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Chloro-diorganotin(IV) Complexes of Pipyridyl Dithiocarbamate: Syntheses and Determination of Kinetic Parameters, Spectral Characteristics and Biocidal Properties

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Organotin complexes of the general formula $R_2Sn(Cl)L$ have been synthesized where R = CH_3, C_2H_5, C_4H_9, C_6H_5, C_7H_7, and L = 1-piperidinecarbodithioic acid. These complexes have been characterized by elemental analysis, FT-IR, ^{1}H NMR and mass spectrometry. The spectroscopic and XRD data shows that the dithiocarbamate ligand acts as a bidentate ligand. These complexes were also tested for biocidal activity. Thermal studies of the reported complexes have been carried out to investigate the degradation pattern and thermal stability while kinetic parameters were calculated from the thermogravometric (TG) trace. Silent features of X-ray structures for (1) and (4) are also given.

Keywords: Chloro-diorganotin(IV) complexes, Dithiocarbamate, S-donor ligand, FT-IR, Mass spectrometry, ^{1}H NMR, Biocidal activity

INTRODUCTION

Since some organotin complexes were found to exhibit the properties of antitumor activity *in vitro*, many series of organotin(IV) complexes have been synthesized and studied in the context of their antitumor potential [1]. Among these efforts to obtain potential antitumor organotin(IV) species, an important strategy is to synthesize organotin(IV) derivatives of biologically relevant substrates. It has been proven that the 2-mercaptopyrimidine (HSPym) and 2-mercapto-4-amino-pyramidine (HSaPym), similar to 2-mercaptopyrimidine nucleosides, are able to inhibit the synthesis of tRNA [2]. Thus they may act as valuable substrates for synthesizing antitumor-active organotin compounds. Moreover, as far as the coordination geometry is concerned, the ligand is interesting, as well. The ligand*'s* own two sulfur atoms and can act as an S,S-bridging ligand.

We synthesized a series of compounds (**1**-**5**) to study their thermal and biological behavior. Two of the compounds, (**2**) and (**5**) have not been previously reported, whereas the synthesis and ^{1}H NMR of the three compounds are reported in the literature [3].

We synthesized these compounds and studied their mass spectrometry, biocidal activity and thermal behavior. Kinetic parameters were calculated from the thermal data while silent features from X-ray data are reported for compounds (**1**) and (**4**) from our earlier findings [4,5].

EXPERIMENTAL

Instrumentation

Melting points were determined in a capillary tube on an

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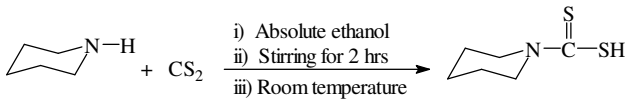
electrothermal melting point apparatus, model MP-D Mitamura Rikero Kogyo (Japan), and are uncorrected. Infrared spectra were recorded on a Perkin Elmer 1000 spectrometer. Electron impact mass spectra (EIMS) were recorded on a Finnigan MAT-312 connected to DPD 11/34 (DEC) computer system. The ^{1}H NMR data were recorded on a Bruker AM-400 MHz spectrometer using DMSO-d_6 as the solvent. Elemental analyses were performed with a model PE-240011 elemental analyzer. The solvent was dried by a previously reported method [6] and dibenzyltin dichloride was synthesized as previously reported [7].

Procedure for Synthesis of 1-Piperidinedithioic Acid (HL)

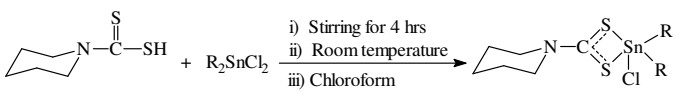
Piperidine (1 mmol) and carbon disulphide (1 mmol) were stirred in a round bottom 100 ml flask in absolute ethanol at room temperature. After stirring for 2 h, yellow precipitates formed and were filtered off and washed with diethylether. The chemical reaction is given below:



Procedure for the Synthesis of Organotin(IV) Derivatives (1)-(5)

These complexes were prepared by reacting the 1-piperidinedithioic acid with diorganotin(IV) halides in a 1:1 molar ratio, in dry chloroform (100 cm^3) in round bottom 250 ml flask. The reaction mixture was stirred at room temperature for 4 h.

The solid product was obtained after slowly evaporating the solvent at room temperature. The solid products were recrystallized in $CHCl_3$ and n-hexane (1:1).



R = Me (**1**), Et (**2**), Bu (**3**), Ph (**4**), and Bz (**5**)

RESULTS AND DISCUSSION

Physical data for the reported complexes (**1**)-(**5**) is given in Table 1. All complexes are solid and having sharp melting points.

FT-IR Spectroscopy

The explicit feature in the infrared spectra of all complexes is the absence of the band in the region 2564 cm^{-1}, which appears in the free ligand as the ν (S–H) vibration. In the far-infrared spectra, strong absorption appears in the range of 448-435 cm^{-1} in the spectra of each of the complexes, which is assigned to Sn-S stretching (see Table 2). All these values are consistent with that detected in a number of organotin(IV)-sulfur derivatives and indicate the formation of a metal-ligand bond through this site [8]. Bands in the range of 1471-1438, 557-511 and 395-335 cm^{-1} indicate the presence of C-N, Sn-C, and Sn-Cl stretching vibrations, respectively.

^{1}H NMR Spectroscopy

In the ^{1}H NMR data of complexes (**2**)-(**5**), the -SH resonance of the ligand is absent which suggests the replacement of -SH proton by organotin(IV) moiety. The ^{1}H NMR data is listed in Table 3. The R groups give signals in the expected range.

The α-CH_2 protons of the diethyltin(IV) derivative resonate as a quartet at 2.48 ppm with ^2J [^{119}Sn, ^{1}H] = 61 Hz, while β-CH_3 protons resonate as a triplet at 1.33 ppm. The dibenzyltin(IV) moiety of compound (**5**) also involves a complex pattern. However, the CH_2 protons of the benzyl moiety show a singlet at 1.25 ppm with ^2J [^{119}Sn, ^{1}H] = 66 Hz. The values of the coupling constant for compounds (**2**), (**3**), and (**5**) suggest the four coordinated geometry in solution [9].

Mass Spectrometry

Molecular ion peaks of low intensity are observed in pipyridyl dithiocarbamate (**HL**), complexes (**1**) and (**4**) at m/z 161, 345 and 369 respectively. Monoisotopic fragments along with their m/z (%) values are given below:

1-Piperidinecarbodithioic acid (HL). $[Pipy\text{-}CS\text{-}SH]^+$ 161 (17.4), $[Pipy\text{-}CS]^+$ 128 (100), $[Pipy\text{-}Cl]^+$ 96 (2.5), $[Pipy]^+$ 84 (46).

Table 1. Physical Data for Free Ligand and its Organotin(IV) Complexes

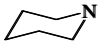
Compound	Empirical formula	M.W.	M.P. (°C)	Yield (%)	Elemental analysis %Calcd. (%Found)			
					C	H	N	S
HL	$C_6H_{11}NS_2$	161	158-160	95	44.72 (44.70)	6.83 (6.81)	8.69 (8.67)	39.75 (39.71)
(**1**)	$C_8H_{11}NS_2ClSn$	345	98	90	27.82 (27.80)	4.63 (4.61)	4.05 (4.02)	18.55 (18.52)
(**2**)	$C_{10}H_{20}NS_2ClSn$	373	167	65	32.17 (32.15)	5.36 (5.35)	3.75 (3.37)	17.15 (17.12)
(**3**)	$C_{14}H_{28}NS_2ClSn$	429	245	78	39.16 (39.14)	6.52 (6.50)	3.26 (3.24)	14.91 (14.90)
(**4**)	$C_{18}H_{20}NS_2ClSn$	469	199	84	46.05 (46.01)	4.26 (4.25)	2.98 (2.96)	13.64 (13.62)
(**5**)	$C_{20}H_{24}NS_2ClSn$	497	203	70	48.28 (48.25)	4.82 (4.80)	2.81 (2.79)	12.87 (12.83)

Table 2. FT-IR Spectral Data (cm^{-1}) for Free Ligand and its Organotin(IV) Complexes

Compound	ν ($_{C-N}$)	ν ($_{C-S}$)	ν ($_{S-H}$)	ν ($_{Sn-C}$)	ν ($_{Sn-Cl}$)	ν ($_{Sn-S}$)
HL	1442 s	1068 s	2546 s	–	–	–
(**1**)	1458 w	1095 s	–	557 m	335 m	435 m
(**2**)	1438 m	1080 m	–	545 m	395 m	427 w
(**3**)	1462 s	1075 m	–	532 s	375 m	411 m
(**4**)	1471 m	1065 s	–	252 m	362 s	448 s
(**5**)	1425 m	1052 m	–	511 s	345 s	439 m

s = strong, m = medium, w = weak.

Table 3. ^{1}H NMR Data (ppm)[a] for Free Ligand and its Organotin(IV) Complexes in DMSO-d_6

Compound		-SH	R
HL	1.41-1.69 m	1.85 s	–
(**2**)	1.49-1.75 m	–	2.48 q [61], 1.33 t (7.5)
(**3**)	1.52-1.72 m	–	0.88 t [68], 1.63-1.68 m, 1.33 m, 2.49 t (7.5)
(**4**)	1.53-1.64 m	–	7.45-7.51 m
(**5**)	1.53-1.66 m	–	1.25s [66], 7.02-7.26 m

[a]s = singlet, t = triplet, q = quartet, m = multiplet.

Complex (1): Dimethyltin(IV) chloro-1-pipyridyl dithiocarbamate. $[(CH_3)_2Sn(\text{-S-CS-Pipy})Cl]^+$ 345 (2.6), $[(CH_3)_2Sn(\text{-S-CS-Pipy})Cl]^+$ 310 (16), $[Sn(\text{-S-CS-Pipy})]^+$ 280 (39), $[Sn(\text{-S-CS-Pipy})_2]^+$ 440 (12), $[Cl\text{-}Sn(CH_3)_2]^+$ 185 (13.3), $[CS\text{-Pipy}]^+$ 128 (89), $[Pipy]^+$ 84 (68), $[S\text{-CS}]^+$ 76 (100), $[Sn\text{-Cl}]^+$ 155 (5.4), $[Sn]^+$ 120 (2.4).

Complex (2): Diethyltin(IV) chloro-1-pipyridyl dithiocarbamate. $[(C_2H_5)_2Sn(\text{-S-CS-Pipy})Cl]^+$ 373 (n.o), $[(C_2H_5)_2Sn(\text{-S-CS-Pipy})]^+$ 338 (13), $[Sn(\text{-S-CS-Pipy})]^+$ 280 (20), $[Sn(\text{-S-CS-Pipy})]^+$ 248 (6.5), $[Pipy\text{-CS}]^+$ 128 (73.6), $[Pipy\text{-Cl}]^+$ 96 (4.1), $[Sn\text{-Cl}]^+$ 155 (30.5).

Complex (3): Dibutyltin(IV) chloro-1-pipyridyl dithiocarbamate. $[(Bu)_2Sn(\text{-S-CS-Pipy})_2Cl]^+$ 429 (n.o), $[(Bu)Sn\text{-Cl}(\text{-S-CS-Pipy})]^+$ 372 (4.9), $[(Bu)Cl\text{-}Sn(S)]^+$ 244 (2.1), $[Bu\text{-Sn-S}]^+$ 209 (3.5), $[Sn\text{-S-C}]^+$ 208 (3.5), $[(Bu)_2Sn\text{-Cl}]^+$ 269 (4.5), $[(Bu)Sn\text{-Cl}]^+$ 212 (10.0), $[Bu]^+$ 57 (100), $[Pipy]^+$ 84 (73.2), $[Sn\text{-Cl}]^+$ 155 (8.9), $[Sn]^+$ 120 (2.1).

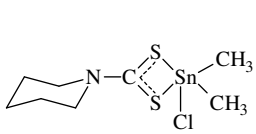
Complex (4): Diphenyltin(IV) chloro-1-pipyridyl dithiocarbamate. $[(Ph)_2Sn(\text{-S-CS-Pipy})_2Cl]^+$ 469 (3.2), $[(Ph)_2Sn(\text{-S-CS-Pipy})]^+$ 434 (30), $[(Ph)Sn\text{-Cl }(\text{-S-CS-Pipy})]^+$ 392 (100), $[(Ph)_2Sn(\text{-S-C})_2S]^+$ 394 (50), $[Cl\text{-}Sn(\text{-S-CS-Pipy})]^+$ 315 (3.2), $[Sn(\text{-S-CS-Pipy})_2]^+$ 440 (11), $[Sn\text{-}(\text{-S-CS-Pipy}]^+$ 280 (39), $[Sn(\text{-S-CS})_2]^+$ 196 (4.5), $[Sn\text{-Cl}]^+$ 155 (20.5), $[Pipy\text{-CS}]^+$ 128 (100), $[(Ph)_2Sn\text{-Cl}]^+$ 386 (3.5), $[(Ph)Sn\text{-Cl}]^+$ 309 (34.4), $[(Ph)_2Sn]^+$ 351 (4.3), $[Sn]^+$ 120 (4.4).

Complex (5): Dibenzyltin(IV) chloro-1-pipyridyl dithiocarbamate. $[(Bez)_2Sn(\text{-S-CS-Pipy})_2Cl]^+$ 497 (n.o), $[Sn(\text{-S-CS-Pipy})Cl]^+$ 315 (27.0), $[(Bez)SnS_2]^+$ 275 (15), $[Sn(\text{-S-CS-Pipy})]^+$ 280 (28.3), $[Pipy\text{-CS}]^+$ 128 (100), $[Pipy]^+$ 84 (78), $[(Bez)Sn\text{-Cl}]^+$ 246 (3.5), $[Sn\text{-Cl}]^+$ 155 (7.7), $[Sn\text{-S}]^+$ 152 (2.6), $[Sn]^+$ 120 (2.0).

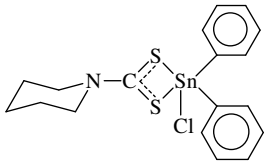
Silent Features of X-ray Analysis

Compound (1) [4]. Monoclinic, Space group = $P2_1/c$, a = 10.817 (3), b = 10.044 (2), c = 12.508 (4) Å, V = 1301.4 (6) $Å^3$, Z = 4, D_{calc} = 1.758 mg m^{-3}, R = 0.022, *w*R = 0.050.

Compound (4) [5]. Orthorhombic, Space group = $P2_12_12_1$, a = 10.281 (1), b = 12.118 (2), c = 15.440 (3) Å, V = 1923.6 (5) $Å^3$, Z = 4, D_{calc} = 1.618 mg m^{-3}, R = 0.023, *w*R = 0.056.



(**1**)



(**4**)

Thermal Studies

Thermal analyses of synthesized complexes (**1**), (**3**) and (**4**) have been carried out to investigate the degradation pattern, thermal stability and purity of each. Some kinetic parameters such as activation energy (E_a), order of reaction (n), enthalpy (ΔH) and entropy (ΔS) were calculated by using Horowitz and Metzger's method [10] and Coats and Redfern's method [11] to verify the thermal stability of the complexes. Results are given in Tables 4 and 5.

In complex (**1**), a two-step decomposition process was observed. The complex was stable at 170 °C. The first step showed the loss of 1/2 C_6H_5Cl group with an 11.25% weight loss (170-220 °C). This step required an activation energy of 17.43 kJ mol^{-1} with an order of 0.7. In the second step (220-230 °C) 1/2 C_6H_5Cl, $C_{12}H_{15}N$ and 1/2 SnS_2 with a 73.58% weight loss, leaving 15.17% as residue. The reaction order was 1.23, with an activation energy of 53.04 kJ mol^{-1}.

Complex (**3**) again followed a two-step decomposition pattern. In the first step, $C_7H_{13}Cl$ and C_7H_{11} groups were eliminated in a temperature range of 160-240 °C with a 45.22% weight loss. This step had an order of 1.11 and required an activation energy of 31.431 kJ mol^{-1}. In the second step (240-370 °C) C_6H_4N and 1/2 SnS_2 evolved with a 37.01% weight loss, leaving 17.77% as residue. This step had an order of 0.87 and an activation energy of 27.12 kJ mol^{-1}.

In the case of complex (**4**), the thermogravimetric trace shows a mass loss over a temperature range of 160-370 °C. This single step decomposition showed a 97% weight loss due to the loss of $C_8H_{16}NCl$ and 1/16 SnS_2 with an order of 3.03 and an activation energy of 35.18 kJ mol^{-1}. A plot of theta *vs*. $\ln\ln W_o/W$ for the thermogravimetric studies of complex (**1**) and (**3**) are given in Figs. 1-3.

Table 4. Thermal Decomposition Pattern of Organotin(IV) Complexes

Compound	Empirical formula	Temp. range (°C)	Evolved components	Residual components	%wt. loss calcd.	%wt. loss obs.
(**1**)	$C_8H_{16}NS_2SnCl$	160-370	$C_8H_{16}NCl$ 15/16 SnS_2	1/16 SnS_2	96.71 3.29(Res.)	96.89 3.11(Res.)
(**3**)	$C_{18}H_{20}NS_2SnCl$	170-220	1/2 C_6H_5Cl	1/2 C_6H_5Cl $C_{12}H_{15}NS_2Sn$	11.99	11.25
		220-310	1/2 C_6H_5Cl, $C_{12}H_{15}N$, 1/2 SnS_2	1/2 SnS_2	67.21 19.4(Res.)	73.58 15.17(Res.)
(**4**)	$C_{20}H_{28}NS_2SnCl$	160-240	$C_7H_{13}Cl$, C_7H_{11}	$C_6S_2NH_4Sn$	43.40	45.22
		240-370	C_6H_4N, 1/2 SnS_2	1/2 SnS_2	36.40 18.3(Res.)	37.01 (17.77(Res.)

Table 5. Kinetic Parameters Calculated from TG Curve for Organotin(IV) Complexes

Compound	Temp. range (°C)	E_a (kJ mol^{-1})	ΔG (kJ mol^{-1})	ΔS (J mol^{-1} K^{-1})	n
(**1**)	160-370	24.8	24.3	28.6	3.0
(**3**)	170-220	17.4	15.7	-86.5	0.7
	220-310	53.0	50.8	171.7	1.2
(**4**)	160-240	31.4	29.6	59.0	1.1
	240-370	27.1	24.9	-96.5	0.9

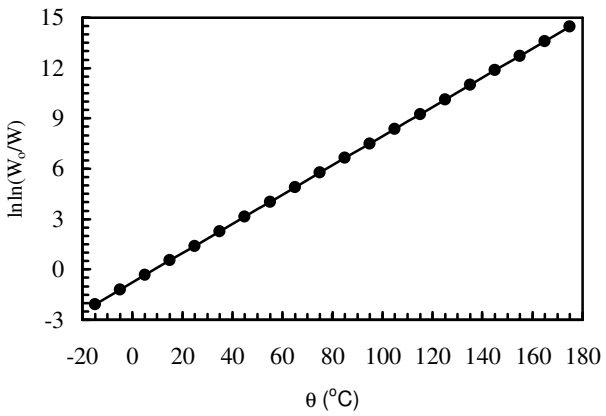


Fig. 1. Plot of theta *vs*. lnlnW_o/W for thermogravimetric analysis of complex (**1**).

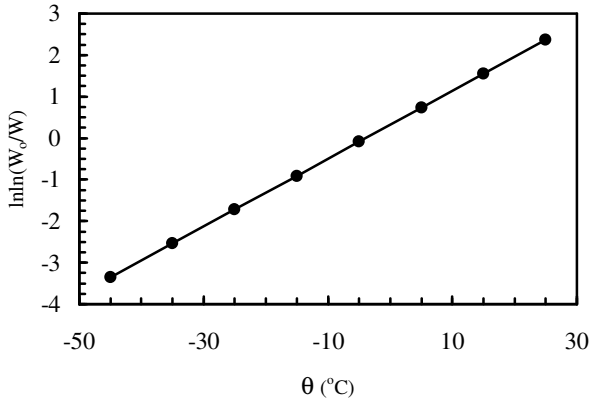


Fig. 2. Plot of theta *vs*. lnlnW_o/W for thermogravimetric analysis of the first decomposition of complex (**3**).

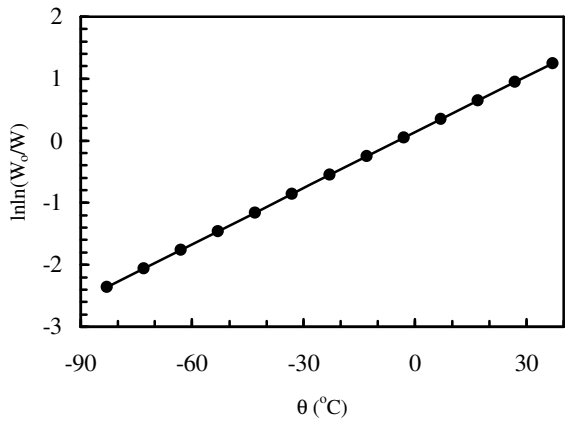


Fig. 3. Plot of theta *vs*. lnlnW$_o$/W for thermogravimetric analysis of the second decomposition of complex (**3**).

Biocidal Activity

Analyses of the antibacterial activity of the free ligand and complexes (**1**)-(**5**) have been carried out against different bacteria using the agar well diffusion method [12]. These results in Table 6 show that all the complexes have significant antibacterial activity.

The synthesized complexes were also tested for antifungal activity against different animal and plant pathogens by the tube diffusion method [13] and results are summarized in. As seen from the results in Table 7, generally all the compounds including the present ligand show markedly lower antifungal activity than the standard drug.

These complexes were also evaluated for cytotoxicity data, using the Brine-Shrimp (*Artemia salina*) bioassay lethality

Table 6. Antibacterial Activity[a] of Free Ligand and its Organotin(IV) Complexes

Bacterium	Standard drug	Zone of inhibition (mm)					
		HL	(**1**)	(**2**)	(**3**)	(**4**)	(**5**)
Escherichia coli	35	–	13	–	12	10	8
Bacillus subtilis	38	13	12	–	15	–	16
Shigella flexneri	32	25	22	23	-	26	20
Staphylococcus aureus	38	10	12	14	10	15	18
Pseudomonas aeruginosa	29	15	13	16	–	18	–
Salmonella typhi	28	30	28	25	30	23	–

[a]Concentration of sample = 3 mg ml^{-1} of DMSO, Size of well = 6 mm, Standard drug = Imipenem.

Table 7. Antifungal Activity[a] Data for Free Ligand and its Organotin(IV) Complexes

Fungus	Standard drug	MIC (μg ml^{-1})	Inhibition (%)					
			HL	(**1**)	(**2**)	(**3**)	(**4**)	(**5**)
Trichophyton longifusum	*Miconazole*	70.0	45	10	10	10	10	10
Candida albicans	*Miconazole*	110.8	45	–	10	35	10	15
Aspergillus flavus	*Amphotericin B*	20.0	–	–	10	10	10	12
Microsporum canis	*Miconazole*	98.4	45	80	55	60	45	40
Fusarium solani	*Miconazole*	73.2	–	20	25	20	20	20
Candida glabrata	*Miconazole*	110.8	–	40	38	25	10	15

[a]Standard drug = Miconazole and Amphotericin B.

Table 8. Brine-Shrimp Toxicity of Free Ligand and its Organotin(IV) Complexes[a]

Compound	Dose ($\mu g\ ml^{-1}$)	No. of shrimp	No. of survivors	LD_{50} ($\mu g\ ml^{-1}$)
HL	1000	30	0	22.94
	100	30	25	
	10	30	22	
(**1**)	1000	30	0	9.18
	100	30	0	
	10	30	15	
(**2**)	1000	30	0	10.21
	100	30	15	
	10	30	15	
(**3**)	1000	30	0	18.01
	100	30	18	
	10	30	28	
(**4**)	1000	30	0	20.01
	100	30	21	
	10	30	30	
(**5**)	1000	30	0	14.05
	100	30	15	
	10	30	0	

[a]Standard drug = Etoposide, LD_{50} ($\mu g\ ml^{-1}$) = 7.46.

method [14]. The results given in Table 8 show that all the complexes, including the ligand, had low LD_{50} values.

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