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Solvent effects on complexation of thallium(I) with guanosine 5′-monophosphate in methanol–water mixtures

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The interaction of guanosine 5′-monophosphate, GMP, with the thallium(I) ion was studied by UV–vis and potentiometric titration methods and ^{31}P NMR spectroscopy. Both NMR spectra and UV–vis titration data have shown that GMP coordinates via guanine to the thallium(I) ion in the pH range 1.5–10. Our study of the system Tl(I) + GMP was performed in water–methanol mixtures with different volume ratios of methanol. The complexation equilibrium in the pH range of study led to the following mononuclear species: $TlH_2(GMP)^+$, TlH(GMP) and $Tl(GMP)^-$, where $(GMP)^{2-}$ represents the fully dissociated ligand. The formation constants of the species were calculated in the various media at constant temperature (25 °C) and constant ionic strength of sodium perchlorate (0.1 mol dm^{-3}) using a suitable computer program. The formation constants were analyzed in terms of Kamlet and Taft's parameters. A single-parameter correlation of the formation constants, β_{121}, β_{111} and β_{101} vs α (hydrogen-bond donor acidity), β (hydrogen-bond acceptor basicity) and for π^* (dipolarity/polarizability) are relatively poor in all solutions, but multi-parameter correlations represent significant improvements with regard to the single-parameter model. In this work, we have also used the normalized polarity parameter, $E_T{}^N$, alone and in combination with some of the Kamlet–Taft parameters to find a better correlation of the formation constants in different methanol–water mixtures. Copyright © 2007 John Wiley & Sons, Ltd.

KEYWORDS: thallium(I); GMP; formation constant; aqueous methanol solution; solvent effect

INTRODUCTION

Understanding the mechanism of the interaction between a metal ion and nucleic acids or its components (nucleosides, nucleotides) is very important for the interpretation of many biochemical processes in animals and plants, hence there has been increasing interest toward understanding the stereochemistry of complexes formed between metal ions and nucleic acid bases. Moreover, correlations between these interactions and protonation of the bases and hydrogen bonding are very useful in order to elucidate the molecular mechanism.[1] Because thallium compounds are extremely toxic, only a few articles have been reported on its nucleic acid bases complexes.[2–4] The metabolic action and fate of thallium(I) are not clear. Nevertheless, experimental evidence suggests that there are some similarities between the ionic transport of thallium(I) and potassium ion through cell membranes, although intercellular transport of thallium(I) seems to be less rapid than potassium transport. The biological effects of thallium(I) have also been thought to be due to its interference with the metabolism of sulfur-containing compounds. Sulfur-containing compounds have been the main detoxifying drug used in the case of poisoning by metals.[5] The study of the interaction between the thallium(I) and nucleotides, as possible detoxifying agents, could be performed from other approaches than the classical one. Thus, the correlation between the stability constants and the dielectric constants or other similar physical properties can lead to interesting results.

Now, it is understood that, in proteins, active site cavities of enzymes, and in different complexes of nucleotides and nucleosides, the effective dielectric constant is decreased at the

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ligand–water interface and the activity of water is decreased due to the presence of aliphatic or aromatic side chains of the ligand at the location.[6] Therefore, interaction of metal ions with a ligand increases considerably when decreasing the solvent polarity of the medium. This effect is well established for most metal ion complexes of biologically ligands.[2,7,8] Hence, the knowledge of physio-chemical properties of the solvent in order to understand the intermolecular interactions between solute–solvent and also solvent–solvent molecules is required for a proper bench-work.

During the last few years, several experimental and theoretical works dealing with the effect of solvent on intermolecular reactions have been published. Most of these papers are concerned with the effect of solvent on reaction rates. There are surprisingly few articles that exclusively deal with the effect of all properties of the solvent on complexation of some biologically important ligands. The interaction of solvents of different dielectric constants with biological molecules is of importance for understanding the chemistry of *in vivo* processes like enzyme interactions, the assembly of lipids in biomembrans, surfactant aggregation, etc.[9]

In three recent publications,[2,7,8] we have reported that the dielectric constant alone (as believed for many years) cannot serve as a quantitative measurement of the solvent polarity. This property is often inadequate, since the dielectric constant description considers a solvent as a non-structured continuum, not composed of individual solvent molecules with their own solvent–solvent interactions, and does not take into account specific solute–solvent interactions. To obtain a quantitative method for the determination of solvent effects on physical properties, many empirical solvent scales have been devised during the last two decades.[10,11] Among these scales (around 40), the most comprehensive are the solvatochromic ones, but only a few of them have found wider application in the correlation analysis of solvent effects. A quantitative measurement of the solvent polarity has been introduced by Kamlet and Taft.[12,13] Kamlet and Taft's solvatochromic parameters have been used in one-, two- or three-parameter correlations involving different combinations of these parameters that are called linear solvation energy relationships. In general, all of these parameters are more comprehensive measures of the solvent polarity than the dielectric constant or other physical properties. They reflect more reliably the complete picture of all intermolecular forces acting between solute and solvent molecules. In this work, we have also tried to use a combination of another polarity scale devised by Dimorth and Reichardt[10,14] with some of Kamlet and Taft's parameters to obtain a better correlation between them.

EXPERIMENTAL SECTION

Chemicals

Methanol and the sodium salt of GMP were obtained from Merck and Fluka, as analytical reagent-grade material, respectively, and were used without further purification. The NaOH solution was prepared from a titrisol solution (Merck) and its concentration was determined by several titrations with standard HCl. Perchloric acid, sodium perchlorate and thallium(I) nitrate were purchased from Merck as analytical reagent grade materials and were used as received. Dilute perchloric acid solutions were standardized against a standard NaOH solution. All dilute solutions were prepared from double-distilled water with specific conductance = $1.3 \pm 0.1\ \mu\Omega^{-1}\ cm^{-1}$. An aqueous stock solution of the ligand was freshly prepared daily, and its concentration was determined each time by titration with a NaOH solution.

Measurements

Measurements of pH were performed with an Eyela, PHM 2000 instrument. All measurements were carried out at 25 °C and constant ionic strength of 0.1 mol dm^{-3} sodium perchlorate. The pH meter was calibrated for the relevant H^+ concentration with a solution of 0.01 mol dm^{-3} perchloric acid solution 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 $-\log[H^+] = 2.0$.[15] The junction potential corrections were calculated from equation (1):

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

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

The guanosine 5′-monophosphate shown in Fig. 1 may bind with two protons, one at the phosphate group and one at the purine moiety. It was proposed[16] that $H_3(GMP)^+$ releases its first proton from $P(O)(OH)_2$, the second from H^+(N-7), and the third again from the phosphate group. A fourth proton is released in the alkaline pH range from H^+(N-1). The given acidity constants agree well, as far as available, with those

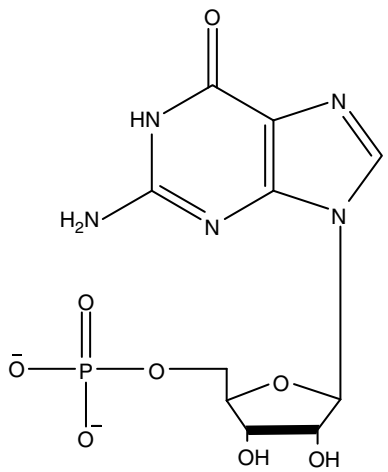

Figure 1. Chemical structure of guanosine 5′-monophosphate, GMP.

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Table 1. Logarithms of the protonation constants of the different species of GMP in various aqueous solutions of methanol at 25 °C and ionic strength of 0.1 mol dm^{-3} ($NaClO_4$)

Dielectric constant[a]	Methanol percent	$\log K^{H}_{H3(GMP)}$	$\log K^{H}_{H2(GMP)}$	$\log K^{H}_{H(GMP)}$	Reference
78.74	0.0%	2.73 ± 0.09	6.42 ± 0.06	9.77 ± 0.11	This work
72.99	10%	2.84 ± 0.08	6.74 ± 0.05	9.97 ± 0.12	This work
70.10	15%	2.91 ± 0.09	6.79 ± 0.08	9.99 ± 0.09	This work
67.11	20%	2.95 ± 0.06	6.85 ± 0.07	10.06 ± 0.08	This work
63.96	25%	2.97 ± 0.07	6.90 ± 0.05	10.15 ± 0.10	This work
60.98	30%	2.98 ± 0.06	6.95 ± 0.04	10.26 ± 0.09	This work
56.36	35%	3.02 ± 0.05	7.05 ± 0.05	10.32 ± 0.08	This work
52.15	40%	3.06 ± 0.08	7.15 ± 0.08	10.46 ± 0.10	This work
78.74	0.0%	2.48	6.25	9.49	16
78.74	0.0%	—	6.66	—	17
78.74	0.0%	—	—	9.94	18

[a] Obtained from Gentile and Cefola.[19]

reported in recent compilations.[16–18] A correlation between the value of the dielectric constant and log *K* calculated using equations (2)–(5) is presented in Table 1.

$$H_3(GMP)^+ \rightleftharpoons H_2(GMP)^{\pm} + H^+ \quad (2a)$$

$$K^{H}_{H3(GMP)} = [H_2(GMP)^{\pm}][H^+]/[H_3(GMP)^+] \quad (2b)$$

$$H_2(GMP)^{\pm} \rightleftharpoons H(GMP)^- + H^+ \quad (3a)$$

$$K^{H}_{H2(GMP)} = [H(GMP)^-][H^+]/[H_2(GMP)^{\pm}] \quad (3b)$$

$$H(GMP)^- \rightleftharpoons (GMP)^{-2} + H^+ \quad (4a)$$

$$K^{H}_{H(GMP)} = [(GMP)^{-2}][H^+]/[H(GMP)^-] \quad (4b)$$

$$(GMP)^{-2} \rightleftharpoons (GMP - H)^{-3} + H^+ \quad (5a)$$

$$K^{H}_{(GMP)} = [(GMP\text{-}H)^{-3}][H^+]/[(GMP)^{-2}] \quad (5b)$$

The release of the first proton from $H_3(GMP)^+$ occurs at very low pH. The comparison of the protonation constants listed in Table 1 and those reported by ^{1}H-NMR shift experiments shows that the second proton in $H_2(GMP)$ is released mainly from H^+(N-7), and the next from the phosphate group, in accord with previous conclusions.[20]

The determination of the hydrogen ion concentration was performed with an Ingold UO 3234 glass electrode and an Ingold UO 3236 calomel electrode. The term pH has significance only in aqueous media. The glass electrode potential in an aqueous solution differs from that in a solution of mixed solvents, and a liquid-junction potential of uncertain magnitude may affect the results. To overcome this difficulty, it was necessary to calibrate the glass electrode in different solvent mixtures. The experimental method outlined by Van Uitert and Hass[21] was employed for this purpose. The pH meter reading *B* in methanol–water mixtures was converted into $[H^+]$ using the equation

$$-\log[H^+] = B + \log \mu_H \quad (6)$$

where the concentration factor μ_H was obtained for the ionic strength 0.1 mol dm^{-3} $NaClO_4$ from the expression $\log \mu_H = \log \mu^\circ_H + \log \gamma_{\pm}$. The value of μ°_H is independent of ionic concentration but is dependent on solvent composition, and $\gamma_{\pm}$ is the mean activity coefficient of perchloric acid in the solvent mixtures. In this work, the values of *B* were recorded in various solvent mixtures containing known concentrations of perchloric acid and sufficient sodium perchlorate to give a constant ionic strength of 0.1 mol dm^{-3}. The differences between the logarithm of known hydrogen-ion concentrations and the corresponding values of *B* were used to calculate values of the correction term $\log \mu_H = \log(\mu^\circ_H \gamma_{\pm})$.

UV–vis spectra were performed using a Shimadzu 2100 spectrophotometer with a Pentium 4 computer and using thermostated matched 10 mm quartz cells. A 50 cm^3 acidic solution of Tl^+, 1.01×10^{-3} mol dm^{-3} for UV–vis studies, was titrated with an alkali solution, 0.1 mol dm^{-3} NaOH, of the ligand, 2.4×10^{-3} mol dm^{-3}, both in the same ionic strength and mole fraction of methanol. The $-\log[H^+]$ and absorbance were measured after addition of 0.1 ml of titrant, and this procedure was extended up to the required $-\log[H^+]$. To exclude carbon dioxide from the system, a steam 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 standard deviations are shown in the text and tables.

To find which functional group of GMP participated in the complexation, the UV spectra of a solution of the free ligand (1.18×10^{-4} mol dm^{-3}) and that of [GMP] = [Tl(I)] = 1.18×10^{-4} mol dm^{-3} were obtained at three different pH values (2.1, 4.9 and 8.9) in the same conditions of temperature and ionic strength.

^{31}P NMR spectra were recorded on a Bruker 300 MHz spectrometer in H_2O–D_2O (1 : 9 by volume), operating at room temperature. The chemical shifts were measured

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relative to phosphoric acid. The solutions were prepared by mixing thallium nitrate and GMP in D_2O–H_2O solution to give a 1 : 1 mole ratio at different pH. The concentration of the samples in NMR measurements was 9.7×10^{-3} mol dm^{-3}.

RESULTS AND DISCUSSION

UV–vis spectra

From above, the solution of free GMP has an absorption maximum at 252.5 and a shoulder at 275–280 nm at pH = 4.9. Upon the addition of Tl(I) ion to GMP, the ligand absorptivity coefficient of 252.5 nm band decreases at pH 4.9 and the absorption maximum is shifted from 252.5 to 256 nm and the ~280 band in free GMP is shifted to ~285 nm upon complex formation, with very little change in the absorption. The UV bands at 252.5 and about 280 nm are attributed to $\pi-\pi^*$ transitions of guanine base.[22,23] Similar results were obtained for the other pH values, Table 2. Therefore, it could be concluded that GMP coordinates via guanine to the thallium ion at the above mentioned pH values.

It should be noted that purine or purine derivatives undergo self-association due to stacking of their nucleic base-ring systems.[24] Neurohr and Mantsch[25] have determined the association formation constant of GMP as 1.3 mol dm^{-3}. In a similar study, Sigel *et al*.[26] have calculated that, in a 0.3 mM solution of a nucleotide more than 99% is present as the monomeric species. Hence, the results presented in this work apply to monomeric species.

^{31}P NMR spectra

The above conclusion was supported by ^{31}P NMR spectra at different pH values; see above and the results in Table 3. No chemical shift modification due to a complexation of the phosphate group of GMP with Tl(I) was noticed (Table 3). Therefore, it was concluded that the phosphate moiety does not participate in the coordination with thallium(I).

Stability constants of complexes

The complex $M_xH_y(GMP)_z^{(x+y-2z)+}$ that is formed is characterized by its stoichiometry ($x:y:z$), where M represents the metal ion. To determine the stability constant of the complexation, equation (7) is defined by β_{xyz}:

$$xM^+ + yH^+ + z(GMP)^{2-} \rightleftharpoons M_xH_y(GMP)_z^{(x+y-2z)+} \quad (7)$$

$$\beta_{xyz} = [M_xH_y(GMP)_z^{(x+y-2z)+}]/([M^+]^x[H^+]^y[GMP^{2-}]^z) \quad (8)$$

The method of determination of the stability constant is based on the relation $A = f(\text{pH})$.[27,28] Absorbance, A, and $-\log[H^+]$ were measured for a solution containing Tl^+ with a large excess of GMP. The UV spectral data correlated with the $[H^+]$ were processed using a computer program,[29] which allows calculation of stability constants for different stoichiometric models.

Considering the protonation constants of the ligands, in acidic pH, the predominant species for complexation is H_2(GMP). In this case, the spectrophotometric titration data were analyzed by using the absorbance of $Tl^+ + GMP$ at wavelengths in the UV range that is given by:

$$A = \varepsilon_M[Tl^+] + \varepsilon_C[\text{complex}] + A_{\text{ligand}} \quad (9)$$

where ε_M and ε_C are the molar absorptivities of Tl^+ and the ligand, respectively.

The mass balance can be expressed as:

$$[Tl^+] = C_M - [\text{complex}] \quad (10)$$

$$[H_2(GMP)] = C_L - [\text{complex}] - [\text{free ligand}] \quad (11)$$

where C_M and C_L are the total concentrations of Tl^+ and GMP, respectively. Substituting equations (8), (10) and (11) into equation (9) gives the final equation for fitting. The method used to determine ε_M was previously described[30] and its values at different wavelengths are used in this work. Using a suitable computer program,[29] the data were fitted to the final equation for estimating the formation constant of equation (7). The Gauss–Newton nonlinear least-squares method was used in the computer program to refine the absorbance by minimizing the error squares sum from equation (12):

$$S = \sum(a_i - b_i)^2 \qquad (i = 1, 2, 3, \ldots) \quad (12)$$

Table 3. ^{31}P NMR chemical shift, δ, as a function of pH for GMP and Tl(I) +GMP in D_2O–H_2O solution (9 : 1 by volume), $[GMP] = [Tl(I)] = 9.7 \times 10^{-3}$ mol dm^{-3}

pH	3.0	4.0	5.0	6.0	7.0	8.0	9.0
δ (ppm) GMP	0.228	0.252	0.377	1.271	1.749	3.562	4.151
δ (ppm) Tl(I) + GMP	0.229	0.261	0.391	1.384	1.858	3.632	4.168

Table 2. The UV bands and absorptivity coefficients of free GMP and GMP +Tl(I) at different pH in equal concentration of GMP and Tl(I) (1.18×10^{-4} mol dm^{-3})

	Maximum wavelength (nm)			Absorptivity coefficient (mol dm^{-3} cm)$^{-1}$		
Species	pH = 2.1	pH = 4.9	pH = 8.9	pH = 2.1	pH = 4.9	pH = 8.9
GMP	255.5	252.5	253	1.02×10^4	1.13×10^4	1.12×10^4
GMP + Tl(I)	260	256	257	8.68×10^3	9.60×10^3	9.43×10^3

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Here a_i is the experimental absorbance and b_i is the calculated one. The computer program consisted of two different kinds of fitting: (a) graphical and (b) numerical. The final selection of the species was based on both graphical and numerical methods, considering in addition the various statistical criteria, i.e. sums of squared residuals and differences of C_M(exp) and C_L(exp) values from calculated ones.

As expected, polynuclear complexes and $[MH_3(GMP)]$, $[MH(GMP)_2]$ and $[MH_2(GMP)_2]$ species were rejected by the computer program (the charges were omitted for simplicity). Values of these parameters for $[MH_3(GMP)]$ were calculated too, but the species was 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 were $[TlH_2(GMP)^+]$, [TlH(GMP)] and $[Tl(GMP)^-]$, resulting in a satisfactory numerical and graphical fitting. The correlation between the average values of these parameters for the wavelengths range used in this study and the log β is listed in Table 4.

In Fig. 2 the equilibrium distribution of various species in $Tl^+ + GMP$ system is shown as a function of $-\log[H^+]$ at two different media (in 0.0 and 30% methanol). The calculations are based on the stability constant values given in Table 4. The curves clearly demonstrate that an increase of the pH is accompanied by an increase in the formation of deprotonated complex species and the stability of the species quite depends upon pH. The most stable complex species at pH = 2.1, 5.0 and 8.5, part A, are $TlH_2(GMP)^+$, TlH(GMP) and $Tl(GMP)^-$, respectively. However, in the presence of methanol, the complex formation shifted to lower pH value which is possibly due to the higher stability constant of the species formed at lower dielectric constant. In 30% methanol, part B, the pH shifts are about 0.2, 0.8 and 2 units for the three complex species, respectively.

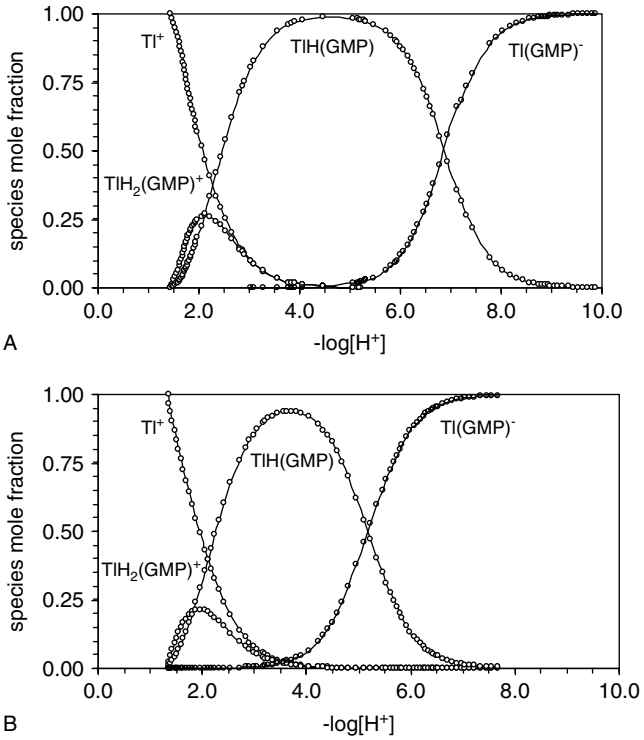

Figure 2. The equilibrium distribution of the species in $Tl^+ + GMP$ system as a function of $-\log[H^+]$ at 25 °C, ionic strength of 0.1 mol dm^{-3} sodium perchlorate: (A) 0.0% methanol; (B) 30% methanol.

Solvent effect

An important quantitative measurement of the solvent polarity has been introduced by Kamlet, Abboud and Taft (KAT).[11]

The KAT equation contains parameters expressing the non-specific as well as specific solute–solvent interactions. The latter should be correlated with solvent Lewis–acidity interactions (hydrogen-bond acceptor, HBA solute, and hydrogen-bond donor, HBD solvent) and solvent Lewis–basicity interactions (HBD solute–HBA solvent), equation (13). This approach has been widely and successfully applied in the correlation analysis of all kind of solvent-dependent processes.[10]

Table 4. Average values for various wavelengths (240–300 nm) of log β_{121}, log β_{111} and log β_{101} for the system $Tl^+ + GMP$ at different methanol–water mixtures, 25 °C, and ionic strength of 0.1 mol dm^{-3} sodium perchlorate

α^a	β^b	π^{*a}	E_T^{Nc}	Methanol (%, by weight)	log β_{121}	log β_{111}	log β_{101}
1.261	0.185	1.137	0.97	0.0	3.88 ± 0.08	4.36 ± 0.06	2.98 ± 0.04
1.176	0.233	1.123	0.93	10	4.13 ± 0.07	4.97 ± 0.05	3.11 ± 0.09
1.139	0.259	1.113	0.91	15	4.27 ± 0.06	5.14 ± 0.06	3.22 ± 0.08
1.107	0.287	1.101	0.89	20	4.39 ± 0.08	5.53 ± 0.08	3.38 ± 0.05
1.079	0.317	1.087	0.88	25	4.62 ± 0.05	5.78 ± 0.09	3.49 ± 0.09
1.055	0.348	1.070	0.86	30	4.83 ± 0.06	6.09 ± 0.04	3.65 ± 0.05
1.037	0.379	1.051	0.84	35	4.92 ± 0.09	6.76 ± 0.06	3.89 ± 0.04
1.023	0.411	1.029	0.82	40	5.01 ± 0.08	7.42 ± 0.05	4.15 ± 0.08

[a,b,c] Obtained from references 31,32 and 33, respectively.

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Using the solvatochromic solvent parameters, α, β, and π^*, which have been introduced in previous reports,[2,7,8] the multiparametric equation, equation (13), has been proposed for use in the so-called linear solvation energy relationship.

$$\log \beta = A_0 + a\alpha + b\beta + p\pi^* \quad (13)$$

where A_0 represents the regression coefficient value, and α represents the solvent hydrogen-bond donor (HBD) acidity, describing the ability of a solvent to donate a proton in a solvent to a solute hydrogen-bond. The α scale extends from 0.0 for non-HBD solvents to about 1.0 for methanol. β is a measure of a solvent hydrogen-bond acceptor (HBA) basicity, and describes the ability of a solvent to accept a proton in a solute to solvent hydrogen-bond. The β scale was selected to extend from 0.0 for non-(HBA) solvents to about 1.0 for hexamethylphosphoric triamide. π^* is the index of the solvent dipolarity/polarizability, which is a measure of the ability of a solvent to stabilize a charge or a dipole by its own dielectric effects. The π^* scale was selected to run from 0.0 for cyclohexanone to 1.0 for dimethylsulfoxide.

In equation (13) the discontinuous polarizability correction term is omitted because the solvent used is not a chlorine compound. The regression coefficients a, b and p in equation (13) measure the relative susceptibilities of the solvent-dependence of $\log \beta$ to the indicated solvent parameters.

In order to explain the obtained $\log \beta$ values through the KAT solvent parameter, the formation constants were correlated with solvent properties by means of single and multiple linear regression analyses by a suitable computer program.[29] We used the Gauss–Newton linear least-squares method in the computer program to refine the $\log \beta$ by minimizing the error squares sum from equation (14). Single-parameter correlations of $\log \beta_{121}$, $\log \beta_{111}$ and $\log \beta_{101}$ in terms of α, β or π^* did not give good results, equations (15)–(17).

$$S = \sum (\log \beta_{exp} - \log \beta_{cal})^2 \quad (14)$$

$$\log \beta_{121} = 9.98 - 4.93\alpha \quad (15a)$$

$$\log \beta_{111} = 18.54 - 11.52\alpha \quad (15b)$$

$$\log \beta_{101} = 8.55 - 4.57\alpha \quad (15c)$$

($n = 8$, $r^2 = 0.95$, 0.97 and 0.84, respectively).

$$\log \beta_{121} = 2.91 + 5.27\beta \quad (16a)$$

$$\log \beta_{111} = 1.88 + 12.83\beta \quad (16b)$$

$$\log \beta_{101} = 1.93 + 5.15\beta \quad (16c)$$

($n = 8$, $r^2 = 0.98$, 0.97 and 0.97, respectively).

$$\log \beta_{121} = 16.12 - 10.66\pi^* \quad (17a)$$

$$\log \beta_{111} = 34.78 - 26.66\pi^* \quad (17b)$$

$$\log \beta_{101} = 15.19 - 10.75\pi^* \quad (17c)$$

($n = 8$, $r^2 = 0.95$, 0.97 and 0.98, respectively).

Applying the multiple-parametric equations (18), significant improvements of the results were noticed.:

$$\log \beta_{121} = -76.49 + 12.89\alpha + 42.23\beta + 49.53\pi^* \quad (18a)$$

$$\log \beta_{111} = 209.82 - 30.82\alpha - 82.57\beta - 133.06\pi^* \quad (18b)$$

$$\log \beta_{101} = 39.68 - 3.86\alpha - 11.36\beta - 26.16\pi^* \quad (18c)$$

($n = 8$, $r^2 = 0.9971$, 0.9961, and 0.9985, respectively).

The coefficients α, β and π^* from equation (18) are very different from those used in equation (17). Variation of these parameters in this new context is: $\pi^* > \beta > \alpha$. This means that the influence of the solvent polarity/polarizability parameter on the Tl(I) + GMP interaction is more important than the other ones. The HBA and HBD parameters are less significant for the studied system.

The analysis of correlation between the values of $\log \beta$ and of the parameters α, β and π^* presented in Table 4 led to the following observations: the solvent polarity parameter of the media, π^*, increases with increasing the mole fraction of water in aqueous solutions of methanol. If the π^* of the media was the only factor for the solvent effect on the complexation, it may be expected that the $\log \beta$ in water would be greater than those of all the other aqueous solutions of methanol. However, the formation constant increases with increasing solvent hydrogen-bond acceptor basicity parameter β, decreases with increasing solvent polarity π^*, and finally increases with decreasing hydrogen-bond donor acidity parameter of the solvents, α, for different methanol–water mixtures, Table 4.

We have also tried to use the polarity scale proposed by Dimroth and Reichardts, E_T, based on the solvatochromic behaviour of pyridinium N-phenoxide betaine dye.[10,14] This dye is the most solvatochromic compound reported to date.[10,14] This scale has now been revised and normalized to $E_T{}^N$, known as the normalized polarity parameter, due to the introduction of SI units. $E_T{}^N$ is related with the ability of a solvent to stabilize charge separation in the dye and has the value of zero for tetramethylsilane, the least polar solvent, and 1.0 for water, the most polar solvent. According to this approach, the formation constants were correlated with $E_T{}^N$ as a single linear regression analysis and then with the multiple regression one with Kamlet and Taft's parameters besides $E_T{}^N$. Single parameter correlation of $\log \beta$ in terms of $E_T{}^N$ did again not give good results, equation (19). However, the multi-parametric equation involving $E_T{}^N$, β and π^* showed a

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Table 5. The percentage contribution of KAT and normalized polarity parameters on the effect of different media on complexation at 25 °C and ionic strength 0.1 mol dm^{-3} $NaClO_4$

Different species	In terms of equation (18)			In terms of equation (20)		
	α	β	π^*	E_T^N	β	π^*
$TlH_2(GMP)^+$	12.3	40.4	47.3	27.3	45.1	27.6
TlH(GMP)	12.5	33.5	54.0	28.2	24.7	47.1
$Tl(GMP)^-$	9.3	27.5	63.2	16.5	19.1	64.4

significant improvement with regard to the single-parameter model, equation (20).

$$\log \beta = A_0 + eE_T^N \quad (19)$$

$$\log \beta_{121} = 11.75 - 8.16E_T^N \quad (19a)$$

$$\log \beta_{111} = 23.37 - 19.84E_T^N \quad (19b)$$

$$\log \beta_{101} = 10.51 - 7.91E_T^N \quad (19c)$$

($n = 8$, $r^2 = 0.97$, 0.97, and 0.94, respectively).

$$\log \beta = A_0 + eE_T^N + b\beta + p\pi^* \quad (20)$$

$$\log \beta_{121} = -20.32 + 10.01E_T^N + 16.51\beta + 10.06\pi^* \quad (20a)$$

$$\log \beta_{111} = 73.15 - 22.65E_T^N - 19.86\beta - 37.91\pi^* \quad (20b)$$

$$\log \beta_{101} = 24.30 - 3.78E_T^N - 4.39\beta - 14.81\pi^* \quad (20c)$$

($n = 8$, $r^2 = 0.998$, 0.996, and 0.999, respectively).

In order to underline the efficiency of the suggested multi-parameter correlations, experimental values of $\log \beta$ are plotted vs their calculated ones from equations (18) and (20) for different aqueous solutions of methanol. It can be seen, Fig. 3, that the experimental and calculated values of $\log \beta$ are in good agreement with each other, $r^2 > 0.99$ in all cases. From the values of the regression coefficients, the contribution of each parameter on a percentage basis was calculated and listed in Table 5.

The observation of this systematic multiple regression analysis leads to the following conclusion: the dipolar/polarizability index of the solvent plays an important role in interpretation of complexation equilibria for the studied systems for both cases of α, β, π^* and β, π^*, E_T^N, Table 5. Unfortunately, these parameters have been determined only for a few aqueous solvent mixtures and so extending the procedure for other solvent systems is limited. However, in our previous studies similar results were obtained for other complex species but again in methanol–water mixtures.[2,7,8] In accordance with our previous experiments and this work the stability of the complexes, which is mainly determined by the metal ion affinity of the purine moiety, increases with increasing the amounts of methanol. This rule seems true not only for the complexes formed by nucleic acid bases[2] but also amino acid (penicillamine) and amino polycarboxilic acid (nitrilotriacetic acid) complex species apparently follow the same policy.[7,8] This could be explained by, upon addition of larger amounts of methanol to the aqueous solution, the activity of water is decreased to the point where poor solvation results for those metal ion sites not occupied by the ligand. Consequently, the poorer solvation leads to an increased affinity of the metal ion sites for other ligating ligands.

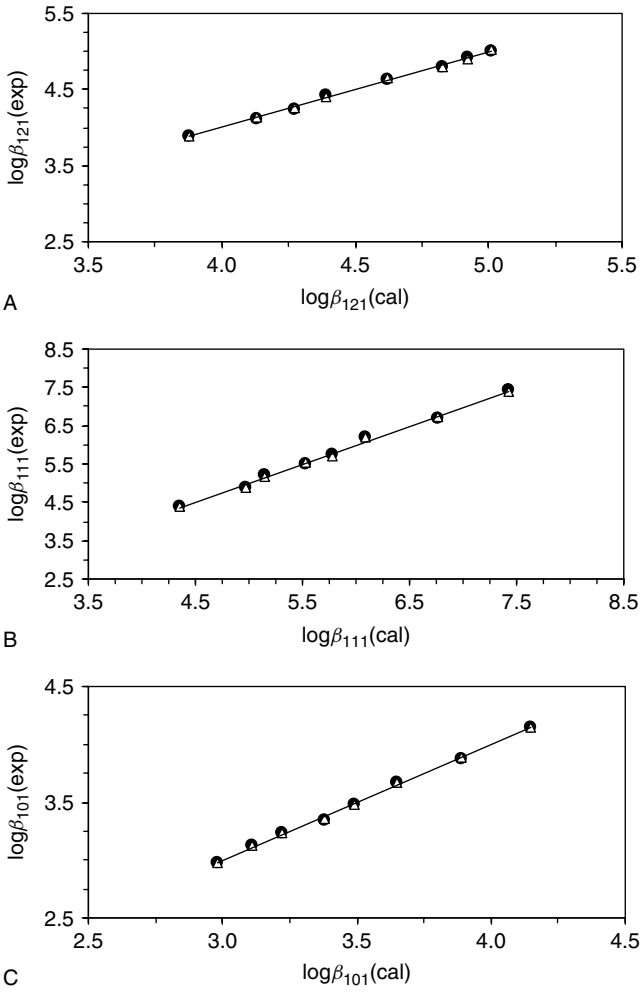

Figure 3. The plots of the experimental values of $\log \beta$ versus the calculated ones: (A) for $TlH_2(GMP)^+$; (B) for TlH(GMP); (C) for $Tl(GMP)^-$, (●) in terms of equation (18) and (△) in terms of equation (20).

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