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Synthesis, structural characterization and bioassay screening of dimeric bis[dicarboxylatotetra-organodistannoxanes]

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Reaction of bis(pyrazol-1-yl)acetic acid with *n*-Bu_2SnO in a 1:1 molar ratio gives dimeric bis[dicarboxylatotetraorganodistannoxanes], $\{[(n\text{-}Bu)_2(Pz_2CHCO_2)Sn]_2O\}_2$ (Pz = pyrazol-1-yl or 3,5-dimethylpyrazol-1-yl), which are characterized by IR and NMR (^1H, ^{13}C and ^{119}Sn) spectra and elemental analyses. The X-ray crystal structure analyses indicate that $\{[(n\text{-}Bu)_2(Pz_2CHCO_2)Sn]_2O\}_2$ is a centrosymmetric dimer with a cyclic Sn_2O_2 unit, in which each tin atom is situated in a distorted trigonal bipyramidal geometry. In addition, bis(3,5-dimethylpyrazol-1-yl)acetic acid in the solid state forms a dimer through two intermolecular O–H···N hydrogen bonds. These organotin derivatives display low fungicide, insecticide and miticide activities, but display certain cytotoxicities for Hela cells *in vitro*. **Copyright © 2005 John Wiley & Sons, Ltd.**

KEYWORDS: organotin(IV) compounds; bis(pyrazol-1-yl)acetate; cluster; X-ray diffraction

INTRODUCTION

Organotin(IV) carboxylate compounds have been extensively investigated for a long time owing to their wide applications in many fields, e.g. as catalysts, stabilizers, pesticides, bactericides and anti-tumor agents, etc.[1–5] Recently, many diorganotin carboxylate compounds have also been synthesized by the dehydration reaction of diorganotin oxides with carboxylic acids and tested for their biological activity.[6–8] The coordination mode of the carboxylate group is usually monodentate, bridging bidentate or chelating bidentate. The tridentate coordination mode of the carboxylate group has also been observed in the diorganotin carboxylate compound.[9] On the other hand, the coordination number and environment of the central tin atom can be easily controlled by using different functionalized carboxylic acids with additional oxygen, sulfur or nitrogen donor groups,[10–14] and substituents linked to the tin atom also have an influence.[15]

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Recently, studies on the heteroscorpionate ligands, e.g. bis(pyrazol-1-yl)acetate, have received increasing attention owing to their advantages, compared with scorpionate ligands, such as polyfunctional donor spheres, being water soluble and stable towards hydrolysis, etc.[16,17] These novel heteroscorpionate ligands have acted as good precursors to form transition-metal complexes. However, limited numbers of main-group metal complexes have been reported.[18] Here, we report the reaction of bis(pyrazol-1-yl)acetic acid with *n*-Bu_2SnO to yield dimeric bis[dicarboxylatotetraorganodistannoxanes].

EXPERIMENTAL

Materials and measurements

Di-*n*-butyltin oxide (*n*-Bu_2SnO),[19] bis(pyrazol-1-yl)acetic acid (**1**) and bis(3,5-dimethylpyrazol-1-yl)acetic acid (**2**)[20] were prepared by the published methods. Multinuclear magnetic resonance spectra were obtained with a Bruker AV300 spectrometer, and the chemical shifts were reported in parts per million with respect to reference standards (internal $SiMe_4$ for ^1H NMR and ^{13}C NMR spectra, external $SnMe_4$ for ^{119}Sn NMR). IR spectral data were obtained from a Bruker

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Equinox55 spectrometer using KBr discs. Elemental analyses were carried out on a Perkin–Elmer 2400C analyzer. Melting temperatures were measured with a PHMK melting-point apparatus and were uncorrected.

Synthesis

*Preparation of dimeric bis[dicarboxylatotetra-organodistannoxane] (**3**)*

A mixture of *n*-Bu_2SnO (0.498 g, 2 mmol) and bis(pyrazol-1-yl)acetic acid (0.384 g, 2 mmol) in anhydrous benzene (30 ml) was stirred and heated at reflux for 6 h to yield a clear solution. After removing the benzene *in vacuo*, the crude product was recrystallized from diethyl ether to afford colorless crystals of **3** (0.73 g, 86%). M.p.: 126–128 °C. ^{1}H NMR ($CDCl_3$): $\delta = 7.67$ (d, 2H), 7.50 (d, 2H), 6.81 (s, 1H), 6.25 (t, 2H), 1.53–1.37 (m, 6H), 1.28–1.19 (m, 4H), 1.08–1.02 (m, 2H), 0.90 (t, 3H), 0.85 (t, 3H). ^{13}C NMR ($CDCl_3$): $\delta = 169.0$ (COO), 140.7, 129.9, 106.9 (carbon atoms of pyrazole ring), 76.1 (CH), 29.1, 28.4, 27.3, 26.9, 26.7, 25.6, 13.6, 13.5 (butyl carbon atoms). ^{119}Sn NMR ($CDCl_3$): $\delta = -190, -192$. IR (KBr, cm^{-1}): ν_{as}(COO) 1669.4, 1622.6, ν_s(COO) 1411.7, 1390.7. Anal. Found: C, 44.59; H, 5.64; N, 13.15. Calc. for $C_{32}H_{50}N_8O_5Sn_2$: C, 44.48; H, 5.79; N, 12.97%.

*Preparation of dimeric bis[dicarboxylatotetra-organodistannoxane] (**4**)*

This compound was obtained similarly using bis(3,5-dimethylpyrazol-1-yl)acetic acid reacted with *n*-Bu_2SnO as described above for **3**. After removing the benzene *in vacuo*, the crude product was recrystallized from CH_2Cl_2–hexane to afford colorless crystals of **4**. Yield: 82%. M. p.: 120–122 °C. ^{1}H NMR ($CDCl_3$): $\delta = 6.67$ (s, 1H), 5.74 (s, 2H), 2.13 (s, 6H), 2.08 (s, 6H), 1.60–1.46 (m, 4H), 1.35–1.12 (m, 8H), 0.93 (t, 3H), 0.85 (t, 3H). ^{13}C NMR ($CDCl_3$): $\delta = 169.3$ (COO), 147.5, 140.8, 106.9 (carbon atoms of pyrazole ring), 74.5 (CH), 28.8, 28.2, 27.4, 27.0, 26.9, 26.8, 13.7, 13.5, 13.4, 11.1 (carbon atoms of butyl and methyl groups of pyrazole ring). ^{119}Sn NMR ($CDCl_3$): $\delta = -193, -195$. IR (KBr, cm^{-1}): ν_{as}(COO) 1685.2, 1616.1, ν_s(COO) 1413.7, 1376.9. Anal. Found: C, 48.45; H, 6.61; N, 11.18. Calc. for $C_{40}H_{66}N_8O_5Sn_2 \cdot 1.25\ H_2O$: C, 48.07; H, 6.86; N, 11.22%.

X-ray crystallography

Colorless crystals of **2** and **4** suitable for X-ray analyses were obtained at −10 °C from their CH_2Cl_2–hexane solutions, and colorless crystals of **3** were obtained by slowly cooling a hot diethyl ether solution. Intensity data were collected at 293 K on a Bruker SMART CCD equipped with graphite-monochromated Mo Kα radiation ($\lambda = 0.710\,73$ Å) using the $\omega - 2\theta$ scan technique. The structures were solved by direct methods and refined by full-matrix least squares on F^2. All non-hydrogen atoms were refined with anisotropic displacement parameters. One butyl group (C37–C40) in **4** was found to be disordered, with two sites discerned in the ratio 75 : 25 (minor component was refined) isotropically. The site occupation factors of three disordered water molecules in **4** were adjusted (0.5 for O8 and O9, 0.25 for O10) to give reasonable thermal parameters, but their hydrogen atoms were not located. Crystallographic data are listed in Table 1.

Table 1. Crystal data and refinement parameters for **2**–**4**

Compound	**2**	**3**	**4**
Formula	$C_{12}H_{16}N_4O_2$	$C_{32}H_{50}N_8O_5Sn_2$	$C_{40}H_{68.5}N_8O_{6.25}Sn_2$
Formula weight	248.29	864.18	998.91
Crystal system	Triclinic	Triclinic	Monoclinic
Space group	$P\bar{1}$	$P\bar{1}$	$C2/c$
a (Å)	8.199(3)	13.081(4)	19.797(8)
b (Å)	9.081(3)	13.565(4)	21.964(9)
c (Å)	9.132(4)	13.744(4)	23.929(10)
α (°)	82.268(6)	63.455(5)	
β (°)	85.279(6)	73.456(6)	99.122(7)
γ (°)	81.436(6)	64.049(5)	
V(Å)^3	664.9(4)	1949.7(10)	10 273(7)
Z	2	2	8
D_c(g cm^{-3})	1.240	1.472	1.292
F(000)	264	876	4116
μ(mm^{-1})	0.088	1.327	1.019
No. of unique reflections	2336	6838	12 265
No. of observed reflections ($I > 2\sigma(I)$)	1751	4686	5919
No. of parameters	169	428	557
Residuals R, R_w	0.041, 0.111	0.037, 0.090	0.059, 0.151
CCDC deposition numbers	266 945	251 918	266 946

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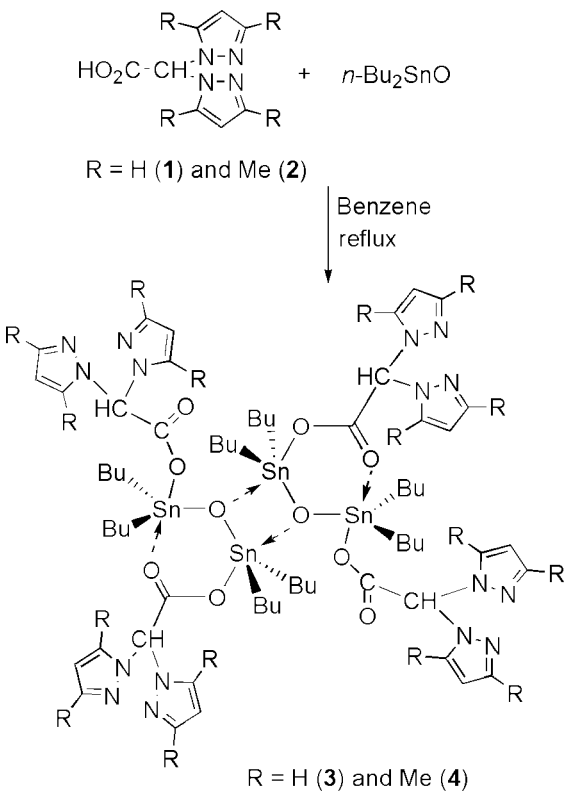
RESULTS AND DISCUSSION

Upon treatment of *n*-Bu_2SnO with bis(pyrazol-1-yl)acetic acid (**1** and **2**) in a 1 : 1 molar ratio in anhydrous benzene, dimeric bis[dicarboxylatotetraorganodistannoxanes] (**3**) and (**4**) are obtained in reasonable yields (Scheme 1), which are soluble in chlorinated solvents at room temperature.

Two types of carbonyl absorption band in the IR spectra of compounds **3** and **4** are observed, implying that carboxylate groups possibly coordinate to the tin atom in a different manner.[8,12,21] Two $\nu_{as}(COO^-)$ bands appear at 1669.4 and 1622.6 cm^{-1} for compound **3**, and at 1685.2 and 1616.1 cm^{-1} for compound **4**, and two $\nu_s COO^-$ bands appear at 1411.7 and 1390.7 cm^{-1} for compound **3**, and at 1413.7 and 1376.9 cm^{-1} for compound **4**. The corresponding differences $\Delta[\nu_{as}(COO^-) - \nu_s(COO^-)]$ are 278.7 and 210.9 cm^{-1} in **3** and 308.3 and 202.4 cm^{-1} in **4**, indicating the monodentate and bidentate coordination modes of the carboxylate groups in the two compounds. This is consistent with the fact that compounds **3** and **4** are centrosymmetric dimers with a cyclic Sn_2O_2 unit, confirmed by the X-ray crystallography. In addition, the ^{119}Sn spectra of the two compounds have also confirmed the presence of endo- and exo-cyclic tin atoms. A pair of resonances of equal intensities are observed at −190 and −192 ppm for compound **3**, and at −193 and −195 ppm for compound **4**. Two sets of butyl signals in the ^1H and ^{13}C NMR spectra also reflect them being attached to different tin atoms. Only one set of NMR signals for bis(pyrazol-1-yl)acetate groups in the two compounds is observed, possibly due to the result of the fast exchange in the coordination behavior of carboxylate groups attached to the endo- and exo-cyclic tin atoms.[8]

In the solid state, molecule **2** forms a dimer through intermolecular O–H···N hydrogen bonds (Fig. 1). Structural parameters, given in the caption to the figure, are comparable to those in bis(3,5-di-*tert*-butylpyrazol-1-yl)acetic acid.[22] A notable difference is found in the N1–C6–N3 angle of 113.1(1)° in **2**, which is slightly smaller than the corresponding angle of 116.0(4)° in the latter structure, a result consistent with less steric hindrance in **2**.

In order to confirm the role of the nitrogen atoms in the bis(pyrazol-1-yl)acetate ligands in **3** and **4**, the structures of these compounds were determined by single-crystal X-ray diffraction. The molecular structures are presented in Figs 2 and 3 and selected bond distances and angles are listed in Table 2. In both structures, the core geometry of the molecule comprises a common centrosymmetric four-membered Sn_2O_2 ring, and each tin atom adopts, to a first approximation, a five-coordinate distorted trigonal bipyramidal geometry with two *cis*-butyl carbon atoms



Scheme 1.

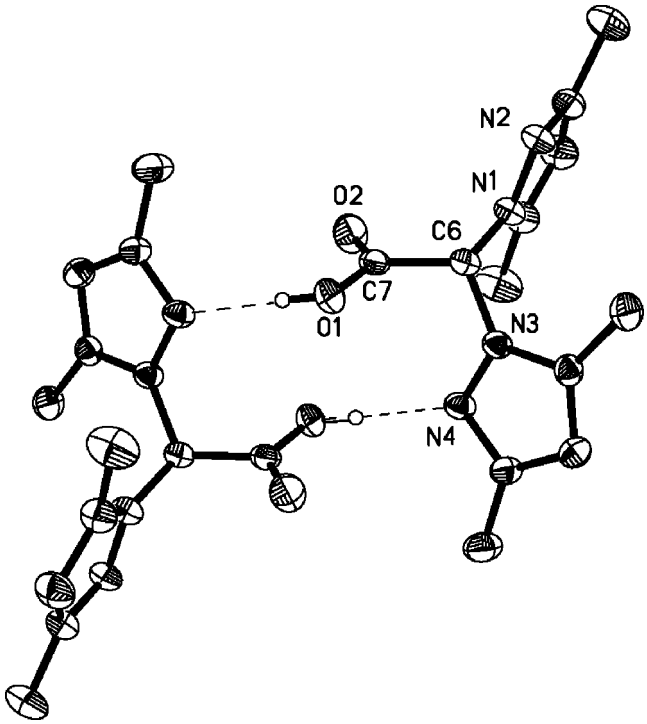


Figure 1. Molecular structure of **2** emphasizing the intermolecular hydrogen bonding interactions. The thermal ellipsoids are drawn at the 30% probability. Key geometric parameters: C6–N1 1.450(2), C7–O1 1.310(2), C7–O2 1.194(2), O–H···N 2.69 Å; N1–C6–N3 113.1(1), O1–C7–O2 126.2(2), C6–C7–O1 111.0(2), C6–C7–O2 122.8(2), O–H···N 177°.

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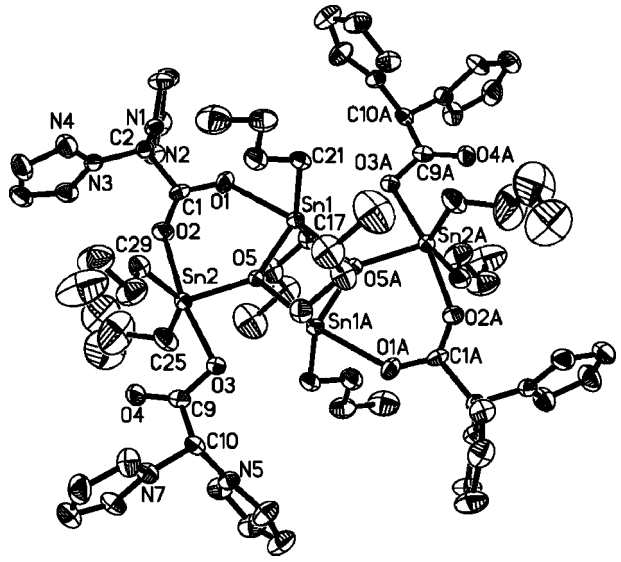

Figure 2. Molecular structure of **3** with the thermal ellipsoids at the 30% probability level. Hydrogen atoms are omitted for clarity. Symmetry operations of 'A' are $-x+2$, $-y+2$, $-z$.

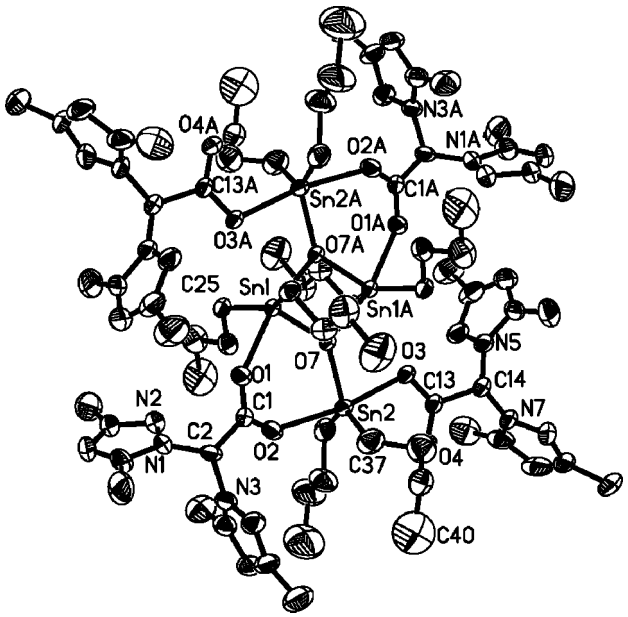

Figure 3. Molecular structure of **4** with the thermal ellipsoids at the 30% probability level. Hydrogen atoms and solvent molecules are omitted for clarity. Symmetry operations of 'A' are $-x+1/2$, $-y+3/2$, $-z+1$.

and three asymmetrically coordinated oxygen atoms. The intramolecular distances of Sn1···O3A and Sn2···O4 in **3** are 2.778 Å and 2.874 Å respectively, and the corresponding distances of Sn1···O3A and Sn2···O4 in **4** are 2.775 Å and 2.936 Å respectively. In **3**, the O1 and O5A atoms for the Sn1 atom and the O2 and O3 atoms for the Sn2 atom occupy the axial sites, and the axial angles of O1–Sn1–O5A and O2–Sn2–O3 are 168.9(1)° and 170.4(1)° respectively. In **4**, the corresponding angles of O1–Sn1–O5A and O2–Sn2–O3 are 166.1(1)° and 170.2(1)° respectively. Unlike in Ph_2SnCl(bdmpaza) (bdmpaza = bis(3,5-dimethylpyrazol-1-yl)acetate),[17] the nitrogen atoms of bis(pyrazol-1-yl)acetates in **3** and **4** do not coordinate the tin atoms. Two bis(pyrazol-1-yl)acetate ligands act as a monodentate ligand by one oxygen atom of the carboxyl group and coordinate each exocyclic tin atom, the two other carboxylates are bridging bidentate ligands and bridge two tin atoms by two oxygen atoms of the carboxyl group.

Table 2. Selected bond length (Å) and angles (°) for compounds **3** and **4**[a]

3		**4**	
Sn1–O1	2.298(4)	Sn1–O1	2.273(5)
Sn1–O5	2.056(3)	Sn1–O7	2.044(4)
Sn1–O5A	2.177(3)	Sn1–O7A	2.179(4)
Sn2–O2	2.261(4)	Sn2–O2	2.285(5)
Sn2–O3	2.193(3)	Sn2–O3	2.200(4)
Sn2–O5	2.019(3)	Sn2–O7	2.019(4)
C1–O1	1.262(6)	C1–O1	1.264(7)
C1–O2	1.213(6)	C1–O2	1.228(8)
C2–N1	1.445(7)	C2–N1	1.458(9)
C2–N3	1.450(6)	C2–N3	1.442(8)
C9–O3	1.289(6)	C13–O3	1.285(7)
C9–O4	1.214(6)	C13–O4	1.220(8)
C10–N5	1.451(6)	C14–N5	1.45(1)
C10–N7	1.448(6)	C14–N7	1.475(9)
C1–O1–Sn1	132.1(3)	C1–O1–Sn1	132.8(4)
C1–O2–Sn2	141.0(4)	C1–O2–Sn2	133.1(5)
Sn1–O5–Sn1A	103.6(1)	Sn1–O7–Sn2	135.9(2)
Sn1–O5–Sn2	136.9(1)	Sn1–O7–Sn1A	104.0(1)
Sn1A–O5–Sn2	119.3(1)	Sn1A–O7–Sn2	119.6(1)
C21–Sn1–O5	108.1(1)	C25–Sn1–O7A	98.8(2)
O1–Sn1–O5A	168.9(1)	O1–Sn1–O7	90.7(1)
O5–Sn1–O5A	76.4(1)	O1–Sn1–O7A	166.1(1)
O2–Sn2–O3	170.4(1)	O7–Sn1–O7A	76.0(1)
O2–Sn2–O5	89.2(1)	O2–Sn2–O3	170.2(1)
O3–Sn2–O5	81.5(1)	O2–Sn2–O7	90.1(1)
O1–C1–O2	125.2(5)	O1–C1–O2	125.7(6)
O3–C9–O4	123.7(5)	O3–C13–O4	125.0(6)
N1–C2–N3	112.2(4)	N1–C2–N3	112.7(6)
N5–C10–N7	111.3(4)	N5–C14–N7	113.5(6)

[a] Symmetry operations of 'A' for **3** are $-x+2$, $-y+2$, $-z$, and $-x+1/2$, $-y+3/2$, $-z+1$ for **4**.

Bioassay screening for fungicidal,[23] insecticidal[24] and miticidal[25] activity indicates that compound **3** has certain fungicidal activities: the inhibition percentages *in vitro* to *Gibberella zeae, Alternaria solani, Cercospora arachidicola, Physalospora piricola* and *Phoma asparagi* are 25.6%, 22.2%, 18.4%, 13.7% and 34.3% respectively. This compound has no

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insecticidal or miticidal activities against *Culex pipiens pallens*, *Mythimna separata* and *Aphis laburni* Kaltenbach. Compound **4** only has 11.1% inhibition to *Alternaria solani in vitro*, and no other fungicidal, insecticidal and miticidal activities are observed.

The cytotoxic activity of compounds **3** and **4** for Hela cells *in vitro* was assayed by the 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl-2*H*-tetrazolium bromide (MTT) method.[26,27] The results show that compound **3** exhibits good cytotoxicities, and its IC_{50} value is 0.75 μM, a relatively higher cytotoxic activity than compound **4** (IC_{50} value of 2.54 μM). It seems that methyl groups in pyrazole rings significantly decrease the cytotoxic activity of compound **4**.

Acknowledgements

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