# Thermodynamic Study of Dimethyltin(IV) Complexes with Nucleoside 5′-Triphosphates*

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The complex formation of $[SnMe_2]^{2+}$ ion with guanosine 5′-triphosphate (GTP), inosine 5′-triphosphate (ITP), cytidine 5′-triphosphate (CTP) and tripolyphosphate(5−) (tpp) has been investigated by means of potentiometric and calorimetric measurements at 25 °C and $I$ = 0.1 mol dm$^{-3}$ ($KNO_3$). On the basis of the thermodynamic parameters, bonding details have been inferred for the main nucleotide complex species, using tpp as reference. The thermodynamic data show that the nitrogen atom [N(1)] of the bases interacts with dimethyltin in the $[SnMe_2L]$ species of GTP and ITP only.

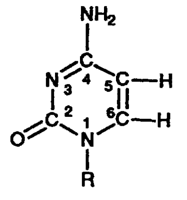
Dimethyltin(IV) compounds have been tested as antitumour drugs since 1929. In a recent paper, Saxena and Huber[1] reviewed the state of the field and pointed out the need 'to study the structure... in solution (especially in aqueous media)'. Organotin(IV) compounds are found both in fresh and marine waters, since they are among the most industrially used organometallic compounds and are also widely used as biocidal agents; this also poses the problem of their presence in the human food chain.[2] In addition, as for many drugs used in chemotherapy, there may be undesirable side-effects of the pharmaceutical use of these compounds.[2] Therefore understanding of the interaction of organotin(IV) compounds with possible biological targets is highly desirable.

With the above in mind, continuing our study on the species distribution[3–5] of dialkyltin(IV), we report on the complex formation of dimethyltin(IV) ($[SnMe_2]^{2+}$) with guanosine 5′-triphosphate (GTP), inosine 5′-triphosphate (ITP), cytidine 5′-triphosphate (CTP) and tripolyphosphate(5−) (tpp). The latter has been studied for the purpose of comparison. These ligands have been chosen (*i*) for a better understanding of the co-ordination chemistry of dimethyltin(IV), to deoxyribonucleic acid (DNA) moieties[6] and (*ii*) because they are present as such in biological systems.

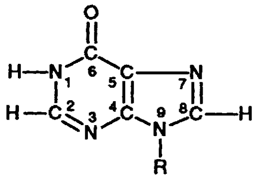
Enthalpy and entropy changes have been obtained from calorimetric measurements. Few such values for proton and metal NTP (nucleoside triphosphate) complexes have so far been reported.[7]

## Experimental

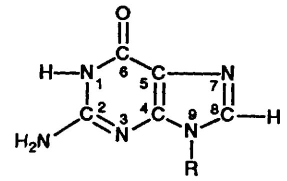
*Chemicals.*—The sodium salts of the nucleoside 5′-triphosphates (Type I, Type III Grade I) were purchased from Sigma and were used without further purification. Pentasodium tripolyphosphate (tpp) was purified by repeated crystallizations from water–ethanol mixtures.[8] Dimethyltin(IV) nitrate was obtained using dimethyltin oxide (ICN Biomedical) as a starting material. The dimethyltin oxide was purified and converted into the nitrate according to a procedure previously described by us.[3]



cytosine, R = H
cytidine, R = β-D-ribofuranosyl



hypoxanthine, R = H
inosine, R = β-D-ribofuranosyl



guanine, R = H
guanosine, R = β-D-ribofuranosyl

*Electromotive Force Measurements.*—The potentiometric measurements were carried out by means of four fully automated sets of apparatus. These made use of Metrohm equipment (burette, E 665; meter, E 654; glass electrodes, EA 109; calomel electrodes, EA 404) and were controlled by an IBM-compatible personal computer. Each computer was able to control two potentiometric set-ups simultaneously by using a program written in our laboratory.

The electrode couples were standardized on the pH = −log $c_{H^+}$ scale by titrating $HNO_3$ with $CO_2$-free KOH.

The solutions were freshly prepared to avoid hydrolysis of nucleoside 5′-triphosphates; in addition, experiments of different duration gave identical results, thus excluding dephosphorylation phenomena. Experimental details for the potentiometric titrations are reported in Table 1.

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* *Non-SI unit employed:* cal = 4.184 J.

**Table 1** Experimental conditions for potentiometric measurements at 25 °C and $I = 0.1$ mol dm$^{-3}$ ($KNO_3$)

| Analytical concentration/mol dm$^{-3}$ | | | | | | | |
|---|---|---|---|---|---|---|---|
| $SnMe_2$ | CTP | ITP | GTP | Titrant KOH | pH range | No. of titrations | No of points |
| | $0.0050 \leqslant c \leqslant 0.0080$ | | | $0.0850 \leqslant c \leqslant 0.1003$ | 3.5–7.1 | 7 | 270 |
| | | $0.0020 \leqslant c \leqslant 0.0022$ | | $0.0844 \leqslant c \leqslant 0.0993$ | 2.0–10.2 | 4 | 232 |
| | | | $0.0020 \leqslant c \leqslant 0.0051$ | $c = 0.0844$ | 2.2–10.6 | 4 | 238 |
| $0.0030 \leqslant c \leqslant 0.0050$ | $0.0040 \leqslant c \leqslant 0.0063$ | | | $0.0998 \leqslant c \leqslant 0.1004$ | 2.2–7.0 | 7 | 281 |
| $0.0030 \leqslant c \leqslant 0.0040$ | | $0.0040 \leqslant c \leqslant 0.0060$ | | $0.0844 \leqslant c \leqslant 0.0993$ | 2.3–8.6 | 6 | 421 |
| $0.0031 \leqslant c \leqslant 0.0040$ | | | $0.0042 \leqslant c \leqslant 0.0046$ | $0.0782 \leqslant c \leqslant 0.1006$ | 2.3–7.6 | 6 | 347 |

The volume of the solutions to be titrated was 20 cm$^3$ in all cases.

**Table 2** Experimental conditions for calorimetric measurements at 25 °C and $I = 0.1$ mol dm$^{-3}$ ($KNO_3$)

| Analytical concentration */mol dm$^{-3}$ | | | | | | | |
|---|---|---|---|---|---|---|---|
| $SnMe_2$ | CTP | ITP | GTP | tpp | pH range | No. of titrations | No of points |
| | $c = 0.0080$ | | | | 7.7–3.4 | 4 | 68 |
| | | $c = 0.0080$ | | | 9.9–1.5 | 4 | 122 |
| | | | $0.0060 \leqslant c \leqslant 0.0090$ | | 9.8–2.0 | 3 | 111 |
| | | | | $c = 0.0080$ | 8.8–2.4 | 6 | 136 |
| $0.0090 \leqslant c \leqslant 0.0091$ | $c = 0.0100$ | | | | 9.0–2.7 | 4 | 400 |
| $0.0080 \leqslant c \leqslant 0.0090$ | | $0.0090 \leqslant c \leqslant 0.0099$ | | | 8.4–2.1 | 3 | 300 |
| $0.0080 \leqslant c \leqslant 0.0090$ | | | $0.0088 \leqslant c \leqslant 0.0099$ | | 8.2–2.2 | 4 | 350 |
| $c = 0.0060$ | | | | $c = 0.0090$ | 9.0–3.9 | 4 | 165 |

The volume of the solutions to be titrated was 25 cm$^3$ in all cases. *For titrant $HNO_3$, $c = 0.5998$ mol dm$^{-3}$ throughout.

*Calorimetric Measurements.*—The calorimetric measurements were performed at 25.000 ± 0.001 °C using a Tronac 450 isoperibolic calorimeter equipped with a 25 cm$^3$ titration Dewar. Solutions containing, in turn, a ligand and a ligand plus the metal ion were titrated with standard $HNO_3$. The titration data, corrected for all non-chemical energy terms determined in separate experiments, were refined to obtain the final $\Delta H^\circ$ of each system. Experimental details for the calorimetric titrations are reported in Table 2.

For calculations and other experimental details see refs. 3 and 5.

## Results and Discussion

*Protonation Constants.*—Agreement of the protonation constant values for CTP, ITP and GTP with values in the literature is good as indicated by Table 3. The protonation constants of tpp have been already reported[5] and are included in Table 3.

*Complex Formation Constants.*—The hydrolytic species of $SnMe_2^{2+}$ and their stability constants were determined previously.[3]

$SnMe_2$–CTP. For the $SnMe_2$–CTP system the species $[SnMe_2(CTP)H_2]$, $[SnMe_2(CTP)H]^-$, $[SnMe_2(CTP)]^{2-}$, $[SnMe_2(CTP)H_{-1}]^{3-}$, $[(SnMe_2)_2(CTP)H]^+$, $[(SnMe_2)_2(CTP)]$, $[(SnMe_2)_2(CTP)H_{-1}]^-$, $[(SnMe_2)_2(CTP)H_{-2}]^{2-}$, $[SnMe_2(CTP)_2H_2]^{4-}$, $[SnMe_2(CTP)_2H]^{5-}$, $[SnMe_2(CTP)_2]^{6-}$, $[(SnMe_2)_2(CTP)_2H_2]^{2-}$, $[(SnMe_2)_2(CTP)_2H]^{3-}$, $[(SnMe_2)_2(CTP)_2]^{4-}$, $[(SnMe_2)_2(CTP)_2H_{-1}]^{5-}$, $[(SnMe_2)_2(CTP)_2H_{-2}]^{6-}$ and $[SnMe_2(CTP)H_3]^+$ were taken into consideration, with the first four as the base model and the others added in different combinations. The base model alone gave high statistical parameters (SUPERQUAD: $\sigma > 3$ and $\chi^2 = 28$). A significant improvement in the statistical parameters ($\sigma = 1.2$ and $\chi^2 = 11$) was obtained by adding $[(SnMe_2)_2(CTP)H]^+$ to the base model.

$SnMe_2$–ITP. For the $SnMe_2$–ITP system the species $[SnMe_2(ITP)H_2]^-$, $[SnMe_2(ITP)H]^{2-}$, $[SnMe_2(ITP)]^{3-}$, $[SnMe_2(ITP)H_{-1}]^{4-}$, $[(SnMe_2)_2(ITP)H]$, $[(SnMe_2)_2(ITP)]^-$, $[(SnMe_2)_2(ITP)H_{-1}]^{2-}$, $[(SnMe_2)_2(ITP)H_{-2}]^{3-}$, $[(SnMe_2)_2(ITP)_2H_2]^{4-}$, $[(SnMe_2)_2(ITP)_2H]^{5-}$, $[(SnMe_2)_2(ITP)_2]^{6-}$, $[(SnMe_2)_2(ITP)_2H_{-1}]^{7-}$, $[(SnMe_2)_2(ITP)_2H_{-2}]^{8-}$, $[SnMe_2(ITP)_2H_2]^{6-}$, $[SnMe_2(ITP)_2H]^{7-}$, $[SnMe_2(ITP)_2]^{8-}$ and $[SnMe_2(ITP)H_3]$ were considered, with the first three as the base model and the others added in different combinations. The 'best' fit (SUPERQUAD: $\sigma = 2.4$ and $\chi^2 = 9$) was obtained with the same set of species as found for CTP, with the exception of the hydrolytic species; in the case of ITP the hydroxo species was always rejected by the computer program.

$SnMe_2$–GTP. For the $SnMe_2$–GTP system the species $[SnMe_2(GTP)H_3]$, $[SnMe_2(GTP)H_2]^-$, $[SnMe_2(GTP)H]^{2-}$, $[SnMe_2(GTP)]^{3-}$, $[SnMe_2(GTP)H_{-1}]^{4-}$, $[(SnMe_2)_2(GTP)H]$, $[(SnMe_2)_2(GTP)]^-$, $[(SnMe_2)_2(GTP)H_{-1}]^{2-}$, $[(SnMe_2)_2(GTP)H_{-2}]^{3-}$, $[(SnMe_2)_2(GTP)_2H_2]^{4-}$, $[(SnMe_2)_2(GTP)_2H]^{5-}$, $[(SnMe_2)_2(GTP)_2H_{-1}]^{7-}$, $[(SnMe_2)_2(GTP)_2]^{6-}$, $[(SnMe_2)_2(GTP)_2H_{-2}]^{8-}$, $[SnMe_2(GTP)_2H_2]^{6-}$, $[SnMe_2(GTP)_2H]^{7-}$ and $[SnMe_2(GTP)_2]^{8-}$ were considered, with the first four as the base model and the others added, as usual, in different combinations. The data were 'best' fitted when offering the computer the 'best' model found for $SnMe_2$-ITP.

The stability constants for the proposed models are reported in Table 4. All the species not shown in the final models were always rejected as 'negative' or as 'excessive' by SUPERQUAD, when added to the base model.

$SnMe_2$–tpp. The formation constants of this system were previously studied[5] and the stability constants are also reported in Table 4.

It may be of some interest that all four systems show the formation of bi- as well as mono-nuclear species. Binuclear species have been reported for the complexes of these ligands with other metals.[16–19] The thermodynamic parameters of protonation for the four systems are reported in Table 3.

The tpp data are determined for comparison, in order to single out the protonation and complexation sites. As expected, thermodynamic data (Table 3) for tpp show that the protonation of phosphate oxygens is entropically driven. We have found the same behaviour for the first step of CTP and the second step of ITP and GTP (Table 3), which all refer to the protonation of phosphate oxygens.[20,21]

**Table 3** The log $K$ values and thermodynamic parameters for the protonation steps of CTP, ITP, GTP and tpp at 25 °C and $I$ = 0.1 mol dm$^{-3}$ ($KNO_3$)[a]

| Reaction | log $K$ | $\Delta G^{\circ}$[b]/ kcal mol$^{-1}$ | $\Delta H^{\circ}$[b]/ kcal mol$^{-1}$ | $\Delta S^{\circ}$[b]/ cal K$^{-1}$ mol$^{-1}$ |
|---|---|---|---|---|
| $H^+ + CTP^{4-} \rightleftharpoons HCTP^{3-}$ | 6.50(2)[b]<br>6.55[c]<br>6.55[d] | −8.86(1) | 0.89(4) | 32.7(1) |
| $H^+ + HCTP^{3-} \rightleftharpoons H_2CTP^{2-}$ | 4.53(2)[b]<br>4.53[c]<br>4.55[d] | −6.18(1) | −4.77(5) | 4.7(2) |
| $H^+ + ITP^{5-} \rightleftharpoons HITP^{4-}$ | 9.06(2)[b]<br>9.1[c]<br>9.26[e] | −12.35(1) | −6.63(5) | 19.2(2) |
| $H^+ + HITP^{4-} \rightleftharpoons H_2ITP^{3-}$ | 6.49(3)[b]<br>6.48[c]<br>6.50[f]<br>6.45[g] | −8.85(1) | 0.93(7) | 32.8(2) |
| $H^+ + H_2ITP^{3-} \rightleftharpoons H_3ITP^{2-}$ | 2.14(3)[b]<br>2.2[c] | −2.92(1) | 1.11(9) | 13.5(3) |
| $H^+ + GTP^{5-} \rightleftharpoons HGTP^{4-}$ | 9.56(1)[b]<br>9.6[c]<br>9.79[e]<br>9.6[h] | −13.04(1) | −7.3(1) | 19.3(3) |
| $H^+ + HGTP^{4-} \rightleftharpoons H_2GTP^{3-}$ | 6.53(1)[b]<br>6.45[c]<br>6.45[f] | −8.90(1) | 0.9(1) | 32.7(4) |
| $H^+ + H_2GTP^{3-} \rightleftharpoons H_3GTP^{2-}$ | 2.92(1)[b]<br>3.2[c]<br>2.94[i] | −3.98(1) | −1.7(1) | 7.6(5) |
| $H^+ + tpp^{5-} \rightleftharpoons Htpp^{4-}$ | 7.97[j] | −10.88 | −0.17(1) | 35.9(1) |
| $H^+ + Htpp^{4-} \rightleftharpoons H_2tpp^{3-}$ | 5.52[j] | −7.55 | 1.50(2) | 30.9(1) |
| $H^+ + H_2tpp^{3-} \rightleftharpoons H_3tpp^{2-}$ | 1.88[j] | −2.58 | 5.26(7) | 20.7(2) |

[a] Standard deviations are given in parentheses. [b] This work. [c] Ref. 9. [d] Ref. 10. [e] Ref. 11. [f] Ref. 12. [g] Ref. 13. [h] Ref. 14. [i] Ref. 15. [j] Ref. 5.

**Table 4** The log β values and thermodynamic parameters of complex formation of $SnMe_2^{2+}$ with CTP, ITP, GTP and tpp at 25 °C and $I$ = mol dm$^{-3}$ ($KNO_3$)[a]

| Reaction | log β | $\Delta G^{\circ}$/ kcal mol$^{-1}$ | $\Delta H^{\circ}$/ kcal mol$^{-1}$ | $\Delta S^{\circ}$/ cal K$^{-1}$ mol$^{-1}$ |
|---|---|---|---|---|
| $2SnMe_2^{2+} + CTP^{4-} + H^+ \rightleftharpoons [(SnMe_2)_2(CTP)H]^+$ | 15.28(2) | −20.83(2) | 7(1) | 93(4) |
| $SnMe_2^{2+} + CTP^{4-} + 2H^+ \rightleftharpoons [SnMe_2(CTP)H_2]$ | 14.92(2) | −20.34(2) | 1.4(3) | 73(1) |
| $SnMe_2^{2+} + CTP^{4-} + H^+ \rightleftharpoons [SnMe_2(CTP)H]^-$ | 12.28(1) | −16.74(1) | −0.5(1) | 4.4(4) |
| $SnMe_2^{2+} + CTP^{4-} \rightleftharpoons [SnMe_2(CTP)]^{2-}$ | 7.77(1) | −10.59(1) | 4.39(9) | 50.2(3) |
| $SnMe_2^{2+} + CTP^{4-} + H_2O \rightleftharpoons [SnMe_2(CTP)H_{-1}]^{3-} + H^+$ | 1.14(1) | −1.55(1) | 9.0(1) | 35.4(4) |
| $2SnMe_2^{2+} + ITP^{5-} + H^+ \rightleftharpoons [(SnMe_2)_2(ITP)H]$ | 20.30(3) | −27.68(3) | 5.3(4) | 110(1) |
| $SnMe_2^{2+} + ITP^{5-} + 2H^+ \rightleftharpoons [SnMe_2(ITP)H_2]^-$ | 19.61(1) | −26.74(1) | −0.6(2) | 87.8(6) |
| $SnMe_2^{2+} + ITP^{5-} + H^+ \rightleftharpoons [SnMe_2(ITP)H]^{2-}$ | 16.82(1) | −22.93(1) | −2.07(9) | 70.0(3) |
| $SnMe_2^{2+} + ITP^{5-} \rightleftharpoons [SnMe_2(ITP)]^{3-}$ | 10.21(1) | −13.92(2) | 2.6(1) | 55.5(4) |
| $2SnMe_2^{2+} + GTP^{5-} + H^+ \rightleftharpoons [(SnMe_2)_2(GTP)H]$ | 21.00(5) | −28.63(5) | 7.5(9) | 121(3) |
| $SnMe_2^{2+} + GTP^{5-} + 3H^+ \rightleftharpoons [SnMe_2(GTP)H_3]$ | 22.56(2) | −30.76(2) | −1.4(4) | 98(1) |
| $SnMe_2^{2+} + GTP^{5-} + 2H^+ \rightleftharpoons [SnMe_2(GTP)H_2]^-$ | 20.42(1) | −27.84(1) | −5.8(4) | 75(2) |
| $SnMe_2^{2+} + GTP^{5-} + H^+ \rightleftharpoons [SnMe_2(GTP)H]^{2-}$ | 17.36(1) | −23.67(1) | −3.0(1) | 69.4(5) |
| $SnMe_2^{2+} + GTP^{5-} \rightleftharpoons [SnMe_2(GTP)]^{3-}$ | 10.69(2) | −14.58(2) | 1.1(2) | 52.6(7) |
| $SnMe_2^{2+} + tpp^{5-} + 2H^+ \rightleftharpoons [SnMe_2(tpp)H_2]^-$ | 17.67[b] | −24.09[b] | 6.2(1) | 103.3(4) |
| $SnMe_2^{2+} + tpp^{5-} + H^+ \rightleftharpoons [SnMe_2(tpp)H]^{2-}$ | 15.02[b] | −20.48[b] | 3.8(1) | 81.8(4) |
| $SnMe_2^{2+} + tpp^{5-} \rightleftharpoons [SnMe_2(tpp)]^{3-}$ | 9.88[b] | −13.47[b] | 3.17(6) | 55.9(2) |
| $2SnMe_2^{2+} + tpp^{5-} \rightleftharpoons [(SnMe_2)_2(tpp)]^-$ | 16.07[b] | −21.91[b] | 5.5(1) | 94.4(4) |
| $SnMe_2^{2+} + 2tpp^{5-} \rightleftharpoons [SnMe_2(tpp)_2]^{8-}$ | 12.11[b] | −16.51[b] | 3.2(2) | 66.3(7) |

[a] Standard deviations are given in parentheses. [b] Ref. 15.

The second step of protonation of CTP is, instead, enthalpically favoured with a negligible entropy contribution; this is as expected for the protonation of N(3)[20] and is typical of cytosine-containing ligands.[9]

The first protonation step of GTP as well as of ITP (Table 3) is both enthalpically and entropically favoured. The negative (favourable) enthalpy term accounts for the involvement of a nitrogen atom, while the positive entropic contribution indicates that desolvation processes, due to charge neutralization, are occurring; this behaviour strongly accounts for the involvement of a negatively charged nitrogen, such as N(1). Furthermore, the protonation constant of GTP is higher than

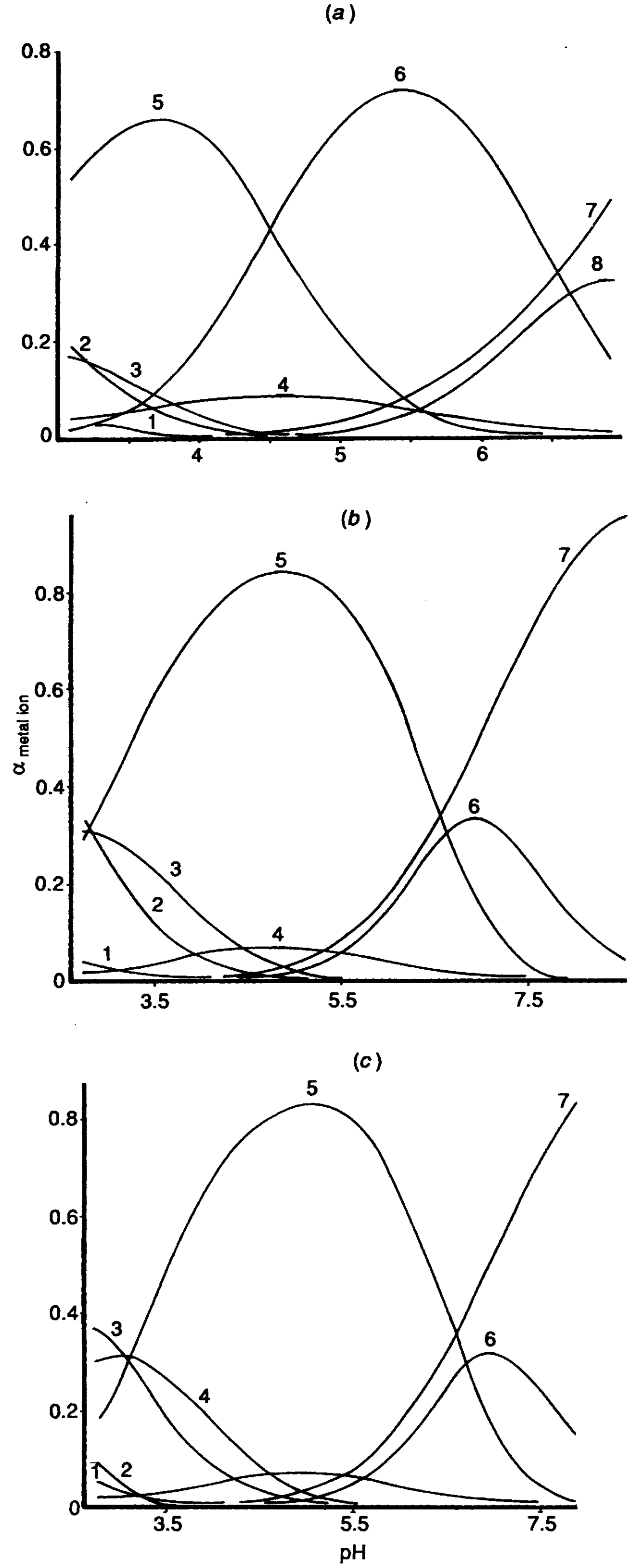

**Fig. 1** Species distribution diagrams: (*a*) $[SnMe_2^{2+}] = [CTP^{4-}] = 4 \times 10^{-3}$ mol dm$^{-3}$; 1, free central ion; 2, $[SnMe_2(CTP)H_2]$; 3, $[(SnMe_2)_2(CTP)H]^+$; 4, $[SnMe_2(OH)]^+$; 5, $[SnMe_2(CTP)H]^-$; 6, $[SnMe_2(CTP)]^{2-}$; 7, $[SnMe_2(OH)_2]$; 8 $[SnMe_2(CTP)H_{-1}]^{3-}$; (*b*) $[SnMe_2^{2+}] = [ITP^{5-}] = 4 \times 10^{-3}$ mol dm$^{-3}$; 1, free central ion; 2, $[SnMe_2(ITP)H_2]^-$; 3, $[(SnMe_2)_2(ITP)H]$; 4, $[SnMe_2(OH)]^+$; 5, $[SnMe_2(ITP)H]^{2-}$; 6, $[SnMe_2(ITP)]^{3-}$; 7, $[SnMe_2(OH)_2]$; (*c*) $[SnMe_2^{2+}] = [GTP^{5-}] = 4 \times 10^{-3}$ mol dm$^{-3}$; 1, free central ion; 2, $[SnMe_2(GTP)H_3]$; 3, $[SnMe_2(GTP)H_2]^-$; 4, $[(SnMe_2)_2(GTP)H]$; 5, $[SnMe_2(GTP)H]^{2-}$; 6, $[SnMe_2(GTP)]^{3-}$; 7, $[SnMe_2(OH)_2]$

that of ITP; the higher basicity results from a more favourable enthalpy term, probably due to the conjugation of N(1) to the exocyclic amino group in the position 2 of the guanosine ring.

The third protonation step [*i.e.* the protonation of N(7)[20]] is also more favoured for GTP than for ITP. This larger stabilization of GTP mainly results from a larger (more favourable) enthalpic contribution (−1.7 *vs.* 1.11 kcal mol$^{-1}$); this can again be ascribed to the influence of the amino group of the guanosine moiety on the heterocyclic ring system. These small $\Delta H^{\circ}$ values, unusual for the protonation of an imidazole nitrogen, are due to the peculiar 'acidic' nature of N(7) which protonates below pH 3.

Species distribution diagrams for CTP, GTP and ITP complexes are shown in Fig. 1.

The formation of all tpp complex species (Table 4) is enthalpy disfavoured and entropy favoured, as expected for the complex formation between two hard ions. The extensive desolvation processes leading to the complexation involve both tpp and $[SnMe_2]^{2+}$. In terms of $\Delta H^{\circ}$ of complexation this means a loss of energy which is not counterbalanced by the formation of bonds, which are essentially ionic in nature.

As already mentioned, knowledge of the thermodynamic parameters concerning the complex formation of tpp with $[SnMe_2]^{2+}$ allows us to ascertain (*i*) whether donor atoms different from phosphate oxygens are involved in the co-ordination sphere of the $[SnMe_2]^{2+}$–NTP species, (*ii*) whether solvophobic interactions between the dimethyltin(IV) methyl groups and the purine or pyrimidine residue of the NTP ligands take place. However, to be consistent, we have to compare the thermodynamic parameters concerning the formation of species having the same charge.

Here, we will discuss the thermodynamic parameters concerning the main species only, which are reported in Table 5 for the sake of clarity. By comparing the thermodynamic data for the ML species of CTP with those for the MLH species of ITP and GTP (which have the same charge, *i.e.* 2−) it is seen that the formation of all these species is entropically driven, while the enthalpy contribution is unfavourable. Moreover, the data are virtually coincident with those found for formation of the MLH species of tpp (charge 2−). This is a clear indication that (*i*) in the above species the organometallic ion co-ordinates through the phosphate oxygens only, (*ii*) there are no solvophobic interactions between the organometallic methyl groups and the purine or pyrimidine residue of NTP, previously suggested for $[SnEt_2]^{2+}$ complexes;[3] this kind of interaction should show up with a more-favourable enthalpy contribution and a less-favourable entropy term[22] with respect to the formation of the M(tpp)H complex where such interactions are not possible.

Also the formation of the ML complexes of GTP and ITP shows an unfavourable enthalpy term and a positive entropy contribution. In particular, the entropy changes are very similar to those found for the formation step of the protonated species of GTP and ITP (Table 5), indicating that the phosphate oxygens are still co-ordinated to the organometallic ion.

On the contrary, the enthalpy contributions, even if still positive, are less unfavourable, by *ca.* 2 and 3 kcal mol$^{-1}$, for the formation of the ML species of ITP and GTP, respectively. This extra enthalpic contribution is very likely due to the co-ordination of the dimethyltin to N(1), which in these complexes is deprotonated. On the other hand, a favourable enthalpic value (−2.1 kcal mol$^{-1}$) for the co-ordination of organometallic tin(IV) to nitrogen has already been reported.[23]

However, the conclusions drawn from the thermodynamic data need further support. The presence of solvophobic interactions in the ML complexes of GTP and ITP could be hidden by the contemporary deprotonation and co-ordination of N(1). In this context, a NMR investigation, presently underway, might be of substantial help.

**Table 5** The log *K* values and thermodynamic parameters for complexation steps of $SnMe_2^{2+}$ with CTP, ITP, GTP and tpp at 25 °C and $I = 0.1$ mol $dm^{-3}$ ($KNO_3$)

| Reaction | log *K* | $\Delta G^\circ$/ kcal $mol^{-1}$ | $\Delta H^\circ$/ kcal $mol^{-1}$ | $\Delta S^\circ$/ cal $K^{-1}$ $mol^{-1}$ |
|---|---|---|---|---|
| $SnMe_2^{2+} + Htpp^{4-} \rightleftharpoons [SnMe_2(tpp)H]^{2-}$ | 7.01 | −9.56 | 4.1 | 50.9 |
| $SnMe_2^{2+} + HITP^{4-} \rightleftharpoons [SnMe_2(ITP)H]^{2-}$ | 7.76 | −10.58 | 4.56 | 50.8 |
| $SnMe_2^{2+} + HGTP^{4-} \rightleftharpoons [SnMe_2(GTP)H]^{2-}$ | 7.80 | −10.63 | 4.3 | 50.1 |
| $SnMe_2^{2+} + CTP^{4-} \rightleftharpoons [SnMe_2(CTP)]^{2-}$ | 7.77 | −10.59 | 4.39 | 50.2 |
| $SnMe_2^{2+} + ITP^{5-} \rightleftharpoons [SnMe_2(ITP)]^{3-}$ | 10.21 | −13.92 | 2.6 | 55.5 |
| $SnMe_2^{2+} + GTP^{5-} \rightleftharpoons [SnMe_2(GTP)]^{3-}$ | 10.69 | −14.58 | 1.1 | 52.6 |

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