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Tin(IV) complexes of 2-benzoylpyridine *N*(4)-phenylthiosemicarbazone: spectral characterization, structural studies and antifungal activity

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Three tin(IV) complexes of 2-benzoylpyridine *N*(4)-phenylthiosemicarbazone (H2Bz4Ph) were prepared: [Sn(L)Cl_3] (1), [BuSn(L)Cl_2] (2) and [$(Bu)_2$Sn(L)Cl] (3), in which L stands for the anionic ligand formed upon complexation with deprotonation and release of HCl. The complexes were characterized by a number of spectroscopic techniques. The crystal structures of H2Bz4Ph and complex 3 were determined. The antifungal activity of the ligand and its tin(IV) complexes was tested against *Candida albicans*. The thiosemicarbazone proved to be more active than the tin(IV) complexes.

KEYWORDS: 2-benzoylpyridine thiosemicarbazone; tin(IV) complexes; crystal structures; antifungal activity

INTRODUCTION

Thiosemicarbazones and their metal complexes present a wide range of pharmacological applications.[1,2] The pharmacological activities of $\alpha(N)$-heterocyclic thiosemicarbazones derived from 2-formyl and 2-acetylpyridine have been extensively investigated,[3–6] but much less attention has been given to the 2-benzoylpyridine analogues. For the latter, a few transition metal complexes have been prepared[7,8] and their activity against the human pathogenic fungi *Aspergillus niger* and *Paecilomyces variotii* has been demonstrated.[8]

On the other hand, tin complexes are known for their biological interest as antitumorals, antibacterials, antifungals and biocides.[9–11] Coordination of tin with thiosemicarbazones could, in principle, give complexes with the therapeutic properties of both metals and ligands. Here, we report the syntheses and spectral (IR, NMR, ^{119}Sn Mössbauer) characterization of tin(IV) complexes of 2-benzoylpyridine *N*(4)-phenylthiosemicarbazone (H2Bz4Ph; see Fig. 1) as well as a structural study of the ligand and its dibutyltin(IV) complex. The antifungal activity of the free thiosemicarbazone and its tin(IV) complexes was investigated against *Candida albicans*.

EXPERIMENTAL

Syntheses

2-Benzoylpyridine *N*(4)-phenylthiosemicarbazone (H2Bz4Ph, HL) was prepared as described in the literature for other 2-benzoylpyridine-derived analogues.[7,8] [Sn(L)Cl_3] (**1**) and [BuSn(L)Cl_2] (**2**) were prepared by mixing an ethanol solution of the ligand with $SnCl_4$ or [Bu$SnCl_3$] in 1 : 1 molar ratio at room temperature with stirring for 4 h. [$(Bu)_2$Sn(L)Cl] (**3**) was obtained by reacting the ligand with [$(Bu)_2SnCl_2$] in ethanol under reflux for 4 h in 1 : 1 molar ratio. The solids were washed with ethanol followed by diethyl ether and dried *in vacuo*. Crystals of H2Bz4Ph could be taken out of

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the ethanol solution and those of **3** from the tetrahydrofuran (THF) solution used for the NMR studies. Both are stable in the air for several hours.

Characterization methods

Partial elemental analyses were performed on a Perkin Elmer CHN 2400 analyzer and atomic absorption measurements on a Hitashi Z8200 equipment. IR spectra were recorded on a Perkin Elmer 283B spectrometer using Nujol mulls between CsI plates; NMR spectra were obtained with a Brucker DRX-400 Avance (400 MHz) spectrometer using dimethyl sulfoxide-(DMSO-d_6) as the solvent and tetramethylsilane (TMS) as internal reference. A YSI model 31 conductivity bridge was employed for molar conductivity measurements. ^{119}Sn NMR spectra were recorded at room temperature and were referred to external $Sn(CH_3)_4$. Mössbauer spectra were obtained from a constant-acceleration spectrometer moving a $CaSnO_3$ source at room temperature. The samples were analyzed at 85 K. All spectra were computer-fitted assuming Lorentzian curves.

X-ray diffraction

Single-crystal X-ray diffraction has been used to investigate the structures of H2Bz4Ph and complex **3**, at room temperature. Data for H2Bz4Ph have been collected in an Enraf–Nonius CAD4 diffractometer, using monochromated Cu Kα radiation ($\lambda = 1.5418$ Å). The lattice parameters were obtained by least-squares fit from 25 accurately centered reflections. A total of 5575 (5525 unique) reflections were collected in the θ–2θ mode. Data for complex **3** were collected in a Stoe–IPDS diffractometer equipped with an image plate detector; monochromated Mo Kα radiation ($\lambda = 0.710\,73$ Å) was used. The diffracted images were recorded with oscillation steps of 1.0° with exposure time of 6 min per frame. A total of 40 149 reflections were collected.

In vitro antifungal activity

C. albicans (ATCC 18804) liquid cultures were prepared in Sabouraud dextrose broth. The cultures were incubated at 37 °C for 24 h. The agar disk diffusion method for assaying antifungal activity was employed. The commercially available antifungal agent nystatin was used as reference.

RESULTS AND DISCUSSION

Table 1 lists the colors, melting points, partial elemental analyses and molar conductivities of the tin(IV) complexes. The data indicate the formation of $[Sn(L)Cl_3]$ (**1**), $[BuSn(L)Cl_2]$ (**2**) and $[(Bu)_2Sn(L)Cl]$ (**3**), in which L represents the anionic ligand (2Bz4Ph), formed upon deprotonation when the thiosemicarbazone coordinates to tin.

IR data

The IR spectral bands most useful for determining the ligands' mode of coordination are given in Table 2. The ν(C=N) band of the ligand at 1590 cm^{-1} shifts to 1527–1542 cm^{-1} in the spectra of the complexes, suggesting coordination of the imine nitrogen.[12] The ν(C=S) band of the thiosemicarbazone at 800 cm^{-1} shifts to 733–740 cm^{-1} in the complexes, indicating complexation of the sulfur. The 60–70 cm^{-1} change is compatible with deprotonation and formation of a C—S

Table 1. Colors, melting points, partial elemental analyses (calculated values in parentheses) and molar conductivities for 2-benzoylpyridine *N*(4)-phenylthiosemicarbazone (H2Bz4Ph) and its tin(IV) complexes

Compound	Color	Melting point[a] (°C)	C (%)	H (%)	N (%)	Sn (%)	Λ_M (Ω^{-1} cm^2 mol^{-1})[b]
H2Bz4Ph	Yellow	141.6–142.7 (d)	68.66 (68.65)	5.07 (4.85)	16.91 (16.85)		
1 $[Sn(2Bz4Ph)Cl_3]$	Yellow	184.1–186.0 (d)	40.18 (41.01)	2.63 (2.72)	9.40 (10.07)	22.52 (21.33)	5.90
2 $[Sn(2Bz4Ph)BuCl_2]$	Orange	230.8–232.0 (d)	47.87 (47.78)	4.06 (4.18)	9.66 (9.69)	19.38 (20.53)	6.07
3 $[Sn(2Bz4Ph)Bu_2Cl]$	Yellow	187.2–188.9 (d)	53.91 (54.07)	5.39 (5.55)	9.35 (9.34)	18.69 (19.79)	1.44

[a] d: decomposition.
[b] 10^3 mol L^{-1} in dimethylformamide.

Table 2. IR absorptions (cm^{-1}) of 2-benzoylpyridine *N*(4)-phenylthiosemicarbazone (H2Bz4Ph) and its tin(IV) complexes[a]

Compound	ν(C=N)	ν(C=S)	ρ(py)	ν(M—C)	ν(M—S)	ν(M—N$_{py}$)	ν(M—Cl)
H2Bz4Ph	1590s	800m	590m				
1 $[Sn(2Bz4Ph)Cl_3]$	1542m	733m	615w		384w	364w	305w
2 $[BuSn(2Bz4Ph)Cl_2]$	1542m	740m	614w	445w	384w	351w	289w
3 $[Bu_2Sn(2Bz4Ph)Cl]$	1527m	736m	611m	428w 419w	375w	342w	283w

[a] s = strong; m = medium; w = weak.

single bond.[12,13] In addition, the in-plane-deformation mode of the pyridine at 590 cm^{-1} in the spectrum of the ligand shifts 20–25 cm^{-1} to higher frequencies in the complexes, indicating coordination of the heteroaromatic nitrogen.[14] The absorptions at 419–445 cm^{-1} were attributed to ν(Sn—C)[15] and those at 375–384 cm^{-1}, 342–364 cm^{-1} and 283–305 cm^{-1} in the spectra of the complexes were assigned to Sn—S,[16] Sn—N$_{py}$[17] and Sn—Cl[18] vibrations respectively.

Mössbauer data

The ^{119}Sn Mössbauer spectra of all complexes were fitted by supposing the existence of one tin site, in agreement with the proposed formulations. Table 3 gives the hyperfine parameters obtained for the complexes, as well as those for the parent salts[19,20] and data for [Sn(FPT)Cl$_3$] (FPT = 2-formylpyridine thiosemicarbazonato), obtained previously by some of us[16] for comparison. The isomer shifts decrease upon coordination due to the variation in the percentage of s character as tin changes from approximately sp^3 hybridization (25% s character) in the tin salts to sp^{3}d^2 (17% s character) in the complexes, with an increase in coordination number of the metal. The quadrupole splitting decreases in going from complex **3** to complex **1**, due to an increase in the symmetry of electronic density distribution around the metal center as the number of different ligands decreases. Interestingly, for [Sn(FPT)Cl$_3$] the absence of any quadrupole splitting in the Mössbauer[16] spectrum shows that it has a highly symmetrical electronic density distribution, which is lost in the analogue with 2-benzoylpyridine *N*(4)-phenylthiosemicarbazone, probably due to sterical and electronic effects of the two phenyl groups in the latter.

NMR data

Table 4 lists all the ^{1}H and ^{13}C NMR assignments for H2Bz4Ph and its tin(IV) complexes in DMSO-d_6. The spectra of the ligand and of complexes **2** and **3** were recorded in CDCl$_3$ as well, but complex **1** is insoluble in this solvent. The ^{1}H resonances were attributed based on chemical shifts, multiplicities and coupling constants. The carbon type (C,

Table 3. ^{119}Sn Mössbauer parameters, isomer shift (IS) and quadrupole splitting (QS) (relative to CaSnO$_3$), of tin(IV) complexes of 2-benzoylpyridine *N*(4)-phenylthiosemicarbazone (H2Bz4Ph) (data from the literature are also included)

Compound	IS (mm s^{-1})	QS (mm s^{-1})	Ref.
1 [Sn(2Bz4Ph)Cl$_3$]	0.65	0.53	
2 [Sn(2Bz4Ph)BuCl$_2$]	1.06	1.88	
3 [Sn(2Bz4Ph)Bu$_2$Cl]	1.53	3.48	
4 [Sn(FPT)Cl$_3$]	0.585	0	16
5 SnCl$_4$	0.82	0	19
6 BuSnCl$_3$	1.31	1.83	20
7 Bu$_2$SnCl$_2$	1.50	3.40	20

Table 4. ^{1}H and ^{13}C NMR signals[a] for 2-benzoylpyridine *N*(4)-phenylthiosemicarbazone (H2Bz4Ph) and its tin(IV) complexes in DMSO-d_6

Attribution	H2Bz4Ph (HL)		[Sn(L)Cl$_3$] (δ)	[Sn(L)BuCl$_2$] (δ)	[Sn(L)Bu$_2$Cl] (δ)	Attribution	H2Bz4Ph		[Sn(L)Cl$_3$] (δ)	[Sn(L)BuCl$_2$] (δ)	[Sn(L)Bu$_2$Cl] (δ)
	Z (δ)	*E* (δ)					*Z* (δ)	*E* (δ)			
N3—H	13.14	10.63	—	—	—	C8=S	176.62	176.45	166.52	172.21	167.00
H6	8.84	8.47	9.20	9.03	9.01	C2	151.46	149.62	138.24	144.70	155.89
H4	8.00	7.87	8.48	8.34	8.06	C6	148.96	148.81	144.80	145.48	147.82
N4—H	10.27	8.96	10.96	10.53	9.87	C7=N	144.04	—	141.28	138.99	139.90
H5	7.55–7.61	7.38–7.47	8.17	7.98	7.72	C4	138.36	136.78	144.60	143.28	139.77
H3	7.34–7.38	8.49	7.89	7.66	7.27	C9	136.78	131.16	129.43	142.50	148.42
						C3	126.34	122.48	128.26	127.23	126.21
						C5	125.18	125.35	129.02	127.95	126.21
						Cα				35.60	34.90
						Cβ				27.60	27.60
						Cγ				25.00	25.40
						Cδ				13.70	13.60
						$^1J(^{119}\mathrm{Sn}^{13}\mathrm{C})$/Hz[b]				934.0	754.6
						$^1J(^{119}\mathrm{Sn}^{13}\mathrm{C})$/Hz				942.6	810.9
						$^2J(^{119}\mathrm{Sn}^{13}\mathrm{C})$/Hz[b]				55.2	45.2
						$^2J(^{119}\mathrm{Sn}^{13}\mathrm{C})$/Hz				53.3	45.0
						$^3J(^{119}\mathrm{Sn}^{13}\mathrm{C})$/Hz[b]				180.5	148.7
						$^3J(^{119}\mathrm{Sn}^{13}\mathrm{C})$/Hz				184.3	140.7

[a] The phenyl hydrogen atoms appear as multiplets in the $\delta = 7.76$–7.19 region in the ligand and in the $\delta = 7.72$–6.84 region in the complexes. The phenyl carbon atoms appear in the $\delta = 130.91$–119.91 range. Carbon atoms α–δ correspond to butyl group.

[b] Measurements carried out in CDCl$_3$

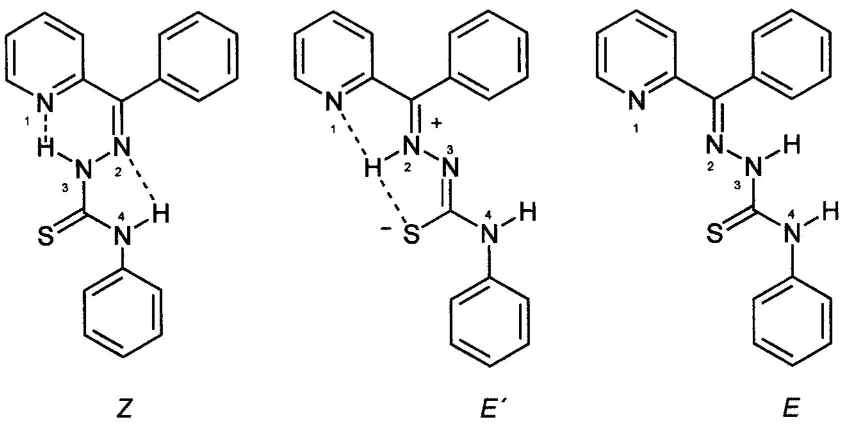

Figure 1. *Z*, *E′* and *E* isomers of 2-benzoylpyridine *N*(4)-phenylthiosemicarbazone (H2Bz4Ph).

CH) was determined by using DEPT135 experiments. The assignments of the protonated carbon atoms were made by two-dimensional heteronuclear-correlated experiments (HMQC) using delay values that correspond to ^1J(C,H). In the spectra of the uncomplexed thiosemicarbazone, the signals are duplicated as a consequence of the existence of structural isomers (see Fig. 1) in solution. The N3—H chemical shifts in DMSO-d_6, $\delta = 13.14$ and $\delta = 10.63$, suggest the presence of the *Z* (70%) and *E* (30%) isomers, in accordance with data reported in the literature for other 2-benzoylpyridine-derived thiosemicarbazones.[21] The high-frequency signal for the *E* form is characteristic of hydrogen bonding with the solvent.[22] In $CDCl_3$, the signals for N3—H were found at $\delta = 14.05$ and $\delta = 9.87$, suggesting the presence of an equivalent mixture of the *Z* and *E′* forms (80%) together with the *E* isomer (20%), as observed for other thiosemicarbazones.[8,14] The *Z* form is present in the solid, as shown by the crystal structure determination of H2Bz4Ph. Moreover, the X-ray diffraction study of complex **3** corroborates the existence of the *E* isomer (see below).

The N3—H signal is absent in the spectra of the complexes, in agreement with deprotonation and formation of an anionic ligand. Upon complexation, the N4—H resonance and the signals of the pyridine hydrogen and carbon atoms undergo significant shifts. In the ^{13}C NMR spectrum, very large shifts occur for C=S, C=N and the pyridine carbon atoms, in accordance with coordination of the sulfur, the imine nitrogen and the heteroaromatic nitrogen, leading to a complex in which the thiosemicarbazone adopts the *E* form. This is also the conformation adopted in the solid, as revealed by the crystal structure determination of complex **3** (see below).

Higher coupling constants $^1J(^{119}Sn^{13}C)$, corresponding to the α carbon of the butyl group, were observed in $CDCl_3$ in relation to the values measured for the starting salts: $SnBuCl_3$, $^1J(^{119}Sn^{13}C) = 648.16$ Hz, $^1J(^{119}Sn^{13}C) = 934.00$ Hz (**2**); $SnBu_2Cl_2$ $^1J(^{119}Sn^{13}C) = 419.69$ Hz, $^1J(^{119}Sn^{13}C) = 754.60$ Hz (**3**). This is in agreement with increasing coordination number in going from the tin(IV) salts to the complexes, as reported in the literature.[23,24] In a coordinating solvent such as DMSO, no significant variations were observed.

The coupling constants $^1J(^{119}Sn^{13}C)$ have been used to determine the value of the C—Sn—C angle θ for complex

Table 5. Crystal data and structure refinement for 2-benzoylpyridine *N*(4)-phenylthiosemicarbazone (H2Bz4Ph) and complex (**3**)

Compound	H2Bz4Ph	Complex (**3**)
Empirical formula	$C_{19}H_{16}N_4S$	$C_{27}H_{33}N_4SSnCl$
Color; habit	Yellow, prism	Yellow, prism
Crystal system	Monoclinic	Monoclinic
Space group	$C2/m$	$P2_1/n$
a (Å)	17.8336(7)	9.8353(5)
b (Å)	9.1202(9)	23.8978(10)
c (Å)	21.8640(13)	12.421(5)
β (°)	105.286(9)	105.033(4)
Volume (Å^3)	3430.3(4)	2819.5(12)
Z	8	4
Formula weight	332.42	599.77
Density, calc. (g/cm^{-3})	1.287	1.413
Absorption coeff. (mm^{-1})	0.196	1.092
F(000)	1392	1224
θ range (°)	2.4–25.7	4.3–39.4
Reflections collected/unique (R_{int})	3303/3196 (0.037)	39 696/12 134 (0.037)
Data $I \geq 2\sigma(I)$/ restraints/ parameters	3196/0/217	12 134/2/307
R_{obs}, R_{all}	0.040, 0.052	0.0436, 0.1186
wR_{2obs}, wR_{2all}	0.130, 0.137	0.1103, 0.1348
CCDC no.	210620	210619

3 in solution using a method described in the literature.[23,24] We found $\theta = 151.8 \pm 21.1$ in $CDCl_3$ and $\theta = 157.4 \pm 21.5$ in DMSO-d_6. These values are close to the angle determined by X-ray crystallography for complex **3**, suggesting that the structure in solution is not much different from that of the solid. Moreover, the similarity of the angles obtained in the two solvents indicates that DMSO is probably not coordinated to the tin center.

The ^{119}Sn NMR study was performed using THF solutions of **1**–**3** and also of the starting salts $SnBuCl_3$, $SnBu_2Cl_2$ and $SnBu_3Cl$ in the same solvent for comparison. As expected, a single resonance was observed for all compounds: $[Sn(2Bz4Ph)Cl_3]$ (**1**), $\delta = -491$; $[Sn(2Bz4Ph)BuCl_2]$ (**2**), $\delta = -353$; $[Sn(2Bz4Ph)Bu_2Cl]$ (**3**), $\delta = -197$. For the precursors we found: $SnBuCl_3$, $\delta = -178$; $SnBu_2Cl_2$, $\delta = 26$; and $SnBu_3Cl$, $\delta = 108$. For $SnCl_4$, $\delta = -150$.[25] All signals are situated in the range of chemical shifts expected for tin(IV) compounds.[25] In view of the resonances observed, the ^{119}Sn nucleus of **1** is more shielded than the nuclei of the other derivatives, followed by those of **2** and **3**. In complex **1** the Sn(IV) center is surrounded by three chloride ions, whereas two and one chloride ions are present in the coordination spheres of **2** and **3** respectively, suggesting that the chloride electron cloud is probably responsible for the shielding effect. In fact, a similar variation is also observed for the butyl-containing organotin compounds, $SnBu_xCl_{4-x}$, ($x = 1$, 2 and 3), indicating again that the variation in the ^{119}Sn chemical shifts seems to relate with replacing Cl^- by butyl groups. Moreover, complexation causes a general effect of moving the ^{119}Sn chemical shifts upfield due to the increase in coordination number of tin, as expected.[18]

Table 6. Selected bond lengths (Å) and angles (°) for H2Bz4Ph

S–C8	1.663(2)	N4–C8	1.343(3)
N4–C15	1.410(2)	N2–C7	1.296(2)
N2–N3	1.362(2)	N3–C8	1.360(2)
N1–C6	1.335(3)	N1–C2	1.343(2)
C8–N4–C15	130.4(2)	N4–C8–N3	114.3(2)
C7–N2–N3	119.4(2)	N4–C8–S	128.0(1)
C8–N3–N2	120.5(2)	N3–C8–S	117.7(1)

Table 7. Selected bond lengths (Å) and angles (°) for **3**

Sn–N2	2.338(19)	N2–N3	1.378(3)
Sn–S	2.507(10)	N2–C7	1.305(3)
Sn–N1	2.581(2)	N3–C8	1.314(3)
Sn–Cl	2.613(7)	N4–C15	1.426(3)
S–C8	1.736(3)	N4–C8	1.358(3)
N1–C2	1.345(3)	C1A–Sn	2.139(3)
N1–C6	1.328(4)	C1B–Sn	2.152(3)
C1B–Sn–C1A	153.10(14)	C2–N1–Sn	114.96(16)
N1–Sn–Cl	131.71(5)	C7–N2–Sn	124.37(16)
N1–Sn–S	142.02(5)	C6–N1–Sn	126.6(2)
N2–Sn–N1	66.19(7)	N3–N2–C7	114.59(19)
N2–Sn–S	75.98(5)	C8–N3–N2	115.48(19)
N2–Sn–Cl	162.07(5)	N4–C8–N3	116.8(2)
N3–N2–Sn	120.92(15)	N4–C8–S	114.96(19)
S–Sn–Cl	86.20(2)	N3–C8–S	128.26(18)
C8–S–Sn	98.51(8)		

Crystal structures

Crystal data and refinement results for H2Bz4Ph and **3** are shown in Table 5, and selected bond distances and angles are collected in Tables 6 and 7 respectively. Perspective views for the asymmetric units of H2Bz4Ph and **3** can be seen in Fig. 2a and b.

As expected, the bond distances in H2Bz4Ph (see Table 6) are very similar to those determined before for H4Bz4Ph,

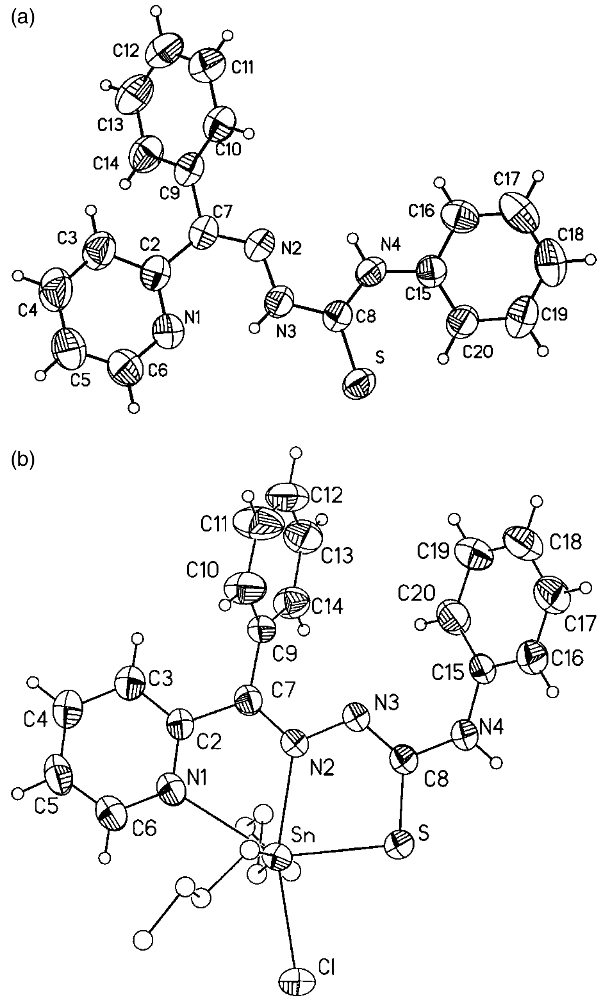

Figure 2. (a) Perspective view of the molecular structure of 2-benzoylpyridine *N*(4)-phenylthiosemicarbazone (H2Bz4Ph); (b) perspective view of the molecular structure of $[(Bu)_2(2Bz4Ph)Cl]$. For the sake of clarity the carbon atoms in the two butyl units are represented with isotropic adp and are not labeled; their corresponding hydrogen atoms have been omitted.

in which the side chain is attached to the 4-position in the pyridine ring.[26] The angles between the plane of the phenyl ring attached to C7 and the plane of the lateral chain are not very different for the two thiosemicarbazones, i.e. 60.14(11)° and 60.89(9)° for H2Bz4Ph and H4Bz4Ph respectively. However, significant differences were found for the angles between the plane of the thiosemicarbazone moiety and the plane of the pyridine ring, which are 10.58(10)° and 52.6(1)° in H2Bz4Ph and H4Bz4Ph respectively, and the angles between the thiosemicarbazone chain and the N(4)—phenyl ring, which are 15.95(8)° and 57.13(8)° respectively. Such dissimilarities are probably responsible for the differences in the angles in the thiosemicarbazone moiety of the two isomers. For example, the C8—N3—N2 angles are 120.5(2)° and 117.7(2)° and the N4—C8—S angles are 128.01(14)° and 125.8(2)° for H2Bz4Ph and H4Bz4Ph respectively.

Interestingly, H2Bz4Ph crystallizes in the *Z* conformation, which is stabilized by a hydrogen bond between N3—H and the heteroaromatic nitrogen. As shown above by the NMR spectra, this is the predominant form in solution as well. On the other hand, H4Bz4Ph crystallizes in the *E* conformation, which is preferred if no N3—H—N1 hydrogen bonding can occur, and this form also predominates in solution.[26] An intramolecular N4—H4· · ·N2 bond is formed as well in both isomers.

Furthermore, comparison with the closely related 2-benzoylpyridine *N*(4)-methyl-*N*(4)-phenylthiosemicarbazone[27] reveals that most bond distances and angles in the thiosemicarbazone moiety are very similar. However, variations were observed in the vicinity of N4 due to the presence of different substituents in the two compounds.

The molecules of complex **3** are associated by an intermolecular N4—H4· · ·Cl bond. The Sn(IV) lies in the center of a very distorted octahedron, formed by the carbon atoms of two *n*-butyl groups, one chloride and the anionic thiosemicarbazone coordinated through an N—N—S tridentate system.

Upon complexation the C8—N3 bond length goes from 1.360(2) Å in H2Bz4Ph to 1.314(3) Å and the C8—S bond distance varies from 1.663(2) Å in H2Bz4Ph to 1.736(3) Å in complex **3** (see Table 7), as a consequence of deprotonation at N3 and formation of an extensively conjugated system involving the thiosemicarbazone moiety and the two rings attached to C7. Therefore, C—S goes from a thione bond in the ligand to a thiolate bond in the complex and C8—N3 from a single bond in H2Bz4Ph to a predominantly double bond in complex **3**. The N2—N3 distance goes from 1.362(2) Å in the ligand to 1.378(3) in **3** and N2—C7 goes from 1.296(2) Å in H2Bz4Ph to 1.305(3) Å in **3**.

From the crystallographic study, a twisting of 180° in the N2—N3 bond of the ligand to match the steric requirements for tridentate coordination was evidenced. As expected, the angles in the thiosemicarbazone moiety undergo significant modifications on coordination (see Table 7). For example, the C8—N3—N2 angle goes from 120.5(2)° in the ligand to 115.48(19)° in complex **3**; the C8—N3—S angle goes from 117.7(1)° in H2Bz4Ph to 128.26(18)° in **3** and the N4—C8—N3 angle from 128.0(1) to 114.96(19)°.

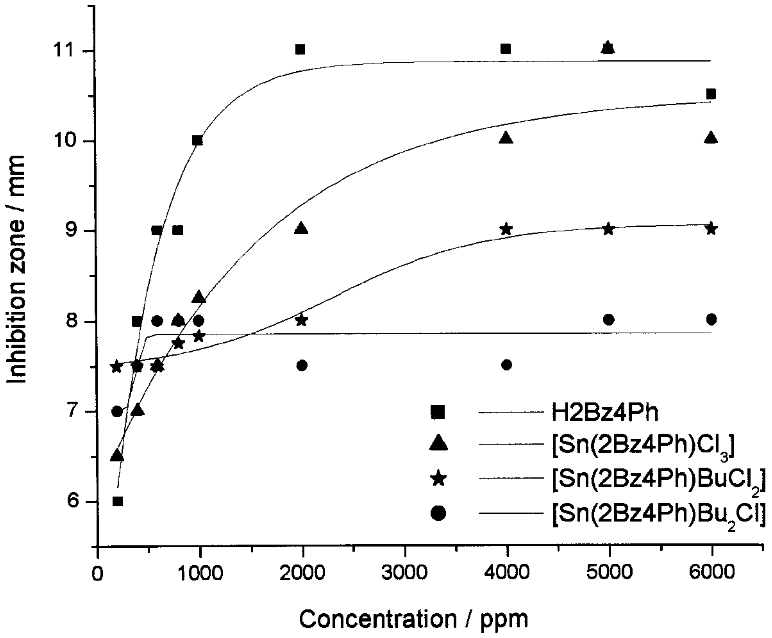

Figure 3. Growth inhibitory activity of 2-benzoylpyridine *N*(4)-phenylthiosemicarbazone (H2Bz4Ph) and its tin(IV) complexes against *C. albicans* (diameter of growth inhibition zone; 6.0 mm = no inhibition). Growth inhibition zones are averages of three values. Inhibition zone for nystatin is 14.0 mm at the maximum dose used.

In the previously prepared compound [Sn(FPT)Cl_3],[16] the C—S bond distance, 1.753(3) Å, is comparable to the C8—S distance obtained for complex **3**, 1.736(3) Å, in accordance with deprotonation upon complexation in both cases. All metal-to-ligand bond distances are bigger in complex **3**, as a consequence of the bulkiness of H2Bz4Ph, as well as of the two butyl groups, which do not allow a closer interaction of the ligand with the tin center.

Antifungal studies

H2Bz4Ph exhibited antifungal activity against *C. albicans*. Though less active than nystatin in the agar disk diffusion method employed in the present work, the activity exhibited by the thiosemicarbazone is still of interest, since resistance to the commercially used drug limits its application. Moreover, the activity of the compound against cultures resistant to nystatin could be higher than against the reference cultures. Upon complexation to tin(IV) the antifungal action decreases (see Fig. 3). Complex **1** is the most effective, but the activity decreases as the chloride ligands are substituted by *n*-butyl groups in complexes **2** and **3**. Metal complexes can act as antifungals by inhibiting enzymes, such as those involved in the biosyntheses of yeast cell walls.[28] The antifungal properties of tin complexes are well known,[29] and some studies report that tin(IV) complexes of thiosemicarbazones could be good candidates as antifungal agents.[30] In the present study, the activity of the thiosemicarbazone was lowered on coordination to tin, probably due to the bulkiness of the complexes, which do not facilitate their permeation through the yeast membrane. In complex **1**, the presence of three chlorine atoms possibly leads to a more lipophilic compound, which could cross the cell membrane better than the other two complexes.

Supplementary data

Crystallographic data for H2Bz4Ph and complex **3** (excluding structure factors) have been deposited at the Cambridge Crystallographic Data Centre as supplementary publication numbers CCDC 210619 and 210620 respectively. Copies of available material can be obtained on application to CCDC, 12, Union Road, Cambridge CB2 IEZ, UK (fax 44-1223-336033 or e-mail: deposit@ccdc.cam.ac.uk).

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