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Original article

Tin(IV) complexes of pyrrolidinedithiocarbamate: synthesis, characterisation and antifungal activity

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Abstract

The reaction of ammonium pyrrolidinedithiocarbamate, $[NH_4\{S_2CN(CH_2)_4\}]$, with $SnCl_2$, $[Sn(C_6H_5)_2Cl_2]$, $[Sn(C_6H_5)_3Cl]$, $[Sn(C_4H_9)_2Cl_2]$ and $[Sn(C_6H_{11})_3Cl]$ produced in good yield the compounds $[Sn\{S_2CN(CH_2)_4\}_2Cl_2]$ **(1)**, $[Sn\{S_2CN(CH_2)_4\}_2Ph_2]$ **(2)**, $[Sn\{S_2CN(CH_2)_4\}Ph_3]$ **(3)**, $[Sn\{S_2CN(CH_2)_4\}_2n\text{-}Bu_2]$ **(4)** and $[Sn\{S_2CN(CH_2)_4\}Cy_3]$ **(5)**. The complexes were characterised by infrared, multinuclear NMR (^1H, $^{13}C\{^1H\}$ and $^{119}Sn\{^1H\}$) and ^{119}Sn Mössbauer spectroscopies. In addition, the crystal structure of **4** was determined by X-ray crystallography. The in vitro antifungal activity of the tin(IV) complexes as well of the ligand was performed on human pathogenic fungi, *Candida albicans*, in concentrations of 0.025; 0.050; 0.100; 0.200; 0.400; 0.800; 1.600 and 3.200 mM. The microorganism presented resistance to the dithiocarbamate ligand and all tin(IV) complexes tested were actives. The highest activity was found for compounds **1** and **4**.

Keywords: Tin(IV) complexes; Dithiocarbamate complexes; Spectroscopic studies; Antifungal activity; *Candida albicans*

1. Introduction

Fungal infections have increased in the last years affecting mainly those patients immuno-compromised [1]. These infections are ordinary in patients whom subdue to immunosuppressive therapy, as in the cases of organ transplantation, critical diseases and patients with AIDS [2,3]. *Candida albicans*, the microorganism in study, can infect the oral and vaginal cavities, skin and, more seriously essential organs [4].

Antifungal therapies include two main classes of compounds: polyene [5] and azole drugs [6]. The former class, which comprises nystatin and amphotericin, act in the membrane of the fungal cell linking to ergosterol. These drugs interfere with the permeability of the membrane, causing losses of macromolecules and ions essentials to the survival process of the fungal cell [7]. The antifungal activity of azole arises from interaction with the sterol-14α-demethyllase (CYP51), involved in the biosynthesis of ergosterol. Interaction CYP51 results in a decreased availability of ergosterol and an accumulation of 14-methylsterols. Changes in ergosterol levels and sterol structure influence the membrane permeability and the activity of several metabolic pathways [7].

The drugs used nowadays normally present problems with resistance and toxicity [8]. Metal-based drugs might represent an alternative therapeutic route. A large number of studies have been reported concerning metal-complexes of 1,10-phenanthroline [9–11], thiosemicarbazones [12,13] and carboxylates [14].

Tin complexes [15–18] as well as dithiocarbamates ligands [19] are known for their biological interest as antifungal, antibacterial and biocide agents. Therefore, the coordination of tin with dithiocarbamates would enhance such biological aspects. Thus, in order to investigate the in vitro antifungal

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activity towards *C. albicans* we have synthesised and characterised a series of tin(IV) complexes with pyrrolidinedithiocarbamate. Here in we describe the outcomes of our investigation.

2. Experimental

2.1. Materials

Carbon disulphide, pyrrolidine, ammoniun hydroxide, tin compounds, dichloromethane, diethylether and ethanol were purchased from Merck, Aldrich, Synth and Quimex and used with no previous treatment. Solvents such as tetrahydrofuran (THF) and hexane, purchased from Synth. were previously dried by standard methods.

2.2. Instruments and techniques

Elemental analyses were performed using a Perkin–Elmer Model PE 2400CHN. Melting points were determined with a digital melting point from Mettler model FP90 with cell of heating model FP82 HT and microscopy from Olympus CH-2.

IR spectra were obtained as KBr plates on a Mattson Galaxy model ST 3000 spectrometer in the 4000–200 cm^{-1} range. NMR spectra were recorded in $CDCl_3$ at 25 °C on a Brucker Avance DRX 400. The values were referenced to internal $SiMe_4$ and $SnMe_4$. ^{119}Sn Mössbauer measurements were performed on a conventional apparatus with the samples at liquid N_2 temperature and a $CaSnO_3$ source kept at room temperature.

2.3. Synthesis of $[NH_4\{S_2CN(CH_2)_4\}]$

To a solution of pyrrolidine (0.64 g, 9 mmol, in 20 cm^3 of diethylether), at 0 °C, was dropped carbon disulphide (0.68 g, 9 mmol). This mixture was stirred for 1 h and ammoniun hydroxide was added. The white solid formed, $[NH_4\{S_2CN(CH_2)_4\}]$, was filtered and re-crystallised from a mixture of water and THF. Yield 85%. Analysis for: $NH_4S_2C_5H_8N$. Found: C, 36.51%; H, 7.28%; N, 8.41%. Calc: C, 36.59%; H, 7.32%; N, 8.54%. M.p. 142–143 °C. IR (cm^{-1}, KBr): 998 (s, ν_{C-S}); 1240 and 1325 (m, ν_{C-N}); 1450 (s, $\nu_{C-N} + \nu_{C=N}$) . ^1H NMR (δ, D_2O): 1.85 (m, 2C**H**$_2$); 3.58 (t, 2NC**H**$_2$). $^{13}C\{^1H\}$ NMR (δ, D_2O): 25.01 (2**C**H_2); 55.27 (2 N**C**H_2); 202.80 (S**C**N).

2.4. Syntheses of complexes

2.4.1. $[Sn\{S_2CN(CH_2)_4\}_2Cl_2]$ (**1**)

In a Schlenk flask, $[NH_4\{S_2CN(CH_2)_4\}]$ (0.98 g, 6 mmol) was dissolved in 50 cm^3 of THF and added to a solution of $SnCl_2$ (0.57 g, 3 mmol) in the same solvent. The mixture was kept stirring for 2 h in an atmosphere of nitrogen. The white solid formed, composed of SnO and NH_4Cl, was separated by filtration from an orange solution. The solvent was removed yielding an orange solid, $[Sn\{S_2CN(CH_2)_4\}_2Cl_2]$. It was re-crystallised in a mixture of hexane/THF and dried *in vacuum*. Yield 80%. Elemental analysis for: $C_{10}H_{16}SnN_2S_4Cl_2$. Found: C, 24.72%; H, 3.30%; N, 5.65%. Calc: C, 24.91%; H, 3.32%; N, 5.81%. M.p. (decomposition) = 200 °C. IR (cm^{-1}, KBr): 303 (m, ν_{Sn-Cl}); 315 (w, ν_{Sn-S}); 949 (s, ν_{C-S}); 1327 (m, ν_{C-N}); 1459 (s, $\nu_{C-N} + \nu_{C=N}$). ^1H NMR (δ, $CDCl_3$): 1.86 (m, 2C**H**$_2$); 3.63 (t, 2NC**H**$_2$). $^{13}C\{^1H\}$ NMR (δ, $CDCl_3$): 26.01 (2**C**H_2); 55.32 (2N**C**H_2); 202.85 (S**C**N). $^{119}Sn\{^1H\}$ NMR (δ, $CHCl_3$): –521.

2.4.2. $[Sn\{S_2CN(CH_2)_4\}_2Ph_2]$ (**2**)

$[NH_4\{S_2CN(CH_2)_4\}]$ (0.98 g, 6 mmol) was dissolved in 20 cm^3 of ethanol and added to a solution of $[Sn(C_6H_5)_2Cl_2]$ (1.03 g, 3 mmol) in the same solvent. The mixture was stirred for 2 h and then the solvent was removed by filtration and a white solid $[Sn\{S_2CN(CH_2)_4\}_2Ph_2]$ **(2)**, was obtained. The ammonium salt was washed with water at 80 °C. Yield 85%. Elemental analysis for: $C_{22}H_{26}SnN_2S_4$. Found: C, 46.62%; H, 4.54%; N, 4.84%. Calc.: C, 46.75%; H, 4.60%; N, 4.95%. M.p.: 222.5–223.1 °C. IR (cm^{-1}, KBr): 385 (m, ν_{Sn-S}); 943 (s, ν_{C-S}); 1247 and 1328 (m, ν_{C-N}); 1495 (s, $\nu_{C-N} + \nu_{C=N}$). ^1H NMR (δ, $CHCl_3$): 1.99 (m, 2C**H**$_2$); 3.64 (t, 2NC**H**$_2$); 7.23–7.90 (m, 2 C_6**H**$_5$). $^{13}C\{^1H\}$ NMR (δ, $CDCl_3$): 26.72; 54.88; 128.10 ($^4J^{119}Sn-^{13}C$ = 83 Hz); 128.34; 134.30 ($^2J^{119}Sn-^{13}C$ = 621 Hz); 151.62; 194.49. $^{119}Sn\{^1H\}$ NMR (δ, $CHCl_3$): –500 ($^1J^{119}Sn-^{13}C$ = 811 Hz).

2.4.3. $[Sn\{S_2CN(CH_2)_4\}Ph_3]$ (**3**)

Prepared accordingly using $[NH_4\{S_2CN(CH_2)_4]$ (0.49 g, 3 mmol) and $[Sn(C_6H_5)_3Cl]$ (1.26 g, 3 mmol) dissolved in 20 cm^3 of ethanol. Yield 89%. Elemental analysis for: $C_{23}H_{23}SnNS_2$. Found: C, 55.47%; H, 4.73%; N, 2.81%. Calc.: C, 55.68%; H, 4.64%; N, 2.82%. M.p.: 171–171.4 °C. IR (cm^{-1}, KBr): 349 (m, ν_{Sn-S}); 949 (s, ν_{C-S}); 1246 (m, ν_{C-N}); 1479 (s, $\nu_{C-N} + \nu_{C=N}$). ^1H NMR (δ, $CDCl_3$): 1.91 (m, 2C**H**$_2$); 3.67 (t, 2NC**H**$_2$); 7.28–7.90 (m, 3 C_6**H**$_5$). $^{13}C\{^1H\}$ NMR (δ, $CDCl_3$): 26.64; 55.05; 128.46; 129.07 ($^3J^{119}Sn-^{13}C$ = 105 Hz); 136.72 ($^2J^{119}Sn-^{13}C$ = 276 Hz); 142.07 ($^1J^{119}Sn-^{13}C$ = 1737 Hz); 191.57. $^{119}Sn\{^1H\}$ NMR (δ, $CHCl_3$): –173 ($^1J^{119}Sn-^{13}C$ = 1897 Hz).

2.4.4. $[Sn\{S_2CN(CH_2)_4\}_2n\text{-}Bu_2]$ (**4**)

Prepared accordingly employing $[NH_4\{S_2CN(CH_2)_4\}]$ (0.98 g, 6 mmol) and $[Sn(C_4H_9)_2Cl_2]$ (0.91 g, 3 mmol) dissolved in 20 cm^3 of dichloromethane. X-ray quality colourless crystals were obtained by cooling an ethanol solution of the compound. Yield 75%. Elemental analysis for: $C_{18}H_{34}SnN_2S_4$. Found: C, 40.99%; H, 6.38%; N, 5.28%. Calc.: C, 41.17%; H, 6.48%; N, 5.34%. M.p.: 110–111 °C. IR (cm^{-1}, KBr): 347 (m, ν_{Sn-S}); 949 (s, ν_{C-S}); 1010 and 1038 (s, $\nu_{C=S}$); 1643 (m, ν_{C-N}). ^1H NMR (δ, $CDCl_3$): 0.93 (t, 2C**H**$_2$CH$_3$); 1.34 (m, 2C**H**$_3$); 1.86 (m, CH$_2$C**H**$_2$CH$_2$); 1.97 (t, SnC**H**$_2$); 2.05 (m, 2C**H**$_2$); 3.76 (t, 2NC**H**$_2$). $^{13}C\{^1H\}$ NMR (δ, $CDCl_3$): 13.81; 26.23; 26.48; 28.53 ($^2J^{119}Sn-^{13}C$ = 144 Hz); 34.21 ($^1J^{119}Sn-^{13}C$ = 1168 Hz); 54.01; 196.04. $^{119}Sn\{^1H\}$ NMR (δ, $CHCl_3$): –307.

*2.4.5. [Sn{$S_2CN(CH_2)_4$}Cy_3] (**5**)*

Similarly prepared using [NH_4{$S_2CN(CH_2)_4$}] (0.49 g, 3 mmol) and [$Sn(C_6H_5)_3Cl$] (1.32 g, 3 mmol) dissolved in 20 cm^3 of ethanol. Yield 88%. Elemental analysis for: $C_{23}H_{41}SnNS_2$. Found: C, 53.57%; H, 7.89%; N, 2.59%. Calc.: C, 53.73%; H, 7.98%; N, 2.73%. M.p. 145.2–147 °C. IR (cm^{-1}, KBr): 350 (ν_{Sn-S}); 958 (ν_{C-S}); 1215 and 1249 (ν_{C-N}); 1489 (s, $\nu_{C-N} + \nu_{C=N}$). ^{1}H NMR (δ, $CDCl_3$): 1.90 (m, 2C**H**$_2$); 3.60 (t, 2NC**H**$_2$); 1.20–2.01 (m, 3C$_6$**H**$_{11}$). ^{13}C{^{1}H} NMR (δ, $CDCl_3$): 23.4; 25.5; 25.6; 26.3; 29.9; 30.6 ($^2J^{119}Sn$–^{13}C = 250 Hz); 39.4 ($^1J^{119}Sn$–^{13}C = 1680 Hz). ^{119}Sn{^{1}H} NMR (δ, $CHCl_3$): –165 ($^1J^{119}Sn$–^{13}C = 1700 Hz).

*2.5. Crystal data collection and processing of complex (**4**)*

Crystals of compound **4** are triclinic with space group *P*-1. The Intensity data for the X-ray crystallographic determination of **4** were collected at 193(2) K on a Bruker APEX diffractometer with Mo Kα, λ = 0.71073 Å, radiation. Programs used: COLLECT, HKL Denzo-Scalepack, WINGX, SHELXS-97 [20], SHELXL-97 and ORTEP-3 [21] and the refinements were carried out on F^2 using SHELXL-97 software [22]. Further details are given in Table 1. All non-H atoms were refined anisotropic. The carbons' H atoms were positioned stereochemically and were refined with fixed individual displacement parameters [Uiso (H) = 1.2 Ueq (C)] using the SHELXL riding model.

Table 1
Crystal data for [$Sn(C_4H_9)_2${$S_2CN(CH_2)_4$}$_2$] (**4**)

Empirical formula	$C_{18}H_{34}N_2S_4Sn$
Molecular weight	525.40
Temperature	193(2) K
Wavelength	0.71073 Å
Crystal system	Triclinic
Space group	*P*-1
United cell dimensions	*a* = 6.9117(4) Å, *b* = 8.9556(6) Å, *c* = 10.3905 [7] Å α = 79.2110(10)°, β = 85.9880(10)°, γ = 69.3410 [10]°
Volume	591.16 [7] Å^3
Z	1
Density (calculated)	1.476 Mg m^{-3}
Absorption coefficient	1.439 mm^{-1}
F(000)	270
Crystal size	0.290 (max), 0.052 (mid), 0.050 (min)
Theta range for data collection	2.47–28.30°
Reflections collected	5215
Independent reflections	5175
Max. and min. transmission	0.65855 (min), 0.87708 (max)
Refinement method	Full-matrix least-squares on F^2
Data/restraints/parameters	5215/8/227
Goodness-of-fit on F^2	1.013
Final *R* indices [*I* > 2sigma(*I*)]	*R*1 = 0.0202 w*R*2 = 0.0492
R indices (all data)	*R*1 = 0.0203 w*R*2 = 0.0493
CCDC reference	267182

2.6. Biological data

2.6.1. Materials and methods

C. albicans (ATCC 18804) was kindly donated by Microbial Laboratory of ICB-UFMG, Sabouraud dextrose agar and broth was obtained from Biobrás S.A. MG, Brazil. The compounds obtained as well as the ligand were studied against *C. albicans* at concentrations of 0.025; 0.050; 0.100; 0.200; 0.400; 0.800; 1.600 and 3.200 mM. The solvent employed was a mixture of dichloromethane/heptane (molar ratio: 2:1).

2.6.2. Antifungal tests

The liquid cultures of *C. albicans* (ATCC 18804) were seeded aerobically in Sabouraud dextrose broth with the cultures incubated at 37 °C for 24 h. Agar disk diffusion test was performed by agar diffusion according the National Committee of Clinical Laboratory Standard Guidelines—NCCLS—(1997). A 0.1 mL aliquot of over-night culture of this microorganism strain corresponding to 0.5 turbidity on the McFarland scale was placed onto 30 mL of Sabouraud dextrose agar. The commercial antifungal agent nystatin (which is about 22 mM) and ethanol were used as positive control. The solvents employed in the experiments, dichloromethane and heptane were tested as a negative control as well as water. The inhibition zone for the commercial nystatin was 14 mm. All the experiments were carried out in sixplicates. The inhibition zones size were considered as sensitive ≥ 11 mm, which could be 3 mm smaller in relation with the control zone diameter, intermediate between 11 and 9 mm and resistant ≤ 9 mm [23]. Finally, the results were statistically analysed by non-parametric test Kruskal Wallis with significance level, $\alpha = 0.05$.

3. Results and discussion

The ligand was prepared by a Lewis acid and base condensation, producing the so-called Schiff Base system, which was satisfactorily characterised. Dithiocarbamates can co-ordinate to metal centres as monodentate ligand, resonance forms **I** and **II**, or in a bidentate fashion **III** and **IV** (Fig. 1) [24].

The complexes were isolated as mixture-free derivatives and showed acceptable melting points, as well as elemental analysis. Compounds **2–5** were obtained as white crystalline solids and **1** was isolated as an orange product. All deriva-

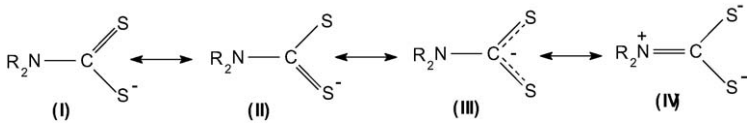

Fig. 1. Possible resonance structures for a generic dithiocarbamate ligand.

tives were air and moisture-stable and readily soluble in polar organic solvents.

The ^{1}H NMR spectra of the complexes in $CDCl_3$ revealed signals for the organic fragments, phenyl, *n*-butyl and cyclohexyl groups in each case. Moreover, the expected ^{13}C resonances revealed first, second, third and fourth-order ^{119}Sn–^{13}C couplings, with values not very different from those found in the literature for organotin compounds [25]. Unlike other reported examples, which normally describe more than one isomer, detected in solution by ^{119}Sn NMR experiments, in our work only one signal was observed in $CHCl_3$ for each compound: $[Sn\{S_2CN(CH_2)_4\}_2Cl_2]$ **(1)**, δ –521; $[Sn\{S_2CN(CH_2)_4\}_2Ph_2]$ **(2)**, δ –500; $[Sn\{S_2CN(CH_2)_4\}Ph_3]$ **(3)**, δ –173; $[Sn\{S_2CN(CH_2)_4\}_2n\text{-}Bu_2]$ **(4)**, δ –307 and $[Sn\{S_2CN(CH_2)_4\}Cy_3]$ **(5)**, δ –165. The coordination number (NC) of the tin centre is one of the interferences in the ^{119}Sn chemical shift. It is suggested in the literature ranges for it, as follows: NC = 6 {δ –300 and –550}; NC = 5 {δ –150 and –250}; and NC = 4 {higher to δ –150}, [26]. However, it must be carefully analysed since tin resonance is strongly dependent upon other factors, such as electronegativity of the ligands, temperature and concentration employed in the experiments. In our case, an increase in the coordination number of the tin atom has effected a large upfield change in ^{119}Sn δ values, comparing complexes **2**, **3** and **5**. In spite of a hexacoordination of the tin atom in complex **1**, the Sn(IV) centre is de-shielded by the two electronnegative chlorine, which can shift the resonance to lower frequency. For complex **4**, the ^{119}Sn NMR technique suggests a hexacoordination rather than a tetrahedral complex. It is an indication that the structure in solution is different from that one obtained by X-ray crystallographic experiment. ^{13}C NMR results can be used to estimate the C–Sn–C angle, by employing methods encountered in the literature, which correlates this angle with the first order ^{119}Sn–^{13}C coupling constant, in solution [27]. The methods have provided the C(11)–Sn–C(15) angle for compound **4** ranging from 187.9 to 195.9°, which is in a total disagreement with the experimental data, 139.35°. It confirms that compound **4** behave differently in solution from solid state. It is possible that in solution compound **4** experience a dynamic exchange going from tetra to hexacoordination through the free sulphur atom of the ligand.

The infrared spectra of the compounds show little changes in the C–S and C–N vibration modes, which was comparable to the free ligand. The ν_{C-S} and $\nu_{C=S}$ stretching frequencies indicate whether the dithiocarbamate acts as a mono or bidentate ligand [28–30]. For compounds **1–3** and **5** it was observed a single band centred in the range of 1000–960 cm^{-1}, suggesting that the carbon–sulphur bond is in fact something between a double and a single bond, which imply that both sulphur coordinates the metal centre. On the other hand for complex **4** it is clearly observed for the carbon–sulphur connection two signals, 1010 and 1038 cm^{-1}, indicating a monocoordination of the ligand throughout one S donor atom, which is according to the X-ray experiment. The Sn–S bands ranged between 300 and 390 cm^{-1} and Sn–Cl for **1** was observed at 303 cm^{-1} [30].

The structure of **2** have been published and **3** has been reviewed recently, both by us [31]. In **2** the Sn atom situates at the centre of an almost perfect octahedral and **3** displays a distorted bipyramidal trigonal geometry. A similar derivative, $[Sn\{S_2CN(CH_2)_4\}_2Me_2]$ have been previously published, and presents hexacoordinated tin atom [32]. In all of them, the ligand presents a bidentate form. Likewise the phenyl derivative prepared by us, complex **4** crystallises in the triclinic system with *P*-1 as space group. X-ray crystallographic study of compound **4**, Table 1 has clearly shown that the Sn(IV) atom locates at the centre of a distorted tetrahedral, where it is surrounded by two butyl groups and two dithiocarbamate ligand, bonded to one sulphur of each one (Fig. 2).

Table 2 comprises the selected bond length and angles. The Sn–S distances, Sn–S(3) = 2.532 and Sn–S(1) = 2.534 Å, in **4** are close to those values found for the methyl derivative and shorter those values found for the phenyl complex. The two Sn–C bonds, Sn–C(11) = 2.132 Å and Sn–C(15) = 2.138 Å, are very close to the same chemical bond detected in the methyl compound.

The angles S(3)–Sn–S(1), C(11)–Sn–C(15) are quite different from those found in the literature, because of the tetrahedral environment at the Sn atom.

The ^{119}Sn Mössbauer spectra of the compounds were fitted supposing the existence of one tin site. Table 3 comprises the hyperfine parameters obtained for the complexes, and for comparison those related to the starting materials [33].

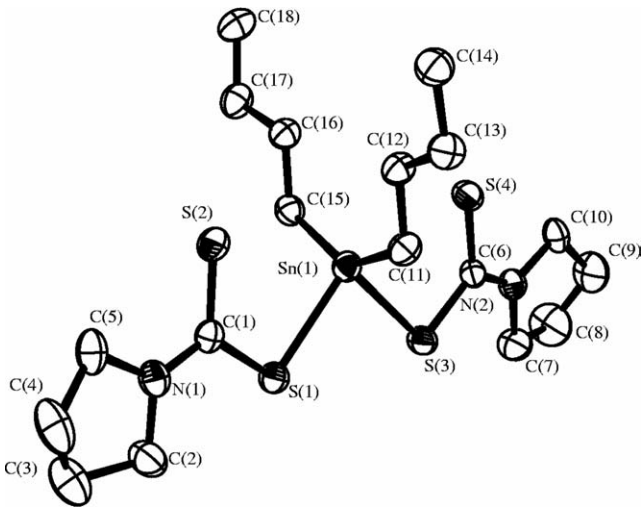

Fig. 2. The molecular structure of **4** and the atom numbering scheme.

Table 2
Selected bond lengths (Å) and angles (°) for complex (**4**)

Sn-S(1)	2.534(6)	Sn-C(11)	2.132(3)
Sn-S(3)	2.532(6)	Sn-C(15)	2.138(2)
C(1)-S(1)	1.732(4)	C(6)-S(4)	1.703(4)
C(1)-S(2)	1.702(4)	C(1)-N(1)	1.332(4)
C(6)-S(3)	1.741(3)	C(6)-N(2)	1.324(4)
C(11)-Sn-C(15)	139.35(9)	C(11)-Sn-S(1)	104.51(7)
S(3)-Sn-S(1)	85.88(2)	C(15)-Sn-S(3)	103.05(7)
C(11)-Sn-S(3)	106.79(7)	C(15)-Sn-S(1)	104.57(7)

Table 3
^{119}Sn Mössbauer parameters, IS and QS

Compounds	IS (mm s^{-1})[a]	QS (mm s^{-1})	Area (%)	Width (mm s^{-1})
1	0.78	1.72	100	0.90
$SnCl_2$	3.71	0.95		
2	1.09	1.72	100	0.90
$[Sn(C_6H_5)_2Cl_2]$	1.38	2.82		
3	1.26	1.65	100	0.90
$[Sn(C_6H_5)_3Cl]$	1.34	2.56		
4	1.58	2.94	100	0.90
$[Sn(C_4H_9)_2Cl_2]$	1.62	3.45		
5	1.37	1.80	100	0.90
$[Sn(C_6H_{11})_3Cl]$ [a]	1.41	2.65		

[a] The errors associated to IS, QS and width are 0.05 mm s^{-1} and 1% for the area. The value for width parameter is 0.90 mm s^{-1} for all complexes.

It is observed a decrease in the isomer shifts (δ) and quadrupole splitting (QS) values for all complexes compared to parent salts, with the exception of complex **1** for which the second parameter increases. All compounds presents spectra characteristic of tin(IV).

The isomer shifts decrease upon coordination due to the variation in the contribution of *s* character in the tin molecular orbital arrangements. The smaller value of the δ parameter in complex **1** might be explained accounting for the withdraw effect of the chlorine atom. The quadrupole splitting is related with the symmetry of electronic density distribution around the Mössbauer atom. In complex **1** the coordination process causes a great deformation in the electronic density at the Sn(IV) centre, resulting in an increase in the quadrupole splitting compared to $SnCl_2$. In complex **4**, the high value of this parameter with relation to other compounds relates to presence of hindering buthyl groups.

3.1. Biological test

The *C. albicans* exhibited resistance against pyrrolidinedithiocarbamate ligand. On the other hand, all complexes have shown remarkable antifungal activity in the screened concentration, 0.025; 0.050; 0.100; 0.200; 0.400; 0.800; 1.600 and 3.200 mM (Table 4 and Fig. 3). The solvents have not shown activity against the microorganism in study.

Some compounds present less active than commercial nystatin, employing the agar disk diffusion method. However the activity exhibited by these tin(IV) complexes might be of interest, since the employed concentration of the compounds is far smaller than that of the commercially available nystatin, which is about 22 mM.

Compounds **2–4** display stable inhibition zones from 0.800 mM. For complexes **1** and **5** the inhibition zones remain stable from 1.600 and 0.200 mM, respectively (see Fig. 3). The large size of the complexes can probably frustrate their penetration through the yeast membrane. In complex **1**, the presence of two chlorine atoms possibly leads to a less hydrophobic compound, which could easily cross the cell membrane compared to the others. The higher activity of complex

Table 4
Inhibition zone (mm) for complexes **1–5** against *C. albicans* (ATCC 18804)

	Inhibition zone (mm)								Complex
	11.0 ± 1	11.4 ± 1	12.0 ± 1	12.0 ± 1	13.6 ± 1	13.8 ± 1	19.5 ± 1	19.7 ± 1	**1**
	8.4 ± 1	8.5 ± 1	9.0 ± 1	9.3 ± 1	9.3 ± 1	10.3 ± 1	10.5 ± 1	10.5 ± 1	**2**
	9.4 ± 1	9.8 ± 1	10.0 ± 1	10.2 ± 1	10.3 ± 1	11.2 ± 1	11.6 ± 1	11.6 ±	**3**
	11.7 ± 1	12.0 ± 1	11.8 ± 1	13.2 ± 1	14.3 ± 1	14.8 ± 1	14.5 ± 1	14.4 ± 1	**4**
	9.0 ± 1	9.8 ± 1	10.0 ± 1	10.8 ± 1	10.7 ± 1	10.7 ± 1	10.7 ± 1	10.7 ± 1	**5**
Concentration (mM)	**0.025**	**0.050**	**0.100**	**0.200**	**0.400**	**0.800**	**1.600**	**3.200**	

Inhibition zone for nystatin = 14 mm.

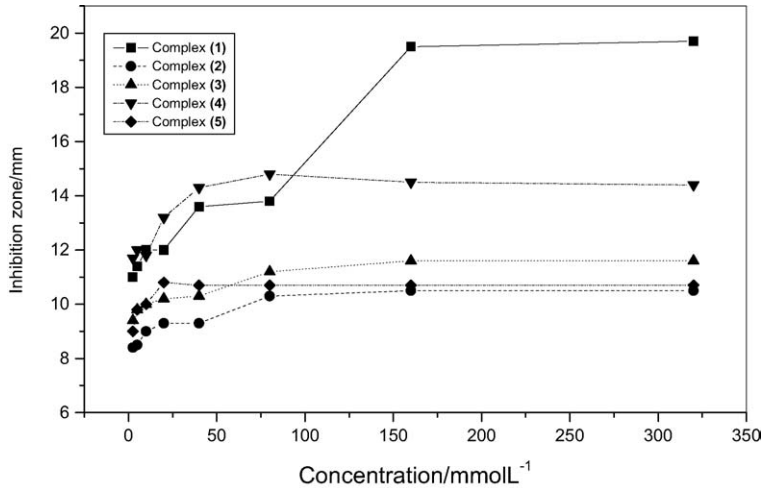

Fig. 3. Inhibition zone versus concentration for complexes **1–5** against.
C. Albicans (ATCC 18804).

4, is probably related to the presence of a monodentate ligand. The two free S atoms might co-ordinate to a molecule in the membrane essentials to the survival of the fungal cell.

4. Supplementary data

Crystallographic data for the structural analysis for complex **4** have been deposited at the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, UK, and are available on request quoting the deposition numbers CCDC 267182.

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