Organometallics **2000,** *19,* 703−706

$^{13}C-^{119}Sn$ Correlation NMR in Solution and Solid-State CP/MAS NMR of Bis(tributylstannyl(IV)) *O*-5,6-Isopropylidene-L-(+)-ascorbate†

A. Lyčka*

Research Institute for Organic Syntheses, CZ-532 18 Pardubice-Rybitví, Czech Republic

D. Micák and J. Holeček

Department of General and Inorganic Chemistry, University of Pardubice,
CZ-532 10 Pardubice, Czech Republic

M. Biesemans, J. C. Martins, and R. Willem*

High Resolution NMR Centre and Unit of General and Organic Chemistry, Free University of
Brussels (VUB), Pleinlaan 2, B-1050 Brussels, Belgium

Received September 23, 1999

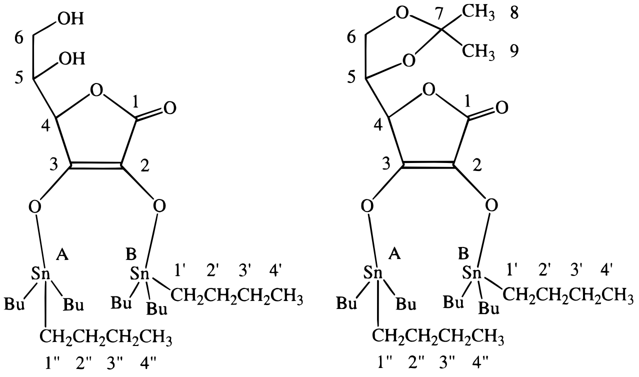
Summary: Various NMR correlation techniques, $^{1}H-^{13}C$ HMQC, $^{1}H-^{13}C$ HMBC, $^{1}H-^{119}Sn$ HMQC with gradient enhancement, and $^{13}C-^{119}Sn$ HMQC, enabled a full resonance assignment and the solution structure elucidation of bis(tributylstannyl(IV)) L*-(+)-ascorbate (***1***) and O-5,6-isopropylidene-*L*-(+)-ascorbate (***2***) in deuteriochloroform. Double heteronuclear $^{13}C-^{119}Sn$ HMQC spectroscopy appeared indispensable for discriminating between $^{2}J(^{13}C-O-^{119}Sn)$ and $^{3}J(^{13}C=C-O-^{119}Sn)$ coupling pathways involving quaternary carbon atoms and provided useful information about the relative magnitudes of $^{2}J(^{13}C-^{119}Sn)$ and $^{3}J(^{13}C-^{119}Sn)$ coupling constants, as they turned out to have an uncommon coupling size sequence. While the tin atoms in compounds* **1** *and* **2** *are four-coordinate in solution, ^{117}Sn CP/MAS NMR reveals that compound* **2** *has one four-coordinate and one five-coordinate tin atom in the solid state.*

Introduction

Organotin derivatives of bio-organic compounds have attracted growing interest because of their biological properties.[1] This raises the issue of their detailed structural elucidation using multinuclear 2D NMR techniques in solution, as recently illustrated for a tin derivative of erythromycin A.[2] Tin derivatives of another natural compound of interest, ascorbic acid, have been recently reported by Casas et al.,[3] who investigated NMR spectra of dimethyltin(IV) and dibutyltin(IV) L-(+)-ascorbates in aqueous solutions and in the solid state.

This study reports the synthesis and structure determination in solution and solid state of two novel tin-containing derivatives of ascorbic acid, i.e., bis(tributylstannyl(IV)) L-(+)-ascorbate (**1**) and bis(tributylstannyl(IV)) *O*-5,6-isopropylidene L-(+)-ascorbate (**2**) (Scheme 1).

Scheme 1



1 2

We present a full resonance and structure assignment strategy using $^{13}C-^{119}Sn$ correlation NMR as an essential tool in solution as well as ^{13}C and ^{117}Sn CP/MAS NMR for the solid state. Double heteronuclear $^{13}C-^{119}Sn$ correlation NMR, so far only described once by Berger and Mitchell,[4] turned out necessary to discriminate between two pairs of $^{2}J(^{13}C-O-^{119}Sn)$ and $^{3}J(^{13}C=C-O-^{119}Sn)$ coupling pathways involving quaternary carbon atoms. It enabled us to obtain interesting information with regards to the relative magnitudes of $^{2}J(^{13}C-^{119}Sn)$ and $^{3}J(^{13}C-^{119}Sn)$ coupling constants which are of relevance to structural organotin chemistry. ^{13}C and ^{117}Sn CP/MAS NMR experiments provide information on the coordination at tin in the solid state of compound **2**, which, unfortunately, appeared unsuitable for X-ray diffraction analysis.

Experimental Section

Syntheses. Bis(tributylstannyl(IV)) L-(+)-Ascorbate (1). To Bu_3SnOCH_3 (1.85 g, 5.76 mmol)[5] in 10 mL of dry ethanol in a 50 mL Schlenk tube was added L-(+)ascorbic acid (0.507 g, 2.88 mmol) in 20 mL of dry ethanol. The mixture was heated under argon atmosphere at 80 °C until the acid

---

† Dedicated to Prof. Dr. K.-H. Thiele on the occasion of his 70th birthday.

(1) de Vos, D.; Willem, R.; Gielen, M.; van Wingerden, K. E.; Nooter, K. *Metal Based Drugs* **1998**, *5*, 179.

(2) Martins, J. C.; Willem, R.; Mercier, F. A. G.; Gielen, M.; Biesemans, M. *J. Am. Chem. Soc.* **1999**, *121*, 3284.

(3) Casas, J. S.; Castano, M. V.; Garcia-Tasende, M. S.; Péres-Alvarez, T.; Sánches, A.; Sordo, J. *J. Inorg. Biochem.* **1996**, *65*, 97.

(4) Berger, S.; Mitchell, T. N. *Organometallics* **1992**, *11*, 3481.

(5) Alleston, D. L.; Davies, A. G. *J. Chem. Soc.* **1962**, 2050.

10.1021/om9907526 CCC: $19.00
Publication on Web 01/21/2000

was completely dissolved. Subsequently, the volume of the solution was reduced to 50% by distillation under normal pressure. The residual solvent was removed by distillation in vacuo. The product was a yellowish liquid that darkens upon standing at room temperature. Yield of isolated product: 1.92 g (88%). Anal. Found: C, 47.36; H, 7.78; Sn, 31.44. Calcd for $C_{30}H_{60}O_6Sn_2$: C, 47.78; H, 8.02; Sn, 31.48.

Bis(tributylstannyl(IV)) *O*-5,6-Isopropylidene-L-(+)-ascorbate (2). Compound **2** was prepared analogously to compound **1** from 1.41 g (4.39 mmol) of Bu_3SnOCH_3 and *O*-5,6-isopropylidene-L-(+)ascorbic acid (0.475 g, 2.20 mmol). A white solid was obtained. Yield of isolated product: 1.77 g (86%). Mp: 57−59 °C. Anal. Found: C, 49.79; H, 8.20; Sn, 30.23. Calcd for $C_{33}H_{64}O_6Sn_2$: C, 49.90; H, 8.12; Sn, 29.89.

NMR Measurements. The ^{1}H (360.13 MHz), ^{13}C (90.56 MHz), and ^{119}Sn (134.35 MHz) NMR spectra were recorded at 300 K from deuteriochloroform solutions on a Bruker AMX 360 spectrometer equipped with a 5 mm broadband probe and a 5 mm broadband inverse probe with z-shielding. ^{1}H and ^{13}C chemical shifts were referred to internal $Si(CH_3)_4$ ($\delta = 0.00$), and ^{119}Sn chemical shifts were referred to external neat $Sn(CH_3)_4$ placed in a coaxial capillary ($\delta = 0.00$).

The ^{13}C (125.79 MHz)−^{119}Sn (186.53 MHz) HMQC spectrum[4] was recorded at 303 K on a Bruker AMX 500 instrument equipped with a Silicon Graphics SGIO2 computer and a BSMS digital lock, using a ^{13}C spectral width of 190 ppm and a ^{119}Sn spectral width of 12 ppm, with appropriate folding of the low-frequency ^{119}Sn resonance (SnB) along F_1 in order to improve digital resolution. Eight FIDs of 16K data points were recorded with 3840 scans and a recycling delay of 10 s. The delay for heteronuclear coupling evolution was set to 28 ms. ^{1}H decoupling was applied during acquisition. Processing consisted of zero-filling in F_1 to 32 K (no zero-filling in F_2), followed by a sine-bell multiplication and magnitude FT calculation.

The gradient enhanced ^{1}H−^{13}C HMQC, ^{1}H−^{13}C HMBC, and ^{1}H−^{119}Sn HMQC 2D spectra were recorded as explained previously.[6]

^{13}C (62.90 MHz) and ^{117}Sn (89.13 MHz) CP/MAS NMR spectra of compound **2** were recorded on a Bruker DRX 250 spectrometer. Compound **2** was packed in a standard 4 mm ZrO_2 rotor. The ^{117}Sn Hartmann−Hahn cross-polarization match was set with tetracyclohexyltin using a ^{1}H 90° pulse of 5 μs. Cross-polarization contact time and recycling delay were set to 2 ms and 4 s, respectively. Two spinning rates (5 and 9 kHz) were used to identify the isotropic chemical shift. The number of scans varied between 200 and 800. ^{117}Sn chemical shifts were referred to tetracyclohexyltin ($\delta = -97.35$) taken as a secondary reference. The principal components of the ^{117}Sn shielding tensors were analyzed according to Herzfeld and Berger[7] using WINFIT software.[8] They are reported, following Haeberlen's notation,[9] as the isotropic chemical shift [$\delta_{iso} = -\sigma_{iso} = -(\sigma_{11} + \sigma_{22} + \sigma_{33})/3$] (ppm), the anisotropy ($\zeta = \sigma_{33} - \sigma_{iso}$), and the asymmetry ($\eta = |\sigma_{22} - \sigma_{11}|/|\sigma_{33} - \sigma_{iso}|$), σ_{11}, σ_{22}, and σ_{33} being the three components of the shielding tensor expressed in its principal axis system with the following rule: $|\sigma_{33} - \sigma_{iso}| \geq |\sigma_{11} - \sigma_{iso}| \geq |\sigma_{22} - \sigma_{iso}|$. With this convention, ζ is signed and expressed in ppm.

Results and Discussion

The complete, final $^{117/119}$Sn and ^{13}C resonance assignments for compounds **1** and **2**, including scalar coupling data, are given in Table 1.

Table 1. ^{119}Sn and ^{13}C Chemical Shifts (ppm) and $^nJ(^{119}Sn-^{13}C)$ Coupling Constants[a] (values in Hz) for Compounds 1 and 2 in $CDCl_3$ and/or the Solid State

	1 ($CDCl_3$)	**2** (solid)	**2** ($CDCl_3$)
C1	174.7 $^3J = 9$	178.5	174.7 $^3J = 9$
C2	122.5 $^3J = 9$; $^2J = 23$	120.4	122.8 $^3J = 9$; $^2J = 23$
C3	155.3 $^3J = 12$; $^2J = 29$	164.3	155.2 $^3J = 12$; $^2J = 26$
C4	77.9 $^3J = 9$	75.4 or 74.3	77.1 $^3J = 9$
C5	72.1	74.3 or 75.4	76.1
C6	63.4	65.5	65.5
C7		115.0	109.3
C8, C9[b]		26.7−28.5[e]	26.2, 25.7
C1′[c]	17.8 ($^1J = 364$)	17.1−21.2[f]	18.0 ($^1J = 365$)
C1″[d]	18.0 ($^1J = 349$)	17.1−21.2[f]	18.0 ($^1J = 350$)
C2′[c]	27.7 ($^2J = 18$)	26.7−28.5[e]	27.8 ($^2J = 18$)
C2″[d]	27.5 ($^2J = 20$)	26.7−28.5[e]	27.6 ($^2J = 21$)
C3′[c]	26.9 ($^3J = 64$)	26.7−28.5[e]	27.0 ($^3J = 64$)
C3″[d]	27.0 ($^3J = 66$)	26.7−28.5[e]	26.9 ($^3J = 68$)
C4′, C4″	13.5	12.6−14.4	13.5
^{119}Sn	123.6 (SnB) 152.5 (SnA)	112.0 (SnB) 18.1 (SnA)	118.6 (SnB) 146.0 (SnA)

[a] $^nJ = {}^nJ(^{13}C-^{119}Sn)$ (n = 1, 2, or 3). [b] Diastereotopic methyl groups. [c] Bu_3SnB. [d] Bu_3SnA. [e] Overlapping ranges of ^{13}C signals for C8, C9, C2′, C2″, C3′, C3″. [f] Overlapping ranges of ^{13}C signals for C1′ and C1″.

The solution assignment, as explained below for **2**, is extrapolated to **1**, on the basis of their very similar NMR data, while the solid-state ^{13}C assignment for **2** (**1** is a liquid) is based on a comparison of ^{13}C data in solution and solid states.

The assignments are pairwise not evident for the olefinic quaternary carbons C2 and C3, the tertiary carbons C4 and C5, and the tin atoms SnA and SnB. Furthermore, the ^{13}C assignment of the butyl carbons to the tin atom to which the butyl group is bound is likewise not straightforward. Compound **2** poses the question of the correct assignment of the $^2J(^{13}C-O-^{119}Sn)$ and $^3J(^{13}C=C-O-^{119}Sn)$ coupling pathways for the quaternary carbons C2 and C3 to the tin atoms SnB and SnA to which they are respectively linked through a bridging oxygen atom. While it is well recognized[10] that usually $^2J(^{13}C-^{119}Sn)$ coupling constants are smaller than $^3J(^{13}C-^{119}Sn)$ ones in aliphatic carbon chains, this rule is far from being applicable without risk to errors to the $^2J(^{13}C-O-^{119}Sn)$ and $^3J(^{13}C=C-O-^{119}Sn)$ coupling pathways.

Compound **2** displays two well-separated and narrow ^{119}Sn resonances at 146.0 and 118.6 ppm. Also in the ^{13}C spectrum, two sets of signals are associated with all carbons of the two Bu_3Sn groups (except for the methyl ones; Figure 1a).

The ^{1}H NMR signals of the butyl group protons are not sufficiently separated to be assigned by a 2D ^{1}H−^{13}C HMQC spectrum. By contrast, the characteristic ^{1}H4 doublet, appearing at 4.32 ppm, well separated from the ^{1}H5 and ^{1}H6 multiplets around 4.0 ppm, allows the identification of the ^{13}C4 resonance through their ^{1}H−^{13}C HMQC cross-peak, the identification of the ^{13}C5 resonance then following logically. The ^{13}C6 resonance is easily identified from its different DEPT pattern.

---

(6) Willem, R.; Bouhdid, A.; Kayser, F.; Delmotte, A.; Gielen, M.; Martins, J. C.; Biesemans, M.; Tiekink, E. R. T. *Organometallics* **1996**, *15*, 1920.

(7) Herzfeld, J.; Berger, A. E. *J. Chem. Phys.* **1980**, *73*, 6021.

(8) Massiot, D.; Thiele, H.; Germanus, A. *Bruker Rep.* **1994**, *140*, 43.

(9) Haeberlen, U. *Adv. Magn. Reson. Suppl.* **1976**, 1.

(10) Wrackmeyer, B. *Annu. Rep. NMR Spectrosc.* **1985**, *16*, 73.

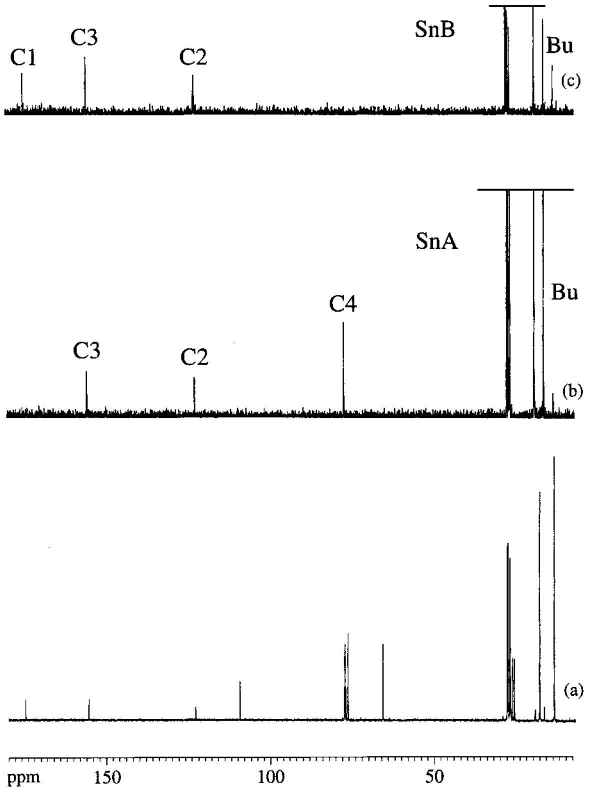


Figure 1. (a) ^{13}C NMR spectrum of compound **2**. (b) Cross-section, parallel to the ^{13}C axis, of its 2D ^{13}C$-$^{119}Sn HMQC spectrum at the ^{119}Sn resonance frequency of tin atom SnA (146.0 ppm) in F_1. (c) Cross-section of the 2D ^{13}C$-$^{119}Sn HMQC spectrum at the ^{119}Sn resonance frequency of tin atom SnB (118.6 ppm).

The application of a 2D ^{1}H$-$^{119}Sn heteronuclear correlation[6,11] allows the ^{119}Sn resonances to be identified. Thus the high-frequency ^{119}Sn resonance at 146.0 ppm displays an intense correlation cross-peak with the ^{1}H4 resonance and a weaker one with the ^{1}H5 resonance; by contrast the low-frequency ^{119}Sn resonance at 118.6 ppm displays only a weak cross-peak with the ^{1}H4 resonance and none with the ^{1}H5 one. This assigns the ^{119}Sn resonance at 146.0 ppm to the tin atom SnA bound to carbon C3, the one at 118.6 ppm to the SnB tin atom bound to carbon C2, in line with a prediction resulting from the fact that the ^{119}Sn NMR resonance is high-frequency shifted for the tin atom bound to the oxygen of the more acidic starting acid (pK_A(C3OH) = 4.03; pK_A(C2OH) = 11.3).[3] The ^{119}Sn resonance assignment being achieved, the ^{13}C resonances of the butyl groups are then easily assigned to their respective tin atoms through their ^{n}J(^{119}Sn$-$^{13}C) coupling satellites, which are well visible at the feet of the ^{119}Sn resonances in the standard ^{119}Sn spectrum.

Identification of the ^{13}C2 and ^{13}C3 resonances is possible from the 2D ^{1}H$-$^{13}C HMBC spectrum. The ^{13}C resonance at 155.2 ppm displays ^{1}H$-$^{13}C HMBC cross-peaks with the ^{1}H4 and ^{1}H5 resonances, while, by contrast, that at 122.8 ppm correlates solely with the ^{1}H4 resonance. The ^{13}C resonances at 155.2 and 122.8 ppm are therefore assigned to the C3 and C2 carbon atoms, respectively, in accordance with ^{13}C literature data[12] on β,γ-olefinic ketones. The ^{13}C2 and ^{13}C3 resonances both display two pairs of unresolved ^{n}J-(^{13}C$-$$^{119/117}$Sn) satellites amounting to ca. 9 and 25 Hz, arising all from ^{2}J(^{13}C$-$O$-$$^{119/117}$Sn) and ^{3}J(^{13}C=C$-O-$$^{119/117}$Sn) coupling pathways involving both SnA and SnB atoms.

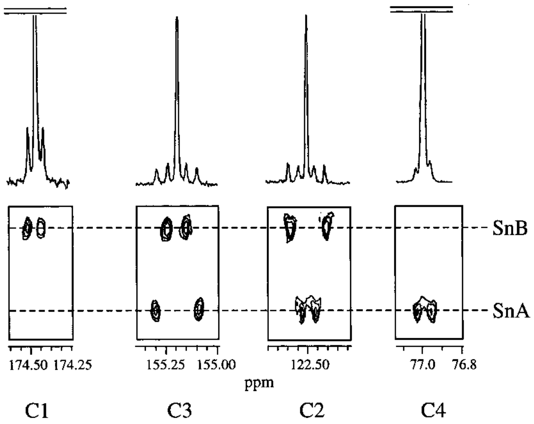


Figure 2. Expansions, at the resonance frequencies of the ^{13}C resonances of carbons C1, C3, C2, and C4 along F_2, of the 2D contour plot of the ^{13}C$-$^{119}Sn HMQC spectrum of compound **2**; the ^{119}Sn resonance chemical shift scales along F_1 are not given because the signal SnB does not appear at its actual chemical shift, having been folded into F_1 (see Experimental Section).

None of the 2D correlation techniques used above enables one to unambiguously discriminate between the ^{2}J and ^{3}J couplings, unless empirical assumptions are formulated as to their relative sizes.[10] This issue can be addressed most efficiently by a ^{13}C$-$^{119}Sn double heteronuclear HMQC experiment.[4] In addition, one such single experiment enables one to check the self-consistency of the ^{13}C and ^{119}Sn assignments proposed above from several 2D experiments.

Although it is customary to use the most sensitive nucleus for detection in a X$-$Y correlation,[13] we decided to detect ^{13}C nuclei for the following reasons: (i) ^{13}C resonances are commonly much sharper than those of ^{119}Sn, while we wanted to detect quite small coupling constants; (ii) the ^{119}Sn spectral window is narrower, in the present case, than the ^{13}C one, and, moreover, a folding can be used to minimize the 2D data matrix at a given digital resolution in the F_1 (^{119}Sn) dimension, since only two ^{119}Sn resonances are present. The preparation delay was set to the compromise ^{n}J(^{13}C$-$^{119}Sn) coupling value of 18 Hz.

Figure 1b,c shows the two-row cross-sections of the 2D ^{13}C$-$^{119}Sn HMQC spectrum at both ^{119}Sn resonance frequencies, confirming the above assignments of both the SnA/SnB and the C2/C3 atom pairs. Figure 2 shows an expansion of the contour plots obtained in the 2D ^{13}C$-$^{119}Sn HMQC spectrum for the ^{13}C2 and ^{13}C3 resonances of interest, as well as for the ^{13}C1 and ^{13}C4 ones, the only ones of the ascorbate moiety to show ^{13}C$-$^{119}Sn HMQC correlations.

---

(11) Kayser, F.; Biesemans, M.; Gielen, M.; Willem, R. In *Advanced Applications of NMR to Organometallic Chemistry*; Gielen, M., Willem, R., Wrackmeyer, B., Eds.; John Wiley: Chichester, 1996; Chapter 3, p 45.

(12) Kalinowski, H. O.; Berger, S.; Braun, S. *Carbon-13 NMR Spectroscopy*; John Wiley: Chichester, 1988.

(13) Berger, S.; Fäcke T.; Wagner, R. In *Advanced Applications of NMR to Organometallic Chemistry*; Gielen, M., Willem, R., Wrackmeyer, B., Eds.; John Wiley: Chichester, 1996; Chapter 2, p 29.

The cross-peak pairs associated with the ^{119}SnB resonance show that the ^{13}C2$-$^{119}SnB correlation doublet exhibits a larger scalar coupling splitting than the ^{13}C3$-$^{119}SnB doublet, which unambiguously demonstrates that the $^2J(^{13}\text{C2}-\text{O}-^{119}\text{SnB})$ coupling constant is larger than the $^3J(^{13}\text{C3}{=}\text{C2}-\text{O}-^{119}\text{SnB})$ one. Analogously, the cross-peak pairs associated with the ^{119}SnA resonance show that the ^{13}C3$-$^{119}SnA correlation doublet exhibits a larger scalar coupling splitting than the ^{13}C2$-$^{119}SnA doublet, which again unambiguously demonstrates that the $^2J(^{13}\text{C3}-\text{O}-^{119}\text{SnA})$ coupling constant is larger than the $^3J(^{13}\text{C2}{=}\text{C3}-\text{O}-^{119}\text{SnA})$ one. This uncommon coupling size sequence[10] for $^2J(^{13}\text{C}-^{119}\text{Sn})$ and $^3J(^{13}\text{C}-^{119}\text{Sn})$ coupling constants is worth stressing, because it can be of prime importance in resonance assignments as well as solution structure elucidations of organotin compounds in general.

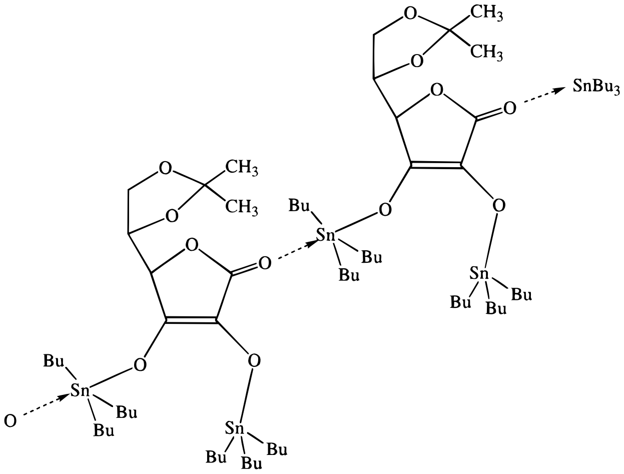
The ^{117}Sn CP/MAS NMR spectrum of compound **2** (SnB $\delta_{\text{iso}} = 112.0$, $\sigma_{11} = \sigma_{22} = -95.2$ and $\sigma_{33} = -145.7$, $\eta = 0$, $\zeta = 33.7$; SnA $\delta_{\text{iso}} = 18.1$, $\sigma_{11} = \sigma_{22} = 74.5$ and $\sigma_{33} = -203.2$, $\eta = 0$, $\zeta = 185.1$) reveals that SnB is four-coordinate, while SnA is five-coordinate in the solid state.[14] This can be explained by an intermolecular coordination involving the carbonyl oxygen and the C3$-$O$-$SnA tin atom, as illustrated in Scheme 2.

Further evidence for the existence of such an intermolecular coordination is found in the ^{13}C chemical shift differences between the solution and solid states which are largest at the level of the C3 (respectively 155.2 vs 164.3 ppm) and C=O (respectively 174.7 vs 178.5 ppm) carbon atoms. An alternative explanation, where the O1 carbonyl oxygen would coordinate the SnB atom, either intra- or intermolecularly, cannot explain satisfactorily the dramatic ^{13}C chemical shift change at C3.

Conclusion

The solution-state structure of compounds **2** and **1** was unambiguously elucidated by various 2D correlation techniques. Especially the ^{13}C$-$^{119}Sn HMQC experiment proved to be indispensable for discriminating between $^2J(^{13}\text{C}-^{119}\text{Sn})$ and $^3J(^{13}\text{C}-^{119}\text{Sn})$ coupling pathways involving quaternary carbon atoms, revealing that the sequence $^3J(^{13}\text{C}-^{119}\text{Sn}) > {}^2J(^{13}\text{C}-^{119}\text{Sn})$ usually observed in aliphatic chains[10] is not applicable to $^2J(^{13}\text{C}-\text{O}-^{119}\text{Sn})$ and $^3J(^{13}\text{C}{=}\text{C}-\text{O}-^{119}\text{Sn})$ coupling pathways.

Scheme 2



From the five-coordination of only one tin atom, together with the ^{13}C chemical shift differences between solution and solid states, an intermolecular coordination between SnA and the carbonyl oxygen is proposed for compound **2** in the solid state.

Acknowledgment. A.L. and J.H. thank the Grant Agency of the Czech Republic for financial support (Grant No. 203/97/0502) and the Ministry of Education, Youth and Sports of the Czech Republic, associated with the European Union in the COST 8.20 program. R.W. and M.B. acknowledge financial support from the Fund for Scientific Research Flanders (Belgium; Grant FWO G.0192.98) and the Research Council of the "Vrije Universiteit Brussel".

Supporting Information Available: ^{117}Sn CP/MAS NMR spectrum of **2**. This material is available free of charge via the Internet at http://pubs.acs.org.

OM9907526

---

(14) Sebald, A. In *Advanced Applications of NMR to Organometallic Chemistry*; Gielen, M., Willem, R., Wrackmeyer, B., Eds.; John Wiley: Chichester, 1996; Chapter 5, p 123.