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C,N-chelated triorganotin(IV) diesters of 4-ketopimelic acid and their fungicidal activity†

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The set of four triorganotin(IV) diesters of 4-ketopimelic acid containing {2-[$(CH_3)_2NCH_2$]C_6H_4}- as a C,N-chelating ligand was prepared. Their structures were studied by the help of IR, NMR and X-ray crystallographic techniques in the case of {{2-[$(CH_3)_2NCH_2$]C_6H_4}$SnPh_2$}$_2$[$(OOCCH_2CH_2)_2C{=}O$]. All these compounds are monomeric both in solid state and solution with five-coordinated tin atoms and medium strong intramolecular Sn–N connection. The antimycotical activity of these compound was studied and compared with the triorganotin(IV) derivatives of 4-ketopimelic acid and antimycotical drugs in clinical use.

Keywords: triorganotin(IV) diesters; ketopimelic acid; C,N-chelate; NMR; X-ray

Introduction

There is a long-standing interest in chemistry of triorganotin(IV) esters of carboxylic acids both in academia and industry, because of known catalytic and medical activity.[1,2] The structures of these compounds are well established and have been studied by X-ray,[3] Mössbauer and CP MAS NMR techniques in the solid state, and mainly multinuclear NMR techniques in solution.[1] The tin atom in these compounds can be four-coordinated [Fig. 1(A)] or five-coordinated with major occurrence in the solid state. In this case, the tin atom is surrounded by three carbon atoms originating from organo groups and two oxygen atoms from one asymmetrically bidentate carboxylate [intramolecularly chelated, Fig. 1(B)] or two different carboxylate groups [intermolecularly bridging, Fig. 1(C)]. The compounds where the intermolecularly bridging bond fashion is taking place form the infinite polymeric networks in the solid state,[3] which can often be fragmented into oligomeric or monomeric particles in solution of various solvents.[4] Another structural motif in polymeric and/or chelate arrangement can be revealed when a further donor atom is implemented as a part of the carboxylate ligand into the tin coordination sphere.[3]

Little is known about the properties and structure of diesters of dicarboxylic acids. To the best of our knowledge, only a few papers have been published on the structure of triorganotin diesters of dicarboxylic acids[5] and certain others on the structure of ester adducts and complex compounds.[6]

In our previous work, we have been interested in structure of organotin carboxylates containing mainly one organotin fragment in solutions of different solvents.[4] Recently, we have been interested in systems where two or more non-equivalent organotin groups exist, caused by chemical or geometrical (sterical) non-equivalency or dynamic exchange and in studying and comparing such phenomena both in the solid state and in solution. In very recent paper,[7] we selected the triorganotin diesters of ketopimelic acid in order to observe two equivalent or non-equivalent tin fragments depending on sterical hindrance of organic substituents and the possibility of formation of seven-membered ring through the plausible intramolecular interaction of the tin atom with the ketonic oxygen. This phenomenon was unfortunately not observed, but we found that five of these compounds are polymeric in the solid state and depolymerize upon dissolving in non-coordinating and/or addition of coordinating solvent to monomeric particles that are four-coordinated, or complexes with a donor solvent with a five-coordinated tin central atom. The tricyclohexyltin derivative is dimeric in the solid state and monomeric in solution. This led us to the idea of employing a C,N-chelating ligand, known as a stabilizing element of monomeric structures,[8] to this class of compounds and of comparing the properties of such compounds with respect to their biological and antimycotical activities.

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† *Dedicated to Professor Jaroslav Holeček on the occasion of his 75th birthday in recognition of his outstanding contributions to the area of organometallic chemistry.*

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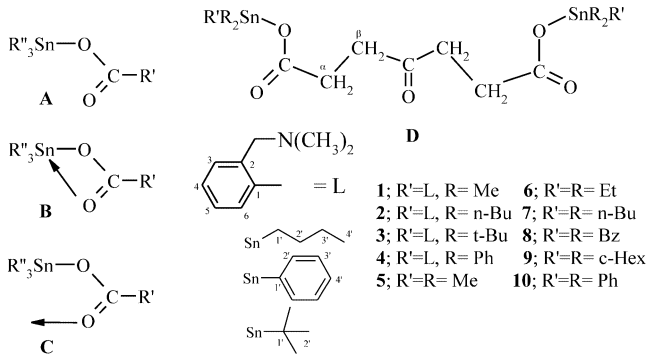

Figure 1. Possible structural motifs and numbering scheme for the studied compounds.

Experimental Section

General remarks

All syntheses were made in air. 4-Ketopimelic acid (4-oxoheptanedioic acid), potassium tert-butoxide and dichloromethane were obtained from commercial sources (Sigma-Aldrich) and used without further purification. Triorganotin chlorides were prepared according to the literature.[9]

Bis{[2-(dimethylaminomethyl)phenyl]dimethyltin}-4-oxoheptanedioate (1)

Compound **1** was prepared from 4-ketopimelic acid (0.16 g; 0.92 mmol), 0.30 g of {2-[$(CH_3)_2NCH_2$]C_6H_4}$SnMe_2Cl$ (0.94 mmol) and potassium tert-butoxide (0.22g; 2.0 mmol) in refluxing dichloromethane (30 ml) for 2 h. The mixture gave the pure oily product in filtrate (0.305 g; 88%, based on tin). ^{1}H NMR ($CDCl_3$, 300 K, ppm): 7.80 [2H, d, H-6, $^3J(^{119}Sn,^1H)$ = 60.5 Hz, $^3J(^1H,^1H)$ = 6.8 Hz], 7.28 (4H, m, H-4,5), 7.03 [2H, d, H-3, $^3J(^1H,^1H)$ = 6.9 Hz], 3.53 (4H, s, NCH_2), 2.76 [4H, t, α-H, $^3J(^1H,^1H)$ = 6.7 Hz], 2.59 [4H, t, α-H, $^3J(^1H,^1H)$ = 6.7 Hz], 2.24 (12H, s, NCH_3), 0.57 [12H, s, H-1′, $^3J(^{119/117}Sn,^1H)$ = 66.8 Hz].$^{13}C\{^1H\}$ NMR ($CDCl_3$, 300 K, ppm): 209.17 (*C*=O), 177.53 (*C*OOSn), 142.19 [C-2, $^2J(^{119/117}Sn,^{13}C)$ = 42.9 Hz], 141.00 [C-1, $^1J(^{119}Sn,^{13}C)$ = 744.5 Hz], 137.20 [C-6, $^2J(^{119/117}Sn,^{13}C)$ = 42.9 Hz], 128.94 [C-4, $^4J(^{119/117}Sn,^{13}C)$ = 12.7 Hz], 127.82 [C-5, $^3J(^{119/117}Sn,^{13}C)$ = 64.4 Hz], 126.51 [C-4, $^3J(^{119/117}Sn,^{13}C)$ = 64.4 Hz], 64.85 [NCH_2, $^nJ(^{119}Sn,^{13}C)$ = 28.7 Hz], 45.09 (NCH_3), 38.62 (C-α), 30.13 (C-α), −3.29 [C-1′, $^1J(^{119}Sn,^{13}C)$ = 536.0 Hz].^{119}Sn $\{^1H\}$ NMR ($CDCl_3$, 300 K, ppm): −77.99. Positive-ion MS: *m/z* 1024 $[M + LSn(CH_3)_2]^+$, 20%; *m/z* 284 $[LSn(CH_3)_2]^+$, 100%. Negative-ion MS: *m/z* 775 $[M + Cl]^-$, 14%; *m/z* 456 $[M - LSn(CH_3)_2]^-$, 100%. IR analysis (neat): 1716 [ν(CO), m], 1643 + 1635 [$\nu_{as}(CO_2)$, vs], 1460 (s), 1363 [$\nu_s(CO_2)$, s-b], 1268 (s), 1098 (s), 1010 (s), 773 (s), 752 (s), 546 (m) cm^{-1}. Elemental analysis $C_{29}H_{44}N_2O_5Sn_2$, found: C, 47.2%; H, 6.1%; N, 3.9%. Calculated C, 47.19%; H, 6.01%, N, 3.80%.

Bis{[2-(dimethylaminomethyl)phenyl]di(*n*-butyl)tin}-4-oxoheptanedioate (2)

This compound was prepared similarly to **1** from 0.129 g (0.74 mmol) of 4-ketopimelic acid 0.2 g of *t*-BuOK (1.82 mmol) and 0.3 g {2-[$(CH_3)_2NCH_2$]C_6H_4}$Sn(n\text{-}Bu)_2Cl$ (0.745 mmol). Yellowish oil, yield 0.311g (92%). ^{1}H NMR ($CDCl_3$, 300 K, ppm): 7.82 [2H, d, H-6, $^3J(^{119}Sn,^1H)$ = 54.5 Hz, $^3J(^1H,^1H)$ = 6.9 Hz], 7.26 (4H, m, H-4,5), 7.07 [2H, d, H-3, $^3J(^1H,^1H)$ = 7.3 Hz], 3.53 (4H, s, NCH_2), 2.80 [4H, t, α-H, $^3J(^1H,^1H)$ = 6.8 Hz], 2.62 [4H, t, α-H, $^3J(^1H,^1H)$ = 6.8 Hz], 2.27 (12H, s, NCH_3), 1.56 (4H, m, C-1′), 1.31 (8H, m, C-2′, 3′), 0.85 [12H, s, H-4′, $^3J(^1H,^1H)$ = 7.3 Hz].$^{13}C\{^1H\}$ NMR ($CDCl_3$, 300 K, ppm): 208.83 (*C*=O), 177.23 (*C*OOSn), 142.52 [C-2, $^2J(^{119/117}Sn,^{13}C)$ = 37.2 Hz], 141.40 [C-1, $^1J(^{119}Sn,^{13}C)$ = 654.8 Hz], 137.48 [C-3, $^2J(^{119/117}Sn,^{13}C)$ = 30.4 Hz], 128.61 [C-4, $^4J(^{119/117}Sn,^{13}C)$ = 12.9 Hz], 127.49 [C-5, $^3J(^{119/117}Sn,^{13}C)$ = 56.6 Hz], 126.62 [C-4, $^3J(^{119/117}Sn,^{13}C)$ = 54.7 Hz], 65.42 [NCH_2, $^nJ(^{119/117}Sn,^{13}C)$ = 21.5 Hz], 45.43 (NCH_3), 38.71 (C-α), 30.12 (C-α), 27.89 [C-2′, $^2J(^{119/117}Sn,^{13}C)$ = 30.1 Hz], 26.81 [C-3′, $^3J(^{119/117}Sn,^{13}C)$ = 88.1 Hz], 16.22 [C-1′, $^1J(^{119}Sn,^{13}C)$ = 514.9 Hz], 13.48 (C-4′).^{119}Sn $\{^1H\}$ NMR ($CDCl_3$, 300 K, ppm): −77.99. Positive-ion MS: *m/z* 1276 $[M + LSn(C_4H_9)_2]^+$, 4%; *m/z* 368 $[LSn(C_4H_9)_2]^+$, 100%; *m/z* 254 $[LSn(C_4H_9)_2]^+$, 11%. Negative-ion MS: *m/z* 540 $[M - LSn(C_4H_9)_2]^-$, 100%. IR analysis (neat): 1717 [ν(CO), m], 1642 [$\nu_{as}(CO_2)$, vs], 1461 (m), 1358 [$\nu_s(CO_2)$, s-b], 1262 (s), 1096 (s), 1015 (s), 801 (vs), 750 (m) cm^{-1}. Elemental analysis for $C_{41}H_{68}N_2O_5Sn_2$, found: C, 54.2%; H, 7.6%; N, 3.2%. Calculated C, 54.33%; H, 7.56%, N, 3.09%.

Bis{[2-(dimethylaminomethyl)phenyl]di(*t*-butyl)tin}-4-oxoheptanedioate (3)

The compound was prepared similarly to **1** from 0.129 g (0.74 mmol) of 4-ketopimelic acid 0.2 g of *t*-BuOK (1.82 mmol) and 0.3 g {2-[$(CH_3)_2NCH_2$]C_6H_4}$Sn(t\text{-}Bu)_2Cl$ (0.745 mmol). Yellowish oil, yield 0.318g (94%). ^{1}H NMR ($CDCl_3$, 300 K, ppm): 7.59 [2H, d, H-6, $^3J(^{119}Sn,^1H)$ = 52.6 Hz, $^3J(^1H,^1H)$ = 6.8 Hz)], 7.23 (4H, m, H-4,5), 7.13 (2H, d, H-3), 3.44 (4H, s, NCH_2), 2.77 [4H, t, α-H, $^3J(^1H,^1H)$ = 6.7 Hz], 2.63 [4H, t, α-H, $^3J(^1H,^1H)$ = 6.7 Hz], 2.20 (12H, s, NCH_3), 1.33 [18H, s, C-2′, $^3J(^{119}Sn,^1H)$ = 92.9 Hz].$^{13}C\{^1H\}$ NMR ($CDCl_3$, 300 K, ppm): 208.53 (*C*=O), 176.96 (*C*OOSn), 143.91 (C-2, broad), 142.72 (C-1, broad), 137.48 (C-3, broad), 129.09 (C-4, broad), 128.56 (C-5, broad), 127.23 (C-4, broad), 67.37 (NCH_2, broad), 45.43 (NCH_3, broad), 38.19 (C-α, broad), 30.87 (C-α, broad), 39.2 (C1′, broad), 31.32 [C-2′, $^1J(^{119}Sn,^{13}C)$ = 25.4 Hz].^{119}Sn $\{^1H\}$ NMR ($CDCl_3$, 300 K, ppm): −60.6. Positive-ion MS: *m/z* 384 $[LSnO(C_4H_9)_2]^+$, 100%; *m/z* 368 $[LSn(C_4H_9)_2]^+$, 88%; *m/z* 270 $[LSnO]^+$, 55%; *m/z* 254 $[LSnO]^+$, 96%. Negative-ion MS: *m/z* 540 $[M - LSn(C_4H_9)_2]^-$, 100%. IR analysis (neat): 1720 [ν(CO), m], 1651 [$\nu_{as}(CO_2)$, vs], 1465 (s), 1364 ($\nu_s(CO_2)$, s), 1263(s), 1164(s), 1097(s), 1015 (s), 749 (s), 584 (s), 509 (s) cm^{-1}. Elemental analysis for $C_{41}H_{68}N_2O_5Sn_2$, found: C, 54.3%; H, 7.7%; N, 3.0%. Calculated C, 54.33%; H, 7.56%, N, 3.09%.

Bis{[2-(dimethylaminomethyl)phenyl]diphenyltin}-4-oxoheptanedioate (4)

The compound was prepared similarly to **1** from 0.039 g (0.224 mmol) of 4-ketopimelic acid 0.06 g of *t*-BuOK (0.545 mmol) and 0.1 g {2-[$(CH_3)_2NCH_2$]C_6H_4}$SnPh_2Cl$ (0.225 mmol). Crystallized by addition of hexane to the filtrate. White powder, m.p. >260 °C, yield 0.091 g (82%). ^{1}H NMR ($CDCl_3$, 300 K, ppm): 7.96 [2H, d, H-6, $^3J(^{119}Sn,^1H)$ = 67.7 Hz, $^3J(^1H,^1H)$ = 6.7 Hz], 7.60 [4H, d, H-2′, $^3J(^{119}Sn,^1H)$ = 64.8 Hz, $^3J(^1H,^1H)$ = 6.9 Hz], 7.25 (12H, m, H-4,5,2′), 7.00 (14H, m, H-3,3′,4′), 3.46 (4H, s, NCH_2), 2.37 (4H, broad, α-H), 2.28 (4H, t, α-H, broad), 1.62 (12H, s, NCH_3).$^{13}C\{^1H\}$ NMR ($CDCl_3$, 300 K, ppm): 208.91 (*C*=O), 177.25 (*C*OOSn), 142.95 [C-2, $^2J(^{119/117}Sn,^{13}C)$ = 41.7 Hz], 138.51 [C-1, $^1J(^{119}Sn,^{13}C)$ = 817.2 Hz], 140.84 [C-1′, $^1J(^{119}Sn,^{13}C)$ = 799.5 Hz], 128.5 (C-4), 126.7 [C(3); $^4J(^{119/117}Sn,^{13}C$ = 55.9 Hz)]; 136.0 [C(2′); $^2J(^{119/117}Sn,^{13}C$ = 45.3 Hz)], 136.5 [C(3′); $^3J(^{119/117}Sn,^{13}C$ =

45.3 Hz)], 128.5 [C(4′)], 127.49 [C-5, $^{3}J(^{119/117}Sn,^{13}C)$ = 55.2 Hz], 126.62 [C-6, $^{3}J(^{119/117}Sn,^{13}C)$ = 54.2 Hz], 64.73 [NCH_2, $^{n}J(^{119/117}Sn,^{13}C)$ = 24.9 Hz], 45.53 (NCH_3), 38.70 (C-α), 30.15 (C-α). ^{119}Sn {^{1}H} NMR ($CDCl_3$, 300 K, ppm): −219.0. Positive-ion MS: *m/z* 1396 $[M + LSn(C_6H_5)_2]^+$, 3%; *m/z* 408 $[LSn(C_6H_5)_2]^+$, 100%; *m/z* 363 $[LSn(C_6H_5)_2\text{-}(CH_3)_2NH]^+$, 21%. Negative-ion MS: *m/z* 540 $[M - LSn(C_6H_5)_2]^-$, 38%; *m/z* 408 $[LSn(C_6H_5)_2]^-$, 100%. IR analysis (KBr): 1716 [ν(CO), m], 1644 [$\nu_{as}(CO_2)$, vs], 1430 (s), 1362 [$\nu_s(CO_2)$, s-b], 1263 (s), 1098 (s), 1077 (s), 1011 (s) 843 (s) 731 (vs), 699 (vs), 454 (s) cm^{-1}. Elemental analysis for $C_{49}H_{52}N_2O_5Sn_2$, found: C, 59.7%; H, 5.4%; N, 3.0%. Calculated C, 59.67%; H, 5.31%, N, 2.84%.

NMR spectroscopy

The ^{1}H (500.13 MHz), ^{13}C (125.76 MHz) and ^{119}Sn (186.50 MHz) NMR spectra of all compounds in $CDCl_3$ (30–50 mg in 0.6 ml) were recorded at ambient temperature on a Bruker Avance 500 spectrometer equipped with a 5 mm broadband probe with *z*-gradient. The ^{13}C and ^{1}H chemical shifts were referred to the signal of $CDCl_3$ (respectively residual $CHCl_3$) [$\delta(^{13}C) = 77.0$, $\delta(^{1}H) = 7.25$] and the ^{119}Sn chemical shifts were referred to external neat tetramethylstannane [$\delta(^{119}Sn) = 0.0$]. Two-dimensional *gs*(gradient selected)-H,H-COSY, *gs*-^{1}H-^{13}C – HSQC, *gs*-^{1}H-^{13}C – HMBC and *gs*-^{1}H-^{15}N-HMBC[10,11] spectra were recorded using standard microprograms provided by Bruker. ^{119}Sn NMR spectra were measured using the inverse gated-decoupling mode. The ^{1}H and ^{13}C chemical shifts were assigned from gs (gradient selected)-H,H-COSY, *gs*-^{1}H-^{13}C and *gs*-^{1}H-^{13}C-HMBC[10,11] spectra [optimized for $^{1}J(^{13}C,^{1}H)$ *ca* 150 Hz and $^{3}J(^{13}C,^{1}H)$ *ca* 8 Hz, respectively].

Mass spectrometry

Positive-ion and negative-ion electrospray ionization (ESI) mass spectra were measured on an Esquire 3000 ion trap analyzer (Bruker Daltonics, Bremen, Germany) in the range *m/z* 50–1500. The samples were dissolved in methanol and analyzed by direct infusion at the flow rate 5 µl min^{-1}. The selected precursor ions were further analyzed by MS/MS analyses under the following conditions: the isolation width $m/z = 8$ for ions containing one tin atom and $m/z = 12$ for ions containing more tin atoms, the collision amplitude in the range 0.8–1.0 V depending on the precursor ion stability, the ion source temperature 300 °C, the tuning parameter compound stability 100%, the flow rate and the pressure of nitrogen 4 l/min and 10 psi, respectively.

IR spectroscopy

IR spectra were recorded on Perkin-Elmer 684 spectrophotometer KBr pellet or neat, respectively, in laboratory conditions.

X-ray crystallography

The single crystals of **4** were grown from *ca* 5% CH_2Cl_2 solution into which hexane was charged via slow vapour diffusion in air. The X-ray data were collected on a Nonius KappaCCD diffractometer fitted with MoK_α radiation ($\lambda = 0.71073$ Å) at 150(1) K. The absorption correction was performed using a gaussian procedure,[12] the structure was solved by direct-methods (SIR92[13]) and full-matrix least-squares refinements on F^2 were carried out using the program SHELXL97.[14] Partial occupancy of solvated water was applied.

Crystallographic data for **4**: $1/2H_2O$; $C_{49}H_{53}N_2O_{5.5}Sn_2$, M = 995.37, monoclinic, $P2_1/n$, a = 9.8240(6), b = 28.265(3), c = 15.7760(16) Å, β = 97.025(9)°, Z = 4, V = 4347.7(7) $Å^3$, $D_c = 1.534$ g cm^{-3}, $\mu = 1.201$ mm^{-1}, $T_{min} = 0.718$, $T_{max} = 0.807$; 42 415 reflections measured ($\theta_{max} = 27.5°$), 9981 independent ($R_{int} = 0.072$), 7259 with $I > 2\sigma(I)$, 532 parameters, $S = 1.01$, *R1* (observed data) = 0.044, *wR2* (all data) = 0.102; max, min residual electron density = 0.845, −1.298 $eÅ^{-3}$. CCDC Deposition number: 672 494.

In vitro antifungal screening

The *in vitro* testing was carried out by the modified microdilution broth method according to the M27-A guideline (NCCLS 1997). Quality control strains (*Candida albicans* ATCC 90 028, *Candida parapsilosis* ATCC 22 019, *Candida krusei* ATCC 6258) and amphotericin B (Sigma), fluconazole (Pfizer), ketoconazole (Janssen-Cilag, Beerse) as reference drugs were involved. All fungal strains were passaged on Sabouraud dextrose agar at 35 °C prior to being tested.

The minimum inhibitory concentration (MIC) and the minimum fungicidal concentration (MFC) were determined by the following method.[15] Dimethyl sulfoxide (DMSO) served as a diluent for all compounds tested. DMSO did not exceed the final concentration of 2%. RPMI 1640 (Sevapharma, Prague) medium supplemented with L-glutamine and buffered with 0.165 M morpholinepropanesulfonic acid (Serva) to pH 7.0 using 10 M NaOH as a test medium. Each well of the microdilution tray was filled with 200 µl of the RPMI 1640 medium with a diluted compound tested and then inoculated with 10 l of suspension of a given fungal strain in sterile water. Fungal inoculum was prepared to give a final size of $5 \times 10^3 \pm 0.2$ CFU ml^{-1}. The trays were incubated at 35 °C and the MICs read after 24 and 48 h. Owing to slow growth, *Trichophyton mentagrophytes* strain was read at 72 and 120 h. The MICs were determined visually and defined as 80% inhibition of the growth of control.

Results and Discussion

The studied compounds – bis[triorganotin(IV)] esters of 4-ketopimelic (4-oxoheptanedioic) acid **5**–**10** – were prepared by published methods.[7] Compounds containing C,N-chelating ligands (**1**–**4**) were prepared by reaction of appropriate organotin(IV) chloride with excess of 4-ketopimelic acid (2 equiv.) and potassium tert-butoxide in refluxing dichlormethane. When the correct molar ratio was used only unsatisfactorily pure compounds were isolated. All reactions gave after purification by crystallization and washing by chloroform–hexane mixture satisfactory (88% of **1**) to nearly quantitative yields (92% for **2**) of analytically pure products. All attempts to prepare triorganotin monoesters of 4-ketopimelic acid failed. The purity of **1**–**4** was checked by elemental analysis, ESI-MS spectrometry and NMR measurements. All these compounds studied are stable on air for longer than one year.

The results of electrospray ionisation (ESI) mass spectrometry measurements the both in positive- and negative-ion modes are summarized in the Experimental section. The main mechanism of the ion formation is the cleavage of the most labile bond between tin and oxygen in the molecules yielding two complementary ions, where positively charged species $[LSnR_2]^+$ (R = *t*-C_4H_9; C_4H_9; C_6H_5 and CH_3) are observed in the positive-ion mode and the negatively charged species $[M - LSnR_2]^-$ in the negative-ion mode of electrospray ionization mass spectrometry. Proposed structures of individual ions are supported by tandem mass spectrometric

Table 1. Selected parameters of IR (cm^{-1}) and NMR (ppm) spectra for **1**–**4**

Compound (R)/parameter	Medium	ν(C=O)	$\nu_{as}(CO_2)$	$\nu_s(CO_2)$	δ (^{119}Sn) in $CDCl_3$
1 (Me)	Neat	1716	1643, 1635	1363	−78.0
2 (*n*-Bu)	Neat	1717	1642	1358	−86.2
3 (*t*-Bu)	Neat	1720	1651	1364	−60.6
4 (Ph)	KBr disk	1716	1644	1362	−219.0

experiments. CO_2, alkene, alkane, H_2O, toluene, benzene, etc., are the characteristic neutral losses in MS/MS spectra. The presence of unusual adducts with solvent is not observed compared to compounds presented in previous work.[7] In case of compound **3**, where R corresponds to tert-butyl, the ions *m/z* 384 $[LSnO(C_4H_9)_2]^+$ and *m/z* 270 $[LSnO]^+$ are observed in the first-order positive-ion mode. This behavior is probably caused by steric reasons of terc-butyl group.[16]

Structure of 1–4

IR spectroscopy

The significant tool for evaluation of organotin carboxylate structure is IR spectroscopy, especially the values of ν_{as} and ν_s for CO_2 group.[17] These values and ν(C=O) for **1**–**4** are collected in Table 1. The ν(C=O) values for **1**–**4** are slightly higher than the same parameter of free 4-ketopimelic acid (1695 cm^{-1})[17c] or polymeric **5**–**10** (~1705 cm^{-1}),[7] which indicates no interaction of ketonic function and tin. The $\nu_{as}(CO_2)$ (1635–1651 cm^{-1}) and $\nu_s(CO_2)$ (~1360 cm^{-1}) values reported earlier for a monomeric–pseudobidentate structure were found for all compounds, which is in strong contrast to previously reported spectra of **5**–**10**. The differences in Sn–O bond lengths [Sn1–O2 2.133(3) vs Sn1–O3 2.930(3) Å and Sn2–O4 2.120(3) vs Sn2–O5 2.992(3) Å] are more than 0.8 Å, and the Sn1–O3 and Sn2–O5 separations are out of range of the sum of van der Waal's radii for Sn and O atoms, so we can suggest the monodentate carboxylate bond fashion.

NMR spectroscopy

The structures of **1**–**4** were studied in solution of $CDCl_3$ using a multinuclear NMR approach. Compound **3** reveals a medium broad set of signals in ^{1}H NMR spectrum which corresponds with the steric hindrance of *t*-Bu groups; on the other hand, **1, 2** and **4** reveal one set of sharp and resolved signals in ^{1}H NMR spectra indicating the geometrical equivalency of organotin moieties and both parts of the acid at room temperature (at least on the NMR time scale). Only one signal was observed for **1**–**4** in ^{119}Sn NMR spectrum in the same solvent at room temperature. The chemical shift values (Table 1) of these signals for **1**–**4** are in accordance with the values found for five-coordinated tin in a solution of non-coordinating solvent[9,18] and organotin(IV) carboxylates containing C,N-chelating ligand,[19] but more negative (~40 ppm) than was found for corresponding halides (LR_2SnX),[8,9] which confirms the results of IR spectra on a pseudobidentate fashion of C(=O)–O–Sn moiety.[4b,20] The ^{13}C NMR spectra revealed three parameters that are useful for structural study: (i) the δ [^{13}C(C=O)] value for all compounds was found in the narrow range (~208 ppm) typical for non-coordinated ketonic groups; (ii) δ [$^{13}C(CO_2)$] are typical for a monodentate carboxylic group (~177 ppm); and (iii) the average angle C–Sn–C = 126 and 123° common for the trigonal bipyramidal vicinity of tin atom was calculated from the values of $^1J(^{119}Sn,^{13}C)$ for **2** and **4** in chloroform.[18b,c]

X-ray diffraction

The crystallization attempts to prepare solvent-free single crystals failed and the only success was the preparation of crystals by the long standing of the solution in air, where the desired molecule was hydrated by a half-molar equivalent of water molecules. The solid state structure of **4** was determined by diffraction techniques. The molecular organization of **4** can be described as two independent pentacoordinated tin fragments with distance Sn1–Sn2 8.659(3) Å connected by a J-shaped (Fig. 2) dicarboxylic acid bridge. The supramolecular architecture observed for non-chelated organotin compounds previously,[3b,7] is not taking place in **4**. A possible hydrogen bridge between O5 and O1W with the distance 2.855(4) Å and the further contact of the O1W atom to one of the hydrogen atoms [2.575(5) Å] of the dimethylamino group of adjacent molecule is the only serious communication in the crystal lattice. Both tin atoms are five-coordinated, with mutually very similar coordination geometries of distorted trigonal bipyramid (Σ of C–Sn–C angles, 355.6 and 355.9°), by three aryl carbon, one oxygen and one nitrogen atoms. In addition the second oxygen (O3 and O5) atoms of the carboxylic groups interact very slightly with tin atoms. There is no interaction of tin atoms with adjacent carboxylates as found for diesters of terephthalic,[5c] succinic[5d] and acetylenedicarboxylic[5c] acids.

The intramolecularly bonded nitrogen atoms of the $CH_2N(CH_3)_2$ groups and the O atom of the carboxylate groups are located in apical positions [Sn1–O2 2.133(3) and Sn2–O4 2.120(3) Å] for **4** [similar to that found for triphenyltin benzoate 2.073(2)Å and previously published organotin derivatives carboxylates containing C,N-chelating ligands].[19,21,22] The monodentate or pseudomonodentate mode of coordination of carboxylate units is reflected in the disparate C–O bond distances (see Fig. 2 caption), the longer separation between C–O being associated with the stronger Sn–O interaction. The Sn–N distances [2.575(3) and 2.564(3) Å] are in the range of relatively strong intramolecular contacts. A further comparison can be made for the N–Sn–O angles, which are in line with previously published structures.

In vitro antifungal activity

Three sets of organotin compounds were tested *in vitro*. The first set are compounds **1**–**4**, containing C,N-chelate and 4-ketopimelate ligands; the second set (**5**–**10**) are compounds without a C,N-chelating ligand; and the third set are starting C,N-chelated chlorides (**1a**–**4a**), see Table 2. Generally the set of non-chelated ketopimelates is the most efficient one and starting chlorides reveal much lower activity. The *in vitro* antifungal effect of the compounds with alkyl substituents was found to be slightly higher than for the aryl substituted ones, especially in the case of *n*-butyl substituted ones. The values for all compounds were comparable with that for the antimycotic drugs (ketoconazole, fluconazole, amphotericin B)[23] used for the treatment of systemic mycoses, but less active than the previously published tributyltin(IV) compounds with four-coordinated tin atom.[24]

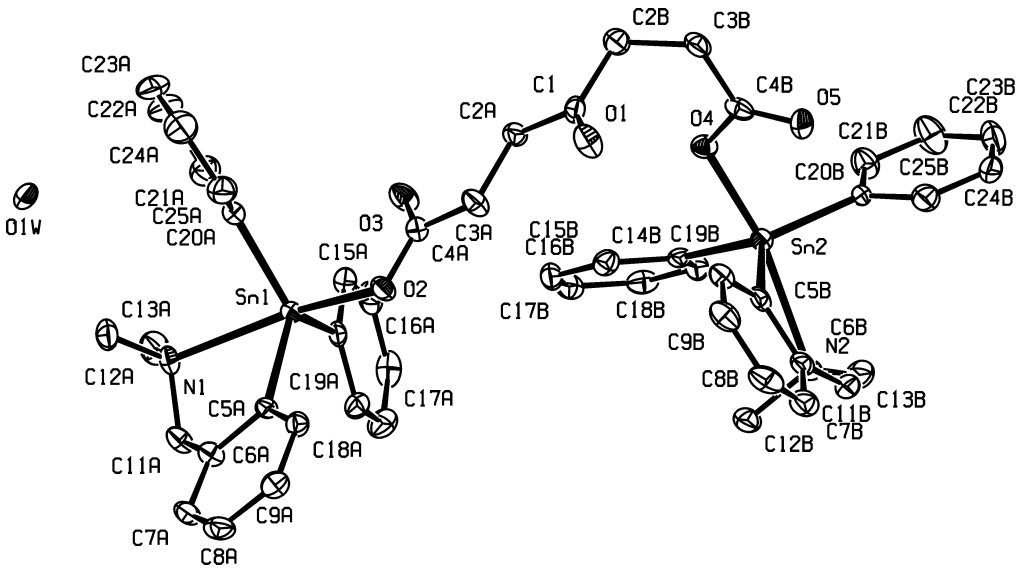

Figure 2. Molecular structure of compound **4** · $1/2H_2O$ with atom numbering scheme (ORTEP 50% probability level); hydrogen atoms are omitted for clarity. Selected interatomic distances (Å) and angles (deg): Sn1–C14A 2.106(4), Sn1–C20A 2.120(4), Sn1–C5A 2.129(4), Sn1–O2 2.133(3), Sn1–O3 2.930(3), Sn1–O1 7.061(3), Sn1–O1W 5.573(5), Sn1–N1 2.575(3), Sn2–O4 2.120(3), Sn2–O5 2.992(3), Sn2–O1 4.895(3), Sn2–C20B 2.123(4), Sn2–C5B 2.130(4), Sn2–C14B 2.137(4), Sn2–N2 2.564(3), O3–C4A 1.215(5), C4B–O4 1.307(5), C4B–O5 1.225(5), O2–C4A 1.304(5), C1–O1 1.205(5), C14A–Sn1–C20A 121.86(16), C14A–Sn1–C5A 114.00(15), C20A–Sn1–C5A 119.40(16), O2–Sn1–N1 164.87(11), C20B–Sn2–C5B 120.61(15), C20B–Sn2–C14B 114.01(16), C5B–Sn2–C14B 121.25(15), O4–Sn2–N2 166.37(11).

Table 2. Antimycotical activity of studied compounds [MIC/IC80 (μmol l^{-1})]

Strain (code)		1	2	3	4	5	6	7	10	1a	2a	3a
CA	24 h	3.9	0.98	7.81	7.81	15.63	0.98	<0.49	<3.91	31.25	1.95	15.63
	48 h	15.62	3.9	15.62	7.81	62.5	1.95	<0.49	<3.91	>125	7.81	62.5
CT	24 h	125	3.9	62.5	7.81	62.5	3.91	<0.49	<3.91	>125	3.91	62.5
	48 h	250	7.81	62.5	15.62	250	62.5	0.98	<3.91	>125	15.63	250
CK	24 h	250	3.9	3.9	7.81	15.63	1.95	<0.49	<3.91	125	3.91	3.91
	48 h	250	3.9	3.9	7.81	31.25	1.95	<0.49	<3.91	>125	7.81	7.81
CG	24 h	250	15.62	125	31.25	7.81	7.81	0.49	<3.91	125	15.63	250
	48 h	500	15.62	250	31.25	125	62.5	0.98	<3.91	>125	62.5	500
TB	24 h	31.25	1.95	15.62	15.62	31.25	1.95	1.95	<3.91	62.5	1.95	31.25
	48 h	125	7.81	62.5	31.25	250	7.81	1.95	<3.91	>125	7.81	62.5
AF	24 h	125	3.9	125	15.62	15.63	1.95	0.98	<3.91	125	1.95	125
	48 h	125	7.81	250	31.25	125	1.95	0.98	<3.91	125	7.81	125
AC	24 h	62.5	0.98	15.62	7.81	125	0.98	0.49	<3.91	>125	0.98	15.63
	48 h	62.5	0.98	15.62	7.81	125	0.98	0.98	<3.91	>125	1.95	62.5
TM	72 h	1.95	0.98	3.9	3.9	3.91	0.49	<0.49	<3.91	<3.91	0.98	7.81
	120 h	3.91	0.49	<0.49	<3.91	<3.91	0.98	7.81	<3.91	<3.91	0.98	7.81

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