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Interaction of dimethyltin(IV) dichloride with 5′-IMP and 5′-UMP

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The formation constants of the species formed in the systems H^++ dimethyltin(IV) + 5′-IMP and 5′-UMP, H^+ + 5′-IMP and H^+ + 5′-UMP have been determined in aqueous solution in the pH range 1.5–9.5 at constant temperature (25 °C) and constant ionic strength (0.1 mol dm^{-3} $NaClO_4$), using spectrophotometric and potentiometric techniques. ^1H and ^{31}P NMR investigations in aqueous solution confirmed the species formation. The precipitated complexes of IMP and UMP by $Me_2Sn(IV)^{2+}$ at low pH values were characterized by elemental analysis and FTIR spectroscopy methods, the bonding sites of the ligands were determined and ruled out purine and pyrimidine moieties (N-7 and N-1 in IMP and N-3 in UMP, respectively) while a bidentated coordination of the phosphate group is concluded in both cases. Finally, the experiments revealed the existence of complexes with trigonal bipyramidal structures that is in agreement with similar systems resulted previously.

Keywords: dimethyltin(IV) dichloride; inosine 5′-monophosphate; uridine 5′-monophosphate; stability and protonation constants

Introduction

Organotin(IV) compounds have been shown to have high antitumor activity *in vitro* in a wide variety of human tumors.[1–16] The increasing interest in the chemistry and biochemistry of organotin complexes has led to extended studies on their interactions with different naturally occurring ligands, e.g. carbohydrates, nucleic acid derivatives, amino acids and peptides.[2–11] Several papers revealed the coordination behavior of organotin cations toward biomolecules containing different types of donor atoms, including both solid-state and solution studies.[17–21]

Organotin compounds are generally very toxic, even at low concentrations, and are found in both fresh and marine waters, since they are among the most industrially used organometallic compounds and are also widely used as biocidal agents. This causes the problem of the presence of organotin compounds in the human food chain.[22] In addition, as for many drugs used in chemotherapy, there may be undesirable side-effects of the pharmaceutical use of these compounds. Therefore understanding of the interaction of organotin compounds with possible biological targets is highly desirable. In spite of these effects, the mechanism of action of these drugs in the living cell is not well understood. The activity of these compounds led to the hypothesis that these drugs hydrolyze easily in aqueous media and transport the active part (R_2Sn) inside the cells where it possibly reacts with DNA.[23] Some recent reviews point out the lack of solution equilibrium studies that could provide essential information on the bioactivity of di- or trialkyltin(IV) ions towards amino acids, peptides and nucleotides.[6,16–18]

Recently, we reported the complexation of dimethyltin(IV) cation with GMP and AMP in aqueous solution and have shown that the purine moiety is not involved in coordination and that the interactions are limited to the phosphate site of the ligands.[2] Continuing our study on the species distribution of dimethyltin(IV), we report on the complex formation of dimethyltin(IV) ($[Me_2Sn]^{2+}$) with uridine 5′-monophosphate (UMP) and inosine 5′-monophosphate (IMP) over a wide pH range. The formation of three complex species are proposed, of which two were isolated in solid states and characterized using FTIR spectroscopy and elemental analysis. To verify the different donor groups in the complexes, ^1H NMR and ^{31}P NMR spectroscopy were used in D_2O–H_2O solutions.

Experimental

Chemicals

Dimethyltin(IV)dichloride, sodium salts of inosine and uridine 5′-monophosphate were obtained from Fluka as reagent-grade materials and were used without further purification. Sodium perchlorate was from Merck and was dried under vacuum at room temperature for at least 48 h before use. NaOH solution was prepared from a titrisol solution (Merck) and its concentration was determined by several titrations with standard HCl solution. Perchloric acid was from Merck and was used as supplied. The aqueous stock solutions of the ligands were freshly prepared daily, and their concentrations were determined each time by titration with NaOH solution. All dilute solutions were prepared from double-distilled water with conductance equal to 1.3 ± 0.1 μS.

Measurements

All measurements were carried out at 25 °C. The ionic strength was maintained at 0.1 mol dm^{-3} with sodium perchlorate. A Jenway research pH-meter, model 3520, was used for pH measurements. The hydrogen ion concentration was measured with a combined electrode (Jenway). The pH-meter was calibrated for the relevant H^+ concentration with a solution of 0.01 mol dm^{-3} perchloric

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acid containing 0.09 mol dm^{-3} sodium perchlorate (for adjusting the ionic strength to 0.1 mol dm^{-3}). For this standard solution, we set $-\log[H^+] = 2.00$.[24] Junction potential corrections were calculated from equation (1):

$$-\log[H^+]_{real} = -\log[H^+]_{measured} + a + b[H^+]_{measured} \quad (1)$$

where a and b were determined by measuring of hydrogen ion concentration for two different solution of $HClO_4$ with sufficient $NaClO_4$ to adjust the ionic media.

Procedure

A 50 ml acidic solution of dimethyltin(IV) dichloride (2.0×10^{-3} mol dm^{-3}) was titrated with an alkali solution, 0.1 mol dm^{-3} NaOH, of the ligands (2×10^{-4} to 5×10^{-4} mol dm^{-3} of IMP and UMP), both of the same ionic strength. The absorbance and $-\log[H^+]$ were measured after addition of a few drops of titrant, and this procedure extended up to the required $-\log[H^+]$. To exclude carbon dioxide from the system, a stream of purified nitrogen was passed through a sodium chloride solution and then bubbled slowly through the reaction solution. In all cases, the procedure was repeated at least three times and the resulting average values and corresponding deviations from the average are shown in the text and tables.

The complex $M_xH_yL_z^{(2x+y-nz)}$ that formed is characterized by its stoichiometry ($x:y:z$), where M and L represent the metal ion and IMP or UMP, respectively. To determine the stability constant of the complexation, equation (2) is defined by β_{xyz}:

$$xM^{2+} + yH^+ + zL^{n-} \rightleftarrows M_xH_yL_z^{(2x+y-nz)} \quad (2)$$

$$\beta_{xyz} = [M_xH_yL_z^{(2x+y-nz)}]/([M^{2+}]^x[H^+]^y[L^{n-}]^z) \quad (3)$$

Determinations of the stability constant, β_{xyz}, based on the relation $A = f(pH)$[25,26] were performed using the computer program Squad. Absorbance, A, and $-\log[H^+]$ were measured for a solution containing dimethyltin(IV) and IMP or UMP. Treatments of the spectrophotometric data (270–290 in intervals of 0.5 nm) obtained during the titrations as a function of the H^+ concentration, were conducted using the computer program. The program allows calculation of the stability constants for different stoichiometry models.

Spectroscopy measurements

Spectrophotometric measurements were performed on a UV–vis Shimadzu 2100 spectrophotometer with a Pentium 4 computer and using thermostated matched 10 mm quartz cells. The measurement cell was a flow-type. A Masterflex pump allowed circulation of the solution under study from the potentiometric cell to the spectrophotometric cell, so the absorbance and $-\log[H^+]$ of the solution could be measured simultaneously.

^{1}H NMR spectra of the ligand and the complexes were recorded on a Bruker DRX-300 MHz spectrometer in H_2O–D_2O (1:1 by volume) using TMS as an external reference. ^{31}P NMR spectra were recorded on the same spectrometer in H_2O–D_2O (1:9 by volume) operating at room temperature. The chemical shifts are given relative to phosphoric acid. The solutions were prepared by mixing $Me_2Sn(IV)$ with Na_2(5′-IMP or UMP) in H_2O–D_2O solution to give a 1:1 mole ratio. The concentrations of the NMR samples were 1 mM in case of ^{1}H and 0.5 mM for ^{31}P NMR.

Other methods

FTIR spectra were obtained on a Bruker, Bomem 100 spectrometer, in the range 4000–500 cm^{-1} using KBr pellets. Sample for microanalysis was dried in vacuum to constant mass. Elemental analysis (C, H, N) was performed with a Fison instrument CHNSO-1108 elemental analyzer.

Elemental analysis

When the concentrations of the ligands are higher than 0.005 mol dm^{-3}, a white precipitate is formed in the pH range 3–5 during the titration of both IMP and UMP by dimethyltin(IV). The hydrolysis products of dimethyltin(IV) are soluble at this concentration and there was no precipitation during the titration of the ligands alone. So, we concluded that the solid products were attributed to the formation of MHL and ML species. The precipitates were collected by filtration, dried at room temperature by vacuum and characterized by means of FTIR. The metal-to-ligand ratios in $Me_2Sn(IV)^{2+}$-IMP and UMP were determined by elemental analysis (found: C 28.01, H 3.62, N 10.78% and C 26.95, H 3.77, N 5.62% for IMP and UMP, respectively; calculated for Me_2Sn-IMP,H_2O [$C_{12}H_{19}N_4O_9PSn$]: C 28.09, H 3.71, N 10.92%; and Me_2Sn-UMP,H_2O [$C_{11}H_{19}N_2O_{10}PSn$]: C 27.01, H 3.89, N 5.73%).

Results and Discussion

The stepwise acidity constants of (IMP^{2-}) and (UMP^{2-})

The protonation constants of IMP and UMP have been determined spectrophotometrically based on the relation $A = f(pH)$.[25] The measured absorbance, A (270–290 nm in the interval of 0.5 nm), and $-\log[H^+]$ from the spectrophotometric titration were conducted using the computer program Squad.[27,28] The data in the computer program were fitted for equations (4)–(7) by minimizing the error squares sum of the experimental absorbances from the calculated ones. The program allows calculation of the protonation constants with different stoichiometries. The number of experimental points (absorbance vs $-\log[H^+]$) was more than 30 (maximum 40) for each titration run. During the experiments, the solutions were stable and the absorbance values did not change with time.

The results obtained using spectrophotometric and potentiometric pH titrations for the various acidity constants of the proton donors of the ligands, equations (4)–(7), are listed in Table 1 together with the values reported before.[29–31] The nucleoside 5′-monophosphate (NMP^{2-}) shown in Scheme 1 may bind with two protons at the phosphate group and one at the purine moiety, (N-7), in IMP. It was proposed[32] that $H_3(IMP)^+$ releases its first proton from $P(O)(OH)_2$, the second one from H^+ (N-7) and the third one again from the phosphate group. A forth proton is released in the alkaline pH range from the neutral H(N-1) site. These steps are expressed by the following equilibria:

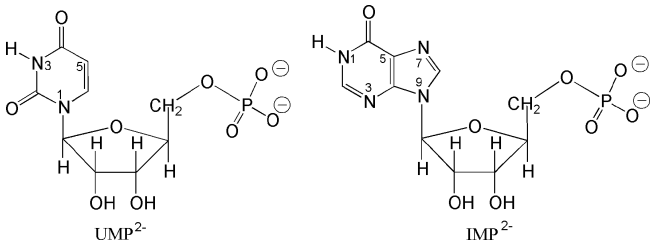
$$H_3(NMP)^+ \; \Phi H_2(NMP) + H^+ \quad (4a)$$

$$H_2(NMP) \; \Phi H(NMP)^- + H^+ \quad (5a)$$

$$H(NMP)^- \; \Phi (NMP)^{2-} + H^+ \quad (6a)$$

$$(NMP)^{2-} \; \Phi (NMP\text{-}H) + H^+ \quad (7a)$$

However, UMP may carry two protons at its phosphate group and therefore the equilibria (5) and (6) must be considered. In this case



Scheme 1. Structures of inosine 5′-monophosphate (IMP) and uridine 5′-monophosphate (UMP).

Table 1. Protonation constants of different species of IMP and UMP considered in this work by spectrophotometric titration in aqueous solution at 25 °C and ionic strength 0.1 mol dm^{-3} ($NaClO_4$)

Species	log K^{H}_{H3} (NMP)	log K^{H}_{H2} (NMP)	log K^{H}_{H} (NMP)	log K^{H} (NMP)	Reference
IMP	–	1.54 ± 0.03	5.91 ± 0.06	8.99 ± 0.05	This work
UMP	–	–	5.74 ± 0.04	9.47 ± 0.06	This work
IMP	0.45	1.30	6.22	9.02	[29]
IMP	–	1.54	6.04	8.88	[30]
UMP	–	0.7	6.15	9.45	[31]
UMP	–	1.02	5.88	9.44	[30]

a third proton from the H(N-3) unit of the neutral pyrimidine ring residue may also be released in the upper pH range, leading to the additional equilibrium, equation (5). To complete the discussion, it should be added that a fifth and a fourth proton may be released at pH > 12 from the ribose groups in IMP and UMP, respectively. The last deprotonation of both nucleosides was not considered further in this work. Also, it should be noted that the release of the first proton from the both nucleosides occurs at very low pH (pK < 1). The assignments agree well with previous conclusions.[32–34]

Hydrolysis of dimethyltin(IV)dichloride

The hydrolysis of $Me_2Sn(IV)^{2+}$ has been investigated in different media by some authors.[35,36] We performed earlier spectrophotometric titrations to obtain these data in various ionic strengths (0.1–1.0 mol dm^{-3}) $NaClO_4$ and NaCl media.[1] The hydrolysis constants of the hydrolyzed species were determined as before[1] and are listed in Table 2. The detected species and their formation constants are in good agreement with those reported earlier and show the strong tendency of dimethyltin(IV) to hydrolysis in aqueous solution to form various hydrolyzed species.[35,36]

Table 2. Average values of hydrolysis constants, β_{pq}, for $Me_2Sn(IV)^{2+}$ species in aqueous solution at 25 °C and ionic strength 0.1 mol dm^{-3} ($NaClO_4$), where p and q represent $Me_2Sn(IV)$ and hydroxyl ions, respectively, the values reported in literature are also listed

$-\log\beta_{11}$	$-\log\beta_{12}$	$-\log\beta_{13}$	$-\log\beta_{22}$	$-\log\beta_{23}$	Reference
3.12 ± 0.03	8.43 ± 0.04	19.45 ± 0.09	4.86 ± 0.05	9.74 ± 0.08	This work
3.25	8.54	–	5.05	9.81	[35]
3.12	8.45	19.48	5.2	9.7	[36]

Complexation of IMP and UMP by dimethyltin(IV)

One of the main obstacles in studying metal ion systems with nucleotide derivatives in solution is the known as the self-association of them. This means low concentration of the ligands must be employed in the experiments, a condition usually fulfilled with UV-spectroscopic studies. In similar studies Sigel *et al*.[32–34] have demonstrated that in 1–5 mM solution about 95–97% of the total NMP exists in the monomeric form. With the indicated problem in mind we decided to study the complexes of IMP and UMP with dimethyltin(IV) in aqueous solution by evaluating precise stability data from spectrophotometric titrations.

Considering equations (2) and (3), different models including MHL, ML, $MH_{-1}L$ and several polynuclear and protonated species were tested by the program. As expected, polynuclear complexes were systematically rejected by the computer program, as also were MH_2L_2, MHL_2 and ML_2 (the charges were omitted for simplicity). A value for MH_3L species (in both cases of IMP and UMP) was also calculated by the program, but the species were not considered further, because the estimated error in its formation constant was unacceptable, and its inclusion does not improve the goodness of the fit. The models finally chosen, formed by MHL, ML and $MH_{-1}L$ for IMP and UMP besides the hydrolysis products of $Me_2Sn(IV)^{2+}$, resulted in satisfactory numerical and graphical fitting. The calculated average values of the stability constants for different experiments are listed in Table 3. Figure 1 is shown as a

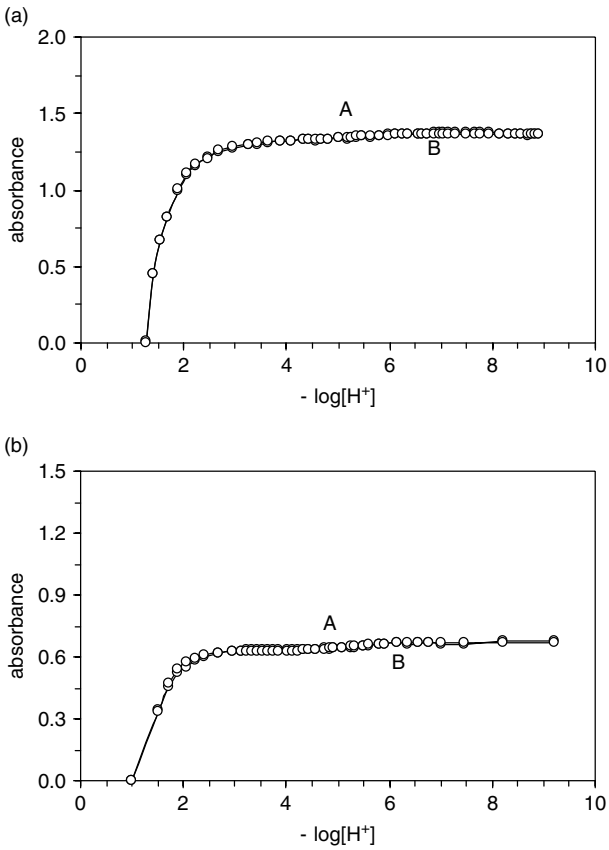


Figure 1. A typical graphical fitting for the complexation of dimethyltin(IV) at 25 °C and 0.1 mol dm^{-3} sodium perchlorate: (a) by IMP at 279 nm and (b) by UMP at 278 nm; in both cases (A) and (B) are experimental and calculated absorbances, respectively.

Table 3. Average values of the stability constants for the systems $Me_2Sn(IV)^{2+}$ + IMP and UMP at 25 °C and ionic strength 0.1 mol dm^{-3} ($NaClO_4$)

Species	log β_{111}	log β_{101}	log β_{1-11}
IMP	8.83 ± 0.01	7.82 ± 0.03	6.88 ± 0.04
UMP	8.42 ± 0.05	7.40 ± 0.03	8.35 ± 0.05

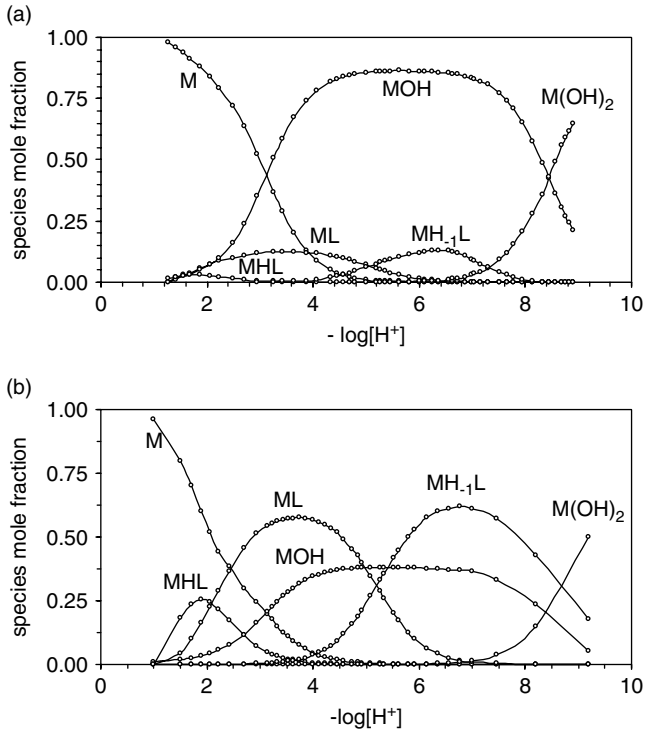


Figure 2. Species distribution diagram of the $Me_2Sn(IV)$-IMP (a), and UMP (b) systems ([$Me_2Sn(IV)$] = 2.0×10^{-3}, [IMP] = 4.94×10^{-4} and [UMP] = 4.05×10^{-4} mol dm^{-3}) at 25 °C and 0.1 mol dm^{-3} ($NaClO_4$).

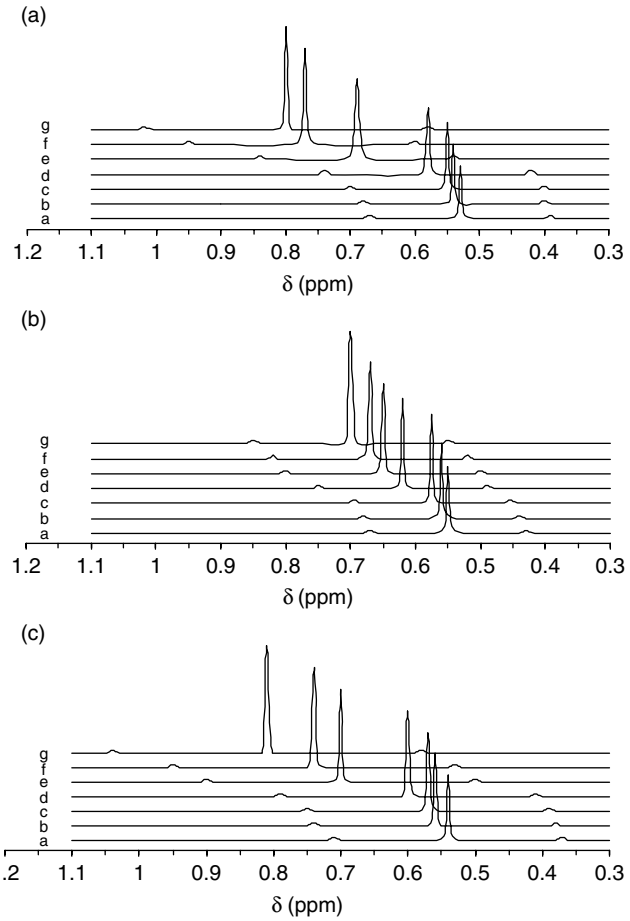


Figure 3. ^{1}H-NMR spectra in the Me proton range for $Me_2Sn(IV)$ alone (a); the 1 : 1 $Me_2Sn(IV)$-IMP system (b); and the 1 : 1 $Me_2Sn(IV)$-UMP system (c), as a function of pH. Curves: (a) a–g, pH 9.53, 8.74, 7.73, 5.11, 4.20, 2.06 and 1.96, respectively; (b) a–g, pH 9.40, 8.49, 7.08, 5.82, 4.70, 3.71 and 2.13, respectively; (c) a–g, pH 9.03, 7.38, 6.30, 5.65, 4.30, 3.50 and 2.50, respectively.

typical example of graphical fitting for the observed and calculated absorbances from the computer program.

During the spectrophotometric titration of IMP and UMP by dimethyltin(IV) no precipitation was observed (in the condition of UV–vis measurements). The species distribution curves depicted in Fig. 2 reveal similar behavior for the two ligands towards $(CH_3)_2Sn(IV)^{2+}$ and demonstrates that complexes with a 1 : 1 ligand-to-metal ion ratio were formed. There was no evidence of the presence of polynuclear species in solution.

Figure 3 exhibits ^{1}H NMR of methyl signals at different pH values and Fig. 4 shows a plot of the $^2J(Sn-^1H)$ as a function of pH. As can be seen, the $^2J(Sn-^1H)$ values increase with decreasing the pH in NMR titration, which indicates that a complex species besides $(CH_3)_2Sn(IV)$ exists in solution at low pH values. The species most probably is MH_2L, which forms on the monodentate coordination of the ligands through their phosphate groups. At such low pH values (below 1), it was very difficult to fit the species matrix and determine the stability constant of this species. However, at higher pH (pH 1.2–2.8 for IMP and pH ≈ 1.1–3.5 for UMP) MHL species is formed from MH_2L on deprotonation of the phosphate group of IMP and UMP ($MH_2L \rightleftarrows MHL + H^+$). The species formed at different pH values were found to be in different protonation states. In acidic, neutral and alkaline pH range, two deprotonation processes take place for both systems (pH ≈ 1.5–6 and 4–8 for IMP; pH ≈ 1.2–6.5 and 3.9–9 for UMP, respectively), resulting in formation of the ML and $MH_{-1}L$ species, $MHL \rightleftarrows ML + H^+$ and $ML \rightleftarrows MH_{-1}L + H^+$. The first reaction is due to the deprotonation of the neutral H(N-1) and H(N-3) units of purine and pyrimidine bases in IMP and UMP, respectively, and the second reaction is attributed to the deprotonation of a coordinated H_2O molecule in both cases, resulting in the formation of a mixed hydroxo complex, Fig. 2. Evaluation of the titration curves, for both systems, shows that only hydrolyzed species, $M(OH)_2$, is present at higher pH.

Lockhart and Manders studied the correlation of $^2J(Sn-^1H)$ and Me–Sn–Me angle in 25 methyltin(IV) compounds.[37] They proposed an empirical quadratic expression in terms of $^2J(Sn-^1H)$ to determine the C–Sn–C angle. It was found that these values provide useful information on the C–Sn–C bond angle of the compounds in a sample and indirectly on the possible coordination numbers and geometry around the Sn atom.

Two-bond coupling, $^2J(Sn-^1H)$, of the $Me_2Sn(IV)^{2+}$ alone and its complexes with IMP and UMP were determined via the ^{1}H NMR spectra at different pH. It can be seen, Fig. 3, that the signal of the methyl protons in $Me_2Sn(IV)^{2+}$ is sharp for both systems and has almost the same chemical shift as in the solution of

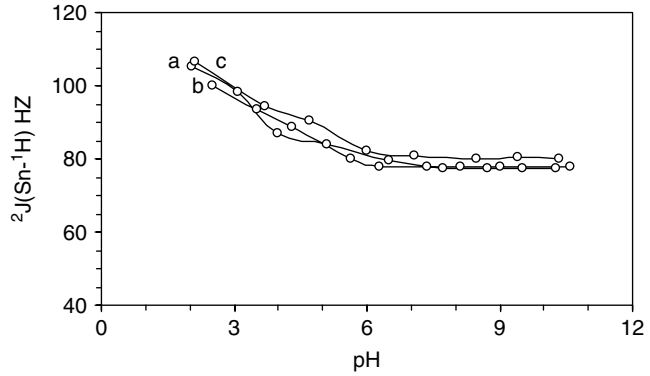


Figure 4. Measured coupling constants, $^2J(Sn-^1H)$, of Me protons in solutions of (a) 1 : 1 $Me_2Sn(IV)$-AMP system, (b) 1 : 1 $Me_2Sn(IV)$-GMP system, and (c) $Me_2Sn(IV)$ alone, as a function of pH.

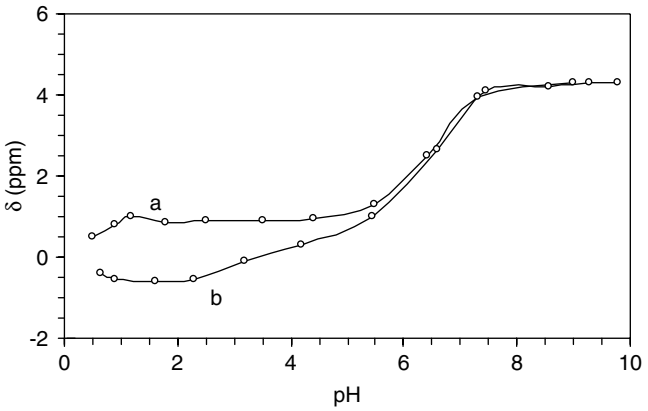
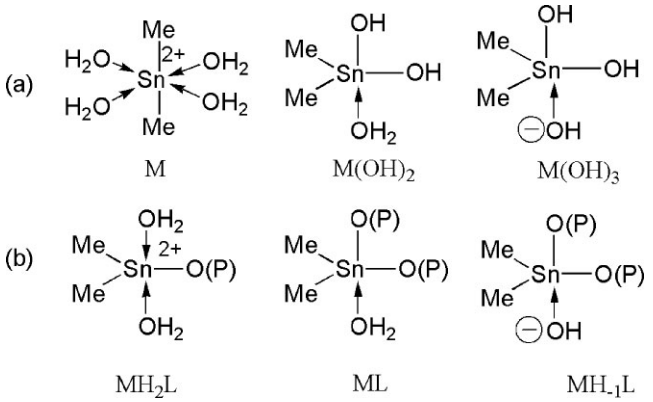


Figure 5. The ^{31}P chemical shifts of IMP (a), and their mixtures with $Me_2Sn(IV)$ (b), vs pH.



Scheme 2. Proposed structure of (a) the hydrolyzed species of dimethyltin(IV) and (b) the complexes of IMP and UMP.

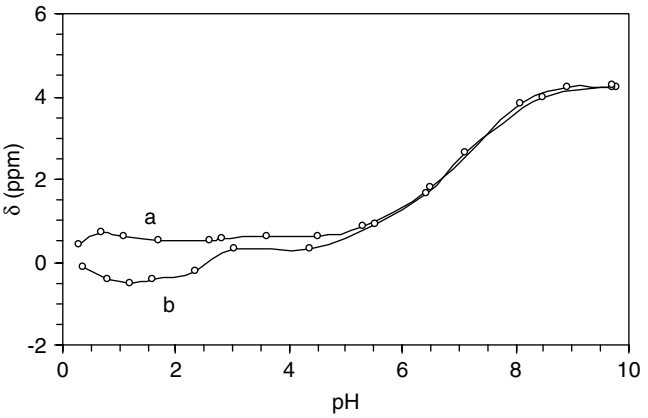


Figure 6. The ^{31}P chemical shifts of UMP (a), and their mixtures with $Me_2Sn(IV)$ (b), vs pH.

$Me_2Sn(IV)^{2+}$ alone. The ^1H NMR titration vs pH of 1 : 1 mixtures of $Me_2Sn(IV)^{2+}$ and IMP or UMP on the other hand, does not show any shift of the adjacent to N-7 and N-1 protons in IMP and N-3 proton in the case of UMP, in the pH range 1.5–9.5, thus excluding Sn(IV) interaction with the purine or pyrimidine rings nitrogens. In similar studies, the same results were observed by Yang *et al*.[20] and Jankovics *et al*.[19] in ^1H NMR and ^{119}Sn Mössbauer spectra for the systems $Et_2Sn(IV)^{2+}$ +5′-GMP, 5′-IMP and $Me_2Sn(IV)^{2+}$ + R5P, GIP, G6P, respectively. At higher pH the $^2J(Sn-^1H)$ values of $Me_2Sn(IV)^{2+}$ are somewhat smaller than the complex systems, Fig. 4, possibly due to a slight distortion of C–Sn–C angle by the coordinated ligand.[37] Using the quadratic equation of Lockhart and Manders,[37] the average C–Sn–C bond angle at low pH (less than 2) and higher pH values (more than 6) for the two species calculated from the coupling constant are 175° and 135°, respectively. On this basis the structures of $Me_2Sn(IV)^{2+}$ and their complexes with IMP and UMP are proposed as an octahedral at low pH and distorted trigonal bipyramidal arrangement at higher pH as shown in Scheme 2.

Figures 5 and 6 present the ^{31}P NMR chemical shifts (δ) of the $Me_2Sn(IV)^{2+}$ and the complexes with IMP and UMP in 1 : 1 stoichiometries in aqueous solution as a function of pH. For the free ligand the chemical shifts of P slightly increase with increasing pH; this can be attributed to the deprotonation of P–OH and delocalization of negative charge over the P moiety. Interestingly, a further increase of pH up to almost 2.5 has no effect on chemical shifts. However, pH values higher than 5 facilitate further deprotonation and delocalization of remaining P–OH and consequently large downfield shifts accrue. It is seen that the presence of $Me_2Sn(IV)^{2+}$ causes an upfield shift in ^{31}P NMR signals of IMP and UMP to a maximum of about 1.5–2 ppm at pH $\approx$ 1.5 for both systems, indicating an Sn(IV) interaction with the pyrophosphate groups. At about pH 3, precipitation starts at higher concentrations. In aqueous solution, it has been suggested that $Me_2Sn(IV)^{2+}$ reacts with phosphate ions to form solid complexes.[19,20] At pH > 6.5, the ^{31}P NMR chemical shift of the free ligands and their mixtures with $Me_2Sn(IV)^{2+}$ present no significant difference and this leads to the conclusion that no tin-phosphate interaction is taking place.

It has been suggested[3] that aqueous solution of $Me_2Sn(IV)$ and $Bu_2Sn(IV)$ interact with 5′-AMP to form solid adducts at pH $\approx$ 3–4. Based on ^{119}Sn Mössbauer and IR spectral studies the adducts were assigned polymeric structures where tin atoms are six-coordinated and bound to the phosphate oxygens of the nucleotides. In another similar study[20] the interaction of 5′-IMP with $Et_2Sn(IV)$ produced a solid adduct at pH $\approx$ 3–4. On the basis of ^{31}P NMR and IR spectra, it was concluded the stoichiometry of the formed complex was $(Et_2Sn)_2(5'\text{-IMP})_2$. However, Willem *et al*.[21] have concluded that, among several possible structures in complexation of $Et_2Sn(IV)$ with nucleotides (5′-CMP, 5′-dCMP and 5′-UMP), only one satisfied all data including the elemental

Table 4. IR absorption bands of the free ligands and the complexes in KBr (cm^{-1})

Assignment	IMP	IMP+ $Me_2Sn(IV)$	UMP	UMP+ $Me_2Sn(IV)$
ν (C=O)	1680, s	1677, s	1677, s	1680, s
Bands of the purine skeleton	1591, w	1589, w	–	–
	1549, w	1547, w		
Bands of the pyrimidine skeleton	–	–	1477, w	1475, w
			1425, w	1422, w
ν (P=O)	1218, m	1207, m	1287, m	1274, m
$\nu_{as}(PO_3)$	1082, s	1101, s	1085, s	1109, s
$\nu_{sym}(PO_3)$	978, m	1001, m	980, m	1001, m

s = strong, m = medium, w = weak, b = broad, sh = shoulder.

analysis. This structure contains two tin atoms bridged by oxygen and a chlorine atom and each tin atom being linked to the phosphate group of the nucleotides at pH ≈ 3–5.5. Recently, the interaction of $Me_2Sn(IV)$ with 5′-AMP has been reported in aqueous solution.[19] Based on ^{31}P NMR, ^{1}H NMR, IR spectra and elemental analysis the authors have concluded a trigonal bipyramidal arrangement in a moderately acidic solution with a bidentated phosphate coordination to $Me_2Sn(IV)$. The same result has been reported earlier in our previous work in complexation of 5′-AMP and 5′-GMP with $Me_2Sn(IV)$.[2]

Characterization of the $Me_2Sn(IV)^{2+}$-IMP and UMP precipitates

The results obtained by elemental analysis (see Experimental section) indicate the formation of complexes with a 1:1 metal-to-ligand ratio. The characteristic IR bands of IMP, UMP, dimethyltin(IV)-IMP and dimethyltin(IV)-UMP are listed in Table 4.

The skeleton vibrations of the purine and pyrimidine rings of the nucleotides in the region 1600–1400 cm^{-1} do not shift in the complexes, indicating the non-existence of any metal ion with the ring nitrogen atoms interactions.[20] On the other hand, considerable changes were observed in phosphate stretching in the range 1300–1000 cm^{-1} of the free ligands and the complexes. This can be explained with the binding of tin to the oxygen of the phosphate.

The arrangement mentioned above confirms that the phosphate group in both cases coordinates to dimethyltin(IV) and the ring nitrogen atoms do not participate in the coordination. Willem *et al*.[21] have studied IR, NMR and electrospray mass spectrometry of diethyltin dichloride complexes with some pyrimidic nucleotides including 5′-CMP, 5′-dCMP and 5′-UMP in aqueous medium. They concluded that $Et_2Sn(IV)$ moiety is involved in bonding with the phosphate group of the ligands studied. This and other findings of similar systems (as mentioned) are in agreement with our result.

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