APPLIED ORGANOMETALLIC CHEMISTRY, VOL. 11, 39–45 (1997)

Organostannate Derivatives of Dicyclohexylammonium Hydrogen 2,6-Pyridinedicarboxylate: Solution/Solid-state ^{13}C, ^{119}Sn NMR and *in vitro* Antitumour Activity of Bis(dicyclohexylammonium) Bis(2,6-pyridinedicarboxylato)dibutylstannate, and the Crystal Structure of its Monohydrate

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Bis(dicyclohexylammonium) bis(2,6-pyridinedicarboxylato)dibutylstannate is assigned seven-fold coordination at tin on the basis of its ^{119}Sn CP/MAS NMR chemical shift ($\delta = -424.9$ ppm). The assignment has been corroborated by a crystal structure determination of its monohydrate, whose tin atom has the *trans*-C_2SnNO_4 pentagonal bipyramidal [Sn–C = 2.040(9), 2.067(8) Å; C–Sn–C = 168.9(5)°] geometry. One 2,6-pyridinedicarboxylato group chelates to the tin atom (Sn–O = 2.234(4), 2.260(4); Sn–N = 2.279(5) Å) whereas the other binds through only one carboxyl –CO_2 end (Sn–O = 2.416(5), 2.441(5) Å). Hydrogen bonds link the cation and the stannate into a linear chain parallel to the *b*-axis. The lattice water molecule is hydrogen-bonded to the free carboxyl end. The anhydrous compound showed higher *in vitro* antitumor activity than those of carboplatin and cisplatin when screened against breast (MCF-7, EVSAT), colonic (WiDr), ovarian (IGROV) and renal (A498) carcinoma, and melanoma (M19 MEL) cell lines. **© 1997 by John Wiley & Sons, Ltd.**

Keywords: organotin; solid-state NMR; crystal structure; antitumor activity

INTRODUCTION

The hydrated dimethyltin, dibutyltin,[1] diphenyltin[2] and ethylphenyltin[3] ester derivatives of 2,6-pyridinedicarboxylic acid when reacted with tetraalkylammonium halides yield tetraalkylammonium diorganohalogeno(2, 6-pyridinedicarboxylato)stannates. As both these classes of compounds exhibit high *in vitro* antitumor activity againsthuman carcinoma,[4] it was anticipated that bis(dicyclohexylammonium) bis(2,6-pyridinedicarboxylato)dibutylstannate would be even more active owing to the presence of a second 2,6-pyridinedicarboxylato entity in the molecule. This study reports the synthesis and characterization of this ammonium stannate as well as its evaluation against several cancer lines.

EXPERIMENTAL

Synthesis and spectroscopy

Dibutyltin oxide was added to a small volume of 95% ethanol containing dicyclohexyamine and 2,6-pyridinedicarboxylic acid (1:2:2 molar proportions) and the solution was heated until the oxide dissolved completely. Slow cooling of the filtered solution afforded clear colorless crystals;

CCC 0268–2605/97/010039–07
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Received 4 September 1995
Accepted 2 February 1996

the crystals rapidly turned opaque when taken out of solution. The C, H and N composition of the opaque material was: C, 59.60; H, 7.99; N, 6.08%. Calcd for $C_{46}H_{72}N_4O_8Sn$: C, 59.55; H, 7.82; N, 6.04%. Infrared (Nujol): 1676, 1655, 1624, 1593, 1556 (asym CO_2), 1266 cm^{-1} (sym CO_2). Tin-119*m* Mössbauer (78 K): isomer shift = 1.37, quadrupole splitting = 4.06, $\Gamma_1 = 0.83$, $\Gamma_2 = 0.83$ mm s^{-1}.

Tin-119 (134.29 MHz) and carbon-13 (90.566 MHz) NMR spectra of saturated solutions of the compound in deuterated chloroform were recorded at 300 K on a Bruker AMX 360 spectrometer equipped with a multinuclear tunable probe; tetramethyltin was used as external reference in the ^{119}Sn NMR whereas $CDCl_3$ served as internal standard in the ^{13}C NMR. The ^{119}Sn (74.6 MHz) and ^{13}C (50.3 MHz) CP/MAS NMR spectra were recorded at 300 K on a Bruker MSL 200 spectrometer. The tin-119 and carbon-13 chemical shifts were referred to tetracyclohexyltin ($\delta = -97.35$ ppm) and the carbonyl signal of glycine ($\delta = 176.0$ ppm) by sample replacement. NMR spectral values are listed in Table 1.

Crystallography

Crystals for diffraction analysis were grown from a solution of the compound in ethanol. An appropriately sized crystal was picked from the mother liquor and immediately sealed in a capillary. The intensities were measured with Mo-Kα radiation (0.71073 Å) on an MAR-research Image Plate System. The crystal was positioned at 75 mm from the image plate in a random orientation; 95 frames were measured at 2° intervals with a counting time of 2 min. Data analysis was carried out with the XDS program.[5] Direct phase determination[6] gave most of the atoms, and the remaining ones were found from difference maps. Both butyl groups are disordered over the C_β to C_δ-atoms but the disorder could only be resolved for one chain; 1,2- and 1,3-related C-atoms were constrained to be at 1.55 ± 0.01 and 2.53 ± 0.02 Å in this chain. The water molecule is also disordered over two positions. Non-H atoms except the disordered butyl (C_β–C_δ) C-atoms were refined anisotropically; H-atoms were generated geometrically and their temperature factors fixed at 1.5 times those of the parents'. Full-matrix least-squares refinements[7] on F^2 converged with a shift-to-error ratio of less than 0.001. Crystal data and structure refinement details are presented in Table 2. Atomic coordinates are listed in Tables 3 and bond distances and angles in Table 4. The structure is shown as a PLUTON[8] plot in Fig. 1.

Table 1 NMR spectral parameters for bis(dicyclohexylammonium) bis (2, 6-pyridinedicarboxylato) dibutylstannate [(cyclo-$C_6H_{11})_2$ $NH_2]_2[(C_4$ $H_9)_2$ $Sn(O_2$ CC_5H_3 $NCO_2)_2$] in $CDCl_3$ and in the solid state (chemical shifts in ppm and coupling constants in Hz)

NMR nucleus	Soluton	Solid state
Sn	−392.0	−424.9
C_α	31.5 (988.2)	30.6, 31.9
C_β	27.4 (46.0)	27.1 (2C)[b]
C_γ	26.2 (165.1)	25.4 (4C)[b]
C_δ	13.3 (< 5)	12.9, 15.3
$-CO_2$	168.5	163.7, 167.3, 169.9, 174.1
$-C_5H_3N$	148.6 (*ortho*)	146.3[a] (2C)[b]
		138.0[a], 155.7[a]
	126.1 (*meta*)	125.8 (4C)[b]
	149.6 (*para*)	148.1[a] (2C)[b]
cyclo-C_6H_{11}	53.2	51.7, 53.6
	29.3	28.1 (4C)[b]
	24.9	24.7 (4C)[b]
	25.3	25.4 (2C)[b]

[a] Interchange of assignment possible. [b] 2C and 4C refer to the number of carbon atoms having the same chemical shifts, based on integral intensities.

In vitro antitumor activity

The anhydrous compound was screened against MCF-7 (mammary cancer), EVSAT (mammary cancer), WiDr (colonic cancer), IGROV (ovarian cancer), M19 MEL (melanoma) and A498 (renal cancer) cell lines by an *in vitro* method.[9] The inhibition dosages (ID_{50}) in water/ethanol (99:1) were found to be 46, 27, 172, 25, 48 and 96 ng ml^{-1}.

RESULTS AND DISCUSSION

Dibutyltin oxide condenses with dicyclohexylammonium hydrogen 2,6-pyridinecarboxylate to form bis(dicyclohexylammonium) bis(2,6-pyridinedicarboxylato)dibutystannate in a one-step synthesis similar to that used for bis(dicyclohexylammonium) bisoxalatodibutylstannate[10] and bis(2-sulfobenzoato)dibutylstannate (Eqn 1).[11]

Table 2 Crystal data and structure refinement for bis(dicyclohexylammonium) bis(2,6-pyridinedicarboxylato)dibutylstannate hydrate

Empirical formula	$C_{46}H_{74}N_4O_9Sn$
Formula weight	945.78
Crystal system	Monoclinic
Space group	$P2_1/a$
Unit cell dimensions	$a=18.825(5)$, $b=13.022(5)$, $c=21.191(5)$ Å, $\beta=105.78(5)°$
Volume	4999(3) Å^3
Z	4
Density (calculated)	1.257 Mg m^{-3}
Absorption coefficient	0.565 mm^{-1}
$F(000)$	2000
Theta range for data collection	2.54–24.92°
Index ranges	$-22\leqslant h\leqslant 22$, $0\leqslant k\leqslant 14$, $-24\leqslant l\leqslant 24$
Reflections collected	15048
Independent reflections	8276 ($R_{int}=0.0387$)
Refinement method	Full-matrix least-squares on F^2
Data/restraints/parameters	8276/15/530
Goodness-of-fit on F^2	1.083
Final R indicates ($I\geqslant 2\sigma(I)$)	$R_1=0.0796$, $wR_2=0.2019$
R indices (all data)	$R_1=0.1061$, $wR_2=0.2211$
Largest diff. peak and hole	0.818 and -1.231 e Å^{-3}

$$\begin{aligned}2(\text{cyclo-}C_6H_{11})_2NH + (\text{n-}C_4H_9)SnO \\ + 2HO_2C\text{-}2\text{-}C_5H_3N\text{-}6\text{-}CO_2H \\ = 2[(\text{cyclo-}C_6H_{11})_2NH_2] \\ [(\text{n-}C_4H_9)_2Sn(O_2C\text{-}2\text{-}C_5H_3N\text{-}6\text{-}CO_2)_2] + H_2O\end{aligned} \quad [1]$$

The solution ^{119}Sn NMR spectrum of the ammonium stannate consists of only one signal, the chemical shift (-392.0 ppm) falling within the range[12] noted for six-coordinate dibutyltin compounds. The ^{13}C NMR spectrum shows only one set of signals for the cation (four signals for cyclo-C_6H_{11}) and anion (four signals for C_4H_9, three for C_5H_3N, one for CO_2). The magnitude of the one-bond coupling constant [$|^1J(^{119}Sn-^{13}C)|=988.2$ Hz] implies an almost linear alignment of the C_2Sn skeleton; the estimated value[13] of the carbon–tin–carbon angle is $173\pm4°$. The observation of only one carboxyl resonance appears to suggest that the four carboxyl groups belonging to the two 2,6-pyridinedicarboxylato ligands are covalently linked to the tin atom, but this bonding mode would lead to two other tin–nitrogen interactions, which were not found in the ^{119}Sn NMR spectrum. A more plausible dynamic model involves a rapid equilibrium between a monodentate ligand that binds through a carboxyl oxygen and a terdentate ligand that chelates to the tin atom. The possibility of strong interactions between the ammonium cation and the stannate anion is ruled out as the chemical shifts of the dicyclohexylammonium units are similar to those of the free counterion.[14]

The tin-119 chemical shift (-429.9 ppm) for the compound in the solid state shows an upfield shift of 35 ppm, a shift that is large enough to argue for an increase in the coordination number of tin from six to seven. This coordination status is supported by the observation of residual dipolar interaction with only one quadrupolar ^{14}N nucleus ($I=1$) that gives rise to tin–nitrogen coupling [$|^1J(^{119}Sn-^{15}N)|\simeq 85$ Hz]. The magnitude of the coupling implies moderately strong tin–nitrogen interaction,[15] so that one 2,6-pyridinedicarboxylato ligand should chelate to the tin atom through its *O*,*N*,*O* atoms (as suggested by the solution measurements). Four carboxyl resonances are observed in the ^{13}C CP/MAS NMR spectrum; three resonances (163.7, 167.3, 16.9. ppm) are assigned to the three carboxyl groups bound to tin, whereas the carboxyl resonance at 174.4 ppm can be confidently assigned to the free carboxyl group. The presence of both bonded and free carboxyl groups is supported by the observation in the infrared spectrum of absorption bands higher than 1650 cm^{-1} (i.e. free carboxyl groups) and

Table 3 Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement parameters ($Å^2 \times 10^3$) for bis(dicyclohexylammonium) bis(2,6-pyridinedicarboxylato)dibutylstannate hydrate

Atom	*x*	*y*	*z*	U_{eq}
Sn(1)	1259 (1)	65 (1)	2833 (1)	54 (1)
O(1)	1199 (3)	1714 (3)	2491 (2)	66 (1)
O(2)	893 (3)	3320 (4)	2621 (3)	72 (1)
O(3)	971 (3)	− 889 (3)	3605 (2)	68 (1)
O(4)	545 (4)	− 953 (5)	4476 (3)	94 (2)
O(5)	1623 (3)	− 1512 (3)	2406 (2)	70 (1)
O(6)	1760 (4)	− 91 (3)	1890 (3)	76 (2)
O(7)	1949 (3)	− 4762 (3)	1588 (2)	57 (1)
O(8)	2042 (3)	− 4910 (3)	575 (2)	66 (1)
O*w*(1)(0.5)	1239 (14)	− 2743 (13)	5000	238 (15)
O*w*(2)(0.5)	2081 (20)	− 2607 (20)	5000	306 (21)
N(1)	793 (3)	1083 (4)	3500 (2)	47 (1)
N(2)	1968 (3)	− 2678 (4)	1481 (2)	46 (1)
N(3)	1636 (3)	3179 (4)	1528 (2)	44 (1)
N(4)	1578 (3)	− 3660 (4)	2568 (2)	51 (1)
C(1)	2343 (4)	262 (7)	3374 (4)	79 (2)
C(2)	2718 (11)	− 295 (18)	4008 (9)	274 (12)
C(3)	3556 (10)	− 37 (18)	4232 (11)	301 (16)
C(4)	3868 (16)	− 378 (29)	4953 (12)	465 (27)
C(5)	275 (6)	− 285 (10)	2179 (5)	138 (5)
C(6) (0.5)	− 157 (9)	29 (15)	1503 (7)	112 (7)
C(7) (0.5)	− 952 (8)	− 368 (17)	1256 (8)	100 (6)
C(8) (0.5)	− 1254 (11)	102 (15)	561 (9)	111 (7)
C(6′) (0.5)	− 465 (8)	19 (14)	2249 (8)	104 (6)
C(7′) (0.5)	− 1072 (8)	− 395 (14)	1663 (7)	97 (6)
C(8′) (0.5)	− 1050 (9)	102 (12)	1007 (7)	71 (4)
C(9)	952 (4)	2432 (5)	2784 (3)	53 (2)
C(10)	705 (3)	2075 (5)	3368 (3)	47 (1)
C(11)	410 (4)	2713 (5)	3756 (3)	64 (2)
C(12)	204 (5)	2264 (6)	4271 (4)	76 (2)
C(13)	299 (4)	1238 (6)	4395 (3)	64 (2)
C(14)	603 (4)	645 (5)	3991 (3)	52 (2)
C(15)	712 (4)	− 488 (6)	4048 (3)	63 (2)
C(16)	1794 (4)	− 1040 (5)	1949 (3)	58 (2)
C(17)	2035 (3)	− 1667 (4)	1447 (3)	44 (1)
C(18)	2297 (4)	− 1183 (5)	972 (3)	57 (2)
C(19)	2493 (4)	− 1787 (5)	517 (3)	61 (2)
C(20)	2416 (4)	− 2823 (5)	544 (3)	57 (2)
C(21)	2147 (3)	− 3257 (4)	1029 (3)	42 (1)
C(22)	2033 (3)	− 4395 (5)	1053 (3)	45 (1)
C(23)	1088 (3)	3000 (5)	880 (3)	49 (1)
C(24)	446 (4)	3724 (5)	824 (4)	68 (2)
C(25)	− 107 (4)	3615 (7)	158 (4)	80 (2)
C(26)	− 364 (5)	2511 (7)	26 (5)	93 (3)
C(27)	282 (5)	1789 (7)	119 (4)	85 (2)
C(28)	828 (4)	1900 (5)	785 (4)	65 (2)
C(29)	2300 (3)	2505 (5)	1715 (3)	49 (1)
C(30)	2800 (4)	2875 (6)	2355 (3)	65 (2)
C(31)	3483 (5)	2218 (7)	2562 (5)	91 (3)
C(32)	3890 (4)	2159 (8)	2047 (5)	90 (3)
C(33)	3379 (5)	1800 (7)	1410 (4)	85 (2)
C(34)	2699 (4)	2483 (6)	1189 (4)	68 (2)
C(35)	2187 (4)	− 3843 (5)	3172 (3)	65 (2)
C(36)	2889 (5)	− 3449 (8)	3061 (4)	88 (3)
C(37)	3539 (6)	− 3642 (10)	3645 (6)	126 (4)
C(38)	3600 (7)	− 4746 (11)	3827 (7)	130 (4)
C(39)	2901 (9)	− 5158 (10)	3938 (6)	148 (6)
C(40)	2237 (6)	− 4950 (6)	3359 (5)	96 (3)
C(41)	815 (4)	− 3993 (5)	2541 (4)	64 (2)
C(42)	334 (4)	− 3709 (6)	1882 (4)	76 (2)
C(43)	− 464 (5)	− 4061 (9)	1808 (6)	113 (3)
C(44)	− 763 (6)	− 3611 (10)	2351 (8)	136 (5)
C(45)	− 249 (6)	− 3891 (10)	3010 (7)	132 (4)
C(46)	541 (5)	− 3541 (7)	3090 (5)	91 (3)

U_{eq} is defined as one-third of the trace of the orthogonalized $\boldsymbol{U}_{ij}$ tensor.

below 1600 cm^{-1} (i.e. coordinated carboxyl groups). The non-equivalence of the butyl, pyridyl and cyclohexyl groups is shown by the observation of two sets of signals for each of these groups.

The Mössbauer quadrupole splitting (4.06 $mm\,s^{-1}$) for this compound lies in the upper limit for diorganotin compounds, and the magnitude specifies a *trans*-alignment[16] of the butyl groups, either in an octahedral or in a pentagonal bipyramidal geometry.

Bis(dicyclohexylammonium) bis(2,6-pyridinedicarboxylato)dibutylstannate when recrystallized from ethanol contains water in the crystal structure (Fig. 1). The water molecule is disordered, and is linked to only one carbonyl oxygen [O···O=2.75(2) Å] (Fig. 2). Hydrogen-bonding interactions involving the water molecule are generally extensive in organotin hydrates,[17] but the presence of only one interaction in the ammonium stannate suggests that the anhydrous compound adopts an essentially identical solid-state structure.

The tin atom shows *trans*-pentagonal bipyramidal coordination [Sn–C = 2.040(9), 2.067(8) Å; C–Sn–C = 168.9(5), $\Sigma_{\text{equatorial plane}}$ = 360(1)°] (Fig. 1). One 2,6-pyridinedicarboxylato ligand chelates to tin through its *O*,*N*,*O* ends [Sn–O = 2.234(4), 2.260(4); Sn–N = 2.279(5) Å], and bond dimensions involving this portion of the stannate dianion compare well with those found[1–3] in aquadiorganotin 2,6-pyridinedicarboxylates. The other 2,6-pyridinedicarboxylato group binds to the tin atom through the two oxygen atoms of one carboxyl group [Sn–O = 2.416(5), 2.441(5) Å] in

Table 4 Bond lengths (Å) and angles (°)

Sn(1)–C(1)	2.067 (8)	C(1)–Sn(1)–C(5)	168.9 (5)
Sn(1)–C(5)	2.040 (9)	C(1)–Sn(1)–N(1)	94.1 (3)
Sn(1)–N(1)	2.279 (5)	C(1)–Sn(1)–O(1)	90.9 (3)
Sn(1)–O(1)	2.260 (4)	C(1)–Sn(1)–O(3)	93.6 (3)
Sn(1)–O(3)	2.234 (4)	C(1)–Sn(1)–O(5)	88.6 (3)
Sn(1)–O(5)	2.416 (5)	C(1)–Sn(1)–O(6)	85.4 (3)
Sn(1)–O(6)	2.441 (5)	C(5)–Sn(1)–N(1)	96.9 (4)
O(1)–C(9)	1.276 (8)	C(5)–Sn(1)–O(1)	92.1 (4)
O(2)–C(9)	1.204 (7)	C(5)–Sn(1)–O(3)	91.0 (4)
O(3)–C(15)	1.281 (8)	C(5)–Sn(1)–O(5)	81.6 (4)
O(4)–C(15)	1.202 (8)	C(5)–Sn(1)–O(6)	84.6 (4)
O(5)–C(16)	1.261 (7)	N(1)–Sn(1)–O(1)	69.6 (2)
O(6)–C(16)	1.243 (7)	N(1)–Sn(1)–O(3)	70.1 (2)
O(7)–C(22)	1.279 (7)	N(1)–Sn(1)–O(5)	157.2 (2)
O(8)–C(22)	1.217 (7)	N(1)–Sn(1)–O(6)	148.8 (2)
N(1)–C(14)	1.317 (7)	O(1)–Sn(1)–O(3)	139.7 (2)
N(1)–C(10)	1.323 (8)	O(1)–Sn(1)–O(5)	133.0 (2)
N(2)–C(17)	1.325 (7)	O(1)–Sn(1)–O(6)	79.2 (2)
N(2)–C(21)	1.333 (7)	O(3)–Sn(1)–O(5)	87.2 (2)
N(3)–C(29)	1.490 (7)	O(3)–Sn(1)–O(6)	141.1 (2)
N(3)–C(23)	1.495 (7)	O(5)–Sn(1)–O(6)	53.9 (2)
N(4)–C(35)	1.487 (9)	Sn(1)–N(1)–C(10)	119.0 (4)
N(4)–C(41)	1.485 (8)	Sn(1)–N(1)–C(14)	118.1 (4)
C(1)–C(2)	1.521 (9)	Sn(1)–O(1)–C(9)	122.2 (4)
C(2)–C(3)	1.56 (1)	Sn(1)–O(3)–C(15)	121.7 (4)
C(3)–C(4)	1.55 (1)	Sn(1)–O(5)–N(4)	140.9 (2)
C(5)–C(6)	1.499 (9)	Sn(1)–O(5)–C(16)	91.8 (4)
C(6)–C(7)	1.54 (1)	Sn(1)–O(6)–C(16)	91.1 (4)
C(7)–C(8)	1.56 (1)	C(10)–N(1)–C(14)	122.9 (5)
C(5)–C(6′)	1.49 (1)	C(17)–N(2)–C(21)	118.5 (5)
C(6′)–C(7′)	1.54 (1)	C(29)–N(3)–C(23)	118.3 (5)
C(7′)–C(8′)	1.54 (1)	C(35)–N(4)–C(41)	119.9 (5)
C(9)–C(10)	1.509 (8)	Sn(1)–C(1)–C(2)	125.5 (9)
C(10)–C(11)	1.387 (9)	C(1)–C(2)–C(3)	111 (1)
C(11)–C(12)	1.38 (1)	C(2)–C(3)–C(4)	109 (1)
C(12)–C(13)	1.36 (1)	Sn(1)–C(5)–C(6)	138 (1)
C(13)–C(14)	1.387 (9)	C(5)–C(6)–C(7)	117 (1)
C(14)–C(15)	1.49 (1)	C(6)–C(7)–C(8)	105 (1)
C(16)–C(17)	1.506 (8)	Sn(1)–C(5)–C(6′)	125 (1)
C(17)–C(18)	1.387 (8)	C(5)–C(6′)–C(7′)	110 (1)
C(18)–C(19)	1.371 (9)	C(6′)–C(7′)–C(8′)	113 (1)
C(19)–C(20)	1.359 (9)	O(1)–C(9)–O(2)	125.6 (6)
C(20)–C(21)	1.385 (8)	O(1)–C(9)–C(10)	114.0 (5)
C(21)–C(22)	1.500 (8)	O(2)–C(9)–C(10)	120.4 (6)
C(23)–C(28)	1.510 (9)	N(1)–C(10)–C(9)	115.1 (5)
C(23)–C(24)	1.511 (9)	N(1)–C(10)–C(11)	120.5 (6)
C(24)–C(25)	1.52 (1)	C(9)–C(10)–C(11)	124.4 (6)
C(25)–C(26)	1.52 (1)	C(10)–C(11)–C(12)	117.3 (7)
C(26)–C(27)	1.51 (1)	C(11)–C(12)–C(13)	121.1 (7)
C(27)–C(28)	1.51 (1)	C(12)–C(13)–C(14)	118.7 (6)
C(29)–C(30)	1.504 (9)	N(1)–C(14)–C(13)	119.5 (6)
C(29)–C(34)	1.504 (9)	N(1)–C(14)–C(15)	115.6 (6)
C(30)–C(31)	1.51 (1)	C(13)–C(14)–C(15)	124.9 (6)
C(31)–C(32)	1.50 (1)	O(3)–C(15)–O(4)	125.2 (8)
C(32)–C(33)	1.50 (1)	O(3)–C(15)–C(14)	114.6 (5)
C(33)–C(34)	1.53 (1)	O(4)–C(15)–C(14)	120.1 (7)
C(35)–C(40)	1.49 (1)	O(5)–C(16)–O(6)	123.1 (6)

Table 4 Continued

C(35)–C(36)	1.50 (1)	O(5)–C(16)–C(17)	117.9 (5)
C(36)–C(37)	1.51 (1)	O(6)–C(16)–C(17)	119.0 (6)
C(37)–C(38)	1.48 (2)	N(2)–C(17)–C(16)	116.7 (5)
C(38)–C(39)	1.50 (2)	N(2)–C(17)–C(18)	123.3 (6)
C(39)–C(40)	1.52 (2)	C(16)–C(17)–C(18)	120.1 (5)
C(41)–C(42)	1.49 (1)	C(17)–C(18)–C(19)	117.8 (6)
C(41)–C(46)	1.52 (1)	C(18)–C(19)–C(20)	119.2 (6)
C(42)–C(43)	1.54 (1)	C(19)–C(20)–C(21)	120.0 (6)
C(43)–C(44)	1.53 (2)	N(2)–C(21)–C(20)	121.2 (5)
C(44)–C(45)	1.51 (2)	N(2)–C(21)–C(22)	117.9 (5)
C(45)–C(46)	1.52 (1)	C(20)–C(21)–C(22)	120.9 (5)
N(3)···O(2)	3.020 (7)	O(7)–C(22)–O(8)	124.3 (6)
N(3)···O(7)≠1[a]	2.742 (7)	O(7)–C(22)–C(21)	116.9 (5)
N(4)···O(5)	2.823 (7)	O(8)–C(22)–C(21)	118.8 (5)
N(4)···O(7)	2.766 (7)	N(3)–C(23)–C(24)	108.2 (5)
O(4)···O*v*1	2.75 (2)	N(3)–C(23)–C(28)	112.8 (5)
		C(23)–C(24)–C(25)	110.2 (6)
		C(24)–C(25)–C(26)	111.4 (7)
		C(25)–C(26)–C(27)	111.1 (7)
		C(26)–C(27)–C(28)	112.6 (7)
		C(27)–C(28)–C(23)	109.2 (6)
		C(28)–C(23)–C(24)	111.0 (6)
		N(3)–C(29)–C(30)	109.0 (5)
		N(3)–C(29)–C(34)	111.4 (5)
		C(29)–C(30)–C(31)	110.9 (6)
		C(30)–C(31)–C(32)	112.5 (7)
		C(31)–C(32)–C(33)	109.9 (7)
		C(32)–C(33)–C(34)	111.9 (7)
		C(33)–C(34)–C(29)	109.2 (6)
		C(34)–C(29)–C(30)	111.0 (6)
		N(4)–C(35)–C(36)	108.5 (6)
		N(4)–C(35)–C(40)	111.2 (6)
		C(35)–C(36)–C(37)	111.7 (8)
		C(36)–C(37)–C(38)	111 (1)
		C(37)–C(38)–C(39)	112 (1)
		C(38)–C(39)–C(40)	112 (1)
		C(39)–C(40)–C(35)	111.5 (9)
		C(40)–C(35)–C(36)	112.3 (8)
		N(4)–C(41)–C(42)	107.4 (6)
		N(4)–C(41)–C(46)	112.6 (6)
		C(41)–C(42)–C(43)	110.5 (8)
		C(42)–C(43)–C(44)	111.0 (9)
		C(43)–C(44)–C(45)	109.2 (9)
		C(44)–C(45)–C(46)	113.0 (9)
		C(45)–C(46)–C(41)	109.0 (9)
		C(46)–C(41)–C(42)	112.0 (7)

[a] Translational code: ≠1 = *x*, 1 − *y*, *z*.

an isobidentate manner; the free carboxyl group is hydrogen-bonded to the disordered water molecule. This ligand is additionally hydrogen-bonded to a dicyclohexylammonium cation [N···O = 2.766(7), 2.823(7) Å] to form a nearly planar eight-membered N—C—C—O···N···O—C—C—N ring. The pair of tin–oxygen bond lengths

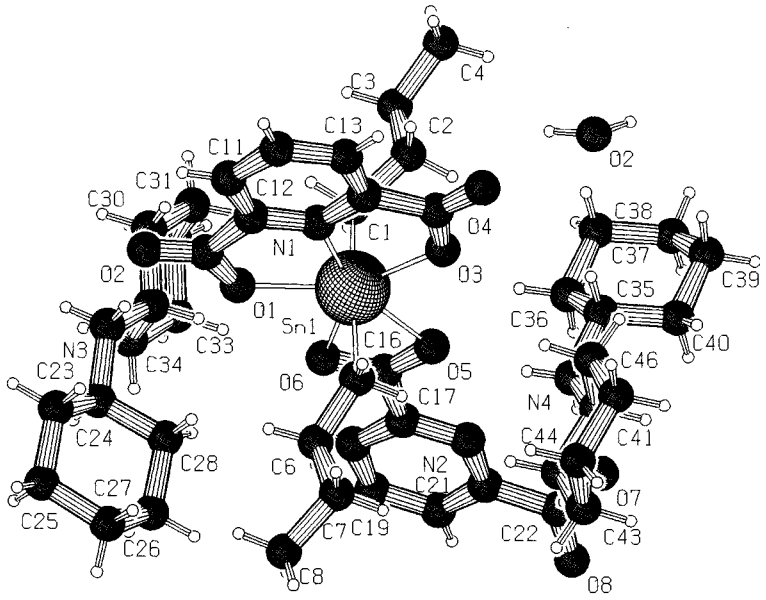

Figure 1 Atom labeling scheme for bis(dicyclohexylammonium) bis(2,6-pyridinedicarboxylato)dibutylstannate hydrate. The water molecule is disordered over two positions.

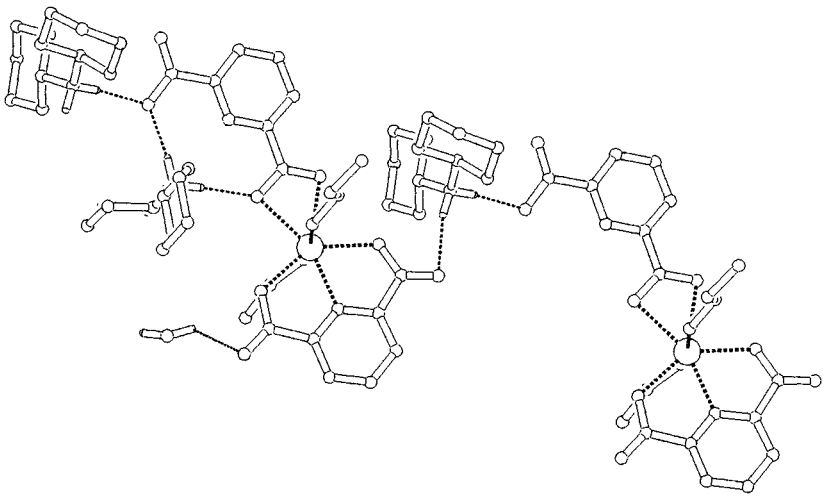

Figure 2 The polymeric chain of bis(dicyclohexylammonium) bis(2,6-pyridinedicarboxylato)dibutylstannate hydrate.

contrasts with that [2.234(5), 2.439(7) Å] found in seven-coordinate carboxyl-chelated aquadibutylbis(phenylacetato)tin.[18] The stannate is linked into chains by hydrogen bonding involving the other counterion [N···O=2.742(7), 3.020(7) Å].

The anhydrous compound, when screened against selected human tumor cell lines (MCF-7 46, WiDr 172 ng ml^{-1}), is more active *in vitro* than carboplatin (MCF-7 10 500, WiDr 3500 ng mL^{-1}), cisplatin (MCV-7 1400, WiDr 1550 ng ml^{-1}) and 5-fluorouracil (MCF-7 350, WiDr 440 ng ml^{-1}), but is less active than methotrexate (MCE-7 15, WiDr 7 ng ml^{-1}) and doxorubicin (MCF-7 25, WiDr 18 ng ml^{-1}). Aquadibutyltin 2,6-pyridinedicarboxylate itself is less active against MCF-7 (54 ng ml^{-1}) but it is more active against WiDr (76 ng ml^{-1}), whereas the 1:1 compound with tetraethylammonium chloride shows much lower activity (MCF-7 118, WiDr 220 ng ml^{-1})[4] compared with these neoplastic drugs.

Acknowledgements We thank Dr D. de Vos (Pharmachemie, Haarlem, The Netherlands), Mr H. J. Kolker, Dr J. Verweij, Professor Dr G. Stoter and Dr J. H. M. Schellens (Laboratory of Exerimental Chemotherapy and Pharmacology, Department of Medical Oncology, Rotterdam Cancer Institute, Rotterdam, The Netherlands) for performing the *in vitro* tests. This research has been supported by the National Science Council for R & D, Malaysia (2-07-04-06), the Grant Agency of the Czech Republic (94/203/0024), the Belgium Nationaal Fonds voor Wetenschappelijk Onderzoek (S2/5 CD F198), the Human Capital and Mobility Programme of the European Community (Contract No. ERBCHRXCT920016) and the SERC, UK. The Image Plate System was purchased through the funds of the University of Reading.

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