Equilibrium studies of diethyltin(IV) dichloride and divinyltin(IV) dichloride with 1-(2-aminoethyl)-pyrrolidine

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Abstract

The interaction of diethyltin(IV) (DET) and divinyltin(IV) (DVT) with 1-(2-aminoethyl)-pyrrolidine (AEPY) was investigated using potentiometric technique at ionic strength of 0.1 mol dm−3 NaNO3. The hydrolysis constants of diethyltin(IV) and divinyltin(IV) cations and the stepwise formation constants of the complexes formed in solution were calculated at different temperatures and in solutions of dioxane-water solutions of different compositions. The stoichiometry and stability constants for the complexes formed were reported. The results showed the formation of 1:1 complex and the corresponding hydroxo complexes. The concentration distributions of the various complex species were evaluated as a function of pH. The thermodynamic parameters ΔH° and ΔS° calculated from the temperature dependence of the equilibrium constants were investigated for DET and DVT complexes with AEPY. The equilibrium constant for the displacement of 1-(2-aminoethyl)-pyrrolidine coordinated to diorganotin(IV) by thymine and thymidine as representative examples of DNA constituents was calculated from calculations based upon equilibrium properties. The results are expected to contribute to the chemistry of tin(IV) based anticancer agents.

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1. Introduction

The biological aspects of pyrrolidine derivatives have got attention as they have selective inhibition activity [1] against matrix metalloproteinase-2 and characteristics of potent anti-tumour activity [2–4]. Copper(II) complex of pyrrolidine dithiocarbamate has been reported to have potent anti-cancer activity against cisplatin resistant neuroblastoma cells [5]. Recently pyrrolidine based inhibitors of the drug resistant mutant of HIV-1 protease have been reported [6]. Pt(II) derivatives of 1,2 alkyl substituted 3-aminopyrrolidines showed antiproliferative activity [7,8]. A variety of organotin complexes structurally related to cis-platin and its derivatives [9] have been investigated for their antitumour properties [10,11]. Among organotin, dialkyl derivatives exhibit greater antitumour activity than the corresponding mono-, tri-, and tetra-alkyl derivatives [12]. If one ranks specific alkyl organotins in terms of antitumour activity of the parent compounds, the diethyl derivatives have the highest activity in vivo provided that one takes no
cognizance of their toxicity [13]. The antitumour activity of diorganotin(IV) compounds of the type R2SnX2L, where L is generally bidentate ligand has been reported [14]. The coordinated ligand plays an important role in this activity as it favors the transport of diorganotin(IV) into the cell. The mechanism of antitumour activity is based on the dissociation of the ligand with subsequent binding to DNA. In the case of nitrogen bearing ligands [15], increasing stability is thought to reduce activity by hindering the dissociation of the ligand that is necessary for binding between tin and DNA. Therefore, there is a relationship between the stability of the organotin compounds and their antitumour activity. During the last two decades, the interest of many scientists in the chemistry of methyl, ethyl, and butyl derivatives of tin(IV) has risen, but very rare studies are available on the solution chemistry of divinyltin(IV). Also, to the best of our knowledge the literature contains no studies regarding the stability constants of DVT and DET complexes with 1-(2-aminoethyl)-pyrrolidine (AEPY) (Scheme 1) in dioxane-water mixtures. As part of our project dealing with the study of metal complexes of expected biological activity [16–20] and as a continuation of our previous studies on organotin(IV) complexes [21–23], the present paper aims to study the diethyltin(IV) and divinyltin(IV) complex formation equilibria with 1-(2-aminoethyl)-pyrrolidine (AEPY). AEPY is selected due to the hydrophobic nature of pyrrolidine moiety, which may help its organotin(IV) complex to transport...
across membranes. In the present study, the complex formation equilibria of the complexes formed in solution was investigated. The stoichiometry and stability constants of the complexes formed in solution were determined at different temperatures and in dioxane-water solutions of different compositions.

2. Experimental

2.1. Materials and reagents

Diethyltin(iv) dichloride and divinyltin(iv) were supplied by Merck Chem. Co. 1-(2-aminoethyl)-pyrrolidine was provided by Sigma Chemicals Co. Carbonate-free NaOH solutions (titrant) was prepared by diluting the content of BDH concentrated volumetric solution vials. These solutions were systematically checked by titration against potassium hydrogen phthalate solution. All solutions were prepared in deionized H₂O.

2.2. Instruments

Potentiometric measurements were made using a Metrohm 686 titroprocessor equipped with a 665 Dosimat (Switzerland-Herisau). A thermostatted glass-cell was used equipped with a magnetic stirring system, a combined Metrohm glass electrode (6.0220.100), a thermoelectric probe, a microburet delivery tube and a salt bridge connected with the reference cell filled with 3 mol dm⁻³ KCl solution in which Ag/AgCl electrode was dipped. The titroprocessor and electrode were calibrated with standard buffer solutions, potassium hydrogen phthalate (pH 4.008) and a mixture of KH₂PO₄ and Na₂HPO₄ (pH 6.865) at 25 °C.

2.3. Procedure and measurements

The following mixtures were prepared and titrated potentiometrically with 0.05 M NaOH solution.

A- 40 ml of solution containing 1.25 × 10⁻³ mol dm⁻³ of ligand (H₂AEPY), of constant ionic strength 0.1 mol dm⁻³, (adjusted with NaNO₃);
B- 40 ml of solution containing 1.25 × 10⁻³ mol dm⁻³ of DET/DVT cation and 0.1 mol dm⁻³ NaNO₃;
C- 40 ml of solution containing 1.25 × 10⁻³ mol dm⁻³ DET/DVT cation, 1.25 × 10⁻²/2.50 × 10⁻² mol dm⁻³ ligand (H₂AEPY) and 0.1 mol dm⁻³ NaNO₃;

The proton dissociation constants of the protonated AEPY were determined potentiometrically by titrating mixture (A). The hydrolysis constants of DET and DVT were determined by titrating mixture (B). The formation constants of DET and DVT complexes with AEPY were determined by titrating mixture (C). All titrations were performed in a purified N₂ atmosphere, using aqueous 0.05 mol dm⁻³ NaOH as titrant. The pH is plotted against p[H]. The relationship pH - p[H] = 0.05 was observed. [OH⁻] value was calculated using a pKw value of 13.921 at 25 °C [21]. The ionic strength was adjusted to 0.1 mol dm⁻³ by using of of NaNO₃. For the variable temperature studies the following values of pKw were employed: at 20 °C (pKw = 14.126), at 30 °C (pKw = 13.753) and at 35 °C (pKw = 13.660) [21]. As is known, pH-meters read −log aH⁺ (pH), whereas the potentiometric method we used for the calculation of stability constants requires −log[H⁺] (p[H]). Hence, the first step in computations was to convert the pH-meter readings (B) recorded in dioxane-water solutions to hydrogen ion concentration [H⁺]. This can be achieved by using the widely used relation given by the Van Uitert and Hass equation, Eq. (1) [24] as shown below,

\[-\log_{10}[H^+] = B + \log_{10}U_H \tag{1}\]

where log₁₀Uₜ is the correction factor for the solvent composition and ionic strength for which B is read. Values of pKw in dioxane-water mixtures were taken from [25].

The equilibrium constants evaluated from the titration data (summarized in Table 1) were determined by titrating mixture (B) recorded in dioxane-water solutions to hydrogen ion concentration [H⁺]. The formation constants are as follows: 10⁻¹ (DET₂⁺ + H₂O ⇌ DET(OH)⁺ + H⁺), 10⁻² (DET⁺ + 2H₂O ⇌ DET(OH)₂ + 2H⁺), 10⁻³ (DET⁻ + 3H₂O ⇌ DET(OH)₃⁻ + 3H⁺), (11 DET⁺ + L = DET(L)⁺), 10⁻⁴ (DET⁻ + L + 2H₂O = DET(L)(OH)²⁺ + H⁺) and 111 (DET⁻ + L + 3H⁺ = DET(L)(OH)₃⁻).

2.4. Data processing

Calculations were performed using the computer program MINIQUAD-76 [26]. The program was described in detail with all FORTRAN commands in Ref. [27]. The stoichiometry and stability constants of the complexes formed were determined by trying various
Table 2

Formation constants of diethyltin(IV) complexes with AEPY.

<table>
<thead>
<tr>
<th>p q r</th>
<th>log10 K</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>15 °C</td>
</tr>
<tr>
<td>1 0 1</td>
<td>16.28 (0.07)</td>
</tr>
<tr>
<td>1 1 0</td>
<td>9.15 (0.02)</td>
</tr>
<tr>
<td>1 1 1</td>
<td>15.30 (0.04)</td>
</tr>
<tr>
<td>1 0 3</td>
<td>10.37 (0.07)</td>
</tr>
<tr>
<td>1 1 1</td>
<td>15.28 (0.07)</td>
</tr>
</tbody>
</table>

a and b as in Table 1.

Table 3

Thermodynamic parameters for the equilibria of diethyltin(IV) or divinyltin(IV), DVT-AEPY and DET-AEPY complexes in aqueous solution at 0.1 M NaNO₃ at different temperatures.

<table>
<thead>
<tr>
<th>Equilibrium</th>
<th>ΔH°(kJ mol⁻¹)</th>
<th>ΔS°(J K⁻¹ mol⁻¹)</th>
<th>ΔG°(kJ mol⁻¹)</th>
</tr>
</thead>
<tbody>
<tr>
<td>DET</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1) M(H₂O)₄⁺ + OH⁻ = M(H₂O)(OH)⁻ + H₂O</td>
<td>-121.3</td>
<td>154.3</td>
<td>-58.1 (5)</td>
</tr>
<tr>
<td>2) M(H₂O)₂(OH)⁻ + OH⁻ = M(H₂O)(OH)₂⁻ + H₂O</td>
<td>-2.85 (3)</td>
<td>146 (1)</td>
<td>-46.5 (5)</td>
</tr>
<tr>
<td>3) M(H₂O)(OH)⁺ + OH⁻ = M(H₂O)(OH)₃⁻</td>
<td>62.4 (6)</td>
<td>269 (3)</td>
<td>-17.9 (5)</td>
</tr>
<tr>
<td>DVT</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4) M(H₂O)₂⁺ + OH⁻ = M(H₂O)(OH)⁺ + H₂O</td>
<td>-216.3</td>
<td>141 (2)</td>
<td>-63.9 (5)</td>
</tr>
<tr>
<td>5) M(H₂O)⁺ + OH⁻ = M(H₂O)(OH)₂⁺</td>
<td>-2.85 (3)</td>
<td>146 (1)</td>
<td>-46.5 (5)</td>
</tr>
<tr>
<td>6) M(H₂O)(OH)⁺ + OH⁻ = M(H₂O)(OH)₂⁺</td>
<td>-3.13 (2)</td>
<td>68 (4)</td>
<td>-23.5 (4)</td>
</tr>
<tr>
<td>7) M(H₂O)(OH)⁻ + OH⁻ = M(H₂O)(OH)₂⁻</td>
<td>-8.97 (4)</td>
<td>21 (3)</td>
<td>-15.3 (4)</td>
</tr>
<tr>
<td>L = AEPY</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8) L⁻ + H⁺ = LH⁺</td>
<td>-40.5 (3)</td>
<td>44.8 (3)</td>
<td>-53.9 (4)</td>
</tr>
<tr>
<td>9) LH⁻ + H⁺ = LH⁺²⁻</td>
<td>-45.5 (3)</td>
<td>16 (2)</td>
<td>-50.4 (6)</td>
</tr>
<tr>
<td>DET-AEPY</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10) M(H₂O)₄⁺ + L⁻ = M(H₂O)(L)²⁻ + 3H₂O</td>
<td>40.8 (4)</td>
<td>33.6 (3)</td>
<td>-58.6 (5)</td>
</tr>
<tr>
<td>11) M(H₂O)₂⁺ + L⁻ = M(H₂O)(L)⁺²⁺</td>
<td>-30.9 (3)</td>
<td>3.0 (8)</td>
<td>-32.0 (5)</td>
</tr>
<tr>
<td>12) M(H₂O)⁺ + L⁻ = MOH(L)⁺ + H₂O</td>
<td>-100 (0.3)</td>
<td>62 (0.5)</td>
<td>-118 (5)</td>
</tr>
<tr>
<td>(DET-AEPY)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>13) M(H₂O)₄⁺ + L⁻ = MOH(L)²⁻ + 3H₂O</td>
<td>802 (5)</td>
<td>501 (3)</td>
<td>-230 (6)</td>
</tr>
<tr>
<td>14) M(H₂O)₂⁺ + H₂O⁺ = MOH²⁺ + H₂O</td>
<td>-22.8 (3)</td>
<td>13 (2)</td>
<td>-26.8 (5)</td>
</tr>
<tr>
<td>15) M(H₂O)⁺ + L⁻ = MOH(L)⁺ + H₂O</td>
<td>-829 (4)</td>
<td>150 (9.2)</td>
<td>-1279 (4)</td>
</tr>
</tbody>
</table>

* Where M is (Ethyl)₂Sn or (Vinyl)₂Sn; standard deviations (in the last digit) are given in parentheses.

2.5. Molecular modeling studies

An attempt to gain a better insight on the molecular structure of the complexes, geometric optimization and conformation analysis has performed using semi-empirical method PM3 as implemented in HyperChem 7.5 [29]. The structures of diorganotin compounds of AEPY were optimized with semi-empirical method PM3 (Parametric Method-3). A gradient of 0.01 kcal/Å was set as a convergence criterion in all the molecular mechanics and quantum calculations. The lowest energy structure was used for each molecule to calculate physicochemical properties.

3. Results and discussion

The proton dissociation constants of the diprotonated 1→(2-aminoethyl)-pyrrolidine (AEPY) ligand were determined under the same experimental conditions of ionic strength and temperature which are used for the study of diethylth(IV) and divinylth(IV) complex equilibria. The results of protonation and complex formation equilibria are given in Tables 1–5.

3.1. Protonation constants of AEPY ligand

1→(2-Aminoethyl)pyrrolidine (AEPY) has two basic nitrogen atoms, Scheme 2. The AEPY solution is prepared in acid medium to protonate 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 [26,27]. Also, the accepted model gave small values for standard deviation and sum of square of residuals. The fitted model was tested by comparing the experimental titration data points and the theoretical curve calculated from the values of the acid dissociation constant of the ligand and the formation constants of the corresponding complexes. The results are summarized in Tables 1–6. The species distribution diagrams were obtained using the program SPECIES [28] under the experimental condition employed.
Scheme 2. Acid-base equilibria of AEPY.

Fig. 1. Concentration distribution of various species as a function of pH in the AEPY system (at concentration of 1.25 mmol/l for AEPY).

Fig. 2. Potentiometric titration curves for the DET-AEPY system.
the nitrogen atoms. The stoichiometric protonation constants of the investigated AEPY ligand were determined in aqueous solution at different temperatures and these constants are given in Table 1. The AEPY ligand studied here have two protonation constants (9.42 and 6.66 at 25 °C). This is also illustrated in the species distribution of the AEPY ligand in Fig. 1. The validity of the model was tested by comparing the experimental and simulated data. The good agreement reveals the validity of the model. In acidic solution, AEPY initially exists in the fully protonated form as H2L+2. By rising of pH, the species H2L+2 loses its first proton forming HL+, which is the predominant species at pH from 6.6 to 9.2 with maximum concentration percentage of 90.5% at pH = 8. As pH increases, the second proton begins deprotonation forming the full deprotonated species L which is the predominant species at pH > 9.2.

**Scheme 3.** Complex formation equilibria of DET with AEPY.

![Scheme 3](image)

**Fig. 3.** Concentration distribution diagram of various species as a function of pH in the DET-AEPY system (at concentration of 1.25 mmol/l for DET & AEPY).

**Fig. 4.** Potentiometric titration curves for the DVT-AEPY system.
Fig. 5. Concentration distribution diagram of various species as a function of pH in the DVT-AEPY system (at concentration of 1.25 mmol/l for DVT & AEPY).

Fig. 6. Effect of temperature on protonation of AEPY ligand.
3.2. Acid-base chemistry of dialkyltin(IV) ion

The acid-base chemistry of dialkyltin(IV) has been characterized by fitting the potentiometric data to various acid-base models. The fitted model, according to the aforementioned method of calculation, was found to be consistent with the mono-, di- and trihydroxo-organotin (IV) \([\text{Et}_2\text{Sn(OH)}_n\text{], where } n = 1, 2 \text{ and } 3]\). For divinyltin(IV) system, the species formed are mono-, di- and tetrahydroxo-organotin (IV) \([\text{DVT}_2\text{Sn(OH)}_n\text{, where } n = 1, 2, 3 \text{ and } 4}\).

3.3. Complex formation equilibria involving DET-AEPY

Potentiometric titration curves of the diethyltin(IV)-AEPY system is shown in Fig. 2. In the organotin complex curve, there is a significant lowering from that of free AEPY indicating formation of organotin complexes by release of protons. The titration data were fitted at 25 °C was fitted with a model composed of the 110, 11–1 and 111 species (Table 1). The pKₐ of coordinated water molecule is calculated by Eq. (4) [16,18,30].

\[
\text{pK}_a = \log \beta_{110} - \log \beta_{11-1}
\]  

(4)

The calculated pKₐ value \((7.0)\) is higher than that of water molecule coordinated to the free diethyltin(IV) ion \((3.69)\). This may be due to the elongation of Sn(IV)-H₂O bond caused by the coordination of 1-(2-aminoethyl)-pyrrolidine (Scheme 3).

The concentration distribution diagram of DET-AEPY complex (Fig. 3) as a function of pH provides a useful picture of the organotin binding with pyrrolidine. The complex \((111)\) starts to predominates from pH 2.7 and reaches a maximum concentration of 13.5% at pH = 4. The complex \((110)\) starts to form at pH = 3.6 and reaches a maximum concentration of 29% at pH = 6.0. The hydroxo complex \((11-1)\) starts to form at pH = 5.3 and predominates from pH 7.9 to 9.7 with maximum concentration of 59% at pH = 8.4.

3.4. Complex formation equilibria involving DVT-AEPY

Potentiometric titration curves of the divinyltin(IV)-AEPY system is shown in Fig. 4. The titration data were fitted at 25 °C with a model composed of the 110, 11–1, 11–2 and 111 species (Table 2). The calculated pKₐ value 6.86 at 25 °C. It is higher than that of water molecule coordinated to the free divinyltin(IV) ion \((2.74)\).

![Fig. 7. Effect of temperature on logK of DET-AEP complexes.](image)
The concentration distribution diagram of divinyltin(IV)-1-(2-aminoethyl) pyrrolidine complex is given in Fig. 5. The complex (111) predominates from pH = 1.7 to 4.6 and reaches a maximum concentration of 77% at pH = 3.2. The complex (110) starts to form at pH = 3 and reaches a maximum concentration of 68% at pH = 5.7. The hydroxo complex (11-1) starts to form at pH = 5 and predominates with maximum concentration of 79.3% at pH = 8.2. It is interesting to find that the complex species (110) and (11-1) are predominating in the pH range 5.7 to 8.2, i.e. in the physiological pH range.

3.5. Effect of temperature

The thermodynamic parameters are useful tools for studying metal-ligand chemical interactions and understanding the relative stability of the formed complexes. The thermodynamic parameters of the \( \Delta H^o \), \( \Delta S^o \) and \( \Delta G^o \) associated with the protonation of AEPY and its complex formation with diethyltin(IV) and divinyltin(IV) species were calculated by using Eqs. (5)–(7) [31,32]

\[
\Delta G = -2.303 \text{ RT } \log K = 2.303 \text{ RT } pK^H
\]

\[
-2 \cdot 303 \text{ RT } \log K = \Delta H - T \Delta S
\]

\( \log K = \frac{\Delta S}{2.303R} - \frac{\Delta H}{2 \cdot 303R T} \)  \hspace{1cm} (7)

where \( K \) is the formation constant, determined potentiometrically at different temperatures (Table 1), \( R \) is the universal gas constant and \( T \) is the temperature in Kelvin. Values of \( \Delta H^o \) (Table 3) were estimated from plotting \( \log K \) vs. \( 1/T \) (Figs. 6–8) while those of the entropy change (\( \Delta S^o \)) (Table 3) were estimated from the intercept of Eq. (7). From the obtained results, the following information can be concluded:

a) The thermodynamic processes accompanying the protonation reactions are:
   i) the neutralization reaction, which is an exothermic process;
   ii) the desolvation of ions, which is an endothermic process; and
   iii) the change in the configuration and the arrangements of the hydrogen bonds around the free and protonated ligands.

b) The \( \log_{10} K \) values decrease with increasing temperature revealing that the acidity increases with increasing temperature.

c) The protonation reactions of AEPY have positive entropy; this may be due to increased disorder as a result of desolvation processes and the breaking of hydrogen bonds.

Fig. 8. Effect of temperature on logK of DVT-AEPY complexes.
d) Surprisingly, the complexation reactions (3) and (5) for diethyltin (IV)-AEPY and divinyltin(IV)-AEPY are endothermic with $\Delta H^\circ$ value of 40.8 and 80.2 kJ mol$^{-1}$ respectively (Table 3). This is similar to what was found by Kramer-Schnabel [33] and can be interpreted as above by assuming that the enthalpy change is a net summation of two opposing effects, i.e. the exothermic complexation and the endothermic liberation of ordered water of hydration and breaking of hydrogen bonds. This is confirmed by large $\Delta S^\circ$, value of 337 J K$^{-1}$ mol$^{-1}$ for DET-AEPY and 503 J K$^{-1}$ mol$^{-1}$ for DVT-AEPY complexes, giving negative $\Delta G^\circ$ value of $-59.6$ kJ mol$^{-1}$ and $-230$ kJ mol$^{-1}$ for DET-AEPY and DVT-AEPY complexes respectively.

e) The positive values of $\Delta S^\circ$ confirmed that the complexation process is entropically favorable.
f) All values of $\Delta G^\circ$ for complexation are negative, indicating the spontaneity of the coordination process.

3.6. Effect of solvent

It is well established that the “effective” or “equivalent solution” dielectric constants in protein [33,34] or active site cavities of enzymes [35] are small compared to that in bulk water. Estimates for the dielectric constants in such locations range from 30 to 70 [33–35]. Hence by using aqueous solutions containing ~10–50% dioxane, one may expect to simulate to some degree the situation in active site cavities [36], hence to extrapolate the data to physiological conditions. The solvent effect on the acid dissociation constants of a ligand [22] can be summarized as follows.

(i) As the solvent dielectric constant decreases, the $pK_a$ of the ligand increases and vice versa.

(ii) On decreasing the extent of hydrogen bonding in water by an organic solvent, the proton-accepting properties of the water increases, and consequently the $pK_a$ of the ligand decreases.

(iii) Increasing proton solvation by an organic solvent is accompanied by a decrease in the $pK_a$ of ligand.

Careful examination of media effects on the equilibrium constants (Tables 4 and 5) reveals the following features:

1) The stoichiometric protonation constants of AEPY given in Table 4 and Fig. 9 are related to the following equilibria:

\[
L + H^+ = HL^+ \quad K_1 = [L^+] / [L][H^+] \tag{8}
\]

\[
\log \beta_{\text{H}^+} \quad \log \beta_{\text{H}^+}
\]

Fig. 9. Effect of dioxane on protonation constants of AEPY.
\[
\text{HL}^+ + \text{H}^+ \rightleftharpoons \text{H}_2\text{L}^2+ \\
K_2 = \frac{[\text{H}_2\text{L}^2+]}{[\text{HL}^+][\text{H}^+]} 
\]

(9)

The protonation constant \((K_1)\) is related to the protonation of the \(\text{NH}_2\) group while \((K_2)\) is related to the protonation of the \(\text{N-pyrrolidine}\) atom.

2) The failure of the cationic acids of \((-\text{NH}^+)\) to conform to the electrostatic model has been discussed in terms of relative importance of the solvent effect (ii and iii). The nonelectrostatic contribution to the change in \(\log K_{\text{NH}^+}\) has been regarded as representing the sum of medium effects for individual ions [37]. This means that, the decrease of \(\log K_{\text{NH}^+}\) values with increasing dioxane content can be interpreted by nonelectrostatic forces, which could include geometrical aspects, hydrogen bonding and solute-solvent interactions. This behaviour is in agreement with that proposed for oximes [38] and cephradines [39].

3) The formation constants of diethyltin(IV) and divinyltin(IV) complexes with AEPY decrease upon addition of dioxane (Figs. 10 and 11) to an aqueous solution of the corresponding species. This can be explained by better solvation of hydrophobic species \((\text{CH}_3)_3\text{Sn}^+\) and \((\text{CH}_3)_2\text{SnCl}\) by dioxane resulting in lowering complex stability. This behaviour is in agreement with that proposed for alkyltin(IV) complexes with \(\beta\)-glucosamine [40], inosine [41] and iminobismethylphosphonic acid [25].

3.7. Quantum chemical calculations and solution equilibrium studies

Energy minimization studies were carried out on the basis of the semi-empirical PM3 level provided by HyperChem 7.5 software. The most stable structures for the AEPY and its diorganotin complexes obtained (Figs. 12–14) were subsequently optimized to the closest local minimum at the semiempirical level using PM3 parameterizations.

![Fig. 10. Effect of dioxane on logβ of DET-AEPY.](image-url)
The values of the following parameters: the highest occupied molecular orbital energy ($E_{\text{HOMO}}$), the lowest unoccupied molecular orbital energy ($E_{\text{LUMO}}$), the difference between HOMO and LUMO energy levels ($\Delta E$), Mulliken electronegativity ($\chi$), chemical potential ($\Pi$), global hardness ($\eta$), global softness ($S$) and global electrophilicity ($\omega$) [42–45] have been calculated [46] using semi-empirical PM3 method as implemented in HyperChem [29]. In a first step, the molecular geometries of all compounds were fully optimized in the gas phase to gradients of 0.01 kcal·mol$^{-1}$ Å$^{-1}$ and afterwards the molecular descriptors were determined.

Eqs. (10)–(15) are used in calculations of molecular parameters as given below:

\[
\chi = -\frac{1}{2} \left( E_{\text{LUMO}} - E_{\text{HOMO}} \right) \tag{10}
\]

\[
\Pi = -\chi \tag{11}
\]

\[
\eta = \frac{1}{2} \left( E_{\text{LUMO}} - E_{\text{HOMO}} \right) \tag{12}
\]

\[
S = \frac{1}{2\eta} \tag{13}
\]

\[
\omega = \frac{\Pi^2}{2\eta} \tag{14}
\]

\[
\sigma = \frac{1}{\eta} \tag{15}
\]

The concepts of the parameters $\chi$ and $\Pi$ are related to each other. The inverse of the global hardness is designated as the absolute softness $\sigma$.

To support the formation and stability of these complexes in solution, we have optimized first the structure of AEPY as given in Fig. 12, indicating that both N-pyrrolidine and amino group of the side chain are in the same direction and participate in coordination forming five-membered chelate ring upon complexation as given in Figs. 13 and 14.

Fig. 11. Effect of dioxane on log($\beta$) of DVT-AEPY.
Also, we have discussed the highest occupied molecular orbital-lowest unoccupied molecular orbital (HOMO–LUMO) gap for the complexes (see Fig. 15 and Table 6) in order to correlate the experimental results of stability constants with the calculated molecular parameters of the complexes (Table 6).

The calculations for the molecular parameters support the experimental formation constant. The HOMO–LUMO gap is used as a direct indicator of stability [47,48]. A large HOMO–LUMO gap increases stability and decreases chemical reactivity. The results show the following trend in HOMO–LUMO gap for the complexes:

\[ \text{DVT–AEPY} > \text{DET–AEPY} \]

DVT-AEPY complex has a large energy gap \( (\Delta E = 7.49) \) than DET-AEPY complex \( (\Delta E = 6.65) \). A large HOMO–LUMO gap is in accord with the experimental formation constant values.

According to the maximum hardness principle, greater hardness \( (\eta) \) causes more stability in the molecule [49]. Absolute hardness is half of the HOMO–LUMO energy gap. The hardness \( (\eta) \) calculated for the complexes shown in Table 6. The hardness parameter of the complexes follows this sequence DVT-AEPY \( (\eta = 3.75) \) > DET-AEPY \( (\eta = 3.32) \) which

![Fig. 12. The optimized geometry of AEpy along with the atom numbering scheme.](image)

![Fig. 13. The optimized geometry of DVT-AEPY along with the atom numbering scheme.](image)

![Fig. 14. The optimized geometry of DET-AEPY along with the atom numbering scheme.](image)
is also in accord with the energy gap and formation constants of the diorganotin complexes.

4. Conclusion

The present investigation describes the complex formation equilibria of diethyltin(IV) and divinyltin(IV) with 2-aminoethylypyridoline. The complexes formed are of stoichiometric coefficients 110, 111 and 11. The stability constants were determined and the concentration distribution diagrams were evaluated. The thermodynamic parameters ΔH° and ΔS° were determined and discussed. The study of the effect of dielectric constant of the medium on the stability constants of the complexes was investigated. The complexes are more favored in biological environments of lower dielectric constant.

The molecular properties of the structures such as dipole moment, hardness, the highest occupied molecular orbital–lowest unoccupied molecular orbital (HOMO–LUMO) gap were calculated. These calculations have shown that the trend in HOMO–LUMO gap for the complexes follows the order: DVT-AEPY > DET-AEPY, this finding is in agreement with the experimental formation constants of these complexes.

References


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