Ternary Complexes of Co(II) with Adenosine 5′-Mono-, 5′-Di-, and 5′-Triphosphates as Primary Ligands and Some Biologically Important Zwitterionic Buffers as Secondary Ligands

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Potentiometric measurements have been made at 25.0 ± 0.1 °C and ionic strength I = 0.1 mol dm^{-3} KNO_3 for the interaction of adenosine 5′-mono-, 5′-di-, and 5′-triphosphates (AMP, ADP, and ATP) and Co(II) with biologically important secondary ligand zwitterionic buffers *N*,*N*-bis(2-hydroxyethyl)-2-aminoethanesulfonic acid (BES), *N*-[tris(hydroxymethyl)methyl]-2-aminoethanesulfonic acid (TES), *N*,*N*-bis(2-hydroxyethyl)glycine (Bicine), and *N*-[tris(hydroxymethyl)methyl]-3-aminopropanesulfonic acid (TAPS) in a 1:1:1: ratio and the formation of various 1:1:1 mixed ligand complex species inferred from the potentiometric pH titration curves. Initial estimates of the formation constants of the resulting species and the acid dissociation constants of the resulting species and the acid dissociation constants of AMP, ADP, ATP, and secondary ligands have been refined with the SUPERQUAD computer program. In some Co(II) ternary systems the interligand interactions have been found to be most effective in deciding the stability of the ternary complexes formed in solution. Stabilities of mixed ligand complexes increase in the order AMP < ADP < ATP. The trend in stability constants of the mixed-ligand complexes of the zwitterionic buffer ligands is in the order TAPS > Bicine > TES > BES.

Introduction

The formation of metal ion complexes is among the prominent interactions in nature (*1*–*3*), and zwitterionic buffers are important hydrogen ion buffers in biological systems, while ribonucleotides adenosine 5′-mono, 5′-di-, and 5′-triphosphates (AMP, ADP, and ATP) are important substrates for many enzymic reactions (*4*–*7*). Ternary complexes of transition divalent metal ions with AMP, ADP, and ATP and other secondary ligands have been investigated (*8*). For an improved understanding of the mechanism leading to mixed ligand complexes of the type Co(II) + nucleotide + zwitterionic buffer ligands (Co(II) + NU + L), where nucleotide = AMP, ADP, or ATP and zwitterionic buffer ligands = BES, Bicine, TAPS, or TES, have been investigated by potentiometric pH titrations to determine the stability constants of the complexes formed as these systems mimic many biological reactions (Co(II) ion + buffer + substrate interactions) and also may be considered as models for enzyme + Co(II) ion + substrate complexes.

Experimental Section

Materials and Solutions. Adenosine 5′-monophosphoric acid disodium salt ($C_{10}H_{12}N_5Na_2O_7P{\cdot}H_2O$, $Na_2AMP{\cdot}H_2O$), adenosine 5′-diphosphoric acid disodium salt ($C_{10}H_{13}N_5Na_2O_{10}P_2{\cdot}2H_2O$, $Na_2ADP{\cdot}2H_2O$), and adenosine 5′-triphosphoric acid disodium salt ($C_{10}H_{14}N_5Na_2O_{13}P_3{\cdot}3H_2O$, $Na_2ATP{\cdot}3H_2O$) were purchased from Sigma Chemical Co. and were used without purification. The amount of free phosphates initially present in the nucleotides was determined (*9*). It was found to be 2% for ATP and 3% for ADP and AMP. To account for this and to prepare metal ion nucleotide solutions in a 1:1 molar ratio, we determined, by potentiometric pH titrations, the molar mass of these nucleotides. *N*,*N*-Bis(2-hydroxyethyl)-2-aminoethanesulfonic acid (BES), N-[tris(hydroxymethyl)methyl]-2-aminoethanesulfonic acid (TES), *N*,*N*-bis(2-hydroxyethyl)glycine (Bicine), and *N*-[tris(hydroxymethyl)methyl]-3-aminopropanesulfonic acid (TAPS) were analytical grade (Merck) with a purity of 99% by mass and were further purified according to Perrin (*10*). $Co(NO_3)_2{\cdot}6H_2O$, nitric acid, and NaOH were from Merck p.a. Stock solutions were prepared using distilled, CO_2-free water. The concentration of NaOH used for the titrations was determined by titration with a standard solution of potassium hydrogen phthalate (Merck AG). On the basis of three replicate measurements, the concentration was found to be 0.0318 ± 0.0004 mol dm^{-3}. HNO_3 solutions were prepared and standardized potentiometrically with tris(hydroxymethyl)aminomethane. On the basis of three replicate measurements the concentration was found to be 0.0041 ± 0.0005 mol dm^{-3}. The concentrations of the metal ion stock solutions were determined by titration with ethylenediaminetetraacetic acid (EDTA). The concentration of the metal ion was found to be 0.0010 ± 0.0004 mol dm^{-3}.

Apparatus. Potentiometric pH measurements were made on the solutions in a double-walled glass vessel using a Beckman Model 4500 digital pH meter with a precision of ±0.1 mV. The potentiometric system was connected to a glass electrode (Metrohm 1028) connected to a double junction reference electrode (Orion 9020). The titrant was delivered by an Amel 882 dispenser, readable to 1 μL. The measurement cell was kept at a temperature constant within ±0.10 °C, and a magnetic stirrer was used. Purified nitrogen was bubbled through the solutions during titrations.

Procedure. The test solution was titrated with standard CO_2-free NaOH. The electrodes were calibrated, in both the acidic and alkaline regions, by titrating 0.01 mol dm^{-3} nitric acid with standard sodium hydroxide under the same experimental conditions.

The concentration of free hydrogen ion, C_{H^+}, at each point of the titration is related to the measured emf, $E°$, of the

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cell by the Nernst equation

$$E = E^\circ + Q \log C_{H^+} \quad (1)$$

where E° is a constant which includes the standard potential of the glass electrode and Q is the slope of the glass electrode response. The value of E° for the electrode was determined from a Gran plot derived from a separate titration of nitric acid with standard NaOH solution under the same temperature and medium conditions as for the test solution titration. The results so obtained were analyzed by the nonlinear least-squares computer program ESAB2M (*11*) to refine E° and the autoprotolysis constant of water, K_w. During these calculation the K_w was refined until the best value for Q was obtained. The results obtained indicated the reversible Nernstian response of the glass electrode used.

In order to avoid hydrolysis prior to the potentiometric measurements, a known mass of the nucleotides as solid was added to the reaction vessel just prior to performing the titration. The solutions titrated can be presented according to the following scheme: HNO_3 (a); HNO_3 + nucleotide (b); HNO_3 + nucleotide + Co(II) (c); HNO_3 + zwitterionic buffer ligand (d); HNO_3 + zwitterionic buffer ligand + Co(II) (e); HNO_3 + nucleotide + zwitterionic buffer ligand + Co(II) (f). A constant ionic strength was obtained with 0.1 mol dm^{-3} KNO_3, and the total volume was kept constant at 25 cm^3.

Results and Discussion

To calculate the initial estimates of the stability constants of the ternary complexes of Co(II) with AMP, ADP, ATP, and BES, Bicine, TAPS, or TES, the following equations were used:

$$\mathrm{Co(II)(NU)} + \mathrm{L} \rightleftharpoons \mathrm{Co(II)(NU)(L)} \quad (2)$$

$$K^{\mathrm{Co(II)(NU)}}_{\mathrm{Co(II)(NU)(L)}} = \frac{[\mathrm{Co(II)(NU)(L)}]}{[\mathrm{Co(II)(NU)}][\mathrm{L}]} \quad (3)$$

$$I = 0.1 \text{ mol dm}^{-3} (KNO_3),\ t = 25\ ^\circ\mathrm{C}$$

$$\mathrm{Co(II)} + \mathrm{NU} \rightleftharpoons \mathrm{Co(II)(NU)} \quad (4)$$

$$K^{\mathrm{Co(II)}}_{\mathrm{Co(II)(NU)}} = \frac{[\mathrm{Co(II)(NU)}]}{[\mathrm{Co(II)}][\mathrm{Nu}]} \quad (5)$$

$$\mathrm{Co(II)} + \mathrm{L} \rightleftharpoons \mathrm{Co(II)(L)} \quad (6)$$

$$K^{\mathrm{Co(II)}}_{\mathrm{Co(II)(L)}} = \frac{[\mathrm{Co(II)(L)}]}{[\mathrm{Co(II)}][\mathrm{L}]} \quad (7)$$

L = zwitterionic buffer ligands (BES, Bicine, TAPS, and TES) and NU = nucleotide (AMP, ADP, and ATP). In addition the protonation and complexation reactions of the free phosphate initially present in solutions have been included in the calculations to get better conditional stability constants. The overall stability constant $\beta^{\mathrm{Co(II)}}_{\mathrm{Co(II)(NU)(L)}}$ may be represented by

$$\mathrm{Co(II)} + \mathrm{NU} + \mathrm{L} \rightleftharpoons \mathrm{Co(II)(NU)(L)} \quad (8)$$

$$\beta^{\mathrm{Co(II)}}_{\mathrm{Co(II)(NU)(L)}} = \frac{[\mathrm{Co(II)(NU)(L)}]}{[\mathrm{Co(II)}][\mathrm{NU}][\mathrm{L}]} = K^{\mathrm{Co(II)(NU)}}_{\mathrm{Co(II)(NU)(L)}} K^{\mathrm{Co(II)}}_{\mathrm{Co(II)(NU)}} \quad (9)$$

Formation constants and protonation constants were refined with the SUPERQUAD computer program (*12*). All the calculations were performed on an IBM XT 286 personal computer. The constants were refined by minimizing U, defined by

$$U = \Sigma W_i (E_{obs} - E_{calc})^2 \quad (10)$$

where E_{obs} and E_{calc} refer to the measured potential and that calculated from eq 1. The weighting factor W_i is defined as the reciprocal of the estimated variance of measurement

$$W_i = 1/\sigma^2 = 1/[\sigma_E{}^2 + (\delta E/\delta V)^2 \sigma_V{}^2] \quad (11)$$

where σ_E and σ_V are the estimated variances of the potential and volume readings, respectively. The quality of fit was judged by the values of the sample standard deviation, S, and the goodness of fix, X^2 (Pearson's test). At σ_E = 0.1 mV (0.001 pH error) and σ_V = 0.005 mL, the values of S in different sets of titrations were between 1.0 and 1.8 and X^2 was between 12.0 and 13.0. The scatter of residuals (E_{obs} − E_{calc}) vs pH was reasonably random, without any significant systematic trends, thus indicating a good fit of the experimental data.

At the experimental pH values used in the calculation in this work the interfering effects of hydroxy complexes are negligible . Thus, the secondary ligand, L, combines with the binary 1:1 Co(II)(NU){[Co(II)(AMP)], [Co(II)-

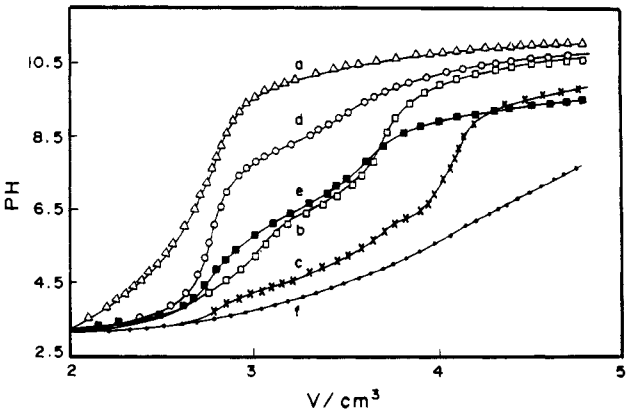

Figure 1. pH against volume of 0.0318 mol dm^{-3} NaOH for the Co(II) + ATP + bicine system at 25 °C and I = 0.1 mol dm^{-3} KNO_3: (a) 0.0041 mol dm^{-3} HNO_3; (b) solution a + 1 × 10^{-3} mol dm^{-3} ATP; (c) solution b + 1 × 10^{-3} mol dm^{-3} Co(II); (d) solution a + 1 × 10^{-3} mol dm^{-3} bicine; (e) solution d + 1 × 10^{-3} mol dm^{-3} Co(II); (f) solution e + 1 × 10^{-3} mol dm^{-3} ATP.

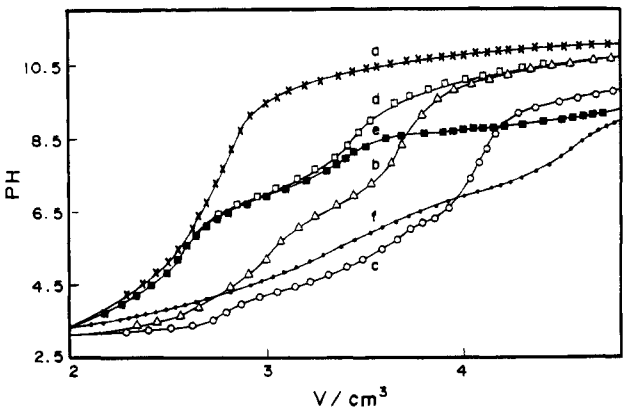

Figure 2. pH against volume of 0.0318 mol dm^{-3} NaOH for the Co(II) + ATP + BES system at 25 °C and I = 0.1 mol dm^{-3} KNO: (a) 0.0041 mol dm^{-3} HNO_3; (b) solution a + 1 × 10^{-3} mol dm^{-3} ATP; (c) solution b + 1 × 10^{-3} mol dm^{-3} Co(II); (d) solution a + 1 × 10^{-3} mol dm^{-3} BES; (e) solution d + 1 × 10^{-3} mol dm^{-3} Co(II); (f) solution e + 1 × 10^{-3} mol dm^{-3} ATP.

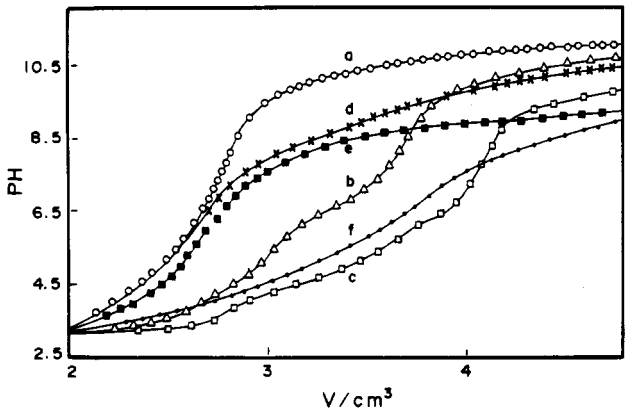

Figure 3. pH against volume of 0.0318 mol dm^{-3} NaOH for the Co(II) + ATP + TAPS system at 25 °C and I = 0.1 mol dm^{-3} KNO_3: (a) 0.0041 mol dm^{-3} HNO_3; (b) solution a + 1 × 10^{-3} mol dm^{-3} ATP; (c) solution b + 1 × 10^{-3} mol dm^{-3} Co(II); (d) solution a + 1 × 10^{-3} mol dm^{-3} TAPS; (e) solution d + 1 × 10^{-3} mol dm^{-3} Co(II); (f) solution e + 1 × 10^{-3} mol dm^{-3} ATP.

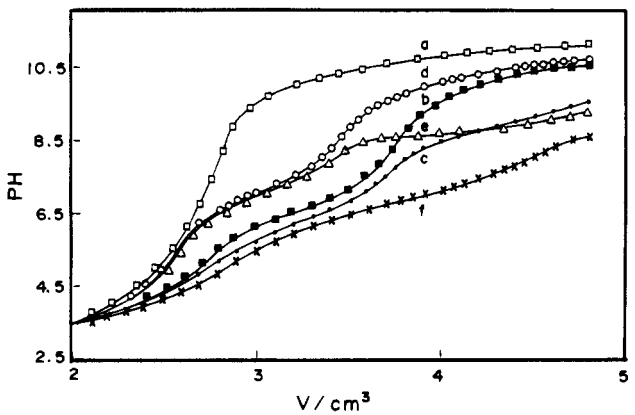

Figure 4. pH against volume of 0.0318 mol dm^{-3} NaOH for the Co(II) + ADP + BES system at 25 °C and I = 0.1 mol dm^{-3} KNO_3: (a) 0.0041 mol dm^{-3} HNO_3; (b) solution a + 1 × 10^{-3} mol dm^{-3} ADP; (c) solution b + 1 × 10^{-3} mol dm^{-3} Co(II); (d) solution a + 1 × 10^{-3} mol dm^{-3} BES; (e) solution d + 1 × 10^{-3} mol dm^{-3} Co(II); (f) solution e + 1 × 10^{-3} mol dm^{-3} ADP.

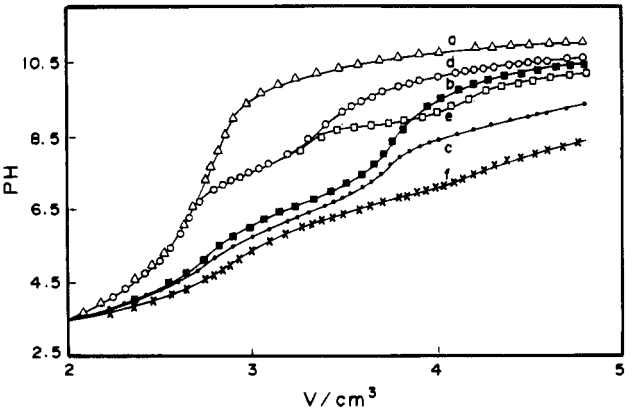

Figure 5. pH against volume of 0.0318 mol dm^{-3} NaOH for the Co(II) + ADP + TES system at 25 °C and I = 0.1 mol dm^{-3} KNO_3: (a) 0.0041 mol dm^{-3} HNO_3; (b) solution a + 1 × 10^{-3} mol dm^{-3} ADP; (c) solution b + 1 × 10^{-3} mol dm^{-3} Co(II); (d) solution a + 1 × 10^{-3} mol dm^{-3} TES; (e) solution d + 1 × 10^{-3} mol dm^{-3} Co(II); (f) solution e + 1 × 10^{-3} mol dm^{-3} ADP.

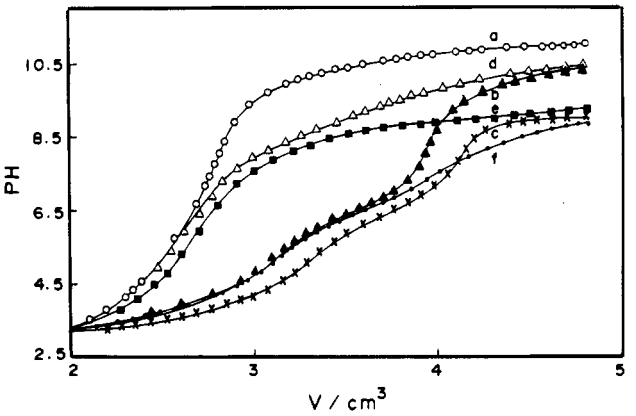

Figure 6. pH against volume of 0.0318 mol dm^{-3} NaOH for the Co(II) + AMP + TAPS system at 25 °C and I = 0.1 mol dm^{-3} KNO_3: (a) 0.0041 mol dm^{-3} HNO_3; (b) solution a + 1 × 10^{-3} mol dm^{-3} ADP; (c) solution b + 1 × 10^{-3} mol dm^{-3} Co(II); (d) solution a + 1 × 10^{-3} mol dm^{-3} TAPS; (e) solution d + 1 × 10^{-3} mol dm^{-3} Co(II); (f) solution e + 1 × 10^{-3} mol dm^{-3} AMP.

$(ADP)^-$], and $[Co(II)(ATP)]^{2-}$} complex in a manner similar to its interaction with aquated metal ions $[Co(H_2O)_6]^{2+}$ in solutions. Thus, the initial estimates of the stability constants of the ternary complexes formed in solution have been determined using the Rossotti and Irving formula (*13*). These values were then refined using the SUPERQUAD computer program (*12*).

The acidity constants determined at 25 °C of BES (pK_a = 7.09 ± 0.02), Bicine (pK_a = 8.29 ± 0.02), TAPS (pK_a = 8.35 ± 0.03), and TES (pK_a = 7.40 ± 0.03) and the stability constants of their binary Co(II) complexes are in good agreement with those found in the literature (*14*, *15*).

The two acid formation constant values for AMP (pK_{a1} = 3.81 ± 0.03, pK_{a2} = 6.24 ± 0.03), ADP (pK_{a1} = 3.94 ± 0.03, pK_{a2} = 6.38 ± 0.04), and ATP (pK_{a1} = 4.05 ± 0.03, pK_{a2} = 6.51 ± 0.03) and the stability constants of their Co(II) complexes were determined from the titration curves, and the results were found to agree well with those reported in the literature (*16*). The plus/minus values refer to statistically determined uncertainties at small 95% confidence intervals of the reported values.

In the case of ADP and ATP the monoprotonated complexes, i.e., Co(HADP) and $Co(HATP)^-$, were taken into consideration. The calculated values of log $K^{Co}_{Co(HADP)}$ = 2.03 and log $K^{Co}_{Co(HATP)^-}$ = 2.64 also agree favorably with the literature (*16*).

It is concluded that the N_1H^+ group is the site of ring proton ionization (*17*) ($pK_a \approx 4$) in adenine and adenosine and presumably in the ribonucleotide derivatives AMP, ADP, and ATP as well. The second proton ionization constant was attributed to the phosphate groups. The sites for proton ionization from the phosphate chain of the adenine nucleotides have been discussed (*18*).

The pK values for primary ionizations of the adenine nucleotides AMP, ADP, and ATP have been estimated as follows: AMP (one primary phosphate hydrogen), 1.0; ADP (two primary phosphate hydrogens), 1.0 and 2.0; ATP (three primary phosphate hydrogens), 1.0, 1.0, and 2.0 (*19*). Given these pK values at the lower pH initial conditions of the experiments described in this work (pH 3–3.4) roughly 10% of the final primary phosphate hydrogen would be un-ionized for ATP and ADP. At lower pH values even more primary phosphate hydrogen would be un-ionized, including the pK = 1.0 phosphate ionizations. Therefore, the net charge on the phosphate chain of ATP and ADP at pH < 3 would be an average value for several differently protonated species. NMR studies of ATP and ADP as a function of pH indicate that the $pK \approx 7$ ionization is from the γ-phosphate in ATP and the β-phosphate group in ADP (*20*). Coordination of Co(II) with the phosphate groups of ribonucleotides has been demonstrated in aqueous solutions for AMP, ADP, and/or ATP by potentiometric

Table 1. Formation Constants for the Binary Co(II) + Nucleotide or Zwitterionic Buffer Ligand Complexes and Those for the Mixed Ligand Complexes Co(II) + Nucleotide + Zwitterionic Buffer Ligand at 25.00 ± 0.10 °C and I = 0.1 mol dm^{-3} KNO_3

ligand	$\log K^{Co(II)}_{Co(II)(NU)}$ or $\log K^{Co(II)}_{Co(II)(LU)}$	$\log K^{Co(II)(AMP)}_{Co(II)(AMP)(L)}$	$\log K^{Co(II)(ADP)}_{Co(II)(ADP)(L)}$	$\log K^{Co(II)(ATP)}_{Co(II)(ATP)(L)}$	$\log \beta^{Co(II)}_{Co(II)(AMP)(L)}$	$\log \beta^{Co(II)}_{Co(II)(ADP)(L)}$	$\log \beta^{Co(II)}_{Co(II)(ATP)(L)}$	$\Delta \log K_1$[a]	$\Delta \log K_2$[a]	$\Delta \log K_3$[a]
AMP	2.61 ± 0.03									
ADP	4.41 ± 0.02									
ATP	5.11 ± 0.02									
BES	3.03 ± 0.01	3.19 ± 0.02	3.80 ± 0.01	4.17 ± 0.03	5.80	8.21	9.28	0.16	0.77	1.14
Bicine	3.51 ± 0.03	3.86 ± 0.01	4.29 ± 0.03	4.52 ± 0.02	6.47	8.70	9.63	0.35	0.78	1.01
TAPS	4.21 ± 0.02	4.15 ± 0.03	4.47 ± 0.02	4.78 ± 0.02	6.76	8.88	9.89	−0.06	0.26	0.57
TES	3.06 ± 0.02	3.52 ± 0.02	4.06 ± 0.02	4.42 ± 0.03	6.13	8.47	9.53	0.46	1.00	1.36

[a] $\Delta \log K_1 = \log K^{Co(II)(AMP)}_{Co(II)(AMP)(L)} - \log K^{Co(II)}_{Co(II)(L)}$, $\Delta \log K_2 = \log K^{Co(II)(ADP)}_{Co(II)(ADP)(L)} - \log K^{Co(II)}_{Co(II)(L)}$, and $\Delta \log K_3 = \log K^{Co(II)(ATP)}_{Co(II)(ATP)(L)} - \log K^{Co(II)}_{Co(II)(L)}$.

(*21*) studies. A Raman spectral study (*22*) of Co(II)–ATP interactions shows the Co(II) to bind the base moiety and to promote intramolecular base–phosphate interaction. Proton NMR data indicate that Co(II) binds the adenine ring of ADP (*23*) and ATP (*23*, *24*). Since the C_8H peak is broadened (*23*), coordination apparently occurs at the N_7 site of ADP and ATP with possible participation from the C_6NH_2 group (*25*). Support for the binding of a metal ion to the base moiety of ATP is found in a proton NMR and kinetic study (*26*). The experimental data were accounted for by assuming that a water molecule forms a bridge between the Co(II) and the N_7 site. The remaining metal coordination sites were phosphate oxygen atoms.

In Figures 1–6 representative sets of experimental titration curves obtained according to the sequence described in the Experimental Section for the different Co(II) + NU + L systems studied are displayed. It is observed that the Co(II) + NU titration curve (c) diverges from the nucleotide curve (b) in the lower pH range (pH ≃ 3.5 for Co(II) + AMP + TAPS and Co(II) + ADP + BES and pH ≃ 3.3 for Co(II) + ATP + Bicine, Co(II) + ATP + BES, and Co(II) + ATP + TAPS systems), denoting the formation of the Co(II) + NU complex.

Generally, the complex titration curves show an inflection after addition of 2 mol of base per 1 mol of the nucleotide (AMP, ADP, or ATP). This indicates that simultaneous dissociation of two protons from AMP while in the case of ADP and ATP the complex species Co(HADP), Co(ADP), Co(HATP)$^-$, and Co(ATP) have been formed in solution. Co(II) + NU is quite stable up to high pH values; i.e., it has no tendency to form hydroxy complexes. With respect to the titration curves of the Co(II) + L binary complex solutions studied, one may deduce that these complexes begin to form at pH > 3.30 for Co(II) + TAPS and Co(II) + Bicine systems and at pH > 7.50 for Co(II) + BES and Co(II) + TES systems. Generally, for all Co(II) + L complexes studied precipitation occurred at pH > 10.5. In all cases no calculations have been performed beyond the precipitation point; hence, the hydroxy species likely to be formed after this point could not be studied.

For the titration curves of the ternary systems studied (Co(II) + NU + L) one observes that the C and F are well separated at a pH > 3.2 for Co(II) + ATP + Bicine and at a pH > 3.5 for Co(II) + ADP + BES and Co(II) + ADP + TES systems. For Co(II) + AMP + TAPS, Co(II) + ATP + BES, and Co(II) + ATP + TAPS systems the separations between C and F occur at pH > 7.5, pH > 6.6, and pH > 7.7, respectively. This behavior reveals that in these pH ranges coordination of the secondary ligand, zwitterionic buffer, and Co(II) + NU starts.

Examination of the different formation constant values listed in Table 1 clearly reveals that the formation constant of the mixed ligand complexes increases in the order AMP < ADP < ATP. Though many studies in solution favored the phosphate group rather than the base as the primary metal binding site, the simultaneous binding of Co(II) ion to the N_7 site of the adenine residue (*27*, *28*) and phosphate may also be reported in the mixed ligand complexes formed in the present work. Thus, the Co(II) bound to the base moiety may promote intramolecular base–phosphate interaction. Thus, the mixed ligands studied may be considered as relatively simple models from which information may be gained about the properties of nucleotides and their base moieties regarding the strength of their interactions with the biologically important zwitterionic buffer ligands (BES, Bicine, TAPS, and TES) and even insight into the factors which influence the strength is thus becoming available as these systems may mimic enzyme–metal ion–substrate complexes. Our investigation confirmed the formation of mixed ligand complexes of the type Co(II) + NU + L (where L = BES, Bicine, TAPS, and TES) in solution; hence, great reservations should be exercised in employing BES, Bicine, TAPS, or TES as buffers in systems containing Co(II) ions and AMP, ADP, or ATP.

With respect to the secondary ligands, the formation constants of the mixed ligand complexes decreases in the following order: TAPS > Bicine > TES > BES. This behavior can be interpreted in terms of the basicities of the secondary ligand zwitterionic buffer used. It is well known that the increase in basicity of a ligand increases the stability of its metal complexes.

$\Delta \log K$ defined by eq 12 is a measure of the stability of the ternary complexes with respect to the binary complexes. $\Delta \log K$ values are positive for some of the inves-

$$\Delta \log K = \log K^{Co(II)(NU)}_{Co(II)(NU)(L)} - \log K^{Co(II)}_{Co(II)(L)} \qquad (12)$$

tigated ternary complexes (Table 1). The higher stability constants of ternary complexes compared with the binary systems may be attributed to the interligand interactions or some cooperativity between the coordinate ligands, possibly H-bond formation. This also may be explained on the basis of the π acceptor qualities of the adenine base. Thus, the π-electron-donating tendency of the Co(II) ion to the antibonding π^* orbitals of heteroaromatic N base, such as adenine base, causes strengthening of the Co(II)–N bond. Due to the π-acceptor qualities of the adenine base (i.e., back-donation from metal to ligand), the d-electron content on the metal decreases, which renders the metal more electrophilic. The interaction of the p-electrons of the phosphate O atoms with the metal will increase to a greater extent and consequently influence the stability of ternary complexes.

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