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1-芳基-3,5-二甲基吡唑-4-羧酸有机锡酯的合成、结构及杀菌活性研究

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摘要: 由 1-芳基-3,5-二甲基吡唑-4-羧酸与适当的有机锡反应, 合成表征了一系列的 1-芳基-3,5-二甲基吡唑-4-羧酸有机锡酯(**1~14**),并通过单晶衍射确定了 1-苯基-3,5-二甲基吡唑-4-羧酸三乙基锡酯(**7**)的结构。该化合物与一分子水共同结晶,通过分子间 O–H···O 及 O–H···N 氢键形成二维网状结构。杀菌活性筛选表明新合成的化合物对于番茄早疫菌、花生褐斑菌、小麦赤霉菌、苹果轮纹菌及灰霉菌全部具有良好的生长抑制作用。1-苯基-3,5-二甲基吡唑-4-羧酸三乙基锡酯及 1-(2-吡啶基)-3,5-二甲基吡唑-4-羧酸三乙基锡酯在 50 μg·mL^{-1} 浓度下的体外实验中表现出很高的生长抑制率。对于高活性的三取代锡羧酸酯进行了 EC_{50} 值的测定,结果表明 1-(2-吡啶基)-3,5-二甲基吡唑-4-羧酸三乙基锡酯对苹果轮纹菌的 EC_{50} 值为 0.06 μg·mL^{-1},对小麦赤霉菌的 EC_{50} 值为 0.14 μg·mL^{-1}。

关键词: 有机锡羧酸酯; 1-芳基-3,5-二甲基吡唑-4-羧酸; 晶体结构; 杀菌活性
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Synthesis, Structure and Fungicidal Activity of Organotin 1-Aryl-3,5-dimethylpyrazole-4-carboxylates

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Abstract: A series of organotin 1-phenyl-3,5-dimethylpyrazole-4-carboxylates and 1-(2-pyridyl)-3,5-dimethylpyrazole-4-carboxylates (**1~14**) have been obtained and characterized by IR, NMR (^{1}H, ^{13}C and ^{119}Sn) and elemental analysis. The structure of triethyltin 1-phenyl-3,5-dimethylpyrazole-4-carboxylate **7** has been further confirmed by X-ray diffraction crystallography. This complex crystallizes with a molecule of water and forms an infinite 2D network through intermolecular O–H···O and O–H···N hydrogen bonds. Fungicide screening indicates that all complexes display good growth inhibition against Alternaria solani, Cercospora arachidicola, Gibberella zeae, Physalospora piricola and Botrytis cinerea. Moreover, high growth inhibition percentage at 50 μg·mL^{-1} was observed in vitro in case of triorganotin 1-phenyl-3,5-dimethylpyrazole-4-carboxylates and 1-(2-pyridyl)-3,5-dimethylpyrazole-4-carboxylates. The corresponding EC_{50} of these highly active triorganotin carboxylates have been detected. The value of EC_{50} of triethyltin 1-(2-pyridyl)-3,5-dimethylpyrazole-4-carboxylate is only 0.06 μg·mL^{-1} against Physalospora piricola and 0.14 μg·mL^{-1} against Gibberella zeae, respectively. CCDC: 823104, **7**.

Key words: organotin carboxylate; 1-aryl-3,5-dimethylpyrazole-4-carboxylic acid; crystal structure; fungicidal activity

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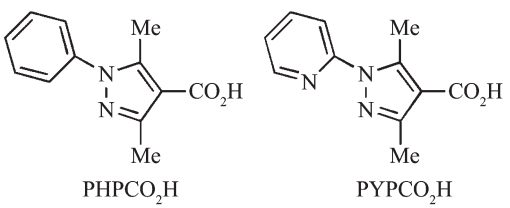
0 Introduction

Organotin derivatives have been extensively used in the industrial and agricultural fields because of their significant biological activities, despite the fact that their toxicity and environmental effects partially limit their applications. Among these organotin derivatives, organotin carboxylates have been extensively investigated for a long time due to their remarkable structural diversity[1-2] as well as biological importance, for example as pesticidal, antibacterial, antitumor agents and wood preservatives[3-6]. In recent years, there is an increasing interest in the introduction of sulfur- or nitrogen-functionalized carboxylic acids to acquire organotin carboxylates with various and fascinating structures and different bioactivities[7-14]. Moreover, to obtain pharmacological profile better than or different from the free ligands, the synthesis of organotin derivatives by using the biologically active ligands has drawn progressive attention recently[15-16]. Pyrazole and their derivatives possess versatile biological activities, such as acaricidal, pesticidal and antibacterial activities[17-21]. Many commercially available agrochemicals with pyrazolyl groups have demonstrated their important role all over the world, such as fungicide pyraclostrobin. On the other hand, pyrazole and their derivatives have been extensively adopted as ligands to transition metals due to their variable coordination modes[22]. Taking into consideration of the important biological applications of organotin carboxylates as well as pyrazole and their derivatives, exploiting the biological activity of organotin carboxylates containing pyrazole should be encouraging. Herein we report the synthesis of a series of organotin carboxylates of 1-aryl-3,5-dimethylpyrazole-4-carboxylic acids (Scheme 1) and their preliminary biological investigations.



Scheme 1　Structures of 1-aryl-3,5-dimethylpyrazole-4-carboxylic acids

1 Experimental

1.1 Materials and measurements

IR spectra were obtained from a Nicolet 380 spectrometer as KBr discs. Multinuclear NMR spectra were recorded with a Bruker 400 spectrometer using $CDCl_3$ as solvent unless otherwise noted, and the chemical shifts were reported in ppm with respect to reference standards (internal $SiMe_4$ for ^1H NMR and ^{13}C NMR spectra, external $SnMe_4$ for ^{119}Sn NMR). 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 were uncorrected. 1-Phenyl-3,5-dimethylpyrazole-4-carboxylic acid ($PHPCO_2H$)[23] and $(CH_3CO)_2CHCO_2Et$[24] were prepared by the known methods.

1.2 Synthesis of 1-(2-Pyridyl)-3,5-dimethylpyrazole-4-carboxylic acid ($PYPCO_2H$)

The solution of $(CH_3CO)_2CHCO_2Et$ (9.59 g, 60 mmol) and 2-pyridylhydrazine (6.56 g, 60 mmol) in methanol (13 mL) was stirred overnight at room temperature. After filtration, methanol was removed in vacuo to yield viscous oil. A solution of KOH (18.0 g) in 60 mL of H_2O was added to the oil, and the mixture was stirred at reflux for 10 h. After cooling to room temperature, the reaction mixture was acidified to a pH value of 4 with concentrated HCl to yield yellow solids, which were filtered off, washed with water, and dried in air to give 1-(2-pyridyl)-3,5-dimethylpyrazole-4-carboxylic acid. Yield: 1.31 g (10%); m.p. 232~234 ℃. ^1H NMR (DMSO-d_6): δ 2.38, 2.78 (s, s, 3H, 3H, CH_3), 7.42, 7.77, 8.00, 8.52 (t, J=5.8 Hz, d, J=8.1 Hz, t, J=7.7 Hz, d, J=4.0 Hz, 1H, 1H, 1H, 1H, pyridyl protons) ppm. ^{13}C NMR (DMSO-d_6): δ 13.1, 14.2 (CH_3), 112.1 (C^4 of pyrazole), 117.6, 122.7, 139.2, 145.1, 147.8, 150.9, 152.1 (pyridyl carbons as well as C^3 and C^5 of pyrazole), 165.1 (C=O) ppm. IR (cm^{-1}): ν(C=O) 1 678.

1.3 Synthesis of $\{[(PHPCO_2)Sn(n\text{-}Bu)_2]_2O\}_2$ (1)

The mixture of $PHPCO_2H$ (0.22 g, 1 mmol) and $(n\text{-}Bu)_2SnO$ (0.25 g, 1 mmol) in anhydrous benzene (50 mL) was stirred and heated at reflux for 8 h. After

removing benzene in vacuo, the crude product was recrystallized from hexanes to yield yellow solids of **1**. Yield: 0.33 g (72%); m.p. 126~129 ℃. ^{1}H NMR: δ 0.72~0.92 (m, 6H, CH_2CH_3), 1.11~1.78 (m, 12H, $CH_2CH_2CH_2$), 2.44, 2.46 (s, s, 3H, 3H, 3- and 5-CH_3 of pyrazole), 7.33~7.40 (m, 5H, C_6H_5) ppm. ^{13}C NMR: δ 12.7, 14.5, 26.8, 27.0, 27.7, 27.8, 31.6, 32.6 (*n*-butyl carbons, signals are broadened by J (^{13}C-$^{119/117}$Sn)) 13.6, 13.7 (3- and 5-CH_3 of pyrazole), 113.7 (C^4 of pyrazole), 125.6, 128.2, 129.2, 139.1 (C_6H_5) 143.9, 151.7 (C^3 and C^5 of pyrazole), 171.8 (C=O) ppm. ^{119}Sn NMR: δ −221.9, −280.1 ppm. IR (cm^{-1}): ν_{as} (COO) 1 599, ν_s(COO) 1 381. Anal. Calcd. for $C_{80}H_{116}N_8O_{10}Sn_4$(%): C, 52.66; H, 6.41; N, 6.14. Found(%): C, 52.66; H, 6.75; N, 6.05.

1.4 Synthesis of $(PHPCO_2)_2Sn(n\text{-}Bu)_2$ (2)

This complex was obtained similarly by the reaction of $PHPCO_2H$ (0.43 g, 2 mmol) and $(n\text{-}Bu)_2SnO$ (0.25 g, 1 mmol) as described above for **1**. After removing the solvent, viscous oil was obtained, which was washed with benzene/hexanes (1:1, *V*/*V*) to give slightly yellow oil of **2**. Yield: 0.40 g (60%). ^{1}H NMR: δ 0.84 (t, J=7.3 Hz, 3H, CH_2CH_3), 1.30~1.40, 1.60~1.80 (m, m, 2H, 4H, $CH_2CH_2CH_2$), 2.47, 2.50 (s, s, 3H, 3H, 3- and 5-CH_3 of pyrazole), 7.35~7.42 (m, 5H, C_6H_5) ppm. ^{13}C NMR: δ 13.0, 23.9, 25.2, 25.7 (*n*-butyl carbons, signals are broadened by J(^{13}C-$^{119/117}$Sn)), 11.5, 12.6 (3- and 5-CH_3 of pyrazole), 109.8 (C^4 of pyrazole), 124.5, 127.3, 128.2, 137.9 (C_6H_5), 144.0, 151.3 (C^3 and C^5 of pyrazole), 172.5 (C=O) ppm. ^{119}Sn NMR: δ −139.7 ppm. IR (cm^{-1}): ν_{as}(COO) 1 585, ν_s(COO) 1 383. Anal. Calcd. for $C_{32}H_{40}N_4O_4Sn$(%): C, 57.94; H, 6.08; N, 8.45. Found(%): C, 57.55; H, 6.37; N, 8.83.

1.5 Synthesis of $\{[(PHPCO_2)SnEt_2]_2O\}_2$ (3)

This complex was obtained similarly using Et_2SnO instead of $(n\text{-}Bu)_2SnO$ as described above for **1**. After removing the solvent, the crude product was recrystallized from CH_2Cl_2/hexanes to give white crystals of **3**. Yield: 70%; m.p. 226~228 ℃. ^{1}H NMR: δ 1.37, 1.41 (t, J=7.5 Hz, t, J=7.6 Hz, 3H, 3H, CH_2CH_3), 1.54, 1.64 (q, J=7.5 Hz, q, J=7.6 Hz, 2H, 2H, CH_2CH_3), 2.54, 2.56 (s, s, 3H, 3H, 3- and 5-CH_3 of pyrazole), 7.41~7.48 (m, 5H, C_6H_5) ppm. ^{13}C NMR: δ 12.8, 14.6 (CH_2CH_3), 19.2, 25.3 (CH_2CH_3, signals are broadened by ^1J(^{13}C-$^{119/117}$Sn)), 10.1, 10.2 (3- and 5-CH_3 of pyrazole), 113.5 (C^4 of pyrazole), 125.6, 128.2, 129.1, 139.1 (C_6H_5), 144.1, 151.8 (C^3 and C^5 of pyrazole), 172.0 (C =O) ppm. ^{119}Sn NMR: δ −222.5, −273.3 ppm. IR (cm^{-1}): ν_{as}(COO) 1 593, ν_s(COO) 1 380. Anal. Calcd. for $C_{64}H_{84}N_8O_{10}Sn_4$ (%): C, 48.04; H, 5.29; N, 7.00. Found(%): C, 48.42; H, 5.07; N, 6.73.

1.6 Synthesis of $(PHPCO_2)_2SnEt_2$ (4)

This complex was obtained similarly by the reaction of $PHPCO_2H$ (0.43 g, 2 mmol) and Et_2SnO (0.19 g, 1 mmol) as described above for **1**. After removing the solvent, the crude product was recrystallized from CH_2Cl_2/hexanes to give slightly yellow solids of **4**. Yield: 0.47 g (77%); m.p. 123~126 ℃. ^{1}H NMR: δ 1.31 (t, J=7.9 Hz, 3H, CH_2CH_3), 1.70 (q, J=7.9 Hz, 2H, CH_2CH_3), 2.47, 2.49 (s, s, 3H, 3H, 3- and 5-CH_3 of pyrazole), 7.34~7.41 (m, 5H, C_6H_5) ppm. ^{13}C NMR: δ 8.0 (CH_2CH_3, ^2J (^{13}C-$^{119/117}$Sn)=21 Hz), 11.6 (CH_2CH_3, signal is broadened by ^1J(^{13}C-$^{119/117}$Sn)), 13.0, 11.6, 13.0, 16.4 (3- and 5-CH_3 of pyrazole), 109.6 (C^4 of pyrazole), 124.6, 127.4, 128.2, 137.8 (C_6H_5), 144.1, 151.3 (C^3 and C^5 of pyrazole), 171.9 (C=O) ppm. ^{119}Sn NMR: δ −144.5 ppm. IR (cm^{-1}): ν_{as}(COO) 1 674, ν_s(COO) 1 427. Anal. Calcd. for $C_{28}H_{32}N_4O_4Sn$(%): C, 55.38; H, 5.31; N, 9.23. Found(%): C, 54.96; H, 5.65; N, 8.86.

1.7 Synthesis of $(PHPCO_2)SnPh_3$ (5)

This complex was obtained similarly by the reaction of $PHPCO_2H$ (0.22 g, 1 mmol) and $(Ph_3Sn)_2O$ (0.36 g, 0.5 mmol) as described above for **1**. After removing the solvent, the crude product was recrystallized from hexanes to give white crystals of **5**. Yield: 0.55 g (97%); m.p. 110~112 ℃. ^{1}H NMR: δ 2.57, 2.59 (s, s, 3H, 3H, CH_3), 7.37~7.80 (m, 5H, NC_6H_5), 7.44~7.47 (m, 15H, SnC_6H_5) ppm. ^{13}C NMR: δ 12.8, 14.4 (CH_3), 110.7 (C^4 of pyrazole), 125.6, 128.4, 128.9 (^3J(^{13}C-$^{119/117}$Sn) =63 Hz), 129.2, 130.0, 136.9 (^{23}J(^{13}C-$^{119/117}$Sn)= 48 Hz), 139.0, 139.1 (C_6H_5), 145.2, 152.4 (C^3 and C^5 of pyrazole), 170.9 (C=O) ppm. ^{119}Sn NMR: δ −120.7 ppm. IR (cm^{-1}): ν_{as}(COO) 15 87, ν_s(COO) 1 339. Anal. Calcd. for $C_{30}H_{26}N_2O_2Sn$(%): C, 63.75; H, 4.64; N, 4.96. Found (%): C, 64.16; H, 4.12; N, 5.04.

1.8 Synthesis of $(PHPCO_2)Sn(n\text{-}Bu)_3$ (6)

This complex was obtained similarly by the reaction

of $PHPCO_2H$ (0.22 g, 1 mmol) and $(n\text{-}Bu_3Sn)_2O$ (0.30 g, 0.5 mmol) as described above for **1**. After removing the solvent, the residual was extracted by hot hexanes. After removing hexanes, yellow oil was obtained. Yield: 0.49 g (87%). ^1H NMR: δ 0.84 (t, J=7.3 Hz, 9H, CH_2CH_3), 1.23~1.33, 1.55~1.63 (m, m, 12H, 6H, $CH_2CH_2CH_2$), 2.42, 2.44 (s, s, 3H, 3H, 3- and 5-CH_3 of pyrazole), 7.30~7.36 (m, 5H, C_6H_5) ppm. ^{13}C NMR: δ 11.6, 13.2 (3- and 5-CH_3 of pyrazole), 12.7, 15.5 ($^1J(^{13}C\text{-}^{119/117}Sn)$=361/345 Hz], 26.0 ($^3J(^{13}C\text{-}^{119/117}Sn)$=63 Hz), 26.9 ($^2J(^{13}C\text{-}^{119/117}Sn)$=21 Hz) ($n$-butyl carbons), 111.2 ($C^4$ of pyrazole), 124.5, 127.1, 128.1, 138.1 (C_6H_5), 143.1, 150.8 (C^3 and C^5 of pyrazole), 168.4 (C=O) ppm. ^{119}Sn NMR: δ 102.8 ppm. IR (cm^{-1}): ν_{as}(COO) 1 628, ν_s(COO) 1 341. Anal. Calcd. for $C_{24}H_{38}N_2O_2Sn$(%): C, 57.05; H, 7.58; N, 5.54. Found(%): C, 57.09; H, 7.60; N, 5.93.

1.9 Synthesis of $(PHPCO_2)SnEt_3$ (7)

This complex was obtained similarly by the reaction of $PHPCO_2H$ (0.22 g, 1 mmol) and $(Et_3Sn)_2O$ (0.21 g, 0.5 mmol) as described above for **1**. After removing the solvent, the crude product was recrystallized from hexanes to give slightly yellow solids of **7**. Yield: 0.39 g (93%); m.p. 59~61 ℃. ^1H NMR: δ 1.22~1.44 (m, 15H, CH_2CH_3), 2.51, 2.53 (s, s, 3H, 3H, 3- and 5-CH_3 of pyrazole), 7.39~7.49 (m, 5H, C_6H_5) ppm. ^{13}C NMR: δ 7.9 ($^1J(^{13}C\text{-}^{119/117}Sn)$=369/353 Hz), 10.0 ($^2J(^{13}C\text{-}^{119/117}Sn)$=26 Hz) (ethyl carbons), 12.6, 14.3 (3- and 5-CH_3 of pyrazole), 112.1 (C^4 of pyrazole), 125.6, 128.2, 129.1, 139.1 (C_6H_5), 144.2, 151.9 (C^3 and C^5 of pyrazole), 169.6 (C=O) ppm. ^{119}Sn NMR: δ 101.4 ppm. IR (cm^{-1}): ν_{as}(COO) 1674, ν_s(COO) 1 358. Anal. Calcd. for $C_{18}H_{26}N_2O_2Sn\cdot H_2O$(%): C, 49.23; H, 6.43; N, 6.38. Found(%): C, 49.73; H, 6.23; N, 6.23.

1.10 Synthesis of $(PHPCO_2)SnCy_3$ (8) (Cy=cyclohexyl)

This complex was obtained similarly by the reaction of $PHPCO_2H$ (0.22 g, 1 mmol) and tricyclohexyltin hydroxide (0.39 g, 1 mmol) as described above for **1**. After removing the solvent, the crude product was recrystallized from hexanes to give slightly yellow solids of **8**. Yield: 0.53 g (91%); m.p. 115~116 ℃. ^1H NMR: δ 1.33~1.38, 1.66~1.76, 1.93~2.05 (m, m, m, 9H, 15H, 9H, C_6H_{11}), 2.53, 2.55 (s, s, 3H, 3H, 3- and 5-CH_3 of pyrazole), 7.40~7.50 (m, 5H, C_6H_5) ppm. ^{13}C NMR: δ 12.7, 14.4 (3- and 5-CH_3 of pyrazole), 27.0, 29.0 ($^3J(^{13}C\text{-}^{119/117}Sn)$=64 Hz), 31.2 ($^2J(^{13}C\text{-}^{119/117}Sn)$=15 Hz), 33.6 ($^1J(^{13}C\text{-}^{119/117}Sn)$=344/328 Hz) (cyclohexyl carbons), 112.6 (C^4 of pyrazole), 125.6, 128.1, 129.1, 139.2 (C_6H_5), 144.0, 151.7 (C^3 and C^5 of pyrazole), 169.2 (C=O) ppm. ^{119}Sn NMR: δ 10.9 ppm. IR (cm^{-1}): ν_{as} (COO) 1 617, ν_s(COO) 1 348. Anal. Calcd. for $C_{30}H_{44}N_2O_2Sn$(%): C, 61.76; H, 7.60; N, 4.80. Found(%): C, 61.61; H, 7.12; N, 4.75.

1.11 Synthesis of $\{[(PYPCO_2)SnEt_2]_2O\}_2$ (9)

This complex was obtained similarly by the reaction of $PYPCO_2H$ (0.22 g, 1 mmol) and Et_2SnO (0.19 g, 1 mmol) as described above for **1**. After removing the solvent, the crude product was recrystallized from CH_2Cl_2/hexanes to give slightly yellow solids of **9**. Yield: 0.25 g (62%); m.p. 235~236 ℃. ^1H NMR: δ 1.36, 1.38 (t, J=7.2 Hz, t, J=7.4 Hz, 3H, 3H, CH_2CH_3), 1.54, 1.64 (q, J=7.2 Hz, q, J=7.4 Hz, 2H, 2H, CH_2CH_3), 2.56, 2.90 (s, s, 3H, 3H, 3- and 5-CH_3 of pyrazole), 7.26, 7.78, 7.84, 8.50 (t, J=6.4 Hz, d, J=8.1 Hz, td, J=7.7 Hz, 1.5 Hz, d, J=4.1 Hz, 1H, 1H, 1H, 1H, pyridyl protons) ppm. ^{13}C NMR: δ 10.0, 14.8, 19.2, 25.3 (ethyl carbons, signals are broadened by $J(^{13}C\text{-}^{119/117}Sn)$), 10.2, 13.6 (3- and 5-$CH_3$ of pyrazole), 114.8 (C^4 of pyrazole), 117.9, 122.0, 138.4, 147.8 152.5 (pyridyl carbons), 145.6, 152.9 (C^3 and C^5 of pyrazole), 171.9 (C=O) ppm. ^{119}Sn NMR: δ −221.1, −271.2 ppm. IR (cm^{-1}): ν_{as} (COO) 1 586, ν_s(COO) 1 357. Anal. Calcd. for $C_{60}H_{80}N_{12}O_{10}Sn_4\cdot 0.25CH_2Cl_2$(%): C, 44.13; H, 4.96; N, 10.21. Found(%): C, 44.37; H, 4.70; N, 10.22.

1.12 Synthesis of $(PYPCO_2)_2SnEt_2$ (10)

This complex was obtained similarly by the reaction of $PYPCO_2H$ (0.43 g, 2 mmol) and Et_2SnO (0.19 g, 1 mmol) as described above for **1**. After removing the solvent, the crude product was recrystallized from CH_2Cl_2/hexanes to give orange-yellow solids of **10**. Yield: 0.38 g (62%); m.p. 143~146 ℃. ^1H NMR: δ 1.30 (t, J=6.6 Hz, 3H, CH_2CH_3), 1.69 (q, J=6.6 Hz, 2H, CH_2CH_3), 2.48, 2.84 (s, s, 3H, 3H, 3- and 5-CH_3 of pyrazole), 7.18, 7.71, 7.76, 8.42 (t, J=6.3 Hz, d, J=8.0 Hz, td, J=7.7 Hz, 1.2 Hz, d, J=4.5 Hz, 1H, 1H, 1H, 1H,

pyridyl protons) ppm. ^{13}C NMR: δ 8.0 (CH_2CH_3, ^2J(^{13}C-$^{119/117}$Sn)=21 Hz), 16.4 (CH_2CH_3, signal is broadened by ^1J (^{13}C-$^{119/117}$Sn)), 12.5, 13.2 (3- and 5-CH_3 of pyrazole), 111.0 (C^4 of pyrazole), 116.8, 121.1, 137.4, 146.9 151.7 (pyridyl carbons), 145.7, 151.8 (C^3 and C^5 of pyrazole), 172.6 (C=O) ppm. ^{119}Sn NMR: δ −143.2 ppm. IR (cm^{-1}): ν_{as}(COO) 1 675, ν_s (COO) 1 377. Anal. Calcd. for $C_{26}H_{30}N_6O_4Sn\cdot0.25C_6H_{14}$(%): C, 52.36; H, 5.35; N, 13.32. Found(%): C, 51.90; H, 5.81; N, 13.04.

1.13 Synthesis of (PYPCO$_2$)SnPh$_3$ (11)

This complex was obtained similarly by the reaction of $PYPCO_2H$ (0.22 g, 1 mmol) and $(Ph_3Sn)_2O$ (0.36 g, 0.5 mmol) as described above for **1**. After removing the solvent, the crude product was recrystallized from hexanes to slightly yellow solids of **11**. Yield: 0.52 g (92%); m.p. 122~124 ℃. ^{1}H NMR: δ 2.57, 2.92 (s, s, 3H, 3H, CH_3), 7.21~7.23, 7.42~7.47, 7.74~7.82 (m, m, m, 1H, 9H, 8H, C_6H_5 and pyridyl protons), 8.47 (dd, J= 4.9 Hz, 0.9 Hz, 1H, pyridyl proton) ppm. ^{13}C NMR: δ 13.7, 14.6 (CH_3), 112.1 (C^4 of pyrazole), 117.8, 122.1, 128.9 (^3J (^{13}C-$^{119/117}$Sn)=63 Hz), 130.0, 136.9 (^2J(^{13}C-$^{119/117}$Sn)=48 Hz), 138.4, 139.1, 147.9, 152.9 (phenyl and pyridyl carbons), 146.8, 152.8 (C^3 and C^5 of pyrazole), 170.8 (C=O) ppm. ^{119}Sn NMR: δ −119.8 ppm. IR (cm^{-1}): ν_{as}(COO) 1 630, ν_s(COO) 1 380. Anal. Calcd. for $C_{29}H_{25}N_3O_2Sn$(%): C, 61.51; H, 4.45; N, 7.42. Found(%): C, 61.14; H, 4.93; N, 7.35.

1.14 Synthesis of (PYPCO$_2$)Sn(*n*-Bu)$_3$ (12)

This complex was obtained similarly by the reaction of $PYPCO_2H$ (0.22 g, 1 mmol) and $(n\text{-}Bu_3Sn)_2O$ (0.30 g, 0.5 mmol) as described above for **1**. After removing the solvent, the residual was extracted by hot hexanes. After removing hexanes, yellow oil was obtained. Yield: 0.43 g (76%). ^{1}H NMR: δ 0.83 (t, J=6.7 Hz, 9H, CH_2CH_3), 1.16~1.31, 1.48~1.68 (m, m, 12H, 6H, $CH_2CH_2CH_2$), 2.42, 2.78 (s, s, 3H, 3H, 3- and 5-CH_3 of pyrazole), 7.18, 7.76~7.70, 8.37 (t, J=6.2 Hz, m, d, J=4.2 Hz, 1H, 2H, 1H, pyridyl protons) ppm. ^{13}C NMR: δ 13.5, 14.4 (3- and 5-CH_3 of pyrazole), 13.6, 16.5 (^1J(^{13}C-$^{119/117}$Sn)=361/345 Hz), 27.0 (^3J (^{13}C-$^{119/117}$Sn)=63 Hz), 27.9 (^2J(^{13}C-$^{119/117}$Sn)=21 Hz) (*n*-butyl carbons), 113.6 (C^4 of pyrazole), 117.6, 121.8, 138.3, 147.7, 152.9 (pyridyl carbons), 145.7, 152.4 (C^3 and C^5 of pyrazole), 169.4 (C=O) ppm. ^{119}Sn NMR: δ 103.5 ppm. IR (cm^{-1}): ν_{as}(COO) 1 630, ν_s(COO) 1 380. Anal. Calcd. for $C_{23}H_{37}N_3O_2Sn$ (%): C, 54.57; H, 7.37; N, 8.30. Found (%): C, 54.51; H, 7.47; N, 8.59.

1.15 Synthesis of (PYPCO$_2$)SnEt$_3$ (13)

This complex was obtained similarly by the reaction of $PYPCO_2H$ (0.22 g, 1 mmol) and $(Et_3Sn)_2O$ (0.21 g, 0.5 mmol) as described above for **1**. After removing the solvent, the crude product was recrystallized from hexanes to give slightly yellow solids of **13**. Yield: 0.28 g (64%); m.p. 51~53 ℃. ^{1}H NMR: δ 1.19~1.46 (m, 15H, CH_2CH_3), 2.52, 2.88 (s, s, 3H, 3H, 3- and 5-CH_3 of pyrazole), 7.21~7.24, 7.75~7.83, 8.47 (m, m, d, J=4.7 Hz, 1H, 2H, 1H, pyridyl protons) ppm. ^{13}C NMR: δ 7.9 (^1J(^{13}C-$^{119/117}$Sn)=370/353 Hz), 9.9 (^2J(^{13}C-$^{119/117}$Sn)=26 Hz) (ethyl carbons), 13.5, 14.5 (3- and 5-CH_3 of pyrazole), 113.5 (C^4 of pyrazole), 117.7, 121.9, 138.3, 147.8, 153.0 (pyridyl carbons), 145.7, 152.4 (C^3 and C^5 of pyrazole), 169.5 (C=O) ppm. ^{119}Sn NMR: δ 102.2 ppm. IR (cm^{-1}): ν_{as}(COO) 1 674, ν_s(COO) 1 357. Anal. Calcd. for $C_{17}H_{25}N_3O_2Sn\cdot H_2O$ (%): C, 46.39; H, 6.18; N, 9.55. Found(%): C, 46.72; H, 5.97; N, 9.97.

1.16 Synthesis of (PYPCO$_2$)SnCy$_3$ (14)

This complex was obtained similarly by the reaction of $PYPCO_2H$ (0.22 g, 1 mmol) and tricyclohexyltin hydroxide (0.39 g, 1 mmol) as described above for **1**. After removing the solvent, the crude product was recrystallized from hexanes to give slightly yellow solids of **14**. Yield: 0.54 g (92%); m.p. 70~71 ℃. ^{1}H NMR: δ 1.23~1.29, 1.57~1.67, 1.86~1.92 (m, m, m, 9H, 15H, 9H, C_6H_{11}), 2.44, 2.79 (s, s, 3H, 3H, 3- and 5-CH_3 of pyrazole), 7.13~7.16, 7.67~7.75, 8.39 (m, m, d, J=4.7 Hz, 1H, 2H, 1H, pyridyl protons) ppm. ^{13}C NMR: δ 13.6, 14.6 (3- and 5-CH_3 of pyrazole), 27.0, 28.9 (^3J (^{13}C-$^{119/117}$Sn)=64 Hz), 31.2 (^2J(^{13}C-$^{119/117}$Sn)=18 Hz), 33.6 (^1J(^{13}C-$^{119/117}$Sn)=343/328 Hz) (cyclohexyl carbons), 114.0 (C^4 of pyrazole), 117.8, 121.9, 138.3, 147.8, 153.0 (pyridyl carbons), 145.5, 152.4 (C^3 and C^5 of pyrazole), 169.2 (C=O) ppm. ^{119}Sn NMR: δ 11.6 ppm. IR (cm^{-1}): ν_{as}(COO) 1629, ν_s(COO) 1 337. Anal. Calcd. for $C_{29}H_{43}N_3O_2Sn$(%): C, 59.60; H, 7.42; N, 7.19. Found(%): C, 59.54; H, 7.81; N, 6.74.

Table 1　Crystal data and refinement parameters for $7\cdot H_2O$

Formula	$C_{18}H_{28}N_2O_3Sn$	T / K	293(2)
Formula weight	439.13	D_c / (g·cm^{-3})	1.446
Crystal size / mm	0.40×0.40×0.40	F(000)	896
Crystal system	Monoclinic	μ / mm^{-1}	1.283
Space group	$P2_1/c$	No. of collected reflections	17 166
a / nm	1.097 5(2)	No. of unique reflections	3 552 (R_{int}=0.030 7)
b / nm	1.233 2(3)	No. of observed reflections ($I>2\sigma(I)$)	3 196
c / nm	1.660 2(6)	No. of parameters	222
β / (°)	116.12(2)	Goodness-of-fit	1.167
V / nm^3	2.018(1)	Residuals R, wR ($I>2\sigma(I)$)	0.028 5, 0.059 9
Z	4		

1.17　Crystal structure determination

Crystals of complex **7** suitable for X-ray analyses were obtained by slow diffusion of hexanes into its CH_2Cl_2 solution at room temperature. This complex crystallized with a molecule of water. All intensity data were collected at 293 (2) K on a SCX-MINI CCD detector with graphite monochromated Mo $K\alpha$ radiation (λ=0.071 073 nm) using the ω scan mode. Semi-empirical absorption corrections were applied using the Crystalclear program[25]. The structures were solved by direct methods and difference Fourier map using SHELXS of the SHELXTL package and refined with SHELXL[26] by full-matrix least-squares on F^2. All non-hydrogen atoms were refined anisotropically. Crystallographic data are listed in Table 1.

CCDC: 823104, **7**.

2　Results and discussion

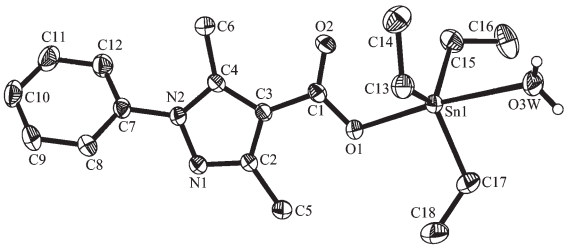
2.1　Synthesis and characterization of complexes

It has been reported that the structures of the organotin carboxylates are variable with different ratio of starting materials. Reaction of 1-phenyl-3,5-dimethylpyrazole-4-carboxylic acid ($PHPCO_2H$) and 1-(2-pyridyl)-3,5-dimethylpyrazole-4-carboxylic acid ($PYPCO_2H$) with R_2SnO in a 1∶1 molar ratio gave dimeric complexes $\{[(PHPCO_2)SnR_2]_2O\}_2$ (R=^{n}Bu (**1**) and Et (**3**)) and $\{[(PYPCO_2)SnEt_2]_2O\}_2$ (**9**), which have been characterized by elemental analyses, IR and NMR spectroscopy. The spectroscopic data support the suggested dimeric structure with a cyclic Sn_2O_2 unit. For example, the ^{1}H and ^{13}C NMR spectra of these three complexes display two sets of butyl signals for **1** as well as ethyl signals for **3** and **9**, respectively. In addition, their ^{119}Sn spectra exhibit a pair of resonances of equal intensities between −220 and −280 ppm for the endo- and exo-cyclic tin atoms, which are comparable to the reported values for other dimeric distannoxanes[1].

Diorganotin dicarboxylates $(PHPCO_2)_2SnR_2$ (R=^{n}Bu (**2**) and Et (**4**)) and $(PYPCO_2)_2SnEt_2$ (**10**) were obtained by the reaction of the corresponding acid with R_2SnO in a 2∶1 molar ratio. These complexes have been characterized by IR and NMR spectra. One ^{119}Sn NMR signal was observed in these diorganotin derivatives (−139.7 ppm in **2**, −144.5 ppm in **4** and −143.2 ppm in **10**, respectively), which is comparable to those reported for diorganotin dicarboxylates with a skewed trapezoidal bipyramid geometry[1]. In addition, triorganotin derivatives of $(PHPCO_2)SnR_3$ and $(PYPCO_2)SnR_3$ (R=Ph (**5**) and (**11**), ^{n}Bu (**6**) and (**12**), Et (**7**) and (**13**) as well as cyclohexyl (**8**) and (**14**)) were obtained by the similar reaction of these two acids with $(R_3Sn)_2O$ or tricyclohexyltin hydroxide. The ^{119}Sn chemical shifts as well as the $^nJ(^{13}C\text{-}^{119/117}Sn)$ coupling constants of triorganotin derivatives display that the tin atoms in these complexes are four-coordinate in solution[27-28]. It is worthy of note that the characteristic absorption of the ester carbonyl in complexes **4**, **7**, **10** and **13** is observed at *ca.* 1 674 cm^{-1}, markedly higher than those in other complexes, indicating that the interactions of the carboxyl oxygen atom with the tin atom are relatively weak in these complexes, which is

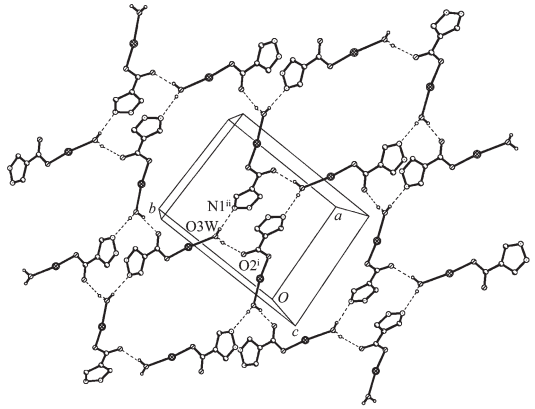
subsequently confirmed by the X-ray analysis of complex **7**.

The structure of complex **7** has been further investigated by X-ray crystallography, which is presented in Fig.1. One molecule of H_2O coordinates to the tin atom, inducing the tin atom to adopt a five-coordinate distorted trigonal bipyramidal geometry with two oxygen atoms occupying the apical positions. The axial O1-Sn1-O3W angle is 173.20(8)°, and significantly derivates from 180°. The carboxylic ligand adopts a monodentate coordination mode. In addition, two asymmetric Sn-O bonds are observed. The Sn1-O1 bond (0.217 4(2) nm) is significantly shorter than the Sn1-O3W (0.251 5(2) nm) bond. Moreover, the non-bond Sn1…O2 distance (0.304(1) nm) is markedly longer than the covalent Sn1-O1 bond distance, indicating that the interactions between Sn1 and O2 atoms are very weak[1], which is consistent with the result of the IR spectrum of this complex. Although the pyrazolyl nitrogen atom does not directly participate in the coordination to the tin atom in this complex, it plays crucial roles in constructing the integral multidimensional structure by forming intermolecular hydrogen bond with the hydrogen atom of the coordinated water (Fig.2). Thus this complex extends further, constructing an interesting infinite 2D network through the intermolecular O3W–H…O2 and O3W–H…N1 hydrogen bonds, and the units of 12-membered ring and 24-membered ring are repeated in this 2D network structure.



Key geometric parameters: Sn1-O1 0.2174(2), Sn1…O2 0.304(1), Sn1-O3W 0.251 5(2), C1-O1 0.1288(3), C1-O2 0.1233(3) nm; O1-Sn1-O3W 173.20(8)°, C13-Sn1-O1 95.2(1)°, C13-Sn1-O3W 82.8(1)°, C15-Sn1-C17 115.1(2)°, C4-N2-C7 129.1(2)°, O1-C1-O2 123.3(3)°

Fig.1 Molecular structure of **7**·H_2O with thermal ellipsoids are drawn at the 30% probability level



O3W–H…O2^{i} 0.196 6 nm, O3W–H…N1^{ii} 0.213 8 nm; Symmetry code: ^{i} $-x+2$, $y+0.5$, $-z+1.5$, ^{ii} $x+1$, $-y+1.5$, $z+0.5$, phenyl and methyl groups on the pyrazole rings and the ethyl groups on the tin atoms have been omitted for clarity

Fig.2 Infinite 2D network of **7**·H_2O through hydrogen bonds

2.2 Fungicidal activities

The preliminary evaluation of fungicidal activities of all complexes was carried out according to the published procedures[13-14]. The tested results are summarized in Tables 2, 3 and 4, respectively. The preliminary biological screening (Table 2) shows that all complexes display a certain degree of activity against the tested fungi at 50 $\mu g \cdot mL^{-1}$. In addition, triorganotin carboxylates exhibit more active than the free acid ligands. Moreover, triorganotin carboxylates have higher inhibition percentage than the dimeric distannoxanes and diorganotin carboxylates, similar to the results reported previously[14,29-30]. Among all the complexes, tri(*n*-butyl)tin (**6** and **12**) and triethyltin (**7** and **13**) carboxylates are most promising, displaying 100% inhibition of all five types of fungi at 50 $g \cdot mL^{-1}$, and these complexes are more active against Alternaria solani than the positive control (propiconazole). The precision toxicity of these high active triorganotin carboxylates was further tested and the corresponding values of EC_{50} are listed in Tables 3 and 4, respectively. The results show that these triorganotin carboxylates are highly toxic to five tested fungi. Furthermore, it seems that the toxicity of triorganotin 1-(2-pyridyl)-3,5-dimethylpyrazole-4-carboxylates is higher than that of triorganotin 1-phenyl-3,5-dimethyl-pyrazole-4-carboxylates against the corresponding

Table 2　Fungicidal activities of complexes and the free acid ligands (50 μg·mL^{-1})

Complex	*Alternaria solani*	*Cercospora arachidicola*	*Physalospora piricola*	*Gibberella zeae*	*Botrytis cinerea*
1	29.7	26.2	28.1	18.8	28.6
2	29.7	33.3	40.6	34.4	47.6
3	23.0	28.6	29.2	21.9	48.8
4	33.8	40.5	37.5	53.1	77.4
5	58.1	76.2	95.8	78.1	88.1
6	100.0	100.0	100.0	100.0	100.0
7	100.0	100.0	100.0	100.0	100.0
8	47.5	83.3	98.1	65.9	95.6
9	20.3	31.0	21.9	34.4	36.9
10	18.9	28.6	34.4	18.8	51.2
11	62.2	83.3	97.9	93.8	82.2
12	98.7	100.0	100.0	100.0	100.0
13	100.0	100.0	100.0	100.0	100.0
14	70.0	76.7	96.2	63.4	94.2
$PHPCO_2H$	20.3	33.3	35.4	40.6	71.4
$PYPCO_2H$	12.2	26.2	36.5	18.8	61.9
Propiconazole	89.2	100.0	100.0	100.0	100.0

Table 3　EC_{50} determination of complexes 5~7[a]

	Regression equation (*y*)			R^2			EC_{50} / (μg·mL^{-1})		
	5	**6**	**7**	**5**	**6**	**7**	**5**	**6**	**7**
AS	ND	y=0.930 5x+4.962 7	y=1.910 1x+4.209 4	ND	0.960 9	0.986 8	ND	1.1	2.59
CA	ND	y=1.378 8x+4.359 6	y=2.081 5x+4.822 9	ND	0.965 9	0.959 2	ND	2.91	1.22
GZ	ND	y=0.995 3x+5.111 7	y=1.871 5x+6.016 7	ND	0.941 3	0.976 6	ND	0.77	0.29
PP	y=1.095 1x+4.728 0	y=1.045 9x+5.087 2	y=1.799 7x+6.294 9	0.910 8	0.937 3	0.946 6	3.03	0.83	0.19
BC	y=1.255 3x+4.538 5	y=2.056 5x+3.831 0	y=2.303 5x+4.279 1	0.973 1	0.970 8	0.975 4	2.33	3.70	2.06

[a]Name of Fungi: Alternaria solani (AS), Cercospora arachidicola (CA), Gibberella zeae (GZ), Physalospora piricola (PP) and Botrytis cinerea (BC), ND: not detected.

Table 4　EC_{50} determination of complexes 11~13[a]

	Regression equation (*y*)			R^2			EC_{50} / (μg·mL^{-1})		
	11	**12**	**13**	**11**	**12**	**13**	**11**	**12**	**13**
AS	y=1.013 9x+4.921 3	y=0.825 2x+5.013 6	y=1.234 3x+4.515 1	0.988 3	0.988 2	0.95	1.2	0.96	2.47
CA	y=1.211 7x+4.934 1	y=0.912 8x+4.942 5	y=2.230 0x+5.489 5	0.993 8	0.952 2	0.984 8	1.13	1.16	0.60
GZ	ND	y=0.662 2x+5.088 8	y=1.687 0x+6.450 1	ND	0.886 3	0.930 2	ND	0.73	0.14
PP	y=0.924 9x+4.643 0	y=0.968 2x+5.099 8	y=1284 8x+0.578 7	0.862 6	0.984 8	0.936 4	2.43	0.79	0.06
BC	y=0.603 1x+5.404 8	y=1.476 4x+4.271 8	y=2.202 6x+4.544 7	0.957 6	0.947 6	0.990 3	0.21	3.12	1.61

[a] Abbreviations of names of fungi are the same as those in Table 3.

tested fungi. For example, the values of EC_{50} of triethyltin 1-(2-pyridyl)-3,5-dimethylpyrazole-4-carboxylate are 0.06 μg·mL^{-1} against Physalospora piricola and 0.14 μg·mL^{-1} against Gibberella zeae, respectively, while the corresponding values of EC_{50} of triethyltin 1-phenyl-3,5-dimethylpyrazole-4-carboxylate are 0.19 μg·mL^{-1} against Physalospora piricola and 0.29 μg·mL^{-1} against Gibberella zeae, respectively.

3　Conclusions

In conclusion, a series of organotin 1-aryl-3,5-dimethylpyrazole-4-carboxylates have been obtained

and characterized. These complexes display good fungicidal activities *in vitro*. Being especially encouraging, relatively high growth inhibition percentage was observed in case of triorganotin derivatives.

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