Synthesis and Structural Studies of Diorganotin Iminodiacetates

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(Received January 17, 1989; revised June 26, 1989)

Abstract

The compounds of formula $HN(CH_2CO_2)_2SnR_2$ with $R = CH_3$ or n-C_4H_9 have been synthesised. The crystal structure of the dimethyltin compound is reported, along with some ^1H, ^{13}C and IR spectroscopic data for both the dimethyl and di-n-butyl compounds. The crystals are monoclinic, space group $P2_1/n$, $a = 10.1912(6)$, $b = 7.0715(4)$, $c = 14.9713(8)$ Å, $\beta = 108.540(10)°$, $V = 1022.94$ Å^3, $Z = 4$, $D_{calc} = 1.934$ Mg m^{-3}, $\mu = 2.46$ mm^{-1}, final $R = 2.1\%$ for 1174 significant observed reflections. The complex crystallises as a dimer, with a seven-coordinate distorted pentagonal bipyramidal structure around the two tin atoms, the methyl groups occupying the apical positions. The ligand behaves as a planar tridentate via the imine nitrogen and oxygen atoms from each of the two carboxylate groups. The sixth position in the coordination sphere is taken up by the oxygen atom of a coordinated water molecule while the seventh site is filled by a shared oxygen from the other organotin moiety in the dimer. The bridging oxygens are each coordinated to both tin atoms.

The structure of the dibutyltin complex is believed to be the same as that of the dimethyltin complex.

Introduction

The success of cisplatin and its second generation derivatives [1, 2] as antitumour agents had led to the investigation of antitumour activity in a variety of organotin complexes [3–5] structurally related to these active platinum compounds. Recent reports of the activity of certain diorganotin derivatives of pyridine 2,10-dicarboxylic acid and some related compounds [6, 7] against the P388 lymphocytic leukemia tumour, both *in vitro* and *in vivo*, has led us to synthesise a series of diorganotin iminodiacetates, two of which are described herein. These are the compounds of formula $HN(CH_2CO_2)_2SnR_2$ with $R = CH_3$ or n-C_4H_9. A full X-ray structural analysis of the dimethyltin compound has been carried out and the results are reported, along with a variety of spectroscopic data for both the dimethyl and di-n-butyl compounds.

Experimental

Chemicals and Reagents

These were purchased from the Aldrich Chemical Company and used without further purification.

Preparation of Complexes

The diorganotin carboxylates were readily prepared according to the following reaction

$$HN(CH_2COOH)_2 + R_2SnO \longrightarrow HN(CH_2CO_2)_2SnR_2 + H_2O$$

Iminodiacetic acid (1.3 g, 10 mmol) and either dimethyl- or dibutyltin oxide (10 mmol) were mixed with benzene in a round-bottomed flask. The mixture was refluxed for 3 h; the water produced during the reaction being removed azeotropically using a Dean–Stark apparatus. After reflux, the mixture was cooled before filtration. The products were recrystallised from a 1:1 water/ethanol mixture, and obtained as white, crystalline monohydrates.

Analytical and melting point data, along with the yields obtained, are as follows.

$NH(CH_2COO)_2Sn(CH_3)_2 \cdot H_2O$: melting point (m.p.) 283–285 °C (dec.), yield 70%. Calc. [for

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0020-1693/89/$3.50

$C_6H_{13}NO_5Sn$]: C, 24.19; H, 4.41; N, 4.70. Found: C, 24.26; H, 4.51; N, 4.72%.

$NH(CH_2COO)_2Sn(C_4H_9)_2 \cdot H_2O$: m.p. 212–216 °C, yield 65%. Calc. [for $C_{12}H_{25}NO_5Sn$]: C, 37.72; H, 6.61; N, 3.67. Found: C, 37.60; H, 6.87; N, 3.86%.

Microanalyses were performed at the Chemistry Department, National University of Singapore, Singapore.

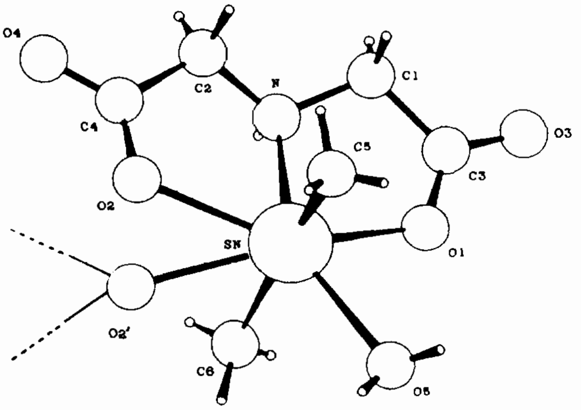

Fig. 1. Structure of the complex and atomic numbering scheme.

NMR Spectra

These were obtained with either a Perkin-Elmer R12B or a Varian CFT-20 spectrometer with deuterochloroform as solvent.

IR Spectra

These were recorded using a Nicolet instrument with the samples as nujol mulls or in KBr disks.

Crystal Data

Monoclinic, space group $P2_1/n$, $a = 10.1912(6)$, $b = 7.0715(4)$, $c = 14.9713(8)$ Å, $\beta = 108.540(10)°$, $V = 1022.94$ Å^3, $Z = 4$, $D_{calc} = 1.934$ Mg m^{-3}, $\mu = 2.46$ mm^{-1}.

Intensity Data

Intensity data were collected from a 0.1 × 0.1 × 0.1 mm while rod-shaped crystal to $2\theta_{max} = 45°$, using graphite monochromatised Mo Kα radiation.

A total of 4659 reflections were measured on a CAD4-diffractometer with the NRCCAD control program [8] and profile analysis [9] using the $\theta/2\theta$ scanning mode. Of the reflections measured, 1330 were unique, of which 1174 were considered significant, with $I_{net} > 2.5\sigma(I_{net})$. Absorption corrections were not necessary ($\mu = 2.46$ mm^{-1}) [λ Mo Kα = 0.70932 Å].

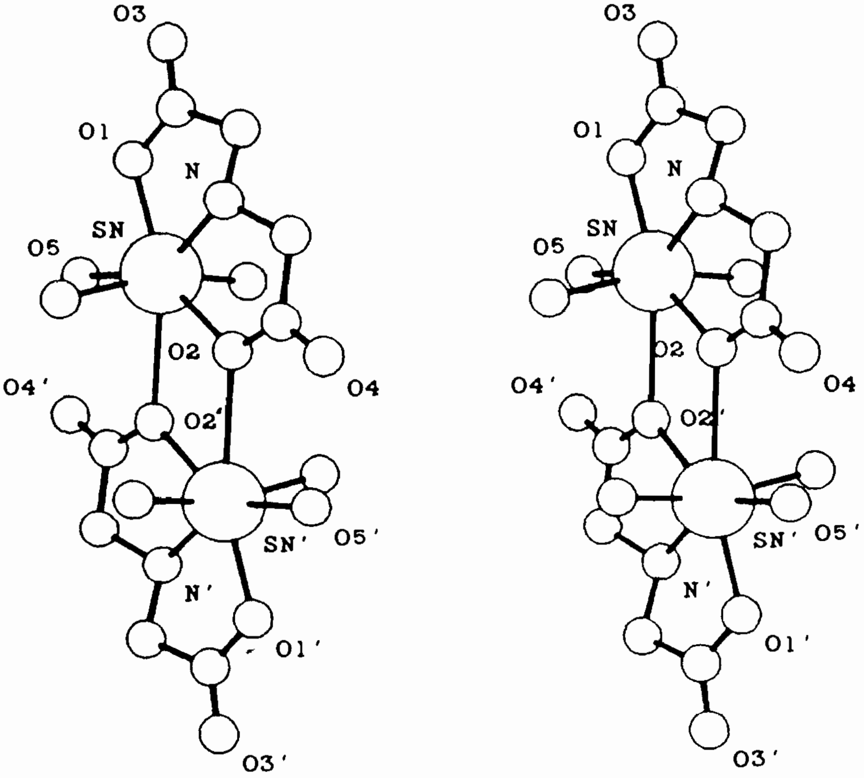

Fig. 2. A stereoscopic view of the dimer.

TABLE 1. Positional and isotropic thermal parameters[a]

	x	y	z	B_{iso}[b]
Sn	0.37665(3)	0.53874(5)	0.093131(22)	2.207(15)
O1	0.2573(3)	0.5752(5)	0.19113(20)	2.55(16)
O2	0.5602(3)	0.3621(4)	0.06890(21)	2.38(16)
O3	0.2525(3)	0.5495(5)	0.33750(20)	2.79(16)
O4	0.7333(3)	0.1615(5)	0.13292(21)	3.31(18)
O5	0.2094(4)	0.7760(6)	0.0258(3)	2.99(22)
N	0.4637(4)	0.3338(6)	0.2162(3)	2.02(21)
C1	0.4441(5)	0.4134(8)	0.3021(3)	2.2(3)
C2	0.6032(5)	0.2674(8)	0.2285(4)	2.3(3)
C3	0.3084(4)	0.5192(7)	0.2765(3)	2.13(23)
C4	0.6350(5)	0.2602(7)	0.1354(3)	2.08(24)
C5	0.5153(8)	0.7586(11)	0.1481(6)	3.4(4)
C6	0.2349(8)	0.3636(11)	−0.0032(5)	3.4(3)
H51	0.219(5)	0.801(7)	−0.018(3)	2.7(16)
H52	0.213(5)	0.868(6)	0.058(3)	2.2(13)
HN	0.422(4)	0.240(6)	0.202(3)	1.4(12)
H1A	0.516(4)	0.504(6)	0.332(3)	1.6(10)
H1B	0.449(4)	0.320(6)	0.342(3)	1.3(10)
H2A	0.665(4)	0.354(6)	0.269(3)	2.4(11)
H2B	0.624(4)	0.148(6)	0.259(3)	2.8(12)
H5A	0.590(5)	0.720(7)	0.197(4)	3.9(15)
H5B	0.538(6)	0.801(9)	0.114(4)	4.9(23)
H5C	0.478(6)	0.838(9)	0.163(4)	5.9(23)
H6A	0.174(6)	0.350(9)	0.013(4)	5.5(21)
H6B	0.208(6)	0.426(9)	−0.066(4)	8.8(21)
H6C	0.269(5)	0.261(7)	−0.001(4)	3.3(16)

[a] e.s.d.s refer to the last digit printed. [b] B_{iso} is the mean of the principal axes of the thermal ellipsoid.

Structure Solution and Refinement

The structure was solved using direct methods. The H atoms were located on a difference map and their positional parameters were refined together with isotropic thermal parameters, while the other atoms were refined anisotropically by full-matrix least-squares. The final residuals are $R_f = 0.021$ and $R_w = 0.017$ for the significant reflections and $R_f = 0.029$ and $R_w = 0.018$ for all reflections. In the final D map, the deepest hole showed a density of -0.330 e/Å^3 and the highest peak, a density of 0.460 e/Å^3. Weights based on counting statistics were used throughout. All calculations were performed with the NRCVAX system of programs [10]. Literature values [11] were used for the scattering factors.

Results and Discussion

The complex crystallises as a dimer, with each of the two tin atoms in a seven-coordinate environment. The structure of one of the complex organotin moieties and the atomic numbering scheme are shown in Fig. 1, while a stereoscopic view of the dimer is given in Fig. 2. The final atomic positional parameters and the equivalent isotropic temperature factors are given in Table 1. Table 2 lists the bond distances and angles. The ^{1}H and ^{13}C NMR data are listed in Table 3 and the IR data are given in Table 4.

The tin atoms are seven-coordinate, with the ligand behaving as a tridentate via the imine nitrogen and an oxygen atom from each of the two carboxylate groups; three further positions in the coordination sphere are taken up by two methyl groups and the oxygen of a water molecule, while the seventh position is filled by a shared carboxylate oxygen (O2′) from the other organotin unit in the dimer. The geometry around the tin atoms is approximately pentagonal bipyramidal, with the methyl groups occupying the apical positions. The arrangement is similar to those reported for the pentagonal bipyramidal diorganotin complexes of quinquedentate hydrazone ligands [12, 13], and to that of the diphenyltin complex of pyridine-2,6-dicarboxylic acid [7]. The structure of the latter compound differs from the one reported here with regard to the identity of the bridging carboxylate oxygen – in the case of the diphenyltin complex of pyridine-2,6-dicarboxylic acid, it is one of the 'free' carboxylic oxygens which binds to another tin atom, whereas in the present instance, one of the coordinated carboxylate oxygen atoms also acts as the bridge to the second tin atom.

TABLE 2. Bond distances (Å) and angles (°)[a]

Sn–O(1)	2.199(3)	O(2)–C(4)	1.269(6)
Sn–O(2)	2.371(3)	O(3)–C(3)	1.240(6)
Sn–O(5)	2.376(4)	O(4)–C(4)	1.232(6)
Sn–N	2.290(4)	N–C(1)	1.475(6)
Sn–C(5)	2.087(7)	N–C(2)	1.453(7)
Sn–C(6)	2.092(7)	C(1)–C(3)	1.511(7)
Sn–O(2′)	2.790(3)	C(2)–C(4)	1.528(7)
O(1)–C(3)	1.279(5)		
O(1)–Sn–O(2)	142.62(11)	O(5)–Sn–C(6)	83.2(3)
O(1)–Sn–O(2′)[b]	151.69(10)	N–Sn–C(5)	96.6(3)
O(1)–Sn–O(5)	74.08(13)	N–Sn–C(6)	100.68(25)
O(1)–Sn–N	72.08(13)	C(5)–Sn–C(6)	161.0(3)
O(1)–Sn–C(5)	95.7(3)	Sn–O(1)–C(3)	119.6(3)
O(1)–Sn–C(6)	97.00(24)	Sn–O(2)–C(4)	119.0(3)
O(2)–Sn–O(2′)	65.67(9)	Sn–N–C(1)	109.6(3)
O(2)–Sn–O(5)	143.30(13)	Sn–N–C(2)	114.8(3)
O(2)–Sn–N	70.55(12)	C(1)–N–C(2)	114.2(4)
O(2)–Sn–C(5)	89.1(3)	N–C(1)–C(3)	109.5(4)
O(2)–Sn–C(6)	89.32(25)	N–C(2)–C(4)	112.2(4)
O(2′)–Sn–O(5)	77.68(12)	O(1)–C(3)–O(3)	123.1(4)
O(2′)–Sn–N	136.15(12)	O(1)–C(3)–C(1)	117.2(4)
O(2′)–Sn–C(5)	80.8(3)	O(3)–C(3)–C(1)	119.7(4)
O(2′)–Sn–C(6)	81.32(22)	O(2)–C(4)–O(4)	126.1(4)
O(5)–Sn–N	146.15(15)	O(2)–C(4)–C(2)	116.6(4)
O(5)–Sn–C(5)	86.9(3)	O(4)–C(4)–C(2)	117.2(4)

[a] Standard deviations are given in parentheses. [b] O(2′) is the symmetry equivalent of O(2) at $1 - x, 1 - y, -z$.

TABLE 3. NMR data for iminodiacetic acid and its derivatives

Compound	Solvent	Chemical shift (ppm)			
		^{1}H		^{13}C	
		CH_2	NH/H_2O	CH_2	C=O
$HN(CH_2COONa)_2$[a]	D_2O	3.1	4.7		
$HN(CH_2COOH)_2$	D_2O			49.22	171.09
$CH_3N(CH_2COOH)_2$[a]	DMSO	3.5			
$CH_3N(CH_2COOH)_2$	D_2O			58.48	170.20
$HN(CH_2COOMe)_2$	$CDCl_3$			51.84	172.26
$HN(CH_2COO)_2SnMe_2 \cdot H_2O$	DMSO	3.4	3.3	49.91	170.79
$HN(CH_2COO)_2SnBu_2 \cdot H_2O$	DMSO	3.3	3.4	49.99	170.50

[a] Data from the Aldrich Library of NMR spectra.

TABLE 4. IR Data of iminodiacetic acid complexes and related compounds

Compound	Infrared absorptions (cm^{-1})				
	ν(O–H)	ν(N–H)	ν(C=O)	ν(Sn–C$_{as}$)	ν(Sn–C$_{sym}$)
$HN(CH_2COO)_2SnMe_2 \cdot H_2O$	3200	3120(s)	1642, 1600	574(m)	500(w)
$HN(CH_2COO)_2SnBu_2 \cdot H_2O$	3220	3160(s)	1620	540(m)	480(w)
$HN(CH_2COOH)_2$			1700		
$HN(CH_2COONa)_2$[a]		3400, 3300	1660		

[a] Data from the Aldrich Library of infrared spectra.

The ligand is not symmetrically bound to the tin, but is slightly skewed, with Sn–O bond lengths of 2.199(3) (Sn–O1) and 2.371(3) Å (Sn–O2). These differences are not unexpected in view of the bonding description outlined above, in which one of the carboxylate oxygens (O2) is bound to two different tin atoms, bridging the organotin units and leading to a reduction in electron density on this oxygen, which in turn weakens and lengthens its bonds to tin. Other ligands with two oxygen donors are also reported to bind to tin(IV) in an asymmetric fashion and show two different Sn–O bond lengths [13–16].

The Sn–N distance of 2.289(4) is within the range 2.266–2.337 Å reported for other seven-coordinate diorganotin complexes [13].

The Sn–O(H_2O) distance of 2.376(4) Å is intermediate between those observed for coordinated water molecules in the six-coordinate triphenyltin complexes of 1,10-phenanthroline [17], 2.420(3) Å, and 3-(2-(1,10-phenanthrolyl))-5,6-diphenyl-1,2,4-triazine [18] 2.359(4) Å, but a little longer than the 2.271(3) Å reported for that in the comparable seven-coordinate diphenyltin complex of pyridine-2,6-dicarboxylic acid [7].

The spectroscopic data for the dimethyltin and the dibutyltin iminodiacetate complexes isolated are very similar. The proton NMR spectra (Table 3) show that the absorptions due to NH and H_2O protons overlap with those of the methylene protons. The methylene proton absorptions for the dimethyltin and di-n-butyltin complexes are 3.4 and 3.5 ppm, respectively, about the same as those observed for dimethyl iminodiacetate (3.5 ppm), *N*-methyl iminodiacetic acid (3.5 ppm) and sodium iminodiacetate (3.1 ppm). The ^{13}C NMR data show that the chemical shifts for the CH_2 and C=O carbon atoms are almost the same for iminodiacetic acid and its derivatives, including both of the diorganotin complexes. The IR data for both complexes (Table 4) are consistent with the structure and show the presence of a water molecule. The observed downfield shifts in the N–H and C–O stretching frequencies relative to the uncoordinated ligand are consistent with the presence of a coordinated imine nitrogen and coordinated carboxylate groups in the complexes. Furthermore, the asymmetric Sn–C(Me) stretching vibration is markedly more intense than the corresponding symmetric vibration for both complexes, as expected for *trans*-methyl groups [19].

The marked similarities in the spectra of the two complexes, taken together with the stoichiometric and preparative similarities, provide strong evidence that the di-n-butyltin complex has the same structure as that of the dimethyltin complex reported here.

Acknowledgements

We thank one of the referees for pointing out an error in the data interpretation. Financial assistance from the Natural Sciences and Engineering Research Council Canada, Laurentian University Research Fund, Universiti Sains Malaysia and Datuk Keramat Smelting is gratefully acknowledged.

References

1 B. Rosenberg, L. VanCamp and T. Krigas, *Nature (London), 205* (1965) 698.

2 J. L. van der Veer and J. Reedijk, *Chem. Br., 20* (1988) 775.

3 A. J. Crowe and P. J. Smith, *Chem. Ind.,* (1980) 200.

4 A. J. Crowe, P. J. Smith and G. Atassi, *Chem.-Biol. Interact., 32* (1980) 171.

5 A. J. Crowe, P. J. Smith, C. J. Cardin, H. E. Parge and F. E. Smith, *Cancer Lett., 24* (1984) 45.

6 G. Ruisi, A. Silvestri, M. T. LoGiudice, R. Barbieri, G. Atassi, F. Huber, K. Gratz and L. Lamartina, *J. Inorg. Biochem., 25* (1985) 229.

7 M. Gielen, E. Joosen, T. Mancilla, K. Jurkschat, C. Roobol, J. Bernheim, G. Atassi, F. Huber, E. Hoffmann, H. Preut and B. Mahieu, *Main Group Metal Chem., 10* (1987) 148.

8 Y. Le Page, P. S. White and E. J. Gabe, *A.C.A. Annual Meeting, Hamilton, Ontario, Canada, June 1986,* Abstract PA23.

9 E. J. Gabe, F. L. Lee and Y. Le Page, *Int. Union Crystallogr. Summer School Crystallographic Computing, Mulheim, F.R.G., 1985,* p. 167.

10 D. F. Grant and E. J. Gabe, *J. App. Crystallogr., 11* (1978) 114.

11 *International Tables for X-ray Crystallography,* Vol. 4, Kynoch Press, Birmingham, U.K., and edn., 1974, p. 99.

12 C. Pelizzi, G. Pelizzi and G. Predieri, *J. Organomet. Chem., 263* (1984) 9.

13 C. Carini, G. Pelizzi, P. Tarasconi, C. Pelizzi, K. C. Molloy and P. C. Waterfield, *J. Chem. Soc., Dalton Trans.,* (1989) 289.

14 P. G. Harrison, T. J. King and R. C. Phillips, *J. Chem. Soc., Dalton Trans.,* (1976) 2317.

15 P. G. Harrison, T. J. King and J. A. Richards, *J. Chem. Soc., Dalton Trans.,* (1975) 826.

16 T. Kimura, N. Yasuoka, N. Kasai and M. Kakudo, *Bull. Chem. Soc. Jpn., 45* (1972) 1649.

17 E. J. Gabe, F. L. Lee and F. E. Smith, *Inorg. Chim. Acta, 90* (1984) L11.

18 M. F. C. Ladd, D. C. Povey and F. E. Smith, *J. Crystallogr. Spectrosc. Res., 14* (1984) 249.

19 V. S. Petrosyan, N. S. Yashina and O. A. Rentov, *Adv. Organomet., Chem., 14* (1976) 63.