Egypt. J. Anal.Chem, Vol. 24, PP. 43- 61 (2015)

Potentiometric Studies of Dimethyltin(IV) Complexes with Homopiperazine.

M. R. Shehata, M. M. Shoukry and A. M. Abdel-Wahab

Department of Chemistry, Faculty of Science, Cairo University, Giza, Egypt.

Summary: The coordination of homopiperazine with dimethyltin(IV) (DMT) was investigated at 25^{o}C and 0.1 mol L^{-1} ionic strength in water for dimethyltin(IV). The mixed-ligand complexes of dimethyltin(IV) with homopiperazine and DNA constituents were investigated. The formation constants are calculated using the non-linear least-square program MINIQUAD-75. The concentration distribution of the various complex species was evaluated as a function of pH.

Introduction

A tremendous research is directed towards the design of non-platinum chemotherapeutics with the aim to optimize the features of classical platinum drugs constituting the basic cisplatin framework viz.: their toxic side effects, inherent intrinsic resistance and high cost [(1)]. Among the noteworthy, dimethyltins have emerged as a promising class of cancer chemotherapeutics.

It has well established that dimethyltin(IV) compounds are very important in cancer chemotherapy because of their apoptotic inducing character [(2,3)]. During last few years it is noticeable that dimethyltin compounds occupy an important place in cancer chemotherapy reports [(4-7)]. Blower described thirty interesting inorganic pharmaceuticals, four of which are tin compounds [(8)]. Numerous didimethyltin (IV) derivatives have been found to exhibit high in vivo cytotoxicity against P388 lymphocytic leukaemia but to exhibit less or no activity against other murine systems [(9-14)]. However, the new in vitro human tumour cell screening tests have once again demonstrated the potential of dimethyltin complexes, some of which

have exhibited high activity [15] and thus interest in them has been revitalized.

Dimethyltin(IV) compounds are involved in cancer treatment via different mechanisms at the molecular level. The binding ability of dimethyltin compounds towards DNA, the ultimate drug target depends on the DNA structure. The phosphate group of DNA sugar backbones usually acts as an anchoring site and nitrogen of DNA base binding is extremely effective, this often resulting in the stabilization of the tin centre as an octahedral stable species [16]. The antitumour activity of the coordination compounds $R_2SnX_2L_2$ is controlled by the nature of R, leaving groups (X) and the ligand (L). The coordinated ligand (L) favoures in some way the transport of the drugs into cells, while the antitumour activity would be exerted by the dimethyltin(IV) moiety dissociated from the complex [17]. The latter would interact with nucleic acids, similarly as in the case of the widely used anticancer drug cisplatin. Therefore, there is a relationship between the stability of the dimethyltin(IV) compounds and their antitumour activity. In conjuction with our previous studies on dimethyltin(IV) complexes [18-22], the present paper aims to study the complex formation equilibria of dimethyltin(IV) with homopiperazine. The solid complexes were prepared and characterized.

Experimental

Materials

Dimethyltin(IV) dichloride (DMT) is obtained from Sigma-Aldrich Chem. Co.. Homopiperazine was obtained from Acros Organics. The DNA constituents, inosine, inosine-5´-monophosphate, thymine, uracil and uridine were provided by Sigma Chemical Co. Carbonate-free NaOH (titrant) was prepared and standardized against potassium hydrogen phthalate solution.

Potentiometric measurements were made using a Metrohm 686 titroprocessor equipped with a 665 Dosimat (Switzerland). The titroprocessor and electrode were calibrated with standard buffer solutions,

prepared according to NBS specifications [23]. The titrations were carried out in a purified N_2 atmosphere using a titration vessel described previously [24]. The temperature was maintained constant by a Colora ultrathermostat. Homopiperazine solution was prepared in the protonated form by dissolving in HCl solution. The protonation constants of homopiperazine were determined by titrating 40ml of homopiperazine solution, 2.5 x 10^{-3} mol L^{-1} with of standardized 0.05M NaOH solution. The hydrolysis constants of DMT were determined by titrating 40ml solution, 2.5 x 10^{-3} mol L^{-1} with standardized 0.05M of NaOH solution. The formation constants of dimethyltin(IV) complexes were determined by titrating 40 mL of solution containing homopiperazine (2.5 x 10^{-3} mol L^{-1}) and dimethyltin(IV) with concentrations 1.25x10^{-3} mol L^{-1}. The formation constants of the ternary complexes were determined by titrating solution 1:1:2 mixture of dimethyltin(IV), homopiperazine and DNA constituents, with concentration of 1.25x10^{-3}, 1.25x10^{-3} and 2.5 x 10^{-3} mol L^{-1}; respectively.

The titration was performed at 25°C in water for DMT and 0.1M ionic strength adjusted with NaCl solution. The pK_w in dioxane-water solution was determined as described previously [22,25]. For this purpose, various amounts of standard NaOH solution were added to a solution of 0.1M ionic strength adjusted with NaCl solution. The $[OH^-]$ was calculated from the amount of base added. The $[H^+]$ was calculated from the pH value. The product of $[OH^-]$ and $[H^+]$ was taken. The mean value obtained in this way for the log concentration product is pK_w = 14.23, 14.50, 14.92, 15.12, and 15.63 for 25.0, 37.5, 50.0, 62.5, and 75.0% dioxane-water solution.

The equilibrium constants of the binary complexes were evaluated from titration data, defined by Eq. (1) and Eq. (2).

$$p(M) + q(L) + r(H) \rightleftharpoons [(M)_p(L)_q(H)_r] \qquad (1)$$

$$\beta_{pqr} = \frac{[(M)_p(L)_q(H)_r]}{[M]^p [L]^q [H]^r} \qquad (2)$$

Where M, L and H represent dimethyltin(IV), homopiperazine and proton respectively. The calculations were performed using the computer program MINIQUAD-75 [26]. The stoichiometries and stability constants of the complexes formed were determined by trying various possible composition models. The model selected gave the best statistical fit and was chemically consistent with the titration data without giving any systematic drifts in the magnitudes of various residuals, as described elsewhere [26]. **Table 1** lists the equilibrium constants together with their standard deviations as obtained from the program MINIQUAD-75. The concentration distribution diagrams were obtained using the program SPECIES [27].

Synthesis

The complex DMT (HPIP) was synthesised by mixing homopiperazine (1mM) and dimethyltin(IV) (1mM) in 20 ml methanol. The mixture was stirred for 2 hours. The resulting white powder precipitate was filtered and washed thoroughly with diethyl ether (Yield 90%). (Found: C, 26.4; H, 5.8; N, 8.7 %. $C_7H_{18}N_2SnCl_2$ M.Wt., 319.85, calcd.: C, 26.29; H, 5.67; N, 8.76 %)

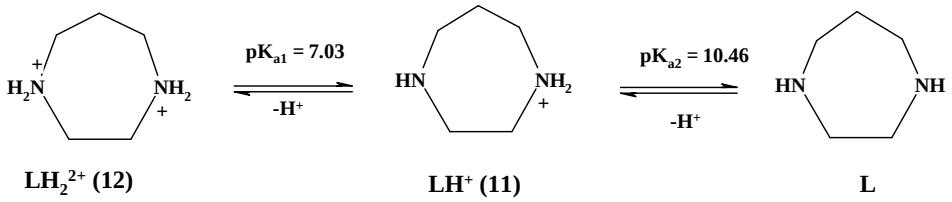
The solid complex was characterized by elemental analysis; Analysis of carbon, hydrogen and nitrogen was carried out on an Automatic analyzer CHNS- Vario EL III- Elmentar-Germany. Thermal analysis (TGA and DTG) were performed in nitrogen atmosphere with TGA-50 shimadzu thermogravimetric analyzer and DTA-50 Shimadzu thermal analyzer. The potential characteristics are as follows: Heating rate: 10K min^{-1}, Sample size: 10-15mg for TGA. Temperature range: room temperature to 600 ^oC.

Results and discussion

Complex formation equilibria of binary complexes

The acid-dissociation constants of the protonated homopiperazine, **Scheme 1**, were determined under the same experimental conditions of ionic strength, solvent composition and temperature which are used for the study of dimethyltin complex equilibria. The overall protonation constants ($\log\beta_{11}$ and $\log\beta_{12}$) were calculated. The values obtained are in

good agreement with the literature data [28] after considering changes in experimental condition.



Scheme 1. Acid-base equilibria of HPIP ligand.

The hydrolysis of the dimethyltin(IV) cation in aqueous solution was studied by several research groups [29-33]. The potentiometric data were fitted considering the formation of the species 10-1, 10-2, 10-3, 10-4 and 20-2.

The potentiometric titration curves of homopiperazine in the presence and absence of dimethyltin(IV) are compared. The complex titration curve is significantly lower than homopiperazine curve as shown in **Figure 1**. This corresponds to the formation of a complex species through release of a hydrogen ion.

The complex formation equilibria of dimethyltin (IV) with homopiperazine is characterized by fitting the potentiometric data to various models. The best model was found to be consistent with the formation of the complexes with stoichiometric coefficients 110, 111, 11-1 and 11-2.

The pK$_a$ of coordinated water molecule is calculated by Eq. 3.

$$pK_a = \log \beta_{110} - \log \beta_{11-1} \qquad (3)$$

The calculated value is 6.96 for dimethyltin(IV) complex. This value is higher than that of water molecule coordinated to the corresponding free dimethyltin(IV) ion. This may be due to the elongation of Sn(IV)-H_2O bond caused by the coordination of homopiperazine.

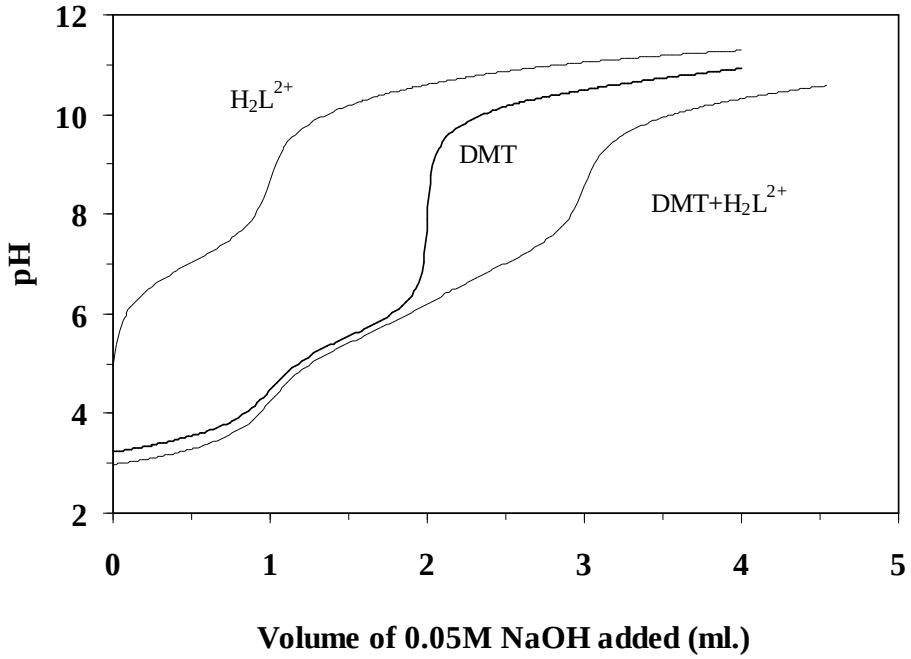
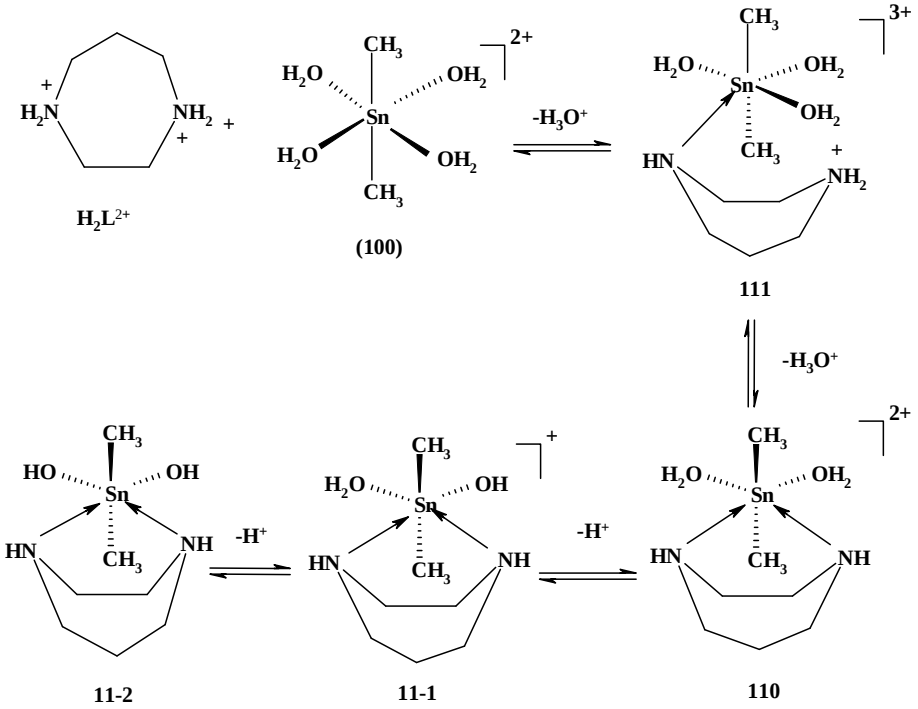


Figure.1. Potentiometric titration curve of HPIP (0.05mmoles) in presence and absence of DMT.



Scheme 2. Complex species of DMT-HPIP system.

The concentration distribution diagram of DMT-HPIP, **Figure 2**, provides a useful picture of the dimethyltin binding with HPIP as a function of pH. The protonated

complex, 111, predominates at lower pH between pH = 2.2 and 5.6 and reaches a maximum concentration of 70.8% at pH = 3.6. The deprotonated complex 110 predominates between pH = 5.6 and 7.0 with maximum concentration of 50.5% at pH = 6.2. The hydrolyzed form 11-1 predominates between pH = 7.0 and 10.4 with maximum formation percentage of 67% at pH = 8.6. It is interesting to note that the main species in the physiological pH range are 110 and 11-1 complex species.

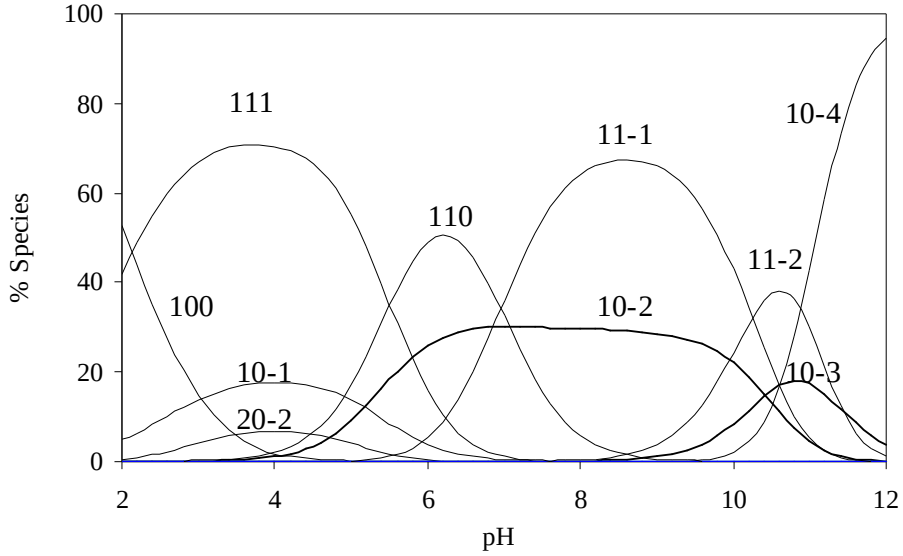


Figure.2. Concentration distribution of various species as a function of pH in the HPIP-DMT system (at concentration of 1.25 mmol/ liter of both HPIP and DMT).

Ternary complexes of DMT-HP with DNA constituents.

The formation of ternary complexes of DMT-HP with DNA constituents(1:2) has been studied and the results are shown in **Table 1**.

The formation of ternary complexes DMT-HP with DNA constituents is indicated by the titration curve of DMT+HP+Inosine (as a representative of DNA constituent) with 0.05M solution of standardized NaOH which is lower than that for DMT+HP, **Figure 3**. The lowering of the curve in presence of inosine is due to complex formation with DMT+HP.

The concentration distribution curve of ternary complexes, **Figure 4** show the formation of ternary complex 1110 in the physiological pH range, with maximum concentration of 53%. Similar curves were found for Inosine-5´-monophosphate, uracil, thymine and uridine, which show the formation of the ternary complexes 1110 in the physiological pH range.

Table 1. Equilibrium constants of binary and ternary complexes of DMT and HP with DNA at 25ºC and 0.1M NaCl.

$ML_1L_2H^a$		$ML_1L_2H^a$	$\log \beta^{Pb}$
	OH^-		HP
1 0 0 -1	-3.03(0.01)	0 1 0 1	10.46(1)
1 0 0 -2	-8.21(0.01)	0 1 0 2	17.49(2)
1 0 0 -3	-18.63(0.03)	1 1 0 0	13.02(2)
1 0 0 -4	-29.24(0.02)	1 1 0 1	18.53(3)
2 0 0 -2	-3.12(0.01)	1 1 0-1	6.06(2)
		1 1 0-2	-4.19(5)
	Inosine		Inosine-5´-monophosphate
0 0 1 1	8.80(0.01)	0 0 1 1	9.02(0.01)
1 0 1 0	8.13(0.03)	0 0 1 2	15.20(0.01)
1 0 2 0	14.82(0.03)	1 0 1 0	11.90(0.02)
1 1 1 0	18.50(0.05)	1 0 2 0	19.37(0.03)
1 1 2 0	22.24(0.06)	1 1 1 0	23.22(0.06)
		1 1 2 0	26.75(0.03)
	Uracil		Thymine
0 0 1 1	9.18(0.01)	0 0 1 1	9.58(0.01)
1 0 1 0	9.34(0.02)	1 0 1 0	9.61(0.02)
1 0 2 0	16.60(0.03)	1 0 2 0	16.96(0.04)
1 1 1 0	18.83(0.05)	1 1 1 0	19.40(0.05)
1 1 2 0	22.49(0.07)	1 1 2 0	23.06(0.04)
	Uridine		
0 0 1 1	9.11(0.01)		
1 0 1 0	9.21(0.02)		
1 0 2 0	16.49(0.03)		
1 1 1 0	19.70(0.03)		
1 1 2 0	23.94(0.04)		

[a],M, L_1, L_2 and H are the stoichiometric coefficient corresponding to DMT, HP, DNA and H, respectively; [b]Standard deviations are given in parentheses Sum of square of residuals are less than $5x10^{-7}$.

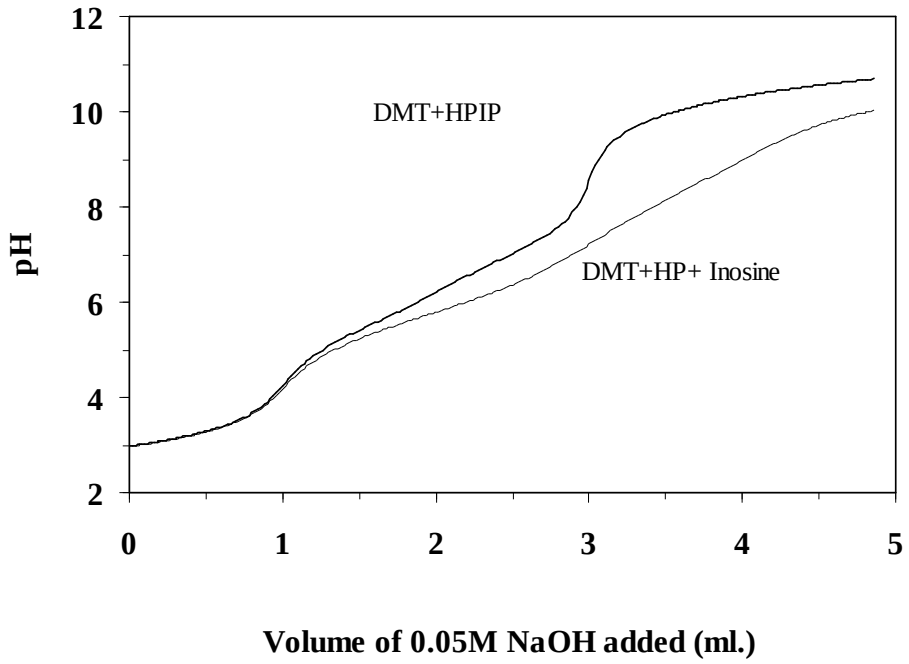


Figure 3. Potentiometric titration curve of DMT-HPIP (0.05mmoles) in presence and absence of Inosine (0.10 mmoles).

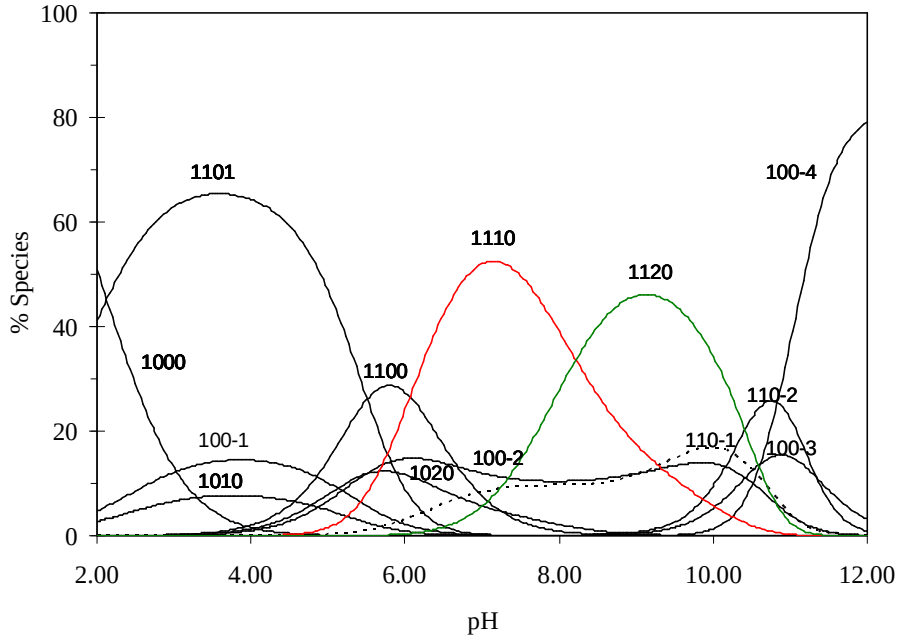


Figure.4. Concentration distribution of various species as a function of pH in the DMT-HPIP-Inosine system (at concentration of 1.25 mmol/ liter of both HPIP and DMT and 2.50 mmol/liter of inosine).

Effect of temperature on protonation of HPIP

Dissociation constants of protonated HPIP, H_2L^{2+} at different temperatures and 0.1M ionic strength are given in **Table 2**.

The thermodynamic parameters ΔH° and ΔS° were obtained by a linear least squares fit of lnk vs.1/T (ln K = –ΔH°/RT + ΔS°/R), leading to an intercept at ΔS°/R and a slope of –ΔH°/R. The results obtained are summarized in **Table 3** and interpreted as follows:

The thermodynamic parameters ΔH°, ΔS° and ΔG° are summarized in **Table 3**, and interpreted as follow: The protonated reactions of HPIP (1) and (2) are exothermic. Three factors affect protonation reactions: **(i)** the interaction of hydrogen ion with HPIP is exothermic process, **(ii)** desolvation of HPIP which is an endothermic **(iii)** the configuration and the rearrangement of the hydrogen bonds around the free and protonated HPIP. The positive ΔS° in equations (1) and (2) indicates that HPIP (L) is highly solvated by water molecules (more order) than the protonated ligand, HL^+ and the protonated ligand, HL^+ is more solvated by water molecules (more order) than the protonated ligand, H_2L^{2+}.

Effect of temperature on the hydrolysis of DMT

The logβ values of hydrolysis of DMT at different temperatures are given in **Table 2**.

The formation constant for the hydrolyzed species of dimethyltin(IV) β_{OH} can be calculated for the species 10-1, taken as an example, as:

$$\log \beta_{OH} = pK_w + \log \beta_{10\text{-}1}$$

The thermodynamic parameters ΔH° and ΔS° were obtained by a linear least squares fit of lnk vs.1/T (ln K = –ΔH°/RT + ΔS°/R), leading to an intercept at ΔS°/R and a slope of –ΔH°/R. The results obtained are summarized in **Table 3** and interpreted as follows:

The hydrolysis reactions are accompanied by endothermic liberation of ordered water of hydration from the reactants to form bulk water of greater disorder and are accompanied by significant increase in entropy. However, the ΔH° values in **Table 3** can be considered as the net summation of two opposing effects, namely the exothermic hydrolysis reaction and the endothermic liberation of ordered coordinated water molecules. Surprisingly reaction (3) in **Table 3**, the formation of the species 10-1, is an endothermic one and it has a very large change in entropy ($\Delta S° = 325.2\ JK^{-1}Mol^{-1}$) due to the release of first molecule of water of hydration. This contributes more negative value to the free energy change $\Delta G° = -62.2\ kJMol^{-1}$. Thus, the endothermic liberation of the ordered strongly bound first water molecule exceeds the exothermic hydrolysis reaction. The formation of 10-2, reaction (4), has negative $\Delta H° = -16.9\ kJMol^{-1}$, the entropy change is only 110 $JK^{-1}Mol^{-1}$, which indicates that the second water molecule in not as strongly bound as the first one. So, the exothermic hydrolysis reaction

exceeds the endothermic liberation of the second water molecule. The net free energy change for reaction (4), $\Delta G° = -49.5$ kJMol^{-1}, is less negative than that of reaction (3).

Reactions (5) and (6) have more negative $\Delta H°$ values compared to reactions (3) and (4). The negative $\Delta S°$ values in reactions (5) and (6) indicate that water molecules are less bound, so the disordering resulting from the release of weakly bound water molecules are less than ordering resulting from hydrolysis reactions.

Reaction (7), the formation of species 20-2, is the dimerization reaction which has negative $\Delta H°$ and positive $\Delta S°$.

Table 2. Effect of temperature on protonation constants of HPIP, hydrolysis of DMT and formation constants of DMT-HPIP complexes in water at different temperatures and 0.1M ionic strength.

M L H[a]	logβ[b]		
	15 °C	20 °C	25 °C
0 1 1	10.71(0.01)	10.57(0.01)	10.46(0.01)
0 1 2	17.93(0.02)	17.68(0.02)	17.49(0.02)
1 0 -1	-3.56(0.01)	-3.31(0.01)	-3.03(0.01)
1 0 -2	-9.05(0.01)	-8.64(0.01)	-8.21(0.01)
1 0 -3	-19.64(0.04)	-19.12(0.05)	-18.63(0.03)
1 0 -4	-30.41(0.04)	-29.76(0.02)	-29.24(0.02)
2 0 -2	-4.23(0.01)	- 3.77(0.01)	-3.12(0.01)
1 1 0	13.82(0.06)	13.53(0.06)	13.02(0.06)
1 1 1	19.63(0.03)	19.30(0.03)	18.53(0.03)
1 1 -1	6.65(0.02)	6.49(0.02)	6.06 (0.02)
1 1 -2	-3.78(0.05)	-3.88(0.05)	-4.19(0.05)
	30 °C	35 °C	
0 1 1	10.29(0.03)	10.16(0.01)	
0 1 2	17.22(0.02)	16.98(0.02)	
1 0 -1	-2.81(0.01)	-2.49(0.02)	
1 0 -2	-7.91(0.02)	-7.54(0.02)	
1 0 -3	-18.22(0.05)	-17.76(0.06)	
1 0 -4	-28.71(0.02)	-28.20(0.03)	
2 0 -2	-2.87(0.02)	-2.27(0.03)	
1 1 0	12.78(0.06)	12.03(0.06)	
1 1 1	17.670.03)	16.39(0.03)	
1 1 -1	5.89(0.02)	5.21(0.02)	
1 1 -2	-4.26(0.05)	-4.92(0.05)	

[a]M, L and H are the stoichiometric coefficient corresponding to DMT, HPIP and H^+, respectively; [b]Standard deviations are given in parentheses; Sum of square of residuals are less than $5x10^{-7}$.

Effect of temperature on the stability constant of DMT- HPIP complexes

The stability constants of DMT-HPIP complexes at different temperatures are given in **Table 2**. The thermodynamic parameters ΔH° and ΔS° were obtained by a linear least squares fit of lnk vs.1/T ($\ln K = -\Delta H°/RT + \Delta S°/R$), leading to an intercept at ΔS°/R and a slope of –ΔH°/R. The results obtained are summarized in **Table 3** and interpreted as follows:

The thermodynamic parameters, ΔH°, ΔS° and ΔG°, of DMT-HPIP complexes are given in **Table 3**. The complexation reaction (8) between DMT and HPIP is exothermic with ΔH° value of -146.7 kJ mol^{-1}. The formation reactions 9 to 11 are exothermic as usual,

Table 3. Thermodynamic parameters for the equilibria of DMT-HPIP complexes.

Equilibrium[a]	ΔH° $kJMol^{-1}$	ΔS° JK^{-1} Mol^{-1}	ΔG° $kJMol^{-1}$
1) $L + H^+ \rightleftharpoons LH^+$	-46.8(0.7)	42.6(0.7)	-59.5(0.8)
2) $LH^+ + H^+ \rightleftharpoons LH_2^{2+}$	-33.3(0.6)	22.7(0.4)	-40.1(0.5)
3) $M(H_2O)_4^{2+} + OH^- \rightleftharpoons M(H_2O)_3(OH)^+ + H_2O$	34.9(0.5)	325.2(2.6)	-62.2(0.8)
4) $M(H_2O)_3(OH)^+ + OH^- \rightleftharpoons M(H_2O)_2(OH)_2 + H_2O$	-16.9(0.3)	109.5(1.2)	-49.5(0.5)
5) $M(H_2O)_2(OH)_2 + OH^- \rightleftharpoons M(H_2O)(OH)^-_3 + H_2O$	- 23.8(0.4)	-12.9 (0.3)	-20.0(0.4)
6) $M(H_2O)(OH)_3^- + OH^- \rightleftharpoons M(OH)_4^{2-} + H_2O$	-27.2(0.4)	-27.7(0.4)	-18.9(0.4)
7)$[2M(H_2O)_3(OH)]^+ \rightleftharpoons (H_2O)_2M(OH)_2M(H_2O)_2^{2+} + 2H_2O$	-15.5(0.3)	2.23(0.06)	-16.1(0.3)
8) $[M(H_2O)_4]^{2+} + L \rightleftharpoons [M(H_2O)_2L]^{2+} + 2H_2O$	-146.7(1.2)	-242.9(1.3)	-74.3(0.6)
9)$[M(H_2O)_2L]^{2+} + H_3O^+ \rightleftharpoons [M(H_2O)_3LH]^{3+}$	-127.6(1.1)	-327.6(2.2)	-30.0(0.3)
10) $[M(H_2O)_2L]^{2+} + OH^- \rightleftharpoons [M(H_2O)(OH)L]^+ + H_2O$	-25.8(0.3)	46.1(0.5)	-39.6(0.4)
11)$[M(H_2O)(OH)L]^+ + OH^- \rightleftharpoons M(OH)_2L + H_2O$	-26.8(0.3)	-20.3(0.3)	-20.8(0.3)

[a] where M is DMT; standard deviations are given in parentheses.

Effect of solvent on stability constants of DMT-HPIP

Formation constants of DMT complexes with HPIP decreases with increasing of dioxane content in the medium **Table 4, and Figure 5**. This may be explained in terms of solvation of hydrophobic homopiperazine with the non-polar dioxane. This will lead to a decreasing in the stability of homopiperazine-$(CH_3)Sn^{+2}$ complexes. These results are in accordance with those found for $(CH_3)_2Sn^{2+}$-glycoxamine [34].

Table 4. Effect of solvent on protonation constants of HPIP, hydrolysis of DMT and formation constants of DMT-HPIP complexes in dioxane water mixture (v/v) solutions of different compositions at 25 °C and 0.1M ionic strength.

M L H[a]	logβ[b]		
	12.5 %	25 %	37.5 %
0 1 1	10.13(0.01)	9.83(0.01)	9.64(0.03)
0 1 2	16.92(0.03)	16.51(0.04)	16.09(0.07)
1 0 -1	-3.27(0.01)	-3.39(0.00)	-3.53(0.01)
1 0 -2	-8.70(0.02)	-8.99(0.01)	-9.23(0.01)
1 0 -3	-19.39(0.06)	-19.83(0.01)	-20.18(0.02)
1 0 -4	-30.28(0.03)	-31.30(0.01)	-31.83(0.01)
2 0 -2	-3.71(0.02)	-3.92(0.01)	-4.17(0.01)
1 1 0	12.81(0.06)	12.32(0.06)	11.73(0.06)
1 1 1	17.88(0.03)	16.87(0.03)	16.10(0.03)
1 1 -1	5.94(0.02)	5.62(0.02)	5.43(0.02)
1 1 -2	-3.76(0.05)	-3.36(0.05)	-3.11(0.05)
	50 %	62.5 %	75 %
0 1 1	9.49(0.01)	9.23(0.01)	9.13(0.01)
0 1 2	15.81(0.02)	15.57(0.02)	15.29(0.02)
1 0 -1	-3.60(0.01)	-3.68(0.01)	-3.98(0.02)
1 0 -2	-9.43(0.01)	-9.62(0.02)	-9.93(0.05)
1 0 -3	-20.58(0.02)	-20.89(0.04)	-21.35(0.09)
1 0 -4	-32.52(0.02)	-33.26(0.05)	-33.74(0.08)
2 0 -2	-4.30(0.01)	-4.47(0.01)	-4.90(0.01)
1 1 0	11.12(0.06)	10.83(0.06)	10.32(0.06)
1 1 1	15.15(0.03)	14.81(0.03)	13.82(0.03)
1 1 -1	5.32(0.02)	5.17(0.02)	4.95(0.02)
1 1 -2	-2.99(0.05)	-2.89(0.05)	-2.47(0.05)

[a]M, L and H are the stoichiometric coefficient corresponding to DMT, HPIP and H^+, respectively; [b]Standard deviations are given in parentheses; Sum of square of residuals are less than $5x10^{-7}$.

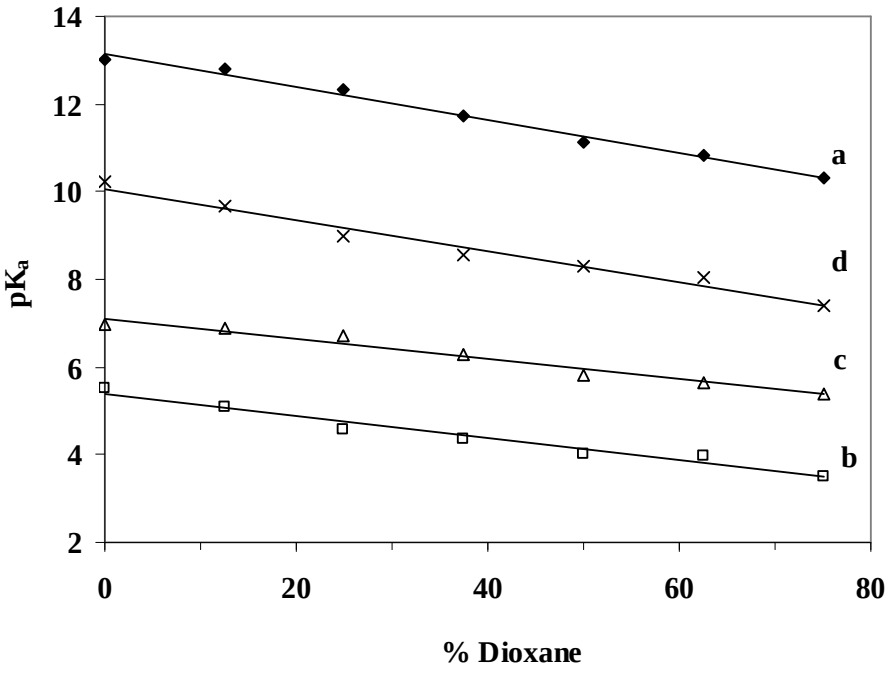


Figure.5. Effect of solvent on log β_{110} (a), pK_a of protonated complex species (111) (b), pK_{a1} and pK_{a2} of first and second coordinated water (c) and (d) respectively of DMT-HPIP system: **Scheme 2**.

Thermogravimetric studies TGA

The TGA for the solid complex was carried out within a temperature range from room temperature up to 600 °C. The percent losses in mass and thermal effects accompanying the changes in the solid complex on heating are shown in **Table 5**. As shown in the TG curve there is no mass loss below 188 which confirm the elemental analysis data that no water of crystallization is founded in the complex. The TGA curve shows two steps, The first step shows the loss of HP ligand + $2CH_3$ + one chloride. The second step shows the loss of the other Chloride, the residue of 37.3% corresponding to Sn, which has a theoretical value of 37.1%, **Figure 6**.

Table 5. Scheme for TGA mass loss of $Sn(CH_3)_2HPCl_2$ complex in the temperature range ~33 to 600°C with heating rate of 10 degree/min.

Assignment Loss	TGA °C	DTG °C	%Wt Loss Found (Calcd)
$HP(C_5H_{12}N_2) + 2CH_3 + Cl$	188 - 300	260	51.0 (51.7)
Cl	300 - 360	325	11.7 (11.1)

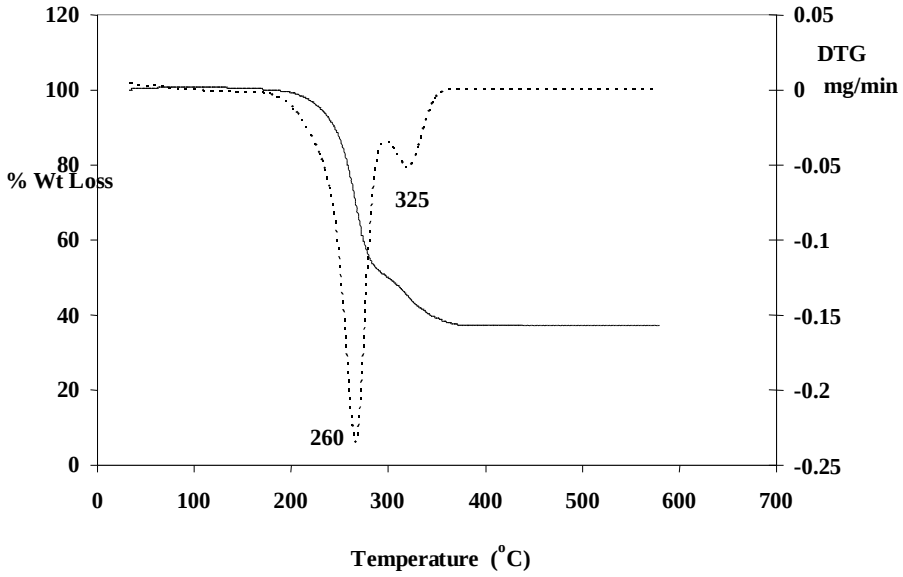


Figure.6. TGA (solid) and DTG (dotted) curves of DMT-HPIP complex.

Conclusion

The present investigation describes complex formation equilibria of homopiperazine with dimethyltin(IV). The results show the formation of 1:1 complexes. The formation of ternary complexes of HP-DMT-DNA (IV) was investigated. The results reveal to what extent DNA, the major target in tumour therapy can coordinate to homopiperazine and interact with dimethyltin(IV). These data are expected to contribute to the chemistry of dimethyltin(IV) compounds as apotential antitumor agents. Further investigation on the formation of the ternary complex with DNA will be carried out in future using advanced NMR measurements.

References

1. A. Kotsakis, D. Hatzidaki, L. Vamvakas, N. Vardakis, A. Kalykakis, V. Bozionelou, N. Androulakis, K. Kalbakis, Z. Saridaki, V. Georgoulias and S. Angelaki, *Anticancer Res.*, **3**, 4335 (2010).
2. C. Pellerito, P.D. Agati, T. Fiore, C. Mansueto, V. Mansueto, G. Stocco, L. Nagy and L. Pellerito, *J. Inorg. Biochem.*, **99**, 1294-1305 (2005).
3. F. Cima, L. Ballarin, Appl. Organomet. Chem., **13**, 697, (1999).
4. M.N. Shuaibu, H. Kanbara, T. Yanagi, A. Ichinose, D.A. Ameh, J.J. Bonire and A.J. Nok, *Parasitolog. Res.*, **91**, 5-11 (2003).
5. C.R. Jan, B.P. Jiann, Y.C. Lu, H.T. Chang, W. Su, W.C. Chen, C.C. Yu, J.K. Huang, *Life Sci.*, **70**, 1337-1345 (2002).
6. M.P. Samuel, D. de Vos, D. Raveendra, J.A.R.P. Sarma and S. Roy, *Bioorg. Med. Chem. Lett.*, **12**, 61-64 (2002).
7. W.D. Siegmann-Louda, E.C. Carraher Jr., F. Pflueger, J. Coleman. S. Harless, H. Luing, Polym. Master Sci. Eng., **82,** 83 Preprints (2000).
8. P. J. Blower, *Annu. Rep. Prog. Chem., Sect. A.*, **100**, 633-658 (2004).
9. M. Gielen and R. Willem, *Anticancer Drugs*, **12,** 269-271 (1992).
10. A.J. Crowe, in: S.P. Fricker (Ed.), Metal Compounds in Cancer Therapy, Chapman and Hall, London, p. 147-179 (1994).
11. S.K. Hadjikakou and N. Hadjiliadis, *Coord. Chem. Rev.*, **253**, 235-249 (2009).
12. A.J. Crowe, P.J. Smith, C.J. Cardin, H.E. Parge and F.E. Smith, *Cancer Lett.*, **24**, 45-48 (1984).
13. M. Gielen, D. De Vos, A. Et-toubami, M. Boualam, A. Khloufi and R. Willem, *In Vivo.*, **7**, 171-174 (1993).
14. A. Yahyi, A. El-touhami, R. Yahyaoui and R. Touzani, *Lett Drug Des Discov.*, **7**, 534-540 (2010).
15. M. Gielen, *Metal-Based Drugs*, **1**, 213-219 (1994).

16. S. Tabassum and C. Pettinari, *J. Organomet. Chem.*, **691**, 1761-1766 (2006).
17. N. Muhammad, A. Shah, Z. Rehman, S. Shuja, S. Ali, R. Qureshi, A. Meetsma and M.N. Nair, *J.Organomet. Chem.*, **694**, 3431-3437 (2009).
18. A.Sh. Al-Alousi, M.R. Shehata, M.M. Shoukry and N. Mahmoud, *Chemical Speciation and Bioavailability.*, **21**, 1-6 (2009).
19. A. Al-Najjar, M.M.A. Mohamed, M.R. Shehata and M.M. Shoukry, *Annali di Chim.*, **96**, 97-107 (2006).
20. A.A. Al-Najjar, M.M.A. Mohamed and M.M. Shoukry, *J. Coord. Chem.*, **59**, 193-206 (2006).
21. M.M.A. Mohamed, M.M. Shoukry, *Chem. & Pharm. Bulletin (Japan)*, **49**, 253-257 (2001).
22. O. Al-Flaijj, M.R. Shehata, M.M.A. Mohamed and M.M. Shoukry.. *Monatsh. Fur Chem.*, **132**, 349-366 (2001).
23. R. G. Bates, "Determination of pH-Theory and Practice" 2nd Edit, Wiley Interscience (1975).
24. M.M. Shoukry, W.M. Hosny and M.M. Khalil, *Transition Met. Chem.*, **20**, 252-255 (1995).
25. R.J. Motekaitis, A.E. Martell and D.A. Nelson, *Inorg. Chem.*, **23**, 275-283 (1984).
26. P. Gans, A. Sabatini and A. Vacca, Inorg. Chim. Acta., **18**, 237 (1976).
27. L. Pettit, University of Leeds, U.K., Personal Communication, 1993.
28. D.D. Perrin, Stability Constants of Metal-Ion Complexes: Part B, Organic Ligands, Pergamon Press, Oxford, 1979.
29. G. Arena, R. Cali, A. Contino, A. Musumeci, S. Musumeci and R. Purrello, *Inorg. Chim. Acta*, **237**, 187-191 (1995).
30. T. Natsume, S. Aizawa, K. Hatano and S. Funahshi, *J. Chem. Soc. Dalton Trans.*, 2749-2753 (1994).
31. M.J. Hynes and J. O'Dowd, *J. Chem. Soc. Dalton Trans.*, 563-566 (1987).

32. C. De Stefano, C. Foti, A. Gianguzza, M. Martino, L. Pellerito and S. Sammartano. *J. Chem. Eng. Data.*, **41**, 511-515 (1996).

33. C. Foti, A. Gianguzza, F.J. Millero and S. Sammartano, *Aquat. Geochem.*, **5**, 381-398 (1999).

34. L.C. Mun, M.A. Hapipah, S.K. Shin, A.S. Murestri and L.K. Mun, *Applied Organomet. Chem.*, **26**, 310-319 (2012).