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Stability of ternary metal ion complexes formed by imidazole and the anion of *N,N*-bis(2-hydroxyethyl)glycine (Bicine)*. Observation of a relatively high stability of the Zn(Bicinate)(imidazole)$^+$ complex

Liang-nian Ji**, Nicolas A. Corfù and Helmut Sigel†

Institute of Inorganic Chemistry, University of Basel, Spitalstrasse 51, CH-4056 Basel (Switzerland)

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Abstract

The acidity constant of H(imidazole)$^+$ and the stability constants of the binary 1:1 complexes formed between Co^{2+}, Ni^{2+}, Cu^{2+}, Zn^{2+} or Cd^{2+} (M^{2+}) and imidazole (Im) were determined by potentiometric pH titration in aqueous solution ($I = 0.1$ M, $NaNO_3$; 25 °C). The stabilities of the ternary complexes containing in addition *N,N*-bis(2-hydroxyethyl)glycinate (Bic$^-$) were also measured. This information allows the position of the following equilibrium to be quantified: $M(Bic)^+ + M(Im)^{2+} \rightleftharpoons M(Bic)(Im)^+ + M^{2+}$. The ternary systems with Co^{2+}, Ni^{2+}, Cu^{2+} and Cd^{2+} show the properties expected from previous experience. However, the result for the Zn^{2+} system is most surprising: the position of the mentioned equilibrium is at the right side, i.e. $\Delta \log K_{Zn} = \log K^{M(Bic)}_{M(Bic)(Im)} - \log K^{M}_{M(Im)} = 2.81 - 2.50 = 0.31 \pm 0.04$. This high relative stability of the ternary Zn(Bic)(Im)$^+$ complex is explained by a reduction of the coordination number of Zn^{2+} from 6 to 4 (or 5) upon coordination of imidazole, which entropically favors the formation of the ternary complex. The equilibrium constants measured earlier for the corresponding systems with nitrilotriacetate (Nta^{3-}) also fit into the indicated picture. The relevance of these observations for biological systems is briefly discussed.

Introduction

N,N-Bis(2-hydroxyethyl)glycine (= Bicine), first prepared in 1926 by Kiprianov [2], became a popular buffer substance through the work of Good *et al.* in 1966 [3], and therefore Bicine actually is often addressed as one of 'Good's' buffers (e.g. refs. 4 and 5). By now it is well known that the anion of Bicine, i.e. Bicinate††, is an excellent metal ion chelator and quite a number of stability constants for M(Bicinate)$^+$ complexes have been measured [3, 5–12]. It has also repeatedly been emphasized that the use of Bicine as a pH buffer in biochemical, medical or any other studies under the assumption that only little (or no) interaction with (divalent) metal ions occurs is not justified [5, 12, 13]; the use of this buffer warrants great care to prevent misleading results and conclusions.

It is evident that the basic metal ion-binding core of Bicinate is the glycinate-type part of the molecule (see Fig. 1). However, by a detailed mathematical treatment the previous conclusion [5, 6, 12] on the participation of the hydroxyethyl groups in complex formation was confirmed [14]. Moreover, evidence was provided [14] that for the metal ions Co^{2+}, Ni^{2+}, Cu^{2+} and Zn^{2+} only about 0.5% of M(Bicinate)$^+$ exist as a species with a glycinate-type binding mode to which we shall refer from now on as $M(Bic)^+_{op}$. In the case of Co^{2+}, Ni^{2+} and Zn^{2+} another approximately 10 to 15% have in addition one of the two hydroxy groups coordinated whereas for the largest part, i.e. in the remaining 85 to 90%, Bicinate actually acts as a tetradentate ligand; these two latter mentioned species are designated as $M(Bic)^+_{cl(1)}$ and $M(Bic)^+_{cl(2)}$ indicating that either one or both hydroxy groups are also coordinated. For Cu^{2+}, due to its Jahn–Teller distorted

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**Work done at the University of Basel during a leave from the Zhongshan University, Guangzhou, People's Republic of China.

†Author to whom correspondence should be addressed.

††Abbreviations: ATP^{4-}, adenosine 5′-triphosphate; Bic$^-$, abbreviation for Bicinate as used in formula; Bicinate, monoanion of Bicine; Bicine, *N,N*-bis(2-hydroxyethyl)glycine; Im, imidazole; M^{2+}, divalent metal ion; $M(Bic)^+_{cl(1)}$, M(Bicinate)$^+$ species with one hydroxy group coordinated to M^{2+}; $M(Bic)^+_{cl(2)}$, M(Bicinate)$^+$ species with both hydroxy groups coordinated to M^{2+}; $M(Bic)^+_{op}$, Bicinate coordinated to M^{2+} in a glycinate-type mode only; Nta^{3-}, nitrilotriacetate; UTP^{4-}, uridine 5′-triphosphate.

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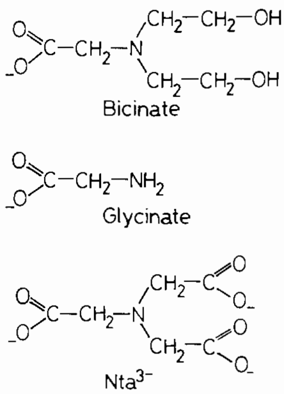

Fig. 1. Chemical formula of *N*,*N*-bis(2-hydroxyethyl)glycinate (=Bicinate or $\mathrm{Bic^-}$) and nitrilotriacetate ($\mathrm{Nta^{3-}}$), as well as of their parent compound glycinate.

(octahedral) coordination sphere [15], one expects that the apical interaction is weaker and indeed for $\mathrm{Cu(Bic)^{+}_{cl(1)}}$ and $\mathrm{Cu(Bic)^{+}_{cl(2)}}$ about 40 and 60%, respectively, have been estimated [14]. However, despite the largely tetradentate binding of Bicinate and consequently its significant saturation of metal ion-coordination spheres, $\mathrm{M(Bicinate)^+}$ complexes of the mentioned metal ions are well able to bind a further ligand and to form ternary complexes, e.g. with 1,10-phenanthroline [16] or ATP [12].

The fact that Bicinate acts to a large part as a tetradentate ligand, especially towards $\mathrm{Co^{2+}}$, $\mathrm{Ni^{2+}}$ and $\mathrm{Zn^{2+}}$ [14], means that the structure of the $\mathrm{M(Bicinate)^+}$ complexes is quite similar to the corresponding complexes with nitrilotriacetate ($\mathrm{Nta^{3-}}$; see Fig. 1). Indeed, if one considers the iminodiacetate moiety as the central binding core in $\mathrm{M(Nta)^-}$ complexes [17], one may calculate that the third acetate residue participates in more than 99.8% [18] of the $\mathrm{M(Nta)^-}$ species in metal ion binding proving that $\mathrm{Nta^{3-}}$ is a tetradentate ligand. In a previous study on ternary $\mathrm{M(Nta)^-}$/imidazole systems [19] it was shown that rather stable mixed ligand complexes are formed [19]. This observation, together with the fact that Bicine, as buffer substance, and imidazole (groups), as part of biological ligands, often appear together in biochemical studies prompted us to investigate the ternary $\mathrm{M(Bicinate)^+}$/imidazole systems, with $\mathrm{M^{2+}} = \mathrm{Co^{2+}}, \mathrm{Ni^{2+}}, \mathrm{Cu^{2+}}, \mathrm{Zn^{2+}}$ and $\mathrm{Cd^{2+}}$. A further factor facilitating this decision is our long standing interest in metal ion–buffer interactions [12, 20].

Experimental

Materials

N,*N*-Bis(2-hydroxyethyl)glycine (Bicine) was from Sigma Chemical Co., St. Louis, MO, USA. The disodium salt of ethylene-*N*,*N*,*N'*,*N'*-tetraacetic acid ($\mathrm{Na_2H_2EDTA}$), potassium hydrogen phthalate, imidazole, $\mathrm{HNO_3}$, NaOH (Titrisol) and the nitrate salts of $\mathrm{Na^+}$, $\mathrm{Co^{2+}}$, $\mathrm{Ni^{2+}}$, $\mathrm{Cu^{2+}}$, $\mathrm{Zn^{2+}}$ and $\mathrm{Cd^{2+}}$ (all pro analysi) were from Merck AG, Darmstadt, Germany. All solutions were prepared with distilled $\mathrm{CO_2}$-free water.

The titer of the NaOH used for the titrations was determined with potassium hydrogen phthalate. The exact concentrations of the imidazole solutions used in the titration experiments with the metal ions (titrated in the presence of an excess of $\mathrm{HNO_3}$; see also below) were measured by titrations with NaOH. The concentrations of the stock solutions of the metal ions were established with EDTA.

Potentiometric pH titrations

The pH titrations were carried out with a Metrohm E536 potentiograph, E655 dosimat and 6.0202.100 (JC) combined, single junction, macro glass electrodes. The buffer solutions (pH 4.64, 7.00 and 9.00; these are based on the scale of the US National Bureau of Standards) used for calibration were also from Metrohm AG, Herisau, Switzerland. The direct pH meter readings were used in the calculations of the acidity constants, i.e. these constants are so-called practical, 'mixed' or Brønsted constants [10, 21]. The negative logarithms of these practical acidity constants given for aqueous solutions at $I=0.1$ M ($\mathrm{NaNO_3}$) and 25 °C may be converted into the corresponding concentration constants by subtracting 0.02 log unit [21]; this conversion term contains both the junction potential of the glass electrode and the hydrogen ion activity coefficient [21, 22]. It should be noted that for the stability constants of metal ion complexes no conversion is necessary.

It may be added that in the described calculation procedure the ionic product of water (K_w) and the mentioned 'combined' term of 0.02 log unit for converting the measured data into $\mathrm{H^+}$ concentration do *not* enter into the calculations, because we evaluate the *differences* in NaOH consumption between two corresponding solutions, i.e. always solutions with and without ligand are titrated (see the following section). The advantage of this procedure is (aside from not needing K_w and the conversion term) that impurities in the solvent or in the salts, as well as systematic errors, etc., cancel to a large part [21].

Determination of equilibrium constants

The acidity constant $K^{\mathrm{H}}_{\mathrm{H(Im)}}$ of protonated imidazole was determined by titrating 50 ml of aqueous 0.85 mM $\mathrm{HNO_3}$ ($I=0.1$ M, $\mathrm{NaNO_3}$; 25 °C) in the presence and absence of 0.7 mM imidazole under $\mathrm{N_2}$ with 1 ml of 0.05 M NaOH and by using the differences in NaOH consumption between such a pair of titrations for the calculations. The value for $K^{\mathrm{H}}_{\mathrm{H(Im)}}$ was calculated from 16 independent pairs of such titrations by a curve-fitting procedure with a Newton-Gauss non-linear least-squares program within the pH range determined by about 3 and 97% neutralization for the equilibrium $H(Im)^+/Im$. The calculation was carried out with a Hewlett-Packard Vectra 60PC MSDOS desk-computer connected with a Brother M-1509 printer and a Graphtec 3100 plotter.

The stability constants $K^{M}_{M(Im)}$ and $K^{M(Bic)}_{M(Bic)(Im)}$ of the binary $M(Im)^{2+}$ and ternary $M(Bicinate)(Im)^+$ complexes, respectively, were measured under the same conditions used for the pair-wise acidity-constant titrations, i.e. $I = 0.1$ M ($NaNO_3$), 25 °C and $[Im] = 0.7$ mM, but $NaNO_3$ was partially or fully replaced by $M(NO_3)_2$. For the binary M^{2+}/Im systems titrations were made with $[M^{2+}] = 8.333$ mM (hence, $Im{:}M^{2+} = 1{:}12$) and 4.167 mM ($Im{:}M^{2+} = 1{:}6$) for Co^{2+}, Ni^{2+}, Cu^{2+}, Zn^{2+} and Cd^{2+}; for Co^{2+}, Zn^{2+} and Cd^{2+} also the conditions with $[M^{2+}] = 0.01667$ M ($Im{:}M^{2+} = 1{:}24$) and for Ni^{2+} with $[M^{2+}] = 0.0333$ M ($Im{:}M^{2+} = 1{:}48$) were used. For the ternary M^{2+}/Bicine/Im systems the conditions were exactly the same as for the binary ones except that now M^{2+} was always replaced by M^{2+}/Bicinate in a 1:1 ratio. Under the conditions with the lowest Bicinate concentration, i.e. $Im{:}M^{2+}{:}Bicinate = 1{:}6{:}6$, the $M(Bicinate)^+$ complexes are formed in the pH ranges used for the calculations (see below) to at least 85% with Co^{2+}, Zn^{2+} and Cd^{2+}, to 90% with Ni^{2+} and 95% with Cu^{2+} (calculated with the values for $K^{M}_{M(Bic)}$ from [7, 12]). Of course, under the conditions with $Im{:}M^{2+}{:}Bicinate = 1{:}12{:}12$ (and the higher ratios) the total concentrations of M^{2+} and Bicinate were larger and consequently the formation degrees of the $M(Bicinate)^+$ complexes are even greater than those given above. It should be emphasized that in all the cases the results are independent within the error limits of the total concentration of M^{2+} or of M^{2+}/Bicinate. Each final result for $K^{M}_{M(Im)}$ and $K^{M(Bic)}_{M(Bic)(Im)}$ is the average of six independent pairs of titrations.

The stability constants $K^{M}_{M(Im)}$ and $K^{M(Bic)}_{M(Bic)(Im)}$ were calculated in two ways. (i) By taking into account the species H^+, $H(Im)^+$, Im, M^{2+} and $M(Im)^{2+}$ in the case of the binary systems and H^+, $H(Im)^+$, Im, $M(Bicinate)^+$ and $M(Bicinate)(Im)^+$ for the ternary systems, and by collecting the data every 0.1 pH unit from about 5% complex formation to a neutralization degree of about 90% or to the beginning of the hydrolysis of $M(aq)^{2+}$ or $M(Bicinate)(aq)^+$; these hydrolysis reactions were evident from the titrations without imidazole. (ii) The curve-fitting procedure described above for the calculation of $K^{H}_{H(Im)}$ was also used to determine an *apparent* acidity constant, K'_a, for the deprotonation of $H(Im)^+$ in the presence of a relatively large (and hence during the titration constant) excess of M^{2+} or M^{2+}/Bicinate. The experimental data used for the calculation of K'_a again covered the pH range between about 3 and 97% neutralization where possible; of course, the collection of the data was not carried into the pH range in which hydrolysis occurs (see above). Values for $K^{M}_{M(Im)}$ and $K^{M(Bic)}_{M(Bic)(Im)}$ were calculated [23, 24] with eqn. (1):

$$K^{M}_{M(Im)} \text{ or } K^{M(Bic)}_{M(Bic)(Im)} = \frac{K'_a - K^{H}_{H(Im)}}{K^{H}_{H(Im)}[M^{2+}]_{tot}} \qquad (1)$$

The agreement of the results obtained from the two evaluation procedures was excellent, but for principle reasons in the present case the first method is somewhat more appealing; therefore these values were finally used.

Results and discussion

Stability of complexes

The acidity constant of monoprotonated imidazole (eqn. (2)) and the stability constants of the binary $M(Im)^{2+}$ (eqn. (3)) and ternary $M(Bicinate)(Im)^+$ complexes (eqn. (4)) were determined by potentiometric pH titrations for aqueous solutions ($I = 0.1$ M, $NaNO_3$; 25 °C):

$$H(Im)^+ \rightleftharpoons Im + H^+ \qquad (2a)$$

$$K^{H}_{H(Im)} = [Im][H^+]/[H(Im)^+] \qquad (2b)$$

$$M^{2+} + Im \rightleftharpoons M(Im)^{2+} \qquad (3a)$$

$$K^{M}_{M(Im)} = [M(Im)^{2+}]/([M^{2+}][Im]) \qquad (3b)$$

$$M(Bic)^+ + Im \rightleftharpoons M(Bic)(Im)^+ \qquad (4a)$$

$$K^{M(Bic)}_{M(Bic)(Im)} = [M(Bic)(Im)^+]/([M(Bic)^+][Im]) \qquad (4b)$$

It may be added that the formation degree of the $M(Bicinate)^+$ complexes under the experimental conditions employed is high enough to allow the evaluation of the ternary systems directly according to equilibrium (4a) (see 'Experimental'). The obtained results are listed in Table 1.

The acidity constant of $H(Im)^+$ (eqn. (2)), i.e. $pK^{H}_{H(Im)} = 7.05 \pm 0.01$, is in excellent agreement with earlier determinations in our laboratory [19, 25] (an observation which confirms again the previous conclusion [21] about the constancy of the term for the conversion from the practical into the concentration pH scale (see ref. 21)), as well as with many values given in the literature [7, 8, 11, 26]. Similarly, the stability constants measured now for the binary $M(Im)^{2+}$ complexes agree perfectly with our previous results [25] and also with the average values obtained from constants listed in the literature [7–9, 26] (see Table 1 of ref. 19). The stability constants given in the third column

TABLE 1. Logarithms of the stability constants for binary M(imidazole)$^{2+}$ (eqn. (3)) and ternary M(Bicinate)(imidazole)$^{+}$ complexes (eqn. (4)), together with the stability differences $\Delta \log K_M$ (eqn. (7)) for aqueous solutions at 25 °C and $I=0.1$ M (NaNO$_3$)[a]

M^{2+}	$\log K^{M}_{M(Im)}$	$\log K^{M(Bic)}_{M(Bic)(Im)}$	$\Delta \log K_M$
Co^{2+}	2.43 ± 0.02	2.38 ± 0.04	-0.05 ± 0.04
Ni^{2+}	3.04 ± 0.01	2.96 ± 0.01	-0.08 ± 0.01
Cu^{2+}	4.22 ± 0.02	4.11 ± 0.02	-0.11 ± 0.03
Zn^{2+}	2.50 ± 0.02	2.81 ± 0.03	0.31 ± 0.04
Cd^{2+}	2.74 ± 0.03	2.24 ± 0.03	-0.50 ± 0.04

[a] Acidity constant of H(Im)$^+$: $pK^{H}_{H(Im)} = 7.05 \pm 0.01$ (3σ). The error limits given are *three times* the standard error of the mean value (3σ) or the sum of the probable systematic errors, whichever is larger; the error limits for $\Delta \log K_M$ were calculated according to the error propagation after Gauss.

of Table 1, i.e. for the ternary M(Bicinate)(Im)$^+$ complexes, to our knowledge are determined here for the first time.

Comparison of the stabilities of binary M(Im)$^{2+}$ and ternary M(Bicinate)(Im)$^{+}$ complexes

A common way to quantify the stability of mixed ligand complexes is based on a comparison with the corresponding binary parent complexes, i.e. by determining the position of equilibrium (5) [27, 28]:

$$M(Bic)^+ + M(Im)^{2+} \rightleftharpoons M(Bic)(Im)^+ + M^{2+} \qquad (5)$$

The corresponding equilibrium constant is defined by eqn. (6):

$$10^{\Delta \log K_M} = [M(Bic)(Im)^+][M^{2+}]/([M(Bic)^+][M(Im)^{2+}]) \qquad (6)$$

Values for this constant follow [23, 27, 28] from relation (7):

$$\Delta \log K_M = \log K^{M(Im)}_{M(Im)(Bic)} - \log K^{M}_{M(Bic)} = \log K^{M(Bic)}_{M(Bic)(Im)} - \log K^{M}_{M(Im)} \qquad (7)$$

It may be added that in case further identification of $\Delta \log K_M$ for a certain equilibrium is needed, this will be given by additional subscripts like $\Delta \log K_{Zn/Bic/Im}$ meaning that the corresponding value refers to the ternary Zn^{2+}–Bicinate–imidazole system.

According to the general rule for binary complexes, $K_1 > K_2$... (see, for example, refs. 7–11, 26), one expects by analogy that equilibrium (5) is on its left side, i.e. for $\Delta \log K_M$ (eqn. (7)) *negative* values are expected. Indeed, statistical (st) reasonings [19, 27] lead to the same conclusion: a monodentate ligand entering an octahedral (oh) coordination sphere has six possibilities for binding, while only two remain if four are already occupied by Bicinate (see 'Introduction' and ref. 14); as the probability for dissociation is the same, namely 1, in the binary and the ternary complex the statistical value for $\Delta \log K_{st/oh}$ is $\log(2/6) = -0.5$. For Cu^{2+} a value is more difficult to assess [27]: assuming a square-planar (sp) or a distorted octahedral (do) coordination sphere one may conclude [19] that the value is log(1/4) or log (1/6) and hence, $\Delta \log K_{st/sp/do} = -0.6$ or -0.8, i.e. $\Delta \log K_{st/Cu} \simeq -0.7$ appears as a reasonable estimate.

Comparison of the mentioned statistical values, $\Delta \log K_{st}$, with the experimental results for $\Delta \log K_M$ listed in the fourth column of Table 1 indicates that only the Cd^{2+}/Bicinate/Im system behaves as predicted by the statistics. The corresponding ternary complexes with Co^{2+}, Ni^{2+}, Cu^{2+} and Zn^{2+} are clearly more stable than expected. Indeed, this observation agrees with the experience [19, 23, 27–29] that mixed ligand complexes formed by a metal ion of the second half of the 3d series, an O donor (what Bicinate is to a large part) and a heteroaromatic N base with π-accepting properties, like imidazole [30, 31], are especially stable; an observation for ligand combinations that are also reflected in biological systems [29, 31, 32].

The special properties of Zn(Bicinate)(Im)$^{+}$ and of the related Zn(Nta)(Im)$^{-}$ complex

At this point it seems interesting to compare the $\Delta \log K_M$ values of the two related ternary systems, i.e. M^{2+}–Bicinate–Im and M^{2+}–Nta–Im (see also 'Introduction'); these data are collected in Table 2. It is evident that the $\Delta \log K_M$ values for the Co^{2+}, Ni^{2+} and Cu^{2+} systems with Nta^{3-} and imidazole [19] are somewhat larger than those with Bicinate and Im; this result has its origin probably in the coordination of the negatively charged oxygens of the carboxylate groups of Nta^{3-} (see also Fig. 1), which should make the π-accepting properties of imidazole somewhat more effective. However, the most unexpected result of Table 2 is certainly the rather high relative stability of the ternary Zn(Bicinate)(Im)$^+$ complex: in this case a *positive* value of about 0.3 for $\Delta \log K_{Zn/Bic/Im}$ is observed

TABLE 2. Comparison of the relative stabilities of ternary M(Bicinate)(Im)$^+$ and M(Nta)(Im)$^-$ complexes[a] in aqueous solutions at 25 °C and $I=0.1$ M[b]

M^{2+}	$\Delta \log K_{M/Bic/Im}$[c]	$\Delta \log K_{M/Nta/Im}$[d]
Co^{2+}	-0.05 ± 0.04	0.02 ± 0.04
Ni^{2+}	-0.08 ± 0.01	0.02 ± 0.03
Cu^{2+}	-0.11 ± 0.03	0.25 ± 0.03
Zn^{2+}	0.31 ± 0.04	0.16 ± 0.03[e]
Cd^{2+}	-0.50 ± 0.04	

[a] Compare equilibrium (5) and eqns. (6) and (7). [b] All error limits (3σ) were calculated according to the error propagation after Gauss. [c] From Table 1. [d] From ref. 19. [e] If $\log K^{Zn}_{Zn(Im)} = 2.51$ ([25]; see also Table 1) is used for the calculation one obtains $\log K_{Zn/Nta/Im} = 0.22 \pm 0.03$.

and this means that equilibrium (5) is on its right hand side. Moreover, also the ternary Zn(Nta)(Im)$^-$ complex shows a relatively high stability if compared to that of the Co(Nta)(Im)$^-$ or Ni(Nta)(Im)$^-$ complexes.

This effect of a relative stability enhancement for the Zn^{2+} complexes is clearly beyond the effect that may be attributed to the combination of an O donor ligand and a heteroaromatic π-accepting amine [23, 28–31, 33]. It seems to us that the explanation for the above observation is linked to the varying coordination sphere of Zn^{2+}, which apparently easily switches from coordination number 6 to 4 or 5 [34, 35]. On this basis the results of Table 2 may be explained: if Bicinate and Nta^{3-} bind to an octahedral Zn^{2+}, and there is a very high probability for this structure [14], and if upon the further binding of imidazole the coordination number is reduced to 4 or 5 two water molecules are released upon the coordination of the monodentate ligand. Such a process is entropically favored and would therefore explain the special properties observed for the Zn^{2+} systems. Clearly, for Co^{2+}, Ni^{2+} or Cd^{2+} with their more well defined octahedral coordination spheres such a process is considerably less probable.

If one assumes an equilibrium between octahedral and tetrahedral Zn^{2+} complexes, even a finer detail in Table 2 may be explained. If the coordination of the monodentate imidazole to Zn(Bicinate)$^{2+}$ or Zn(Nta)$^-$ enforces coordination number four, one of the hydroxy or carboxylate groups from Bicinate or Nta^{3-}, respectively, has to be released from the coordination sphere of the metal ion. This is an unfavorable process and expected to be especially pronounced for a more tightly bound carboxylate group. Indeed, the relative stability increase between the ternary Co^{2+} (or Ni^{2+}) and Zn^{2+} complexes is somewhat less pronounced in the case of Nta^{3-} (see column 3 of Table 2) than with Bicinate (column 2); the first mentioned ligand is expected to act in about 99.8% of the Zn^{2+} complexes as a tetradentate ligand (see 'Introduction') while Bicinate does this only in about 85% [14] of the complexed species.

Conclusions

The present study on the ternary M(Bicinate)(Im)$^+$ complexes confirms previous conclusions [5, 12–14] about the care that should be exercised if Bicine is employed as a pH buffer in the presence of metal ions. It is quite evident that Bicinate may not only complex with free M^{2+} ions but also with already coordinated M^{2+} species giving thus rise to the formation of ternary complexes and then to possibly undesired and unexpected properties.

Considering the often observed [35–39] adaptability of Zn^{2+} coordination spheres in biological systems, the described results for the Zn(Bicinate)(Im)$^+$ and Zn(Nta)(Im)$^-$ complexes as well as the given explanations are meaningful. An incoming substrate is favorably bound, and enhances also the Lewis acidity of Zn^{2+}, if the coordination number is *reduced* and thus more water (or other bound sites or) molecules are released; not to speak of the fact that this property allows in addition that now during a reactive transition a further donor site can easily be bound *without* the necessity to release another group from the coordination sphere. Tentatively one may also conclude from the available data that the shift from coordination number 6 to 5 or 4 is favored by the participation of N donor ligands (or sites). Again a request in accordance with the observed situation in biological systems where the extremely versatile [15, 31, 40, 41] imidazole group is often involved [29, 36b, 37]. Finally, it is evident that more such low-molecular-weight Zn^{2+} systems should be studied and a more quantitative evaluation regarding the changes of the coordination number should be attempted.

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