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Complexation of L-Cystine with Metal Cations

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The complexation equilibria of L-cystine, H_2L, with the Cu^{2+}, Al^{3+}, and Fe^{3+} ions have been studied at 25 °C and in 3 $mol\cdot dm^{-3}$ $NaClO_4$ ionic medium by potentiometric measurements with a glass electrode. The concentrations of ligand (C_L) and metal ions M^{z+} (C_M) were varied between ($0.5\cdot 10^{-3}$ and $5\cdot 10^{-3}$) $mol\cdot dm^{-3}$, and the ligand-to-metal ratio was varied between 1 and 10 ($1 \le C_L/C_M \le 10$). The hydrogen ion concentration was decreased stepwise to the incipient precipitation of a basic salt of each metal. The experimental data have been explained with the formation of the complexes: CuL, CuL_2^{2-}, $Cu(HL)_2$, and $Cu_2(HL)^{3+}$; AlL^+ and AlL_2^-; and FeL^+ and FeL_2^-. Equilibrium formation constants are given for the investigated ionic medium as well as for the infinite dilution reference state, evaluated by the specific ion interaction theory (SIT).

Introduction

In recent years, we have been interested in a systematic study concerning the complexing power of L-cystine, H_2L, toward metal ions of biological interest. L-Cystine results from cysteine oxidation with the formation of a disulfide bridge and displays four protonation sites (Figure 1).

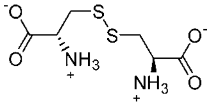

Figure 1. Structure of L-cystine, H_2L.

The two most basic protonation steps for L-cystine relate to its two amino groups, whereas the two most acidic steps correspond to its two carboxylate functions. Both types of donor sites are likely to participate in metal coordination; in addition, the disulfide bond may also be involved in some specific cases. The interaction of cations with L-cystine is more important than that with cysteine that is rapidly oxidized in human blood.[1] For this reason, L-cystine is the predominant species in this fluid. Despite its relevance, L-cystine has been investigated less than other sulfur-containing amino acids due to its limited solubility in water.[2] For this reason, in a previous work[3] we have determined the solubility as well as the acidic constants of this ligand in $NaClO_4$ solutions at different ionic strengths. The potentiometric data, in combination with solubility measurements of H_2L in pure water and in $NaClO_4$ solutions, were processed by the specific ion interaction theory (SIT)[4,5] to yield acidic constants at the infinite dilution reference state and interaction coefficients of the cationic and anionic forms of L-cystine with the perchlorate and sodium ions, respectively. Those data are necessary to evaluate the complexation between ligand and metal ions at the constant ionic medium as well as at the infinite dilution reference state.

Furthermore, the solubility of L-cystine increases proportionally with the ionic medium concentration.[3] For this reason, in this work, the complexation equilibria of this ligand with the Cu^{2+}, Al^{3+}, and Fe^{3+} ions have been studied at 25 °C and in 3 $mol\cdot dm^{-3}$ $NaClO_4$ ionic medium by potentiometric measurements with a glass electrode. The adoption of the constant ionic medium method, proposed by Biedermann and Sillèn,[6] was necessary to minimize activity coefficient variation in spite of the change of the reagent concentrations. In this way, it was possible to substitute activities with concentrations in the calculations and to minimize the residual liquid junction potential, that is, its difference between potential readings due to the hydrogen ion.

Materials and Methods

Instrumentation. The cell arrangement was similar to the one described by Forsling et al.[7] Ag/AgCl electrodes were prepared according to Brown.[8] Glass electrodes, manufactured by Metrohm, were of the 6.0133.100 type. They acquired a constant potential within 10 min after the addition of the reagents and remained unchanged to within ± 0.1 mV for several hours. The titrations were carried out with a programmable computer-controlled data acquisition switch unit 34970 A supplied by Hewlett-Packard. The EMF values were measured with a precision of $\pm\ 10^{-5}$ V using an OPA 111 low-noise precision DIFET operational amplifier. A slow stream of nitrogen gas was passed through four bottles (**a**−**d**) containing (**a**) 1 $mol\cdot dm^{-3}$ NaOH, (**b**) 1 $mol\cdot dm^{-3}$ H_2SO_4, (**c**) twice distilled water, and (**d**) 3 $mol\cdot dm^{-3}$ $NaClO_4$ and then into the test solutions, stirred during titrations, through the gas inlet tube. During the EMF measurements, the cell assembly was placed in a thermostat kept at (25.0 ± 0.1) °C.

Reagents and Analysis. A perchloric acid stock solution was prepared and standardized as described previously.[9] A sodium perchlorate stock solution was prepared and standardized according to Biedermann.[10] Sodium hydroxide titrant solutions were obtained by dilution of a saturated solution filtered on a Gooch crucible (G4) in a nitrogen atmosphere. The hydroxide concentration was determined by titration with standardized $HClO_4$ using methyl-red as a visual indicator. The results agreed to within 0.1 %. Purissimum grade (≥ 99.0 % Aldrich p.a.) L-cystine product was used without further purification. It was kept in a desiccator over silica gel. Copper(II) perchlorate stock solutions were prepared by dissolving CuO in a slight excess of standardized $HClO_4$. The oxide was obtained by heating, at 500 °C, $Cu(NO_3)_2\cdot 4H_2O$ prepared from electrolytic copper

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99.99 % and HNO_3. The Cu(II) concentration in the stock solutions was determined by electrogravimetry and iodometry. The results agreed to 0.1 %. The hydrogen ion concentration was derived by $[ClO_4^-] = [H^+] + 2[Cu(II)]$. Aluminum(III) perchlorate was prepared and standardized as reported by Ciavatta and Iuliano.[11] Iron(III) perchlorate was prepared and standardized as reported by Ciavatta et al.[12]

All solutions were prepared with twice distilled water.

Potentiometric Measurements. The complexation equilibria have been studied, at 25 °C and in 3 $mol \cdot dm^{-3}$ $NaClO_4$, by measuring with a glass electrode the competition of the L-cystine, H_2L, for the metal and H^+ ions.

The potentiometric measurements, performed as titrations, were performed with cell (G)

$$\text{RE/Test Solution/Glass Electrode} \qquad \text{(G)}$$

where RE, reference electrode, = Ag/AgCl/0.01 $mol \cdot dm^{-3}$ $AgClO_4$, 2.99 $mol \cdot dm^{-3}$ $NaClO_4$/3 $mol \cdot dm^{-3}$ $NaClO_4$, and Test Solution = C_M $mol \cdot dm^{-3}$ $M(ClO_4)_z$, C_L $mol \cdot dm^{-3}$ H_2L, C_A $mol \cdot dm^{-3}$ $HClO_4$, and C_B $mol \cdot dm^{-3}$ NaOH, $(3-z\,C_M-C_A-C_B)$ $mol \cdot dm^{-3}$ $NaClO_4$. The metal and the ligand concentrations, C_M and C_L, respectively, ranged from $(0.5 \cdot 10^{-3}$ to $5 \cdot 10^{-3})$ $mol \cdot dm^{-3}$, the upper limit being imposed by the limited solubility of the ligand. The ligand-to-metal ratio was varied between 1 and 10 ($1 \leq C_L/C_M \leq 10$), with the only exception of the system being L-cystine$-Cu^{2+}$, which was further investigated also at $C_M = 2C_L$. The hydrogen ion concentration was varied from $10^{-1.5}$ $mol \cdot dm^{-3}$ to incipient precipitation of a basic salt of each metal, whose formation depends on the particular metal ion and the specific ligand-to-metal ratio.

Since the effects of composition changes on activity coefficients can be considered negligible, the EMF of cell (G) can be written, in millivolts, at the temperature of 25 °C, as

$$E = E° + 59.16 \log[H^+] + E_j \qquad (1)$$

where $E°$ is constant in each series of measurements, and E_j is the liquid junction potential which is a function of $[H^+]$ only.[6] In a previous study, we have found[9] $E_j = -17[H^+]$ in 3 $mol \cdot dm^{-3}$ $NaClO_4$.

Each titration was divided in two parts. In the first part, $E°$ was determined in the absence of M^{z+} ions, and the acidity was decreased stepwise by coulometric generation of OH^- ions with the circuit (C)

$$-\text{Pt/Test Solution/AE}+ \qquad \text{(C)}$$

where AE, auxiliary electrode, = 3 M $NaClO_4$/0.1 M NaCl, 2.9 M $NaClO_4/Hg_2Cl_2/Hg$.

Assuming that the only reactions occurring at the cathode are $H^+ + e^- \rightarrow 1/2H_2$ and $H_2O + e^- \rightarrow 1/2H_2 + OH^-$, then in the Test Solution of a given volume V dm^3, $C_B = \mu F\ 10^{-6}/V$ $mol \cdot dm^{-3}$, where μF stands for the microfaradays passed through the cell.

In the second part, for the investigation of metal ion complexes, alkalification was achieved by adding NaOH.

The primary C_M, C_L, C_A, C_B, and $[H^+]$ data represent the basis of the treatment to obtain the equilibrium constants.

Table 1. Summary of the Relevant Data Taken in Four Titrations for the System L-Cystine$-Cu^{2+}$

C_M / $(mol \cdot dm^{-3})$	C_L / $(mol \cdot dm^{-3})$	pH_{range}
$1.5 \cdot 10^{-3}$	$1.5 \cdot 10^{-3}$	2.4 to 3.5
$2.5 \cdot 10^{-3}$	$5 \cdot 10^{-3}$	2.2 to 3.8
$0.5 \cdot 10^{-3}$	$5 \cdot 10^{-3}$	2.7 to 4.0
$4 \cdot 10^{-3}$	$2 \cdot 10^{-3}$	2.0 to 3.1

Results and Discussion

The general equilibrium can be written, schematically, for all four systems as eq 2

$$pM^{z+} + rH_2L \rightleftarrows M_pH_{-q}(H_2L)_r^{(zp-q)} + qH^+, \quad \beta_{pqr} \qquad (2)$$

The most probable p, q, and r values and the corresponding constants β_{pqr} were computed by a numerical approach based on the least-squares procedure using the program SUPERQUAD.[13] The minimum of the function $U = \Sigma w_i(E_{exp} - E_{calc})$ was sought, where w_i represents a statistical weight assigned to each point. Calculations of the chi-square statistic have been considered to test the fit between a theoretical frequency distribution and a frequency distribution of observed data.

In the numerical treatment, the equilibrium constants concerning the species formed according to equilibria 3 to 6 and determined in a previous work[3] have been maintained invariant

$$L^{2-} + H^+ \rightleftarrows HL^- \qquad \log K_1 = 9.50 \qquad (3)$$

$$HL^- + H^+ \rightleftarrows H_2L \qquad \log K_2 = 8.50 \qquad (4)$$

$$H_2L + H^+ \rightleftarrows H_3L^+ \qquad \log K_3 = 2.352 \qquad (5)$$

$$H_3L^+ + H^+ \rightleftarrows H_4L^{2+} \qquad \log K_4 = 1.960 \qquad (6)$$

The single systems were treated separately.

System L-Cystine$-Cu^{2+}$. The data comprise four titrations with 67 data points. A summary of the relevant data taken in all titrations si reported in Table 1.

The principal cationic hydrolysis product of Cu^{2+} has been established as $Cu_2(OH)_2^{2+}$ by several studies in 3 $mol \cdot dm^{-3}$ perchlorate media.[14] In this work, in the numerical treatment the equilibrium constants for this dominant hydrolysis product of the copper(II) ion were fixed because it is well-known from the literature.[15] The numerical evaluation started assuming the presence of only CuL (Model 1), but the standard deviation is higher than the experimental uncertainty. Various models were tested by adding one single species; the best agreement was obtained with the polynuclear complex $Cu_2(HL)^{3+}$ (Model 2) with a consequent diminution of the function U equal to 37 %. To confirm the presence of this species, it was further investigated at a ligand-to-metal ratio $C_M = 2C_L$.

An additional improvement was reached including in the previous model the species CuL_2^{2-} (Model 3); on the other hand, on adding the complex $Cu(HL)_2$ (Model 4), the fit is significantly improved. The various steps of calculations are illustrated in Table 2.

Table 2. Best Set of log $\beta_{pqr}(\sigma)$ for the System L-Cystine−Cu^{2+}

species	model 1	model 2	model 3	model 4
CuL	−3.4 ± 0.1	−3.48 ± 0.09	−3.57 ± 0.09	−4.4 ± 0.3
CuL_2^{2-}			−9.2 ± 0.3	−8.56 ± 0.09
$Cu(HL)_2$				−0.79 ± 0.06
$Cu_2(HL)^{3+}$		−1.4 ± 0.3	−1.46 ± 0.02	−1.44 ± 0.06
σ, mV	2.17	1.74	1.14	0.31
χ^2	48.22	45.36	23.39	10.25
U, mV^2	$3.0 \cdot 10^{2}$	$1.9 \cdot 10^{2}$	$8.01 \cdot 10^{1}$	5.76

The refined equilibrium constants are used to represent the distribution of copper(II) in the different species (Figure 2); this gives some confidence to the presence of such complexes.

System L-Cystine−Al^{3+}. The data comprise four titrations with 63 data points. A summary of the relevant data taken in all titrations is reported in Table 3.

Like many other cations, Al^{3+} can be hydrolyzed extensively to form solutions of mononuclear as well as polynuclear hydroxide complexes which can be stable indefinitely. In this work, we have considered the complexes $AlOH^{2+}$, $Al(OH)_2^{+}$, and $Al_3(OH)_4^{5+}$ which are the dominant hydrolysis products in our experimental conditions. The relative equilibrium constants were taken from the literature[15] and in the computational evaluation were invariant.

Model 1 considers only the presence of AlL^{+}, but the standard deviation was considerably high. The introduction of AlL_2^{-} (Model 2) lowers σ about five times. As no other species lowered the minimum, Model 2 was assumed as the best describing the data, also in consideration that the standard deviation (σ) is comparable with the experimental uncertainty. The various steps of calculations are illustrated in Table 4.

Using the values of the constants reported in Table 4 (Model 2), a distribution diagram was constructed (Figure 3).

As can be seen in Figure 3 when the analytical concentrations of ligand are greater than those of the metal, e.g., $C_L = 5 \cdot 10^{-3}$ $mol \cdot dm^{-3}$ and $C_M = 0.5 \cdot 10^{-3}$ $mol \cdot dm^{-3}$, AlL^{+} and AlL_2^{-} reach a significant percentage, and they are predominant over the hydrolysis product.

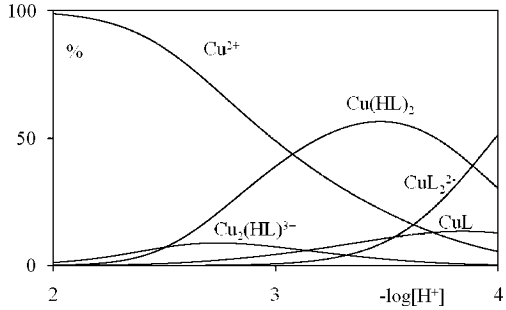

Figure 2. Distribution of the Cu(II) species in $C_L = 5 \cdot 10^{-3}$ $mol \cdot dm^{-3}$ and $C_M = 2.5 \cdot 10^{-3}$ $mol \cdot dm^{-3}$.

Table 3. Summary of the Relevant Data Taken in Four Titrations for the System L-Cystine−Al^{3+}

C_M ($mol \cdot dm^{-3}$)	C_L ($mol \cdot dm^{-3}$)	pH_{range}
$0.5 \cdot 10^{-3}$	$5 \cdot 10^{-3}$	2.5 to 4.5
$2 \cdot 10^{-3}$	$4 \cdot 10^{-3}$	2.3 to 5.2
$5 \cdot 10^{-3}$	$5 \cdot 10^{-3}$	2.2 to 4.8
$1.5 \cdot 10^{-3}$	$4.5 \cdot 10^{-3}$	2.4 to 5.0

Table 4. Best Set of log $\beta_{pqr}(\sigma)$ for the System L-Cystine−Al^{3+}

species	model 1	model 2
AlL^{+}	−6.88 ± 0.05	−6.97 ± 0.03
AlL_2^{-}		−14.73 ± 0.02
σ, mV	2.72	0.51
χ^2	22.27	10.00
U, mV^2	$1.7 \cdot 10^{2}$	5.68

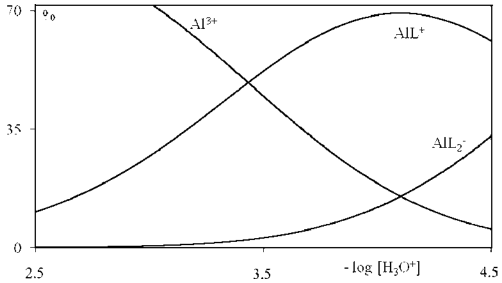

Figure 3. Distribution of the Al(III) species in $C_L = 5 \cdot 10^{-3}$ $mol \cdot dm^{-3}$ and $C_M = 0.5 \cdot 10^{-3}$ $mol \cdot dm^{-3}$.

Table 5. Summary of the Relevant Data Taken in Five Titrations for the System L-Cystine−Fe^{3+}

C_M ($mol \cdot dm^{-3}$)	C_L ($mol \cdot dm^{-3}$)	pH_{range}
$0.5 \cdot 10^{-3}$	$5 \cdot 10^{-3}$	1.5 to 3.5
$2 \cdot 10^{-3}$	$4 \cdot 10^{-3}$	1.3 to 3.2
$5 \cdot 10^{-3}$	$5 \cdot 10^{-3}$	1.2 to 3.0
$2.5 \cdot 10^{-3}$	$2.5 \cdot 10^{-3}$	1.2 to 3.2
$1.5 \cdot 10^{-3}$	$4.5 \cdot 10^{-3}$	1.4 to 3.3

Table 6. Best Set of log $\beta_{pqr}(\sigma)$ for the System L-Cystine−Fe^{3+}

species	model 1	model 2
FeL^{+}	−3.5 ± 0.1	−3.12 ± 0.04
FeL_2^{-}		−7.89 ± 0.08
σ, mV	0.44	0.26
χ^2	14.98	5.26
U, mV^2	23.89	8.12

System L-Cystine−Fe^{3+}. The experimental data consist of 76 data points collected in five titrations. A summary of the relevant data taken in all titrations is reported in Table 5.

The hydrolysis of the ferric ion, which begins at about pH = 1, was examined by Hedström[16] at 25 °C in 3 $mol \cdot dm^{-3}$ $NaClO_4$ using a calomel electrode in combination with glass and Fe^{3+}/Fe^{2+} electrodes. The results of this study have been widely quoted and have been confirmed by other authors.[14] The species $Fe(OH)^{2+}$, $Fe(OH)_2^{+}$, and $Fe_2(OH)_2^{4+}$ were identified by Hedström, and their formation quotients have been used in the numerical estimation of the equilibrium formation constants of the complexes between L-cystine and Fe^{3+}. Results of the calculations are reported in Table 6.

Model 1, which considers the presence of FeL^{+}, is the best model with only one species. The introduction of FeL_2^{-} (Model 2) lowered the minimum of the square error sum significantly, and the standard deviation (σ) is comparable with the experimental uncertainty. No other species, introduced to improve the fit, was retained. To visualize our results, the distribution diagram, reported in Figure 4, was constructed.

All the proposed species reach a concentration level of, at least, 30 % of the total metal; therefore, meaningful concentrations were obtained for a correct definition of the equilibrium constants.

Extrapolation to Infinite Dilution Reference State. The main conclusion of this work is that, concerning the complexation equilibria of L-cystine, H_2L, with the Cu^{2+}, Al^{3+}, and Fe^{3+} ions, the species CuL, CuL_2^{2-}, $Cu(HL)_2$ and $Cu_2(HL)^{3+}$, AlL^{+} and AlL_2^{-}, and FeL^{+} and FeL_2^{-} are formed in an appreciable amount in acidic solutions before the precipitation of basic salts. Modeling in natural systems requires the knowledge of the formation constants valid in the dilution reference state.

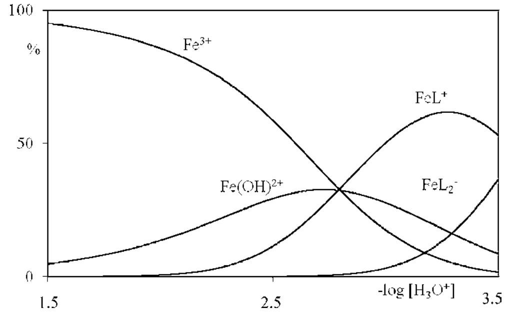

Figure 4. Distribution of the Fe(III) species in $C_L = 5 \cdot 10^{-3}$ mol·dm^{-3} and $C_M = 0.5 \cdot 10^{-3}$ mol·dm^{-3}.

Extrapolation to zero ionic strength was carried out by assuming the validity of the SIT.[4,5] To convert molar into molal quantities, the factor 1.166 (3 mol·dm^{-3} NaClO$_4$) was used.[14] According to the theory, the activity coefficient, γ_i, of the species i with charge z_i can be expressed at 25 °C in aqueous solutions as

$$\log \gamma_i = -z_i^2 D + \Sigma b(\mathrm{i,k}) m_k \quad (7)$$

where $D = 0.51(\sqrt{3.5})/(1 + 1.5(\sqrt{3.5}))$, and b is the specific interaction coefficient of i with species k of molality m_k. Interaction coefficients depend on the ionic strength, but the variation in the range $(0.5 \le I \le 3.5)$ m is sufficiently low that they may be assumed as constants. As a further simplification, interaction coefficients of ions with the same charge type are nearly zero.

According to equilibrium 2 and indicating with $°\beta_{pqr}$ the constant at zero ionic strength, the variation of the various equilibrium constants determined in this work can be expressed, for the system L-cystine−Cu^{2+}, as

$$\log °\beta_{121} = \log \beta_{121} + 2D - \log \gamma_{H_2L} + [b(\mathrm{CuL, NaClO_4}) + 2b(\mathrm{H^+, ClO_4^-}) - b(\mathrm{Cu^{2+}, ClO_4^-})] \cdot 3.5 \quad (8)$$

$$\log °\beta_{142} = \log \beta_{142} - 4D - 2 \log \gamma_{H_2L} + [b(\mathrm{CuL_2^{2-}, Na^+}) + 4b(\mathrm{H^+, ClO_4^-}) - b(\mathrm{Cu^{2+}, ClO_4^-})] \cdot 3.5 \quad (9)$$

$$\log °\beta_{122} = \log \beta_{122} + 2D - 2 \log \gamma_{H_2L} + [b(\mathrm{Cu(HL)_2, NaClO_4}) + 2b(\mathrm{H^+, ClO_4^-}) - b(\mathrm{Cu^{2+}, ClO_4^-})] \cdot 3.5 \quad (10)$$

$$\log °\beta_{211} = \log \beta_{211} - 2D - \log \gamma_{H_2L} + [b(\mathrm{Cu_2(HL)^{3+}, ClO_4^-}) + b(\mathrm{H^+, ClO_4^-}) - 2b(\mathrm{Cu^{2+}, ClO_4^-})] \cdot 3.5 \quad (11)$$

for the system L-cystine−Al^{3+} as

$$\log °\beta_{121} = \log \beta_{121} + 6D - \gamma_{H_2L} + [b(\mathrm{AlL^+, ClO_4^-}) + 2b(\mathrm{H^+, ClO_4^-}) - b(\mathrm{Al^{3+}, ClO_4^-})] \cdot 3.5 \quad (12)$$

$$\log °\beta_{142} = \log \beta_{142} + 4D - 2 \log \gamma_{H_2L} + [b(\mathrm{AlL_2^-, Na^+}) + 4b(\mathrm{H^+, ClO_4^-}) - b(\mathrm{Al^{3+}, ClO_4^-})] \cdot 3.5 \quad (13)$$

and for the system L-cystine−Fe^{3+}, as

$$\log °\beta_{121} = \log \beta_{121} + 6D - \log \gamma_{H_2L} + [b(\mathrm{FeL^+, ClO_4^-}) + 2b(\mathrm{H^+, ClO_4^-}) - b(\mathrm{Fe^{3+}, ClO_4^-})] \cdot 3.5 \quad (14)$$

$$\log °\beta_{142} = \log \beta_{142} + 4D - 2 \log \gamma_{H_2L} + [b(\mathrm{FeL_2^-, Na^+}) + 4b(\mathrm{H^+, ClO_4^-}) - b(\mathrm{Fe^{3+}, ClO_4^-})] \cdot 3.5 \quad (15)$$

The activity coefficient, γ_{H2L}, of L-cystine has been obtained as the ratio (solubility in water)/(solubility in 3.5 m NaClO$_4$) in a previous work.[3]

Some b(i,k) values, needed for the calculations, have been deduced from various sources. From ref 3, $b(\mathrm{L^{2-}, Na^+}) = 0.29$ and $b(\mathrm{HL^-, Na^+}) = 0.14$; from ref 4, $b(\mathrm{H^+, ClO_4^-}) = 0.14$, $b(\mathrm{Cu^{2+}, ClO_4^-}) = 0.32$; from ref 11, $b(\mathrm{Al^{3+}, ClO_4^-}) = 0.46$; and from ref 17, $b(\mathrm{Fe^{3+}, ClO_4^-}) = 0.56$. The b(i,k) values for the complexes of stoichiometry (1,2,1), (1,4,2), and (1,2,2) can be estimated on the basis of empirical rules, suggested by Ciavatta.[5] For the complex Cu$_2$(HL)$^{3+}$, the probable specific ion interaction coefficient is deduced from empirical rules derived from plausible structure of the species (Figure 5).

The short-range interaction of the complex with medium ions takes place in reduced amounts according to the accessible contact area. From the collected coefficient values, the interaction of the complexes with medium ions, accounting that the coordination of metal cations is six, should be: $b(\mathrm{Cu_2(HL)^{3+}, ClO_4^-}) = (2 \cdot 5/6) b(\mathrm{Cu^{2+}, ClO_4^-}) = 0.53$. The results of extrapolation are collected in Table 7.

The uncertainties assigned to the constants stem primarily from interaction coefficients of complexes, which are estimated as probable within (± 0.05 or ± 0.1) kg mol^{-1}.

Comparison with Literature Data. L-Cystine is poorly soluble in neutral aqueous media; therefore, studies on metal complex formation and even protonation equilibria of this amino acid have thus been seriously hampered. As a consequence, corresponding data available in the literature are rather limited. In

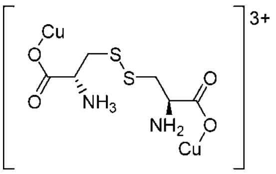

Figure 5. Plausible structure of the complex Cu$_2$(HL)$^{3+}$.

Table 7. Survey of the Formation Constants of the M^{z+}−H$_2$L Systems at 25 °C at the Infinite Dilution Reference State

log $°\beta_{pqr}$	Cu^{2+}	Al^{3+}	Fe^{3+}
log $°\beta_{121}$	-3.6 ± 0.2	-5.4 ± 0.1[a]	-1.7 ± 0.1
log $°\beta_{142}$	-8.9 ± 0.2	-13.4 ± 0.1	-6.8 ± 0.2
log $°\beta_{122}$	-1.1 ± 0.1	/	/
log $°\beta_{211}$	-2.6 ± 0.1	/	/

[a] The extrapolation at the infinite dilution reference state starting from the value obtained by Bohrer et al.[1] for this species is −8.0.

the case of the system L-cystine−Cu^{2+}, the available values were obtained at different temperatures,[18] i.e., 20 °C and 37 °C, and for this reason, it was not possible to make any comparison.

Stability constants for the Fe^{3+} complexes of L-cystine were not found in the literature, while for the system L-cystine−Al^{3+}, Bohrer et al.[1] have found, at 25 °C and in 0.01 M KCl, the following species: AlL^+, Al(OH)L, $Al(OH)_2L^-$, and $Al(OH)_3L^{2-}$. Due to the difference of the ionic medium, the comparison of the values for the only common species, i.e., AlL^+, has been made on the basis of extrapolated values of the equilibrium constant at the infinite dilution reference state (see Table 7). The remarkable difference between the values of the equilibrium constant for AlL^+ is likely due to the absence, in our experimental conditions, of any hydrolytic species, which are predominant in the pH range investigated by Bohrer. Instead, as can be seen in Figure 3, in our experimental conditions the AlL^+ complex is the predominant complex, and for this reason the equilibrium constant for this species is more stable.

Abbreviations Used

H_2L	L-cystine
M^{z+}	metal cation of charge $z+$
β_{pqr}	equilibrium constant for $pM^{z+} + rH_2L \rightleftarrows (M)_pH_q(H_2L)_r^{(zp-q)} + qH^+$
C_M, C_L, C_B, and C_A	molarity ($mol \cdot dm^{-3}$) of metal cations, L-cystine, NaOH, and $HClO_4$, respectively
b(i,k)	interaction coefficient between species “i” and “k”
γ_i	activity coefficient of species “i” on the molal scale
[i]	molar concentration of species “i”

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