APPLIED ORGANOMETALLIC CHEMISTRY
Appl. Organometal. Chem. **13**, 595–603 (1999)

The Interaction of S,N-coordinated Dimethyltin(IV) Derivatives with Deoxyribonucleic Acid: Structure and Dynamics by ^{119}Sn Mössbauer Spectroscopy

Renato Barbieri,[1]* Friedo Huber,[2] Arturo Silvestri,[1] Giuseppe Ruisi,[1] Mario Rossi,[1] Giampaolo Barone[1] and Adriana Barbieri Paulsen[3]
[1]Dipartimento di Chimica Inorganica, Università di Palermo, Viale delle Scienze, I-90128 Palermo, Italy
[2]Fachbereich Chemie, Universität Dortmund, D-44221 Dortmund, Germany
[3]Institut für Physik, Medizinische Universität Lübeck, Ratzeburger Allee 160, D-23538 Lübeck, Germany

Complexes $Me_2SnCl(SPy)$ and $Me_2SnCl(SPym)$ (HSPy = 2-mercaptopyridine; HSPym = 2-mercaptopyrimidine), from ethanol solutions, interact with aqueous calf-thymus DNA yielding condensed phases with probable $Me_2Sn(SPy,SPym)$ (DNA monomer) stoichiometries of 1:1; the condensation of DNA is inferred originated from electrostatic bonding between complex cations $Me_2Sn(SPy,SPym)^+$ and the phosphate oxygen of the phosphodiester groups. Octahedral-or trigonal-bipyramidal tin environments are inferred from the point-charge model treatment of the ^{119}Sn Mössbauer parameter nuclear quadrupole splitting, considering the bonding by S and N, or only S donor atoms from the ligand, as well as possible coordination by H_2O molecules. The dynamics of tin atoms in the condensed systems $Me_2Sn(SPym)$ (DNA monomer), in both gel and lyophilized phases, have been investigated by variable-temperature ^{119}Sn Mössbauer spectroscopy, obtaining evidence of a general correspondence as reported in the literature for the lyophilized condensates $Alk_2Sn(DNA\ monomer)_2$; possible analogies for $Me_2Sn(SPym)$ (DNA monomer) and $Alk_2Sn(DNA\ monomer)_2$ in DNA bonding, and structures of tin environments, are discussed. 'Neutral' complexes, such as $Me_2Sn(SPy)_2$, neither induce DNA condensation, nor bind to DNA in solution phases.

Keywords: organotin; DNA; Mössbauer; structure

Received 18 August 1998; accepted 22 February 1999

INTRODUCTION

The structure of tin environments, and the dynamics of tin nuclei in condensed phases (gelled and lyophilized), obtained by the interaction of calf-thymus deoxyribonucleic acid (DNA) with $MeSnCl_3$, R_2SnCl_2, R_3SnCl (R = alkyl,aryl), have previously been investigated by ^{119}Sn Mössbauer spectroscopy;[1–4] model systems in aqueous phases have been studied.[5] Research in the field, reported in the present paper, has been extended to the interaction of DNA with dimethyltin(IV) moieties coordinated by 2-mercaptopyridine (HSPy) and 2-mercaptopyrimidine (HSPym) (footnotes a and b in Table 1), the complexes being characterized by chelation of tin by S,N donor ligand atoms.[6–8] These heterocycles belong to the same class as the nucleic acid bases, and the occurrence of HSPym has been detected in RNA.[9]

Triorganotin(IV) in an oligodeoxyribonucleotide,[10] and thiobases in relation to nucleosides, nucleotides and nucleic acids,[11,12] have recently been investigated.

Thiol sulfur–tin bonds in $Me_2Sn(IV)$ complexes with $^-$SPy and $^-$SPym are expected to persist even in water and ethanol solutions, and in the ternary

* Correspondence to: Professor Renato Barbieri, Dipartimento di Chimica Inorganica, Università di Palermo, Viale delle Scienze, I-90128 Palermo, Italy.
Contract/grant sponsor: Ministero per l'Università e la Ricerca Scientifica e Tecnologica.
Contract/grant sponsor: Fonds der Chemischer Industrie.
Contract/grant sponsor: European Community.

 CCC 0268–2605/99/080595–09 $17.50

Table 1 ^{119}Sn Mössbauer hyperfine parameters for complexes of $Me_2Sn(IV)$ with 2-mercaptopyridine (HSPy)[a] and 2-mercaptopyrimidine (HSPym)[b] in frozen ethanol solutions, and in pellets (gel) or supernatants obtained by interaction with calf thymus DNA (see Experimental section) (T = 77.3 K)

No.	Compound or system	δ[c](mm s^{-1})	ΔE[d] (mm s^{-1})	Γ[e] (mm s^{-1})
1	$Me_2SnCl(SPy)$ in EtOH	1.31	2.98	1.01
2	$Me_2Sn(SPy)$(DNA monomer)[f]			
	Doublet A	1.25	4.29	0.75
	Doublet B	1.15	3.11	0.97
3	$Me_2SnCl(SPym)$ in EtOH	1.31[g]	3.22[g]	0.92[g]
4	$Me_2Sn(SPym)$(DNA monomer)[f]			
	Doublet A	1.31	4.43	0.79
	Doublet B	1.22	3.13	0.97
5	$Me_2Sn(SPy)_2$ in EtOH	1.35	2.58	0.82
6	$Me_2Sn(SPy)_2$ + DNA, supernatant	1.34	2.68	0.77

[a] Thiol form 

[b] Thiol form 

[c] Isomer shift with respect to room-temperature $CaSnO_3$. Average data.
[d] Nuclear quadrupole splitting. Average data.
[e] Full width at half height of the resonant peaks $\Gamma_1 = \Gamma_2$ imposed in the fit. Average data.
[f] Gelled DNA condensates obtained from $Me_2SnCl(SPy)$ + DNA and $Me_2SnCl(SPym)$ + DNA, r = 1.0.
[g] Ref. 8.

systems dimethyltin(IV)–$^-$SPy, $^-$SPym–DNA condensates, accounting for the large stability constants shown by Sn–S bonds detected for example in $Me_3Sn(IV)$–SR derivatives.[13]

The interaction of metal complexes with nucleic acids, polynucleotides, and constituent molecules, has been widely investigated.[14–20] In the context of organotin(IV) coordination chemistry, the binding of Et_2SnCl_2(*o*-phenanthroline) to nucleotides and plasmid DNA has recently been reported.[21] Results concerning such ternary systems would help in the interpretation of structure–activity relationships in the context of antitumor properties of organotin(IV) derivatives.[22]

EXPERIMENTAL

Me_2SnCl_2 was prepared by literature methods (see Refs 6 and 8), or was obtained from Schering; 2-mercaptopyridine and 2-mercaptopyrimidine were from Fluka Chemie AG. Calf thymus DNA, mol.wt $\simeq 10^6$, was from Serva Feinbiochemica, and the buffer tris(hydroxymethyl)aminomethane [Tris; $(HOCH_2)_3C(NH_2)$] from Sigma. Other reagents and solvents were Carlo Erba products.

The complexes formed by $Me_2Sn(IV)$ with $^-$SPy and $^-$SPym (Table 1) were obtained by the procedures reported in Refs 6 and 8.

The concentration of solutions of calf-thymus DNA employed in the present work, in triply distilled water, was in the range 15–20 mM (in monomer units, mol.wt = 315);[23] they were buffered to pH $\approx$ 8 by 1 mM Tris, in the presence of 0.1 mM ethylenediamine tetra-acetate (EDTA).

The DNA monomer concentrations were determined by UV spectrophotometry (ε_{260} = 7000 M^{-1} cm^{-1}).[23]

The systems and absorber samples for studying the interactions of dimethyltin(IV) complexes and DNA (Table 1), were obtained by adding ethanol solutions of $Me_2Sn(IV)$ 2-mercaptopyridinates and 2-mercaptopyrimidinates to DNA in aqueous Tris–EDTA, the molar ratios of complex and DNA monomer being held at 1:1. Systems **2** and **4** (Table 1) yielded condensed phases, which were separated by centrifugation, the pellets and supernatants being submitted to Mössbauer spectroscopy. System **6** yielded a solution, from which a DNA pellet was obtained by addition of NaCl (0.1 M in the resulting solution) and C_2H_5OH (2 vols), i.e., the conditions for obtaining gelled DNA by salting-out.[24]

The ^{119}Sn Mössbauer parameters determined for the condensed phases of systems **2** and **4** (Table 1),

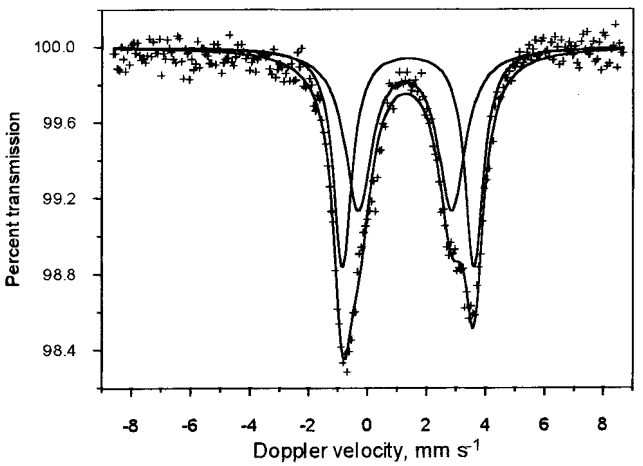


Figure 1 The ^{119}Sn Mössbauer spectrum of Me_2Sn(SPy)(DNA monomer), system **2** in Table 1, and fitting with two symmetric doublets.

from spectra such as that shown in Fig. 1, were independent of the procedure of addition of the ethanolic solutions of the complexes to DNA (dropwise, or addition in one or two steps). Moreover, it has been determined that: (i) ethanol solutions of the complexes (**1, 3, 5** in Table 1) were not influenced by addition of H_2O (up to 50% by volume) with respect to the solubility of the complexes; (ii) DNA in Tris–EDTA solutions did not undergo condensation by addition of C_2H_5OH up to ~50% by volume.

The formation of dimethyltin(IV) complex–DNA condensates (**2** and **4** in Table 1) was monitored by UV spectrophotometry of the supernatants, as well as of the pellets redissolved in aqueous Tris–EDTA (λ_{max} = 260 nm, ε = 7000 for DNA monomer[23]), the occurrence of Me_2Sn^{IV} in the two phases being monitored by the absorption, ε, of the Mössbauer spectral lines, and also accounting for the UV spectra of the Me_2Sn(IV) –$^-$SPy and $^-$SPym complexes (M. Rossi, unpublished results). In fact, the $^-$SPy complexes of Me_2Sn(IV) and MeSn(IV) showed, *inter alia*, absorption bands with $\lambda_{max} \approx$ 269–273 and ≈ 340–346 nm, while the related $^-$SPym complexes gave $\lambda_{max} \approx$ 272–273 nm, in 1 mM Tris–0.1 mM EDTA–1% C_2H_5OH (M. Rossi, unpublished results. A. Barbieri Paulsen, unpublished results.); these absorption bands correspond to data reported for aqueous solutions of the ligands (H)SPy (as well as for *N*-methylpyridine-2-thione), pH = 3.1–7.0,[25,26] and (H)SPym, pH = 13.[27,28]

The apparatus, procedures, and data reduction for ^{119}Sn Mössbauer spectroscopy at 77.3 K as well as in the studies of ^{119}Sn dynamics by variable-temperature measurements (vtMs) were as previously described.[3] The UV–Vis spectra were measured with a Perkin-Elmer Lambda 15 spectrophotometer. Measurements of pH were effected with a Crison 2002 instrument, equipped with an Ingold glass electrode. The conductances and molecular weights of the Me_2Sn(IV)–$^-$SPy and –$^-$SPym complexes in ethanol solutions (**1, 3, 5** in Table 1) were measured with a conductivity meter (Radiometer CDM 83) and with a vapor pressure osmometer (Gonotec Osmomat 070). Lyophilized samples employed in dynamics studies of Me_2Sn-(SPym)–DNA condensates (Table 2) were obtained with Heto lyophilizers.

RESULTS AND DISCUSSION

First, solutions of complexes Me_2SnCl(SPy), Me_2SnCl(SPym) and $Me_2Sn(SPy)_2$ in ethanol were investigated, in order to interpret correctly their possible interaction with DNA in ethanol–water solutions.

Molar conductances Λ_M (corrected for solvent conductivity) at 25 °C, and van't Hoff *i* factors at 37 °C (by vapor pressure osmometry), have been determined. Representative ranges of the data obtained we report below.

(a) Me_2SnCl(SPy), 7.08–0.18 mM in C_2H_5OH: Λ_M = 0.61–4.20 S cm^2 mol^{-1}. Me_2SnCl(SPy), 3.93–8.18 mM in C_2H_5OH: *i* = 1.10–1.44.

Table 2 ^{119}Sn Mössbauer hyperfine parameters and molecular dynamics data functions for $Me_2Sn(SPym)$(DNA monomer) determined by variable-temperature ^{119}Sn Mössbauer spectroscopy (vtMs) on pellets (DNA condensates)

Absorber sample[a]	δ[b] (mm s^{-1})	ΔE[c] (mm s^{-1})	Γ_1, Γ_2[d] (mm s^{-1})	10^2d ln (A_T/$A_{77.3}$)/dT[e] (K^{-1})	ϑ_D[f] (K)	No. of data points (T range, K)[g]
Gel, doublet A	1.342 (±0.016)	4.443 (±0.031)	0.791 (±0.028)			
				−1.228 (0.989)	54.9	10 (77.3–140.5)
Gel, doublet B	1.195 (±0.028)	3.526 (±0.120)	0.945 (±0.044)			
Lyophil., doublet A	1.347 (±0.009)	4.409 (±0.016)	0.708 (±0.037)			
				−1.309 (0.996)	53.2	8 (77.3–240.75)
Lyophil., doublet B	1.183 (±0.010)	3.268 (±0.033)	1.039 (±0.030)			

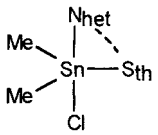
[a] DNA pellet; gel = gelled condensate; lyophil = lyophilized (freeze-dried) condensate. A, B: see Fig. 1 and Table 1.
b–d See footnotes c–e, Table 1; averaged over data in the temperature range 77.3–119.27 K (gel) and 77.3–181.59 K (lyophil). d $\Gamma_1 = \Gamma_2$, imposed in the fitting of the two-line spectra.
[e] Slopes of functions of normalized total areas under the resonant peaks [Lorentzian, $A = (\pi/2)$, ε Γ, ε being the percentage resonant effect] vs T; correlation coefficients in parentheses. Total areas mean the sum of the areas of doublets A + B (Fig. 1) at any given temperature determination in the ranges 77.3 K–T_{max} in each series.
[f] Debye temperatures obtained from the slopes of the collective ln ($A_T/A_{77.3}$) vs T functions (Fig. 3 and Eqn 1). The effective vibrating mass EVM = 575 is assumed to correspond to the $Me_2Sn(SPym)$: DNA monomer stoichiometry 1:1, M = 315 for DNA monomer unit. See text, Results and Discussion section.
[g] The total number of spectra determined, on two series of gels and lyophilized absorbers, respectively, obtained from individual preparations and submitted to vtMs.

(b) $Me_2SnCl(SPym)$, 6.85–0.27 mM in C_2H_5OH: Λ_M = 0.67–3.00 S cm^2 mol^{-1}. $Me_2SnCl(SPym)$, 5.81–8.61 mM in C_2H_5OH: i = 1.08–1.17.
(c) $Me_2Sn(SPy)_2$, 5.91–0.19 mM in C_2H_5OH: Λ_M = 0.07–1.63 S cm^2 mol^{-1}. $Me_2Sn(SPy)_2$, 4.59–7.65 mM in C_2H_5OH: i = 0.99–1.75.

From the data under (a) and (b), it is inferred that molecular, undissociated, species are essentially present in C_2H_5OH solutions, the Λ_M values being consistently lower than those for organotin chlorides in C_2H_5OH, for example.[2] Moreover, i values indicate correspondence between experimental and calculated (monomeric) molecular weights; this is in analogy to findings for $CHCl_3$ solutions.[6–8]

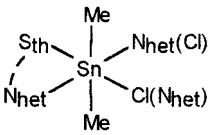
The configuration of the tin environments in the (frozen) ethanol solutions (a)–(c) (*vide supra*) has been inferred from ^{119}Sn Mössbauer spectroscopy,[29] the structures in the glassy phase reflecting those in solution at room temperature.[2,5,29] The measured Mössbauer parameters are reported in Table 1 (**1, 3, 5, 6**), and related structural assignments are in Fig 2. The latter concern the point-charge model treatment[29] of ΔE, nuclear quadrupole splitting parameters, by the 'literal' version,[29] idealized regular structures being assumed to occur. The narrowness of the linewidths, Γ (Table 1, **1, 3, 5, 6**), indicates the occurrence of a single tin coordination site in each complex. Taking into account also that: (i) a large series of $^-$SPy and $^-$SPym complexes of $R_nSn(IV)$ moieties in $CDCl_3$ and $(CD_3)_2SO$ solutions maintain chelation of tin by S and N donor atoms, according to IR and ^{1}H, ^{13}C- and ^{119}Sn-NMR spectroscopic data;[6–8] (ii) the complex $Me_2SnCl(SPym)$, **3** in Table 1, possibly polymeric in the solid state (Ib, Fig. 2), is monomeric in $CDCl_3$ solution;[8] in comparison with solid-state structures, it is assumed that the structural variations occurring in ethanol solutions of the complexes **1, 3** and **5** (Table 1) concern only the possible coordination of C_2H_5OH molecules to tin centers (II and III, Fig. 2). The latter would be expected to take place especially for tin species being five-coordinated in the solid state, e.g. as detected for $Ph_2SnCl(SPy)$ in $(CD_3)_2SO$ solution, by ^{13}C- and ^{119}Sn-NMR.[6] The ethanol solution structures II and III (Fig. 2), are consequently assumed to occur, and are also in accord with the rule of Clark *et al.*,[30] i.e. ($|\Delta E_{calcd}| - |\Delta E_{exp}|$) $\leq$ 0.4 mms^{-1}; then, these species would eventually interact with DNA in the condensation process (see the Experimental section).

Multivalent cations cause DNA condensation *'in vitro'* by counterion association to phospho-



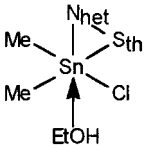
(I a) (Ref. 6)

ΔE_{calcd} = -2.94
(solid state:
ΔE_{exp} = 2.78)



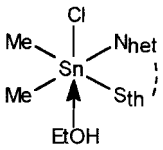
(I b) (Ref. 8)

ΔE_{calcd} = 3.42; 3.50
(solid state:
ΔE_{exp} = 3.20-3.53)



(II)

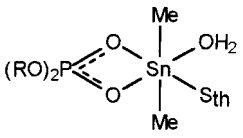
ΔE_{calcd} = -2.91



(III)

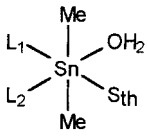
ΔE_{calcd} = -3.14

Complexes **1** and **3**, Table 1: solids such as (I a), (I b) turn to (II) or (III), or assume structure (I a), in ethanol solution



(IV)

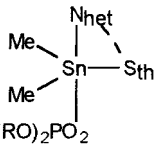
ΔE_{calcd} = 4.09



(V)

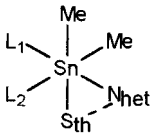
$L_1 = H_2O$,
$L_2 = (RO)_2PO_2^-$:
ΔE_{calcd} = 4.10

$L_1 = (RO)_2PO_2^-$,
$L_2 = H_2O$:
ΔE_{calcd} = 4.12



(VI)

ΔE_{calcd} = -3.19

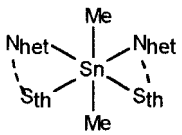


(VII)

$L_1 = (RO)_2PO_2^-$,
$L_2 = H_2O$:
ΔE_{calcd} = -2.78

$L_1 = H_2O$,
$L_2 = (RO)_2PO_2^-$:
ΔE_{calcd} = -2.82

Systems **2** and **4**, Table 1: (IV) or (V), doublet A; (VI) or (VII), doublet B



(VIII) (Ref. 6)

ΔE_{calcd} = 2.80
(solid state: ΔE_{exp} = 2.55)

Systems **5** and **6**, Table 1

Figure 2 Point-charge model idealized regular structures for the environment of tin in complexes $Me_2SnCl(SPy,SPym)$ and $Me_2Sn(SPy)_2$ in the solid state and in solution phases (**1, 3, 5, 6** in Table 1), and for gelled condensates $Me_2Sn(SPy,SPym)$ (DNA monomer) (**2** and **4** in Table 1). Partial nuclear quadrupole splittings, pqs, employed in the calculations are from Refs 3, 6–8 and 29. The pqs value $([CH_3OH]–[Hal])^{oct} = +0.16$ mm s^{-1}, Ref. 40, has been employed for C_2H_5OH. ΔE_{calcd} data are in mm s^{-1}. N_{het}, S_{th}: Table 1, footnotes a, b.

diester groups;[31] condensed DNA phases have been obtained by addition of organotin(IV) chlorides, in aqueous (acidic) or ethanol solutions, to aqueous calf-thymus DNA.[1–4] In this context, DNA condensation by ethanolic $Me_2SnCl(SPy)$ and $Me_2SnCl(SPym)$, systems **2** and **4** in Table 1, is analogously interpreted in terms of electrostatic interaction of complex cations $Me_2Sn(SPy)^+$ and $Me_2Sn(SPym)^+$ with a phosphodiester group of calf-thymus DNA, in line with Cl^- dissociation in ethanol solution (although quite limited) detected by conductivity and osmometry (*vide supra*); the Cl^- dissociation would be expected to increase consistently in the final solutions of the organotin complex and DNA in ~50% EtOH in H_2O, considering the dissociation of Me_2SnCl_2 and Me_3SnCl in water.[32] The condensed DNA phases would then consist of $Me_2Sn(SPy)$(DNA monomer) and $Me_2Sn(SPym)$(DNA monomer) species, respectively. These show four-line ^{119}Sn Mössbauer spectra, as exemplified in Fig. 1.

The assumptions above correspond to hypotheses advanced for the interpretation of the interaction of the complex Et_2SnCl_2(*o*-phenanthroline) with DNA in aqueous solution,[21] where after dissociation of Cl^- the resulting complex cation would bind to a phosphodiester group of DNA,[21] in line with the principles of counterion association.[33]

The complex $Me_2Sn(SPy)_2$ does not provoke DNA condensation; by salting-out of DNA from the $Me_2Sn(SPy)_2$ + DNA solution, and separation of the gelled DNA condensate, it has been determined that the complex remains essentially in the solution phase, the ^{119}Sn Mössbauer parameters corresponding to the values shown in ethanol solution as well as in the solid state (**5** and **6**, Table 1 and Fig. 2). Consequently, structure VIII (Fig. 2) is inferred to be maintained in the solid state and in ethanol solution, without interacting with DNA.

Studies are under way in our laboratory on the nature of the 'neutral' complexes Me_2SnL_2 and $MeSnL_3$ (L = $^-$SPy, $^-$SPym) by interaction of DNA in solution phase. The complexes could intercalate into the DNA double helix through $^-$SPy and $^-$SPym, which would be in accordance with the observed lack of DNA condensation.[34] Besides, intercalation into DNA by ligands coordinated to metal centers has been detected in a number of systems,[16,18–20] including Et_2SnCl_2–(*o*-phenanthroline)–DNA.[21] Anyway, in the case of $Me_2Sn(SPy)_2$–DNA, no variations of Mössbauer parameters occur with respect to data for solid-state and ethanol solutions (e.g. Table 1, **5** and **6;** Fig. 2, VIII). This suggests lack of any type of interaction, including intercalation of the coordinated ligand into the DNA double helix; in the latter case the C–Sn–C moiety would be expected to undergo distortion due to steric hindrance effects, which would provoke variations, at least in the ^{119}Sn Mössbauer ΔE parameters.[29]

According to the assumed persistence of structure VIII (Fig. 2) for $Me_2Sn(SPy)_2$ in ethanol, as well as in water–ethanol solution in the presence of buffered DNA (**5** and **6** in Table 1), analogous structural features concerning the persistence of S and N chelation to Sn may be expected to occur in the systems **2** and **4** (Table 1). In fact, the Lewis acidity of tin in $Me_2SnCl(SPy)$ and $Me_2SnCl(SPym)$ should be greater than in $Me_2Sn(SPy)_2$, also in the presence of DNA. This assumption is in line with X-ray crystallographic data. Thus, Sn–N bond lengths decrease, as in the series $Ph_2Sn(SPy)_2$,[35] $Ph_2SnCl(SPy)$[6] ≈ $PhSn(SPy)_3$,[7] $Sn(SPy)_4 \cdot 2HSPy$,[36] $SnCl_2(SPy)_2$,[37] the Sn–S bond lengths being practically constant.[6,7,35–37] On the other hand, when dissociation of tin–ligand bonds occurs in the course of the DNA condensation process, this would concern only N→Sn bonds, e.g. in line with the stability constants reported for $Me_3Sn(IV)$ complexes,[13] $Sn–S_{thiol}$ > tin-phosphate (including mononucleotides) > $Sn–N_{het}$ (from pyridine).[13] Lastly, H_2O coordination to tin centers would possibly occur.

On these grounds, accounting also for the preferential *cis* configuration for two phosphodiester groups bound to tin in intra-chain interactions,[2,3] the possible point-charge model structures for tin environments in systems **2** and **4** (Table 1), obtained as described above, are reported in Fig. 2 (IV–VII), according to Clark's rule.[30] These trigonal-bipyramidal structures (obeying the Muetterties and Schunn rule, with the most electronegative groups being located in apical positions[38]) and also the octahedral structures are in accord with generally established geometries of tin environments in $R_2Sn(IV)$ complexes.[29]

The occurrence of two tin sites in the gelled condensates $Me_2Sn(SPy,SPym)$ (DNA monomer) (**2** and **4** in Table 1; Fig. 1; structures IV–VII in Fig. 2), has been detected also in $Alk_2Sn(DNA\ monomer)_2$ freeze-dried condensates,[3] which has been interpreted in terms of the persistence of the same type of structure for the tin environment, differing only in the C–Sn–C angle.[3] The latter could be assumed also for the ternary systems investigated here. Instead, condensates obtained by interaction of DNA with Alk_2SnCl_2 and Ph_2SnCl_2 in C_2H_5OH solutions are reported to show two-line ^{119}Sn

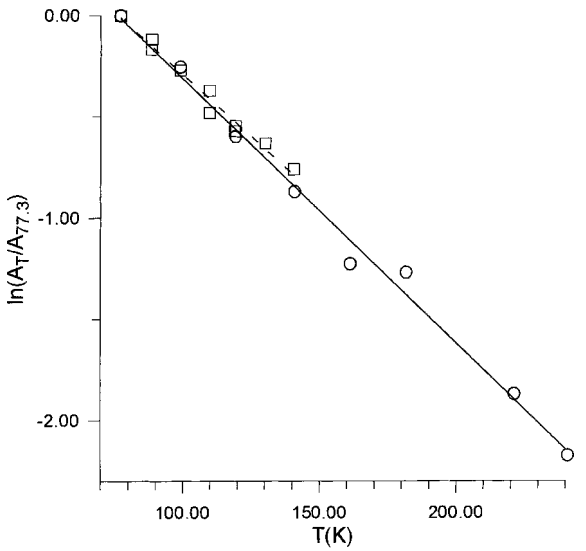


Figure 3 Functions ln ($A_T/A_{77.3}$) vs T for Me_2Sn(SPym)(DNA monomer) condensates, gel (□) and lyophilized (○). A = total Lorentzian area under the ^{119}Sn Mössbauer peaks (Table 2 and Fig. 1); all data points determined are reported (Table 2). Lines are least-squares fits $y = ax + b$ where slopes a are in Table 2 [$a = 10^2$ d ln ($A_T/A_{77.3}$)/dT] and intercepts b are as follows: (□) 0.938; (○) 0.997.

Mössbauer spectra, i.e. one doublet, in the gel phases,[1,2] analogous to R_3SnCl–DNA systems in both gels[2] and freeze-dried specimens.[3]

Additional information on the nature of the interaction of complexes $Me_2SnCl(L)$ (L = $^-$SPy, $^-$SPym) with DNA (Table 1 and Figs 1, 2) has been extracted from the dynamics of tin by variable-temperature Mössbauer spectroscopy (vtMs) as determined for the representative system Me_2Sn(SPym)(DNA monomer) on gelled as well as freeze-dried condensates.

The vtMs parameters A_T (the total area under the resonant peaks at variable temperature) were treated according to the 'relative' recoil-free fraction (f_a^{rel}) approach,[3,29,39] according to which the Lamb–Mössbauer factors (f_a) are estimated through the slope of the function ln $A_T(T)$ (Eqn 1):[3,29,39]

$$\frac{d(\ln A_T)}{dT} = \frac{(d \ln f_a)}{dT} = \frac{-3E_\gamma^2}{Mc^2k\theta_D^2} \qquad [1]$$

where A_T is the total area under the resonant peaks at a given temperature T, E_γ is the energy of the Mössbauer transition, M is the mass of the molecular unit taken as the effective vibrating mass (EVM), k is the Boltzmann constant and ∂_D the Debye temperature.[3,29,39] The mean-square displacement of the Mössbauer atom, $<x^2>$, is obtained by Eqn 2 [3,29,39]

$$f_a = \exp(-k^2\langle x^2\rangle) \qquad [2]$$

k being the wave vector of γ-rays.

The results obtained are reported in Table 2; functions ln ($A_T/A_{77.3}$) vs T, $f_a^{rel}(T)$ and $<x^2>(T)$ are shown in Fig. 3 and Fig. 4. The following inferences are made, being discussed in connection with data reported for Alk_2Sn(DNA monomer)$_2$, Alk_3Sn(DNA monomer) and $MeSnCl_n$(DNA monomer)$_{3-n}$:[3,4]

(i) In the T ranges investigated (Table 2 and Figs 3 and 4), parameters δ, ΔE and Γ are invariant (Table 2) and functions ln $A_T(T)$, ln $f_a(T)$ and $<x^2>(T)$ are linear (Figs 3 and 4), which excludes phase and glass transitions[3] for Me_2Sn(SPym)(DNA monomer) in both gelled and lyophilized condensed phases; these trends are in line with data reported for Alk_2Sn(DNA monomer)$_2$ and Alk_3Sn(DNA monomer) in lyophilized[3] and gelled[4] phases, respectively, as well as for gelled and lyophilized $MeSnCl_n$(DNA monomer)$_{3-n}$.[4]

(ii) The slopes of functions ln $A_T(T)$, the magnitudes of the Debye temperature ∂_D, and the values of ln $f_a(T)$ and $<x^2>(T)$ (Table 2 and Figs 3 and 4), concerning gelled and

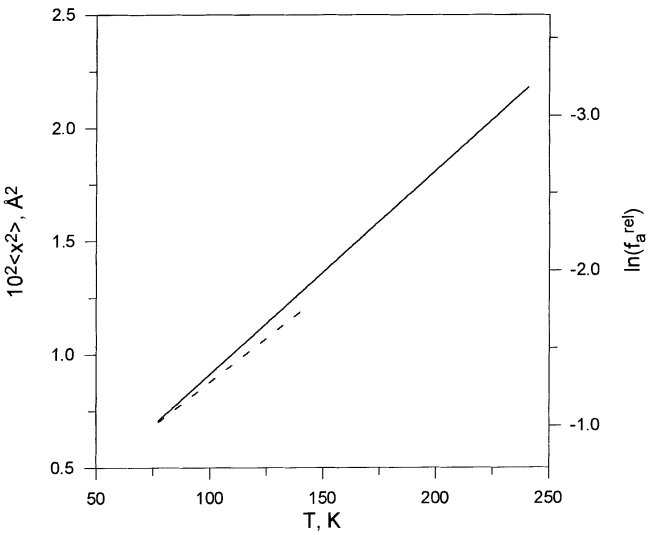


Figure 4 Recoil-free fractions of the absorber ^{119}Sn nuclei, f_a^{rel}, and the corresponding mean-square displacements of ^{119}Sn, $<x^2>$, as a function of temperature, for $Me_2Sn(SPym)$(DNA monomer) condensates, gel (- - -) and lyophilized (—). See text.

lyophilized condensates [$Me_2Sn(SPym)$(DNA monomer)], are almost mutually coincident. These findings correspond to trends detected for $MeSnCl_n$(DNA monomer)$_{3-n}$ condensates[4] [e.g. slopes $\ln A_T(T) = -0.866$ to $-0.944\,K^{-1}$ for gelled and lyophilized phases[4]].

The correspondence of the hyperfine parameters for $Me_2Sn(SPym)$(DNA monomer) in the gel and lyophilized condensed phases (Tables 1 and 2) then implies the persistence of structures such as IV–VII (Fig. 2), independently of the water content and temperature of the system. These trends are at variance with findings concerning Alk_2Sn(DNA monomer)$_2$ systems, where freeze-drying of the condensates creates a second tin coordination site, with respect to the single site occurring in the gelled phases,[1–3] and causes variations in the dynamical functions and parameters [e.g. the slope $\ln A_T(T)$ in Et_2Sn(DNA monomer)$_2$ is $-1.724\,K^{-1}$ in gelled[4] and $-1.250\,K^{-1}$ in lyophilized[3] condensates, analogous trends being detected for Et_3Sn(DNA monomer)[3,4]].

CONCLUSIONS

$Me_2SnCl(SPy,SPym)$ and $Me_2Sn(SPy)_2$ in C_2H_5OH solutions maintain their respective solid-state structures as far as chelation of tin by S and N donor ligand atoms is concerned; a limited dissociation into $Me_2Sn(SPy,SPym)^+$ and Cl^- is inferred to take place, producing a cationic complex species.

Tin atoms in the cationic complex species would be coordinated by DNA phosphodiester oxygen, with organotin/DNA monomer stoichiometry of 1:1, causing the DNA condensation. The latter does not occur with $Me_2Sn(SPy)_2$, presumably due to its insufficient dissociation. A close analogy with DNA condensation by Alk_2Sn(IV), Alk_3Sn(IV) and MeSn(IV) is then inferred.[1–4]

Tin coordination sites in the gelled and lyophilized $Me_2Sn(SPy,SPym)$ (DNA monomer) condensates show the same ^{119}Sn Mössbauer hyperfine parameters, i.e. corresponding to the structures of tin coordination environments: from a point-charge model treatment of the quadrupole splittings ΔE, inherent in the experimental four-line spectra (Fig. 1), ligands $^-$SPy and $^-$SPym would chelate Sn through S and N atoms in coordination type B (Fig. 2; trigonal-bipyramidal or *cis*-Me_2 octahedral structures VI and VII), while only S–Sn bonds would persist in coordination type A (Fig. 2; octahedral structures IV and V), according to data in Tables 1 and 2. The partial ligand dissociation of type A compounds may be a consequence of the occurrence of interaction of tin-coordinated $^-$SPy and $^-$SPym ligands with an adjacent DNA double helix in the toroidal[3] condensates.

The dynamics of tin in the ternary systems ligand–organotin(IV) species–nucleic acid investigated here, in both gelled and lyophilized DNA condensates, show a strict similarity with data inherent to lyophilized $Alk_2Sn(DNA\ monomer)_2$ condensates,[3] which suggests a correspondence in the mode of binding to DNA, as well as in the possible toroidal DNA[3] interchain interaction, in the two classes of DNA condensates.

The structure and dynamics of tin environments in the ternary systems are then independent of the H_2O content in the DNA condensed phases, analogously to findings[4] inherent in $MeSnCl_n(DNA\ monomer)_{3-n}$, and contrary[3] to $Alk_2Sn(DNA\ monomer)_2$ and $Alk_3Sn(DNA\ monomer)$ condensates.

REFERENCES

1. R. Barbieri and A. Silvestri, *J. Inorg. Biochem.* **41**, 31 (1991).
2. R. Barbieri, A. Silvestri, A. M. Giuliani, V. Piro, F. Di Simone and G. Madonia, *J. Chem. Soc., Dalton Trans.* 585 (1992).
3. R. Barbieri, G. Ruisi, A. Silvestri, A. M. Giuliani, A. Barbieri, G. Spina, F. Pieralli and F. Del Giallo, *J. Chem. Soc., Dalton Trans.* 467 (1995), and references therein.
4. S. Posante, Dissertation, University of Palermo, Italy (1996).
5. R. Barbieri, A. Silvestri and V. Piro, *J. Chem. Soc., Dalton Trans.* 3605 (1990).
6. R. Schmiedgen, F. Huber, H. Preut, G. Ruisi and R. Barbieri, *Appl. Organometal. Chem.* **8**, 397 (1994).
7. F. Huber, R. Schmiedgen, M. Schürmann, R. Barbieri, G. Ruisi and A. Silvestri, *Appl. Organometal. Chem.* **11**, 869 (1997).
8. R. Schmiedgen, F. Huber, A. Silvestri, G. Ruisi, M. Rossi and R. Barbieri, *Appl. Organometal. Chem.* **12**, 861 (1998), and references therein.
9. See, for example: J. Carbon, H. David and M. H. Studier, *Science* **161**, 1146 (1968).
10. H. Dougan, J. B. Hobbs, J. I. Weitz and D. M. Lyster, *Nucleic Acids Res.* **25**, 2897 (1997).
11. R. G. Kuimelis and K. P. Nambiar, *Nucleic Acid Res.* **22**, 1429 (1994).
12. K. Singh, B. Groth Vasselli, P. N. Farnsworth and D. K. Rai, *Res. Commun. Mol. Pathol. Pharmacol.*, **94**, 129 (1996).
13. M. J. Hynes and M. O'Dowd, *J. Chem. Soc., Dalton Trans.* 563 (1987).
14. A. Sigel and H. Sigel (eds) *Metal Ions in Biological Systems*, Vols 32 and 33 M. Dekker, New York, 1996.
15. G. Berthon (ed.), *Handbook of Metal–Ligand Interactions in Biological Fluids. Bioinorganic Chemistry* Vols 1 and 2, M. Dekker, New York, 1995.
16. M. Cusumano, M. L. Di Pietro and A. Giannetto, *Chem. Commun.* 2527 (1996).
17. W. Harada, T. Nojima, A. Shibayama, H. Ueda, H. Shindo and M. Chikira, *J. Inorg. Biochem.* **64**, 273 (1996).
18. M. Kharatishvili, M. Mathieson and N. Farrell, *Inorg. Chim. Acta*, **255**, 1 (1997).
19. S. Mahadevan and M. Palaniandavar, *Inorg. Chim. Acta* **254**, 291 (1997).
20. F. Zamora, V. M. González, J. M. Pérez, J. R. Masaguer, C. Alonso and C. Navarro Ranninger, *Appl. Organometal. Chem.* **11**, 491 (1997).
21. Q. Li, P. Yang, H. Wang and M. Guo, *J. Inorg. Biochem.* **64**, 181 (1996).
22. See, for example: B. K. Keppler (ed.), *Metal Complexes in Cancer Chemotherapy*, VCH Verlags-gesellschaft, Weinheim, New York, 1993.
23. S. D. Kennedy and R. G. Bryant, *Biophys. J.* **50**, 669 (1986).
24. See, for example: L. Grossman and K. Moldave (eds), *Nucleic Acids*, Part B, Vol. XII of *Methods in Enzymology*, Colowick, S. P. and Kaplan, N. O. (eds), Academic Press, New York, 1968.
25. A. Albert and G. B. Barlin, *J. Chem. Soc.* 2384 (1959).
26. R. A. Jones and A. R. Katritzky, *J. Chem. Soc.* 3610 (1958).
27. M. P. V. Boarland and J. F. W. McOmie, *J. Chem. Soc.* 3716 (1952).
28. J. Kister, D. Bouin-Roubaud, L. Bouscasse and J. Metzger, *Spectrosc. Lett.* **13**, 1 (1980).
29. See, for example: R. Barbieri, F. Huber, L. Pellerito, G. Ruisi and A. Silvestri, ^{119m}Sn Mössbauer studies on tin compounds. In: *Chemistry of Tin*, Smith, P. J. (ed.), Blackie Academic and Professional, London, 1998, Chapter 14, p. 496, and references therein.
30. M. G. Clark, A. G. Maddock and R. H. Platt, *J. Chem. Soc., Dalton Trans.* 281 (1972).
31. See, for example: V. A. Bloomfield, *Biopolymers* **44**, 269 (1998), and references therein.
32. See, for example: R. S. Tobias, *Organometal. Chem. Rev.* **1**, 93 (1966).
33. E. Nordmeier, *Macromol. Chem. Phys.* **196**, 1321 (1995).
34. See for example Z. Reich, R. Ghirlando, T. Arad, S. Weinberger and A. Minsky, *J. Biol. Chem.* **265**, 16004 (1990).
35. R. Schmiedgen, F. Huber and H. Preut, *Acta Crystallogr. Sect. C* **49**, 1735 (1993).
36. L. C. Damude, P. A. W. Dean, V. Manivannan, R. S. Srivastava and J. J. Vittal, *Can. J. Chem.* **68**, 1323 (1990).
37. M. Masaki, S. Matsunami and H. Ueda, *Bull. Chem. Soc. Jpn.* **51**, 3298 (1978).
38. E. L. Muetterties and R. A. Schunn, *Q. Rev. Chem. Soc.* **20**, 245 (1966).
39. R. Barbieri, A. Silvestri, L. Pellerito, A. Gennaro, M. Petrera and N. Burriesci, *J. Chem. Soc., Dalton Trans.* 1983 (1980), and references therein.
40. G. Ruisi, A. Silvestri, M. T. Lo Giudice, R. Barbieri, G. Atassi, F. Huber, K. Grätz and L. Lamartina, *J. Inorg. Biochem.* **25**, 229 (1985).

