Inorganica Chimica Acta

LETTER

Crystal Structures and Antitumour Activity of 2-(2′-pyridyl)benzothiazole and its Organotin Complex

HU SHENG-ZHI*, SHI DASHUANG and HUANG TAISHAN

Department of Chemistry, Xiamen University, Xiamen, Fujian (China)

WAN JIAZHU and HUANG ZEXING

Department of Chemistry, Hua Chiao University, Chuanzhou, Fujian (China)

YANG JINLONG and XU CHENGHUI

Shanghai Institute of Materials, Academia Sinica, Shanghai (China)

(Received October 16, 1989; revised March 6, 1990)

Thioanilides of α-picolinic acid are known to function as chelate compounds and exhibit a wide variety of biological properties [1–3]. In the earlier papers [4–5] concerning the crystal structures of α-picoline-*p*-toluidide and *o*-toluidide, as well as their organotin complexes, we reported that the former undergoes an intramolecular ring closure at the thiol sulfur and a phenyl carbon atom on the one hand, and both undergo a configurational transformation from each original structure during the coordination on the other hand.

Although the antitumour activity of organotin compounds including N⌒N chelating ligand has been extensively studied [6], which led to the conclusion that the active compounds had average Sn–N bond lengths ⩾2.39 Å, whereas those with average Sn–N bond lengths <2.39 Å were inactive, structural studies of more complexes of the same type are essential. In this paper we report the crystal structures of the title compounds and their antitumour activity *in vitro* towards the P388 lymphocytic leukaemia tumour as well. The structure of complex **2** is of particular interest since its average Sn–N bond length 2.515(5) Å is the longest one among those have been reported so far to our knowledge.

*Author to whom correspondence should be addressed.

Experimental

Preparation

The title compounds were prepared according to the procedures described in a previous paper [5]. *Anal.* For ligand **1**: Found: C, 68.08; H, 2.37; N, 13.15. Calc. for $C_{12}H_8N_2S$: C, 67.89; H, 3.81; N, 13.19%. For complex **2**: Found: C, 42.07; H, 3.94; N, 6.02. Calc. for $C_{16}H_{18}N_2SCl_2Sn$: C, 41.79; H, 3.94; N, 6.09%.

X-ray Analysis

Crystallographic measurements were carried out on an Enraf-Nonius CAD-4 diffractometer with graphite-monochromated Mo Kα (λ = 0.7107 Å) at room temperature. Intensity data were corrected for absorption. Table 1 contains details of crystal data, data collection and structure solution for compounds **1** and **2**. All computations were performed on a PDP 11/44 computer with the SDP program package. In both structures, full-matrix anisotropic refinement for non-hydrogen atoms was used. Hydrogens were located from difference-Fourier synthesis and were included in the refinement at fixed positions with their isotropic B values set invariant at 5 Å^2. Residuals R and R_w are defined as: $R = \Sigma[|F_o - F_c|]/\Sigma F_o$ and $R_w = (\Sigma w[|F_o - F_c|]^2/$

TABLE 1. Crystal data for ligand **1** and $[SnEt_2Cl_2 \cdot L]$ (**2**)

	1	**2**
Formula	$C_{12}H_8N_2S$	$C_{16}H_{18}N_2SCl_2Sn$
M_r	212.3	460.0
a (Å)	13.912(2)	13.963(2)
b (Å)	13.074(2)	9.425(4)
c (Å)	11.186(2)	27.444(4)
V (Å^3)	2034.6	3611.7
Z	8	8
ρ_c (g cm^{-3})	1.386	1.692
ρ_o (g cm^{-3})	1.34(1)	
F (000)	880	1824
μ(Mo Kα) (cm^{-1})	2.77	18.24
Space group	$Pca2_1$	$Pna2_1$
Scan type	$\omega-2\theta$	$\omega-2\theta$
2θ max (°)	50	56
Unique data measured	2078	4294
Observed data with $I \geqslant 3\sigma(I)$	1656	3188
Crystal size (mm)	0.10 × 0.10 × 0.40	0.15 × 0.10 × 0.40
Structure solution	Direct method	Patterson
R	0.054	0.034
R_w	0.053	0.036
$w = [\sigma^2(F_o) + (pF_o)^2]^{-1}$, p	0.02	0.015

0020-1693/90/$3.50

TABLE 2. Atomic positional parameters ($\times 10^4$)

Atom	Ligand (1)							
	Molecule 1				Molecule 2			
	x/a	*y/b*	*z/c*	B_{eq}	*x/a*	*y/b*	*z/c*	B_{eq}
S	5498(1)	1381(1)	5173	4.81(3)	7787(1)	3796(1)	10093(2)	3.41(2)
N1	4217(4)	2987(5)	5992(6)	5.2(1)	9103(4)	5401(4)	10958(5)	4.5(1)
N2	5360(4)	867(4)	7395(5)	4.3(1)	8033(3)	3177(4)	12255(5)	3.2(1)
C1	3651(6)	3785(6)	6224(9)	6.2(2)	9644(6)	6231(6)	11235(8)	5.9(2)
C2	3332(5)	4032(6)	7365(9)	6.3(2)	10003(6)	6415(6)	12357(9)	6.0(2)
C3	3583(6)	3413(7)	8296(7)	5.7(2)	9809(5)	5723(6)	13238(7)	5.1(2)
C4	4156(5)	2577(6)	8106(7)	4.9(2)	9267(5)	4867(5)	12978(6)	4.0(1)
C5	4473(4)	2391(5)	6931(8)	4.4(1)	8916(4)	4753(4)	11831(6)	3.2(1)
C6	5082(5)	1533(6)	6648(7)	4.8(2)	8297(4)	3880(5)	11534(6)	3.2(1)
C7	5955(5)	135(5)	6839(7)	4.2(1)	7404(4)	2493(4)	11748(5)	2.9(1)
C8	6138(5)	288(5)	5604(6)	4.2(1)	7168(4)	2704(4)	10528(5)	3.0(1)
C9	6696(5)	−369(6)	4973(8)	5.3(2)	6520(4)	2102(5)	9915(5)	3.6(1)
C10	7105(6)	−1189(6)	5523(8)	6.2(2)	6133(5)	1270(5)	10486(6)	4.0(1)
C11	6931(6)	−1344(6)	6752(8)	5.7(2)	6378(5)	1032(5)	11688(6)	4.3(1)
C12	6364(6)	−691(6)	7406(8)	5.4(2)	7009(4)	1641(5)	12296(6)	3.6(1)
	$[SnEt_2Cl_2 \cdot L]$ (2)							
	Molecule 1				Molecule 2			
	x/a	*y/b*	*z/c*	B_{eq}	*x/a*	*y/b*	*z/c*	B_{eq}
Sn	9324.8(4)	6560.1(6)	23117(4)	3.22(1)	8217.5(4)	1541.5(6)	0	2.98(1)
Cl1	7964(2)	8048(3)	2616(1)	5.03(6)	9585(2)	3015(3)	−310(1)	4.71(6)
Cl2	10282(2)	8374(3)	1889(2)	6.54(8)	7265(2)	3357(3)	416(1)	5.67(7)
S	9018(2)	1356(2)	2563(1)	3.62(5)	8529(2)	−3675(2)	−246(1)	3.57(5)
N1	10505(6)	4707(8)	2066(3)	3.3(2)	7043(5)	−3088(8)	226(3)	3.1(2)
N2	8855(6)	4063(8)	2584(3)	3.5(2)	8683(5)	−937(7)	−274(3)	3.0(1)
C1	11325.4(4)	5038.5(6)	1831.6(3)	4.0(2)	6239(7)	−10(10)	4581(4)	3.8(2)
C2	11950(7)	3970(10)	1673(4)	4.4(2)	5600(6)	−1020(10)	622(4)	4.3(2)
C3	11709(6)	2566(9)	1762(3)	3.1(2)	5793(9)	−2410(10)	559(5)	5.6(3)
C4	10928(7)	2270(10)	1991(4)	3.4(2)	6668(7)	−2780(10)	285(4)	3.4(2)
C5	10301(6)	3320(10)	2156(3)	3.1(2)	7243(6)	−1695(9)	141(3)	2.8(2)
C6	9418(7)	3073(9)	2430(4)	3.3(2)	8141(6)	−1975(8)	−125(3)	2.4(2)
C7	8062(6)	3514(9)	2818(3)	3.0(2)	9491(6)	−1433(9)	−516(3)	3.0(2)
C8	8020(7)	2042(9)	2843(4)	3.1(2)	9522(6)	−2952(9)	−544(3)	2.8(2)
C9	7263(8)	1380(10)	3067(4)	4.1(2)	10269(7)	−3670(10)	−780(4)	3.8(2)
C10	6563(8)	2190(10)	3284(4)	4.6(2)	10980(7)	−2830(10)	−958(4)	3.7(2)
C11	6578(7)	3660(10)	3240(4)	4.3(2)	10956(8)	−1360(10)	−958(4)	4.1(2)
C12	7301(8)	4380(10)	3015(4)	4.0(2)	10199(7)	−690(10)	−729(4)	3.7(2)
C13	8514(9)	5910(10)	1682(5)	5.1(3)	9054(8)	910(10)	607(4)	4.4(2)
C14	8200(5)	6930(20)	1320(6)	8.0(4)	9300(10)	2060(20)	948(5)	7.5(4)
C15	10000(10)	6530(20)	3024(6)	7.7(4)	7488(9)	1620(10)	−684(4)	5.0(3)
C16	10260(10)	7850(20)	3232(6)	8.9(5)	7350(10)	3030(10)	−902(7)	8.7(4)

$\Sigma w|F_o|^2)^{1/2}$. Final parameters are listed in Table 2. Bond distances and angles are given in Table 3.

Antitumour activity test

Following the previously described method [4], the activity of the ligand **1** and the complex **2** *in vitro* towards P388 lymphocytic leukaemia tumour was determined for primary screening. The inhibiting ratios (%) of the complex **2** in final concentrations 100, 10 and 1 μg/ml are 96.4, 95.9 and 97.4 respectively, which present a striking contrast to those of the ligand **1** of 35.7, 29.6 and 10.7 μg/ml respectively.

Results and Discussion

2-(2'-Pyridyl)benzothiazole (1)

Two independent molecules which have nearly the same structure (Fig. 1) were observed in each

TABLE 3. Bond distances (Å) and angles (°)

Ligand (1)	Molecule 1	Molecule 2
S–C6	1.760(4)	1.764(3)
S–C8	1.751(3)	1.737(3)
N1–C1	1.333(5)	1.357(3)
N1–C5	1.355(5)	1.318(4)
N2–C6	1.268(4)	1.276(4)
N2–C7	1.409(4)	1.373(3)
C1–C2	1.389(7)	1.373(6)
C2–C3	1.364(6)	1.364(5)
C3–C4	1.370(5)	1.381(4)
C4–C5	1.408(5)	1.381(4)
C5–C6	1.441(5)	1.468(4)
C7–C8	1.418(5)	1.430(4)
C7–C12	1.376(5)	1.385(4)
C8–C9	1.356(5)	1.380(4)
C9–C10	1.361(5)	1.372(4)
C10–C11	1.411(5)	1.421(4)
C11–C12	1.373(5)	1.367(4)
C6–S–C8	90.1(2)	89.7(1)
C1–N1–C5	117.0(4)	117.0(3)
C6–N2–C7	110.8(3)	113.0(2)
N1–C1–C2	123.3(4)	123.4(3)
C1–C2–C3	118.8(4)	118.2(3)
C2–C3–C4	120.3(4)	119.5(3)
C3–C4–C5	117.7(4)	118.5(3)
N1–C5–C4	122.8(3)	123.3(3)
N1–C5–C6	115.6(4)	116.6(3)
C4–C5–C6	121.5(4)	120.1(3)
S–C6–N2	116.1(3)	114.7(2)
S–C6–C5	119.2(3)	119.4(2)
N2–C6–C5	124.8(4)	125.8(3)
N2–C7–C8	116.1(3)	114.5(2)
N2–C7–C12	124.9(4)	126.4(3)
C8–C7–C12	119.0(4)	119.1(3)
S–C8–C7	107.0(3)	108.2(2)
S–C8–C9	131.6(3)	130.8(2)
C7–C8–C9	121.4(3)	121.0(3)
C8–C9–C10	120.2(4)	118.5(3)
C9–C10–C11	118.8(4)	121.4(3)
C10–C11–C12	121.9(4)	119.8(3)
C7–C12–C11	118.7(4)	120.3(3)
[$SnEt_2Cl_2$·L] (2)		
Sn–C11	2.505(2)	2.509(2)
Sn–C12	2.461(2)	2.450(2)
Sn–N1	2.494(4)	2.472(4)
Sn–N2	2.555(6)	2.539(5)
Sn–C13	2.156(8)	2.120(7)
Sn–C15	2.171(11)	2.137(8)
S–C6	1.750(6)	1.724(6)
S–C8	1.718(8)	1.748(7)
N1–C1	1.351(5)	1.321(7)
N1–C5	1.357(7)	1.358(7)
N2–C6	1.291(7)	1.303(7)
N2–C7	1.380(8)	1.390(8)
C1–C2	1.399(7)	1.383(8)
C2–C3	1.391(9)	1.348(11)
C3–C4	1.288(13)	1.48(2)
C4–C5	1.400(8)	1.361(9)
C5–C6	1.463(8)	1.473(8)
C7–C8	1.391(8)	1.434(8)
C7–C12	1.442(10)	1.345(9)
C8–C9	1.372(10)	1.401(9)
C9–C10	1.376(12)	1.363(10)
C10–C11	1.383(10)	1.386(9)
C11–C12	1.365(10)	1.381(9)
C13–C14	1.458(15)	1.476(13)
C15–C16	1.412(15)	1.465(12)
C11–Sn–C12	100.40(7)	100.63(7)
C11–Sn–N1	169.5(1)	168.5(1)
C11–Sn–N2	102.9(1)	102.3(1)
C11–Sn–C13	91.7(2)	90.1(2)
C11–Sn–C15	92.0(3)	92.6(2)
C12–Sn–N1	90.0(1)	90.9(1)
C12–Sn–N2	156.5(1)	156.9(1)
C12–Sn–C13	96.1(3)	97.4(2)
C12–Sn–C15	101.4(3)	97.2(3)
N1–Sn–N2	66.6(2)	66.1(2)
N1–Sn–C13	86.0(2)	88.3(2)
N1–Sn–C15	87.0(3)	86.0(2)
N2–Sn–C13	80.5(3)	80.4(3)
N2–Sn–C15	80.7(3)	83.9(3)
C13–Sn–C15	161.2(4)	164.3(3)
C6–S–C8	90.2(3)	88.7(3)
C1–N1–C5	119.1(4)	117.6(5)
C6–N2–C7	111.7(6)	111.7(5)
N1–C1–C2	120.7(3)	123.9(5)
C1–C2–C3	118.6(6)	120.0(8)
C2–C3–C4	119.8(6)	117.4(9)
C3–C4–C5	122.2(6)	117.3(7)
N1–C5–C4	119.4(6)	123.6(6)
N1–C5–C6	115.2(5)	115.7(5)
C4–C5–C6	125.4(6)	120.8(5)
S–C6–N2	114.0(5)	117.0(4)
S–C6–C5	121.6(5)	121.9(4)
N2–C6–C5	124.4(6)	121.0(5)
N2–C7–C8	115.5(6)	112.7(5)
N2–C7–C12	123.7(6)	129.0(6)
C8–C7–C12	120.8(6)	118.3(6)
S–C8–C7	108.6(5)	109.9(5)
S–C8–C9	131.0(6)	128.2(6)
C7–C8–C9	120.5(7)	121.9(6)
C8–C9–C10	119.3(7)	115.3(6)
C9–C10–C11	120.3(7)	124.4(7)
C10–C11–C12	123.1(7)	118.2(7)
C7–C12–C11	115.7(6)	121.6(6)
Sn–N1–C1	121.8(3)	122.3(4)
Sn–N1–C5	119.0(4)	119.9(3)
Sn–N2–C6	114.4(5)	116.7(4)
Sn–N2–C7	133.4(4)	131.2(4)
Sn–C13–C14	121.1(7)	114.9(7)
Sn–C15–C16	117.7(9)	116.9(7)

asymmetric unit. Both molecules are almost planar to within ±0.055(6) Å in one of the two independent molecules, the other ±0.102(8) Å, and the C(5)–C(6) bond lengths of 1.441(5) and 1.468(4) Å

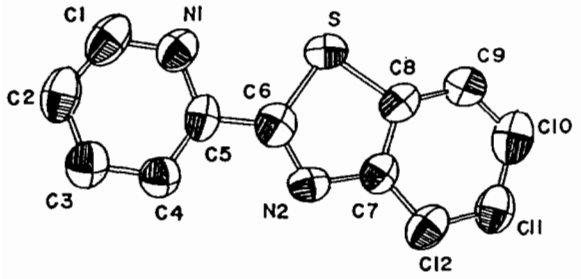

Fig. 1. ORTEP drawing of ligand 1.

indicate that the molecules have a conjugated system. As in the cases of α-thiopicoline-*p*-toluidide [4] and α-thiopicoline-*m*-toluidide [7], the sulfur atom is attached to the phenyl carbon atom to form a benzothiazole ring. This kind of oxidative intramolecular ring closure reaction has also been observed in the tridentate sulfur-containing Schiff bases [8]. All bond lengths and angles fall in the normal ranges and neither remarkable intermolecular contacts nor possible disorder between N(1) and C(4) in the structure have been observed.

[$SnEt_2Cl_2$·L] (2)

There are also two molecules in each asymmetric unit. As in the case of the organotin complex of 2-(2′-pyridyl)-6-methylbenzothiazole [4], the tin atom is located in a distorted octahedral environment with two pyridine-like nitrogen atoms from the organic ligand (Fig. 2). That the tin atom prefers to coordinate with the nitrogen rather than the sulfur atom can be rationalized by Pearson's hard and soft acid–base concept, except in the case of that of the [$SnEt_2Cl$·L] complex (L = α-thiopicoline-*o*-toluidide) due to spatial hindrance [7]. The energy barrier of transformation of the ligands in the isomeric process calculated by the molecular mechanics calculations using the MMPM program [7] is *c.* 6 kcal/mol, which allows the ligands to choose the favourable mode of coordination.

As a whole, the bond lengths of both the ligands and the [$SnEt_2Cl_2$] complex undergo no significant change on coordination. However, the average Sn–N bond lengths ranged from 2.361(5) Å for the complex of α-thiopicoline-*o*-toluidide [5], 2.485(4) Å for that of 2-(2′-pyridyl)-6-methylbenzothiazole [4], 2.500(4) Å for that of 2-(2′-pyridyl)-5-methylbenzothiazole [7], to 2.515(5) Å for that

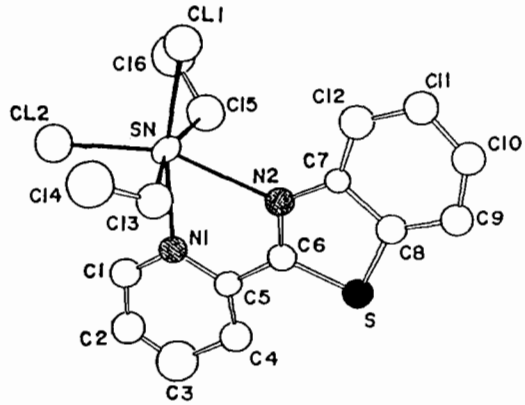

Fig. 2. ORTEP drawing of complex 2.

of the title complex. As a result, the latter shows very high antitumour activity as was expected.

Supplementary Material

Lists of hydrogen parameters, anisotropic temperature factors, torsion angles and structure factors are available from the authors.

Acknowledgement

This research was supported by the National Science Foundation of China.

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