative-ion mode.

For illustration of the above mentioned characterization power, we have chosen to use the ESI mass spectra of [2,6-bis(dimethylaminomethyl)phenyl]diphenyltin selenocyanate, which one depicted in Fig. 2. Figure 2a shows the magnified region of the full scan mass spectrum with the characteristic isotopic peaks of tin, which are in reasonable agreement with theoretical relative abundances. No other ions were observed in the full scan positive-ion mass spectrum; hence only the selected part of the spectrum is shown in Fig. 2. To obtain additional structural information, the ion *m/z* 465 was isolated in the ion trap and collisionally activated to induce fragmentation. The resulting MS/MS spectrum (Fig. 2b) yields many fragment ions, which are

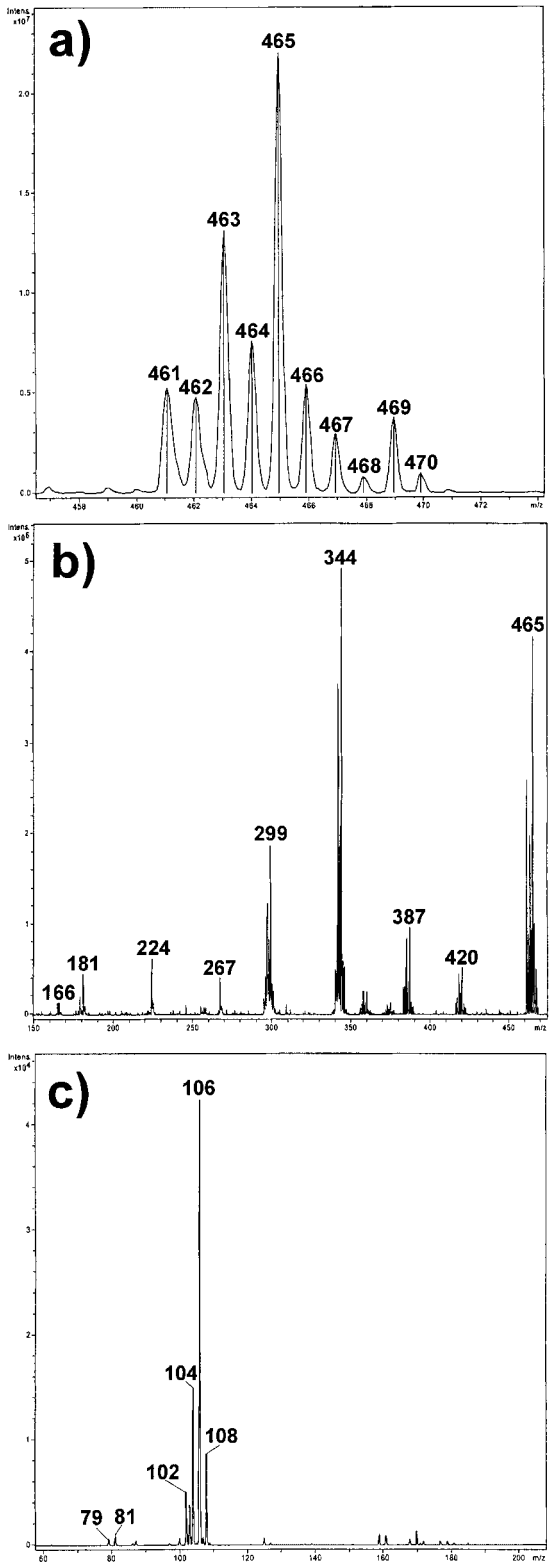

Figure 2. ESI mass spectra of [2,6-bis(dimethylamino)methyl] phenyldiphenyltin selenocyanate: (a) positive-ion full scan mass spectrum with magnified region of $C_{24}H_{29}N_2Sn$; (b) positive-ion MS/MS spectrum of *m/z* 465; (c) negative-ion full scan mass spectrum.

listed in the Experimental section with their suggested interpretations. The isotopic pattern of tin enables easy identification, as to whether the particular fragment ion contains a tin atom. The characteristic neutral losses are CH_3NHCH_3 (*m/z* 45), $CH_3N{=}CH_2$ (*m/z* 43), C_6H_6 (*m/z* 78) and Sn (*m/z* 120), which is in accordance with the structure of the cation. The positive-ion mass spectra were identical for all the compounds studied. The negative-ion ESI mass spectrum of [2,6-bis(dimethylaminomethyl)phenyl]diphenyltin selenocyanate (Fig. 2c) illustrated the identification of the anionic part of the molecule. Small amounts (<2%) of unreacted bromide can be observed in Fig. 2c (*m/z* 79 and 81). The same approach was applied for all compounds studied.

Solid-state structure study

For the solid-state study, four compounds were chosen as representative samples: monoatomic (Br^-, **1**), linear (SCN^-, **3**), tetrahedral (BF_4^-, **4**) and octahedral (PF_6^-, **7**) anion. ^{13}C and ^{119}Sn RAMP CP/MAS spectra and crystallographic results were obtained in this set.

^{13}C and ^{119}Sn RAMP CP/MAS NMR

All ^{13}C RAMP CP/MAS NMR spectra reveal one set of signals for CH_2 and CH_3 aliphatic carbon atoms and the correct number of signals for aromatic carbon atoms (see Experimental), which is proof of the $CH_2N(CH_3)_2$ group's equivalence. In the case of compound **3**, the carbon from the SCN^- group was not assigned.

In all cases the ^{119}Sn RAMP CP/MAS NMR spectra reveal one isotropic signal (for $\delta(^{119}Sn)_{iso}$ values, see Experimental), which is split into a triplet with integral ratios 1:4:4 as a result of residual quadrupolar splitting by two equivalent quadrupolar ^{14}N nuclei.[9] This signal pattern is clear proof of the compound's structure. The equidistant lengths between each of the two $CH_2N(CH_3)_2$ groups in the 1:4:4 signal pattern indirectly evaluates the strength of the intramolecular interactions between Sn—N in the solid state: 138.3 Hz for **1**, 99.8 Hz for **3**, 118.3 Hz for **4** and: 114.5 Hz for **7** (Fig. 3).

Crystallography

Selected parameters in the crystal structures of compounds **1, 3, 4** and **7** are collected in Table 4 and ORTEP drawings with a numbering scheme for compounds **3** and **4** are depicted in Figs. 4 and 5 respectively. The crystal structures of **1** and **7** have been published previously.[11,12] The crystal structures of **3** and **4** are disordered in the anionic parts, and in the case of **1** and **4** the water molecule is incorporated into the structures.

Solution-state structure study

All compounds prepared are soluble (200 mg/100 ml/room temperature) in water and rather insoluble in non-coordinating solvents. The molar conductivities (see Table 1) of 10^{-3} M solutions in acetonitrile show them all to be ionogenic in this solvent.[13] This finding is in good agreement with the

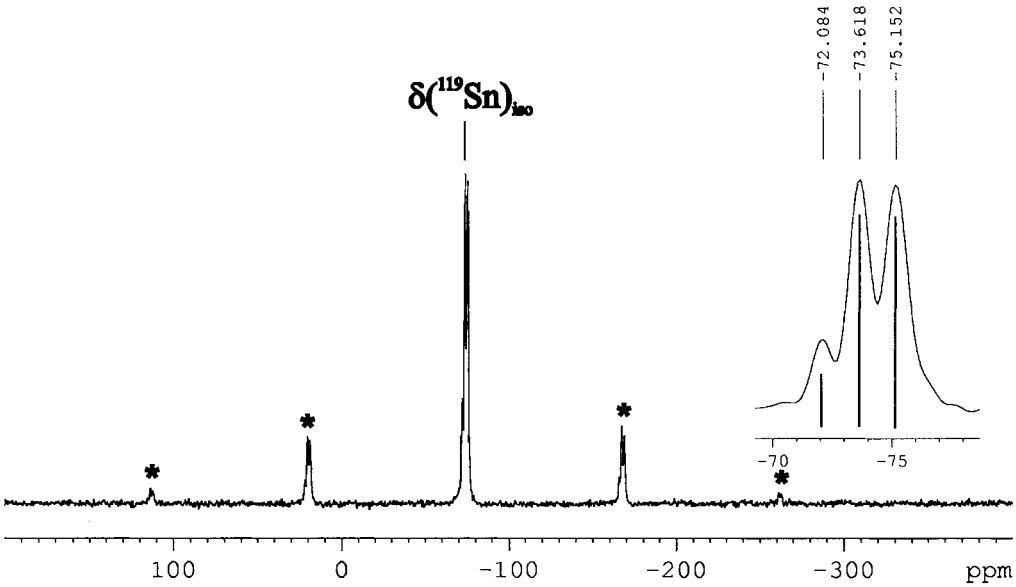

Figure 3. ^{119}Sn RAMP CP/MAS NMR spectrum of **7** and detail of the central signal with the 'stick model' of its residual quadrupolar splitting (1:4:4); spinning side bands are marked with asterisks.

premise that the structures are the same in solutions of non-coordinating solvents and in the solid state.

The values of chemical shifts in the ^{119}Sn NMR spectra of compound **1** in $CDCl_3$ (−69.5 ppm) and DMSO-d_6 (−66.7 ppm) demonstrate the same structure (ionic) in solution in both solvents and in the solid state (chemical shift in solid-state NMR spectra differs only slightly (−71.6 ppm) from those obtained from solution spectra). We were not able to obtain low-temperature and other nuclei (^{119}Sn, ^{15}N, ^{13}C) NMR spectra, which would give more information about the structure of this type of compounds,[8] due to low solubility of the compounds in non-coordinating solvents or fluxional processes inducing broad unresolved signals in these spectra.

All ^{1}H NMR spectra measured in $CDCl_3$ (300 K) (see Table 2) reveal the same pattern: one set of signals for CH_2, CH_3 and the aromatic part of molecules. The values of $\delta(^1H)$ for the methylene and methyl groups of all compounds studied are upfield shifted compared with the free ligand 1,3-

Table 4. Selected geometric parameters (Å, °) for **1**, **3**, **4**, and **7**

Compound/ parameter[a]	**1** (Ref. 11)	**3**	**4**	**7** (Ref. 12)
Sn—N1	2.440(1)	2.416(3)	2.416(1)	2.410(2)
Sn—N1^i	2.440(1)	2.416(3)	2.416(1)	2.415(2)
Sn—C(11)	2.093(2)	2.096(6)	2.090(2)	2.092(3)
Sn—C(21)	2.141(2)	2.126(4)	2.128(2)	2.131(3)
Sn—C(21)^i	2.141(2)	2.126(4)	2.128(2)	2.122(3)
N(1)—Sn—N(1)^i	152.18(7)	151.4(2)	152.04(7)	152.03(8)
C(11)—Sn—C(21)	124.95(4)	126.1(1)	124.83(4)	126.6(1)
C(11)—Sn—C(21)^i	124.95(4)	126.1(1)	124.83(4)	118.3(1)
N(1)—Sn—C(11)	76.09(3)	75.69(9)	76.02(3)	75.68(9)
N(1)—Sn—C(21)	99.48(5)	100.1(1)	100.23(5)	99.74(9)
C(21)—Sn—N(1)^i	96.36(5)	96.6(1)	95.64(5)	95.56(9)

[a] Symmetry code: for **1** (i) -*x*, *y*, $\frac{3}{2}$ -*z*; for **3** (i) 1 -*x*, *y*, $\frac{1}{2}$ -*z*; for **4** (i) 1 -*x*, *y*, $\frac{3}{2}$ -*z*; for **7** (i) -*x*, *y*, $\frac{3}{2}$ -*z*.

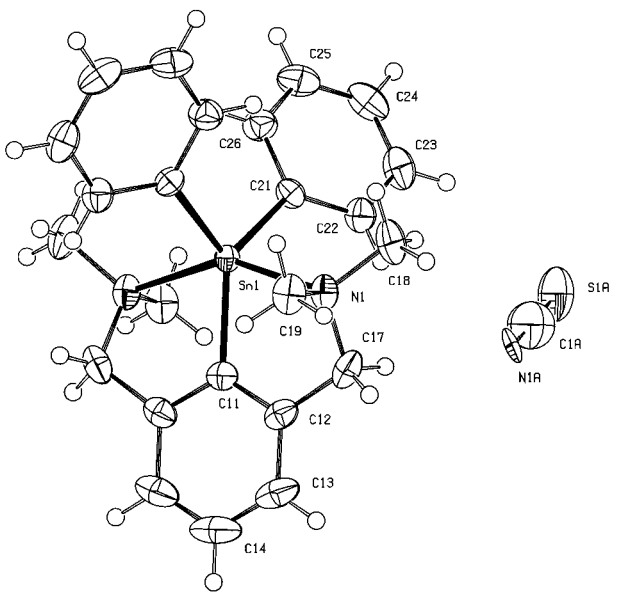

Figure 4. Molecular structure of **3** showing the atom labelling scheme for symmetrically independent atoms. Thermal ellipsoids are drawn at the 50% probability level. Only one position of the disordered anion is displayed for clarity.

Table 5. *In vitro* antifungal activity of [2,6-bis(dimethylaminomethyl)phenyl]diphenyltin(IV) derivatives determined by microdilution broth method

	MIC (μmol l^{-1})[a, b]							
	TM	CA	CT	CK	CG	TB	AF	AC
Compound[c]	72 h 120 h	24 h 48 h	24 h 48 h	24 h 48 h	24 h 48 h	24 h 48 h	24 h 48 h	24 h 48 h
1,3-Bis(dimethyl-aminomethyl)benzene	125 125	250 >250	>250 >250	>250 >250	>250 >250	250 >250	31.25 250	>250 >250
1	1.95 1.95	15.63 125	250 250	7.81 15.63	125 250	>250 >250	7.81 15.63	7.81 15.63
2	31.25 31.25	31.25 62.5	62.5 125	62.5 62.5	62.5 62.5	62.5 125	31.25 62.5	62.5 62.5
3	62.5 62.5	62.5 62.5	125 250	62.5 125	62.5 125	125 125	62.5 125	62.5 125
4	62.5 62.5	>250 >250	>250 >250	125 >250	>250 >250	>250 >250	125 >250	125 >250
5	>250 >250	>250 >250	>250 >250	>250 >250	>250 >250	>250 >250	>250 >250	>250 >250
6	31.25 31.25	15.63 31.25	62.5 125	31.25 62.5	31.25 62.5	31.25 125	15.63 62.5	31.25 31.25
7	1.95 1.95	7.81 15.63	62.5 >125	3.91 7.81	15.63 >125	>125 >125	7.81 15.63	7.81 7.81
Ketoconazole	0.98 1.95	0.12 0.12	1.95 3.91	3.91 3.91	0.24 0.98	0.12 0.24	15.63 15.63	32.25 32.25
Fluconazole	26.1 52.2	0.82 1.63	1.63 >417.9	52.2 104.5	13.1 52.2	3.26 6.53	>417.9 >417.9	>417.9 >417.9
Amphotericin B	2.16 2.16	1.08 2.16	2.16 4.33	2.16 4.33	2.16 2.16	0.27 0.27	0.27 0.54	0.54 2.16

[a] CA: *C. albicans* ATCC 44859; TB: *Trichosporon beigelii* 1188; CT: *Candida tropicalis* 156; TM: *T. mentagrophytes* 445; CK: *C. krusei* E28; AF: *Aspergillus fumigatus* 231; CG: *Candida glabrata* 20/I; AC: *Absidia corymbifera* 272.
[b] The limit of maximum concentration tested of a given compound was given with its solubility in DMSO.
[c] See Fig. 1.

bis(dimethylaminomethyl)benzene (3.38 ppm for CH_2 and 2.19 ppm for CH_3),[14] due to coordination of $CH_2N(CH_3)_2$ groups to the tin centre.[14] The magnitude of $^3J(^{119}Sn,^1H)$ (on *ortho* protons of phenyl rings; see Table 2) is in good agreement with the concept of Sn—N donor–acceptor bond and azastannacycle(s) formation (values of 64.8–73.2 Hz obtained for compounds **1–7** reveal small but significant changes in comparison with compound without C,N-chelating rings).[15] The spectral patterns and chemical shifts of ^1H NMR spectra of compound **1** remain unchanged going from coordinating DMSO-d_6 to non-coordinating $CDCl_3$. All the above-mentioned NMR parameters agree with the concept of a five-coordinated tin central atom with two nitrogen atoms *trans* axial and all three carbon atoms in equatorial positions of a trigonal bipyramid, which is compensated by the anionic part of the complex in solution, just as in the solid state.

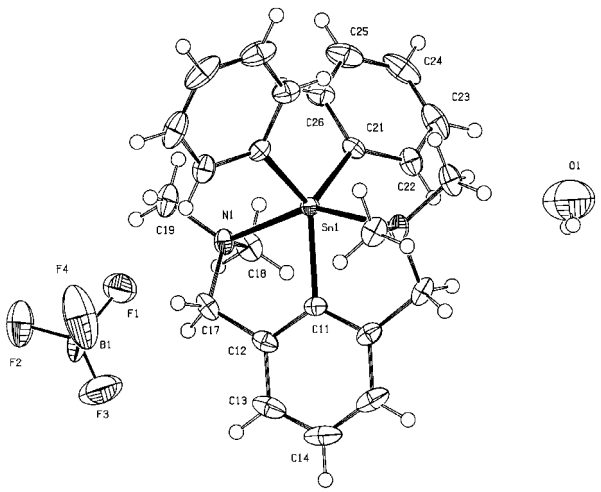

Figure 5. Molecular structure of **4** showing the atom labelling scheme for symmetrically independent atoms. Thermal ellipsoids are drawn at the 50% probability level. The second position of the disordered anion was omitted for clarity.

In vitro antifungal activity

In vitro antifungal results (MIC) against the fungal strains tested are summarized in Table 5 for compounds **1–7**, as well as for the starting compound 1,3-bis(dimethylaminomethyl)-benzene and for conventional antimycotic drugs (ketoconazol, fluconazole, amphotericin B). From the values of MIC, we can conclude that the *in vitro* antifungal effect of the most ionic compounds **1** and **7** (evaluated by molar conductivity) was comparable to that of the above-mentioned antimycotic drugs for the treatment of systemic mycoses (Table 5).

Acknowledgements

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