JOURNAL OF AGRICULTURAL AND FOOD CHEMISTRY
ARTICLE

J. Agric. Food Chem. 2010, 58, 2715–2719 2715
DOI:10.1021/jf902168d

# Synthesis and Biological Activity of Organotin 4-Methyl-1,2,3-thiadiazole-5-carboxylates and Benzo[1,2,3]thiadiazole-7-carboxylates†

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A series of organotin 4-methyl-1,2,3-thiadiazole-5-carboxylates and benzo[1,2,3]thiadiazole-7-carboxylates have been synthesized and characterized by NMR ($^1$H, $^{13}$C, and $^{119}$Sn), IR, and elemental analyses. The structure of the dimeric complex $\{[(BTHCO_2)SnEt_2]_2O\}_2$ (BTH represents benzo-[1,2,3]thiadiazol-7-yl) has been further confirmed by X-ray diffraction crystallography. Assessment for fungicidal activity indicates that all of the newly synthesized compounds exhibit good growth inhibition against *Alternaria solani*, *Cercospora arachidicola*, *Gibberella zeae*, *Physalospora piricola*, and *Botrytis cinerea*. High growth inhibition percentage at 50 $\mu$g/mL was obtained in vitro in the case of triorganotin 4-methyl-1,2,3-thiadiazole-5-carboxylates and benzo[1,2,3]thiadiazole-7-carboxylates. The corresponding $EC_{50}$ values of these triorganotin carboxylates have been detected, and values of $EC_{50}$ as low as 0.12 $\mu$g/mL against *P. piricola* and 0.16 $\mu$g/mL against *G. zeae*, respectively, were observed for triethyltin benzo[1,2,3]thiadiazole-7-carboxylate.

**KEYWORDS: Organotin carboxylate; 4-methyl-1,2,3-thiadiazole-5-carboxylic acid; benzo[1,2,3]thiadiazole-7-carboxylic acid; fungicide**

## INTRODUCTION

Benefiting from their significant biological activities, organotin derivatives have been explored extensively for applications in industrial and agricultural fields despite their toxicity and environmental effects partially limiting their application. Among these organotin compounds, organotin carboxylates have received particular attention owing to their remarkable structural diversity (*1*−*3*) as well as biological importance, for example, as pesticidal, antibacterial, and antitumor agents and wood preservatives (*4*−*6*). Existing investigations have proved that the biological activities of organotin carboxylates greatly depend on their coordination structures, which are markedly related to the properties of the carboxylic acid ligands and the organic substituents bonded to the tin atoms. Thus, the synthesis of organotin derivatives from biologically active ligands has drawn increasing attention in recent years (*7*, *8*) in the efforts to obtain better or different pharmacological profiles than the free ligands. Since their first synthesis, the derivatives of 1,2,3-thiadiazole and benzo[1,2,3]thiadiazole have manifested their versatile biological activities, such as antitumor, antibacterial, and antiallergic activities (*9*−*12*). Some 1,2,3-thiadiazole-5-carboxylic and benzo-[1,2,3]thiadiazole-7-carboxylic derivatives, such as *N*-(3-chloro-4-methylphenyl)-4-methyl-1,2,3-thiadiazole-5-carboxamide as well as benzo[1,2,3]thiadiazole-7-carbothionic acid *S*-methyl ester, have been commercially available plant activators. Taking into consideration the important biological applications of organotin carboxylates and thiadiazole carboxylic derivatives, exploring the biological activities of organotin thiadiazole carboxylates should be quite significant and promising. Here we report chemical and preliminary biological investigations on organotin 4-methyl-1,2,3-thiadiazole-5-carboxylates and benzo[1,2,3]thiadiazole-7-carboxylates.

## EXPERIMENTAL PROCEDURES

Multinuclear NMR spectra were obtained with a Bruker 600 spectrometer using $CDCl_3$ as solvent unless otherwise noted, and the chemical shifts are reported in parts per million with respect to reference standards (internal $SiMe_4$ for $^1$H NMR and $^{13}$C NMR spectra, external $SnMe_4$ for $^{119}$Sn NMR). IR spectra were obtained from a Nicolet 380 spectrometer as KBr disks. Elemental analyses were carried out on an Elementar Vairo EL analyzer. Melting points were measured with an X-4 digital micro melting-point apparatus and are uncorrected.

**Synthesis of $\{[(BTHCO_2)Sn(n\text{-}Bu)_2]_2O\}_2$ (1) (BTH = Benzo-[1,2,3]thiadiazol-7-yl).** The mixture of benzo[1,2,3]thiadiazole-7-carboxylic acid ($BTHCO_2H$) (0.18 g, 1 mmol) and $(n\text{-}Bu)_2SnO$ (0.25 g, 1 mmol) in anhydrous benzene (50 mL) was stirred and refluxed for 8 h. After removal of benzene in vacuo, the crude product was recrystallized from benzene/hexane to afford orange crystals of **1**: yield, 0.20 g (48%); mp, 228−231 °C; $^1$H NMR, $\delta$ 0.69 (t, $J$ = 6.5 Hz, 3H, $CH_3$), 0.86 (t, $J$ = 6.7 Hz, 3H, $CH_3$), 1.23−1.27 (m, 2H, $CH_2$), 1.40−1.43 (m, 2H, $CH_2$),

†Part of the ECUST-Qian Pesticide Cluster.

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Published on Web 12/16/2009

1.62−1.81 (m, 8H, C$H_2$), 7.94 (t, $J$ = 6.9 Hz, 1H, C$_6H_3$), 8.41 (d, $J$ = 6.4 Hz, 1H, C$_6H_3$), 8.92 (d, $J$ = 7.6 Hz, 1H, C$_6H_3$); $^{13}$C NMR, $\delta$ 13.6, 13.8, 26.8, 26.9, 27.7, 28.1, 29.0, 31.8 (*n*-butyl carbons), 126.3, 127.5, 128.5, 130.6, 141.2, 159.1 (C$_6$H$_3$), 171.1 (*C*OO); $^{119}$Sn NMR, $\delta$ −204.8, −218.8; IR (cm$^{-1}$), $\nu_{as}$ (COO) 1599, $\nu_s$ (COO) 1370. Anal. Calcd for $C_{60}H_{84}N_8O_{10}S_4Sn_4$: C, 42.88; H, 5.04; N, 6.67%. Found: C, 42.99; H, 4.56; N, 6.76%.

**Synthesis of (BTHCO$_2$)$_2$Sn(*n*-Bu)$_2$ (2).** The mixture of BTHCO$_2$H (0.36 g, 2 mmol) and (*n*-Bu)$_2$SnO (0.25 g, 1 mmol) in anhydrous benzene (50 mL) was stirred and refluxed for 8 h. After removal of benzene in vacuo, the crude product was recrystallized from benzene to afford orange solids of **2**: yield, 0.24 g (41%); mp, 191−194 °C; $^1$H NMR, $\delta$ 0.88 (t, $J$ = 7.3 Hz, 3H, C$H_3$), 1.42−1.46 (m, 2H, C$H_2$), 1.77−1.81 (m, 2H, C$H_2$), 1.94−1.95 (m, 2H, C$H_2$), 7.83 (t, $J$ = 7.9 Hz, 1H, C$_6H_3$), 8.55 (d, $J$ = 7.0 Hz, 1H, C$_6H_3$), 8.89 (d, $J$ = 7.8 Hz, 1H, C$_6H_3$); $^{13}$C NMR, $\delta$ 13.5, 26.0, 26.3, 26.7 (*n*-butyl carbons), 125.3, 127.2, 128.8, 131.8, 141.3, 158.8 (C$_6$H$_3$), 173.3 (*C*OO); $^{119}$Sn NMR, $\delta$ −126.5; IR (cm$^{-1}$), $\nu_{as}$ (COO) 1604, $\nu_s$ (COO) 1377. Anal. Calcd for $C_{22}H_{24}N_4O_4S_2Sn$: C, 44.69; H, 4.09; N, 9.48%. Found: C, 44.48; H, 4.24; N, 9.98%.

**Synthesis of {[(BTHCO$_2$)SnEt$_2$]$_2$O}$_2$ (3).** This complex was obtained similarly using Et$_2$SnO instead of (*n*-Bu)$_2$SnO as described above for **1**. The crude product was recrystallized from $CH_2Cl_2$/hexane to afford yellow solids of **3**: yield, 0.16 g (44%); mp, 310 °C (dec); $^1$H NMR, $\delta$ 1.42 (t, $J$ = 7.8 Hz, 3H, C$H_3$), 1.47 (t, $J$ = 7.8 Hz, 3H, C$H_3$), 1.74−1.85 (m, 4H, C$H_2$), 7.94 (s, br, 1H, C$_6H_3$), 8.44 (d, $J$ = 5.9 Hz, 1H, C$_6H_3$), 8.92 (d, $J$ = 7.6 Hz, 1H, C$_6H_3$); $^{13}$C NMR, $\delta$ 10.0, 10.3, 21.1, 24.5 (ethyl carbons), 126.0, 127.4, 128.3, 130.4, 141.0, 158.9 (C$_6$H$_3$), 170.9 (*C*OO); $^{119}$Sn NMR, $\delta$ −205.1, −215.9; IR (cm$^{-1}$), $\nu_{as}$ (COO) 1600, $\nu_s$ (COO) 1395. Anal. Calcd for $C_{44}H_{52}N_8O_{10}S_4Sn_4\cdot 0.5CH_2Cl_2$: C, 35.07; H, 3.53; N, 7.27%. Found: C, 34.87; H, 3.08; N, 7.58%.

**Synthesis of (BTHCO$_2$)$_2$SnEt$_2$ (4).** This complex was obtained similarly using Et$_2$SnO instead of (*n*-Bu)$_2$SnO as described above for **2**: yellow solids; yield, 0.42 g (77%); mp, 174−178 °C; $^1$H NMR, $\delta$ 1.41 (t, $J$ = 7.6 Hz, 3H, C$H_3$), 1.76−1.93 (m, 2H, C$H_2$), 7.83 (t, $J$ = 7.7 Hz, 1H, C$_6H_3$), 8.55 (d, $J$ = 7.2 Hz, 1H, C$_6H_3$), 8.91 (d, $J$ = 8.2 Hz, 1H, C$_6H_3$); $^{13}$C NMR, $\delta$ 9.3, 19.0 (ethyl carbons), 123.6, 127.4, 129.0, 132.0, 141.5, 159.0 (C$_6$H$_3$), 173.5 (*C*OO); $^{119}$Sn NMR, $\delta$ −133.0; IR (cm$^{-1}$), $\nu_{as}$ (COO) 1604, $\nu_s$ (COO) 1371. Anal. Calcd for $C_{18}H_{16}N_4O_4S_2Sn\cdot 2H_2O\cdot 0.5C_6H_6$: C, 41.33; H, 3.80; N, 9.18%. Found: C, 41.54; H, 3.90; N, 9.57%.

**Synthesis of BTHCO$_2$SnPh$_3$ (5).** This complex was obtained similarly using (Ph$_3$Sn)$_2$O instead of (*n*-Bu)$_2$SnO as described above for **2**: slightly yellow crystals; yield, 0.40 g (76%); mp, 173−175 °C; $^1$H NMR, $\delta$ 7.50−7.54 (m, 9H, C$_6H_5$), 7.74 (t, $J$ = 7.8 Hz, 1H, C$_6H_3$), 7.83−7.93 (m, 6H, C$_6H_5$), 8.48 (d, $J$ = 7.2 Hz, 1H, C$_6H_3$), 8.80 (d, $J$ = 8.1 Hz, 1H, C$_6H_3$); $^{13}$C NMR, $\delta$ 124.2, 127.1, 128.1, 129.1, 130.6, 131.7, 136.9, 137.5, 141.4, 158.6 (C$_6$H$_5$ and C$_6$H$_3$), 169.8 (*C*OO); $^{119}$Sn NMR, $\delta$ −89.3; IR (cm$^{-1}$), $\nu_{as}$ (COO) 1636, $\nu_s$ (COO) 1339. Anal. Calcd for $C_{25}H_{18}N_2O_2SSn$: C, 56.74; H, 3.43; N, 5.29%. Found: C, 56.69; H, 3.56; N, 5.34%.

**Synthesis of BTHCO$_2$Sn(*n*-Bu)$_3$ (6).** This complex was obtained similarly using (*n*-Bu$_3$Sn)$_2$O instead of (*n*-Bu)$_2$SnO as described above for **2**: yellow crystals; yield, 0.82 g (87%); mp, 45−47 °C; $^1$H NMR, $\delta$ 0.94 (t, $J$ = 7.3 Hz, 9H, C$H_3$), 1.40−1.46 (m, 12H, C$H_2$), 1.69−1.74 (m, 6H, C$H_2$), 7.71 (t, $J$ = 7.3 Hz, 1H, C$_6H_3$), 8.36 (d, $J$ = 7.2 Hz, 1H, C$_6H_3$), 8.75 (d, $J$ = 8.1 Hz, 1H, C$_6H_3$); $^{13}$C NMR, $\delta$ 13.7, 17.1, 27.1, 27.8 (*n*-butyl carbons), 125.5, 127.1, 127.5, 131.0, 141.1, 158.6 (C$_6$H$_3$), 168.8 (*C*OO); $^{119}$Sn NMR, $\delta$ 138.4; IR (cm$^{-1}$), $\nu_{as}$ (COO) 1613, $\nu_s$ (COO) 1357. Anal. Calcd for $C_{19}H_{30}N_2O_2SSn$: C, 48.63; H, 6.44; N, 5.97%. Found: C, 49.14; H, 5.93; N, 5.92%.

**Synthesis of BTHCO$_2$SnEt$_3$ (7).** This complex was obtained similarly using (Et$_3$Sn)$_2$O instead of (*n*-Bu)$_2$SnO as described above for **2**. The crude product was recrystallized from hexane to afford yellow solids of **7**: yield, 0.73 g (95%); mp, 66−68 °C; $^1$H NMR, $\delta$ 1.26−1.49 (m, 15H, C$_2H_5$), 7.74 (t, $J$ = 7.8 Hz, 1H, C$_6H_3$), 8.40 (d, $J$ = 7.2 Hz, 1H, C$_6H_3$), 8.78 (d, $J$ = 8.2 Hz, 1H, C$_6H_3$); $^{13}$C NMR, $\delta$ 8.5, 9.9 (ethyl carbons), 125.3, 127.1, 127.6, 131.1, 141.1, 158.6 (C$_6$H$_3$), 169.0 (*C*OO); $^{119}$Sn NMR, $\delta$ 135.3; IR (cm$^{-1}$), $\nu_{as}$ (COO) 1605, $\nu_s$ (COO) 1365. Anal. Calcd for $C_{13}H_{18}N_2O_2SSn$: C, 40.55; H, 4.71; N, 7.27%. Found: C, 40.59; H, 5.03; N, 7.27%.

**Synthesis of BTHCO$_2$SnCy$_3$ (8).** This complex was obtained similarly using tricyclohexyltin hydroxide instead of (*n*-Bu)$_2$SnO as described above for **1**. The crude product was recrystallized from hexane to afford yellow crystals of **8**: yield, 0.50 g (91%); mp 99−101 °C. $^1$H NMR, $\delta$ 1.31−1.43 (m, 12H, C$_6H_{11}$), 1.66−1.82 (m, 15H, C$_6H_{11}$), 2.00−2.10 (m, 6H, C$_6H_{11}$), 7.73 (t, $J$ = 8.0 Hz, 1H, C$_6H_3$), 8.39 (d, $J$ = 6.8 Hz, 1H, C$_6H_3$), 8.76 (d, $J$ = 7.6 Hz, 1H, C$_6H_3$); $^{13}$C NMR, $\delta$ 26.9, 28.9, 31.1, 34.5 (cyclohexyl carbons), 125.6, 127.1, 127.4, 131.1, 141.1, 158.5 (C$_6$H$_3$), 168.7 (*C*OO); $^{119}$Sn NMR, $\delta$ 40.5; IR (cm$^{-1}$), $\nu_{as}$ (COO) 1620, $\nu_s$ (COO) 1359. Anal. Calcd for $C_{25}H_{36}N_2O_2SSn$: C, 54.86; H, 6.63; N, 5.12%. Found: C, 54.97; H, 6.51; N, 4.89%.

**Synthesis of {[(TDLCO$_2$)Sn(*n*-Bu)$_2$]$_2$O}$_2$ (9) (TDL = 4-Methyl-1,2,3-thiadiazol-5-yl).** This complex was obtained similarly using 4-methyl-1,2,3-thiadiazole-5-carboxylic acid (TDLCO$_2$H) instead of BTHCO$_2$H as described above for **1**. The crude product was recrystallized from hexane to afford white crystals of **9**: yield, 0.22 g (57%); mp, 160−162 °C; $^1$H NMR, $\delta$ 0.83−0.96 (m, 12H, C$_4H_9$), 1.31−1.40 (m, 8H, C$_4H_9$), 1.62−1.73 (m, 16H, C$_4H_9$), 2.95 (s, br, 6H, C$H_3$); $^{13}$C NMR, $\delta$ 13.5, 13.6, 26.7, 13.9, 27.1, 27.4, 27.8, 28.9, 31.0, 31.1 (*n*-butyl carbons and *C*H$_3$), 143.4, 161.2 (C$_2$N$_2$S), 165.7 (*C*OO); $^{119}$Sn NMR, $\delta$ −200.3, −206.1; IR (cm$^{-1}$), $\nu_{as}$ (COO) 1645, $\nu_s$ (COO) 1400. Anal. Calcd for $C_{48}H_{84}N_8O_{10}S_4Sn_4$: C, 37.53; H, 5.51; N, 7.29%. Found: C, 37.51; H, 5.72; N, 7.68%.

**Synthesis of (TDLCO$_2$)$_2$Sn(*n*-Bu)$_2$ (10).** This complex was obtained similarly using TDLCO$_2$H instead of BTHCO$_2$H as described above for **2**: slightly yellow solids; yield, 0.32 g (62%); mp, 158−160 °C; $^1$H NMR, $\delta$ 0.93 (t, $J$ = 7.3 Hz, 3H, CH$_2$C$H_3$), 1.42−1.46 (m, 2H, C$H_2$), 1.73−1.78 (m, 2H, C$H_2$), 1.84−1.94 (m, 2H, C$H_2$), 3.00 (s, 3H, C$_2$N$_2$SC$H_3$); $^{13}$C NMR, $\delta$ 13.5, 13.9, 26.0, 26.3, 26.6 (*n*-butyl carbons and *C*H$_3$), 140.5, 162.2 (C$_2$N$_2$S), 168.1 (*C*OO); $^{119}$Sn NMR, $\delta$ −115.8; IR (cm$^{-1}$), $\nu_{as}$ (COO) 1618, $\nu_s$ (COO) 1359. Anal. Calcd for $C_{16}H_{24}N_4O_4S_2Sn$: C, 37.01; H, 4.66; N, 10.79%. Found: C, 37.27; H, 4.44; N, 10.57%.

**Synthesis of {[(TDLCO$_2$)SnEt$_2$]$_2$O}$_2$ (11).** The mixture of TDLCO$_2$H (0.14 g, 1 mmol) and Et$_2$SnO (0.19 g, 1 mmol) in anhydrous benzene (50 mL) was stirred and refluxed for 8 h. After removal of benzene in vacuo, the crude product was recrystallized from benzene/hexane to afford white crystals of **11**: yield, 0.20 g (61%); mp, 208−210 °C; $^1$H NMR, $\delta$ 1.37 (t, $J$ = 7.8 Hz, 3H, CH$_2$C$H_3$), 1.40 (t, $J$ = 7.8 Hz, 3H, CH$_2$C$H_3$), 1.63−1.67 (m, 4H, C$H_2$CH$_3$), 2.99 (s, 3H, C$_2$N$_2$SC$H_3$); $^{13}$C NMR, $\delta$ 9.8, 10.1, 14.0, 21.1, 23.9 (ethyl carbons and *C*H$_3$), 143.3, 161.4 (C$_2$N$_2$S), 165.7 (*C*OO); $^{119}$Sn NMR, $\delta$ −200.4, −202.7; IR (cm$^{-1}$), $\nu_{as}$ (COO) 1621, $\nu_s$ (COO) 1399. Anal. Calcd for $C_{32}H_{52}N_8O_{10}S_4Sn_4$: C, 29.30; H, 4.00; N, 8.54%. Found: C, 29.51; H, 4.05; N, 8.75%.

**Synthesis of (TDLCO$_2$)$_2$SnEt$_2$ (12).** This complex was obtained similarly by the reaction of TDLCO$_2$H with Et$_2$SnO as described above for **11**, but in a 2:1 (acid/Et$_2$SnO) molar ratio. The crude product was recrystallized from hexane to afford white crystals of **12**: yield, 0.30 g (63%); mp, 106−108 °C; $^1$H NMR, $\delta$ 1.40 (t, $J$ = 7.9 Hz, 3H, CH$_2$C$H_3$), 1.86 (s, br, 2H, C$H_2$CH$_3$), 2.99 (s, 3H, C$_2$N$_2$SC$H_3$); $^{13}$C NMR, $\delta$ 9.0, 13.9, 19.0 (ethyl carbons and *C*H$_3$), 140.7, 162.2 (C$_2$N$_2$S), 168.2 (*C*OO); $^{119}$Sn NMR, $\delta$ −121.0; IR (cm$^{-1}$), $\nu_{as}$ (COO) 1634, $\nu_s$ (COO) 1398. Anal. Calcd for $C_{12}H_{16}N_4O_4S_2Sn$: C, 31.12; H, 3.48; N, 12.10%. Found: C, 31.15; H, 3.48; N, 12.41%.

**Synthesis of TDLCO$_2$SnPh$_3$ (13).** The mixture of TDLCO$_2$H (0.14 g, 1 mmol) and (Ph$_3$Sn)$_2$O (0.36 g, 0.5 mmol) in anhydrous benzene (50 mL) was stirred and refluxed for 8 h. After removal of benzene in vacuo, the crude product was recrystallized from benzene/hexane to afford yellow solids of **13**: yield, 0.37 g (75%); mp, 71−73 °C; $^1$H NMR, $\delta$ 2.94 (s, 3H, C$H_3$), 7.52, 7.74−7.84 (s, br, m, 9H, 6H, C$_6H_5$); $^{13}$C NMR, $\delta$ 13.9 (*C*H$_3$), 129.2, 130.7, 136.9, 137.1 (C$_6$H$_5$), 141.8, 161.7 (C$_2$N$_2$S), 164.6 (*C*OO); $^{119}$Sn NMR, $\delta$ −86.0; IR (cm$^{-1}$), $\nu_{as}$ (COO) 1633, $\nu_s$ (COO) 1395. Anal. Calcd for $C_{22}H_{18}N_2O_2SSn\cdot 2H_2O$: C, 49.93; H, 4.19; N, 5.29%. Found: C, 49.50; H, 4.31; N, 5.51%.

**Synthesis of TDLCO$_2$Sn(*n*-Bu)$_3$ (14).** This complex was obtained similarly using (*n*-Bu$_3$Sn)$_2$O instead of (Ph$_3$Sn)$_2$O as described above for **13**. The crude product was recrystallized from hexane to afford yellow crystals of **14**: yield, 0.71 g (87%); mp, 45−47 °C; $^1$H NMR, $\delta$ 0.91 (t, $J$ = 7.3 Hz, 9H, C$H_2$C$H_3$), 1.34−1.40 (m, 12H, C$H_2$), 1.63−1.68 (m, 6H, C$H_2$), 2.92 (s, 3H, C$_2$N$_2$SC$H_3$); $^{13}$C NMR, $\delta$ 13.6, 13.7, 17.0, 27.0, 27.8 (*n*-butyl carbons and C$_2$N$_2$SC$H_3$), 143.3, 160.9 (C$_2$N$_2$S), 163.8 (*C*OO); $^{119}$Sn NMR, $\delta$ 142.7; IR (cm$^{-1}$), $\nu_{as}$ (COO) 1662, $\nu_s$ (COO)

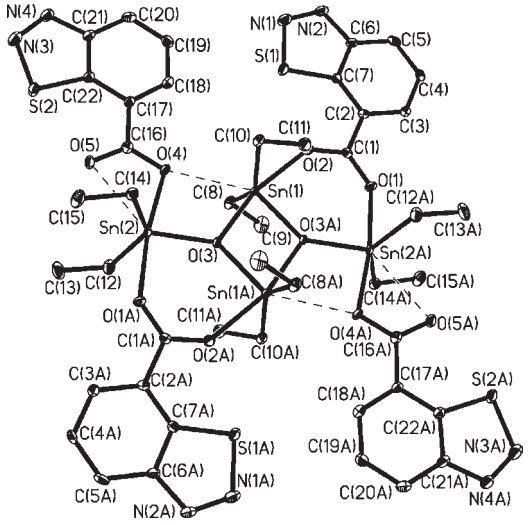


**Figure 1.** Molecular structure of complex **3** with the thermal ellipsoids at the 30% probability level. The uncoordinated solvent molecules and hydrogen atoms are omitted for clarity. Selected bond distances and angles: Sn(1)−O(2), 2.272(2) Å; Sn(1)−O(3), 2.155(2) Å; Sn(1)−O(3A), 2.053(2) Å; Sn(2)−O(1A), 2.295(2) Å; Sn(2)−O(3), 2.021(1) Å; Sn(2)−O(4), 2.202(2) Å; Sn(1)···O(4), 2.72(9) Å; Sn(2)···O(5), 2.78(4) Å; C(1)−O(1), 1.253(4) Å; C(1)−O(2), 1.266(4) Å; C(16)−O(4), 1.288(4) Å; C(16)−O(5), 1.233(4) Å. O(1)−C(1)−O(2), 125.3(3)°; O(4)−C(16)−O(5), 122.4(3)°; O(3)−Sn(1)−O(3A), 76.76(8)°; O(2)−Sn(1)−O(3), 165.87(8)°; Sn(1)−O(3)−Sn(1A), 103.24(8)°; Sn(2)−O(3)−Sn(1A), 138.1(1)°; O(4)−Sn(2)−O(1A), 172.16(8)°; O(3A)−Sn(1)−C(10), 107.0(1)°; C(8)−Sn(1)−C(10), 143.9(1)°; O(3)−Sn(2)−C(12), 112.3(1)°; C(12)−Sn(2)−C(14), 135.8(1)°. Symmetric operations: $A = 1 - x, 1 - y, - z$.

1328. Anal. Calcd for $C_{16}H_{30}N_2O_2SSn$: C, 44.36; H, 6.98; N, 6.47%. Found: C, 44.74; H, 7.12; N, 6.39%.

**Synthesis of $TDLCO_2SnEt_3$ (15).** This complex was obtained similarly using $(Et_3Sn)_2O$ instead of $(Ph_3Sn)_2O$ as described above for **13**. The crude product was recrystallized from hexane to afford yellow crystals of **15**: yield, 0.56 g (80%); mp, 65−67 °C; $^1$H NMR, $\delta$ 1.20−1.44 (m, 15H, $CH_2CH_3$), 2.93 (s, 3H, $C_2N_2SCH_3$); $^{13}$C NMR, $\delta$ 8.6, 9.8, 13.7 (ethyl carbons and $C_2N_2SCH_3$), 143.1, 161.0 ($C_2N_2S$), 163.9 (*C*OO); $^{119}$Sn NMR, $\delta$ 139.0; IR (cm$^{-1}$), $\nu_{as}$ (COO) 1656, $\nu_s$ (COO) 1378. Anal. Calcd for $C_{10}H_{18}N_2O_2SSn$: C, 34.41; H, 5.20; N, 8.03%. Found: C, 34.56; H, 5.44; N, 7.99%.

**Synthesis of $TDLCO_2SnCy_3$ (16).** This complex was obtained similarly using tricyclohexyltin hydroxide instead of $Et_2SnO$ as described above for **13**. The crude product was recrystallized from hexane to afford white crystals of **16**: yield, 0.47 g (92%); mp, 103−104 °C; $^1$H NMR, $\delta$ 1.26−1.36 (m, 9H, $C_6H_{11}$), 1.61−1.69 (m, 15H, $C_6H_{11}$), 1.87−2.00 (m, 9H, $C_6H_{11}$), 2.86 (s, 3H, $CH_3$); $^{13}$C NMR, $\delta$ 13.8, 26.8, 28.8, 31.1, 34.5 (cyclohexyl carbons and $CH_3$), 143.5, 160.7 ($C_2N_2S$), 163.6 (*C*OO); $^{119}$Sn NMR, $\delta$ 45.7; IR (cm$^{-1}$), $\nu_{as}$ (COO) 1647, $\nu_s$ (COO) 1362. Anal. Calcd for $C_{22}H_{36}N_2O_2SSn$: C, 51.68; H, 7.10; N, 5.48%. Found: C, 51.51; H, 7.59; N, 5.76%.

**Crystal Structure Determination.** Crystals of complex **3** suitable for X-ray analyses were obtained by slow diffusion of hexane into its benzene solution at room temperature. All intensity data were collected with a Rigaku Saturn CCD detector using graphite monochromated Mo Kα radiation ($\lambda$ = 0.71073 Å) at 113(2) K. The structure was resolved by the direct method and refined by full-matrix least-squares on $F^2$. All non-hydrogen atoms were refined anisotropically.

Crystal data for $3 \cdot 2C_6H_6$: $C_{56}H_{64}N_8O_{10}S_4Sn_4$, $M_r$ = 1612.27, triclinic, space group, $P\bar{1}$, $a$ = 11.008(2) Å, $b$ = 12.502(3) Å, $c$ = 13.118(3) Å, $\alpha$ = 74.75(3)°, $\beta$ = 71.81(3)°, $\gamma$ = 65.93(3)°, $V$ = 1546.7(5) Å$^3$, $Z$ = 1, $D_{calcd}$ = 1.731 g cm$^{-3}$; 5403 unique reflections were used for refinement ($R_{int}$ = 0.0267), final $R$ indices [$I > 2\sigma(I)$] were $R_1$ = 0.0252 and $wR_2$ = 0.0654.

**Table 1.** Fungicidal Activities of Complexes and Free Acid Ligands (Growth Inhibition Percentage)

| complex | *Alternaria solani* | *Cercospora arachidicola* | *Physalospora piricola* | *Gibberella zeae* | *Botrytis cinerea* |
|---|---|---|---|---|---|
| **1** | 9.77 | 10.26 | 34.84 | 45.24 | 21.62 |
| **2** | 19.80 | 23.08 | 27.29 | 58.33 | 29.73 |
| **3** | 14.79 | 20.51 | 24.46 | 41.67 | 26.13 |
| **4** | 32.33 | 20.51 | 36.73 | 50.00 | 43.24 |
| **5** | 92.48 | 71.79 | 97.17 | 54.76 | 91.89 |
| **6** | 92.48 | 97.44 | 97.17 | 92.86 | 98.20 |
| **7** | 100 | 100 | 100 | 100 | 100 |
| **8** | 50.00 | 76.67 | 92.45 | 50.00 | 94.12 |
| **9** | 54.89 | 23.08 | 54.67 | 55.95 | 41.44 |
| **10** | 32.33 | 15.38 | 55.62 | 57.14 | 35.14 |
| **11** | 27.32 | 30.77 | 48.06 | 33.33 | 31.53 |
| **12** | 32.33 | 23.08 | 47.12 | 36.90 | 50.45 |
| **13** | 92.48 | 66.67 | 95.28 | 59.52 | 76.58 |
| **14** | 100 | 100 | 100 | 98.81 | 100 |
| **15** | 100 | 100 | 100 | 100 | 100 |
| **16** | 72.50 | 86.67 | 92.45 | 80.49 | 91.18 |
| $BTHCO_2H$[a] | 42.36 | 30.77 | 40.51 | 60.71 | 72.07 |
| $TDLCO_2H$[b] | 77.44 | 74.36 | 84.89 | 88.10 | 96.40 |
| positive control[c] | 89.19 | 100 | 100 | 100 | 100 |

[a] $BTHCO_2H$, benzo[1,2,3]thiadiazole-7-carboxylic acid. [b] $TDLCO_2H$, 4-methyl-1,2,3-thiadiazole-5-carboxylic acid. [c] Positive control, propiconazole.

## RESULTS AND DISCUSSION

**Synthesis and Characterization of Compounds.** Reaction of 4-methyl-1,2,3-thiadiazole-5-carboxylic acid or benzo[1,2,3]thiadiazole-7-carboxylic acid with $R_2SnO$ (R = Et or $^n$Bu) in a 1:1 molar ratio in anhydrous benzene yields dimeric complexes $\{[(BTHCO_2)SnR_2]_2O\}_2$ (R = $^n$Bu (**1**) and Et (**3**); BTH = benzo-[1,2,3]thiadiazol-7-yl) and $\{[(TDLCO_2)Sn(n\text{-}Bu)_2]_2O\}_2$ (R = $^n$Bu (**9**) and Et (**11**); TDL = 4-methyl-1,2,3-thiadiazole-5-yl). Upon treatment of these two acids with $R_2SnO$ in a 2:1 molar ratio, complexes $(BTHCO_2)_2SnR_2$ (R = $^n$Bu (**2**) and Et (**4**)) and $(TDLCO_2)_2SnR_2$ (R = $^n$Bu (**10**) and Et (**12**)) were obtained. In addition, triorganotin derivatives $(BTHCO_2)SnR_3$ (R = Ph (**5**), $^n$Bu (**6**), Et (**7**) and cyclohexyl (**8**)) and $(TDLCO_2)SnR_3$ (R = Ph (**13**), $^n$Bu (**14**), Et (**15**), and cyclohexyl (**16**)) were synthesized by the reaction of the corresponding acid with $(R_3Sn)_2O$ or tricyclohexyltin hydroxide. All complexes have been characterized by IR, NMR, and elemental analyses. The NMR spectra of these complexes support the suggested structures. For instance, the $^1$H and $^{13}$C NMR spectra of dimeric complexes **1** and **3** as well as **9** and **11** exhibit two sets of butyl signals for **1** and **9** as well as ethyl signals for **3** and **11**, respectively. Furthermore, their $^{119}$Sn spectra also display the presence of *endo*- and *exo*-cyclic tin atoms. A pair of resonances of equal intensities is observed between −200 and −219 ppm in these four complexes, which are comparable with the reported values for other dimeric distannoxanes (*1*).

The structure of complex **3** has been confirmed further by X-ray crystallography. The molecular structure of **3**, as presented in **Figure 1**, shows a tetranuclear distannoxane structure, in which the nitrogen and sulfur atoms do not coordinate to the tin atom. The crystallographically unique carboxylic ligands display different coordination modes. One acts as a bridging bidentate ligand by two oxygen atoms of the carboxyl group, whereas the other is only a monodentate ligand by the carboxylate oxygen. Each tin atom adopts a five-coordinate distorted trigonal bipyramidal geometry with two oxygen atoms (O(2) and O(3) for Sn(1) as well as O(4) and O(1A) for Sn(2)) occupying the apical positions. In addition, the axial O−Sn−O angles (O(2)−Sn(1)−O(3) 165.87(8)° and O(4)−Sn(2)−O(1A) 172.16(8)°) significantly

**Table 2.** $EC_{50}$ Determination of Complexes **5**−**7**[a]

| | regression eq ($y$) | | | $R^2$ | | | $EC_{50}$ ($\mu$g/mL) | | |
|---|---|---|---|---|---|---|---|---|---|
| fungus tested | **5** | **6** | **7** | **5** | **6** | **7** | **5** | **6** | **7** |
| AS | $y = 0.9579x + 4.7025$ | $y = 1.3002x + 4.5155$ | $y = 1.8645x + 4.4336$ | 0.9844 | 0.9794 | 0.9424 | 2.04 | 2.36 | 2.01 |
| CA | nd | $y = 1.8400x + 4.0601$ | $y = 2.1551x + 5.0425$ | nd | 0.9765 | 0.9337 | nd | 3.24 | 0.96 |
| GZ | nd | $y = 1.0357x + 5.0426$ | $y = 1.5108x + 6.2180$ | nd | 0.9804 | 0.9709 | nd | 0.91 | 0.16 |
| PP | $y = 1.1254x + 4.7721$ | $y = 1.2652x + 4.9708$ | $y = 1.2635x + 6.1817$ | 0.9821 | 0.9236 | 0.9659 | 1.59 | 1.05 | 0.12 |
| BC | $y = 0.8297x + 4.8854$ | $y = 2.5663x + 4.2149$ | $y = 2.4061x + 4.0689$ | 0.9435 | 0.9717 | 0.9629 | 1.37 | 2.02 | 2.44 |

[a] Abbreviations: AS, *Alternaria solani*; CA, *Cercospora arachidicola*; GA, *Gibberella zeae*; PP, *Physalospora piricola*; BC, *Botrytis cinerea*; nd, not detected (it is no meaning to test because of the lower fungus growth inhibition activity).

**Table 3.** $EC_{50}$ Determination of Complexes **13**−**15**[a]

| | regression eq ($y$) | | | $R^2$ | | | $EC_{50}$ ($\mu$g/mL) | | |
|---|---|---|---|---|---|---|---|---|---|
| fungus tested | **13** | **14** | **15** | **13** | **14** | **15** | **13** | **14** | **15** |
| AS | $y = 0.8493x + 4.7278$ | $y = 1.4413x + 4.5565$ | $y = 2.0080x + 4.5872$ | 0.9988 | 0.9743 | 0.9593 | 2.09 | 2.03 | 1.61 |
| CA | nd | $y = 2.5168x + 4.0293$ | $y = 1.9638x + 4.8461$ | nd | 0.9676 | 0.9650 | nd | 2.43 | 1.20 |
| GZ | nd | $y = 0.8245x + 5.2558$ | $y = 1.5336x + 5.4733$ | nd | 0.9473 | 0.9745 | nd | 0.49 | 0.49 |
| PP | $y = 0.7187x + 4.6537$ | $y = 1.4145x + 4.8104$ | $y = 1.8526x + 5.9681$ | 0.9419 | 0.9730 | 0.9695 | 3.03 | 1.36 | 0.30 |
| BC | nd | $y = 3.0661x + 3.6554$ | $y = 2.2467x + 4.6800$ | nd | 0.9577 | 0.8639 | nd | 2.74 | 1.39 |

[a] Abbreviations: AS, *Alternaria solani*; CA, *Cercospora arachidicola*; GZ, *Gibberella zeae*; PP, *Physalospora piricola*; BC, *Botrytis cinerea*; nd, not detected (it is no meaning to test because of the lower fungus growth inhibition activity).

deviate from 180°. The nonbond Sn···O distances (Sn(1)···O(4) 2.72(9) and Sn(2)···O(5) 2.78(4) Å) are longer than the relevant covalent Sn−O bond distances (Sn(1)−O(2) 2.272(2) and Sn(2)−O(4) 2.202(2) Å), but significantly shorter than the sum of the van der Waals radii for the Sn and O atoms of 3.57 Å (*13*), indicating the presence of some weak interactions between the Sn(1) and O(4) as well as Sn(2) and O(5) atoms despite not much influence on the geometry of the tin atom.

**Fungicidal Activity.** The preliminary evaluation of fungicidal activities of all complexes was carried out according to the following procedures. The stock solution of complexes was prepared at 500 $\mu$g/mL using DMF as the solvent. The working solution (50 $\mu$g/mL) was obtained by diluting the stock solution (0.1 mL) with sterilized water (0.9 mL) in a 10 cm diameter Petri dish. The plate was prepared by adding potato dextrose agar (PDA, 9 mL) to the Petri dish. Before the solidification of PDA, it was thoroughly mixed by shaking or turning around the Petri dish in the sterilized operation desk. Fungus was inoculated and cultured in the culture tank at 24−26 °C. The diameter of fungus spread was measured 2 days later. Growth inhibition was then calculated using the corresponding control. Fungi used in this study included *Alternaria solani*, *Cercospora arachidicola*, *Gibberella zeae*, *Physalospora piricola*, and *Botrytis cinerea*. Precision toxicity measurements were carried out according to the above-mentioned methods by the determination of growth inhibition of specific fungi using the same complex in five to seven different concentrations. The $EC_{50}$ was calculated by the linear regression of logarithm of the concentration with probability of the corresponding growth inhibition by Excel (*16*). The tested results are summarized in **Tables 1**, **2**, and **3**, respectively.

The data in **Table 1** show that all compounds display certain activity against the tested fungi in a low concentration. Moreover, triorganotin carboxylates show much higher activity than the dimeric tetranuclear complexes and diorganotin derivatives, as reported previously (*14*, *15*). In addition, these triorganotin carboxylates are observed to be more active against the tested fungi than the corresponding free acid ligand. Complexes **7**, **14**, and **15** display 100% inhibition of all five species of fungi at 50 g/mL, and they are also found to be more active against *A. solani* than the positive control (propiconazole). The precision toxicity of these highly active triorganotin carboxylates was further tested, and the values of $EC_{50}$ are listed in **Tables 2** and **3**, which show that all six of these complexes are highly toxic to the five tested fungi. Among these six complexes, the value of $EC_{50}$ of triethyltin benzo[1,2,3]thiadiazole-7-carboxylate is only 0.12 $\mu$g/mL against *P. piricola* and 0.16 $\mu$g/mL against *G. zeae*, respectively. These results indicate that organotin compounds containing benzo[1,2,3]thiadiazole or 1,2,3-thiadiazole are wide-spectrum fungicide leads.

## ABBREVIATIONS USED

AS, *Alternaria solani*; BC, *Botrytis cinerea*; BTH, benzo[1,2,3]-thiadiazole-7-carbothionic acid *S*-methyl ester; $BTHCO_2H$, benzo[1,2,3]thiadiazole-7-carboxylic acid; CA, *Cercospora arachidicola*; $CDCl_3$, deuteriated chloroform; $^{13}C$ NMR, $^{13}C$ nuclear magnetic resonance; DMF, *N*,*N*-dimethylformamide; $EC_{50}$, median effective concentration; GZ, *Gibberella zeae*; $^1H$ NMR, $^1H$ nuclear magnetic resonance; IR, infrared spectroscopy; nd, not detected; PDA, potato dextrose agar; PP, *Physalospora piricola*; $^{119}Sn$ NMR, $^{119}Sn$ nuclear magnetic resonance; TDL, tiadinil; $TDLCO_2H$, 4-methyl-1,2,3-thiadiazole-5- carboxylic acid.

**Supporting Information Available:** Crystal data of complex **3**: crystal.cif. This information is available free of charge via the Internet at http://pubs.acs.org.

## LITERATURE CITED

(1) Chandrasekhar, V.; Nagendran, S.; Baskar, V. Organotin assemblies containing Sn−O bonds. *Coord. Chem. Rev.* **2002**, *235*, 1–52.
(2) Holmes, R. R. Organotin cluster chemistry. *Acc. Chem. Res.* **1989**, *22*, 190–197.
(3) Tiekink, E. R. T. Structural chemistry of organotin carboxylates: a review of the crystallographic literature. *Appl. Organomet. Chem.* **1991**, *5*, 1–23.
(4) Gielen, M. Organotin compounds and their therapeutic potential: a report from the Organometallic Chemistry Department of the Free University Brussels. *Appl. Organomet. Chem.* **2002**, *16*, 481–494.
(5) Baul, T. S. B. Antimicrobial activity of organotin(IV) compounds: a review. *Appl. Organomet. Chem.* **2008**, *22*, 195–204.
(6) Hadjikakou, S. K.; Hadjiliadis, N. Antiproliferative and anti-tumor activity of organotin compounds. *Coord. Chem. Rev.* **2009**, *253*, 235–249.
(7) Kovala-Demertzi, D. Recent advances on non-steroidal anti-inflammatory drugs, NSAIDs: organotin complexes of NSAIDs. *J. Organomet. Chem.* **2006**, *691*, 1767–1774.

(8) Pellerito, L.; Nagy, L. Organotin(IV)$^{n+}$ complexes formed with biologically active ligands: equilibrium and structural studies, and some biological aspects. *Coord. Chem. Rev.* **2002**, *224*, 111–150.
(9) Kunz, W.; Schurter, R.; Maetzke, T. The chemistry of benzothiadiazole plant activators. *Pestic. Sci.* **1997**, *50*, 275–282.
(10) Yasuda, M.; Kusajima, M.; Nakajima, M.; Akutsu, K.; Kudo, T.; Yoshida, S.; Nakashita, H. Thiadiazole carboxylic acid moiety of tiadinil, SV-03, induces systemic acquired resistance in tobacco without salicylic acid accumulation. *J. Pestic. Sci.* **2006**, *31*, 329–334.
(11) Fan, Z. J.; Shi, Z. G.; Zhang, H. K.; Liu, X. F.; Bao, L. L.; Ma, L.; Zuo, X.; Zheng, Q. X.; Mi, N. Synthesis and biological activity evaluation of 1,2,3-thiadiazole derivatives as potential elicitors with highly systemic acquired resistance. *J. Agric. Food Chem.* **2009**, *57*, 4279–4286.
(12) Bakulev, V. A.; Dehaem W. *The Chemistry of 1,2,3-Thiadiazole*; Wiley: New York, 2004.
(13) Szorcsik, A.; Nagy, L.; Deák, A.; Scopelliti, M.; Fekete, Z. A.; Császár, A.; Pellerito, C.; Pellerito, L. Preparation and structural studies on the $^{t}Bu_2Sn$(IV) complexes with aromatic mono- and dicarboxylic acids containing hetero {N} donor atom. *J. Organomet. Chem.* **2004**, *689*, 2762–2769.
(14) Danish, M.; Alt, H. G.; Badshah, A.; Ali, S.; Mazhar, M. Organotin esters of 3-(2-furanyl)-2-propenoic acid: their characterization and biological activity. *J. Organomet. Chem.* **1995**, *486*, 51–56.
(15) Rauf, M. K.; Saeed, M. A.; Imtiaz-ud-Din, B. M.; Badshah, A.; Mirza, B. Synthesis, characterization and biological activities of some new organotin(IV)derivatives: crystal structure of $[(SnPh_3)(OOCC_6H_4OH)]$ and $[(SnMe_3)_2(OOC)_2C_6Cl_4(DMSO)_2]$. *J. Organomet. Chem.* **2008**, *693*, 3043–3048.
(16) Fan, Z. J.; Yang, Z. K.; Zhang, H. K.; Mi, N.; Wang, H.; Cai, F.; Zuo, X.; Zheng, Q. X.; Song, H. B. Synthesis, crystal structure, and biological activity of 4-methyl-1,2,3-thiadiazole containing 1,2,4-triazolo-[3,4-*b*][1,3,4]-thiadiazoles. *J. Agric. Food Chem.* **2010**, doi: 10.1021/jf9029628.

**Received for review June 24, 2009. Revised manuscript received August 15, 2009. Accepted November 19, 2009. This work was funded partly by grants from the Specialized Research Fund for the Doctoral Program of Higher Education of China (20070055043), the Foundation of the Ministry of Education of China for Returned Scholars, the National Key Project for Basic Research (No. 2003CB114402 and 2010CB126105), the National Natural Science Foundation of China (No. 20872071 and 20672062), the Tianjin Natural Science Foundation (No. 07JCYBJC01200), and the International Collaboration Program of the National Natural Science Foundation of China (No. 20911120069).**