Synthesis and Characterization of Diphenylmethyltin(IV) Mono-, Di-, and Trichloroacetate

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ABSTRACT: *Diphenylmethyltin(IV) mono-, di-, and trichloroacetate have been synthesized and characterized by infrared, ^1H, ^{13}C, ^{119}Sn NMR, and mass spectroscopy. Infrared spectroscopy indicates that the prepared organotin carboxylates possess chain polymer structures. NMR data show that the mono- and dichloro derivatives do not retain the solid state structure in solution.* © 2003 Wiley Periodicals, Inc. Heteroatom Chem 14:18–22, 2003; Published online in Wiley InterScience (www.interscience.wiley.com). DOI 10.1002/hc.10059

INTRODUCTION

Recent interest in organotin carboxylates is stimulated because of their in vitro antitumor activities [1,2]. A broad range of activities against human tumor cell lines for di- and triorganotin carboxylates has been reported [1–4]. Triphenyltin phenylacetate with an ID_{50} value of 4 ng ml^{-1} shows higher activity than cis-platin, a clinically known drug with an ID_{50} value of 1400 ng ml^{-1} [5], against the mammary tumor MCF-7 [4]. Recent works also reveal higher antitumor activities for di- and triorganotin fluoro-substituted carboxylates than than their non-fluorinated analogs [1]. For instance, the ID_{50} values of 15, 18, 45, and 650 ng ml^{-1} are observed for 4-FC$_6$H$_4$CO$_2$SnPh$_3$, 3,5-FC$_6$H$_3$CO$_2$SnPh$_3$,

C$_6$F$_5$CO$_2$SnPh$_3$, and C$_6$H$_5$CO$_2$SnPh$_3$, respectively [1]. Despite vast data of in vitro antitumor activities of organotin carboxylates, no simple trend among them can be established. To date, there is no clear picture on the antitumor activity cause of organotin carboxylates from structural and coordination chemistry points of view and a considerable amount of research has to be performed for their elucidation. Consequently, search for finding effective organotin compounds against a broader panel of cell lines remains mostly based on trial and error.

However, it is well known that the toxicity of organotin compounds decreases with increasing length of alkyl-substituted groups on tin [6], and it has been suggested that the perfluoro compounds facilitate drug transport to tumor [7]. Interestingly, tributyltin benzoate exhibits higher activity than triphenyltin benzoate against several human tumor cell lines [1]. This clearly demonstrates the significant role of organic substituent groups on tin. Although synthesis and characterization of organotin carboxylates have been widely investigated [8,9], there is only a limited number of studies on the preparation of organotin carboxylates with mixed alkyl/aryl substituent groups on tin [10, M. M. Amini, Y. Farhanghi, and Z. Salarvand, unpublished work.]. By realizing the importance of organic substituent groups in tin in vitro antitumor activity, it may be possible to tailor such activity by introducing certain number of alkyl and aryl groups at tin. Therefore, synthesis and characterization of new organotin carboxylates will be fruitful in this respect. In this paper, we report on the synthesis and characterization of

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diphenylmethyltin(IV) mono-, di-, and trichloroacetate, a new series of organotin carboxylates.

EXPERIMENTAL

Diphenylmethyltin iodide was prepared via tin–phenyl cleavage of triphenylmethyltin by elemental iodine [11], and triphenylmethyltin was prepared according to the literature procedure by reacting triphenyltin chloride with methyllithium or methylmagnesium bromide [12]. Diphenylmethyltin mono- and dichloroacetate were prepared from the reaction of diphenylmethyltin iodide with the corresponding silver acetate in methanol in 83 and 47% yields, respectively. The silver iodide was removed by filtration and the resulting solid obtained from the filtrate was recrystallized from methanol or chloroform. Diphenylmethyltin trichloroacetate was synthesized in 54% yield by reacting trichloroacetic acid with diphenylmethyltin iodide in ethanol in the presence of Ag_2O. The silver iodide was removed and diphenylmethyltin trichloroacetate was recrystallized from ethanol.

The ^1H NMR spectra of diphenylmethyltin mono- and dichloroacetate were recorded in $CDCl_3$ and CD_3OD and their ^{13}C NMR spectra in CD_3OD (vs. Me_4Si in ppm) using the Brucker Spectrospin 300 MHz spectrometer. The ^{119}Sn NMR spectra of diphenylmethyltin mono- and dichloroacetate were obtained in $CDCl_3$ (vs. Me_4Sn in ppm) on a Bruker Advance DRX-500 MHz spectrometer. Because of the insufficient solubility of diphenylmethyltin trichloroacetate in $CDCl_3$ and CD_3OD, the ^1H and ^{119}Sn NMR spectra of this compound were recorded in DMSO. The mass spectroscopy was performed on a Hewlett-Packard 5973 instrument at 70 eV. Infrared spectra were recorded (KBr pellets) on a Bomem MB-100 FT-IR spectrometer. Elemental analyses were determined using a Heraeus CHN Rapid analyzer. Melting points were uncorrected.

$(C_6H_5)_2CH_3SnOC(O)CH_2Cl$: m.p. 92–94°C. Anal. calcd. for $C_{15}H_{15}O_2ClSn$ (%): C, 47.23; H, 3.96. Found: C, 46.55; H, 3.90. Mass spectrum data, tin-bearing fragments: m/e 382 $[(C_6H_5)_2CH_3SnOC(O)CH_2Cl]^+$, 367 $[(C_6H_5)_2SnOC(O)CH_2Cl]^+$, 347 $[(C_6H_5)_2CH_3SnOC(O)CH_2]^+$, 305 $[C_6H_5CH_3SnOC(O)CH_2Cl]^+$, 289 $[(C_6H_5)_2CH_3Sn]^+$, 197 $[C_6H_5Sn]^+$, 120 $[Sn]^+$. Mass numbers are based upon ^1H, ^{12}C, ^{35}Cl, ^{16}O, and ^{120}Sn.

$(C_6H_5)_2CH_3SnOC(O)CHCl_2$: m.p. 124°C. Anal. calcd. for $C_{15}H_{14}O_2Cl_2Sn$ (%): C, 43.32; H, 3.39. Found: C, 42.12; H, 3.29. Mass spectrum data, tin-bearing fragments: m/e 346 $[(C_6H_5)_2CH_3SnOC(O)CH]^+$, 339 $[C_6H_5CH_3SnOC(O)CHCl_2]^+$, 289 $[(C_6H_5)_2$-

$CH_3Sn]^+$, 269 $[C_6H_5CH_3SnOC(O)CH]^+$, 247 $[SnOC(O)CHCl_2]^+$, 197 $[C_6H_5Sn]^+$, 120 $[Sn]^+$.

$(C_6H_5)_2CH_3SnOC(O)CCl_3$: m.p. > 300°C. Anal. calcd. for $C_{15}H_{13}O_2Cl_3Sn$ (%): C, 40.01; H, 2.91. Found: C, 39.02; H, 2.73. Mass spectrum data, tin-bearing fragments: m/e 415 $[(C_6H_5)_2CH_3SnOC(O)CCl_2]^+$, 373 $[C_6H_5CH_3SnOC(O)CCl_3]^+$, 358 $[C_6H_5SnOC(O)CCl_3]^+$, 323 $[C_6H_5SnOC(O)CCl_2]^+$, 226 $[CH_3SnOC(O)CCl]^+$, 197 $[C_6H_5Sn]^+$, 120 $[Sn]^+$ Infrared, ^1H, ^{13}C, and ^{119}Sn NMR data for the prepared compounds are listed in Table 1.

RESULTS AND DISCUSSION

Triorganotin carboxylates, as shown in Fig. 1, adopt several types of structure in the solid state [8]. The crystal structures of several triorganotin carboxylates demonstrate that the pentacoordinated tin stabilized through bridging carboxylate is mostly favored [13]. In the simplest triorganotin carboxylates, trimethyltin acetate, the oxygen atom of the acetate and the carbonyl oxygen of the acetate occupy the apical positions in the C_3SnO_2 polyhedron, a common feature in triorganotin compounds [14], to form a polymer with zig-zag configuration. The bridging carboxylate in organotin compounds is simply followed by infrared spectroscopy with shift of $\nu(CO_2)$ bands, as compared to the parent carboxylic acid. In the infrared spectra of $(C_6H_5)_2CH_3SnOC(O)CH_3$, $(C_6H_5)_2CH_3SnOC(O)CH_2$-$Cl$, $(C_6H_5)_2CH_3SnOC(O)CHCl_2$, and $(C_6H_5)_2CH_3$-$SnOC(O)CCl_3$ the $\nu_{asym}(CO_2)$ and $\nu_{sym}(CO_2)$ modes appear at 1548, 1430; 1563, 1431; 1607, 1399; and 1644, 1364 cm^{-1}, respectively. These bands significantly are shifted to the lower energy region in comparison to the corresponding acids, which clearly demonstrate bridged carboxylate structures for them (**A**, see Fig. 1). Furthermore, the single absorption bands corresponding to $\nu(Sn-C)$ in the 540–545 cm^{-1} region for the above triorganotin carboxylates indicate that the SnC_3 moiety is planer, consistent with the suggested structures. In addition, there is a steady increase in $\nu_{asym}(CO_2)$ and decrease in $\nu_{sym}(CO_2)$ modes with increasing halogenation on
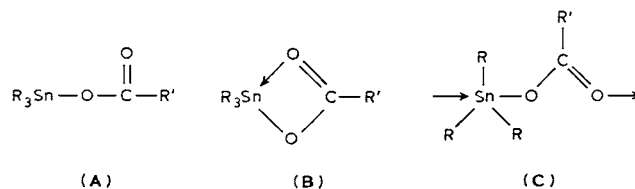

FIGURE 1 The possible geometries for triorganotin carboxylates.

TABLE 1 Infrared, ^{1}H, ^{13}C, and ^{119}Sn NMR Data for Diphenylmethyltin Acetates

Compound	^{1}H NMR	^{13}C NMR[a]	^{119}Sn NMR	IR (cm^{-1})
$(C_6H_5)_2CH_3SnOC(O)CH_2Cl$	δ 1.05 s (3H) δ 4.1 s (2H) δ 7.3–7.8 m (10H) $^2J(^{119}Sn-C-^1H)$, 60 Hz $^2J(^{119}Sn-C-^1H)$, 71 Hz[a]	δ −3.3 (CH_3) δ 42.7 (CH_2) δ 128.5 (C_{meta}, $J^{117/119}Sn-^{13}C$, 265 Hz), δ 129.4 (C_{para}, $J^{117/119}Sn-^{13}C$, 54 Hz) δ 136.2 (C_{ortho}, $J^{117/119}Sn-^{13}C$,183 Hz), δ 141.6 (C_{ipso}, $J^{117/119}Sn-^{13}C$, no[b])	δ 21.6	1563 s, $\nu_{asym}(COO)$ 540 s, $\nu(Sn-CH_3)$
$(C_6H_5)_2CH_3SnOC(O)CHCl_2$	δ 1.09 s (3H) δ 6.0 s (1H) δ 7.3–7.8 m (10H) $^2J(^{119}Sn-C-^1H)$, 61 Hz $^2J(^{119}Sn-C-^1H)$, 71 Hz[a]	δ −0.6 (CH_3) δ 74.2 (CH) δ 129.2 (C_{meta}, $J^{117/119}Sn-^{13}C$, 277 Hz), δ 130.1 (C_{para}, $J^{117/119}Sn-^{13}C$, no) δ 136.6 (C_{ortho}, $J^{117/119}Sn-^{13}C$,185 Hz), δ 142.9 (C_{ipso}, $J^{117/119}Sn-^{13}C$, no) [c][d]	δ 38.7	1607 s, $\nu_{asym}(COO)$ 541 s, $\nu(Sn-CH_3)$
$(C_6H_5)_2CH_3SnOC(O)CCl_3$	δ 1.15 s (3H) δ 7.3–7.7 m (10H) $^2J(^{119}Sn-C-^1H)$, 117 Hz[c]	[c][d]	δ −146.3[c]	
$(C_6H_5)_2CH_3SnOC(O)CH_3$[e]	0.85 s (3H) δ2.0 s (3H) δ 7.3–7.8 m (10H) $^2J(^{119}Sn-C-^1H)$, 59 Hz $^2J(^{119}Sn-C-^1H)$, 70 Hz[a]	δ −4.9 (CH_3) δ 20.8 (CH_3) δ 128.6 (C_{meta}, $J^{117/119}Sn-^{13}C$, 247 Hz), δ 130.2 (C_{para}, $J^{117/119}Sn-^{13}C$, no) δ 136.2 (C_{ortho}, $J^{117/119}Sn-^{13}C$, 214 Hz), δ 139.6 (C_{ipso}, $J^{117/119}Sn-^{13}C$, no)	δ −35.0	1607 s, $\nu_{asym}(COO)$ 541 s, $\nu(Sn-CH_3)$

[a]In CD_3OD.
[b]No: not observed.
[c]Because of insufficient solubility recorded in DMSO.
[d]Insufficient solubility to record ^{13}C NMR.
[e]From reference 11, recorded on JELO-90 spectrometer.

the acetate group. The magnitude of $\nu_{asym} - \nu_{sym}$ ($\Delta\nu$) separation has been used to explain the type of carboxylate structure present [15]. The magnitude of $\nu_{asym} - \nu_{sym}$ ($\Delta\nu$) separation for all diphenylmethyltin acetates are in the expected range for the bridged carboxylate triorganotin acetates. Apparently, with increasing $\Delta\nu$ the interaction of carboxylate group oxygen and the tin atom increases and consequently the polymeric structure tightens. Interestingly, this is parallel with decreases in their solubility. Obviously, it is expected that with increasing halogenation on the acetate group the Lewis basicity of the carbonyl diminishes and the Lewis acidity of tin atom increases. The predominant effect may be revealed only by crystal structure determination. Surprisingly, $\nu_{asym}(CO_2)$ absorption bands of all diphenylmethyltin acetate in the solid state show splitting with frequency separation of about 15–25 cm^{-1}, such splitting observed in solution for dimethyltin chloride acetates, which previously has been attributed to the rotational isomerism [16], may be only because of the lowering symmetry of the SnC_3 skeleton.

The ^{1}H, ^{13}C, and ^{119}Sn NMR data for all triorgantin carboxylates in the present study are given Table 1. The methyl group protons chemical shifts of the diphenylmethyltin moiety clearly are assigned from the hydrogen-tin coupling pattern and resonance intensity. The available $^{2}J(^{119}Sn-C-^{1}H)$ values in a noncoordinating solvent indicate that the diphenylmethyltin acetate and its mono- and dichloro acetate derivatives do not retain solid state structures in solution. The insufficient solubility of diphenylmethyltin trichloroacetate in chloroform did not allow us to record the ^{1}H NMR spectrum and reach a similar conclusion. The increase in the $^{2}J(^{119/117}Sn-C-^{1}H)$ coupling constants from 60 Hz in chloroform to 70–71 Hz in methanol reveals a five-coordinated tin atom in a coordinating solvent for the above mentioned compounds. This value elevates to 117 Hz for trichloroacetate derivatives in DMSO, which shows further extension of the tin coordination number. In fact, similar to other triorganotin acetates [17], polymeric solid state structures of diphenylmethyltin acetates in solution depolymerize to their monomers as a four-coordinated species and then coordination of solvent returns it to the five- or six-coordinated status. The $^{2}J(^{119}Sn-C-^{1}H)$ value also slightly increases with increasing chlorine substitution on the acetate group, a trend which is similar to that found for trimethyltin chloroacetates and opposite to that of dimethyltin chloride chloroacetates [16]. The increase in $^{2}J(^{119}Sn-C-^{1}H)$ values with increase in chlorine substitution on the acetate group may be interpreted as an increase in Lewis

acidity of tin rather than as a significant reduction in Lewis basicity of the carboxylate carbonyl oxygen. However, the values clearly exhibit the presence of tetra-coordinated tin in noncoordinating solvents [18]. The increase in chemical shifts of the acetate group protons with increasing halogenation on the acetate group is believed to be due to the electron-withdrawing nature of chlorine; the similar effect on the methyltin protons is less drastic.

The ^{13}C resonances of the aromatic part are assigned according to signal intensities, chemical shifts and aromatic $^{n}J(^{117/119}Sn-^{13}C)$ coupling constants (4,9). The ortho, meta and para carbon–tin couplings are observed for the diphenyltin moieties whereas the ispo carbon–tin coupling are not visible. The reason for this is not known at this time; however, it seems that because of the multiple coupling splitting of ispo and methyl carbons to tin, the tin satellites are dispersed. Probably, this behavior is a feature of mixed alkyl/aryl substituted triorganotin compounds. Although the $^{1}J(^{117/119}Sn-^{13}C_{ispo})$ coupling constants for the title compounds are not visible, which according to Holecek and Tiekink are good indicators of the coordination number of tin in triorganotin compounds [19,20], the chemical shift of ispo carbons at 139.6, 141.6, and 142.9 ppm reveal a five coordinated tin atom for the present triorganotin carboxylates in methanol [20].

The ^{119}Sn NMR chemical shifts in chloroform are also in the expected range for tetra-coordinated tin compounds, which confirms that the solid structure is not intact in solution [21], and their trend in chemical shifts is likewise to the acetate group protons in the ^{1}H NMR.

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