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# Comparison of the Coordination Tendency of Amino Acids, Nucleobases, or Mononucleotides Toward the Monomeric and Dimeric Lanthanide Complexes with Biologically Important Compounds

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**ABSTRACT:** The formation of monomeric and dimeric binary and ternary complexes of Eu(III), Gd(III), Dy(III), and Pr(III) with primary ligand 2-amino-6-oxy 8-azapurine (8-azaguanine) and amino acids amino-succinic acid (aspartic acid), 2-amino-propanoic acid (D-alanine), (L-alanine), 2-amino-4-methyl thiobutanoic acid (methionine), 2-amino succinamic acid (asparagine), 2-amino 4-methyl pentanoic acid (DL-leucine), 2-amino-3-indolyl propanoic acid (L-tryptophan), 2-amino 3-(4-hydroxyphenyl)-propanoic acid (L-tyrosine), 2-amino-3-imidazole propanoic acid (histidine), 2-amino-5-guanidino pentanoic acid (arginine), and 4-amino-5-oxo-pentanoic acid amide (glutamine); or nucleotides adenosine 5′-triphosphate (5′-ATP), adenosine 5′-diphosphate (5′-ADP), adenosine 5′-monophosphate (5′-AMP), adenosine 5′-monophosphate (5′-GMP), inosine 5′-monophosphate (5′-IMP), or nucleobases (uracil, 5-aminouracil, dihydrouracil); and with zwitterionic buffers (primary ligands) 4-(2-hydroxyethyl) piperazine-1-propane sulfonic acid (EPPS), 3-(*N*-morpholino)-2-hydroxypropane sulfonic acid (MOPSO), 3-(cycloxylamino)-1-propane sulfonic acid (CAPS), *N*-(tris(hydroxy methyl)-methyl)-2-amino-ethane sulfonic acid (TES), 3-(cyclohexyl amino)-2-hydroxy-1-propane sulfonic acid (CAPSO), *N*-(tris(hydroxy methyl)-methyl)-3-amino propane sulfonic acid (TAPS), *N*-(2-acetamido)-2-aminoethane sulfonic acid (ACES), 2-morpholinoethane sulfonic acid (MES), piperazine 1,4-bis(2-ethane sulfonic acid) (PIPES), *N*-(1,1-dimethyl-2-hydroxy ethyl)-3-amino 2-hydroxypropane sulfonic acid (AMPSO), *N*-(2-acetamido)-imino-diacetic acid (ADA); and nucleobases 6-amino-purine (adenine), 2-amino-6-oxypurine (guanine), 2-amino-6-oxy 8-azapurine (8-azaguanine), 5-methyl pyrimidine (thymine), 2,4-dioxypyrimidine (uracil), 5-amino 2,4-dioxypyrimidine (5-aminouracil), and 5,6-dihydro-2,4-dioxypyrimidine (dihydrouracil), has been studied potentiometrically at (25.0 ± 0.1) °C and ionic strength $I$ = 0.1 mol·dm$^{-3}$ ($KNO_3$). The acid−base properties of ligands were investigated and discussed. The formation of the 1:1 and 2:1 binary and 1:1:1 and 2:1:1 ternary complexes are inferred from the corresponding titration curves. The stability constants of the binary and ternary systems were evaluated. Initial estimates of the formation constants of the resulting species and the protonation constants of the different ligands used have been refined with SUPERQUAD computer program.

## INTRODUCTION

A number of structural analogues of the natural purines and pyrimidines are now known to be capable of replacing the corresponding bases in nucleic acids. These include: 5-chloro, 5-bromo, and 5-iodo-uracils, which can replace thymine in DNA,[1] and 2-thiouracil, which can be incorporated into tobacco mosaic virus RNA.[2,3] 8-Azaguanine can replace guanine in several ribonucleic acids. With most organisms the proportion of ribonucleic acid and guanine replaced by 8-azaguanine is low, but in *Bacillus cereus* RNA this proportion can be as high as 40 %.

The 8-azapurines and substituted triazoles offered a series of analogues of purines and their possible precursors, all differing from the correspondingly natural derivatives only by the replacement of the CH group in the 8 position of the purines by a nitrogen atom.

One may speculate on the differences between guanine and 8-azaguanine which are responsible for the failure of 8-azaguanine-containing RNA to function normally. The replacement of the CH group in the purine 8 position by a nitrogen atom changes the shape of the purine ring to a small degree and considerably alters other properties of the molecule. In particular, the dissociation constants of the 6-oxo and 2-amino groups of 8-azaguanine are lower than those of guanine. This may affect the ability of an 8-azaguanine residue in a nucleic acid to participate in a hydrogen-bonded structure involving those substituent groups.[4]

Cellular resistance to 8-azaguanine is usually due to reduced or absent activity of HPRT enzyme. Cell deficient in this enzyme activity cannot convert the abnormal purine into its corresponding ribonucleotide, thus preventing its lethal incorporation into nucleic acids.

Some of the zwitterionic buffers like piperazine 1,4-bis(2-ethane sulfonic acid) (PIPES) are substituted taurine derivatives. Taurine is derived directly from the breakdown of food, but the

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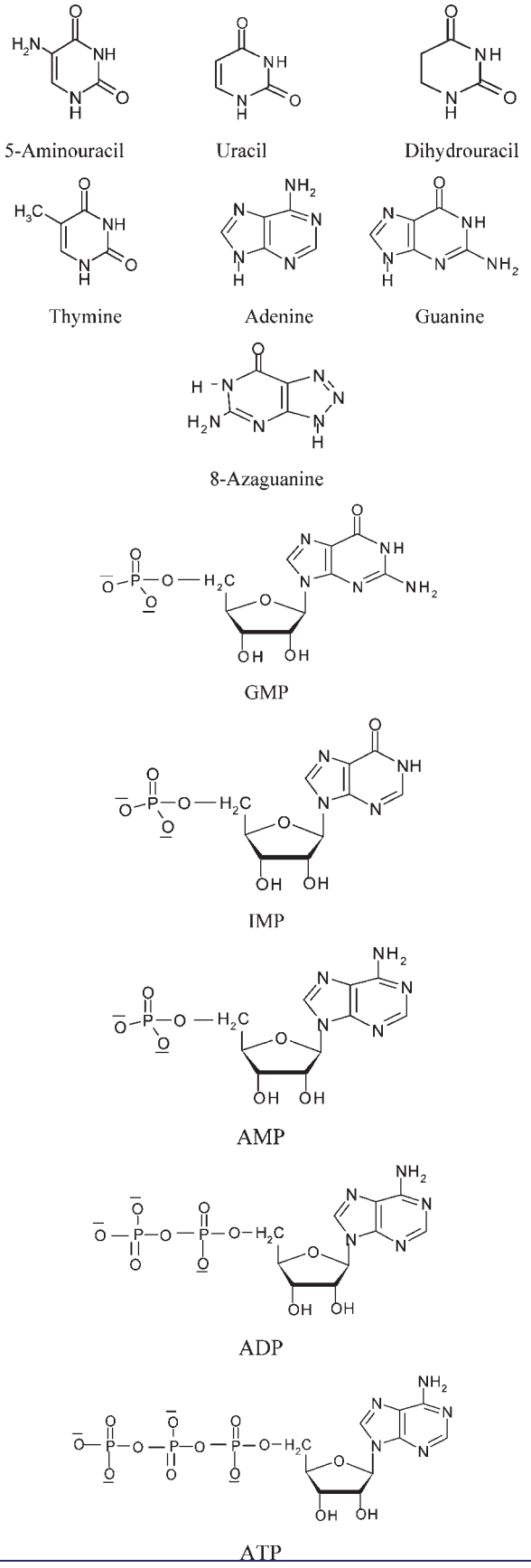
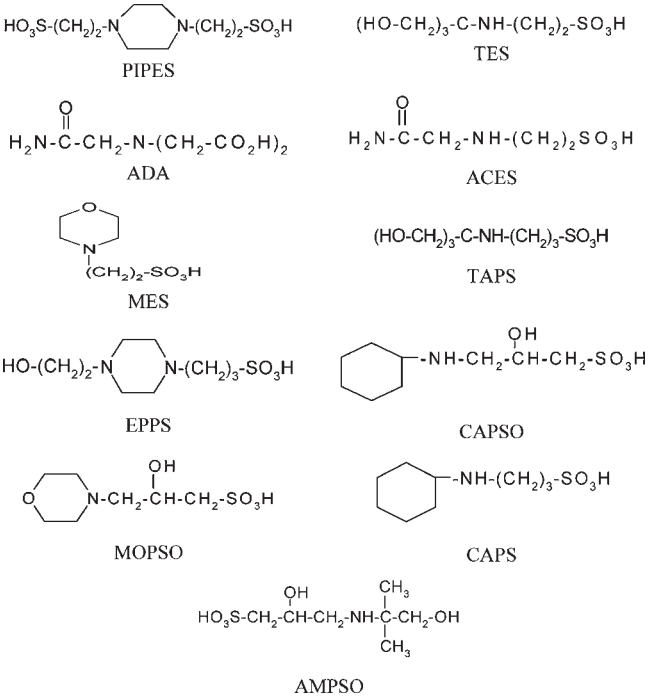
**Scheme 1. Structures of Nucleotides and Nucleobases under Investigation**




**Scheme 2. Structures of Zwitterionic Buffers under Investigation**




body can produce its own taurine from the essential amino acid methionine and its related nonessential amino acid cysteine. Taurine is found abundantly in tissues that are excitable, rich in membranes, and that generate oxidants. Thus, it is the most prevalent of all of the amino acids in the tissues comprising the skeletal and cardiac muscles and the brain. It is critical to the proper function of the brain, heart, lungs, and blood. Because it performs key functions in cholesterol metabolism related to bile acids, it is essential to the role of the liver, pancreas, and gall bladder. It is also a key in the renal function of the kidney. Taurine is essential for vision, directly to execute muscular motion and control, and indirectly to prevent disorders such as diabetes and cancer.[5] Some of the systems under investigation mimic taurine−metal ion−DNA or taurine−metal ion−protein interactions in biological systems and can be considered as models for development of possible drugs.

The ternary complexes of the type Ln(III) + nucleotide + zwitterionic buffer or Ln(III) + nucleobase + zwitterionic buffer may be considered as relatively simple models from which information may be gained about the properties of nucleotides adenosine 5′-monophosphate (5′-AMP), adenosine 5′-diphosphate (5′-ADP), adenosine 5′-triphosphate (5′-ATP), and inosine 5′-monophosphate (5′-IMP) and their base moieties regarding the strength of their interactions with the biologically important zwitterionic buffer ligands 4-(2-hydroxyethyl) piperazine-1-propane sulfonicacid (EPPS), 3-(*N*-morpholino)-2-hydroxypropane sulfonic acid (MOPSO), 3-(cyclo-xylamino)-1-propane sulfonic acid (CAPS), *N*-(tris(hydroxy methyl)-methyl)-2-amino-ethane sulfonic acid (TES), 3-(cyclohexyl amino)-2-hydroxy-1-propane sulfonic acid (CAPSO), *N*-(tris(hydroxy methyl)-methyl)-3-amino propane sulfonic acid (TAPS), *N*-(2-acetamido)-2-aminoethane sulfonic acid (ACES), PIPES, *N*-(1,1-dimethyl-2-hydroxy ethyl)-3-amino 2-hydroxypropane sulfonic acid (AMPSO), and *N*-(2-acetamido)-imino-diacetic acid

(ADA). Insight into the factors which influence the strength is thus becoming available, as these systems may mimic the biological process in which lanthanide complexes may be involved in the catalytic cleavage of DNA and RNA. Cleavage of nucleotides and of DNA or RNA by lanthanide catalysts is an area of much activity.[6] In particular, lanthanide ions and their complexes are known to be excellent catalysts for the hydrolysis of biozide-type phenyl phosphate esters, of DNA, and of related oligonucleotides. Different trivalent lanthanide ions have been reported to show different efficiencies.[7]

Good et al.[8,9] described 12 buffers which were useful for most common biological applications, having p$K_a$ values between 6.1 and 8.4. Most of these buffers were zwitterionic, capable of possessing both positive and negative charges. The nature of the original Good's buffers made them particularly suitable for biological applications because their buffering capacity was independent of temperature and concentration.

They were very soluble in water but poorly soluble in organic solvents; this property made it difficult for the buffers to traverse cellular membranes or accumulate within biological systems. The reduced ion effects observed with these buffers allowed the preparation of solutions from concentrated stocks with minimal pH effects from the dilution of buffer components.

In continuation of our previous work on ternary complexes containing nuclobase, amino acids, zwitterionic buffers, and nucleotides[10−15] the mixed ligand complexes of the type Ln(III) + nucleotide + zwitterionic buffer ligands, Ln(III) + nucleobase + zwitterionic buffer ligands, and Ln(III) + nucleobase + amino acids have been investigated by potentiometric pH-titrations to determine the formation constants of the monomeric and dimeric normal and protonated mixed ligand complexes formed in solution.

## EXPERIMENTAL SECTION

**Material and Solutions.** All materials employed in the present investigation were of analytical reagent grade products. [6-Amino-purine] $C_5H_5N_5$ (adenine), [2-amino-6-oxypurine] $C_5H_5N_5O$ (guanine), [2-amino-6-oxy 8-azapurine] $C_4H_4N_4O$ (8-azaguanine), [5-methyl pyrimidine] $C_5H_6N_2O_2$ (thymine), [2,4-dioxypyrimidine] $C_4H_4N_2O_2$ (uracil), [5-amino 2,4-dioxypyrimidine] $C_4H_5N_3O_2$ (5-aminouracil), [5,6 dihydro-2,4-dioxy pyrimidine] $C_4H_6N_2O_2$ (dihydrouracil), [adenosine 5′-triphosphate dissodium salt hydrate] $C_{10}H_{14}N_5Na_2O_{13}P_3 \cdot 3H_2O$ (ATP), [adenosine-5′-diphosphate sodium salt] $C_{10}H_{14}N_5NaO_{10}P_2$ (ADP), [adenosine 5′-monophosphoric acid monohydrate] $C_{10}H_{14}N_5O_7P \cdot H_2O$ (AMP), [guanosine 5′-monophosphate dissodium salt] $C_{10}H_{12}N_5Na_2O_8P$ (GMP), and [inosine 5′-monophosphate dissodium salt] $C_{10}H_{11}N_4Na_2O_8P$ (IMP) were purchased from Sigma Chemical Co. and were used without purification. The amount of free phosphates initially present in the nucleotides was determined.[16] To account for this and to prepare metal ion nucleotide solutions of exactly a 1:1 ratio, we also determined, by potentiometric pH titration, the molecular mass of these nucleotides and nucleobases.[17] Fresh solid ligand was weighed out for each titration to avoid hydrolysis prior to the potentiometric measurements.

Chemical structures of adenine, guanine, 8-azaguanine, thymine, uracil, 5-aminouracil, dihydrouracil, ATP, ADP, AMP, GMP, and IMP in their dominating conformation are shown in Scheme 1.

ACES, CAPS, MES, PIPES, TAPS, TES, ADA, EPPS, AMPSO, CAPSO, and MOPSO were purchased from Sigma Chemical Co. (St. Louis, MO). We determined by potentiometric pH titration the molecular mass of these zwitterions to verify/determine the purity, especially for acidic/basic contaminants. We observed the high purity of the buffers used. The structures of the biologically important zwitterionic buffer under investigation are given in Scheme 2.

[Amino succinic acid] $C_4H_7NO_2$ (aspartic acid), [2-amino-propanoic acid] $C_3H_7NO_2$ (D-alanine) and (L-alanine), [2-amino-4-methyl thiobutanoic acid] $C_5H_{11}NO_2S$ (methionine), [2-amino-succinamic acid] $C_4H_8N_2O_3$ (asparagine), [2-amino-4-methyl pentanoic acid] $C_6H_{13}NO_2$ (DL-leucine), [2-amino-3-indolyl propanoic acid] $C_{11}H_{12}N_2O_2$ (L-tryptophan), [2-amino-3-(4-hydroxyphenyl)-propanoic acid] $C_9H_{11}NO_3$ (L-tyrosine), [2-amino-3-imidazole propanoic acid] $C_6H_9N_3O_2$ (histidine), [2-amino-5-guanidino pentanoic acid] $C_6H_{14}N_4O_2$ (arginine), and [4-amino-5-oxo-pentanoic acid amide] $C_5H_{10}N_2O_3$ (glutamine) were used without purification. To account for preparation of metal ion amino acid solutions of exactly a 1:1 ratio, we also determined, by potentiometric pH titration, the molecular mass of these amino acids.

Metal salt $Pr(NO_3)_3 \cdot 5H_2O$, $DyCl_3$ anhydrous, $Gd(NO_3)_3 \cdot 6H_2O$, and $Eu(NO_3)_3 \cdot 5H_2O$ were of the Sigma Chemical Co. Stock solutions (0.01 mol·dm$^{-3}$) of metal salts were prepared by dissolving precisely weighed amount of the salt in bidistilled water. The concentrations of the metal ion stock solutions were determined complexometrically by ethylenediamine tetracetic acid dissodium salt (EDTA) using suitable indicators.

A $CO_2$ free solution of potassium hydroxide (Merck AG) was prepared and standardized against multiple samples of primary standard potassium hydrogen phthalate (Merck AG) under $CO_2$ free conditions. $HNO_3$ solutions were prepared and standardized potentiometrically with tris(hydroxyl methyl)-amino methane. The ionic strength of the studied solutions was adjusted to 0.1 mol·dm$^{-3}$ using stock solution of $KNO_3$ in potentiometric and spectral measurements. $KNO_3$ was from Merck AG.

**Apparatus and Procedure.** The value of the electromotive force (EMF) of the cell was taken with a commercial Fisher Accumet pH/ion meter model 825 MP. The potentiometric system was connected to a glass electrode (Metrohm 1028) connected against a double junction reference electrode (Orion 9020). The temperature was controlled by circulation of water through the jacket from a VEB model E3E ultrathermostat bath and maintained within 25.0 ± 0.1 °C. Pure nitrogen was bubbled through the solution to maintain an inert atmosphere. Efficient stirring of the solution was achieved with a magnetic stirrer. All solutions were prepared in a constant ionic medium, 0.1 mol·dm$^{-3}$ $KNO_3$. The concentration of hydrogen ion was decreased by the addition of potassium hydroxide, prepared in the ionic medium used for the solution.

Gran's method[18] was used to determine $E^{o\prime}$ and $E_j$ so that the hydrogen ion concentration, $h$, could be found from $E$, the measured potential by means of

$$E(\mathrm{mV}) = E^{o\prime} - 59.157 \log h + E_j \quad (1)$$

The protonation constants were then determined by use of the Bjerrum function.[19]

$$\begin{aligned} \overline{n} &= (H_T - h + K_W/h)/A_T \\ &= (\beta_1 h + 2\beta_2 h^2)/(1 + \beta_1 h + \beta_2 h^2) \end{aligned} \quad (2)$$

which is calculated from the experimental quantities, $h$, the total concentration of titratable hydrogen ion $H_T$, and the total reagent concentration $A_T$. p$K_a$ values of the investigated ligands

were determined in water from the overall protonation constants $\beta_1$ and $\beta_2$ calculated by the linearization method of Irving and Rossotti.[20]

Initial estimates of the p$K_a$ values were refined with the ESAB2M computer program.[21]

A detailed description of solution composition used in the determination of the stability constants of complex species is shown as follows:

System 1: Complexes of 8-azaguanine and amino acids, nucleotides, or nucleobases.

(a) $4 \cdot 10^{-4}$ mol·dm$^{-3}$ $HNO_3$ + $1 \cdot 10^{-4}$ mol·dm$^{-3}$ 8-azaguanine (primary ligand).
(b) $4 \cdot 10^{-4}$ mol·dm$^{-3}$ $HNO_3$ + $1 \cdot 10^{-4}$ mol·dm$^{-3}$ amino acids (aspartic acid, asparagine, glutamine, D-alanine, DL-leucine, L-alanine, methionine, L-tryptophan, L-tyrosine, histidine, arginine), nucleotides (ATP, ADP, AMP, GMP, IMP), or nucleobases (uracil, 5-aminouracil, dihydrouracil).
(c) Solution (a) + $1 \cdot 10^{-4}$ mol·dm$^{-3}$ Ln(III).
(d) Solution (b) + $1 \cdot 10^{-4}$ mol·dm$^{-3}$ Ln(III).
(e) Solution (a) + $2 \cdot 10^{-4}$ mol·dm$^{-3}$ Ln(III).
(f) Solution (b) + $2 \cdot 10^{-4}$ mol·dm$^{-3}$ Ln(III).
(g) $4 \cdot 10^{-4}$ mol·dm$^{-3}$ $HNO_3$ + $1 \cdot 10^{-4}$ mol·dm$^{-3}$ 8-azaguanine + $1 \cdot 10^{-4}$ mol·dm$^{-3}$ amino acids or nucleotides or nucleobases + $1 \cdot 10^{-4}$ mol·dm$^{-3}$ Ln(III).
(h) $4 \cdot 10^{-4}$ mol·dm$^{-3}$ $HNO_3$ + $1 \cdot 10^{-4}$ mol·dm$^{-3}$ 8-azaguanine + $1 \cdot 10^{-4}$ mol·dm$^{-3}$ amino acids or nucleotides or nucleobases + $2 \cdot 10^{-4}$ mol·dm$^{-3}$ Ln(III).

System 2: Complexes of zwitterionic buffers and nucleobases.

(a) $4 \cdot 10^{-4}$ mol·dm$^{-3}$ $HNO_3$ + $1 \cdot 10^{-4}$ mol·dm$^{-3}$ zwitterionic buffers (ligand 1), (EPPS, MOPSO, CAPS, TES, CAPSO, TAPS, ACES, PIPES, AMPSO, MES, and ADA).
(b) $4 \cdot 10^{-4}$ mol·dm$^{-3}$ $HNO_3$ + $1 \cdot 10^{-4}$ mol·dm$^{-3}$ nucleobases (adenine, guanine, thymine, uracil, 5-aminouracil, and dihydrouracil).
(c) Solution (a) + $1 \cdot 10^{-4}$ mol·dm$^{-3}$ Ln(III).
(d) Solution (b) + $1 \cdot 10^{-4}$ mol·dm$^{-3}$ Ln(III).
(e) Solution (a) + $2 \cdot 10^{-4}$ mol·dm$^{-3}$ Ln(III).
(f) Solution (b) + $2 \cdot 10^{-4}$ mol·dm$^{-3}$ Ln(III).
(g) $4 \cdot 10^{-4}$ mol·dm$^{-3}$ $HNO_3$ + $1 \cdot 10^{-4}$ mol·dm$^{-3}$ zwitterionic buffers + $1 \cdot 10^{-4}$ mol·dm$^{-3}$ nucleobases + $1 \cdot 10^{-4}$ mol·dm$^{-3}$ Ln(III).
(h) $4 \cdot 10^{-4}$ mol·dm$^{-3}$ $HNO_3$ + $1 \cdot 10^{-4}$ mol·dm$^{-3}$ zwitterionic buffers + $1 \cdot 10^{-4}$ mol·dm$^{-3}$ nucleobases + $2 \cdot 10^{-4}$ mol·dm$^{-3}$ Ln(III).

A constant ionic strength was obtained with 0.1 mol·dm$^{-3}$ $KNO_3$.

For both ligand protonation and metal complex formation equilibria, data were collected over the largest possible pH interval, although a number of experimental points were frequently discarded for the final stability constant calculations, especially within the range where the complexation observed was insignificant.

## RESULTS AND DISCUSSION

**Lanthanide(III) Complexes of 2-Amino-6-oxy-8-azapurine (8-Azaguanine) with Amino Acids, Nucleotides, or Nucleobases.** Equilibrium potentiometric measurements for the interaction of 8-azaguanine and lanthanide metal ions Eu(III), Pr(III), Gd(III), or Dy(III) with amino acids, L-tyrosine, arginine, aspartic acid, glutamine, methionine, L-tryptophan, L-alanine, asparagine, D-alanine, D-histidine, and DL-leucine, nucleotides AMP, ADP, ATP, GMP, and IMP, or nucleobases uracil, 5-aminouracil, and dihydrouracil have been carried out in solution.

The formation of various ternary complex species is inferred from the potentiometric pH titration curves. Initial estimates of the stability constants of the resulting species and the acid dissociation constants of 8-azaguanine, nucleotides, nucleobases, and amino acids have been refined with the SUPERQUAD computer program.[22] The quality of the fit during this refinement was judged by the values of the sample standard deviations and the goodness of fit $\chi^2$ (Pearson's Test). At $\sigma_E$ = 0.1 mV (0.001 pH error) and $\sigma_V$ = 0.005 mL, the values of $S$ in different sets of titrations were between 1.0 and 1.7, and $\chi^2$ was between 12.0 and 13.0. The scatter of residuals ($E_{obs} - E_{calc}$) versus pH was reasonably random, without any significant systematic trends, thus indicating a good fit of the experimental data of the expected model systems under our experimental conditions.

Furthermore, the formation constant values of the different 1:1 or 2:1 Ln(III)−nucleobases, nucleotides, or amino acids have been determined under identical conditions.

The overall complexation reactions involving normal and protonated species are:

$$pM + q8\text{-aza} + rL \leftrightarrow M_p(8\text{-aza})_q(L)_r$$

$$pM + q8\text{-aza} + rL + sH \rightleftharpoons M_p(8\text{-aza})_q(L)_r(H)_s$$

$$\beta_{pqrs} = \frac{M_p(8\text{-aza})_q(L)_r(H)_s}{[M]^p[8\text{-aza}]^q[L]^r[H]^s} \quad (3)$$

in which L = amino acids, nucleotides, or nucleobases ligands, 8-aza = 8-azaguanine, and M = Eu(III), Pr(III), Gd(III), and Dy(III). In addition, the protonation and complexation reactions of the free phosphate ligand initially present in solutions have been included in the calculations to get better conditional stability constants. If the metal ion undergoes significant hydrolysis, as in our case of Eu(III), Pr(III), Gd(III), or Dy(III), the appropriate constants are also included.

The data points collected in the pH range 3.0 to 11.0 were used for the calculations and refinements.

The formation constants of all of the binary and the ternary complexes studied are given in Tables 1 to 12.

The acidity constants of amino acids determined at 25 °C of arginine (p$K_{a2}$ = 8.91 ± 0.02), aspartic acid (p$K_{a2}$ = 9.77 ± 0.02), asparagine (p$K_{a2}$ = 8.70 ± 0.02), D-histidine (p$K_{a2}$ = 5.94 ± 0.02), DL-leucine (p$K_{a2}$ = 9.24 ± 0.02), L-tryptophan (p$K_{a2}$ = 9.25 ± 0.02), glutamine (p$K_{a2}$ = 9.25 ± 0.02), methionine (p$K_{a2}$ = 9.37 ± 0.02), D-alanine (p$K_{a2}$ = 9.54 ± 0.02), L-tyrosine (p$K_{a2}$ = 9.85 ± 0.02), and L-alanine(p$K_{a2}$ = 8.91 ± 0.02) are in good agreement with those found in the literature.[23]

The acid dissociation constant values are for 8-azaguanine (p$K_{a2}$ = 6.81 ± 0.02); for dihydrouracil (p$K_{a2}$ = 11.5 ± 0.02); for 5-aminouracil (p$K_{a2}$ = 9.15 ± 0.02); and for uracil (p$K_{a2}$ = 9.30 ± 0.02). The acid dissociation constant values are for nucleo tides GMP (p$K_{a1}$ = 2.45 ± 0.04), (p$K_{a2}$ = 6.38 ± 0.04)), (p$K_{a3}$ = 9.48 ± 0.04); for IMP (p$K_{a2}$ = 9.01 ± 0.02); for AMP (p$K_{a1}$ = 3.70 ± 0.02), (p$K_{a2}$ = 5.97 ± 0.02); for ADP (p$K_{a1}$ = 3.86 ± 0.02), (p$K_{a2}$ = 6.28 ± 0.02); and for ATP (p$K_{a1}$ = 4.13 ± 0.02), (p$K_{a2}$ = 6.13 ± 0.02) in good agreement with those found in the

**Table 1. Formation Constants for Ln(III) + Amino Acid (AA) (1:1) Binary Complexes at 25.0 ± 0.1 °C and $I$ = 0.1 mol·dm$^{-3}$ $KNO_3$[a]**

| amino acid (AA) | $\log K^{Gd(III)}_{Gd(III)(AA)}$ | $\log K^{Pr(III)}_{Pr(III)(AA)}$ | $\log K^{Dy(III)}_{Dy(III)(AA)}$ | $\log K^{Eu(III)}_{Eu(III)(AA)}$ |
|---|---|---|---|---|
| arginine | 3.31 ± 0.01 | 3.99 ± 0.01 | 3.43 ± 0.03 | 4.09 ± 0.03 |
| asparagine | 3.86 ± 0.02 | 4.23 ± 0.01 | 4.04 ± 0.03 | 4.27 ± 0.03 |
| histidine | 3.68 ± 0.03 | 4.25 ± 0.03 | 4.06 ± 0.01 | 4.27 ± 0.02 |
| DL-leucine | 3.49 ± 0.01 | 4.12 ± 0.01 | 3.92 ± 0.03 | 4.27 ± 0.02 |
| L-tryptophan | 3.76 ± 0.02 | 4.16 ± 0.03 | 4.05 ± 0.02 | 4.29 ± 0.03 |
| L-tyrosine | 3.26 ± 0.03 | 4.14 ± 0.02 | 3.62 ± 0.03 | 4.26 ± 0.03 |
| methionine | 3.47 ± 0.02 | 4.09 ± 0.03 | 4.08 ± 0.02 | 4.27 ± 0.01 |
| D-alanine | 3.60 ± 0.02 | 4.24 ± 0.03 | 4.02 ± 0.03 | 4.28 ± 0.02 |
| L-alanine | 3.85 ± 0.02 | 4.16 ± 0.02 | 3.89 ± 0.03 | 4.28 ± 0.01 |
| aspartic acid | 4.04 ± 0.02 | 4.26 ± 0.03 | 3.94 ± 0.02 | 4.30 ± 0.01 |
| glutamine | 3.64 ± 0.02 | 4.16 ± 0.03 | 4.08 ± 0.03 | 3.70 ± 0.03 |

[a] ± refers to three times standard deviation (3s).

**Table 2. Formation Constants for Ln(III) + Nucleobase (NB) (1:1) Binary Complexes at 25.0 ± 0.1 °C and $I$ = 0.1 mol·dm$^{-3}$ $KNO_3$[a]**

| nucleobase (NB) | $\log K^{Gd(III)}_{Gd(III)(NB)}$ | $\log K^{Pr(III)}_{Pr(III)(NB)}$ | $\log K^{Dy(III)}_{Dy(III)(NB)}$ | $\log K^{Eu(III)}_{Eu(III)(NB)}$ |
|---|---|---|---|---|
| thymine | 3.22 ± 0.03 | 4.17 ± 0.02 | 4.04 ± 0.02 | 4.28 ± 0.03 |
| uracil | 3.27 ± 0.03 | 4.23 ± 0.03 | 3.89 ± 0.02 | 4.29 ± 0.01 |
| adenine | 3.10 ± 0.02 | 4.12 ± 0.03 | 3.91 ± 0.03 | 4.27 ± 0.03 |
| 8-azaguanine | 4.04 ± 0.02 | 4.25 ± 0.03 | 4.23 ± 0.01 | 4.30 ± 0.01 |
| dihydrouracil | 3.21 ± 0.02 | 4.21 ± 0.02 | 4.19 ± 0.03 | 4.28 ± 0.02 |
| 5-aminouracil | 3.58 ± 0.02 | 4.20 ± 0.02 | 4.06 ± 0.01 | 4.26 ± 0.02 |

[a] ± refers to three times standard deviation (3s).

**Table 3. Formation Constants for Ln(III) + Nucleotide (NU) (1:1) Binary Complexes at 25.0 ± 0.1 °C and $I$ = 0.1 mol·dm$^{-3}$ $KNO_3$[a]**

| nucleotide (NU) | $\log K^{Gd(III)}_{Gd(III)(NU)}$ | $\log K^{Pr(III)}_{Pr(III)(NU)}$ | $\log K^{Dy(III)}_{Dy(III)(NU)}$ | $\log K^{Eu(III)}_{Eu(III)(NU)}$ |
|---|---|---|---|---|
| GMP | 4.08 ± 0.01 | 4.23 ± 0.02 | 4.20 ± 0.02 | 4.28 ± 0.02 |
| IMP | 3.91 ± 0.02 | 4.15 ± 0.02 | 4.18 ± 0.01 | 4.28 ± 0.01 |
| ATP | 5.51 ± 0.01 | 4.33 ± 0.01 | 4.36 ± 0.01 | 4.46 ± 0.02 |
| ADP | 4.03 ± 0.01 | 4.03 ± 0.02 | 4.03 ± 0.02 | 4.07 ± 0.01 |
| AMP | 4.63 ± 0.02 | 4.39 ± 0.02 | 4.03 ± 0.02 | 4.03 ± 0.02 |

[a] ± refers to three times standard deviation (3s).

literature.[23] The plus/minus values obtained from SUPERQUAD calculations refer to statistically determined uncertainties at small 95 % confidence intervals of the reported values.

As can be seen in Table 4 the behavior of lanthanide ions in the presence of amino acids is almost the same, reflecting their well-known chemical similarity.

In general, amino acids show a weak binding to lanthanide metals. Formation constant values are always low, and variations for different amino acids are quite small. Despite this, it is possible to observe that the interaction of lanthanides with amino acids is mostly determined by electrostatic interaction. Some observed trends support this idea: (a) an increase in formation constant values is observed as the basicity of ligands increases, (b) stability is also enhanced when more negatively charged ligands are bound to the metal; aspartic acid provide a good example of this point, and (c) a steady increase in formation constants is observed as ionic radii of the lanthanide ions decrease.

Because of the low stability of lanthanide complexes with amino acids, hydrolysis reactions are obvious competing processes. Of course, the extension of hydrolysis depends on the particular ion since the acidity of these f-transition metal ions increases with decreasing ionic radii; thus, the smaller are the lanthanides, the more importance should be given to hydrolysis reactions. The formation of $[Ln(OH)]^{2+}$ and $[Ln(OH)_2]^{4+}$ $[Ln(OH)_5]^{4+}$ has been reported for all lanthanide ions, and a consistent increase in acidity is observed as the charge/radius ratio increases due to the lanthanide contraction. The lanthanide trihydroxides are weakly amphoteric, but those of the heavier metals dissolve in excess base. There is evidence for the formation of $[Ln(OH)_4]$.[24]

In solution nucleotides exist mainly in the so-called anticonformation. Independent of the kind of nucleobase involved or whether a nucleoside mono-, di-, or triphosphate is considered, it is the phosphate residue which determines to a very large part the stability of the complexes formed with the biologically important metal ions.[25] However, for the selectivity and specificity of


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**Table 4. Formation Constants for Ln(III) + 8-Azaguanine + Amino Acid (AA) 1:1:1 Ternary Complexes at 25.0 ± 0.1 °C and $I$ = 0.1 mol·dm$^{-3}$ $KNO_3$[a]**

| amino acid (AA) | $\log K^{Gd(III)}_{Gd(III)(Azaguanine)(AA)}$ | $\log K^{Pr(III)}_{Pr(III)(Azaguanine)(AA)}$ | $\log K^{Dy(III)}_{Dy(III)(Azaguanine)(AA)}$ | $\log K^{Eu(III)}_{Eu(III)(Azaguanine)(AA)}$ |
|---|---|---|---|---|
| arginine | 5.66 ± 0.02[b] | 14.62 ± 0.02[c] | 14.01 ± 0.01[c] | 14.26 ± 0.02[c] |
| | | 3.92 ± 0.02[b] | | 4.30 ± 0.02[b] |
| asparagine | 4.33 ± 0.02[b] | 18.31 ± 0.02[c] | 16.72 ± 0.01[c] | 15.83 ± 0.02[c] |
| | | 4.25 ± 0.02[b] | | 4.31 ± 0.02[b] |
| D-histidine | 4.31 ± 0.02[b] | 4.29 ± 0.01[b] | 13.03 ± 0.01[c] | 4.30 ± 0.01[b] |
| DL-leucine | 4.30 ± 0.02[b] | 18.63 ± 0.02[c] | 16.66 ± 0.01[c] | 18.04 ± 0.02[c] |
| | | 4.19 ± 0.02[b] | | 4.34 ± 0.02[b] |
| L-tryptophan | 4.31 ± 0.02[b] | 16.27 ± 0.02[c] | 15.24 ± 0.02[c] | 16.82 ± 0.01[c] |
| | | 4.24 ± 0.02[b] | | 4.33 ± 0.01[b] |
| L-tyrosine | 20.67 ± 0.02[c] | 15.42 ± 0.01[c] | 15.51 ± 0.01[c] | 15.27 ± 0.01[c] |
| | 4.34 ± 0.02[b] | 4.01 ± 0.01[b] | | 4.27 ± 0.01[b] |
| methionine | 4.32 ± 0.02[b] | 17.92 ± 0.01[c] | 17.54 ± 0.02[c] | 6.01 ± 0.01[b] |
| | | 4.22 ± 0.01[b] | | |
| D-alanine | 4.32 ± 0.02[b] | 21.06 ± 0.02[c] | 18.93 ± 0.02[c] | 18.09 ± 0.02[c] |
| | | 4.26 ± 0.02[b] | | 4.31 ± 0.02[b] |
| L-alanine | 4.33 ± 0.02[b] | 6.07 ± 0.01[b] | 16.87 ± 0.02[c] | 6.53 ± 0.01[b] |
| aspartic acid | 4.50 ± 0.01[b] | 4.28 ± 0.02[b] | 4.37 ± 0.02[b] | 4.42 ± 0.01[b] |
| glutamine | 5.74 ± 0.02[b] | 18.64 ± 0.02[c] | 17.32 ± 0.02[c] | 17.52 ± 0.02[c] |
| | | 4.21 ± 0.02[b] | | 4.33 ± 0.02[b] |

[a] ± refers to three times standard deviation (3s). [b] log formation constant of normal ternary complex. [c] log formation constant of protonated complex.

**Table 5. Formation Constants for Ln(III) + 8-Azaguanine + Nucleotide (NU) 1:1:1 Ternary Complexes at 25.0 ± 0.1 °C and $I$ = 0.1 mol·dm$^{-3}$ $KNO_3$[a]**

| nucleotide (NU) | $\log K^{Gd(III)}_{Gd(III)(Azaguanine)(NU)}$ | $\log K^{Pr(III)}_{Pr(III)(Azaguanine)(NU)}$ | $\log K^{Dy(III)}_{Dy(III)(Azaguanine)(NU)}$ | $\log K^{Eu(III)}_{Eu(III)(Azaguanine)(NU)}$ |
|---|---|---|---|---|
| AMP | 5.36 ± 0.01 | 4.71 ± 0.03 | 4.81 ± 0.03 | 4.79 ± 0.01 |
| ADP | 5.15 ± 0.01 | 4.50 ± 0.01 | 4.68 ± 0.02 | 4.84 ± 0.03 |
| ATP | 4.68 ± 0.02 | 4.55 ± 0.02 | 4.85 ± 0.03 | 4.57 ± 0.01 |
| GMP | 4.42 ± 0.02 | 4.22 ± 0.02 | 16.41 ± 0.01 | 15.57 ± 0.02 |
| IMP | 4.40 ± 0.01 | 4.28 ± 0.02 | 15.87 ± 0.01 | 15.00 ± 0.02 |

[a] ± refers to three times standard deviation (3s).

**Table 6. Formation Constants for Ln(III) + 8-Azaguanine + Nucleobase (NB) 1:1:1 Ternary Complexes at 25.0 ± 0.1 °C and $I$ = 0.1 mol·dm$^{-3}$ $KNO_3$[a]**

| nucleobase (NB) | $\log K^{Gd(III)}_{Gd(III)(Azaguanine)(NB)}$ | $\log K^{Pr(III)}_{Pr(III)(Azaguanine)(NB)}$ | $\log K^{Dy(III)}_{Dy(III)(Azaguanine)(NB)}$ | $\log K^{Eu(III)}_{Eu(III)(Azaguanine)(NB)}$ |
|---|---|---|---|---|
| uracil | 5.90 ± 0.03[b] | 5.18 ± 0.02[b] | 22.36 ± 0.02[c] | 16.63 ± 0.01[c] |
| | | | 4.28 ± 0.03[b] | 4.31 ± 0.01[b] |
| dihydrouracil | 7.55 ± 0.02[b] | 19.00 ± 0.02[c] | 7.68 ± 0.02[b] | 17.68 ± 0.01[c] |
| | | 4.18 ± 0.03[b] | | 4.23 ± 0.03[b] |
| 5-aminouracil | 5.35 ± 0.02[b] | 4.10 ± 0.02[b] | 19.97 ± 0.03[c] | 4.24 ± 0.01[b] |
| | | | 4.34 ± 0.01[b] | |

[a] ± refers to three times standard deviation (3s). [b] log formation constant of normal ternary complex. [c] log formation constant of protonated complex.

reactions involving nucleotides the nucleobase residues are largely responsible. For purine-nucleotide 5′-phosphates the formation of nucleotides was suggested;[26−29] that is, a metal ion coordinated to the phosphate residue of a purine nucleotide may also interact in the dominating anticonformation with N-7 of the purine moiety.

All mono-, di-, and triphosphate monoesters bind one proton rather avidly; that is, this proton is released only in the pH range of about 6.0, and consequently nucleotides are largely present in aqueous solution in the neutral or slightly alkaline (physiological) pH range as $NMP^{2-}$, $NDP^{3-}$, and $NTP^{4-}$. A further proton at the phosphate residue is only loosely bound and consequently accepted only at a rather low pH. For those nucleotides where the nucleobase also accepts a proton, the corresponding values are even lower due to charge repulsion.[30,31] This means that all of the depotonation reactions regarding a "primary" proton from the phosphate residue occur with $pK_a \leq 2$ and are therefore not considered further because they are without relevance in the pH range above 3.0.

**Table 7. Formation Constants for Ln(III) + Amino Acid (AA) (2:1) Dimeric Binary Complexes at 25.0 ± 0.1 °C and $I$ = 0.1 mol·dm$^{-3}$ $KNO_3$[a]**

| amino acid (AA) | $\log K^{Gd(III)(AA)}_{Gd(III)_2(AA)}$ | $\log K^{Pr(III)(AA)}_{Pr(III)_2(AA)}$ | $\log K^{Dy(III)(AA)}_{Dy(III)_2(AA)}$ | $\log K^{Eu(III)(AA)}_{Eu(III)_2(AA)}$ |
|---|---|---|---|---|
| arginine | 4.28 ± 0.01 | 4.26 ± 0.02 | 4.29 ± 0.02 | 4.28 ± 0.01 |
| asparagine | 4.29 ± 0.01 | 4.26 ± 0.02 | 4.30 ± 0.02 | 4.27 ± 0.02 |
| histidine | 4.29 ± 0.02 | 4.27 ± 0.02 | 4.29 ± 0.01 | 4.28 ± 0.02 |
| DL-leucine | 4.29 ± 0.01 | 4.24 ± 0.03 | 4.29 ± 0.02 | 4.30 ± 0.03 |
| L-tryptophan | 4.29 ± 0.02 | 4.25 ± 0.01 | 4.30 ± 0.03 | 4.31 ± 0.03 |
| L-tyrosine | 4.29 ± 0.02 | 4.26 ± 0.02 | 4.30 ± 0.01 | 4.31 ± 0.01 |
| methionine | 4.29 ± 0.01 | 4.32 ± 0.02 | 4.31 ± 0.02 | 4.29 ± 0.03 |
| D-alanine | 4.30 ± 0.02 | 4.29 ± 0.01 | 4.30 ± 0.02 | 4.30 ± 0.03 |
| L-alanine | 4.32 ± 0.03 | 4.25 ± 0.02 | 4.30 ± 0.02 | 4.36 ± 0.01 |
| aspartic acid | 4.42 ± 0.01 | 4.30 ± 0.02 | 4.37 ± 0.02 | 4.47 ± 0.02 |
| glutamine | 4.26 ± 0.02 | 4.25 ± 0.02 | 4.31 ± 0.03 | 4.27 ± 0.03 |

[a] ± refers to three times standard deviation (3s).

**Table 8. Formation Constants Ln(III) + Nucleobase (NB) (2:1) Dimeric Binary Complexes at 25.0 ± 0.1 °C and $I$ = 0.1 mol·dm$^{-3}$ $KNO_3$[a]**

| nucleobase (NB) | $\log K^{Gd(III)(NB)}_{Gd(III)_2(NB)}$ | $\log K^{Pr(III)(NB)}_{Pr(III)_2(NB)}$ | $\log K^{Dy(III)(NB)}_{Dy(III)_2(NB)}$ | $\log K^{Eu(III)(NB)}_{Eu(III)_2(NB)}$ |
|---|---|---|---|---|
| thymine | 4.08 ± 0.03 | 4.27 ± 0.02 | 4.40 ± 0.02 | 4.32 ± 0.01 |
| uracil | 4.30 ± 0.03 | 4.24 ± 0.02 | 4.30 ± 0.03 | 4.32 ± 0.02 |
| adenine | 4.19 ± 0.02 | 4.25 ± 0.02 | 4.29 ± 0.02 | 4.29 ± 0.03 |
| 8-azaguanine | 4.29 ± 0.02 | 4.28 ± ± 0.03 | 4.30 ± 0.03 | 4.30 ± 0.02 |
| 5-aminouracil | 4.24 ± 0.02 | 4.26 ± 0.01 | 4.31 ± 0.02 | 4.27 ± 0.03 |
| dihydrouracil | 3.70 ± 0.01 | 4.42 ± 0.02 | 5.69 ± 0.02 | 4.97 ± 0.02 |

[a] ± refers to three times standard deviation (3s).

**Table 9. Formation Constants for Ln(III) + Nucleotide (NU) (2:1) Dimeric Binary Complexes at 25.0 ± 0.1 °C and $I$ = 0.1 mol·dm$^{-3}$ $KNO_3$[a]**

| nucleotide (NU) | $\log K^{Gd(III)(NU)}_{Gd(III)_2(NU)}$ | $\log K^{Pr(III)(NU)}_{Pr(III)_2(NU)}$ | $\log K^{Dy(III)(NU)}_{Dy(III)_2(NU)}$ | $\log K^{Eu(III)(NU)}_{Eu(III)_2(NU)}$ |
|---|---|---|---|---|
| GMP | 4.35 ± 0.01 | 4.30 ± 0.02 | 4.38 ± 0.02 | 4.32 ± 0.01 |
| IMP | 4.31 ± 0.02 | 4.29 ± 0.03 | 4.35 ± 0.01 | 4.31 ± 0.02 |
| ATP | 4.43 ± 0.02 | 4.31 ± 0.01 | 4.33 ± 0.02 | 4.32 ± 0.02 |
| ADP | 4.31 ± 0.03 | 4.30 ± 0.02 | 4.31 ± 0.02 | 4.31 ± 0.02 |
| AMP | 4.30 ± 0.02 | 4.31 ± 0.01 | 4.31 ± 0.03 | 4.30 ± 0.01 |

[a] ± refers to three times standard deviation (3s).

**Table 10. Formation Constants for Ln(III) + 8-Azaguanine + Amino Acid (AA) (2:1:1) Dimeric Ternary Complexes at 25.0 ± 0.1 °C and $I$ = 0.1 mol·dm$^{-3}$ $KNO_3$[a]**

| amino acid (AA) | $\log K^{Gd(III)(Azaguanine)(AA)}_{Gd(III)_2(Azaguanine)(AA)}$ | $\log K^{Pr(III)(Azaguanine)(AA)}_{Pr(III)_2(Azaguanine)(AA)}$ | $\log K^{Dy(III)(Azaguanine)(AA)}_{Dy(III)_2(Azaguanine)(AA)}$ | $\log K^{Eu(III)(Azaguanine)(AA)}_{Eu(III)_2(Azaguanine)(AA)}$ |
|---|---|---|---|---|
| arginine | 4.29 ± 0.03 | 4.22 ± 0.01 | 4.33 ± 0.02 | 4.33 ± 0.03 |
| asparagine | 4.29 ± 0.02 | 4.25 ± 0.02 | 4.34 ± 0.01 | 4.31 ± 0.01 |
| D-histidine | 4.28 ± 0.02 | 4.26 ± 0.02 | 4.36 ± 0.03 | 4.29 ± 0.03 |
| DL-leucine | 4.28 ± 0.03 | 4.22 ± 0.02 | 4.33 ± 0.02 | 4.35 ± 0.01 |
| L-tryptophan | 4.28 ± 0.02 | 4.26 ± 0.02 | 4.33 ± 0.01 | 4.34 ± 0.01 |
| L-tyrosine | 4.32 ± 0.01 | 4.26 ± 0.01 | 4.32 ± 0.02 | 4.34 ± 0.03 |
| methionine | 4.28 ± 0.02 | 4.22 ± 0.03 | 4.35 ± 0.02 | 4.31 ± 0.02 |
| D-alanine | 4.28 ± 0.01 | 4.25 ± 0.02 | 4.34 ± 0.02 | 4.33 ± 0.02 |
| L-alanine | 4.29 ± 0.01 | 4.27 ± 0.02 | 4.32 ± 0.03 | 4.32 ± 0.02 |
| aspartic acid | 4.29 ± 0.02 | 4.26 ± 0.03 | 4.29 ± 0.01 | 4.30 ± 0.02 |
| glutamine | 4.29 ± 0.02 | 4.23 ± 0.02 | 4.34 ± 0.01 | 4.32 ± 0.02 |

[a] ± refers to three times standard deviation (3s).


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**Table 11. Formation Constants for the Ln(III) + 8-Azaguanine + Nucleotide (NU) (2:1:1) Dimeric Ternary Complexes at 25.0 ± 0.1 °C and $I$ = 0.1 mol·dm$^{-3}$ $KNO_3$[a]**

| nucleotide (NU) | $\log K^{Gd(III)(Azaguanine)(NU)}_{Gd(III)_2(Azaguanine)(NU)}$ | $\log K^{Pr(III)(Azaguanine)(NU)}_{Pr(III)_2(Azaguanine)(NU)}$ | $\log K^{Dy(III)(Azaguanine)(NU)}_{Dy(III)_2(Azaguanine)(NU)}$ | $\log K^{Eu(III)(Azaguanine)(NU)}_{Eu(III)_2(Azaguanine)(NU)}$ |
|---|---|---|---|---|
| AMP | 4.31 ± 0.01 | 4.29 ± 0.03 | 4.31 ± 0.03 | 4.31 ± 0.03 |
| ADP | 4.30 ± 0.01 | 4.30 ± 0.03 | 4.31 ± 0.02 | 4.30 ± 0.03 |
| ATP | 4.30 ± 0.02 | 4.30 ± 0.01 | 4.31 ± 0.02 | 4.30 ± 0.02 |
| GMP | 4.29 ± 0.02 | 4.27 ± 0.01 | 4.43 ± 0.01 | 4.38 ± 0.02 |
| IMP | 4.30 ± 0.02 | 4.28 ± 0.03 | 4.44 ± 0.03 | 4.36 ± 0.01 |

[a] ± refers to three times standard deviation (3s).

**Table 12. Formation Constants for the Ln(III) + 8-Azaguanine + Nucleobase (NB) (2:1:1) Dimeric Ternary Complexes at 25.0 ± 0.1 °C and $I$ = 0.1 mol·dm$^{-3}$ $KNO_3$[a]**

| nucleobase (NB) | $\log K^{Gd(III)(Azaguanine)(NB)}_{Gd(III)_2(Azaguanine)(NB)}$ | $\log K^{Pr(III)(Azaguanine)(NB)}_{Pr(III)_2(Azaguanine)(NB)}$ | $\log K^{Dy(III)(Azaguanine)(NB)}_{Dy(III)_2(Azaguanine)(NB)}$ | $\log K^{Eu(III)(Azaguanine)(NB)}_{Eu(III)_2(Azaguanine)(NB)}$ |
|---|---|---|---|---|
| uracil | 4.26 ± 0.03 | 4.23 ± 0.02 | 4.37 ± 0.02 | 4.33 ± 0.01 |
| dihydrouracil | 3.80 ± 0.01 | 4.26 ± 0.03 | 4.65 ± 0.01 | 4.34 ± 0.03 |
| 5-aminouracil | 4.20 ± 0.01 | 4.24 ± 0.01 | 4.37 ± 0.03 | 4.29 ± 0.02 |

[a] ± refers to three times standard deviation (3s).

**Table 13. Formation Constants for Ln(III) + Zwitterionic Buffer (Z) (1:1) Binary Complexes at 25.0 ± 0.1 °C and $I$ = 0.1 mol·dm$^{-3}$ $KNO_3$[a]**

| zwitterionic buffer (Z) | $\log K^{Gd(III)}_{Gd(III)(Z)}$ | $\log K^{Pr(III)}_{Pr(III)(Z)}$ | $\log K^{Dy(III)}_{Dy(III)(Z)}$ | $\log K^{Eu(III)}_{Eu(III)(Z)}$ |
|---|---|---|---|---|
| ACES | 3.56 ± 0.02 | 4.26 ± 0.01 | 4.18 ± 0.02 | 4.27 ± 0.02 |
| CAPS | 3.68 ± 0.02 | 4.13 ± 0.02 | 4.16 ± 0.01 | 4.28 ± 0.03 |
| CAPSO | 2.74 ± 0.02 | 3.91 ± 0.03 | 4.07 ± 0.02 | 3.75 ± 0.01 |
| EPPS | 3.11 ± 0.03 | 4.18 ± 0.03 | 4.18 ± 0.01 | 4.26 ± 0.02 |
| MES | 3.84 ± 0.02 | 4.26 ± 0.01 | 4.19 ± 0.02 | 4.27 ± 0.03 |
| MOPSO | 3.27 ± 0.02 | 4.18 ± 0.02 | 4.09 ± 0.03 | 4.24 ± 0.01 |
| PIPES | 3.57 ± 0.02 | 4.11 ± 0.01 | 4.03 ± 0.02 | 4.22 ± 0.03 |
| TAPS | 3.30 ± 0.02 | 4.16 ± 0.01 | 4.09 ± 0.01 | 3.99 ± 0.02 |
| TES | 3.17 ± 0.03 | 4.12 ± 0.03 | 4.02 ± 0.02 | 4.21 ± 0.03 |
| ADA | 2.66 ± 0.02 | 1.67 ± 0.02 | 3.53 ± 0.03 | 3.81 ± 0.01 |
| AMPSO | 2.71 ± 0.03 | 3.97 ± 0.02 | 4.12 ± 0.02 | 4.22 ± 0.02 |

[a] ± refers to standard deviation (3s).

The α-phosphate group nucleotide monophosphates is close to the nucleotide residue, and its basicity properties are therefore somewhat affected by this residue. This contrasts with the situation for the nucleoside 5′-phosphates, where the nucleobase moiety does not affected the basicity of the γ-phosphate group due to the large distance between these residues.

The presence of O-6 in the inosine and guanosine residues is evidently crucial for the observation of a somewhat increased complex stability. The factors affecting the binding of metal ion to nucleic acid bases include the affinity of the bases for the metal ion, the nature of the metal ion, the pH of the solution, and the length and structure (single-stranded or duplex) of the polynucleotide. The nature of the metal ion plays an important role in nucleic acid−metal ion interactions. Generally, three groups of metal ions have been distinguished with respect to their binding preferences in interactions with nucleic acids:[32−35] (1) ions preferring oxygen donors, that is, alkali and alkaline earth metal ions, lanthanides, Cr(III), and Fe(III); (2) ions favoring mixed oxygen and nitrogen donors, that is, Mn(II), Fe(II), Zn(II), Co(II), Cd(II), Ni(II), and Cu(II); and (3) ions favoring nitrogen donors, that is, Ag(I), Pd(II), Pt(II), and Hg(II).

Taking into consideration the factors which affect metal nucleotide or nucleobase interactions, one can account for the trend observed for the stability constants of the different ternary complexes including lanthanide metal ions Eu(III), Gd(III), Dy(III), and Pr(III), amino acids, nucleobases, or nucleotides under investigation in the present work. Via the formation of mixed-ligand complexes, certain ligand−ligand associations and interactions may be favored, and thus distinct structures may be created in a way that involves only small changes from an energetic point of view.

**Ternary Complexes of the Type Lanthanide(III)−Zwitterionic Buffer−Nucleobase.** Potentiometric equilibrium measurements for the interaction of nucleobases uracil, 5-aminouracil, adenine, thymine, and dihydrouracil and lanthanide metal ions Eu(III), Pr(III), Gd(III), or Dy(III) with zwitterionic buffers, ACES, CAPS, CAPSO, EPPS, MES, MOPSO, PIPES, TAPS, TES, ADA, and AMPSO have been carried out in aqueous medium.

The formation of various 1:1:1 or 2:1:1 (metal ion/zwitterionic buffer/nucleobase) ternary complex species is inferred from the potentiometric pH titration curves.

**Table 14. Formation Constants for Gd(III) + Zwitterionic Buffer (Z) + Nucleobase (NB) 1:1:1 Ternary Complexes at 25.0 ± 0.1 °C and $I$ = 0.1 mol·dm$^{-3}$ $KNO_3$[a]**

| zwitterionic buffer (Z) | $\log K^{Gd(III)}_{Gd(III)(Uracil)(Z)}$ | $\log K^{Gd(III)}_{Gd(III)(5\text{-}Aminouracil)(Z)}$ | $\log K^{Gd(III)}_{Gd(III)(Dihydrouracil)(Z)}$ | $\log K^{Gd(III)}_{Gd(III)(Adenine)(Z)}$ | $\log K^{Gd(III)}_{Gd(III)(Thymine)(Z)}$ |
|---|---|---|---|---|---|
| ACES | 5.40 ± 0.02[b] | 5.69 ± 0.01[b] | 10.25 ± 0.01[c] | 11.32 ± 0.01[c] | 6.16 ± 0.01[b] |
| | | | | 4.29 ± 0.01[b] | |
| CAPS | 8.20 ± 0.03[c] | 10.23 ± 0.02[c] | 11.13 ± 0.01[c] | 11.20 ± 0.01[c] | 5.73 ± 0.01[b] |
| | 4.46 ± 0.03[b] | | | | |
| CAPSO | 8.01 ± 0.03[c] | 9.10 ± 0.01[c] | 8.53 ± 0.03[c] | 10.20 ± 0.03[c] | 8.54 ± 0.03[c] |
| | | | | 2.54 ± 0.02[b] | 3.60 ± 0.03[b] |
| EPPS | 5.08 ± 0.02[b] | 4.49 ± 0.01[b] | 10.74 ± 0.02[c] | 9.31 ± 0.01[c] | 5.79 ± 0.02[b] |
| | | | | 4.38 ± 0.01[b] | |
| MES | 6.76 ± 0.02[c] | 10.21 ± 0.02[c] | 9.56 ± 0.02[c] | 10.03 ± 0.02[c] | 9.44 ± 0.03[c] |
| | | | | | 4.29 ± 0.01[b] |
| MOPSO | 4.96 ± 0.03[b] | 4.28 ± 0.02[b] | 7.41 ± 0.02[b] | 4.19 ± 0.01[b] | 5.09 ± 0.03[b] |
| PIPES | 6.76 ± 0.03[c] | 7.31 ± 0.02[c] | 8.78 ± 0.01[c] | 9.59 ± 0.02[c] | 9.57 ± 0.02[c] |
| | | | | 4.07 ± 0.02[b] | |
| TAPS | 4.97 ± 0.02[b] | 8.75 ± 0.01[c] | 11.45 ± 0.02[c] | 10.24 ± 0.01[c] | 11.40 ± 0.02[c] |
| | | 4.45 ± 0.01[b] | | | 4.43 ± 0.01[b] |
| TES | 4.24 ± 0.03[b] | 7.75 ± 0.02[c] | 6.26 ± 0.01[b] | 9.28 ± 0.01[c] | 4.72 ± 0.03[b] |
| | | 5.01 ± 0.02[b] | | 4.01 ± 0.01[b] | |
| ADA | 7.17 ± 0.01[c] | 21.97 ± 0.01[c] | 8.76 ± 0.02[c] | 9.29 ± 0.02[c] | - |
| AMPSO | 8.46 ± 0.01[c] | 8.25 ± 0.03[c] | 9.21 ± 0.03[c] | 6.80 ± 0.02[c] | 8.78 ± 0.02[c] |
| | 3.96 ± 0.01[b] | 5.04 ± 0.01[b] | | 3.98 ± 0.02[b] | |

[a] ± refers to three times standard deviation (3s). [b] log formation constant of normal ternary complex. [c] log formation constant of protonated complex.

**Table 15. Formation Constants for Pr (III) + Zwitterionic Buffer (Z) + Nucleobase (NB) 1:1:1 Ternary Complexes at 25.0 ± 0.1 °C and $I$ = 0.1 mol·dm$^{-3}$ $KNO_3$[a]**

| zwitterionic buffer (Z) | $\log K^{Pr(III)}_{Pr(III)(Uracil)(Z)}$ | $\log K^{Pr(III)}_{Pr(III)(5\text{-}Aminouracil)(Z)}$ | $\log K^{Pr(III)}_{Pr(III)(Dihydrouracil)(Z)}$ | $\log K^{Pr(III)}_{Pr(III)(Adenine)(Z)}$ | $\log K^{Pr(III)}_{Pr(III)(Thymine)(Z)}$ |
|---|---|---|---|---|---|
| ACES | 9.84 ± 0.01[c] | 5.57 ± 0.03[b] | 7.78 ± 0.03[b] | 10.39 ± 0.03[c] | 6.09 ± 0.03[b] |
| CAPS | 5.88 ± 0.01[b] | 12.64 ± 0.01[c] | 12.32 ± 0.03[c] | 4.09 ± 0.03[b] | 5.67 ± 0.03[b] |
| CAPSO | 9.66 ± 0.02[c] | 8.62 ± 0.03[c] | 9.96 ± 0.01[c] | 15.59 ± 0.01[d] | 8.95 ± 0.01[c] |
| | | | | 12.72 ± 0.01[c] | |
| EPPS | 5.08 ± 0.02[b] | 12.52 ± 0.03[c] | 10.35 ± 0.01[c] | 11.28 ± 0.01[c] | 9.77 ± 0.03[c] |
| | | 4.96 ± 0.03[b] | | | |
| MES | 5.66 ± 0.01[b] | 5.36 ± 0.03[b] | 10.27 ± 0.03[c] | 12.71 ± 0.01[c] | 13.29 ± 0.01[c] |
| MOPSO | 8.81 ± 0.01[c] | 10.31 ± 0.01[c] | 9.53 ± 0.02[c] | 17.11 ± 0.02[d] | 14.91 ± 0.01[c] |
| | 5.11 ± 0.01[b] | | | 10.67 ± 0.01[c] | |
| PIPES | 10.02 ± 0.01[c] | 14.12 ± 0.02[c] | 12.51 ± 0.02[c] | 17.11 ± 0.02[d] | 4.69 ± 0.02[b] |
| | | | 6.58 ± 0.02[b] | 9.47 ± 0.01[c] | |
| TAPS | 11.30 ± 0.01[c] | 12.60 ± 0.02[c] | 7.64 ± 0.02[b] | 12.72 ± 0.02[c] | 5.45 ± 0.01[b] |
| | 5.01 ± 0.01[b] | 4.92 ± 0.02[b] | | | |
| TES | 8.57 ± 0.02[c] | 8.70 ± 0.01[c] | 8.59 ± 0.01[c] | 13.98 ± 0.02[d] | 11.20 ± 0.01[c] |
| | | 4.75 ± 0.02[b] | | 9.92 ± 0.01[c] | |
| ADA | 11.50 ± 0.02[c] | 9.89 ± 0.02[c] | 19.78 ± 0.02[c] | - | 9.23 ± 0.01[c] |
| AMPSO | - | 11.51 ± 0.02[c] | 12.45 ± 0.02[c] | 12.86 ± 0.01[c] | 13.45 ± 0.01[c] |
| | | | | 3.92 ± 0.01[b] | 4.53 ± 0.01[b] |

[a] ± refers to three times standard deviation (3s). [b] log formation constant of normal ternary complex. [c] log formation constant of protonated complex. [d] log formation constant of diprotonated complex.

Furthermore the formation constant values of the different 1:1 or 2:1 Ln(III)−nucleobases or Ln(III)−zwitterionic buffers have been determined under identical conditions.

All of the initial estimates of the formation constants of the different binary and ternary complexes formed in the present investigation have been refined using SUPERQUAD[23] computer program. During this refinement the overall complexation reaction involving protonation is

$$pM + qNB + rZ + sH \rightleftharpoons M_p(NB)_q(Z)_r(H)_s$$

$$\beta_{pqrs} = \frac{M_p(NB)_q(Z)_r(H)_s}{[M]^p[NB]^q[Z]^r[H]^s} \quad (4)$$


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**Table 16. Formation Constants for Dy(III) + Zwitterionic Buffer (Z) + Nucleobase (NB) 1:1:1 Ternary Complexes at 25.0 ± 0.1 °C and $I$ = 0.1 mol·dm$^{-3}$ $KNO_3$[a]**

| zwitterionic buffer (Z) | log $K^{Dy(III)}_{Dy(III)(Uracil)(Z)}$ | log $K^{Dy(III)}_{Dy(III)(Aminouracil)(Z)}$ | log $K^{Dy(III)}_{Dy(III)(Dihydrouracil)(Z)}$ | log $K^{Dy(III)}_{Dy(III)(Adenine)(Z)}$ | log $K^{Dy(III)}_{Dy(III)(Thymine)(Z)}$ |
|---|---|---|---|---|---|
| ACES | 4.39 ± 0.01[b] | 11.30 ± 0.02[c] | 4.40 ± 0.02[b] | 11.43 ± 0.02[c] | 11.44 ± 0.02[c] |
| | | 4.38 ± 0.02[b] | | 4.40 ± 0.02[b] | |
| CAPS | 11.86 ± 0.01[c] | 10.19 ± 0.02[c] | 13.59 ± 0.02[c] | 5.43 ± 0.02[b] | 6.90 ± 0.01[b] |
| | 6.38 ± 0.02[b] | 6.29 ± 0.02[b] | 8.28 ± 0.02[b] | | |
| CAPSO | 4.54 ± 0.01[b] | 9.65 ± 0.02[c] | 11.22 ± 0.01[c] | 4.16 ± 0.02[b] | 9.72 ± 0.01[c] |
| | | 4.94 ± 0.02[b] | | | |
| EPPS | 9.29 ± 0.01[c] | 8.57 ± 0.02[c] | 11.55 ± 0.01[c] | 8.10 ± 0.02[c] | 9.69 ± 0.02[c] |
| | | 4.53 ± 0.02[b] | | 4.46 ± 0.01[b] | |
| MES | 9.45 ± 0.01[c] | 8.93 ± 0.02[c] | 4.31 ± 0.01[b] | 11.04 ± 0.01[c] | 9.79 ± 0.02[c] |
| | | 4.31 ± 0.02[b] | | | 4.31 ± 0.02[b] |
| MOPSO | 7.85 ± 0.01[c] | 5.99 ± 0.01[b] | 12.11 ± 0.01[c] | 9.38 ± 0.01[c] | 7.88 ± 0.01[c] |
| | | | 4.29 ± 0.01[b] | 4.33 ± 0.01[b] | 6.35 ± 0.01[b] |
| PIPES | 4.29 ± 0.02[b] | 12.75 ± 0.02[c] | 13.09 ± 0.02[c] | 4.29 ± 0.02[b] | 8.60 ± 0.02[c] |
| | | 4.24 ± 0.02[b] | | | |
| TAPS | 10.19 ± 0.02[c] | 12.87 ± 0.02[c] | 4.85 ± 0.02[b] | 4.29 ± 0.02[b] | 11.05 ± 0.03[c] |
| | 4.59 ± 0.02[b] | 4.60 ± 0.02[b] | | | 6.16 ± 0.03[b] |
| TES | 5.64 ± 0.02[b] | 17.01 ± 0.03[d] | 11.24 ± 0.03[c] | 11.31 ± 0.03[c] | 14.70 ± 0.02[d] |
| | | 10.29 ± 0.03[c] | | 4.28 ± 0.02[b] | 8.86 ± 0.02[c] |
| ADA | 9.64 ± 0.030[c] | 11.28 ± 0.02[c] | 12.29 ± 0.02[c] | 10.39 ± 0.02[c] | 11.49 ± 0.01[c] |
| | 3.59 ± 0.02[b] | | | | |
| AMPSO | | 5.36 ± 0.01[b] | - | 4.22 ± 0.01[b] | 10.01 ± 0.01[c] |
| | 4.23 ± 0.01[b] | | | | |

[a] ± refers to three times standard deviation (3s). [b] log formation constant of normal ternary complex. [c] log formation constant of protonated complex. [d] log formation constant of diprotonated complex.

**Table 17. Formation Constants for Eu(III) + Zwitterionic Buffer (Z) + Nucleobase (NB) 1:1:1 Ternary Complexes at 25.0 ± 0.1 °C and $I$ = 0.1 mol·dm$^{-3}$ $KNO_3$[a]**

| zwitterionic buffer (Z) | log $K^{Eu(III)}_{Eu(III)(Uracil)(Z)}$ | log $K^{Eu(III)}_{Eu(III)(5\text{-}Aminouracil)(Z)}$ | log $K^{Eu(III)}_{Eu(III)(Dihydrouracil)(Z)}$ | log $K^{Eu(III)}_{Eu(III)(Adenine)(Z)}$ | log $K^{Eu(III)}_{Eu(III)(Thymine)(Z)}$ |
|---|---|---|---|---|---|
| ACES | 4.38 ± 0.03[b] | 9.62 ± 0.02[c] | 10.07 ± 0.02[c] | 9.28 ± 0.01[c] | 4.35 ± 0.01[b] |
| | | 4.27 ± 0.02[b] | | | |
| CAPS | 6.58 ± 0.03[b] | - | - | 6.57 ± 0.01[b] | 6.40 ± 0.01[b] |
| CAPSO | 8.32 ± 0.03[c] | 9.92 ± 0.02[c] | 9.64 ± 0.02[c] | 9.47 ± 0.02[c] | 8.75 ± 0.02[c] |
| EPPS | 4.82 ± 0.03[b] | 9.80 ± 0.02[c] | 11.74 ± 0.02[c] | 7.31 ± 0.02[c] | 5.79 ± 0.02[b] |
| | | | | 4.38 ± 0.02[b] | |
| MES | 11.50 ± 0.03[c] | 8.64 ± 0.02[c] | 9.56 ± 0.02[c] | 4.32 ± 0.02[b] | 6.43 ± 0.02[b] |
| | 4.27 ± 0.03[b] | 4.27 ± 0.03[b] | | | |
| MOPSO | 7.08 ± 0.02[c] | 4.31 ± 0.03[b] | - | 12.39 ± 0.02[d] | 11.56 ± 0.02[c] |
| | 5.74 ± 0.02[b] | | | | 5.85 ± 0.02[b] |
| PIPES | 7.91 ± 0.02[c] | 7.58 ± 0.03[c] | 7.05 ± 0.02[c] | 4.26 ± 0.02[b] | 10.49 ± 0.02[c] |
| | 5.31 ± 0.02[b] | | | | |
| TAPS | 4.79 ± 0.02[b] | 4.90 ± 0.02[b] | 4.66 ± 0.03[b] | 4.30 ± 0.02[b] | 4.68 ± 0.02[b] |
| TES | 11.73 ± 0.02[c] | 7.96 ± 0.02[c] | - | 11.82 ± 0.03[c] | 12.84 ± 0.02[c] |
| | 5.39 ± 0.02[b] | | | 4.21 ± 0.03[b] | 5.52 ± 0.02[b] |
| ADA | 12.09 ± 0.02[c] | 9.67 ± 0.02[c] | 9.99 ± 0.02[c] | - | |
| AMPSO | 10.08 ± 0.02[c] | 7.71 ± 0.02[c] | 8.82 ± 0.02[c] | 11.59 ± 0.02[d] | 10.04 ± 0.03[c] |
| | 5.74 ± 0.02[b] | | | | 5.32 ± 0.03[b] |

[a] ± refers to three times standard deviation (3s). [b] log formation constant of normal ternary complex. [c] log formation constant of protonated complex. [d] log formation constant of diprotonated complex.

in which Z = zwitterionic buffers ACES, CAPS, CAPSO, EPPS, MES, MOPSO, PIPES, TAPS, TES, ADA, and AMPSO, NB = nucleobases, and M = Eu(III), Pr(III), Gd(III), and Dy(III).

The formation constants of all binary and ternary complexes studied are given in Tables 13 to 22. To the author's knowledge, no data for the ternary complex of the secondary ligand


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**Table 18. Formation Constants for Ln(III) + Zwitterionic Buffer (Z) 2:1:1 Dimeric Ternary Complexes at 25.0 ± 0.1 °C and $I$ = 0.1 mol·dm$^{-3}$ $KNO_3$[a]**

| zwitterionic buffer (Z) | log $K^{Gd(III)(Z)}_{Gd(III)_2(Z)}$ | log $K^{Pr(III)(Z)}_{Pr(III)_2(Z)}$ | log $K^{Dy(III)(Z)}_{Dy(III)_2(Z)}$ | log $K^{Eu(III)(Z)}_{Eu(III)_2(Z)}$ |
|---|---|---|---|---|
| ACES | 4.26 ± 0.02 | 4.28 ± 0.03 | 4.30 ± 0.03 | 4.29 ± 0.02 |
| CAPS | 4.29 ± 0.02 | 4.27 ± 0.03 | 4.51 ± 0.03 | 4.31 ± 0.02 |
| CAPSO | 3.42 ± 0.02 | 4.24 ± 0.03 | 4.32 ± 0.03 | 4.26 ± 0.03 |
| EPPS | 4.21 ± 0.02 | 4.27 ± 0.02 | 4.30 ± 0.02 | 4.28 ± 0.03 |
| MES | 4.13 ± 0.02 | 4.28 ± 0.03 | 4.30 ± 0.02 | 4.28 ± 0.03 |
| MOPSO | 4.23 ± 0.01 | 4.26 ± 0.02 | 4.29 ± 0.03 | 4.26 ± 0.03 |
| PIPES | 4.20 ± 0.02 | 4.24 ± 0.01 | 4.29 ± 0.01 | 4.26 ± 0.01 |
| TAPS | 4.15 ± 0.01 | 4.25 ± 0.01 | 4.29 ± 0.02 | 4.27 ± 0.03 |
| TES | 3.90 ± 0.01 | 4.25 ± 0.01 | 4.29 ± 0.02 | 4.27 ± 0.01 |
| ADA | 3.36 ± 0.02 | 3.97 ± 0.03 | 4.29 ± 0.02 | 4.21 ± 0.02 |
| AMPSO | 4.16 ± 0.03 | 4.24 ± 0.02 | 4.30 ± 0.02 | 4.27 ± 0.02 |

[a] ± refers to three times standard deviation (3s).

**Table 19. Formation Constants for Gd(III) + Zwitterionic Buffer (Z) + Nucleobase (NB) 2:1:1 Dimeric Ternary Complexes at 25.0 ± 0.1 °C and $I$ = 0.1 mol·dm$^{-3}$ $KNO_3$[a]**

| zwitterionic buffer (Z) | log $K^{Gd(III)(Uracil)(Z)}_{Gd(III)_2(Uracil)(Z)}$ | log $K^{Gd(III)(5\text{-}Aminouracil)(Z)}_{Gd(III)_2(5\text{-}Aminouracil)(Z)}$ | log $K^{Gd(III)(Dihydrouracil)(Z)}_{Gd(III)_2(Dihydrouracil)(Z)}$ | log $K^{Gd(III)(Adenine)(Z)}_{Gd(III)_2(Adenine)(Z)}$ | log $K^{Gd(III)(Thymine)(Z)}_{Gd(III)_2(Thymine)(Z)}$ |
|---|---|---|---|---|---|
| ACES | 4.29 ± 0.01 | 4.19 ± 0.02 | 4.06 ± 0.02 | 4.01 ± 0.02 | 4.17 ± 0.01 |
| CAPS | 6.05 ± 0.01 | 4.75 ± 0.02 | 4.44 ± 0.02 | 4.44 ± 0.02 | 3.86 ± 0.01 |
| CAPSO | 4.36 ± 0.02 | 3.44 ± 0.02 | - | - | - |
| EPPS | 4.27 ± 0.01 | 4.19 ± 0.03 | 3.63 ± 0.02 | 4.07 ± 0.02 | 4.23 ± 0.03 |
| MES | 4.30 ± 0.03 | 4.27 ± 0.02 | 3.78 ± 0.03 | 3.86 ± 0.02 | 4.25 ± 0.03 |
| MOPSO | 4.21 ± 0.01 | 3.68 ± 0.03 | 3.00 ± 0.02 | 3.61 ± 0.01 | 2.77 ± 0.03 |
| PIPES | 4.24 ± 0.03 | 3.71 ± 0.03 | 3.19 ± 0.01 | 3.64 ± 0.03 | 3.51 ± 0.03 |
| TAPS | 4.28 ± 0.01 | 3.82 ± 0.01 | 4.08 ± 0.02 | 4.01 ± 0.02 | 4.27 ± 0.02 |
| TES | 4.22 ± 0.03 | 4.44 ± 0.03 | - | - | 2.54 ± 0.02 |
| ADA | 3.81 ± 0.01 | - | - | - | - |
| AMPSO | 4.70 ± 0.03 | 3.84 ± 0.01 | 3.33 ± 0.02 | 3.70 ± 0.02 | 3.25 ± 0.02 |

[a] ± refers to three times standard deviation (3s).

**Table 20. Formation Constants for Pr(III) + Zwitterionic Buffer (Z) + Nucleobase (NB) 2:1:1 Dimeric Ternary Complexes at 25.0 ± 0.1 °C and $I$ = 0.1 mol·dm$^{-3}$ $KNO_3$[a]**

| zwitterionic buffer (Z) | log $K^{Pr(III)(Uracil)(Z)}_{Pr(III)_2(Uracil)(Z)}$ | log $K^{Pr(III)(5\text{-}Aminouracil)(Z)}_{Pr(III)_2(5\text{-}Aminouracil)(Z)}$ | log $K^{Pr(III)(Dihydrouracil)(Z)}_{Pr(III)_2(Dihydrouracil)(Z)}$ | log $K^{Pr(III)(Adenine)(Z)}_{Pr(III)_2(Adenine)(Z)}$ | log $K^{Pr(III)(Thymine)(Z)}_{Pr(III)_2(Thymine)(Z)}$ |
|---|---|---|---|---|---|
| ACES | 4.25 ± 0.03 | 4.23 ± 0.02 | 4.40 ± 0.02 | 4.25 ± 0.02 | 4.25 ± 0.02 |
| CAPS | 4.17 ± 0.03 | 5.76 ± 0.01 | 7.23 ± 0.03 | 4.21 ± 0.01 | 4.20 ± 0.03 |
| CAPSO | 4.85 ± 0.02 | 4.52 ± 0.02 | 7.04 ± 0.01 | 4.81 ± 0.01 | 4.76 ± 0.01 |
| EPPS | 4.23 ± 0.02 | 5.02 ± 0.02 | 4.38 ± 0.03 | 4.33 ± 0.02 | 4.31 ± 0.03 |
| MES | 4.22 ± 0.03 | 4.24 ± 0.01 | 4.25 ± 0.02 | 4.23 ± 0.02 | 4.25 ± 0.03 |
| MOPSO | 4.85 ± 0.01 | 4.66 ± 0.01 | 7.17 ± 0.02 | 4.15 ± 0.02 | 4.18 ± 0.01 |
| PIPES | 4.77 ± 0.01 | 4.83 ± 0.01 | 6.97 ± 0.02 | 4.14 ± 0.03 | 4.16 ± 0.02 |
| TAPS | 4.95 ± 0.03 | 4.78 ± 0.01 | 4.27 ± 0.02 | 4.31 ± 0.01 | 4.22 ± 0.02 |
| TES | 4.80 ± 0.01 | 4.71 ± 0.01 | 4.22 ± 0.03 | 4.17 ± 0.01 | 4.25 ± 0.02 |
| ADA | 3.76 ± 0.03 | 4.00 ± 0.03 | 5.54 ± 0.02 | 3.36 ± 0.01 | 3.75 ± 0.02 |
| AMPSO | 4.68 ± 0.01 | 4.62 ± 0.01 | 6.85 ± 0.02 | 4.12 ± 0.02 | 4.87 ± 0.02 |

[a] ± refers to three times standard deviation (3s).

zwitterionic buffer with the nucleobases under study are available in the literature for comparison.

The acidity constants of nucleobases determined at 25 °C of uracil ($pK_{a2}$ = 9.30 ± 0.02), adenine ($pK_{a2}$ = 4.18 ± 0.02), thymine ($pK_{a2}$ = 9.70 ± 0.02), dihydrouracil ($pK_{a2}$ = 11.5 ± 0.02), and 5-aminouracil ($pK_{a2}$ = 9.16 ± 0.02) show some differences from those reported in literature[24] which may attributed to the high accuracy of the measurements carried out in our present work. The acidity constants of zwitterionic buffers ACES ($pK_{a2}$ = 6.89 ± 0.02), AMPSO ($pK_{a2}$ = 8.77 ± 0.02), CAPS ($pK_{a2}$ = 10.24 ± 0.02), CAPSO ($pK_{a2}$ = 9.60 ± 0.02), EPPS ($pK_{a2}$ = 7.99 ± 0.02), MES ($pK_{a2}$ = 6.19 ± 0.02),

**Table 21. Formation Constants for Dy(III) + Zwitterionic Buffer (Z) + Nucleobase (NB) 2:1:1 Dimeric Ternary Complexes at 25.0 ± 0.1 °C and $I$ = 0.1 mol·dm$^{-3}$ $KNO_3$[a]**

| zwitterionic buffer (Z) | log $K^{Dy(III)(Uracil)(Z)}_{Dy(III)_2(Uracil)(Z)}$ | log $K^{Dy(III)(5\text{-Aminouracil})(Z)}_{Dy(III)_2(5\text{-Aminouracil})(Z)}$ | log $K^{Dy(III)(Dihydrouracil)(Z)}_{Dy(III)_2(Dihydrouracil)(Z)}$ | log $K^{Dy(III)(Adenine)(Z)}_{Dy(III)_2(Adenine)(Z)}$ | log $K^{Dy(III)(Thymine)(Z)}_{Dy(III)_2(Thymine)(Z)}$ |
|---|---|---|---|---|---|
| ACES | 4.29 ± 0.02 | 4.39 ± 0.03 | 4.29 ± 0.01 | 4.38 ± 0.01 | 4.40 ± 0.02 |
| CAPS | 6.72 ± 0.01 | 6.92 ± 0.02 | 8.22 ± 0.02 | 4.29 ± 0.02 | 4.36 ± 0.02 |
| CAPSO | 4.28 ± 0.02 | 5.61 ± 0.03 | 8.32 ± 0.02 | 4.29 ± 0.01 | 6.33 ± 0.02 |
| EPPS | 5.46 ± 0.02 | 4.81 ± 0.02 | 8.18 ± 0.02 | 4.79 ± 0.02 | 4.79 ± 0.02 |
| MES | 4.31 ± 0.02 | 4.31 ± 0.02 | 4.29 ± 0.03 | 4.31 ± 0.01 | 4.31 ± 0.03 |
| MOPSO | 4.33 ± 0.02 | 4.29 ± 0.03 | 8.11 ± 0.02 | 4.34 ± 0.01 | 6.29 ± 0.03 |
| PIPES | 4.28 ± 0.01 | 4.33 ± 0.02 | 8.09 ± 0.02 | 4.29 ± 0.01 | 6.33 ± 0.01 |
| TAPS | 4.83 ± 0.02 | 4.94 ± 0.02 | 4.29 ± 0.02 | 4.29 ± 0.02 | 6.31 ± 0.02 |
| TES | 4.29 ± 0.02 | 4.44 ± 0.01 | 8.04 ± 0.02 | 4.31 ± 0.03 | 6.16 ± 0.01 |
| ADA | 4.75 ± 0.02 | 4.85 ± 0.02 | 7.54 ± 0.02 | 4.28 ± 0.02 | 5.56 ± 0.01 |
| AMPSO | 5.21 ± 0.02 | 4.28 ± 0.01 | 5.33 ± 0.01 | 4.28 ± 0.03 | 6.15 ± 0.01 |

[a] ± refers to three times standard deviation (3s).

**Table 22. Formation Constants for Eu(III) + Zwitterionic Buffer (Z) + Nucleobase (NB) 2:1:1 Dimeric Ternary Complexes at 25.0 ± 0.1 °C and $I$ = 0.1 mol·dm$^{-3}$ $KNO_3$[a]**

| zwitterionic buffer (Z) | log $K^{Eu(III)(Uracil)(Z)}_{Eu(III)_2(Uracil)(Z)}$ | log $K^{Eu(III)(5\text{-Aminouracil})(Z)}_{Eu(III)_2(5\text{-Aminouracil})(Z)}$ | log $K^{Eu(III)(Dihydrouracil)(Z)}_{Eu(III)_2(Dihydrouracil)(Z)}$ | log $K^{Eu(III)(Adenine)(Z)}_{Eu(III)_2(Adenine)(Z)}$ | log $K^{Eu(III)(Thymine)(Z)}_{Eu(III)_2(Thymine)(Z)}$ |
|---|---|---|---|---|---|
| ACES | 4.29 ± 0.01 | 4.29 ± 0.01 | 4.34 ± 0.01 | 4.31 ± 0.02 | 4.29 ± 0.03 |
| CAPS | 4.33 ± 0.03 | 5.81 ± 0.02 | 6.59 ± 0.02 | 4.30 ± 0.01 | 4.30 ± 0.02 |
| CAPSO | 5.76 ± 0.03 | 4.75 ± 0.02 | 7.90 ± 0.01 | 4.29 ± 0.03 | 5.94 ± 0.02 |
| EPPS | 4.29 ± 0.01 | 5.17 ± 0.03 | 4.28 ± 0.02 | 4.28 ± 0.02 | 4.29 ± 0.02 |
| MES | 4.32 ± 0.03 | 4.25 ± 0.02 | 8.02 ± 0.03 | 4.29 ± 0.02 | 4.32 ± 0.02 |
| MOPSO | 5.83 ± 0.01 | 4.28 ± 0.03 | 4.31 ± 0.02 | 4.07 ± 0.02 | 6.07 ± 0.02 |
| PIPES | 5.83 ± 0.01 | 4.85 ± 0.01 | 7.78 ± 0.01 | 4.28 ± 0.01 | 6.09 ± 0.02 |
| TAPS | 4.29 ± 0.03 | 4.22 ± 0.03 | 4.28 ± 0.03 | 4.28 ± 0.03 | 4.28 ± 0.03 |
| TES | 5.85 ± 0.03 | 5.10 ± 0.02 | 4.44 ± 0.02 | 4.30 ± 0.01 | 6.18 ± 0.02 |
| ADA | 5.17 ± 0.02 | 4.31 ± 0.03 | 6.74 ± 0.02 | - | 5.35 ± 0.03 |
| AMPSO | 5.70 ± 0.03 | 4.81 ± 0.02 | 7.68 ± 0.02 | 4.87 ± 0.01 | 5.90 ± 0.03 |

[a] ± refers to three times standard deviation (3s).

MOPSO ($pK_{a2}$ = 6.83 ± 0.02), PIPES ($pK_{a2}$ = 6.63 ± 0.02), TAPS ($pK_{a2}$ = 8.15 ± 0.02), TES ($pK_{a2}$ = 7.54 ± 0.02), and ADA ($pK_{a2}$ = 6.54 ± 0.02) are in good agreement with those found in the literature.[24]

With respect to the titration curves of the [Ln(III) + Z] binary complex solutions (not shown in text), one may deduce that these complexes begin to form at pH > 6.5 for Gd(III) + ACES, at pH > 6.2 for Eu(III) + ACES, and at pH > 5.9 for Eu(III) + ADA systems. For the titration curves of the ternary [Ln(III) + Z+ NB] systems studied (not shown in text), it was observed that the binary and ternary complexes titration curves are well separated at pH > 9.5 for Gd(III) + ACES + uracil, at pH > 9.8 for Gd(III) + ACES + adenine, at pH > 8.8 forEu(III) + ACES + dihydrouracil, and at pH > 8.9 for Eu(III) + ADA + thymine systems.

The Gibbs energy changes $\Delta G^o$ (kJ·mol$^{-1}$) for formation of the normal or protonated ternary complexes have negative values, which reveals the highly favorable and spontaneous behavior of the formation of these complexes.[36]

We conclude that the most favorable ternary systems include Gd(III)−AMPSO−uracil, Gd(III)−CAPS−5-aminouracil, Gd(III)−CAPSO−uracil, Gd(III)−CAPS−adenine, Pr(III)−ACES−adenine, Pr(III)−CAPSO−adenine, Pr(III)−CAPS−dihydrouracil, Eu(III)−TES−thymine, and Eu(III)−ADA−uracil based on the negative values of their Gibbs energy changes, $\Delta G^o$.

Taking into consideration the factors affect metal−nucleobase interactions, which include binding conditions such as pH, temperature, and metal ion concentrations as well as factors associated with the metal ion chemistry, one can account for the trend observed for the stability constants of the different ternary complexes of the type Ln(III) + NB + Z.

Great reservation should be exercised in employing the biologically important zwitterionic buffer ligands in aqueous solutions in systems containing Eu(III), Pr(III), Gd(III), or Dy(III) ions and nucleobases uracil, 5-aminouracil, adenine, thymine, and dihydrouracil. The likelihood for the formation of ternary complexes is also rather high, as demonstrated in the present study with uracil, 5-aminouracil, adenine, thymine, and dihydrouracil; this will affect the properties of these nucleobases in various ways when they are used as substrates. The study of the systems in the present investigation may lead to guidelines for the synthesis of possible antitumor drugs.

The weaker binding of the CAPSate anion to the binary Gd(III) + uracil complex as compared with that of the ADAate

was observed. The effect from the poorer structural matching between the secondary ligands and the Ln(III) + nucleobase complex prevails over that from the basicity, and the binding of the ADAate anion secondary ligand by Gd(III) + nucleobase complexes is weaker than the bonding between the above-mentioned secondary ligand anions and the same binary Gd(III) + nucleobase complex. This rule held for several ternary systems under investigation as shown in the tables collecting the formation constant values for several normal and protonated ternary complexes formed in solution in this study.

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## REFERENCES

(1) Dunn, D. B.; Smith, J. D. Incorporation of halogenated pyrimidines into the deoxyribonucleic acids of Bacterium coli and its bacteriophages. *Nature* **1954**, *174*, 305.

(2) Jenner, R.; Rosseels, J. Incorporation of 2-thiouracil-S35 in the ribose nucleic acid of tobacco mosaic virus. *Biochem. Biophys. Acta* **1953**, *11*, 438.

(3) Matthews, R. E. F. Thiouracil in tobacco mosaic virus. *Biochem. Biophys. Acta* **1956**, *19*, 559.

(4) Smith, J. D.; Matthews, R. E. F. The metabolism of 8-azapurines. *Biochemistry* **1957**, *66* (2), 323–333.

(5) Smayda, R. Review of Therapeutic Benefits of the Amino Acid Taurine, Gorden Conference on Magnesium in Biological Processes and Medicine-Ventura, CA, 2005.

(6) Branum, M. E.; Que, L., Jr. Double-strand DNA hydrolysis by dilanthanide complexes. *J. Biol. Inorg. Chem.* **1999**, *4*, 593–600.

(7) Roigk, A.; Hettich, R.; Schneider, H. I. Unusual Catalyst Concentration Effects in the Hydrolysis of Phenyl phosphate esters and of DNA: A systematic investigation of the lanthanide series. *Inorg. Chem.* **1998**, *37*, 751–756.

(8) Good, N. E.; et al. Hydrogen Ion Buffers for Biological Research. *Biochemistry* **1966**, *5*, 467.

(9) Good, N. E.; Izawa, S. Hydrogen Ion Buffers Methods. *Enzymology* **1972**, *24*, 53.

(10) Azab, H. A.; Orabi, A. S.; El Deghidy, F. S.; Said, H. Ternary Complexes of La(III), Ce(III), Pr(III) or Er(III) with adenosine 5′-mono, 5′-di, and 5′-triphosphate as primary ligands and some biologically important zwitterionic buffers as secondary ligands. *J. Solution Chem.* **2010**, *3*, 319–334.

(11) Azab, H. A.; Abd El-Gawad, I. I.; Kamel, R. M. Ternary Complexes Formed by the Fluorescent Probe Eu(III)-9-Anthracene Carboxylic Acid with Pyrimidine and Purine Nucleobases. *J. Chem. Eng. Data* **2009**, *54*, 3069–3078.

(12) Azab, H. A.; El-Korashy, S. A.; Anwar, Z. M.; Hussein, B. H. M.; Khairy, G. M. Eu(III)-anthracene-9-carboxylic acid as a responsive luminescent bioprobe and its electroanalytical interactions with N-acetyl amino acids, nucleotides and DNA. *J. Chem. Eng. Data* **2010**, *55*, 3130–3141.

(13) Azab, H. A.; Abo El Nour, K. M.; Sherif, S. Metal Ion Complexes Containing Di-, Tripeptides and biologically important zwitterionic buffers. *J. Chem. Eng. Data* **2007**, *52* (2), 381–390.

(14) Anwar, Z. M.; Azab, H. A.; Sokar, M. Metal ion complexes containing nucleobases and some zwitterionic buffers. *J. Chem. Eng. Data* **2004**, *49* (1), 62–72.

(15) Anwar, Z. M.; Azab, H. A. Ternary complexes formed by trivalent lanthanide ions, nucleotides and biological buffers. *J. Chem. Eng. Data* **2001**, *46*, 613–618.

(16) Burrsson, D. H.; Sigel, H. Significance of binary and ternary copper(II) complexes for the promotion and protection of adenosine 5′-di- and triphosphate toward hydrolysis. *Biochem. Biophys. Acta* **1974**, *45*, 343.

(17) Welcher, F. J. *The Analytical Uses of Ethylene diaminetetraacetic acid*; D. Von Nostrand Co., Inc.: Princeton, NJ, 1965.

(18) Gran, G. Determination of the Equivalence Point in Potentiometric Titration Part II. *Analyst* **1952**, *77*, 661.

(19) Bjerrum, N. Chemical equilibrium between the thiocyanate chromic complexes. *Z. Anorg. Allg. Chem.* **1921**, *119*, 179–201. Bjerrum, N. *Chem. Abstr.* **1922**, *16*, 2276.

(20) Irving, H.; Rossotti, H. S. Methods of computing successive stability constants from experimental formation curves. *J. Chem. Soc.* **1953**, 3397–3405.

(21) Wagner, R.; Von Philipsborn, W. Protonation of amino and hydroxypyrimidines. NMR-spectra and structures of mono and dications. *Helv. Chim. Acta* **1970**, *53*, 299.

(22) Gans, P.; Sabatini, A.; Vacca, A. Superquad: An improved general program for computation of formation constants from potentiometric data. *J. Chem. Soc., Dalton Trans.* **1985**, 1195–1200.

(23) Martell, A. E.; Sillen, L. G. *Stability constants of metal ion complexes*; The Chemical Society: London, 1971.

(24) Smith, R. M.; Martell, A. E.; Chen, Y. Critical Evaluation of Stability Constants for Nucleotide Complexes with Protons and Metal Ions and the Accompanying Enthalpy Changes. *Pure Appl. Chem.* **1991**, *63*, 1015–1080.

(25) Baes, C. F.; Mesmer, R. E. *The Hydrolysis of Cations*; Wiley: New York, 1976.

(26) Sigel, H. Interactions of Metal Ions with Nucleotides and Nucleic Acids and their Constituents. *Chem. Soc. Rev.* **1993**, *22*, 255–267.

(27) Cohn, M.; Hughes, T. R., Jr. Effect of Complexing with Divalent Metal Ions. *J. Biol. Chem.* **1962**, *237*, 176–181.

(28) Schneider, P. W.; Brintzinger, H.; Erlenmeyer, H. Zur Struktur der ATP.-Komplexe zweiwertiger Kationen IV. Koordinative Besetzung des Adeninrings. *Helv. Chim. Acta* **1964**, *47*, 992–1002.

(29) Eichhorn, G. L.; Clark, P.; Becker, E. D. Interactions of Metal Ions with Nucleotides and Deoxyribonucleic acids. *Biochemistry* **1966**, *5*, 245–253.

(30) Sigel, H. $Cu^{2+}$-Adenine-Interaction in The $Cu^{2+}$-Complexes of Adenosin-5′- and Adenosin-3′-monophosphat. *Experientia* **1966**, *22*, 497–499.

(31) Sigel, H.; Massoud, S. S.; Corfù, N. A. Comparison of the Extent of Macrochelate Formation in Complexes of Divalent Metal Ions with Guanosine ($GMP^{2-}$), Inosine ($IMP^{2-}$), and Adenosine 5′-Monophosphate ($AMP^{2-}$). The Crucial Role of N-7 Basicity in Metal Ion-Nucleic Base Recognition. *J. Am. Chem. Soc.* **1994**, *116*, 2958–2971.

(32) Corfù, N. A.; Tribolet, R.; Sigel, H. Comparison of the Self-Association Properties of the 5′-Triphosphates of Inosine (ITP), Guanosine (GTP), and Adenosine (ATP). Further Evidence for Ionic Interactions in the Highly Stable Dimeric $[H_2(ATP)]_2^{4-}$ Stack. *Eur. J. Biochem.* **1990**, *191*, 721–735.

(33) Sigel, H. Interactions of Metal Ions with Nucleotides and Nucleic Acids and their Constituent. *Chem. Soc. Rev.* **1993**, *22*, 255–267.

(34) Martin, R. B.; Mariam, Y. H. In *Metal Ions in Biological Systems, Vol. 8, Nucleotides and Derivatives: Their Ligating Ambivalency*; Sigel, H., Ed.; Marcel Dekker: New York, 1979; p 57ff.

(35) Sabat, M. In *Metal Ions in Biological Systems, Vol. 32, Ternary Metal Ion-Nucleic Acid-Base Protein Complexes*; Sigel, A., Sigel, H., Eds.; Marcel Dekker: New York, 1996; p 526ff.

(36) Arivoli, S.; Thenkuzhali, M. Kinetic, mechanistic, thermodynamic and equilibrium studies on the adsorption of Rhodamine B by acid activated low cost carbon. *E-J. Chem.* **2008**, *5*, 187–200.