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# Synthesis, characterization of diorganotin(IV) complexes of *N*-(2-hydroxyarylidene)amino-acetic acid and antitumour screening *in vivo* in Ehrlich ascites carcinoma cells

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**Some new diorganotin(IV) complexes have been prepared by reacting potassium *N*-(2-hydroxyarylidene)aminoacetate with $R_2SnCl_2$(R = Me,$^n$Bu,Ph). The complexes have been characterized by $^1$H,$^{13}$C,$^{119}$Sn NMR, IR and $^{119m}$Sn Mössbauer spectroscopic techniques in combination with elemental analysis. In the solid state, the complexes possess penta- and hexa-coordinated tin centres. The hexa-coordinated tin complexes were found to dissociate in solution, giving rise to penta-coordinated species as revealed by $^{119}$Sn NMR spectroscopy. Antitumour screening *in vivo* of the complexes $L^4SnPh_2$,$L^4SnPh_2{\cdot}Ph_3SnCl$ and $L^4Sn^tBu_2{\cdot}^tBu_2SnCl_2$ ($L^4$ = *N*-(2-hydroxyacetophenone)aminoacetate) is also reported. Copyright © 2001 John Wiley & Sons, Ltd.**

**Keywords: organotin; Schiff bases; amino acid; IR; NMR; antitumour activity; Ehrlich ascites carcinoma cells**

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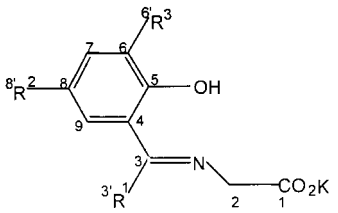
## INTRODUCTION

Interest in organotin(IV) complexes of the *N*-(2-hydroxyarylidene)aminoacetic acid framework is from two perspectives, viz. putative antitumour activity[1] and structural reasons.[2] In this context, we have recently reported the coordination behaviour of *N*-(2-hydroxyacetophenone)glycine towards the $R_2Sn$(IV) moiety;[3,4] the isolated monomeric complexes contain an additional potential oxygen-containing site. These complexes, on further treatment with $R_2SnCl_2$ or $R_3SnCl$, yielded mixed organotin dendritic complexes in which the two tin atoms are connected *via* the carbonyl atoms of the ligand molecule. Such organotin oxo clusters have potential as homogeneous catalysts[5] and in material science.[6,7] In addition, we have also reported a series of triorganotin(IV) derivatives of *N*-(2-hydroxyarylidene)aminoacetic acid.[8] X-ray structural studies of two complexes, *viz.* $Ph_3SnL^1H$ and $Me_3SnL^4H$ (ligand skeleton as described in Fig. 1), reveal a polymeric *trans*-$O_2SnC_3$ trigonal-bipyramidal configuration with the R groups in the equatorial positions and the axial locations occupied by a carboxylate oxygen from the ligand and the phenolic oxygen of the ligand on an adjacent complex. In the case of $Me_3SnL^4H$, the ligands coordinate in the zwitterionic form with the phenolic proton moved to the nearby nitrogen atom.

One of the goals of the present work was to explore the feasibility of using various $R_2Sn$ groups in the synthesis of organotin complexes of potassium *N*-(2-hydroxyarylidene)aminoacetate (LHK, Fig. 1). A second objective was to investigate the



(LHK)

| Abbreviation[a] | $R^1$ | $R^2$ | $R^3$ |
|---|---|---|---|
| $L^1HK$ | H | H | H |
| $L^2HK$ | H | Cl | H |
| $L^3HK$ | H | $NO_2$ | H |
| $L^4HK$ | $CH_3$ | H | H |
| $L^5HK$ | $CH_3$ | H | $CH_3$ |
| $L^6HK$ | $CH_3$ | $CH_3$ | H |

[a] H represents hydroxyl proton.

**Figure 1** The ligands used in present work.

structural consequences of such complexes in relation to their antitumour properties. For later purposes, we selected three different types of complex (see Table 1), *viz.* $L^4SnPh_2$ (**14**), $L^4SnPh_2{\cdot}Ph_3SnCl$ (**15**) and $L^4Sn^tBu_2{\cdot}^tBu_2SnCl_2$ (**16**), which are structurally characterized both in solution and in the solid state and subjected to antitumour activity *in vivo* towards Ehrlich ascites carcinoma (EAC) cells. The complexes **15** and **16** are expected to exhibit enhanced antitumour activity compared with complex **14**, since they contain two organotin moieties.[9]

# EXPERIMENTAL

## Materials

Dimethyltin dichloride (Fluka), diphenyltin dichloride (Aldrich), and di-*n*-butyltin dichloride (Merck) were used as received. The ligands ($L^1HK$–$L^6HK$) and $L^4HNa$ were prepared as described in earlier reports.[3,8] The solvents used in the reactions were dried using standard procedures.

## Measurements

Carbon, hydrogen and nitrogen analyses were performed with a Perkin Elmer 2400 series II instrument. IR spectra in the range 4000–400 $cm^{-1}$ were obtained on a Perkin Elmer 983 spectrophotometer with samples investigated as KBr discs. The $^1H$, $^{13}C$ and $^{119}Sn$ NMR spectra were acquired on a Bruker ACF 300 spectrometer and measured at 300.13 MHz, 75.47 MHz and 111.92 MHz respectively. The $^1H$, $^{13}C$ spectra were referenced to $Me_4Si$ and $^{119}Sn$ chemical shifts were referenced to $Me_4Sn$, all set at 0.00 ppm. $^{119}Sn$ Mössbauer spectra of the complexes in the solid state were obtained at liquid-nitrogen temperature on a conventional constant acceleration spectrometer equipped with a CRYO cryostat and a $^{119}Sn$ Mössbauer source. The velocity calibration was made using a $^{57}Co$ Mössbauer source, and an iron foil enriched to 95% in $^{57}Fe$ (DuPont Pharma Italia, Firenze, Italy) was used as the absorber. The $Ca^{119m}SnO_3$ and $^{57}Co$ sources, 10 mCi, were procured from Ritverc, St Petersburg, Russia. The NORMOS program was used to solve the Mössbauer spectrum of complex $L^4SnPh_2{\cdot}Ph_3SnCl$ (**15**).

## Syntheses

### Preparation of diorganotin(IV) complexes

A typical procedure is described below, using $L^4Sn^nBu_2$ (**10**) as an example.

$^nBu_2SnCl_2$ (0.50 g, 1.64 mmol) in 50 ml of methanol was added dropwise with continuous stirring to a hot methanol solution (50 ml) containing $L^4HK$ (0.378 g, 1.64 mmol). The reaction mixture was stirred at room temperature for 3 h, and the solvent was removed using a rotary evaporator. The dry mass was washed thoroughly with hot hexane, extracted into chloroform and filtered. A pale yellow product was obtained upon concentration of the chloroform. This was then recrystallized from the same solvent to yield pale yellow crystals of the desired product and dried *in vacuo*.

The other diorganotin complexes of *N*-(2-hydroxyarylidene)aminoacetic acids were prepared analogously using appropriate $R_2SnCl_2$ and LHK.

## Biological tests

The organotin(IV) complexes, *viz.* $L^4SnPh_2$ (**14**), $L^4SnPh_2{\cdot}Ph_3SnCl$ (**15**), $L^4Sn\ ^tBu_2{\cdot}^tBu_2SnCl_2$ (**16**) and $L^4HNa$, were dissolved in dimethyl sulfoxide (DMSO) and further diluted with DMSO in order to achieve the required working solution concentration. The animals of the control group were treated with only DMSO solutions (0.1 ml).

Male Swiss-albino mice, aged 7 weeks and weighing about 21–23 g [maintained in the labora-

**Table 1** The physical and analytical data for the diorganotin(IV) complexes

| Complex[a] | Reaction time (h) | Crystallization solvent | Colour | Yield (%) | M.p. (°C) | Elemental analysis: Found (calc.) (%) C | H | N |
|---|---|---|---|---|---|---|---|---|
| **1** $L^1SnMe_2{\cdot}OH_2$ | 2[b] | Chloroform + petroleum ether | Yellow | 59 | 133–135 | 38.30 (38.41) | 4.18 (4.40) | 3.96 (4.07) |
| **2** $L^1Sn^nBu_2{\cdot}OH_2$ | 3[c] | Chloroform | Pale yellow | 72 | 124–125 (123.5)[d] | 47.72 (47.70) | 6.25 (6.36) | 3.29 (3.23) |
| **3** $L^1SnPh_2$ | 3[b] | Chloroform | Yellow | 70 | 190–191 (183.5)[d] | 56.00 (56.04) | 3.78 (3.81) | 3.29 (3.11) |
| **4** $L^2SnMe_2{\cdot}OH_2$ | 2[b] | Benzene + chloroform | Yellow | 30 | 139–140 | 34.90 (34.92) | 3.70 (3.73) | 3.70 (3.70) |
| **5** $L^2Sn^nBu_2{\cdot}OH_2$ | 3[b] | Chloroform | Yellow | 40 | 120–122 | 44.20 (44.14) | 5.52 (5.67) | 3.20 (3.30) |
| **6** $L^2SnPh_2$ | 3[b] | Chloroform | Yellow | 45 | 130–132 | 52.15 (52.06) | 3.42 (3.33) | 2.95 (2.89) |
| **7** $L^3SnMe_2{\cdot}OH_2$ | 2[b] | Chloroform (large volume) | Pale yellow | 47 | >250 | 33.90 (34.15) | 3.20 (3.13) | 7.30 (7.24) |
| **8** $L^3SnPh_2{\cdot}OH_2$ | 3[b] | Chloroform (large volume) | Pale yellow | 26 | 226–228 (dec.) | 49.22 (49.16) | 3.44 (3.54) | 5.50 (5.46) |
| **9** $L^4SnMe_2{\cdot}OH_2$ | 2[b] | Chloroform | Pale yellow | 53 | 210–211 | 40.30 (40.26) | 4.80 (4.79) | 3.90 (3.91) |
| **10** $L^4Sn^nBu_2{\cdot}OH_2$ | 3[c] | Chloroform | Pale yellow | 70 | 77–78 | 49.02 (48.90) | 6.53 (6.61) | 3.33 (3.17) |
| **11** $L^5SnPh_2$ | 3[b] | Chloroform | Yellow | 79 | 170–172 | 57.65 (57.78) | 4.45 (4.43) | 3.00 (2.93) |
| **12** $L^6SnMe_2{\cdot}OH_2$ | 2[b] | Benzene | Pale yellow | 54 | 138–140 | 42.05 (41.98) | 5.15 (5.15) | 3.80 (3.77) |
| **13** $L^6SnPh_2$ | 3[b] | Chloroform | Yellow | 79 | 236–237[e] | 57.70 (57.78) | 4.40 (4.43) | 2.90 (2.93) |

[a] The complexes **14** $L^4SnPh_2$, **15** $L^4SnPh_2{\cdot}Ph_3SnCl$ and **16** $L^4Sn^tBu_2{\cdot}{}^tBu_2SnCl_2$ are included elsewhere for convenience of discussion; for details see Ref. 3.
[b] Method: stirring in methanol.
[c] Method: reflux in methanol–benzene mixture (1:1).
[d] Data taken from Ref. 10.
[e] Data taken from Ref. 4.

tory in communal cages in room under controlled temperature ($27 \pm 3$ °C) and lighting (12 h light/12 h dark) conditions on standard mouse diet (NMC Oil Mills Ltd, Pune, India) and water *ad libitum*] were used in all experiments. One hundred mice were divided randomly into five groups of 20 each.

EAC cells were maintained in 7-week-old male Swiss mice throughout intraperitoneal (i.p.) transplantation of $1 \times 10^6$ viable tumour cells to each mouse. On day 0, five groups of mice received tumour cells ($1 \times 10^6$ per mouse i.p.). On day 2, the complexes to be screened, **14, 15, 16** and $L^4HNa$, were injected (i.p.) into four different groups of mice. One untreated group, which received only DMSO, was kept as a control. Three animals from each group were sacrificed by cervical dislocation on the 12th or 13th day of cell implantation. Ascites fluid volume, packed cell volume and number of cells were then measured. The survival of drug-treated mice over controls was studied in the remainder of the mice.

## RESULTS AND DISCUSSION

Treatment of LHK with $R_2SnCl_2$ in equimolar ratio in methanol or methanol–benzene mixture yielded the diorganotin derivatives of composition $LSnR_2{\cdot}OH_2$ similar to that of the vinyl analogue[3] in most cases, except for complexes **3, 6, 11** and **13**, which were isolated as $LSnR_2$. A typical reaction is described in the Experimental section, whereas the synthetic details and characterization data are summarized in Table 1. The complexes are soluble in chloroform, methanol, ethanol and DMSO.

In our earlier communications[3,4,7] we have reported that the ligands are tridentate, and can coordinate to tin atom *via* an oxygen atom of a carboxylate group, a phenoxide oxygen atom and the imino nitrogen atom, as revealed by X-ray crystallography. On this basis, we discuss the spectroscopic results in relation to the structure of the complexes.

**Table 2** Characteristic IR bands ($cm^{-1}$) for the diorganotin(IV) complexes

| Complex | $\nu(OCO)_{asym}$ | $\nu(OCO)_{sym}$ | $\Delta\nu(OCO)$ | $\nu(C{=}N)$ | $\nu(Ph{-}(CO))$ |
|---|---|---|---|---|---|
| **1** | 1617[a] | 1389 | 228 | 1617[a] | 1286 |
| **2** | 1622 | 1394 | 228 | 1585 | 1249 |
| **3** | 1684 | 1433 | 251 | 1615 | 1214 |
| **4** | 1604[a] | 1382 | 222 | 1604[a] | 1241 |
| **5** | 1612[a] | 1372 | 240 | 1612[a] | 1239 |
| **6** | 1682 | 1441 | 241 | 1602 | 1238 |
| **7** | 1627 | 1398 | 229 | 1587 | 1245 |
| **8** | 1679 | 1431 | 248 | 1616 | 1226 |
| **9** | 1595[a] | 1375 | 220 | 1595[a] | 1235 |
| **10** | 1612[a] | 1372 | 240 | 1612[a] | 1239 |
| **11** | 1686 | 1451 | 235 | 1600 | 1233 |
| **12** | 1593[a] | 1369 | 224 | 1593[a] | 1226 |
| **13** | 1679 | 1450 | 229 | 1616 | 1226 |

[a] Vibrations due to both $\nu(OCO)_{asym}$ and $\nu(C{=}N)$ appeared as an unresolved broad peak.

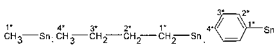
## IR spectra

Diagnostically important IR bands and their assignments are presented in Table 2. The potassium salts of the ligands display two bands at around 1630 $cm^{-1}$ and 1605 $cm^{-1}$ that are assigned to the $\nu(OCO)_{asym}$ and $\nu(C{=}N)$ stretching vibrations respectively, in accord with earlier reports.[3,8,11] In organotin(IV) complexes, these vibrations are shifted considerably owing to coordination through the carboxyl oxygen and the imino nitrogen atoms.[3] The $\nu(OCO)_{sym}$ stretches have been detected and the magnitude of $\Delta\nu(OCO)$ is in the range 220–251 $cm^{-1}$, indicating unidentate bonding through the carboxylate moiety.[8,12] Coordination through the phenolic oxygen atom is reflected in the lower wavelength shifts of the $\nu(Ph{-}(CO))$ vibration when compared with the sodium or potassium salts.[3] A medium intensity band due to Sn—O has been detected at around 540 $cm^{-1}$ in the com-

**Table 3** $^1H$ chemical shifts (ppm)[a] for the diorganotin(IV) complexes

| | Ligand skeleton[b] | | | | | | Sn—R skeleton[c] | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Complex | H-2 | H-6/6′ | H-7 | H-8/8′ | H-9 | H-3′ | 1* | 2* | 3* | 4* |
| **1** | 4.39 | 6.85 | 7.17 | 6.74 | 7.41 | 8.33 | 0.83 (89)[d] | – | – | – |
| **2** | 4.34 | 6.79 | 7.17 | 6.74 | 7.43 | 8.40 | 1.64 | 1.58 | 1.38 | 0.87 |
| **3** | 4.35 | 7.15 | 7.15 | 6.77 | 7.53 | 8.34 | – | 7.89 | 7.45 | 7.45 |
| **4** | 4.36 | 6.67 | 7.65 | – | 7.25 | 8.38 | 0.70 (93)[d] | – | – | – |
| **5** | 4.38 | 6.65 | 7.30 | – | 7.14 | 8.32 | 1.64 | 1.52 | 1.29 | 0.84 |
| **6** | 4.37 | 7.07 | 7.47 | – | 7.16 | 8.34 | – | 7.85 | 7.47 | 7.47 |
| **7** | 4.00 | 6.32 | 7.75 | – | 8.32 | 8.40 | 0.40 (93)[d] | – | – | – |
| **8** | 4.36 | 6.96 | 8.23 | – | 8.43 | 8.76 | – | 7.62 | 7.34 | 7.34 |
| **9** | 4.29 | 6.84 | 7.36 | 6.79 | 7.51 | 2.67 | 0.73 (78)[d] | – | – | – |
| **10** | 4.26 | 6.85 | 7.35 | 6.76 | 7.47 | 2.67 | 1.60 | 1.43 | 1.31 | 0.86 |
| **11** | 4.25 | 2.44 | 7.27 | 6.69 | 7.38 | 2.57 | – | 7.82 | 7.38 | 7.38 |
| **12** | 4.27 | 6.75 | 7.18 | 2.27 | 7.25 | 2.65 | 0.71 (75)[d] | – | – | – |
| **13** | 4.28 | 7.08 | 7.25 | 2.25 | 7.27 | 2.61 | – | 7.87 | 7.39 | 7.39 |

[a] In $CDCl_3$ except for complexes **4**, **7** and **8**, which are in DMSO-$d_6$.
[b] Refer to Fig. 1 for numbering scheme.
[c] Numbering scheme for Sn—R skeleton as shown below:



[d] $J(^1H{-}^{119}Sn)$ (Hz).

**Table 4** $^{13}C$ and $^{119}Sn$ chemical shifts (ppm)[a] for the diorganotin(IV) complexes

| | Ligand skeleton[b] | | | | | | | | | | Sn—R skeleton[b] ($^{n}J(^{13}C–^{119}Sn)$ (Hz)) | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Complex | C-1 | C-2 | C-3 | C-4 | C-5 | C-6 | C-7 | C-8 | C-9 | C-3′/6′/8′ | C-1* | C-2* | C-3* | C-4* | $^{119}Sn$ |
| **1** | 172.5 | 57.9 | 172.3 | 117.7 | 168.1 | 122.9 | 137.2 | 117.5 | 135.3 | – | 0.09 (–[c]) | – | – | – | −203.1 |
| **2** | 172.9 | 57.7 | 171.4 | 117.3 | 169.5 | 122.7 | 138.0 | 117.2 | 135.6 | – | 26.7 (–[c]) | 26.8 (–[c]) | 22.6 (–[c]) | 13.7 (–[c]) | −208.0 |
| **3** | 173.0 | 57.0 | 170.4 | 117.1 | 169.4 | 122.8 | 138.3 | 117.8 | 135.6 | – | 137.6 (–[c]) | 136.4 (57) | 128.9 (91) | 130.8 (23) | −335.4 |
| **4** | 171.7 | 56.6 | 170.1 | 119.3 | 165.1 | 122.9 | 135.0 | 119.2 | 132.4 | – | 0.70 (804) | – | – | – | –[d] |
| **5** | 171.2 | 58.1 | 171.2 | 117.6 | 167.7 | 124.5 | 137.2 | 121.0 | 133.4 | – | 26.1 (–[c]) | 27.0 (33) | 21.1 (85) | 13.5 (–[c]) | −200.0 |
| **6** | 172.1 | 57.3 | 170.2 | 117.6 | 167.9 | 124.6 | 138.2 | 122.1 | 133.7 | – | 137.3 (–[c]) | 136.4 (57) | 129.7 (91) | 131.0 (19) | −335.8 |
| **7** | 171.5 | 56.5 | 170.4 | 135.5 | 170.0 | 121.6 | 131.6 | 115.3 | 129.1 | – | 0.20 (800) | – | – | – | –[d] |
| **8** | 173.0 | 56.8 | 170.4 | 146.0 | 170.0 | 124.8 | 132.8 | 117.5 | 130.4 | – | 137.3 (–[c]) | 134.9 (–[c]) | 129.3 (–[c]) | 130.4 (–[c]) | –[d] |
| **9** | 181.7 | 53.3 | 170.4 | 121.1 | 165.7 | 123.5 | 135.9 | 117.9 | 130.5 | 22.9 | 0.08 (670) | – | – | – | −172.6 |
| **10** | 181.4 | 53.5 | 170.7 | 121.1 | 166.1 | 123.5 | 135.8 | 117.6 | 130.3 | 22.9 | 26.7 (–[c]) | 26.9 (35) | 21.0 (85) | 13.5 (–[c]) | −210.8 |
| **11** | 182.5 | 53.6 | 170.7 | 128.7 | 164.8 | 119.5 | 136.7 | 117.5 | 131.6 | 23.1/16.9 | 137.9 (–[c]) | 136.5 (54) | 128.9 (90) | 130.7 (20) | −349.4 |
| **12** | 181.5 | 53.2 | 170.3 | 126.9 | 163.5 | 123.2 | 137.2 | 120.6 | 129.8 | 22.8/20.5 | 0.30 (677) | – | – | – | −170.1 |
| **13** | 181.9 | 53.5 | 170.3 | 128.2 | 164.4 | 123.6 | 136.7 | 119.9 | 130.2 | 22.7/20.5 | 137.7 (–[c]) | 136.7 (56) | 128.8 (93) | 130.6 (20) | −349.8 |

[a] Refer to Table 3 for the solvents.
[b] Refer to Table 3 for numbering schemes.
[c] Could not be detected.
[d] Not determined.

plexes.[13] Thus, IR data provide reasonable evidence for complexation of the potentially multidentate ligand.

## NMR spectra

The $^{1}H$ and $^{13}C$ NMR data of the diorganotin complexes are shown in Tables 3 and 4 respectively. The $^{1}H$ and $^{13}C$ chemical shift assignments of the diorganotin moiety are straightforward from the multiplicity patterns and/or resonance intensities, whereas the ligand skeletons were assigned by multiplicity patterns and/or resonance intensities of the signals,[3,8] and also by standard distortionless enhancement by polarization transfer (DEPT) experiments. The $^{1}H$ and $^{13}C$ NMR spectra of the complexes show the expected resonances and integration.

In recording $^{119}Sn$ NMR spectra of organotin(IV) complexes in solution, non-coordinating solvents are preferrable to coordinating ones to preclude possible changes in the coordination number of the tin atom. In the present investigation, a few complexes were found to be suitable for recording $^{119}Sn$ NMR spectra in $CDCl_3$ solution. These are listed in Table 4. The $^{119}Sn$ chemical shifts of dialkyltin(IV) complexes occur between $-170$ and $-211$ ppm, which fall well within the range proposed for penta-coordinate tin centres.[14] Thus, $^{119}Sn$ NMR results indicate that the hexa-coordinated structure of diorganotin complexes (as revealed by Mössbauer spectroscopy, *vide infra*) is lost upon dissolution, indicating that a water molecule is not coordinated in solution, similar to that of its divinyltin analogue.[3] Diphenyltin complexes show a sharp resonance between $-335$ and $-350$ ppm indicating a penta-coordinated tin structure in solution, which is consistent with our earlier report.[3]

## Mössbauer data

In order to obtain further structural evidence, the Mössbauer spectra of the representative complexes were recorded in the solid state (Table 5). The spectra of the complexes (except **15**) all display a characteristic doublet absorption, indicating a single tin site. The $R_2Sn$ derivatives show isomer shift $\delta$ values typical of quadrivalent organotin derivatives, similar in alkyl$_2$Sn moieties and higher with respect to $Ph_2Sn$. The quadrupole splitting $\Delta$ values of complexes **2, 7, 8, 9** and **10** are in the range 3.74–3.99 mm $s^{-1}$ in alkyl$_2$Sn and 3.61 mm $s^{-1}$ in $Ph_2Sn$ derivatives, suggesting a distorted *trans*-$R_2Sn$ octahedral structure.[15] The C—Sn—C angles, calculated by the Parish relation,[16] vary from 141 to 170 °. In contrast, complex **14** shows a lower $\Delta$ value, which agrees with a trigonal bipyramidal structure with a calculated C—Sn—C angle of 128 °. The spectrum of **15** (see Fig. 2 of Ref. 3) requires special comment. The spectrum shows asymmetric absorption with large values of full-width at half height, and was fitted as two doublets with different parameter values; hence the occurrence of two different tin sites can be inferred. A doublet shows a $\Delta$ value (2.20 mm $s^{-1}$) that can be set as the lowest in *cis*-$R_2Sn$ trigonal bipyramidal derivatives.[15] This $Ph_2Sn$—$O_2N$ trigonal bipyramidal geometry matches with the X-ray structure[3] except for the C—Sn—C calculated angle; the corresponding $\delta$ value is also low, and this can arise from the electron withdrawl of the ligands to the tin. The second doublet can be attributed to a $Ph_3Sn$ moiety in a trigonal bipyramidal geometry, with the oxygen and chlorine atoms as axial ligands. The percentage areas of the two doublets are similar, indicating equal amounts of di- and tri-organotin moieties.

**Table 5** $^{119}Sn$ Mössbauer parameters (mm $s^{-1}$) for some representative diorganotin(IV) complexes[a]

| Complex | $\delta$ | $\Delta$ | $\Gamma_1$ | $\Gamma_2$ | C—Sn—C (°) |
|---|---|---|---|---|---|
| **2** | 1.33 | 3.79 | 0.92 | 0.92 | 141 |
| **7** | 1.29 | 3.99 | 0.95 | 0.92 | 170 |
| **8** | 1.16 | 3.61 | 1.00 | 1.00 | 159 |
| **9** | 1.21 | 3.74 | 0.90 | 0.92 | 154 |
| **10** | 1.40 | 3.87 | 0.95 | 0.98 | 143 |
| **14** | 1.15 | 2.88 | 0.89 | 0.98 | 128 |
| **15** | 0.75 | 2.20 | 1.00 | 1.00 | 107 |
| | 1.14 | 2.50 | 0.86 | 0.86 | |

[a] $\Gamma_1$ and $\Gamma_2$: line widths.

Thus, the spectroscopic data suggest a six-coordinate structure for the $LSnR_2{\cdot}OH_2$ type complexes in the solid state, owing to coordination of a water molecule. The geometry is distorted octahedral with two R groups occupying the *trans* positions and the equatorial plane by on $NO_3$ donor set similar to that of the vinyl analogue.[3] On the other hand, a distorted trigonal bipyramidal geometry has been suggested for $LSnR_2$-type complexes, with two oxygen atoms defining the axial positions and two phenyl groups and nitrogen in the trigonal plane, as in the case of complex **14**.[3,4]

## Evaluation of antitumour properties

The effect of the organotin complexes **14, 15, 16**

**Table 6** Effect of organotin compounds **14, 15** and **16** and $L^4HNa$ on the survivability of the mouse *in vivo*

| Parameters | Control | $L^4HNa$ | | Organotin compounds | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | **14** | | **15** | | **16** | |
| Dose (mg $kg^{-1}$) | No drug | 6 | 30 | 6 | 30 | 6 | 30 | 6 | 30 |
| Cells ($\times 10^6$) per ml ascites fluid | $168 \pm 10.20$ | $180 \pm 16.32$ | $178.3 \pm 16.5$ | $76 \pm 20.5$ | – | – | – | – | – |
| Total volume (ml) tumour cells + ascites fluid | $7.3 \pm 1.45$ | $5 \pm 0.6$ | $6 \pm 0.6$ | $4 \pm 0.77$ | – | – | – | – | – |
| Total packed cell volume (ml) | $5.2 \pm 0.40$ | $3.1 \pm 0.3$ | $3.5 \pm 0.8$ | $3.1 \pm 0.6$ | – | – | – | – | – |
| Mean survival time (MST) (days) | $32.5 \pm 2.69$ | $30.2 \pm 3.16$ | $29 \pm 3.5$ | $19.1 \pm 4.6$ | 02 | 10 | 02 | 11.2 | 04 |
| T/C[a] (%) | 100 | 93 | 90 | 59 | 6.15 | 30.76 | 6.15 | 35 | 12.3 |

[a] T/C is the ratio of the MST of treated mice to MST of control mice.

and $L^4HNa$ on the survivability of mice is shown in Table 6. $L^4HNa$ is found to be non-toxic to the mice at 30 mg $kg^{-1}$. It has been observed that $L^4HNa$ is highly soluble in water, and a very high dosage (50 mg $kg^{-1}$ in aqueous solution) does not cause the death of any mice. All the organotin complexes studied in the experiment are highly toxic to mice. Complex **14** is less toxic than **15** and **16**. Although the exact cause of toxicity was not studied, it could be due to free radical generation from the organotins to the living system.[13]

T/C values (using the NCI protocol for screening new anticancer drugs)[17] showed that neither $L^4HNa$ nor the organotin complexes possess any antitumour properties. However, some diorganotin complexes of cognate ligands displayed cytotoxicity when tested *in vitro* against MCF-7, EVSA-T, WiDr, IGROV, M19 MEL, A498 and H226 human tumour cell lines.[13] Further studies with the organotin complexes were not undertaken owing to their toxicity; however, studies with $L^4HNa$ are warranted owing to its water solubility and non-toxic nature.

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