Metal Ion-Coordinating Properties of 2′-Deoxyguanosine 5′-Monophosphate ($dGMP^{2-}$)[1] in Aqueous Solution. Quantification of Macrochelate Formation

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Introduction

Nowadays it is well recognized that the reactivity of nucleotides, which are at the crossroads of many metabolic processes, depends on the presence of metal ions.[2] Indeed, over the years a remarkable amount of information on the stability[3] and structure of metal ion complexes formed with nucleotides has been accumulated.[2a,4,5] This is also true for complexes formed with nucleoside 5′-monophosphates,[6] yet only for those containing the ribose ring, whereas hardly any knowledge on nucleotides containing 2′-deoxyribose is available.[3,7]

With the above facts in mind, we have recently studied the metal ion-binding properties of 2′-deoxycytidine 5′-monophosphate[8] and now we are concentrating our efforts on 2′-deoxyguanosine 5′-monophosphate, for which no information[3,7] exists and the properties of which need to be compared with those[5,6b] of guanosine 5′-monophosphate. The structures of these two nucleotides, and of their corresponding nucleosides, are shown in Figure 1.[9] Aside from the fact that the metal ion-binding properties of $dGMP^{2-}$ are important on their own right, and will be reported below for Mg^{2+}, Cu^{2+}, and Zn^{2+} (= M^{2+}), we are accumulating this information also with the aim to understand the acid−base[10] and metal ion-binding properties of the *cis*-$(NH_3)_2Pt(dGuo)(dGMP)$ (cf. ref 11) and *cis*-$(NH_3)_2Pt(dGMP)_2^{2-}$ (cf. ref 12) complexes.

Experimental Section

Materials. The $Na_2(dGMP)$ salt was purchased from Sigma Chemical Co. (St. Louis, MO). All the other reagents are identical with those used previously.[6,11]

Potentiometric pH Titrations. The same equipment, including the computer facilities, was used as was reported recently.[6c,11,13] The concentration of dGMP was such that self-association is certainly negligible.[6b]

The acidity constants $K^{H}_{H_2(dGMP)}$, $K^{H}_{H(dGMP)}$, and K^{H}_{dGMP} for $H_2(dGMP)^{\pm}$ were determined exactly as described[13] by titrating 50 mL of aqueous 1.08 mM HNO_3 (I = 0.1 M ($NaNO_3$); 25 °C) in the presence and absence of 0.3 or 0.4 mM dGMP under N_2 with 3 mL of 0.03 M or 2 mL 0.045 M NaOH. The experimental data, i.e., the differences between two such titrations, were evaluated within the pH range 3.1−10.3, corresponding to about 72 and 85% neutralization for the equilibria $H_2(dGMP)^{\pm}/H(dGMP)^{-}$ and $dGMP^{2-}/(dGMP-H)^{3-}$, respectively. It should be mentioned that these acidity constants are the so-called practical, mixed, or Brønsted constants.[14] Their negative logarithms given for aqueous solutions at I = 0.1 M ($NaNO_3$) and 25 °C may be converted into the corresponding concentration constants by subtracting 0.02 from the listed pK_a values. The results given in Table 1 (vide infra) are the averages of 18 independent pairs of titrations.[13]

The stability constants of the complexes formed between Mg^{2+}, Cu^{2+}, or Zn^{2+} and $H(dGMP)^{-}$ or $dGMP^{2-}$ were determined under the same conditions as given above for the acidity constants, but $NaNO_3$ was partly or fully replaced by $M(NO_3)_2$ (I = 0.1 M; 25 °C). The ligand/M^{2+} ratios were 1:111, 1:89, 1:80, and 1:67 for Mg^{2+}, 1:8, 1:5.6, 1:4, and 1:2.8 for Cu^{2+}, and 1:56, 1:40, 1:28, and 1:20 for Zn^{2+}. The stability constants $K^{M}_{M(H;dGMP)}$ and $K^{M}_{M(dGMP)}$ and the acidity constant $K^{H}_{M(dGMP)}$ (for Mg^{2+} only) were computed for each titration pair with a curve-fitting procedure[15] by taking into account the species H^+, $H_2(dGMP)^{\pm}$, $H(dGMP)^{-}$, $dGMP^{2-}$, M^{2+}, $M(H;dGMP)^{+}$, and M(dGMP); in the case of Mg^{2+}/dGMP, the species $(dGMP-H)^{3-}$ and $M(dGMP-H)^{-}$ were also considered. The experimental data were evaluated from the onset of the titrations up to the pH where hydrolysis of $M(aq)^{2+}$ begins, which was evident from the titrations without dGMP. The calculated constants showed no dependence on the excess amount of M^{2+} used in the experiments. For each system at least eight independent pairs of titrations were made.

Results and Discussion

1. Acidity Constants of $H_3(dGMP)^{+}$ in Comparison with Some Related Data. 2′-Deoxyguanosine 5′-monophosphate ($dGMP^{2-}$), shown in Figure 1, is a tribasic species; it may bind

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(1) Abbreviations: $dGMP^{2-}$, 2′-deoxyguanosine 5′-monophosphate; dGuo, 2′-deoxyguanosine; GMP^{2-}, guanosine 5′-monophosphate; Guo, guanosine; M^{2+}, divalent metal ion; $RibMP^{2-}$, D-ribose 5-monophosphate; $R-PO_3^{2-}$, simple phosphate monoester or phosphonate ligand with R representing a noncoordinating residue (see also legend for Figure 2). Species that are given in the text without a charge either do not carry one or represent the species in general (i.e., independent from their protonation degree); the version that applies is always clear from the context.

(2) For example, see: (a) Sigel, A., Sigel, H., Eds. *Interactions of Metal Ions with Nucleotides, Nucleic Acids, and Their Constituents*; Metal Ions in Biological Systems 32; M. Dekker, Inc.: New York, 1996; pp 1−814. (b) Lippard, S. J.; Berg, J. M. *Principles of Bioinorganic Chemistry*; University Science Books: Mill Valley, CA, 1994. (c) Fraústo da Silva, J. J. R.; Williams, R. J. P. *The Biological Chemistry of the Elements*; Clarendon Press: Oxford, 1991.

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(5) Sigel, H.; Song, B. *Met. Ions Biol. Syst.* **1996**, *32*, 135−205; cf. ref 2a.

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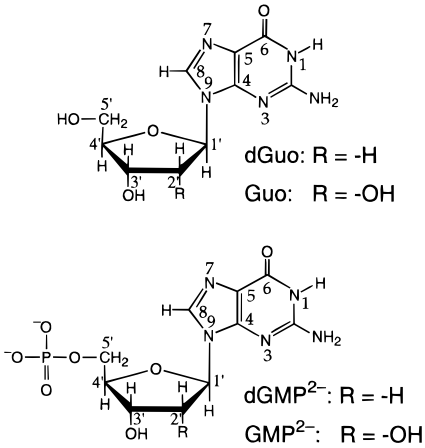

Figure 1. Structures of the guanine derivatives considered in this study. The nucleosides and nucleotides are shown in their dominating anti conformation.[9]

Table 1. Logarithms of the Stability Constants of $M(H;dGMP)^+$ (Eq 1) and M(dGMP) (Eq 2) Complexes As Determined by Potentiometric pH Titrations in Aqueous Solution, Together with the Negative Logarithms for the Acidity Constants of $M(H;dGMP)^+$ (Eqs 4 and 5) and for the Formation of $M(dGMP-H)^-$ (Eq 3) at 25 °C and $I = 0.1$ M ($NaNO_3$)[a]

M^{2+}	$\log K^{M}_{M(H;dGMP)}$ (eq 1)	$\log K^{M}_{M(dGMP)}$ (eq 2)	$pK^{H}_{M(H;dGMP)}$ (eqs 4 and 5)	$pK^{H}_{M(dGMP)}$ (eq 3)
Mg^{2+}	0.5 ± 0.3	1.81 ± 0.04	5.0 ± 0.3	9.13 ± 0.08
Cu^{2+}	2.81 ± 0.06	4.05 ± 0.04	5.05 ± 0.07	
Zn^{2+}	1.76 ± 0.06	2.99 ± 0.05	5.06 ± 0.08	

[a] The error limits given are *three times* the standard error of the mean value or the sum of the probable systematic errors, whichever is larger. The error limits (3σ) of the derived data, in the present case for column 4, were calculated according to the error propagation after Gauss.

two protons at the phosphate group and one at the purine moiety. For $H_3(dGMP)^+$ the first proton is released from the $-P(O)(OH)_2$ group, the second from the H^+(N7) site, and the third one again from the still-monoprotonated phosphate residue; finally, a fourth proton may be released in the alkaline pH range from the H(N1) site. The release of the first proton occurs for $H_3(GMP)^+$ with $pK^{H}_{H_3(GMP)} = 0.3 \pm 0.2$;[6b] consequently, one may asssume that within the given error limits this value also holds for $H_3(dGMP)^+$. Therefore, this deprotonation does not interfere with any acid−base reaction at pH > 2 and thus, it is not relevant for this study.

The results[13] obtained via potentiometric pH titrations (25 °C; $I = 0.1$ M ($NaNO_3$)) for the various acidity constants of the three-proton donor $H_2(dGMP)^{\pm}$ are $pK^{H}_{H_2(dGMP)} = 2.69 \pm 0.03$, $pK^{H}_{H(dGMP)} = 6.29 \pm 0.01$, and $pK^{H}_{dGMP} = 9.56 \pm 0.02$. Those of the related acids $H(dGuo)^+$, $H(RibMP)^-$, $H(Guo)^+$, and $H_2(GMP)^{\pm}$ are $pK^{H}_{H(dGuo)} = 2.30 \pm 0.04$ [H^+(N7)], $pK^{H}_{dGuo} = 9.24 \pm 0.03$ [H(N1)];[11] $pK^{H}_{H(RibMP)} = 6.24 \pm 0.01$ [$-OP(O)_2(OH)^-$];[16] $pK^{H}_{H(Guo)} = 2.11 \pm 0.04$, $pK^{H}_{Guo} = 9.22 \pm 0.01$;[6b] and $pK^{H}_{H_2(GMP)} = 2.48 \pm 0.04$, $pK^{H}_{H(GMP)} = 6.25 \pm 0.02$, and $pK^{H}_{GMP} = 9.49 \pm 0.02$,[6b] respectively. All the acidity constants given are in the order expected on the basis of previous experience.[3,4a,5,9b]

Comparison of the mentioned results reveals that the absence of the 2′-OH group at the ribose moiety enhances the basicity of N7 by $\Delta pK_a \simeq 0.2$. The corresponding effect on the $-PO_3^{2-}$ group and the $(N1)^-$ site is much smaller, but can still be seen. The higher overall basicity of the 2′-deoxy species, compared with the ribose species, probably results from a somewhat poorer solvation by water of the deoxy species due to the absence of the 2′-OH group.

The presence of the 5′-phosphate group enhances the basicity of N7 on average by $\Delta pK_a = 0.38$ and the one of $(N1)^-$ by $\Delta pK_a = 0.30$. The charge effect understandably is slightly more pronounced on N7 than on $(N1)^-$ because in the anti conformation (cf. Figure 1) N7 is somewhat closer to the phosphate group.

2. Stability of the $M(H;dGMP)^+$ and M(dGMP) Complexes. The experimental data of the potentiometric pH titrations of the M^{2+}/dGMP systems can be completely described by considering the mentioned acidity constants of $H_2(dGMP)^{\pm}$ (cf. Section 1) and the following equilibria, 1a−3a:

$$M^{2+} + H(dGMP)^- \rightleftharpoons M(H;dGMP)^+ \quad (1a)$$

$$K^{M}_{M(H;dGMP)} = [M(H;dGMP)^+]/([M^{2+}][H(dGMP)^-]) \quad (1b)$$

$$M^{2+} + dGMP^{2-} \rightleftharpoons M(dGMP) \quad (2a)$$

$$K^{M}_{M(dGMP)} = [M(dGMP)]/([M^{2+}][dGMP^{2-}]) \quad (2b)$$

$$M(dGMP) \rightleftharpoons M(dGMP-H)^- + H^+ \quad (3a)$$

$$K^{H}_{M(dGMP)} = [M(dGMP-H)^-][H^+]/[M(dGMP)] \quad (3b)$$

However, an analysis involving all mentioned equilibria is possible only for the Mg^{2+}/dGMP system. Cu^{2+} and Zn^{2+} form hydroxo complexes; thus, the evaluation of the data was restricted to the pH range below the onset of the formation of these species, and therefore equilibrium 3a could not be considered.

Of course, equilibria 1a and 2a are also connected via equilibrium 4a; the acidity constant of which may be calculated with eq 5:

$$M(H;dGMP)^+ \rightleftharpoons M(dGMP) + H^+ \quad (4a)$$

$$K^{H}_{M(H;dGMP)} = [M(dGMP)][H^+]/[M(H;dGMP)^+] \quad (4b)$$

$$pK_{M(H;dGMP)} = pK^{H}_{H(dGMP)} + \log K^{M}_{M(H;dGMP)} - \log K^{M}_{M(dGMP)} \quad (5)$$

The constants determined for eqs 1, 2, 4, and 3 are listed in columns 2, 3, 4, and 5 of Table 1, respectively. These results are similar to those obtained previously for the corresponding M^{2+}/GMP^{2-} systems (see also Figure 2, vide infra).[17]

Since the analysis of potentiometric pH titrations yields only the amount and distribution of the species of a net charged type, e.g. of $M(H;dGMP)^+$, further information is required to locate the binding sites of the proton and the metal ion. A comparison of the acidity constants of $H_2(dGMP)^{\pm}$, $pK^{H}_{H_2(dGMP)} = 2.69$ and

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(17) An earlier study (see ref 6b) with M^{2+}/GMP systems was carried out with very low concentrations of ligand, and this prevented the detection of the monoprotonated $M(H;GMP)^+$ complexes (see also Section "1.6. A Caveat" in ref 6b). In the repetition of this work with higher ligand concentrations (see p 162 of ref 5) the $M(H;GMP)^+$ species could be detected; the corresponding stability constants are similar to those listed in Table 1 (column 2). The consideration of these species also affected somewhat the results for the M(GMP) complexes: The log stability constants given in ref 5 are 0.27 and 0.14 log units larger for the Cu^{2+} and Zn^{2+} complexes, respectively, than the values given in the earlier study; the constants for Mg(GMP) are identical within the error limits in both studies. However, it needs to be emphasized that these small changes in the stability constants do not affect any of the structural conclusions presented in ref 6b.

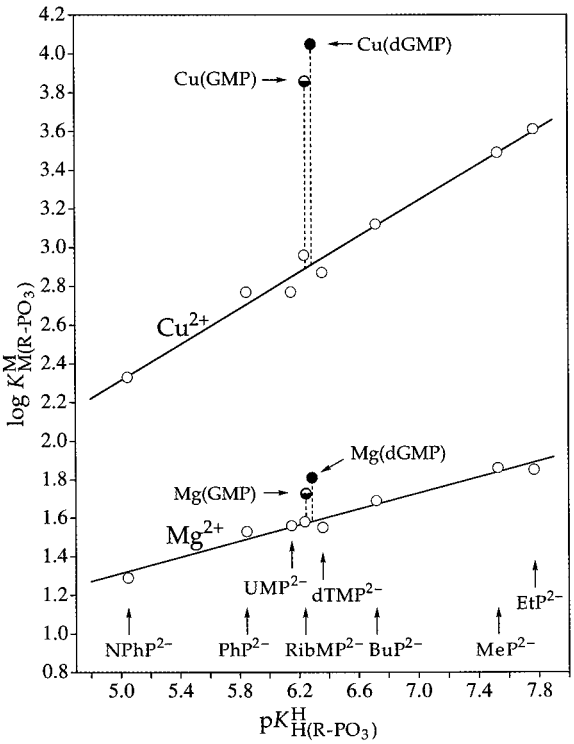
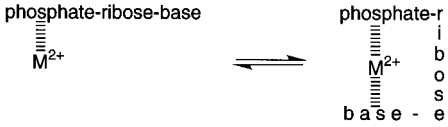


Figure 2. Evidence for an enhanced stability of the Mg^{2+} and Cu^{2+} 1:1 complexes formed with $dGMP^{2-}$ (●) and GMP^{2-} (◒). The latter are shown for comparison (their data are from ref 5), on the basis of the relationship between log $K^{M}_{M(R-PO_3)}$ and $pK^{H}_{H(R-PO_3)}$ for the 1:1 complexes of Mg^{2+} and Cu^{2+} with some simple phosphate monoester or phosphonate ligands ($R-PO_3^{2-}$): 4-nitrophenyl phosphate ($NPhP^{2-}$), phenyl phosphate (PhP^{2-}), uridine 5′-monophosphate (UMP^{2-}), D-ribose 5-monophosphate ($RibMP^{2-}$), thymidine [= 1-(2′-deoxy-β-D-ribofuranosyl)thymine] 5′-monophosphate ($dTMP^{2-}$), *n*-butyl phosphate (BuP^{2-}), methanephosphonate (MeP^{2-}), and ethanephosphonate (EtP^{2-}) (from left to right) (○). The least-squares lines of eqs 7 (Mg^{2+}) and 8 (Cu^{2+}) are drawn through the corresponding eight data sets, which are taken for the phosphate monoesters from ref 16 and for the phosphonates from ref 21. The points due to the equilibrium constants for the M^{2+}/$dGMP^{2-}$ systems (●) are based on the data given in Section 1 and Table 1; those for the M^{2+}/GMP^{2-} systems (◒) are from ref 5. The vertical broken lines emphasize the stability differences to the corresponding reference lines; these differences are equal to log $\Delta_{M(dGMP)}$ for the M(dGMP) complexes (eq 10) and log $\Delta_{M(GMP)}$ for the M(GMP) species. All the plotted equilibrium constant values refer to aqueous solutions at 25 °C and $I = 0.1$ M ($NaNO_3$).

$pK^{H}_{H(dGMP)} = 6.29$ (Section 1), with those of the $M(H;dGMP)^{+}$ complexes (eq 4), which are listed in the fourth column of Table 1, i.e., $pK^{H}_{M(H;dGMP)} \simeq 5.0$, demonstrates that in these complexes the proton must be located at the phosphate group. Hence, the metal ions, at least Cu^{2+} and Zn^{2+}, are probably located at N7 of the guanine residue;[5] this coordination may possibly be somewhat favored in addition by (a) hydrogen bond(s) of (a) metal ion-coordinated water molecule(s) to the carbonyl oxygen at C6 and/or to the phosphate group. A more detailed analysis for the formation degrees of the base- or phosphate-coordinated species is possible[6c,18] but is left to the interested reader.

3. Increased Stability of the M(dGMP) Complexes and Extent of Macrochelate Formation in These Species. From previous studies[6,19] with purine-nucleoside 5′-monophosphates, it is well-known that a metal ion bound at the phosphate group may in addition interact with N7 of the purine moiety because these nucleotides exist in solution preferably in the anti conformation (see Figure 1). This additional interaction gives rise to macrochelate formation as schematically expressed in the intramolecular equilibrium 6:



(6)

Of course, any further interaction of a phosphate-coordinated metal ion in a given nucleotide complex has to result[20] in an increased complex stability.

In earlier studies[16,21] a linear relationship was established between the logarithms of the stability constants of $M(R-PO_3)$ complexes, log $K^{M}_{M(R-PO_3)}$, and the negative logarithms of the acidity constants of the corresponding monoprotonated $H(R-PO_3)^{-}$ species, $pK^{H}_{H(R-PO_3)}$, for several simple phosphate monoester ligands,[16] including methyl phosphate.[22] The points for complexes formed with phosphonates, like methanephosphonate (MeP^{2-}) or ethanephosphonate (EtP^{2-}), also fall on the same straight reference line for a given metal ion.[21] The corresponding straight-line equations for the complexes of Mg^{2+}, Cu^{2+}, or Zn^{2+} and $R-PO_3^{2+}$ ligands (where R is a residue unable to interact with M^{2+}) are given in eqs 7, 8, and 9, respectively:[21]

$$\log K^{Mg}_{Mg(R-PO_3)} = (0.208 \pm 0.015)\cdot pK^{H}_{H(R-PO_3)} + (0.272 \pm 0.097) \quad (7)$$

$$\log K^{Cu}_{Cu(R-PO_3)} = (0.465 \pm 0.025)\cdot pK^{H}_{H(R-PO_3)} - (0.015 \pm 0.164) \quad (8)$$

$$\log K^{Zn}_{Zn(R-PO_3)} = (0.345 \pm 0.026)\cdot pK^{H}_{H(R-PO_3)} - (0.017 \pm 0.171) \quad (9)$$

The error limits of log stability constants calculated with given $pK^{H}_{H(R-PO_3)}$ values and eqs 7, 8, and 9 are ±0.03, ±0.06, and ±0.06 log units (3σ), respectively, in the pK_a range 5−8 (aqueous solution; 25 °C; $I = 0.1$ M ($NaNO_3$); see Tables 5 and 6 in ref 21 or Table 3 in ref 6b).

That the M^{2+} complexes of $dGMP^{2-}$ are more stable than is expected on the basis of the basicity of its phosphate group is evident from the two examples shown in Figure 2. The vertical distances of the data points for the Cu(dGMP) and Mg(dGMP) complexes to their corresponding reference line reflect the mentioned expected stability increase which is similar to the one observed[5] for the analogous M(GMP) complexes,[23] and

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(23) At this point one may also ask: Is there any chelate formation in the Mg(dGMP-H)$^{-}$ species? The above evaluation has shown that for Mg(dGMP) the open isomer dominates (Table 2); to a first approximation this then means that Mg^{2+} in this complex mainly compensates for the 2-fold negative charge of the $-PO_3^{2-}$ residue by its coordination. Indeed, the acidity constant of Mg(dGMP), $pK^{H}_{Mg(dGMP)} = 9.13 \pm 0.08$ (Table 1), is very close to that of the isocharged dGuo, $pK^{H}_{dGuo} = 9.24 \pm 0.03$ (Section 1). The difference $\Delta pK_a = 0.11 \pm 0.08$ is hardly beyond the error limit and indicates that if at all only a small acidification occurs; if taken as real one may estimate a formation degree of 22 ± 14% for the macrochelated isomer of the Mg(dGMP−H)$^{-}$ species, in excellent agreement with the result listed in Table 2 for the $Mg(dGMP)_{cl}$ isomer.

Table 2. Experimentally Determined Stability Constants, log $K^{M}_{M(dGMP)}$, for M(dGMP) Complexes[a] and Calculated Stability Constants, log $K^{M}_{M(dGMP)_{op}}$, for the Corresponding Isomers with a Sole Phosphate Coordination of M^{2+},[b] as Well as the Resulting Stability Differences, log $\Delta_{M(dGMP)}$ (Eq 10) and the Extent of Intramolecular Macrochelate Formation (Eqs 6 and 11−13) in Various M(dGMP) Complexes in Aqueous Solution at 25 °C and $I = 0.1$ M ($NaNO_3$)

M^{2+}	log $K^{M}_{M(dGMP)}$[a] (eqs 2 and 12)	log $K^{M}_{M(dGMP)_{op}}$[b] (eq 12)	log $\Delta_{M(dGMP)}$ (eq 10)	K_I (eqs 11 and 13)	% $M(dGMP)_{cl}$ cf.[c]
Mg^{2+}	1.81 ± 0.04	1.58 ± 0.03	0.23 ± 0.05	0.70 ± 0.20	41 ± 7
Cu^{2+}	4.05 ± 0.04	2.91 ± 0.06	1.14 ± 0.07	12.80 ± 2.29	93 ± 1
Zn^{2+}	2.99 ± 0.05	2.15 ± 0.06	0.84 ± 0.08	5.92 ± 1.24	86 ± 3

[a] See footnote *a* of Table 1. The values given in the second column are taken from column 3 of Table 1. [b] Calculated with $pK^{H}_{H(dGMP)} = 6.29$ (Section 1) and the reference straight-line equations (see also Figure 2) given in eqs 7−9 (see also refs 6b and 21). [c] Calculated according to the equation % $M(dGMP)_{cl} = 100[K_I/(1 + K_I)]$.

which may be defined according to eq 10:

$$\log \Delta = \log \Delta_{M(dGMP)} = \log K^{M}_{M(dGMP)} - \log K^{M}_{M(dGMP)_{op}} \quad (10)$$

where log $K^{M}_{M(dGMP)_{op}}$ refers to the stability of the open species in equilibrium 6 and may be calculated with eqs 7, 8, and 9 and $pK^{H}_{H(dGMP)} = 6.29$ (Section 1).

The stability increase seen in Figure 2 for the M(GMP) complexes being somewhat smaller than that observed for the M(dGMP) complexes originates in the lower basicity of N7 in GMP^{2-} compared with the one in $dGMP^{2-}$ (see Section 1: $pK^{H}_{H(Guo)} = 2.11$ versus $pK^{H}_{H(dGuo)} = 2.30$ or $pK^{H}_{H_2(GMP)} = 2.48$ versus $pK^{H}_{H_2(dGMP)} = 2.69$). That the extent of macrochelate formation depends on the basicity of N7 has been shown before.[5,6b]

On the basis of the stability difference defined in eq 10, the position of equilibrium 6 can be determined. If one designates $M(dGMP)_{cl}$ for the "closed" or macrochelated species and $M(dGMP)_{op}$ for the "open" isomer, the intramolecular and, hence, dimensionless equilibrium constant K_I may be defined by eq 11:

$$K_I = [M(dGMP)_{cl}]/[M(dGMP)_{op}] \quad (11)$$

Of course, when this is taken into account, equilibrium 2a may be rewritten as below:

$$M^{2+} + dGMP^{2-} \overset{K^{M}_{M(dGMP)_{op}}}{\rightleftharpoons} M(dGMP)_{op} \overset{K_I}{\rightleftharpoons} M(dGMP)_{cl} \quad (12)$$

As shown previously,[6] K_I may be calculated according to eq 13:

$$K_I = (K^{M}_{M(dGMP)}/K^{M}_{M(dGMP)_{op}}) - 1 = 10^{\log \Delta} - 1 \quad (13)$$

As the values for log Δ (eq 10) are known, the various complex systems may be evaluated. The corresponding results are summarized in Table 2.

The values for the stability differences log $\Delta_{M(dGMP)}$ given in Table 2 (column 4) reflect the different affinities of the considered metal ions toward nitrogen donor ligands; this affinity is relatively small for Mg^{2+} and quite pronounced for Cu^{2+} or Zn^{2+} leading in the latter instances to stability enhancements in the order of 1 log unit. As a consequence, the formation degree of the macrochelate reaches "only" about 40% with Mg^{2+} whereas that for the other two metal ions is close to 90% (Table 2, column 6). These results may be compared with those[5] for Mg(GMP), Cu(GMP), and Zn(GMP), where the macrochelates form to 31 ± 7% (log Δ = 0.16 ± 0.04), 89 ± 2% (log Δ = 0.97 ± 0.07), and 83 ± 3% (log Δ = 0.69 ± 0.07), respectively. Hence, the formation degrees (and the stability enhancements) of the $M(dGMP)_{cl}$ species are somewhat larger (see Table 2), but the detailed structural aspects discussed previously[6b] for the M(GMP) complexes are also valid here.[23]

In conclusion, in all of the M(dGMP) complexes studied the tendency to form macrochelates is quite pronounced. This is true not only for Cu^{2+} but also in the Mg(dGMP) and Zn(dGMP) systems, where the formation degree of the macrochelates reaches approximately 40 and 85%, respectively. For the solution structures of these complexes under physiological conditions this is remarkable because, via the substrate "fitting" of a given isomer occurring in equilibrium, selectivity may be achieved in a specific reaction pathway.

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