Ternary Complexes in Solution. Comparison of the Coordination Tendency of Some Biologically Important Zwitterionic Buffers toward the Binary Complexes of Some Transition Metal Ions and Some Amino Acids

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Potentiometric equilibrium measurements have been performed at (25.0 ± 0.1) °C and ionic strength I = 0.1 mol dm^{-3} (KNO_3) for the interaction of glycine (aminoethanoic acid), serine (2-amino-3-hydroxypropanoic acid), methionine (2-amino-4-(methylthio)butanoic acid), aspartic acid (aminobutanedioic acid), glutamic acid (2-aminopropanedioic acid), and histidine (α-amino-1*H*-imidazole-4-propanoic acid) and Cu(II), Co(II), Ni(II), Mn(II), and Zn(II) with the biologically important secondary ligand zwitterionic buffers β-hydroxy-4-morpholinepropanesulfonic acid (MOPSO), 4-morpholinepropanesulfonic acid (MOPS), 3-[bis(2-hydroxyethyl)amino]-2-hydroxy-1-propanesulfonic acid (DIPSO), and 3-[*N*-tris(hydroxymethyl)-methyl)amino]-2-hydroxypropanesulfonic acid (TAPSO) in 1:1:1 and 1:1:2 ratios, and the formation of various 1:1:1 ternary complexes and 1:1:2 quaternary complex species was inferred from the potentiometric pH titration curves. Initial estimates of the formation constants of the resulting species and the acid dissociation constants of the different amino acids and secondary ligands studied have been refined with the SUPERQUAD computer program. The order of stability of the different normal ternary complexes in the systems under investigation in terms of metal ion follows generally the trend Cu(II) > Ni(II) > Co(II) > Zn(II) > Mn(II).

Introduction

For the standardization of pH and control of acidity in the physiological region of pH 7 to 9, Good et al. (1966) and Ferguson et al. (1980) have listed hydrogen buffers which are N-substituted amino acids compatible with common biological media. Organic buffers suitable for use in biochemistry now include β-hydroxy-4-morpholinepropanesulfonic acid (MOPSO), 4-morpholinepropanesulfonic acid (MOPS), 3-[bis(2-hydroxyethyl)amino]-2-hydroxy-1-propanesulfonic acid (DIPSO) and 3-[*N*-tris(hydroxymethyl)methyl)amino]-2-hydroxypropanesulfonic acid (TAPSO).

Zwitterionic *N*-substituted aminopropanesulfonic acids show significant advantages over conventional buffers: insignificant penetration through biological membranes, maximum water solubility, and no enzyme substrate or enzyme inhibition properties. Attention has been focused on the zwitterionic buffer TAPSO, for the isoelectric focusing method in analytical separation of protein over a pH gradient of 4−6. It is well-known that ternary coordination plays an important role in biological processes. Ternary complex formation occurs commonly in biological fluids, as several potential ligands are likely to compete for metal ions in vivo, that is, Cu(II), Co(II), Mn(II), and Zn(II). Ternary complexes of transition divalent metal ions with some amino acids and other secondary ligands have been investigated (Shelke and Jahagirdar, 1979; Ghandour et al., 1989; Mahmoud et al., 1989; Reddy et al., 1981; Chandel and Gupta, 1984; De Robertis et al., 1995).

Metal ion complex formations are among the prominent interactions in nature (Eichhorn, 1973; Sigel, 1973), and the glycine, serine, methionine, aspartic acid, glutamic acid and histidine residues are important and versatile binding sites for protein while the zwitterionic buffers MOPSO, MOPS, DIPSO, and TAPSO are equally important and compatible with most media of physiological and biochemical importance. For an improved understanding of the driving forces leading to mixed ligand complexes in biological systems, ternary complexes of the type M(II)−A−Z, where M(II) = Cu(II), Co(II), Ni(II), Mn(II), or Zn (II), A = glycine, serine, methionine, aspartic acid, glutamic acid, or histidine, and Z = MOPSO, MOPS, DIPSO, or TAPSO, have been investigated to determine the stability constants of the complexes formed, as these systems mimic many biological reactions (enzyme−M(II)−buffer interactions).

Experimental Section

Materials and Solutions. Reagent grade β-hydroxy-4-morpholinepropanesulfonic acid (MOPSO), 4-morpholinepropanesulfonic acid (MOPS), 3-[bis(2-hydroxyethyl)amino]-2-hydroxy-1-propanesulfonic acid (DIPSO), and 3-[*N*-tris(hydroxymethyl)methyl)amino]-2-hydroxypropanesulfonic acid (TAPSO) were from Sigma Chemical Co., St. Louis, MO. Potentiometric pH titrations was used to determine the molecular weight of MOPSO, MOPS, DIPSO, and TAPSO to verify/determine the purity, especially for acidic/basic contaminants; the purity averaged 99.5% for the four compounds, with a standard deviation of 0.05%.

Glycine (aminoethanoic acid), serine (2-amino-3-hydroxypropanoic acid), glutamic acid (2-aminopropanedioic acid), aspartic acid (aminobutanedioic acid), methionine (2-amino-4-(methylthio)butanoic acid), and histidine (α-amino-1*H*-imidazole-4-propanoic acid) were biochemical Merck products. All these substances were potentiometrically assayed and proved sufficiently reliable so that further purification was not needed. Copper nitrate ($Cu(NO_3)_2 \cdot 6H_2O$), nickel nitrate ($Ni(NO_3)_2 \cdot 6H_2O$), cobalt nitrate ($Co(NO_3)_2 \cdot 6H_2O$), manganese nitrate ($Mn(NO_3)_2 \cdot 6H_2O$), zinc nitrate ($Zn(NO_3)_2 \cdot 6H_2O$), nitric acid, and KOH were from Merck p.a. Stock solutions were prepared using distilled, CO_2-free water. The concentration of KOH used for the titrations

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was determined by titration with a standard solution of potassium hydrogen phthalate (Merck AG). On the basis of three replicate measurements, the concentrations were found to be (0.0307 ± 0.00004) and (0.0256 ± 0.00004) 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 (0.0040 ± 0.000005) mol dm^{-3}. The ESAB2M computer program (De Stefano et al., 1987) was used for this refinement.

The concentrations of the metal ion stock solutions were determined by titration with ethylenediaminetetraacetic acid (EDTA). The concentration of the metal ions was found to be (0.0010 ± 0.000004) mol dm^{-3}.

Apparatus. Potentiometric pH measurements were performed on the solutions in a double-walled glass vessel at (25 ± 0.1) °C with a commercial Fisher combined electrode, and a magnetic stirrer was used. A Fisher Accumet pH/ion meter Model 825 MP was used. Purified nitrogen was bubbled through the solutions during titrations.

Procedure. The test solution was titrated with standard CO_2-free KOH. The electrodes were calibrated, in both the acidic and alkaline regions, by titrating 0.01 mol dm^{-3} nitric acid with standard potassium 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 cell by the Nernst equation

$$E = E° + Q \log C_{H^+} \quad (1)$$

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 KOH solution under the same temperature and medium conditions as those for the test solution titration. The results so obtained were analyzed by the nonlinear least-squares computer program ESAB2M (De Stefano et al., 1987) to refine $E°$ and the autoprotolysis constant of water K_W. During these calculations, 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. The solutions titrated can be presented according to the following scheme: HNO_3; HNO_3 + amino acid (a); HNO_3 + amino acid + M(II) (b); HNO_3 + zwitterionic buffer ligand (c); HNO_3 + zwitterionic buffer ligand + M(II) (d); HNO_3 + amino acid + zwitterionic buffer ligand + M(II) (e). A constant ionic strength was obtained with 0.1 mol dm^{-3} KNO_3, and the total volume was kept constant at 50 cm^3.

Results and Discussion

Formation constants for the normal ternary complexes and protonation constants for primary and secondary ligands were refined with the SUPERQUAD computer program (Gans et al., 1985). The same computer program has been used by the author in previous publications (Azab et al., 1993, 1994, 1995). The constants were refined by minimizing U, defined by

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

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 the measurement.

$$W_i = 1/\sigma^2 = 1/[\sigma_E^2 + (\delta E/\delta V)^2 \sigma_V^2] \quad (3)$$

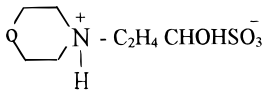
where σ_E and σ_V are the estimated variances of the potential and volume readings, respectively, The quality of the fit was judged by the values of the sample standard deviation S and the goodness of fit X^2 (Pearson's test). At $\sigma_E = 0.1$ mV (0.001 pH error) and $\sigma_V = 0.005$ mL, the values of S in different sets of titrations were between 1.0 and 1.8 and X^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.

At the experimental pH values used in the calculation in this work, the interfering effects of hydroxy complexes are negligible. Thus, the secondary ligand Z combines with the binary 1:1 M(II)−(A) complexes [M(II)−(glycine), M(II)−(serine), M(II)−(methionine), M(II)−(aspartic acid), M(II)−(glutamic acid) and M(II)−(histidine)] in a manner similar to that for its interaction with aquated metal ions in solutions. Thus, the initial estimates of the stability constants of the normal ternary complexes formed in solution have been determined using the Irving and Rossotti formula (Irving and Rossotti, 1953, 1954).

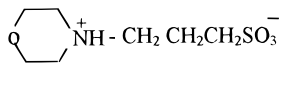
The acidity constants determined at 25 °C of MOPSO ($pK_{a2} = 6.89 \pm 0.02$), MOPS ($pK_{a2} = 7.14 \pm 0.04$), DIPSO ($pK_{a2} = 7.60 \pm 0.03$), and TAPSO ($pK_{a2} = 7.61 \pm 0.02$) are in good agreement with those found in the literature (Sankar and Bates, 1978; Ferguson et al. 1980; Roy et al., 1997). The acid formation constant values for glycine ($pK_{a2} = 9.80 \pm 0.03$), serine ($pK_{a2} = 9.20 \pm 0.03$), methionine ($pK_{a2} = 9.16 \pm 0.04$), aspartic acid ($pK_{a2} = 3.91 \pm 0.03$, $pK_{a3} = 9.74 \pm 0.04$), glutamic acid ($pK_{a2} = 3.98 \pm 0.02$, $pK_{a3} = 9.68 \pm 0.03$), and histidine ($pK_{a2} = 5.96 \pm 0.02$, $pK_{a3} = 9.20 \pm 0.02$) and the stability constants of their Cu(II), Co(II), Ni(II), Mn(II), or Zn(II) complexes were determined from the titration curves, and the results agree fairly well with those reported in the literature (Perrin and Dempsey, 1979; Martin, 1979). The plus/minus values refer to statistically determined uncertainities at small 95% confidence intervals of the reported values.

Initial estimates of the stability constants of different monoprotonated mixed ligand and quaternary complexes formed in solution have been refined with the SUPER QUAD computer program (Gans et al., 1985). Initial estimates of the stability constants of the quaternary complexes have been calculated by the method used by Sinha et al. (1989).

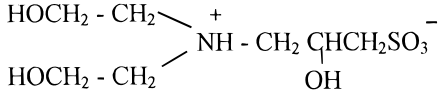
The zwitterionic structures of the ampholytes MOPSO, MOPS, DIPSO, and TAPSO are



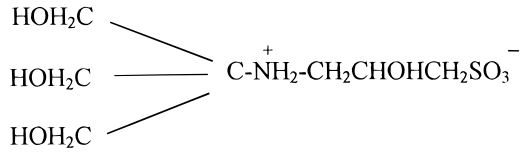
(MOPSO)



(MOPS)



(DIPSO)



(TAPSO)

It is evident that the calculated pK's of MOPSO, MOPS, DIPSO, and TAPSO are lower than that of the parent compound Taurine ($-O_3S(H_2C)_2NH_3^+$), pK_2 = 9.06. This enhancement of acid strength of the NH^+ group in MOPSO, MOPS, DIPSO, and TAPSO is probably due to the steric and inductive effects of the oxygen atoms. The substitution of hydroxyethyl, hydroxymethyl, morpholine, or piperazine groups on the nitrogen atom in Taurine usually lowers the value of pK_2 for the isoelectric dissociation processes.

During the titrations of different M(II)−(A)−(Z) systems it was observed that different 1:1 binary M(II)−amino acid complexes begin to form in the pH range 4.0−6.5 for monocarboxylic amino acids and in the pH range 3.0−4.0 for dicarboxylic amino acids. With respect to the titration curves of the M(II) + Z binary complex solutions, one may deduce that these complexes begin to form at pH > 6.06 for Cu(II) + MOPSO, pH > 5.02 for Cu(II) + TAPSO, pH > 5.41 for Cu(II) + DIPSO, and pH > 3.29 for Co(II) + DIPSO. Generally, for all M(II) + Z 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 (M(II)−A−Z), one observes that b and e are well separated at pH > 8.73 for Cu(II)−glycine−MOPSO, pH > 3.40 for Cu(II)−aspartic acid−MOPSO, pH > 8.30 for Cu(II)−methionine−TAPSO, pH > 6.40 for Zn(II)−methionine−MOPSO, pH > 7.25 for Mn(II)−aspartic acid−TAPSO, pH > 7.40 for Cu(II)−histidine−TAPSO, pH > 7.05 for Cu(II)−glycine−DIPSO, and pH > 8.20 for Co(II)−glycine−DIPSO, respectively. This behavior reveals that in these pH ranges coordination of the secondary ligand, the zwitterionic buffer, and M(II) + A starts.

Examination of the different formation constant values listed in Tables 1−5 clearly reveals that the order of the overall stability of the different normal ternary complexes in the systems under investigation in terms of metal ions follows generally the trend Cu(II) > Ni(II) > Co(II) > Zn(II) > Mn(II) whereas the log $\beta_{M(II)(A)(Z)}$ values of M(II)−serine−MOPS follow the order Cu(II) > Ni(II) > Zn(II) > Mn(II) > Co(II).

To the authors' knowledge, no data for the ternary complexes of the newer buffers MOPSO, MOPS, DIPSO, or TAPSO with glycine, serine, methionine, aspartic acid, glutamic acid, or histidine are available in the literature for comparison.

The observed weaker binding of the TAPSO-ate anion by the binary M(II)−amino acid complexes as compared with that of the MOPSO-ate, MOPS-ate, and DIPSO-ate anions may be attributed to the poorer structural matching between the TAPSO-ate secondary ligand and the M(II)−amino acid complex.

A comparison of the overall stability constants of the M(II)−A−Z ternary systems indicates the higher stabilities of the ternary complexes containing dicarboxylic amino acid (aspartic and glutamic). This behavior can be mainly ascribed to the fact that the dicarboxylic amino acids are much more prone to complex formation than the monocarboxylic amino acids (glycine, serine, or methionine). This

Table 1. Formation Constants for the Binary Cu(II) + Amino Acid (A) or Zwitterionic Buffer (Z) Ligand Complexes Together with the Corresponding Mixed Ligand Complexes Cu(II)−Amino Acid−Zwitterionic Buffer Ligand at 25.0 ± 0.1 °C and I = 0.1 mol·dm^{-3} KNO_3[a]

ligand	$\log K^{Cu(II)}_{Cu(II)(Z)}$	$\log K^{Cu(II)glycine}_{Cu(II)glycine(Z)}$ or $\log \beta^{Cu(II)}_{Cu(II)glycine(Z)}$	$\log K^{Cu(II)serine}_{Cu(II)serine(Z)}$ or $\log \beta^{Cu(II)}_{Cu(II)serine(Z)}$	$\log K^{Cu(II)methionine}_{Cu(II)methionine(Z)}$ or $\log \beta^{Cu(II)}_{Cu(II)methionine(Z)}$	$\log K^{Cu(II)aspartic}_{Cu(II)aspartic(Z)}$ or $\log \beta^{Cu(II)}_{Cu(II)aspartic(Z)}$	$\log K^{Cu(II)glutamic}_{Cu(II)glutamic(Z)}$ or $\log \beta^{Cu(II)}_{Cu(II)glutamic(Z)}$	$\log K^{Cu(II)histidine}_{Cu(II)histidine(Z)}$ or $\log \beta^{Cu(II)}_{Cu(II)histidine(Z)}$
MOPSO	3.81 ± 0.04	3.78 ± 0.02, 11.95 ± 0.03	3.98 ± 0.02, 11.21 ± 0.04	3.80 ± 0.02, 12.06 ± 0.03	4.07 ± 0.01, 12.57 ± 0.03	3.78 ± 0.02, 11.73 ± 0.03	3.63 ± 0.02, 14.13 ± 0.04
MOPS	4.00 ± 0.04	3.66 ± 0.02, 11.83 ± 0.03	3.54 ± 0.02, 10.77 ± 0.04	3.71 ± 0.03, 11.97 ± 0.03	3.86 ± 0.03, 12.36 ± 0.04	4.26 ± 0.02, 12.21 ± 0.03	3.80 ± 0.03, 14.30 ± 0.04
DIPSO	4.71 ± 0.02	3.69 ± 0.03, 11.86 ± 0.03	3.68 ± 0.03, 10.91 ± 0.04	3.42 ± 0.04, 11.68 ± 0.03	3.47 ± 0.04, 11.97 ± 0.04	3.54 ± 0.04, 11.49 ± 0.02	3.53 ± 0.02, 14.03 ± 0.04
TAPSO	4.74 ± 0.02	3.50 ± 0.02, 11.67 ± 0.04	3.46 ± 0.03, 10.69 ± 0.04	3.41 ± 0.02, 11.67 ± 0.04	3.44 ± 0.02, 11.94 ± 0.03	3.47 ± 0.02, 11.42 ± 0.03	3.66 ± 0.03, 14.16 ± 0.03

		$\log \beta^{Cu(II)}_{Cu(II)(A)(Z)_2}$		$-\Delta G^b$/kJ·mol^{-1}			
ligand	$\log K^{Cu(II)}_{Cu(II)(A)}$	Z = MOPSO	Z = MOPS	Z = MOPSO	Z = MOPS	Z = DIPSO	Z = TAPSO
glycine	8.17 ± 0.03	7.50 ± 0.04	6.35 ± 0.03	21.56	20.88	21.05	19.97
serine	7.23 ± 0.03	7.52 ± 0.05	6.40 ± 0.03	22.70	20.19	20.99	19.74
methionine	8.26 ± 0.04	7.62 ± 0.03	6.46 ± 0.02	21.68	21.16	19.51	19.45
aspartic acid	8.50 ± 0.03	7.67 ± 0.03	6.61 ± 0.03	23.22	22.02	19.79	19.62
glutamic acid	7.95 ± 0.03	7.60 ± 0.02	6.56 ± 0.03	21.56	24.30	20.19	19.79
histidine	10.50 ± 0.04	8.10 ± 0.03	6.48 ± 0.02	20.71	21.68	20.14	20.88

[a] $\log \beta^{Cu(II)}_{Cu(II)(A)(Z)} = \log K^{Cu(II)}_{Cu(II)(A)} + \log K^{Cu(II)(A)}_{Cu(II)(A)(Z)}$. $\log \beta^{Cu(II)}_{Cu(II)(A)(Z)_2} = \log K^{Cu(II)(A)}_{Cu(II)(A)(Z)} + \log K^{Cu(II)(A)(Z)}_{Cu(II)(A)(Z)_2}$. ± uncertainties refer to 3 times the standard deviation (3s). [b] ΔG, free energy of formation of the ternary complex: $\Delta G = -2.303RT \log K^{Cu(II)(A)}_{Cu(II)(A)(Z)}$.

Table 2. Formation Constants for the Binary Ni(II) + Amino Acid (A) or Zwitterionic Buffer (Z) Ligand Complexes Together with the Corresponding Mixed Ligand Complexes Ni(II)−Amino Acid−Zwitterionic Buffer Ligand at 25.0 ± 0.1 °C and I = 0.1 mol·dm^{-3} KNO_3[a]

ligand	$\log K^{Ni(II)}_{Ni(II)(Z)}$	$\log K^{Ni(II)glycine}_{Ni(II)glycine(Z)}$ or $\log \beta^{Ni(II)}_{Ni(II)glycine(Z)}$	$\log K^{Ni(II)serine}_{Ni(II)serine(Z)}$ or $\log \beta^{Ni(II)}_{Ni(II)serine(Z)}$	$\log K^{Ni(II)methionine}_{Ni(II)methionine(Z)}$ or $\log \beta^{Ni(II)}_{Ni(II)methionine(Z)}$	$\log K^{Ni(II)aspartic}_{Ni(II)aspartic(Z)}$ or $\log \beta^{Ni(II)}_{Ni(II)aspartic(Z)}$	$\log K^{Ni(II)glutamic}_{Ni(II)glutamic(Z)}$ or $\log \beta^{Ni(II)}_{Ni(II)glutamic(Z)}$	$\log K^{Ni(II)histidine}_{Ni(II)histidine(Z)}$ or $\log \beta^{Ni(II)}_{Ni(II)histidine(Z)}$
MOPSO	3.43 ± 0.02	3.72 ± 0.02, 9.22 ± 0.04	3.85 ± 0.02, 9.47 ± 0.03	3.78 ± 0.03, 9.80 ± 0.03	3.85 ± 0.02, 11.34 ± 0.03	3.83 ± 0.02, 9.64 ± 0.04	3.76 ± 0.02, 12.06 ± 0.05
MOPS	3.45 ± 0.02	3.62 ± 0.03, 9.12 ± 0.03	3.41 ± 0.03, 9.03 ± 0.04	3.45 ± 0.02, 9.47 ± 0.03	3.67 ± 0.02, 11.16 ± 0.03	3.93 ± 0.02, 9.74 ± 0.04	3.58 ± 0.03, 11.88 ± 0.04
DIPSO	3.68 ± 0.02	3.44 ± 0.02, 8.94 ± 0.03	3.15 ± 0.02[b]	3.26 ± 0.02[b]	5.82 ± 0.02[b]	3.46 ± 0.02, 9.27 ± 0.03	3.99 ± 0.02[b]
TAPSO	3.48 ± 0.02	3.66 ± 0.02[b]	3.45 ± 0.02, 9.07 ± 0.03		1.61 ± 0.02[b]		3.68 ± 0.02, 11.98 ± 0.03

ligand	$\log K^{Ni(II)}_{Ni(II)(A)}$	$\log \beta^{Ni(II)}_{Ni(II)(A)(Z)_2}$[c] Z = MOPSO	$\log \beta^{Ni(II)}_{Ni(II)(A)(Z)_2}$[c] Z = MOPS	$-\Delta G$/kJ·mol^{-1}[d] Z = MOPSO	$-\Delta G$/kJ·mol^{-1}[d] Z = MOPS	$-\Delta G$/kJ·mol^{-1}[d] Z = DIPSO	$-\Delta G$/kJ·mol^{-1}[d] Z = TAPSO
glycine	5.50 ± 0.02	7.15 ± 0.02	6.39 ± 0.02	21.22	20.65	19.62	20.88
serine	5.62 ± 0.03	7.58 ± 0.02	6.44 ± 0.04	21.96	19.45	17.97	19.68
methionine	6.02 ± 0.03	7.30 ± 0.03	6.32 ± 0.04	21.56	19.68	18.60	
aspartic acid	7.49 ± 0.04	7.33 ± 0.04	6.53 ± 0.03	21.96	20.94	33.20	9.18
glutamic acid	5.81 ± 0.02	7.32 ± 0.04	6.45 ± 0.02	21.85	22.42	19.74	
histidine	8.30 ± 0.04	7.73 ± 0.03	6.46 ± 0.02	21.45	20.42	22.76	20.99

[a] $\log \beta^{Ni(II)}_{Ni(II)(A)(Z)} = \log K^{Ni(II)}_{Ni(II)(A)} + \log K^{Ni(II)(A)}_{Ni(II)(A)(Z)}$. ± uncertainties refer to 3 times the standard deviation (3s). [b] log formation constant of protonated ternary complex: $\log K^{Ni(II)(HA)}_{Ni(II)(HA)(Z)}$. [c] $\log \beta^{Ni(II)}_{Ni(II)(A)(Z)_2} = \log K^{Ni(II)(A)}_{Ni(II)(A)(Z)} + \log K^{Ni(II)(A)(Z)}_{Ni(II)(A)(Z)_2}$. [d] ΔG, free energy of formation of the normal or protonated ternary complex: $\Delta G = -2.303RT \log K^{Ni(II)(A)}_{Ni(II)(A)(Z)}$ or $-2.303RT \log K^{Ni(II)(HA)}_{Ni(II)(HA)(Z)}$.

Table 3. Formation Constants for the Binary Co(II) + Amino Acid (A) or Zwitterionic Buffer (Z) Ligand Complexes Together with the Corresponding Mixed Ligand Complexes Co(II)−Amino Acid−Zwitterionic Buffer Ligand at 25.0 ± 0.1 °C and I = 0.1 mol·dm^{-3} KNO_3[a]

ligand	$\log K^{Co(II)}_{Co(II)(Z)}$	$\log K^{Co(II)glycine}_{Co(II)glycine(Z)}$ or $\log \beta^{Co(II)}_{Co(II)glycine(Z)}$	$\log K^{Co(II)serine}_{Co(II)serine(Z)}$ or $\log \beta^{Co(II)}_{Co(II)serine(Z)}$	$\log K^{Co(II)methionine}_{Co(II)methionine(Z)}$ or $\log \beta^{Co(II)}_{Co(II)methionine(Z)}$	$\log K^{Co(II)aspartic}_{Co(II)aspartic(Z)}$ or $\log \beta^{Co(II)}_{Co(II)aspartic(Z)}$	$\log K^{Co(II)glutamic}_{Co(II)glutamic(Z)}$ or $\log \beta^{Co(II)}_{Co(II)glutamic(Z)}$	$\log K^{Co(II)histidine}_{Co(II)histidine(Z)}$ or $\log \beta^{Co(II)}_{Co(II)histidine(Z)}$
MOPSO		3.76 ± 0.01, 8.36 ± 0.02	3.77 ± 0.02, 8.00 ± 0.03	3.71 ± 0.02, 8.95 ± 0.02	3.85 ± 0.02, 10.42 ± 0.03	3.84 ± 0.02, 8.14 ± 0.02	3.60 ± 0.02, 10.00 ± 0.03
MOPS	3.41 ± 0.02	3.82 ± 0.02[b]	3.40 ± 0.02, 7.63 ± 0.03	1.89 ± 0.01[b]	3.68 ± 0.02, 10.25 ± 0.04	3.65 ± 0.02, 7.95 ± 0.03	3.68 ± 0.02, 10.08 ± 0.03
DIPSO	3.63 ± 0.02	3.43 ± 0.02, 8.03 ± 0.03		1.20 ± 0.02[b]	2.81 ± 0.02[b]	3.46 ± 0.02, 7.76 ± 0.03	1.60 ± 0.01[b]
TAPSO	3.42 ± 0.02						3.66 ± 0.02, 10.06 ± 0.03

ligand	$\log K^{Co(II)}_{Co(II)(A)}$	$\log \beta^{Co(II)}_{Co(II)(A)(Z)_2}$[c] Z = MOPSO	$\log \beta^{Co(II)}_{Co(II)(A)(Z)_2}$[c] Z = MOPS	$-\Delta G$/kJ·mol^{-1}[d] Z = MOPSO	$-\Delta G$/kJ·mol^{-1}[d] Z = MOPS	$-\Delta G$/kJ·mol^{-1}[d] Z = DIPSO	$-\Delta G$/kJ·mol^{-1}[d] Z = TAPSO
glycine	4.60 ± 0.02	7.01 ± 0.04		21.45	21.79	19.57	
serine	4.23 ± 0.03	7.14 ± 0.02	6.30 ± 0.02	21.51	19.39		
methionine	5.25 ± 0.03	6.91 ± 0.02		21.16	10.78	6.84	
aspartic acid	6.57 ± 0.03	7.64 ± 0.03	6.69 ± 0.03	21.96	20.99	16.03	
glutamic acid	4.30 ± 0.03	7.51 ± 0.03	6.47 ± 0.03	21.91	20.82	19.74	
histidine	6.40 ± 0.02	7.41 ± 0.02	6.54 ± 0.04	20.54	20.99	9.12	20.88

[a] $\log \beta^{Co(II)}_{Co(II)(A)(Z)} = \log K^{Co(II)}_{Co(II)(A)} + \log K^{Co(II)(A)}_{Co(II)(A)(Z)}$. ± uncertainties refer to 3 times the standard deviation (3s). [b] log formation constant of protonated ternary complex: $\log K^{Co(II)(HA)}_{Co(II)(HA)(Z)}$. [c] $\log \beta^{Co(II)(HA)}_{Co(II)(HA)(Z)} = \log K^{Co(II)(A)}_{Co(II)(A)(Z)} + \log K^{Co(II)(A)(Z)}_{Co(II)(A)(Z)_2}$. [d] ΔG, free energy of formation of the normal or protonated ternary complex: $\Delta G = -2.303RT \log K^{Co(II)(A)}_{Co(II)(A)(Z)}$ or $-2.303RT \log K^{Co(II)(HA)}_{Co(II)(HA)(Z)}$.

Table 4. Formation Constants for the Binary Mn(II) + Amino Acid (A) or Zwitterionic Buffer (Z) Ligand Complexes Together with the Corresponding Mixed Ligand Complexes Mn(II)−Amino Acid−Zwitterionic Buffer Ligand at 25.0 ± 0.1 °C and I = 0.1 mol·dm^{-3} KNO_3[a]

ligand	$\log K^{Mn(II)}_{Mn(II)(Z)}$	$\log K^{Mn(II)glycine}_{Mn(II)glycine(Z)}$ or $\log \beta^{Mn(II)}_{Mn(II)glycine(Z)}$	$\log K^{Mn(II)serine}_{Mn(II)serine(Z)}$ or $\log \beta^{Mn(II)}_{Mn(II)serine(Z)}$	$\log K^{Mn(II)methionine}_{Mn(II)methionine(Z)}$ or $\log \beta^{Mn(II)}_{Mn(II)methionine(Z)}$	$\log K^{Mn(II)aspartic}_{Mn(II)aspartic(Z)}$ or $\log \beta^{Mn(II)}_{Mn(II)aspartic(Z)}$	$\log K^{Mn(II)glutamic}_{Mn(II)glutamic(Z)}$ or $\log \beta^{Mn(II)}_{Mn(II)glutamic(Z)}$	$\log K^{Mn(II)histidine}_{Mn(II)histidine(Z)}$ or $\log \beta^{Mn(II)}_{Mn(II)histidine(Z)}$
MOPSO		3.54 ± 0.02, 6.54 ± 0.03	3.53 ± 0.02, 7.88 ± 0.02	3.73 ± 0.03, 8.61 ± 0.03	3.66 ± 0.02, 8.40 ± 0.03	3.70 ± 0.02, 7.81 ± 0.04	3.74 ± 0.02, 6.75 ± 0.02
MOPS	3.54 ± 0.02	2.60 ± 0.02[b]	3.54 ± 0.02, 7.89 ± 0.03	1.89 ± 0.01[b]	3.78 ± 0.02, 8.52 ± 0.02	3.60 ± 0.02, 7.71 ± 0.03	3.49 ± 0.02, 6.50 ± 0.02
DIPSO	3.76 ± 0.02	1.04 ± 0.02[b]		1.20 ± 0.02[b]			
TAPSO	3.44 ± 0.02				1.61 ± 0.01[b]		3.51 ± 0.02, 6.52 ± 0.03

ligand	$\log K^{Mn(II)}_{Mn(II)(A)}$	$\log \beta^{Mn(II)}_{Mn(II)(A)(Z)_2}$[c]		$-\Delta G$/kJ·mol^{-1}[d]			
		Z = MOPSO	Z = MOPS	Z = MOPSO	Z = MOPS	Z = DIPSO	Z = TAPSO
glycine	3.00 ± 0.02	7.22 ± 0.02		20.19	14.83	5.93	
serine	4.35 ± 0.02	7.77 ± 0.03	6.31 ± 0.03	20.14	20.19		
methionine	4.88 ± 0.02	7.37 ± 0.04		21.28	10.78	6.84	
aspartic acid	4.74 ± 0.03	7.81 ± 0.02	6.38 ± 0.03	20.88	21.56		9.18
glutamic acid	4.11 ± 0.03	7.30 ± 0.02	6.50 ± 0.04	21.11	20.54		
histidine	3.01 ± 0.02	7.49 ± 0.03	6.45 ± 0.02	21.33	19.91		20.02

[a] $\log \beta^{Mn(II)}_{Mn(II)(A)(Z)} = \log K^{Mn(II)}_{Mn(II)(A)} + \log K^{Mn(II)(A)}_{Mn(II)(A)(Z)}$. ± uncertainties refer to 3 times the standard deviation (3s). [b] log formation constant of protonated ternary complex: $\log K^{Mn(II)(HA)}_{Mn(II)(HA)(Z)}$. [c] $\log \beta^{Mn(II)}_{Mn(II)(A)(Z)_2} = \log K^{Mn(II)(A)}_{Mn(II)(A)(Z)} + \log K^{Mn(II)(A)(Z)}_{Mn(II)(A)(Z)_2}$. [d] ΔG, free energy of formation of the normal or protonated ternary complex: $\Delta G = -2.303RT \log K^{Mn(II)(A)}_{Mn(II)(A)(Z)}$ or $-2.303RT \log K^{Mn(II)(HA)}_{Mn(II)(HA)(Z)}$.

Table 5. Formation Constants for the Binary Zn(II) + Amino Acid (A) or Zwitterionic Buffer (Z) Ligand Complexes Together with the Corresponding Mixed Ligand Complexes Zn(II)−Amino Acid−Zwitterionic Buffer Ligand at 25.0 ± 0.1 °C and I = 0.1 mol·dm^{-3} KNO_3[a]

ligand	$\log K^{Zn(II)}_{Zn(II)(Z)}$	$\log K^{Zn(II)glycine}_{Zn(II)glycine(Z)}$ or $\log \beta^{Zn(II)}_{Zn(II)glycine(Z)}$	$\log K^{Zn(II)serine}_{Zn(II)serine(Z)}$ or $\log \beta^{Zn(II)}_{Zn(II)serine(Z)}$	$\log K^{Zn(II)methionine}_{Zn(II)methionine(Z)}$ or $\log \beta^{Zn(II)}_{Zn(II)methionine(Z)}$	$\log K^{Zn(II)aspartic}_{Zn(II)aspartic(Z)}$ or $\log \beta^{Zn(II)}_{Zn(II)aspartic(Z)}$	$\log K^{Zn(II)glutamic}_{Zn(II)glutamic(Z)}$ or $\log \beta^{Zn(II)}_{Zn(II)glutamic(Z)}$	$\log K^{Zn(II)histidine}_{Zn(II)histidine(Z)}$ or $\log \beta^{Zn(II)}_{Zn(II)histidine(Z)}$
MOPSO		3.62 ± 0.03, 8.92 ± 0.02	3.61 ± 0.02, 8.71 ± 0.03	3.74 ± 0.04, 8.56 ± 0.02	3.52 ± 0.02, 10.57 ± 0.03	3.48 ± 0.03, 7.98 ± 0.03	4.08 ± 0.02, 10.48 ± 0.03
MOPS	3.63 ± 0.02	2.83 ± 0.03[b]	3.52 ± 0.02, 8.62 ± 0.03	1.89 ± 0.02[b]	3.70 ± 0.02, 10.75 ± 0.03	3.65 ± 0.03[b]	4.15 ± 0.02, 10.55 ± 0.03
DIPSO	3.55 ± 0.02	1.89 ± 0.01[b]		1.78 ± 0.02[b]			2.13 ± 0.02[b]
TAPSO	3.78 ± 0.02	2.13 ± 0.01[b]			1.61 ± 0.01[b]		4.23 ± 0.02, 10.23 ± 0.03

ligand	$\log K^{Zn(II)}_{Zn(II)(A)}$	$\log \beta^{Zn(II)}_{Zn(II)(A)(Z)_2}$[c]		$-\Delta G$/kJ·mol^{-1}[d]			
		Z = MOPSO	Z = MOPS	Z = MOPSO	Z = MOPS	Z = DIPSO	Z = TAPSO
glycine	5.30 ± 0.02	7.28 ± 0.03		20.65	16.14	10.78	12.15
serine	5.10 ± 0.02	7.63 ± 0.03	6.42 ± 0.02	20.59	20.08		
methionine	4.82 ± 0.02	6.97 ± 0.02		21.33	10.78	10.15	
aspartic acid	7.05 ± 0.04	7.65 ± 0.02	7.30 ± 0.03	20.08	21.11		9.18
glutamic acid	4.50 ± 0.02	7.03 ± 0.02		19.85	20.82		
histidine	6.40 ± 0.02	8.50 ± 0.03	6.82 ± 0.04	23.27	23.67	12.15	24.13

[a] $\log \beta^{Zn(II)}_{Zn(II)(A)(Z)} = \log K^{Zn(II)}_{Zn(II)(A)} + \log K^{Zn(II)(A)}_{Zn(II)(A)(Z)}$. ± uncertainties refer to 3 times the standard deviation (3s). [b] log formation constant of protonated ternary complex: $\log K^{Zn(II)(HA)}_{Zn(II)(HA)(Z)}$. [c] $\log \beta^{Zn(II)}_{Zn(II)(A)(Z)_2} = \log K^{Zn(II)(A)}_{Zn(II)(A)(Z)} + \log K^{Zn(II)(A)(Z)}_{Zn(II)(A)(Z)_2}$. [d] ΔG, free energy of formation of the normal or protonated ternary complex: $\Delta G = -2.303RT \log K^{Zn(II)(A)}_{Zn(II)(A)(Z)}$ or $-2.303RT \log K^{Zn(II)(HA)}_{Zn(II)(HA)(Z)}$.

Table 6. Δ log K_M Values for the 1:1:1 M(II)−Amino Acid (A)−Zwitterionic Buffer (Z) Ternary Complexes, As Determined by Potentiometric pH Titrations at 25.0 ± 0.1 °C and I = 0.1 mol·dm^{-3} KNO_3[a]

	Δ log K				
M(II)(A)(Z)	Cu(II)	Co(II)	Ni(II)	Mn(II)	Zn(II)
			M(II)−Glycine−Z		
MOPSO	−0.03		+0.29		
MOPS	−0.34		+0.17		
DIPSO	−1.02	−0.20	−0.24		
TAPSO	−1.24				
			M(II)−Serine−Z		
MOPSO	+0.17		+0.42		
MOPS	−0.46	−0.01	−0.04		−0.11
DIPSO	−1.03				
TAPSO	−1.28		−0.03		
			M(II)−Methionine−Z		
MOPSO	−0.01		+0.35		
MOPS	−0.29				
DIPSO	−1.29				
TAPSO	−1.33				
			M(II)−Aspartic−Z		
MOPSO	+0.26		+0.42		
MOPS	−0.14	+0.27	+0.22	+0.24	+0.07
DIPSO	−1.24				
TAPSO	−1.30				
			M(II)−Glutamic−Z		
MOPSO	−0.03		+0.40		
MOPS	+0.26	+0.24	+0.48	+0.06	
DIPSO	−1.17	−0.17	−0.22		
TAPSO	−1.27				
			M(II)−Histidine−Z		
MOPSO	−0.18		+0.33		
MOPS	−0.20	+0.27	+0.13	−0.05	+0.52
DIPSO	−1.18				
TAPSO	−1.08	+0.24	+0. 20	+0.07	+0.45

[a] $\Delta \log K = \log K^{M(II)(A)}_{M(II)(A)(Z)} - \log K^{M(II)}_{M(II)(Z)}$.

is due to the effective high basicity of the dicarboxylic amino acids as well as their tendency to act as ONO tridentate. Furthermore, with respect to the dicarboxylic amino acids, it is evident that the stability of the binary or mixed ligand complexes containing an aspartic acid residue is higher than that of the corresponding one containing glutamic acid. This behavior can be interpreted in terms of the effective basicity of the free conjugate base of the aspartic acid.

The Δ log K values are positive for some of the investigated ternary complexes (Table 6). The higher stability constants of ternary complexes compared with those of binary systems may be attributed to the interligand interactions or some cooperativity between the coordinated ligands, possibly H-bond formation.

On the basis of a mathematical treatment and SUPERQUAD calculations (Gans et al., 1985) of the titration curves of the systems M(II)−A−MOPSO, it was concluded that there is no formation of protonated ternary complexes in these solutions. This may be explained on the basis of the higher acidity of MOPSO compared to MOPS, DIPSO, or TAPSO, which makes the protonated 1:1:1 complexes of MOPSO with Cu(II), Co(II), Ni(II), Mn(II), or Zn(II) ions and the amino acids (glycine, serine, methionine, aspartic acid, glutamic acid or histidine), strong acids that dissociate readily to the normal 1:1:1 complexes in solution.

It seems evident from the values of the overall formation constants reported in Tables 1−5 that the different chelation modes of the above-mentioned amino acids during the formation of the ternary complexes under investigation overestimate the role of basicity in determining the overall stability of these mixed ligand complexes.

The observed higher stability constants for the ternary complexes containing histidine relative to those of other ternary systems under investigation may be attributed quite possibly to the fact that under this condition the histidine anion bound to Cu(II), Co(II), Ni(II), Mn(II), or Zn(II) ions as terdentate ligand to form the primary complexes which then interacted simultaneously with the zwitterionic buffer ligands to form the ternary complexes. As is shown in Tables 1−5, the overall formation constants of the quaternary complexes with MOPSO as secondary ligand are higher than those for complexes containing MOPS. The quaternary complexes studied, especially those of Cu(II) and Ni(II), may be considered as relatively simple models from which information may be gained about the properties of amino acids and their different structural chemistries regarding the strength of their interactions with the biologically important zwitterionic buffer ligands (MOPSO, MOPS, DIPSO, and TAPSO), and even insight into the factors which influence the strength is thus becoming available, as these systems may mimic the low molecular weight metallopeptides Cu(II)−GGH and Ni(II)−GGH.

Our investigation confirmed the formation of mixed ligand complexes of the type M(II)−A−Z [where A = glycine, serine, methionine, glutamic acid, aspartic acid, and histidine; Z = MOPSO, MOPS, DIPSO, and TAPSO; M(II) = Cu(II), Co(II), Ni(II), Mn(II), and Zn(II)] in solution; hence, great reservations should be exercised in employing these biologically important zwitterionic buffers in systems containing the mentioned metal ions or amino acids.

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