Pure & Appl. Chem., Vol. 67, No. 7, pp. 1117–1240, 1995.
Printed in Great Britain.

INTERNATIONAL UNION OF PURE
AND APPLIED CHEMISTRY

ANALYTICAL CHEMISTRY DIVISION
COMMISSION ON EQUILIBRIUM DATA*

Critical Evaluation of

THE STABILITY CONSTANTS OF METAL COMPLEXES OF AMINO ACIDS† WITH POLAR SIDE CHAINS‡

(Technical Report)

Prepared for publication by

G. BERTHON

INSERM U305, Equipe "Bioréactifs: Spéciation et Biodisponibilité", 38 rue des Trente-six Ponts, F-31400 Toulouse, France

*Membership of the Commission during the period (1989–93) when this report was prepared was as follows:

Chairman: 1989–93 D. G. Tuck (Canada); *Secretary:* 1989–90 O. Yamauchi (Japan); 1990–93 T. Kiss (Hungary); *Titular Members:* A. C. M. Bourg (1989–91; France); A. Braibanti (1989–93; Italy); R. H. Byrne (1991–93; USA); L. H. J. Lajunen (1991–93; Finland); H. K. J. Powell (1989–91; New Zealand); O. Yamauchi (1990–91; Japan); *Associate Members:* R. H. Byrne (1989–91; USA); J. R. Duffield (1991–93; UK); B. Holmberg (1989–93; Sweden); S. Ishiguro (1989–93; Japan); T. A. Kaden (1989–93; Switzerland); S. H. Laurie (1989–93; UK); R. B. Martin (1989–93; USA); P. Paoletti (1989–93; Italy); R. Portanova (1989–93; Italy); S. Sjöberg (1989–93; Sweden); O. Yamauchi (1991–93; Japan); *National Representatives:* C. B. Melios (1991–93; Brazil); M. P. Zhang (1989–93; Chinese Chemical Society); P. Valenta (1989–93; FRG); L. H. J. Lajunen (1989–91; Finland); M. T. Beck (1989–91; Hungary); P. K. Bhattacharya (1989–93; India); M. C. Vaz (1991–93; Portugal); K. I. Popov (1989–93; USSR); L. D. Pettit (1989–91; UK); G. R. Choppin (1989–91; USA).

Names of countries given after Members' names are in accordance with the then prevailing *IUPAC Handbook.*

†Although IUPAC nomenclature recommends "aminocarboxylic acid", the expression "amino acid", more familiar to biochemists to whom this review is predominantly addressed, has been used throughout.

‡**Series Title: Critical Evaluation of Stability Constants of Metal Complexes in Solution**

TABLE OF CONTENTS

Critical evaluation of the stability constants of metal complexes of amino acids* with polar side chains (Technical report)

Abstract

Available experimental data on proton and metal complex equilibria of the seven essential amino acids with polar side chains (i.e. cysteine, cystine, methionine, serine, threonine, asparagine and glutamine) have been critically evaluated. First, the introduction outlines the main structural features of these amino acids as ligands and calls attention to their important roles in biology. A general discussion is also reported on the determination of formation constants and their reliability. In particular, the critical role played by protonation constants as reference parameters for the determination of complex formation constants by glass electrode potentiometry has been emphasized. Coordination enthalpies and entropies are also introduced, and the selection criteria employed in the course of the review are described.

For each of the seven amino acids, a specific chapter then reports (i) protonation constants and their associated enthalpic and entropic changes, (ii) formation constants for binary metal complex species and ternary mixed-ligand complexes with the associated thermodynamic quantities whenever available. For every entry, all data available in the literature are first reported. Then, a selection of recommended or tentative values is proposed for as many sets of specific experimental conditions as possible, in accordance with the criteria given in the introduction and based on considerations developed in corresponding discussions.

1. INTRODUCTION

1-1. Ligand structures and general properties

All of the seven amino acids considered in the present survey are found in proteins and are thus classified as essential. From the chemical point of view, all are optically active and include side chain groups likely to form a chelate ring with a metal ion bound at the α-amino nitrogen. The first three acids contain sulfur as an extra donor atom, each in a different chemical function: a β-thiol in cysteine, a ββ'-disulfide bridge in cystine, and a γ-thioether in methionine. Among the last four, both serine and threonine incorporate a β-hydroxy group whereas asparagine and glutamine include an amide function at their respective β and γ positions.

The above structural characteristics indicate that if these amino acids are to behave as tridentate ligands, cysteine and cystine as well as serine and threonine will form 5-membered chelate rings, methionine and asparagine 6-membered rings, and glutamine 7-membered rings. All other factors being equal, there is a known tendency for side chain chelation to weaken as ring size increases. One would thus a priori expect cysteine, cystine, serine and threonine to be tridentate while glutamine would coordinate metal ions in a glycine-like manner. We shall see later that the actual situation is not that simple, the nature of the side chain groups overriding such structural considerations to determine the coordinative properties of each amino acid (79M).

Concerning the biological role of these amino acids as ligands, cysteine is of particular importance because of the high affinity of its thiol group for soft metal ions. For example, to a challenge from toxic ions such as Cd^{2+}, Hg^{2+} and Pb^{2+}, the first response of the body consists in an increased synthesis of metallothionein by liver and kidney. This small metalloprotein has an exceptionally high content of sulfur, about one third of it being constituted of cysteine residues (83VK). A consequence of this is that metallothionein is also the metalloprotein with the highest known zinc content. In particular,

* Although IUPAC nomenclature recommends "aminocarboxylic acid", the expression "amino acid", more familiar to biochemists to whom this review is predominantly addressed, has been used throughout.

it is owing to the role of metallothionein in zinc homeostasis that this metal can now be used in the treatment of Wilson's disease (83HV). The high affinity of zinc ions for the thiol side group of cysteine will also explain that zinc-cysteine binary and ternary complexes take up a predominant position in the distribution of this metal into its low-molar-mass (l.m.m.) fraction in blood plasma (78BM).

A second reason why cysteine is of particular interest lies in the capacity of its thiol group to oxidise. For example, the ability of cysteine thiol groups to form disulfur bridges will largely contribute to the stabilisation of the three-dimensional conformation of proteins. Oxidation of the -SH group usually takes place in the presence of catalysts, these generally being transient cysteine complexes of various metal ions such as iron(III) and copper(II). From a practical point of view, this implies that if stable complexes are likely to be formed between a ligand and a metal ion in different oxidation states, it will be necessary to reckon with the parallel occurrence of acid-base and redox reactions (79GS). This, added to the propensity of sulfur atoms to give rise to polynuclear complexes, indicates the difficulty of investigating complex equilibria involving cysteine with many transition metal ions.

In comparison with cysteine, other amino acids examined in this review display a much simpler behaviour. With the other two thio-ligands for example, the ether sulfur of methionine is an extremely weak base undergoing protonation in strongly acidic solutions only (72BL). A priori, this weak basicity is not expected to favour coordination in general. According to the HSAB principle however, there is a known tendency for the soft sulfur donor to combine with soft metal ions, and most soft metal ions do effectively coordinate to the methionine thioether. This functional group has even been proposed as a test of "softness" (79M), even though the related effects are rather difficult to generalise (86M). Similarly, only marginal interactions are expected from the above principle between the methionine thioether and metal ions being classified as borderline, and NMR data have confirmed the small involvement of the thioether group in this case. In fact, methionine behaves as a substituted glycine towards most borderline as well as all hard metal ions.

The disulfide bond present in cystine is an even weaker base than the ether sulfur of methionine (73BL), which should predispose it still less to metal coordination. Nevertheless, its involvement in copper(II) coordination has been reported (63HP). From a general point of view, the poor solubility of cystine in neutral aqueous solutions has severely limited the investigation of its metal complex equilibria.

Whether they contain a hydroxy (serine and threonine) or an amide (asparagine and glutamine) side group, the four remaining amino acids largely behave as substituted glycines and bind most metal ions in a bidentate manner.

As far as the optical activity of the above ligands is concerned, it seems that, on the whole, stereoselectivity plays no significant role in the formation of their metal complexes (79PH).

1-2. Formation constants and reliability

In his introductory chapter to the present series of critical evaluations, Beck (77B) wrote that "users of stability data not familiar with this fairly large field may mistakenly conclude from widely diverging values that stability constants are not reliable in general". More recently, computer simulation modelling of the distribution of metal ions in biological fluids has been questioned on the basis that results for copper in blood plasma did not significantly coincide with corresponding experimental observations previously made on this biofluid (79YS, 81S). It was proved later (86BH) that this lack of coincidence actually stemmed from the poor reliability of the stability constants on which the initial models were built (71HP, 73PA, 77ML). Since this problem only involved copper complex equilibria with simple amino acids such as histidine, cystine, glutamine, threonine and serine, one realises what more serious risks of misinterpretations might affect simulations involving equilibria with more complicated ligands.

This illustrates once more the need for reliable stability constants to solve analytical problems such as those encountered in industrial and biological fields, and details of both experimental technique and computational strategy as well as of the experimental conditions under which they have been obtained constitute invaluable information to the well-informed user. For example, it frequently occurs that

several sets of constants give rise to almost identical goodness-of-fit parameters. In such cases, it is important to know by which criteria the "best" set has been selected. A better reliability will normally be expected from results tested on graphical grounds, usually by simulating experimental curves as they would have been obtained from corresponding analytical data in the hypothesis of each possible set (75CM, 84MM, 85MM). It is also important to know which species have been finally discarded, since these could become significant under different concentration conditions.

Easy to prevent though widely spread is the misuse of the so-called distribution curves showing the percentage of a given metal or of a given ligand as a function of pH *for given concentrations of metal and ligand*. This mode of representation is still nowadays considered too often by occasional users - even sometimes by coordination chemists- as an absolute feature of the system, and it may be worthwhile to recall that it should always be stressed by the authors of such curves that these are only pertinent to those reactant concentrations which are being taken into consideration under specific conditions.

In this respect, it should also be borne in mind that the total reactant concentrations on which these curves are based should preferably lie within the limits of the range used to determine the corresponding equilibrium constants. Indeed, outside of this range, some additional equilibria may have to be taken into account while others will become negligible (see above). Nowadays, most equilibrium studies are carried out over large ranges of reactant concentrations and concentration ratios, but these ranges always suffer inevitable limitations due to factors such as variations of activity coefficients for weak complexes, solubility problems, etc, and applications are by definition open to potentially larger regions than those experimentally investigated.

Before analysing equilibrium constants, two important points must be made clear which concern their mode and scale of representation. Formation constants may a priori be expressed in terms of activity or concentration quotients: (i) activity quotients are usually defined as (true) "thermodynamic" constants which are by definition independent of the ionic medium since they refer to the pure solvent taken as the reference state. This character of universality was long considered an advantage (70B), but since these ideal values must be extrapolated from curves which are far from linear or calculated by approximate semi-empirical equations, they are rather difficult to determine and hence do not actually offer a sound basis for reliability; (ii) concentration quotients are usually defined as "stoichiometric" constants. Although less than unity in this case, activity coefficients are kept invariant by the addition of high and constant concentrations of an inert background electrolyte, and reliable constants can be directly determined. Incidentally, these practical constants are also thermodynamic quantities since they refer to a standard state in which activity coefficients are unity at infinite dilution of the reactants in the particular salt medium selected. Generally speaking, it thus seems more desirable to obtain reliable values of stoichiometric constants -even of theoretically limited applicability- rather than less certain values of a priori more universal thermodynamic constants (61RR). In addition, thermodynamic constants never correspond, by definition, to any practical situation where an ionic medium is naturally present such as encountered in biological fluids, whereas stoichiometric constants specific to a given application can always be determined. For all these reasons, stoichiometric constants should systematically be preferred.

Because logarithmic quantities are non-dimensional, it is often forgotten that constant numerical values depend on the units in which activity terms are expressed, the molar concentration scale being the most commonly used. This remark may seem of minor importance, but it nonetheless implies that comparisons between logarithmic constants are permissible for complexes of equivalent stoichiometries only.

Even when this recommendation is satisfied, direct comparisons between formation constants may still be extremely misleading. This is especially the case when the ligands are protonated to different extents at the same pH values. For example, the ML complex of copper with the salicylate dianion will be much less concentrated at pH 7.4 than, say, the same ML species with the dianionic form of a dicarboxylic acid, whereas respective formation constants suggest the opposite (90BB). When simulation models are used to predict the distribution of such complexes, all these considerations are implicitly taken into account in the calculations. In simpler cases, however, approximate guesses should use the notion of conditional constants, which express complex concentrations with respect to ligand concentrations not bound to the metal.

1-3. Protonation constants as references

As pointed out by Pettit in a previous article in the present series of critical evaluations (84P), the pH range within which amino acids interact with protons is particularly suited for the use of proton-ligand equilibria as a reference for metal-ligand system investigations. Titrations in absence and presence of metal ions have thus long been a technique of choice for the determination of metal complex formation constants of amino acids. Unfortunately, frequent utilisation of the pH scale for glass electrode measurements -i.e. made by reference to buffer solutions- has led to a rather confused situation concerning the definition of protonation constants. In older studies especially, the need to establish metal, ligand and acid mass-balance equations in terms of concentrations was reconciled with the use of proton activities by expressing protonation constants in a "mixed" manner (69CP). For example, the protonation constant of a monobasic ligand L is represented by the [LH]/[L].{H} ratio in which [LH] and [L] concentrations are mixed with the proton activity {H}. Although this mode of representation should of course be avoided, it is still sometimes in use. In such cases, corresponding results must be redetermined in the concentration scale when reliable applications are needed.

Since the ligands examined in this survey are essential amino acids, particular emphasis will be placed on the applications of their complex stability constants to problems of biological relevance. In this respect, protonation constants are of high importance. Metal complex formation constants determined with reference to stoichiometric or mixed protonation constants will not vary to a significant extent since the systematic difference between the two standard states will be cancelled when subtracting the results of measurements made in presence and absence of metal. Yet, the simulated distribution of the corresponding metal complexes in a given solution may well be seriously biased (81AB).

In biological fluids indeed, amino acids are generally far more concentrated than the metal ions with which they form the most stable complexes. Under normal circumstances, metal-complexed fractions of these ligands are thus largely negligible with respect to their overall concentrations, which implies that their free concentrations depend almost exclusively on their interactions with protons. Small variations in free ligand concentrations caused by slightly different protonation constants determined with reference to distinct standard states may then entail important discrepancies in the distribution of metal complexes. Concentrations of metal complexes will indeed reflect these variations unevenly, the more so as complexes of high ligand-to-metal ratios as well as mixed-ligand species will usually be predominant (78BM, 80BM, 86BH).

Clearly, the use of stoichiometric protonation constants as references for determining stoichiometric metal complex formation constants should always be preferred. There remains the problem of choosing a calibration procedure. The oldest and most straightforward method consists of titrating a strong acid with a strong base or vice versa under the same experimental conditions (temperature, ionic strength, nature of the background electrolyte) as those used for determining stability constants. Provided that the concentrations of both acid and base are known with high precision, free concentrations of hydrogen as well as hydroxide ions can be calculated for each point of the titration curve. E.m.f.'s of the electrochemical cell comprising a glass electrode and a reference electrode can then be determined as a function of the -log[H] and -log[OH] values in acidic and basic ranges, respectively. The acidic curve will provide a suitable value for the apparent standard potential E° of the electrode pair. Both curves allow a check on the theoretical slope of the glass electrode, whereas their intersection point will yield $pK_w/2$ (72CB).

Of course, this technique suffers theoretical limitations. The main objection against its use is that pH ranges where such calibration curves are effectively linear rarely coincide with the interval experimentally investigated, especially for biological systems. For this reason, the new procedure known as internal calibration has recently gained increasing popularity (84LT). It basically consists in titrating a weak acid (or base) with a strong base (or acid), both electrode parameters and protonation constants being simultaneously calculated by appropriate computer programs for this titration. Actually, all parameters may be allowed to vary, including acid and base concentrations.

This new concept undoubtedly represents a real breakthrough in the theoretical approach to calibration of the glass electrode. Its application to practical problems may also be extremely fruitful. In particular, the facility it offers to optimise the ligand concentration may be of great help in increasing both precision and applicability of protonation constants, provided identical concentrations of ligand (and mineral acid if any) are then used in presence of metal. This facility is extremely valuable when concentration errors are very small, but its application may become hazardous if experimental data are less precise. In general, great care must be taken of the fact that the optimisation of too many variables inevitably leads to indeterminate answers. The use of such a technique thus actually requires more attention from the experimentalist than usual. In particular, it is advisable that ligands be independently titrated before their concentrations are submitted to automatic optimisation. Without particular care, this marvellous "tool" might turn into quite a redoubtable "weapon", and it should not be forgotten that the less difference between experimental and optimised data, the more reliable the corresponding results. It is to some extent rather reassuring to note that one must first rely on the quality of one's experimental work rather than on the "magic" of the computer.

1-4. Coordination enthalpies and entropies

The decomposition of stability constants into their enthalpic and entropic contributions is of fundamental importance to the understanding of the various factors (electronic and steric effects, solute-solvent interactions, etc) that may influence coordination. Enthalpy changes due to coordination reactions can always be obtained from the determination of stability constants at different temperatures according to the van't Hoff relationship

$$\mathrm{d}\log K/\mathrm{d}T = \Delta H/RT^2 .$$

However, reaction enthalpies derived from this approach are generally only approximate since (i) stability constant variations are often too low within the narrow range of temperature investigated to allow calculation of reliable slopes, and (ii) the extension of the temperature range is limited by the fact that enthalpy changes are temperature-dependent and that ΔC_p° values which would permit to correct them through the Kirchoff equation are not usually available. Enthalpy determinations from direct calorimetric measurements are thus highly preferable, the more so as the calculation of correlative entropy changes will accumulate errors from both constants and enthalpies.

1-5. Selection criteria

By taking the above comments into account, a number of criteria have been defined for evaluating stability constants and standard enthalpies and entropies.

The first point concerns the experimental conditions under which these quantities have been determined. Most investigations refer to the normal temperature of 25 °C, but a large number have been carried out at 20 °C while some have been performed at 37 °C. Ionic strength values are also very variable. Formation constants have thus been selected separately for different ionic strength values or intervals at 25 °C, 37 °C and 20 °C whenever possible.

In order to take account of the potential use of amino acid formation constants for biologically relevant applications, particular attention has been paid to the values obtained under physiological conditions (37 °C; I = 0.15 mol dm^{-3}). Among the ionic backgrounds employed, KNO_3 and $NaClO_4$ are not expected to induce significant differences in corresponding constants. However, the use of NaCl may result in distinct values, depending on the affinity of each metal for chloride ions. Concerning this problem, the use of an ionic medium whose anions are likely to form metal complexes on their own should be avoided if one wants to determine thermodynamically "pure" constants. Nevertheless, as biofluids incorporate sodium chloride as a natural constituent, "practical" constants determined in its presence may appear more realistic from the biological point of view. Values determined in sodium chloride solutions have thus been evaluated separately.

Whenever reliable average values could be calculated with a good precision from the results obtained by different authors, recommended (R) or tentative (T) stability constants and associated thermodynamic quantities have been proposed, depending on the reproducibility observed.

For metal complex binary systems, overall formation constants β will normally be expressed according to the general formula

$$\beta_{pqr}=[M_qL_pH_r]/[M]^q[L]^p[H]^r$$

in which the value of r is negative for hydroxo species. For example, the equilibrium

$$M^{2+} + L^{2-} + H_2O \Leftrightarrow MLOH^- + H^+$$

is represented by

$$\beta_{11-1} = [ML(OH)]/[M][L][H]^{-1},$$

with $\log \beta_{11-1} = \log \beta_{ML(OH)} - pK_w$.

Successive stability constants K may sometimes be more expressive than their overall counterparts. This is especially the case for protonation equilibria, whose constants will be expressed according to

$$K_r = \beta_{10r}/\beta_{10(r-1)}.$$

Finally, overall formation constants for mixed-ligand species will also be mentioned when available. They will correspond to the general formula

$$\beta_{pp'qr} = [M_qL_pX_{p'}H_r]/[M]^q[L]^p[X]^{p'}[H]^r$$

where X stands for the extra ligand.

In accordance with these definitions, the enthalpy and entropy changes collected in this review will refer to stepwise equilibria for protonation data, but to overall equilibria for all metal complexes.

2. CYSTEINE - $HSCH_2CH[NH_2]CO_2H$ (2-amino-3-mercaptopropanoic acid, LH_2)

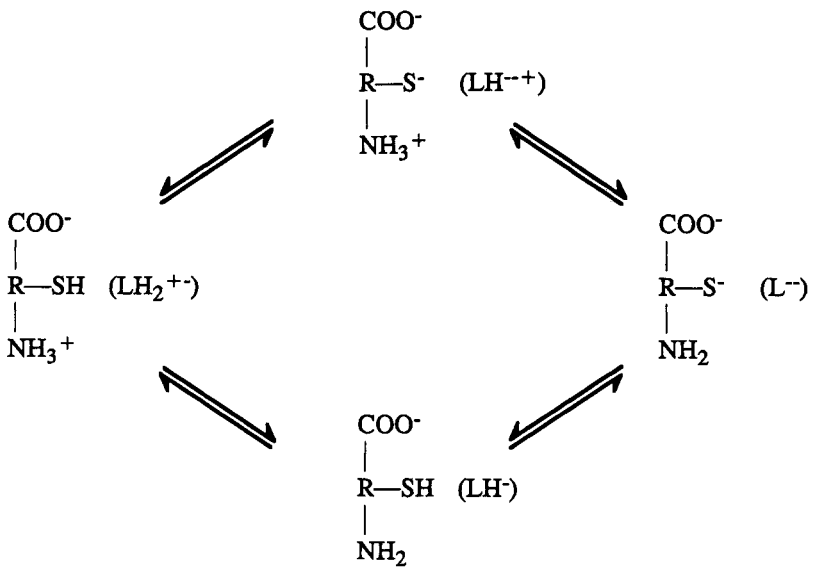
The fully protonated form of cysteine contains three dissociable protons. Clearly, the most acidic of these lies on the carboxylic group. By contrast, assigning the respective sites of the two most basic protonation steps is less straightforward since related constants result from intermingled microscopic processes (79GS). Corresponding microconstants can be determined by the joint use of potentiometric and spectroscopic (69CMa, 72JB, 74WL, 85BC) or calorimetric (64WI) techniques, or through the determination of macroconstants of appropriate chemical derivatives (44RS, 55GN).

With three ionisable protons, cysteine will naturally be prone to protonated complex formation. Moreover, the size of the sulfur atom of its thiol group will facilitate the formation of polynuclear complexes. Both tendencies are confirmed by the following observations.

2-1. Protonation constants of cysteine

The relatively high value of the most basic protonation constant of cysteine ($\log K > 10$) makes its accurate determination difficult since a significant fraction of the protonation curve lies in the pH range where the glass electrode response becomes less reliable. Attempts to correct related systematic deviations have been made (85MM), but the use of optimisation processes to improve electrode data (85MMa) in a range where the repercussion of ligand and acid concentration errors is a maximum may also be hazardous. Similar uncertainties are likely to affect the constant of the most acidic protonation step ($\log K < 2$) since the use of high total concentrations of mineral acid to reach the largest possible protonation numbers may entail significant variations in the ionic strength. For this reason, this constant has often been omitted in the determinations reported in the literature.

The most striking feature of cysteine protonation lies in the difficulty to assign the donating groups involved in its two most basic equilibria. Its mode of ionisation between the two microprocesses described in the following scheme



has been discussed for several decades (44RS, 51SK, 55BB, 55GN, 62EE, 64WI, 65D, 69CM, 69CMa, 72JB, 79GS, 79PB, 85BC). It is now generally accepted that proton ionisation occurs simultaneously from the SH and NH_3^+ groups, but the extent to which LH^{-+} and LH^- individually contribute to the whole equilibrium is all the more difficult to determine as the ratio of their respective concentrations has not only been shown to lie near unity (44RS, 55GN, 72JB), but also to reverse depending on the ionic strength (64WI).

Fortunately, this uncertainty does not affect the precision of the macroconstants to which the determination of metal complex formation constants refers, but one of its undesirable consequences is that some of the constants collected earlier may be misleading. According to Sillén and Martell's tables for example (64SM), references 55TK, 53SK and 44RS are expected to report $\log K_1$ and $\log K_2$ values equal to 10.51 and 8.60, respectively. These values in the corresponding articles actually refer to the microconstants relative to the individual formation of LH^-, as deduced by Rycklan and Schmidt (44RS) from the macroconstants published by Borsook, Ellis and Huffman (37BE) and from their own determinations on homocysteine.

Literature values for the macroconstants are given in Table 2-1. Thermodynamic constants determined at 25 °C in references 37BE, 64WI and 69CM are close to one another, and a recommended value has been calculated. In contrast, no such agreement is observed in mixed constants obtained at 25 °C although the two sets determined at 20 °C and I = 0.1 mol dm^{-3} are quite similar (65D, 68PS) and have been used to propose tentative average values. Tentative values have also been calculated for stoichiometric constants determined at 25 °C in 3.0 mol dm^{-3} $NaClO_4$ (72GW, 76BH), although related $\log K_2$ values differ to a surprising extent.

Concerning the determinations made at 37 °C, mixed constants (71HP) have logically (79ZJ, 81AB, 82BK, 84BP) been found about 0.1 larger than stoichiometric ones (78BM, 80AM, 85CF, 88GG), which roughly corresponds to the correction of 0.12 used by Martell and Smith in their constant tables (74MS, 82MS, 89SM). A fair agreement has been found between stoichiometric values in spite of different background salts (78BM, 80AM, 85CF, 88GG). A recommended average has thus been calculated. Recommended and tentative values for the protonation constants of cysteine are given in Table 2-2.

2-2. Thermodynamic quantities for the protonation of cysteine

Publications reporting determinations of enthalpy and entropy changes for the protonation of cysteine are relatively numerous. Among the seven available (64WI, 66WS, 69CM, 71MB, 72GW, 83BV, 89RF), three refer to the van't Hoff equation, in the 25-45 °C range in one of these (83BV), and between 5 and 95 °C in another, so that particular thermodynamic quantities have been calculated at

25, 50 and 75 °C (69CM). The application made at 30 °C (66WS) seems particularly dubious, as is the case in reference 88MA whose results have been discarded. The other four studies are based on calorimetric measurements (64WI, 71MB, 72GW, 89RF) and should thus a priori be considered more reliable. However, only 64WI, 72GW and 89 RF seem to correspond to the expected standards.

All these values can be seen in Table 2-3, where the subscripts relative to thermodynamic functions correspond to those employed for the stepwise stability constants shown in Tables 2-1 and 2-2.

2-3. Metal complex formation constants

Available overall stability constants for the formation of cysteine metal complexes are reported in Table 2-4. Some of these deserve some comments.

The different experimental conditions used for investigating Cd^{2+}-cysteine equilibria do not allow any comparison among available results. Moreover, the data obtained by polarography in 82NA did not take cysteine protonation into account and have thus been discarded. Consequently, the only reliable constants in this system are those determined at 37 °C (85CF), which have been proposed as tentative (Table 2-5).

The case of Co^{2+} complexation is similar since studies relative to identical temperatures (52A, 65D and 83HS, 83KP) refer to different ionic strengths. Acceptable agreement is observed between constants obtained at 20 °C, especially for ML_2 (52A, 65D). However, these data are far from being corroborated by a more recent study (83HS) in which formation of the polynuclear complexes -also suggested in 83KP- has been taken into consideration, and whose results are thus expected to be more reliable.

A huge discrepancy affects the constants for Cu^{+} complexes (51SKa, 78BK). NH_3 may interfere with the polarographic determinations reported by Stricks and Kolthoff (51SKa), but it is unlikely that it can account for such a large difference. Redox problems are thus to be suspected. No complex could be obtained with the Cu^{2+} form due to its reduction into Cu^{+}, cysteine being simultaneously transformed into cystine. In this respect, it must be noted that Sillén and Martell's Tables (71SM) mistakenly report for Cu^{2+}-cysteine complexes stability constants which actually correspond to those for Cu^{2+}-cystine. The same remark also holds for protonation constants in the same reference (63HP).

There is no agreement among different authors on Hg^{2+} complex stability constants (53P, 53SK, 64LM, 79ZN). Even the related complex stoichiometries vary depending on the above sources. It is also surprising that determinations on this system are so few, given the environmental and biological implications of mercury. Nevertheless, it must be noted that the various organic mercurials which result from the assimilation of this metal by living organisms are more toxic than Hg^{2+} ions (88M). Accordingly, stability constants of cysteine complexes with aryl (76HS) and alkyl (76HS, 78NM, 81JI, 81RR, 83AC) mercury have been determined. For methylmercury, the values in 76HS, 81JI, 81RR and 83AC relative to different ionic strengths are of the same order of magnitude and are thus to be considered as acceptable.

Nickel-cysteine complex equilibria have been investigated by several groups of authors. Acceptable agreement can be noted for the ML_2 constant between the most recent results obtained at 20 °C (20.18 ± 0.03 for references 65D and 68PS), but none is observed at 25 °C (19.5 ± 0.5 for references 56WM, 64LM, 72RJ and 79SG). The formation of ML_2 from ML is more favourable than that of ML from hydrated Ni^{2+} ions, so ML is a minor species at almost all concentrations. This explains the large uncertainty affecting its constant. The existence of M_2L_3 and M_3L_4 polynuclear complexes seems likely, but the distinct experimental conditions used by the different groups of authors who mention this possibility (68PS, 79SG, 85CF) makes impossible any estimation of realistic average values. The three corresponding sets of constants have thus been proposed as tentative (Table 2-5).

For lead-cysteine determinations, the large scale of experimental conditions used precludes any systematic comparison except for the 3.0 mol dm^{-3} $NaClO_4$ medium at 25 °C (73CT, 76CW, 76CWa). The constant found for ML under these conditions is fairly reproducible (13.18 ± 0.03) between two of the above studies (73CT, 76CWa), but there seems to be a misprint in the third (76CW) where log β_{ML} is reported as 12.213 (instead of 13.213?). Moreover, there is no agreement about the stoichiometries of other possible species, although all three investigations have been performed by the

same group of authors. The very important stability of ML with respect to ML_2, which gives the formation curve its particular shape (73CT), is probably at the origin of these discrepancies. It is also worth noting that no polynuclear complex has been mentioned. No set of constants has finally been selected.

Zinc(II)-cysteine complexes have been the most extensively investigated. As is the case with nickel, the formation of ML is less favourable than that of ML_2, and so the corresponding constant cannot be determined with precision. Results of studies considering simple mononuclear species only, which also happen to differ significantly from one another, must be discarded. By contrast, most of those relative to studies mentioning the existence of acidic and polynuclear species are much more reliable (68PS, 71HP, 76CW, 78BM, 79SG, 85CF), especially as far as ML_2 (17.9 ± 0.1 at 37 °C for example), ML_2H and M_3L_4H are concerned. The main discussion still concerns the coexistence of M_2L_3 and M_3L_4 and their respective acidic counterparts, although the second alternative seems more likely (78BM). There is also no general accord about the coexistence of MLH, ML_2H and ML_2H_2, though independently characterised by two groups of authors (78BM, 79SG).

In spite of these remaining uncertainties, all of the six above-mentioned studies agree on the essentials, and there is only one work (80AM) strikingly at variance with this common position. Surprisingly, not only does Arena et al.'s study at 37 °C (80AM) report a constant for ML_2 much lower than the above average, but it also mentions a constant for M_2L_3 nine orders of magnitude below the corresponding values obtained in 78BM, 85CF and 79SG (the latter referring to 25 °C). More than that, it is the only one to report an accurate log β_{ML}, but much larger than log K_2 (= log β_{ML_2} - log β_{ML}), while sulphur-containing ligands are well known to be prone to give the sequence log β_{ML} < log K_2 in their metal complexes. At the very least, these results, as well as their accompanying comments on the validity of earlier blood plasma simulation models (71HP, 78BM), should thus be considered with extreme caution.

To conclude on zinc(II)-cysteine complex equilibria and except for the case just treated, it is very difficult to select objectively a particular set of constants from which average values can be derived. For this reason, we do not propose any other choice than 17.9 for log β_{ML_2}, which is after all the most relevant constant for quantitative biological applications involving this system.

Determinations reported in Table 2-4 for cysteine binary complexes with other metal ions are too restricted to allow significant comparisons or to suggest useful comments.

Table 2-6 reports overall formation constants for mixed-ligand complexes involving cysteine. All the values determined at 25 °C are due to the same group of authors (74RM, 74RMa, 75RM). The MLX constant relative to the zinc(II)-cysteine-citrate system has not been confirmed by a more recent study (78BM) in which no ternary complex could be characterised. The latter finding is substantiated by the fact that the statistical combination of parent binary constants leads to a value situated about four orders of magnitude below the constant reported by Ramamoorthy and Manning (74RMa). This casts doubt on all the results obtained by this group, which should thus be considered with caution.

A large number of formation constants have been determined at 37 °C for mixed-ligand complexes of zinc(II) involving cysteine. This stems from the fact that cysteine is definitely *the* main l.m.m. ligand of zinc(II) in human blood plasma (78BM). Among these results, fair agreement is to be noted between the constants reported by two groups of authors for the MLX and MLXH main species in the zinc(II)-cysteine-histidine system (71HP, 81ABb), MLX_2H being definitely minor (81ABb). It is remarkable that no MLX complex could be found in the zinc(II)-cysteine-glycine and zinc(II)-cysteine-lysine systems (81ABa, 81ABb). Apart from the known poor ability of glycine -and hence of glycine-like amino acids- to give rise to ternary coordination with other aliphatic ligands (72GS), ligand-ligand interactions may also be at the origin of such a priori unexpected results. The stereospecific effect brought to light in the zinc(II)-histidine-threonine system, which will be developed in the threonine chapter, is of particular interest in this respect (81ABa, 81G).

2-4. Thermodynamic quantities for metal complex formation with cysteine

Determinations of thermodynamic quantities relative to the formation of metal cysteine complexes are extremely scarce. In particular, no calorimetric study has been performed on any of the corresponding equilibria. Table 2-7 reports the only available data thus obtained from the van't Hoff equation, among which the values from 76CWa appear to be the most reliable.

Table 2-1. Protonation Constants of Cysteine

Type of constants	Medium (mol dm^{-3})	Temp. (°C)	log K_1	log K_2	log K_3	Ref.
Mixed	0.02	30	10.28	8.18	1.96	27CK
	0.1	10.34	8.14	1.86		
Thermo	0.02-0.18	25	10.78	8.33	1.71	37BE
Thermo	0.01	20	10.28	8.36	1.96	52A
Thermo	0.01	20	10.53	8.53	-	53P
Mixed	0.15 NaCl	25	10.40	8.30	-	55GN
Mixed(?)	0.15 KNO_3	25	10.55	8.48	-	55LM
Mixed	0.1 KCl	25	10.42	8.27	-	56G
Stoichio	0.1 KNO_3	25	10.11	8.13	-	64LM
Thermo	0.02-1.00	25	10.76	8.39	-	64WI
Mixed	0.16 KNO_3	25	10.36	8.21	-	65CM
Mixed	0.1 $NaClO_4$	20	10.472	8.308	1.881	65D
Mixed(?)	0.3	30	10.37	8.15	-	65FC
Mixed(?)	0.1 KCl	30	10.47	8.15	-	66WS
Mixed	0.1 $NaClO_4$	20	10.498	8.335	~2	68PS
Thermo	0.01	5	11.20	8.84	-	69CM
	15	10.89	8.58	-		
	25	10.70	8.37	-		
	35	10.50	8.17	-		
	45	10.34	7.98	-		
	55	10.23	7.85	-		
	65	10.08	7.69	-		
	75	9.93	7.52	-		
	85	9.85	7.38	-		
	95	9.76	7.28	-		
Mixed(?)	0.1 $NaClO_4$	30	10.56	8.27	1.65	70RS
Mixed	0.15 KNO_3	37	10.23	8.07	(1.90)	71HP
Mixed(?)	? $NaClO_4$	20	9.88	7.95	1.90	72GP
Stoichio	3.0 $NaClO_4$	25	10.709	8.784	2.44	72GW
-	-	25	10.25	8.25	-	72JB
Mixed(?)	0.1 KCl	25	10.361	8.178	1.896	72RJ
Mixed(?)	0.2 KNO_3	15	10.53	8.44	2.25	73SR
		25	10.36	8.27	2.28	
		40	10.10	7.99	2.32	
Mixed(?)	0.5(?)	room t	10.48	8.48	2.02	74WL
Mixed(?)	0.5 $NaClO_4$	25	10.55	8.48	1.96	75ZK
Stoichio	3.0 $NaClO_4$	25	10.68	8.64	2.36	76BH
Mixed(?)	?	22	-	8.17	-	76HS
Stoichio	0.1 KNO_3	21	10.42	8.36	2.06	76KS
Stoichio	0.15 $NaClO_4$	37	10.110	7.968	1.972	78BM
Stoichio	0.1 KCl	25	10.87	8.20	1.97	79PB
	16.3% acetonitrile	25	10.67	8.38	2.20	
	34.2% acetonitrile	25	11.00	8.47	2.39	
	53.9% acetonitrile	25	11.33	8.66	2.73	
Mixed	0.15 KNO_3	37	10.21	8.04	-	79ZJ
Stoichio	0.15 $NaClO_4$	37	10.04	7.91	1.81	80AM

cont'd

Values in parentheses are estimates.

Table 2-1. Protonation Constants of Cysteine (continued)

Type of constants	Medium (mol dm^{-3})	Temp. (°C)	log K_1	log K_2	log K_3	Ref.
Mixed(?)	0.1 $NaClO_4$	20	10.750	8.900	2.974	80SD
		35	10.050	8.350	2.365	
		45	10.000	8.255	2.128	
	0.25 $NaClO_4$	20	10.400	8.850	2.535	
		35	10.025	8.325	2.137	
		45	9.950	8.250	1.980	
	0.50 $NaClO_4$	20	10.350	8.775	2.485	
		35	9.855	8.250	1.984	
		45	9.750	8.150	1.879	
	1.0 $NaClO_4$	20	10.300	8.675	1.962	
		35	9.850	8.225	1.533	
		45	9.725	8.100	1.530	
Stoichio	1.0 $NaNO_3$	25	10.15	8.12	1.90	81JI
Mixed(?)	0.1 $NaClO_4$	25	10.36	8.35	1.71	81MC, 84MCb
Stoichio	1.0 $NaClO_4$	25	10.19	8.25	2.09	82BC
Stoichio	0.5 $NaClO_4$	25	10.10	8.15	1.85	82N
Stoichio	0.1 KNO_3	25	10.552	8.244	-	82NM
Mixed	0.1 $NaClO_4$	50	10.36	7.91	1.90	82VN
Mixed	0.1 KNO_3	25	10.37	8.23	1.98	83AC
Mixed	0.1 KCl	26	10.5	8.25	-	83BA
Mixed(?)	0.1 $NaClO_4$	25	10.70	8.37	-	83BV
		35	10.50	8.17	-	
		45	10.34	7.98	-	
Stoichio	0.2 KCl	25	10.16	8.10	1.86	83HS, 88SK
Stoichio	0.1 KNO_3	25	-	8.244	2.308	83NM
Mixed(?)	0.1 KNO_3	15	10.45	8.15	-	84ID
		30	10.35	8.10	-	
Stoichio	0.5 $NaClO_4$	25	10.407	8.286	-	85BC
Stoichio	0.15 NaCl	37	10.102	7.928	1.962	85CF
Mixed(?)	0.1 $NaClO_4$	25	10.75	8.95	2.96	85SN
		35	10.06	8.35	2.35	
		45	10.00	8.26	2.13	
	0.25 $NaClO_4$	25	10.40	8.84	2.53	
		35	10.02	8.33	2.14	
		45	9.95	8.25	2.13	
	0.5 $NaClO_4$	25	10.37	8.77	2.50	
		35	9.85	8.25	1.98	
		45	9.75	8.15	1.88	
	1.0 $NaClO_4$	25	10.35	8.67	1.96	
		35	9.85	8.22	1.53	
		45	9.72	8.10	1.53	
Mixed(?)	1.0 $NaNO_3$	25	10.26	8.07	2.02	88BA
Stoichio	0.15 NaCl	37	10.068	7.911	1.817	88GG
Mixed	0.1 KNO_3	25	10.15	8.16	-	89S

N.B. Other references consulted but rejected: 74PN, 85KR.

Table 2-2. Recommended (R) and Tentative (T) Values for Protonation Constants of Cysteine

Type of constants	Medium (mol dm^{-3})	Temp. (°C)	log K_1	log K_2	log K_3	Ref.
Thermo (R)	0	25	10.75 (±0.05)	8.36 (±0.03)	1.71	37BE, 64WI, 69CM
Mixed (T)	0.1	20	10.48 (±0.01)	8.32 (±0.01)	1.94 (±0.06)	65D, 68PS
Stoichio (T)	3.0 $NaClO_4$	25	10.69 (±0.02)	8.71 (±0.07)	2.40 (±0.04)	72GW, 76BH
Stoichio (R)	0.15	37	10.08 (±0.04)	7.93 (±0.04)	1.89 (±0.08)	78BM, 80AM, 85CF, 88GG

Table 2-3. Thermodynamic Quantities for Cysteine Protonation Equilibria

Method	Medium (mol dm^{-3})	Temp. (°C)	$\Delta H°_1$	$\Delta H°_2$	$\Delta H°_3$ (kJ mol^{-1})	$\Delta S°_1$	$\Delta S°_2$	$\Delta S°_3$ (J K^{-1} mol^{-1})	Ref.
Cal.	→0	25	-34.3	-36.0	-	91.6	39.7	-	64WI
Pot.	0.1 KCl	30	-22.6	-28.9	-	126.0	60.7	-	66WS
Pot.	~0.01	25	-35.1	-35.1	-	87.0	42.2	-	69CM
		50	-29.3	-33.5	-	105.8	47.7	-	
		75	-24.3	-31.8	-	121.7	52.3	-	
Cal.	~0	20	-35.9	-32.2	-				71MB
Cal.	3.0 $NaClO_4$	25	-40.4	-38.8	-1.4	69.5	38.0	50.6	72GW
Pot.	0.1 $NaClO_4$	25	-32.6	-35.6	-	95.0	40.6	-	83BV
Cal.	~0	25	-37.8	-29.2	-2.3	79.5	61.3	25.1	89RF, 89R

(Pot. = potentiometry; Cal. = calorimetry)

Table 2-4. Overall Formation Constants for L-Cysteine Metal Complexes

Metal ion	Method	Medium (mol dm^{-3})	Temp. (°C)	Complex	log β	Ref.
Ag^+	Ag el.	1.0 $NaNO_3$	25	ML	14.00	76ZN
Al^{3+}	Gl.	0.1 $NaClO_4$	25	ML	6.43	74RM
Au^+	Sol.	-	25	ML.LH/ ML_2.H	2.68	79SSb
	NMR	pH 7	-	ML.H/ LH.M	24.18	86LS
				$ML_2.H^2$/ $(LH)^2$.M	28.48	
	Gl.	0.15 KNO_3	20	ML	11.11	79ZJ
			37		12.04	
Au^{3+}	Gl.	0.1 KNO_3	15	ML	14.85	84ID
			30	ML	14.85	
Be^{2+}	Gl.	0.1 KNO_3	15	ML	12.50	84ID
				ML_2	20.00	
			30	ML	12.35	
				ML_2	19.75	
Bi^{3+}	Sp.	0.5 $NaClO_4$	25	MLH	22.38	82N
				ML_2H_2	40.96	
Ca^{2+}	Gl.	0.1 $NaClO_4$	20	ML	2.50	65D
	Gl. (DL-)	0.1 $NaClO_4$	25	ML	1.92	75RM
Cd^{2+}	Pol.	0.15 KNO_3	25	precipitate		55LM
	Pol.	0.2 (phosphate buffer)	25	ML	9.89	66SP
	Gl.	3.0 $NaClO_4$	25	ML	12.875	74WW
				ML_2	19.627	
	Gl. (DL-)	0.1 $NaClO_4$	25	ML	6.45	75RM
	Gl.	0.5 $NaClO_4$	25	ML	(~)8.65	75ZK
				ML_2	(~)14.20	
	Gl.	0.15 $NaNO_3$	25	ML_2H_2	24.58	79ZN
	Gl.	0.15 NaCl	37	ML	10.3	85CF
				MLH_{-1}	2.42	
				ML_2	16.92	
				ML_2H	24.97	
				ML_2H_2	30.93	
				ML_3	19.78	
				ML_3H	29.21	
	Gl.-Cd el.	1.0 $NaNO_3$	25	ML	12.82	88BA
				ML_2	21.72	
				ML_3	27.52	
	DPP	-	-	ML_2	15.3	89WZ
Ce^{3+}	Gl.	→0	20	ML	6.379	80SD
				ML_2	12.567	
			35	ML	6.198	
				ML_2	12.297	
			45	ML	6.005	
				ML_2	11.900	

cont'd

Table 2-4. Overall Formation Constants for L-Cysteine Metal Complexes (continued)

Metal ion	Method	Medium (mol dm^{-3})	Temp. (°C)	Complex	log β	Ref.
	Gl.	0.1 KNO_3	15	ML	13.50	84ID
				ML_2	20.50	
			30	ML	13.40	
				ML_2	20.30	
Co^{2+}	Gl. (DL-)	0.025	20	ML	8.8	52A
				ML_2	16.2	
	Gl.	0.1 $NaClO_4$	20	ML	8.46	65D
				ML_2	16.13	
	Gl.	0.2 KCl	25	ML	8.00	83HS
				ML_2	14.20	
				M_2L_3	26.34	
				M_3L_4	37.98	
				M_3L_4H	43.74	
	Gl.	0.1 $NaClO_4$	25	M_2L_3	27.5	83KP
Co^{3+}	Gl. (DL-)	0.040	20	ML	9.3	52A
				ML_2	16.9	
Cr^{2+}	Gl. (DL-)	-	25	ML	9.77	70FMa
Cr^{3+}	Gl.	0.1 $NaClO_4$	25	ML	8.32	81MC, 84MCb
				ML_2	16.01	
				ML_3	22.95	
	Sp.	0.1 $NaClO_4$	25	ML	8.05	81MC, 84MCb
				ML_2	15.50	
				ML_3	21.82	
	Gl.	0.1 $NaClO_4$	50	MLH	18.33	82VN
				ML_2H	31.83	
				ML_2H_2	35.90	
				M_2L_3	44.49	
Cu^{+}	Pol.	1.0 NH_4Cl	25	ML	19.19	51SKa
	Sp.	1.0	20	ML	11.38	78BK
Cu^{2+}	Pol.	0.17 (phosphate buffer)	25	ML_2	16.0	61KP
NB: Constants in ref. 71SM on Cu^{2+}-cysteine (63HP) actually refer to Cu^{2+}-cystine						
Dy^{3+}	Gl.	0.1 KCl	20	ML	5.0	74PN
	Gl.	→0	20	ML	8.625	80SD
				ML_2	15.625	
			35	ML	8.500	
				ML_2	15.425	
			45	ML	8.325	
				ML_2	15.150	
Er^{3+}	Gl.	→0	20	ML	8.000	80SD
				ML_2	15.790	
			35	ML	7.885	
				ML_2	15.464	
			45	ML	7.755	
				ML_2	15.240	

cont'd

Table 2-4. Overall Formation Constants for L-Cysteine Metal Complexes (continued)

Metal ion	Method	Medium (mol dm^{-3})	Temp. (°C)	Complex	log β	Ref.
Eu^{3+}	Gl.	→0	20	ML	7.525	80SD
				ML_2	14.050	
			35	ML	7.475	
				ML_2	13.975	
			45	ML	7.350	
				ML_2	13.800	
Fe^{2+}	Gl. (DL-)	0.025	20	ML	6.2	52A
	Sol.	→0	25	ML_2	11.77	55TK
				MLH_{-1}	-1.23	
	Gl.	0.1 $NaClO_4$	20	ML	6.66	65D
				ML_2	12.16	
Fe^{3+}	Sol.	→0	25	ML_3	32.01	55TK
				ML_2H_{-1}	19.30	
	Gl.	0.15 KNO_3	20	ML	10.85	79ZJ
				ML_2	14.49	
			37	ML	10.63	
				ML_2	14.01	
Ga^{3+}	Gl.	3.0 $NaClO_4$	25	ML	16.1	76BH
				M(LH)	8.3	
				$M(LH_2)$	2.4	
Gd^{3+}	Gl.	0.1 KCl	20	ML	4.7	74PN
	Gl.	→0	20	ML	7.950	80SD
				ML_2	15.075	
			35	ML	7.825	
				ML_2	14.900	
			45	ML	7.700	
				ML_2	14.700	
Hg^{2+}	Gl. (DL-)	0.025	20	ML	20.5	53P
	Pol.	0.1 KNO_3	25	ML_2	43.57	53SK
				ML_2H	54.37	
				ML_2H_2	61.79	
	Gl.	0.1 KNO_3	25	ML	14.21	64LM
	Hg el.	0.1 $NaNO_3$	25	$M(LH)_2$	39.4	73VB
	Gl.	0.15 $NaNO_3$	25	ML_2H_2	54.92	79ZN
	Hg el.	-	25	ML	37.8	81BC
				ML_2	44.0	
				$M(LH)_2$	38.3	
	Gl.	1.0 KNO_3	25	ML_2	41.80	83DQ
			38	ML_2	41.20	
	Gl.	0.1 $NaNO_3$	25	$(ML_2)H$	8.94	85S
				$(ML_2)H_2$	16.31	
CH_3Hg^{II}						
	Gl.	0.1	25	ML	15.7	61S
	NMR	-	25	MLH(H)	1.95	75RF
				ML(H)	9.05	
	Gl.	-	22	M(LH)	7.19	76HS
				ML(H)	8.92	
				ML(M)	5.96	
	Liq. Part.	1.0 HNa,Cl	25	ML^*	1.71	78NM

cont'd

Table 2-4. Overall Formation Constants for L-Cysteine Metal Complexes (continued)

Metal ion	Method	Medium (mol dm^{-3})	Temp. (°C)	Complex	log β	Ref.
	Gl.	1.0 $NaNO_3$	25	ML	15.70	81JI
				MLH	24.96	
	Gl.	0.3 KNO_3	25	ML	16.67	81RR
				MLH	25.68	
	Gl.	0.1 KNO_3	25	ML	16.46	83AC
				MLH	25.48	
$C_2H_5Hg^{II}$						
	Liq. Part.	1.0 HNa,Cl	25	ML*	1.55	78NM
$C_3H_7Hg^{II}$						
	Liq. Part.	1.0 HNa,Cl	25	ML*	1.49	78NM
* $\log \beta_{ML} = \log \beta_{ML}{}^{*} + \log K_1$						
$C_6H_5Hg^{II}$						
	Gl.	-	22	M(LH)	4.77	76HS
				ML(H)	8.64	
	Solv. ext.	1.0	25	ML_2	16.5	88KS
Ho^{3+}	Gl.	→0	20	ML	8.025	80SD
				ML_2	15.825	
			35	ML	7.900	
				ML_2	15.500	
			45	ML	7.800	
				ML_2	15.250	
In^{3+}	Gl.	0.1 KNO_3	21	ML	14.72	76KS
				ML_2	27.26	
				MLH	18.46	
				ML_2H	31.78	
				ML_2H_2	35.74	
				ML_3	32.20	
La^{3+}	Gl.	0.1 KCl	20	ML	4.9	74PN
	Gl.	→0	20	ML	6.025	80SD
			35	ML	5.875	
			45	ML	5.700	
	Gl.	0.1 KNO_3	15	ML	13.35	84ID
				ML_2	18.65	
			30	ML	13.25	
				ML_2	18.45	
Mg^{2+}	Gl. (DL-)	0.025	20	ML	< 4	52A
	Gl.	0.1 $NaClO_4$	20	ML	2.746	65D
Mn^{2+}	Gl. (DL-)	0.025	20	ML	4.1	52A
	Gl.	0.1 KCl	25	ML	~2	52K
	GL.	0.1 KNO_3	25	ML	4.56	64LM
	Gl.	0.1 $NaClO_4$	20	ML	4.90	65D
				ML_2	8.65	

cont'd

Table 2-4. Overall Formation Constants for L-Cysteine Metal Complexes (continued)

Metal ion	Method	Medium (mol dm^{-3})	Temp. (°C)	Complex	log β	Ref.
Mo^{IV}	Sp.	-	-	MLH	(~)20.5	77L
Mo^{V}	Sp.	1.5-3.0 (acetate buffer)	25	ML	6.0±0.1	63SC
Mo^{VI}	Sp.	1.5 (acetate buffer)	25	ML_3	18±1	63SC
Nd^{3+}	Gl.	→0	20	ML	6.852	80SD
				ML_2	13.522	
			35	ML	6.755	
				ML_2	13.304	
			45	ML	6.698	
				ML_2	13.183	
	Gl.	0.1 KNO_3	15	ML	13.45	84ID
				ML_2	18.75	
			30	ML	13.35	
				ML_2	18.55	
Ni^{2+}	Gl. (DL-)	0.025	20	ML_2	19.3	52A
	Gl.	0.15	25	ML	10.48	56WM
				ML_2	19.79	
	Gl.	0.1 KNO_3	25	ML	9.64	64LM
				ML_2	19.04	
	Gl.	0.1 $NaClO_4$	20	ML	9.83	65D
				ML_2	20.21	
				ML_3	23.08	
	Gl.	0.1 $NaClO_4$	20	ML	~9.0	68PS
				ML_2	20.156	
				MLH	15.426	
				M_2L_3	33.005	
				M_3L_4	45.719	
	Gl.	0.1 KCl	25	ML	9.816	72RJ
				ML_2	20.066	
	Gl.	0.2 KNO_3	15	ML	10.36	73SR
				ML_2	20.10	
			25	ML	10.20	
				ML_2	19.97	
			40	ML	9.95	
				ML_2	19.27	
	Gl.	0.2 KCl	25	ML	8.7	79SG
				ML_2	19.61	
				MLH	14.87	
				ML_2H	24.02	
				M_2L_3	30.3	
				M_3L_4	44.51	
	Gl.	0.15 NaCl	37	ML	9.603	85CF
				ML_2	19.219	
				M_2L_3	31.49	
Pb^{2+}	Pol.	0.15 KNO_3 [with $Pb(ClO_4)_2$	25	ML	12.20	55LM
				ML	12.75]	
	Gl.	0.1 KNO_3	25	ML	11.39	64LM

cont'd

Table 2-4. Overall Formation Constants for L-Cysteine Metal Complexes (continued)

Metal ion	Method	Medium (mol dm^{-3})	Temp. (°C)	Complex	log β	Ref.
	Gl.	0.1 $NaClO_4$	20	ML	12.75	65D
				ML_2	16.91	
				ML_3	19.50	
	Gl.	3.0 $NaClO_4$	25	ML	13.163	73CT
				ML_2	19.203	
				ML_3	22.470	
	Gl.	3.0 $NaClO_4$	25	ML	12.213	76CW
				MLH	17.347	
				ML_2	18.571	
				ML_2H	27.476	
				ML_2H_{-1}	7.331	
	Gl.	3.0 $NaClO_4$	10	ML	13.579	76CWa
				MLH	17.974	
				ML_2H	28.417	
			25	ML	13.207	
				MLH	17.434	
				ML_2H	27.301	
			40	ML	12.828	
				MLH	16.968	
				ML_2H	26.445	
	Gl.	1.0 $NaClO_4$	25	ML	12.20	82BC
				MLH	16.16	
				ML_2	15.90	
				ML_2H	25.10	
				MLH_{-1}	2.04	
	Sp.	0.5 $NaClO_4$	25	ML	12.21	82N
$(CH_3)_3Pb^{IV}$						
	NMR	0.3 KNO_3	25	ML	5.97	81BR
				M(LH)	4.99	
				$M(LH_2)$	0.34	
Pr^{3+}	Gl.	→0	20	ML	6.586	80SD
				ML_2	12.975	
			35	ML	6.398	
				ML_2	12.693	
			45	ML	6.245	
				ML_2	12.345	
	Gl.	0.1 KNO_3	15	ML	13.40	84ID
				ML_2	18.65	
			30	ML	13.30	
				ML_2	18.45	
Pt^{4+}	Gl.	0.1 KNO_3	15	ML	13.40	84ID
				ML_2	18.65	
			30	ML	13.35	
				ML_2	18.50	
Rh^{3+}	Gl.	→0	25	ML	8.60	85SN
				ML_2	11.95	
				ML_3	14.20	
			35	ML	8.25	
				ML_2	11.45	
				ML_3	13.60	

cont'd

Table 2-4. Overall Formation Constants for L-Cysteine Metal Complexes (continued)

Metal ion	Method	Medium (mol dm^{-3})	Temp. (°C)	Complex	log β	Ref.
			45	ML	7.90	
				ML_2	11.00	
				ML_3	13.05	
$Sn(CH_3)_3(H_2O)_2^+$						
	Gl.	0.3 $NaClO_4$	25	ML	10.54	87HO
				ML_2	18.97	
				MLH	15.21	
Sm^{3+}	Gl.	0.1 KCl	20	ML	4.8	74PN
	Gl.	→0	20	ML	7.300	80SD
				ML_2	14.000	
			35	ML	7.150	
				ML_2	13.650	
			45	ML	7.075	
				ML_2	13.475	
Sr^{2+}	Gl.	3.0 KNO_3	25	no evidence of cplx formation		64LM
Tb^{3+}	Gl.	→0	20	ML	7.925	80SD
				ML_2	15.525	
			35	ML	7.875	
				ML_2	15.375	
			45	ML	7.800	
				ML_2	15.225	
Th^{4+}	Gl. (D-)	0.1 KNO_3	25	ML	7.51	83NM
				ML_2	14.80	
	Gl.	0.1 KNO_3	15	ML	14.30	84ID
			30	ML	14.05	
Tm^{3+}	Gl.	→0	20	ML	7.998	80SD
				ML_2	15.897	
			35	ML	7.800	
				ML_2	15.400	
			45	ML	7.698	
				ML_2	15.173	
UO_2^{2+}	Gl.	0.1 $NaClO_4$	30	ML	9.04	70RS, 73RS
	Gl. (D-)	0.1 KNO_3	25	ML	5.84	82NM, 83NM
				ML_2	11.85	
	Gl.	0.1 KNO_3	15	ML	13.80	84ID
				ML_2	22.50	
			30	ML	13.65	
				ML_2	22.20	
VO^{2+}	Gl.	2.25 $NaNO_3$	25	MLH_2	19.9	89CVa
				MLH	16.1	
				ML_2H_4	~39.3	
				ML_2H_3	~35.8	
				ML_2H_2	31.0	
				ML_2H	26.0	
				ML_2	19.2	
				M_2L_2	25.2	

cont'd

Table 2-4. Overall Formation Constants for L-Cysteine Metal Complexes (continued)

Metal ion	Method	Medium (mol dm^{-3})	Temp. (°C)	Complex	log β	Ref.
Y^{3+}	Gl.	0.1 KCl	20	ML	4.9	74PN
Yb^{3+}	Gl.	0.1 KCl	20	ML	5.2	74PN
Zn^{2+}	Gl. (DL-)	0.025	20	ML_2	18.2	52A
	Gl. (DL-)	0.025	20	ML_2	17.1	53P
	Pol.	0.15 KNO_3	25	ML	9.86	55LM
				ML_2	18.70	
	Gl.	0.1 KNO_3	25	ML	9.04	64LM
				ML_2	17.54	
	Gl.	0.1 $NaClO_4$	20	ML	9.67	65D
				ML_2	18.71	
				ML_3	21.64	
	Gl.	0.1 $NaClO_4$	20	ML_2	18.210	68PS
				ML_2H	24.794	
				ML_2H_2	30.553	
				M_3L_4	43.493	
				M_3L_4H	49.517	
	Gl.	0.15 KNO_3	37	ML_2	17.98	71HP
				ML_2H	24.33	
				ML_2H_2	29.86	
				M_3L_4H	48.63	
	Gl.	0.1 KCl	25	ML	9.191	72RJ
				ML_2	18.185	
				ML_2H	24.466	
	(DL-)			ML	9.150	
				ML_2	18.177	
				ML_2H	24.500	
	NMR	0.5 NaCl	31.6	ML	8.91	73H
				ML_2	17.61	
				ML_3	22.41	
	Gl.	3.0 $NaClO_4$	25	ML_2	19.394	76CW
				ML_2H	25.856	
				ML_2H_2	31.879	
				M_3L_4	46.247	
				M_3L_4H	52.503	
	Gl.	0.15 $NaClO_4$	37	(ML	8.60)	78BM
				ML_2	17.905	
				MLH	14.604	
				ML_2H	24.114	
				(ML_2H_2	29.013)	
				M_3L_4	42.278	
				M_3L_4H	48.313	
				$M_3L_4H_2$	54.082	
	(less satisfactory fit)			ML_2	17.913	
				MLH	14.544	
				ML_2H	23.813	
				M_2L_3	29.826	
				M_2L_3H	36.392	
				$M_2L_3H_2$	41.748	
	Gl.	0.2 KCl	25	ML	8.2	79SG
				ML_2	18.05	
				MLH	14.76	
				ML_2H	24.43	
				ML_2H_2	29.93	
				M_2L_3	29.2	
				M_3L_4	42.11	
				M_3L_4H	49.01	

cont'd

Table 2-4. Overall Formation Constants for L-Cysteine Metal Complexes (continued)

Metal ion	Method	Medium (mol dm^{-3})	Temp. (°C)	Complex	log β	Ref.
	Gl.	0.15 $NaNO_3$	25	ML_2H_2	24.50	79ZN
	Gl.	0.15 $NaClO_4$	37	ML	9.17	80AM
				ML_2	17.29	
				ML_2H	23.32	
				M_2L_3	20.75	
	Gl.	0.15 NaCl	37	ML_2	17.77	85CF
				MLH	14.67	
				M_2L_3	30.26	
				M_2L_3H	36.14	
				$M_2L_3H_2$	41.73	
Zr^{4+}	Gl.	0.1 KNO_3	15	ML	14.40	84ID
			30	ML	14.15	

(Gl.= glass electrode potentiometry [as exclusive or main method]; Pol.= polarography; Sp.= spectrophotometry; Sol.= solubility; DPP= differential pulse polarography)

Table 2-5. Recommended (R) and Tentative (T) Overall Formation Constants for L-Cysteine Metal Complexes

Metal ion	Medium (mol dm^{-3})	Temp. (°C)	Complex	log β	Ref.
Cd^{2+} (T)	0.15 NaCl	37	ML	10.3	85CF
			MLH_{-1}	2.42	
			ML_2	16.92	
			ML_2H	24.97	
			ML_2H_2	30.93	
			ML_3	19.78	
Co^{2+} (T)	0.2 KCl	25	ML	8.00	83HS
			ML_2	14.20	
			M_2L_3	26.34	
			M_3L_4	37.98	
			M_3L_4H	43.74	
Ni^{2+} (T)	0.1 $NaClO_4$	20	ML	~9.0	68PS
			ML_2	20.156	
			MLH	15.426	
			M_2L_3	33.005	
			M_3L_4	45.719	
	0.2 KCl	25	ML	8.7	79SG
			ML_2	19.61	
			MLH	14.87	
			ML_2H	24.02	
			M_2L_3	30.3	
			M_3L_4	44.51	
	0.15 NaCl	37	ML	9.603	85CF
			ML_2	19.219	
			M_2L_3	31.49	
Zn^{2+} (R)	0.15	37	ML_2	17.9 (±0.1)	71HP, 78BM, 85CF

Table 2-6. Constants for Mixed-ligand Complexes Involving L-Cysteine

Metal ion	Method	Medium (mol dm^{-3})	Temp. (°C)	Extra ligand (X)	Complex	log β	Ref.
Al^{3+}	Gl.	0.1 $NaClO_4$	25	Phosphate	MLX	15.66	74RM, 75RM
	Gl.	0.1 $NaClO_4$	25	Citrate	MLX	14.90	74RM, 75RM
	Gl.	0.1 $NaClO_4$	25	NTA	MLX	18.89	75RM
Ca^{2+}	Gl.	0.1 $NaClO_4$	25	Phosphate	MLX	8.49	75RM
	Gl.	0.1 $NaClO_4$	25	Citrate	MLX	5.58	75RM
	Gl.	0.1 $NaClO_4$	25	NTA	MLX	8.44	75RM
Cd^{2+}	Gl.	0.1 $NaClO_4$	25	Phosphate	MLX	11.45	75RM
	Gl.	0.1 $NaClO_4$	25	Citrate	MLX	10.82	75RM
	Gl.	0.1 $NaClO_4$	25	NTA	MLX	17.53	75RM
Co^{2+}	Gl.	0.1 $NaClO_4$	24	Bipyridyl	(MX)L	4.45	82SD
				o-phen.	(MX)L	4.30	
Cr^{3+}	Gl.	0.1 $NaClO_4$	50	L-Aspartic acid	MLX	26.03	82VN
					MLXH	29.74	
				L-Glutamic acid	MLX	24.82	
					MLXH	29.53	
					$MLXH_2$	32.55	
Cu^{+}	Sp.	1.0	20	Chloride	MLX	14.43	78BK
Cu^{2+}	Gl.	0.1 $NaClO_4$	24	Bipyridyl	(MX)L	6.00	82SD
				o-phen.	(MX)L	5.90	
Hg^{2+}	Gl.	0.1 KNO_3	30	Dien.	(MX)L	4.47	87SB
			45	Dien.	(MX)L	4.92	
Ni^{2+}	Gl.	0.1 $NaClO_4$	24	Bipyridyl	(MX)L	5.55	82SD
				o-phen.	(MX)L	5.45	
Pb^{2+}	Gl.	0.1 $NaClO_4$	25	Phosphate	MLX	16.53	74RMa
	Gl.	0.1 $NaClO_4$	25	Citrate	MLX	18.27	
	Gl.	0.1 $NaClO_4$	25	NTA	MLX	25.53	
Pd^{2+}	Gl.	0.1 $NaClO_4$	24	Bipyridyl	(MX)L	5.60	82SD
				o-phen.	(MX)L	5.45	
Pt^{2+}	Gl.	-	-	cis-diammine	(MX)L	7.55	82XL
	Sp.	-	-			7.43	
Tb^{3+}	Sp.	-	-	EDTA	(MX)L	3.07	85SB

cont'd

Table 2-6. Constants for Mixed-ligand Complexes Involving L-Cysteine (continued)

Metal ion	Method	Medium (mol dm^{-3})	Temp. (°C)	Extra ligand (X)	Complex	log β	Ref.
Zn^{2+}	Gl.	0.15 KNO_3	37	L-Histidine	MLX	15.23	71HP
					MLXH	21.60	
					MLX_2H	26.50	
	Gl.	0.1 $NaClO_4$	25	Phosphate	MLX	14.14	74RMa
	Gl.	0.1 $NaClO_4$	25	Citrate	MLX	16.59	
	Gl.	0.1 $NaClO_4$	25	NTA	MLX	26.28	
	Gl.	0.15 $NaClO_4$	37	Citrate	no ternary complex in evidence		78BM
	Gl.	0.15 $NaClO_4$	37	Histamine	MLX	14.592	80KB
					MLXH	21.130	
	Gl.	0.15 $NaClO_4$	37	L-Lysine	no ternary complex in evidence		81ABa
	Gl.	0.15 $NaClO_4$	37	L-Histidine	MLX	15.090	81ABb
					MLXH	21.333	
	Gl.	0.15 $NaClO_4$	37	Glycine	MLXH	19.922	81ABb
					ML_2X	16.166	
					ML_2XH	24.752	
					MLX_2	19.747	
	Gl.	0.15 $NaClO_4$	37	L-Phenylalanine	MLX	13.110	81AB
	Gl.	0.15 $NaClO_4$	37	L-Arginine	MLX	13.652	81AB
					MLXH	19.999	
	Gl.	0.1 $NaClO_4$	24	Bipyridyl	(MX)L	5.35	82SD
				o-phen.	(MX)L	5.05	
	Gl.	0.15 NaCl	37	L-Glutamine	MLXH	19.66	85CF
	Gl.	0.1 KNO_3	25	NTA	(MX)L	6.51	89S
					(MX)LH	14.02	

(Gl. = glass electrode potentiometry [as exclusive or main method];
Sp. = spectrophotometry; o-phen. = orthophenanthroline; Dien. = diethylenetriamine)

Table 2-7. Overall Thermodynamic Quantities for L-Cysteine Metal Complex Equilibria

Metal ion	Method	Medium (mol dm^{-3})	Temp. (°C)	Complex	ΔH° (kJ mol^{-1})	ΔS° (J K^{-1} mol^{-1})	Ref.
Ce^{3+}	Pot.	→0	25	ML	-20.8	51	80SD
				ML_2	-31.1	134	
Dy^{3+}	Pot.	→0	25	ML	-14.4	116	80SD
				ML_2	-23.0	220	
Er^{3+}	Pot.	→0	25	ML	-13.2	108	80SD
				ML_2	-37.5	174	
Eu^{3+}	Pot.	→0	25	ML	-5.7	124	80SD
				ML_2	-8.6	239	
Gd^{3+}	Pot.	→0	25	ML	-14.4	103	80SD
				ML_2	-20.1	220	
Hg^{2+}	Pol.	0.1 KNO_3	25	ML_2	-228	67	53SK
				ML_2H	-258	167	
				ML_2H_2	-294	184	
Ho^{3+}	Pot.	→0	25	ML	-14.4	104	80SD
				ML_2	-37.4	175	
La^{3+}	Pot.	→0	25	ML	-17.3	56	80SD
Nd^{3+}	Pot.	→0	25	ML	-11.2	93	80SD
				ML_2	-25.1	173	
Ni^{2+}	Pot.	0.2 KNO_3	25	ML_2	-57.3	188.3	73SR
Pb^{2+}	Pot.	3.0 $NaClO_4$	25	ML	-42.4	110.6	76CWa
				MLH	-56.9	142.9	
				ML_2H	-111.8	147.8	
Pr^{3+}	Pot.	→0	25	ML	-21.7	52	80SD
				ML_2	-32.5	137	
Rh^{3+}	Pot.	→0	25	ML	-61.5	0.0	85SN
				ML_2	-79.5	-0.1	
				ML_3	-97.0	-0.1	
Sm^{3+}	Pot.	→0	25	ML	-17.3	81	80SD
				ML_2	-40.3	130	
Tb^{3+}	Pot.	→0	25	ML	-5.8	132	80SD
				ML_2	-17.3	238	
Tm^{3+}	Pot.	→0	25	ML	-23.2	75	80SD
				ML_2	-57.2	109	

(Pot. = potentiometry; Pol. = polarography)

3. CYSTINE - $HO_2C[NH_2]CHCH_2SSCH_2CH[NH_2]CO_2H$ (3,3'-dithiobis(2-amino-propanoic acid), LH_2)

Cystine results from cysteine oxidation with the formation of a disulfide bridge, and displays four protonation sites whose assignment is more straightforward than that of its reduced counterpart. Clearly, the two most basic protonation steps for 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.

Cystine is poorly soluble in neutral aqueous media. 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 spite of this, a strong incentive for investigating metal ion - essential amino acid interactions has been the discovery that a low but significant fraction of copper(II) and zinc(II) naturally present in blood plasma occurs in the form of amino acid complexes (67NS, 68PO). In particular, cystine-containing mixed-ligand species were originally considered to represent a predominant fraction of the l.m.m. complexes of copper(II) in this biofluid (71HP, 73PA, 77ML, 81MW, 82WF). Copper binary and ternary complex equilibria involving cystine have thus received particular attention in this context.

3-1. Protonation constants of cystine

Due to the poor solubility of cystine in aqueous solution, attempts to determine its protonation constants are not numerous. It is worth noting in this respect that solubility data were used in the past to calculate values which, although approximate, did at least refer to its four protonation steps (26S, 37BE). In contrast with these former studies, more recent investigations using potentiometric back titrations have led to limited information from which equilibrium constants for the two most acidic protonation steps were lacking (63HP, 71HP). It is only recently that all of the four protonation constants have been determined with precision from classical titrations run in such a way that precipitation of the cystine zwitterion could be avoided (81BK). Following this study, two other complete sets of constants were produced, relating to the same conditions of temperature and ionic strength (82HA, 85CF). All constants collected are reported in Table 3-1.

The paucity of the data available for 20°C and 25°C precludes any selection of recommended or tentative averages at these temperatures. In contrast, the five contributions carried out under physiological conditions provide a relatively sound basis for comparison. If we consider the first protonation step (log K_1), an initial remark is in order. When account is taken of factors developed in the preceding chapter, the mixed constant found in 71HP is logically 0.1 log unit higher than its stoichiometric counterpart, whose assessment in 81BK, 82HA and 85CF has been perfectly reproducible and from which a recommended average has been calculated (Table 3-2). This casts doubt on the result obtained by Arena et al. (80AM) which, although claimed to derive from concentration measurements, is almost exactly equivalent to that of 71HP.

The case of the second protonation step is more confused. Whereas the stoichiometric constant determined by Arena et al. (80AM) is once again almost equivalent to the mixed constant obtained in 71HP, which is again a priori abnormal but at least in line with what was observed for log K_1, the values in 82HA and 85CF are lower by 0.2 log units, which seems quite surprising. The only stoichiometric constant to fall within the expected range of the mixed log K_2 of 71HP is that found in 81BK, the difference between both values being exactly the same as between their log K_1 counterparts. Fortunately, the average calculated from all constants -including that in 71HP corrected from its 0.12 activity coefficient increment (see 74MS, 82MS, 89SM)- is relatively close to the constant of 81BK (Table 3-2).

For the third protonation step, the values of log K_3 found in 81BK, on the one hand, and in 82HA and 85CF on the other, are almost identical as was the case for log K_1, whereas the value in 80AM is far higher. The average in Table 3-2 has thus been calculated from refs. 81BK, 82HA and 85CF only.

As for the last protonation step, it is particularly difficult to evaluate the reliability of log K_4 given its low value. At the acidic pH's required for such determinations, the imposed ionic strength (0.15 mol dm^{-3}) is no longer in sufficient excess, and variations in activity coefficients are possible. The only study which discusses experimental details concerning this problem is 81BK. From the reported

protonation curve for which the highest attainable protonation degree is 3.5, the resulting value of 1.36 appears to be a maximum. Thus, the average proposed in Table 3-2, which takes also account of the values found in 82HA and 85CF, should in no case be considered as an underestimate.

3-2. Metal complex formation constants

Primarily because of the poor solubility of the cystine zwitterion, equilibrium studies relative to the formation of metal complexes of this amino acid are extremely limited on the whole. However, on account of the potential role of cystine as a major ligand of the l.m.m. fractions of copper(II) and zinc(II) in blood plasma (67NS, 68PO), quantitative investigations of corresponding complexes were considered a priority by bioinorganic chemists. A few sets of formation constants for cystine complexes with copper(II) and zinc(II) are thus available under physiological conditions. The nickel(II)-cystine system has also been investigated for similar reasons, although to a lesser extent. Table 3-3 reports all these results.

In the first study carried out on copper(II)-cystine interactions, Hawkins and Perrin (63HP) characterised the existence of six complexes, but drew attention to the fact that along with the free Cu^{2+} ion, MLH, ML_2H_2 and M_2L_2 accounted for more than 97% of all the copper(II) present. A careful examination of their results leads to the conclusion that M_2L_2 is largely predominant under the concentration conditions investigated, even for metal-to-ligand ratios as high as 1:3, MLH being the second species by order of decreasing importance.*

The large number of species reported by the above authors may be attributed to the well-known permissiveness (78BM, 84BB) of the SCOGS programme (68S). This interpretation is corroborated by the results later published by the same group (71HP), in which M_2L_2 and MLH are the only species mentioned. A more recent study carried out under similar experimental conditions has led to identical conclusions (81BK), but for the characterisation of an additional M_2L complex made on PSEUDOPLOT (75CM) graphical grounds. Stability constants relative to the species common to the latter two studies are in fair agreement. If one indeed recalculates the MLH constant given in reference 71HP according to the general mode of expression defined in the Introduction, one finds 16.20, compared to 16.08 (81BK), whereas 28.07 and 28.24 have, respectively, been obtained for the M_2L_2 constant (71HP, 81BK). Still more recently, the stoichiometries of the species characterised in 81BK have been confirmed (85CF), but corresponding constants have all been found to be a little lower (Table 3-3), which may be logically expected from determinations made in the NaCl medium (see Chapter 1). Recommended and tentative values have been proposed in Table 3-4.

For nickel(II), only one study has been done of its complexation equilibria with cystine (85CF). Corresponding results are reported in Table 3-3.

As for zinc(II)-cystine interactions, solubility problems made the determination of complex formation constants still more difficult than in the case of copper(II). Four studies are available under the same experimental conditions, but only two of these, issued from the same group of authors (82HA, 85CF), agree on the nature of the complexes formed. No experimental details have been given in the oldest investigation (72GH) on the way nature and stability of the proposed complexes have been determined; corresponding results should thus be considered with caution. On the other hand, the pH range investigated by Arena et al. (80AM) is so limited (5.3-6.4) and the reactant concentrations so low (~0.5 mol dm^{-3}) that, without any information on the formation curve on which the calculations are based, it is difficult to lend credit to the M_2L constant proposed; this is all the more so as protonation as well as cysteine results from the same study (see Chapter 2) have not been selected as reliable.

In contrast, the other two investigations, using either indirect analysis with respect to histidine (82HA), or direct determinations (85CF), not only led to identical stoichiometries but also yielded fairly reproducible constants. The two corresponding species have thus been selected, and their average constants proposed as tentative (Table 3-4).

As a rule, mixed-ligand complexes play an important role in the distribution of metal ion l.m.m. fractions in blood plasma (78BM, 84BP, 86BH). In particular, mixed-ligand species involving cystine

* Incidentally, it may be worth noting that these results have been mistakenly cited under the cysteine heading in ref. 71SM (see section 2-3). Moreover, constants for the sole MLH and ML_2H_2 complexes have been mentioned in ref. 74MS, where they have in addition been wrongly associated with ML and M_2L_2 stoichiometries.

were originally considered to predominate in the l.m.m. fraction of copper(II) in this biofluid (71HP, 73PA, 77ML, 81MW, 82WF). With histidine definitely the main l.m.m. ligand of copper(II) in plasma (84BP, 86BH), studies on copper(II)-cystine-histidine equilibria have taken up an important part of the few investigations carried out on metal-cystine ternary systems.

Among the results of the two groups of authors cited in Table 3-5 (71HP, 84BB), fair agreement is observed for the constant of the $MLXH_2$ species, and a tentative average of 30.56 ± 0.13 may even be proposed. However, the agreement stops there. In particular, none of the MLX and MLXH species characterised by Hallman et al. (71HP) has been confirmed in the more recent study (84BB). The lack of experimental details in 71HP prevents any direct comparison, but data obtained on connected systems allow to reach a clearcut conclusion. In fact, the nonexistence of MLX and MLXH complexes in the copper(II)-cystine-histidine system in 84BB is in line with the lack of evidence for any ternary species in the copper(II)-histamine-cystine system (81BK). The former characterisation of the two MLX and MLXH complexes by Hallman et al. (71HP) has been suggested to result from the above mentioned permissiveness of SCOGS (84BB). In this respect, the discovery of the nonexistence of species initially considered significant by Perrin's school is not an exception. The negligibility of a series of ternary zinc(II) species (81ABb) previously reported to form (71HP) has even been acknowledged by Perrin's group itself (79SP).

The above discussion might appear somewhat superfluous if the consequences of the corresponding results were not so important. As long as the MLX and MLXH constants proposed by Hallman et al. (71HP) were present in the databank used to simulate the distributions of essential metal ions in blood plasma, no coincidence could be obtained with the experimental data formerly collected on copper(II) by Neumann and Sass-Kortsak (67NS). As stated in the introduction, this lack of coincidence had even been advanced as an argument to question the very principle of simulation models in this field (79YS, 81S). The fact that the removal of these constants from the databank in accordance with the results found in ref. 84BB led not only to the expected coincidence between experimental and simulated classifications in blood plasma (84BB) but also (86BH) in the reconstituted serum solutions investigated by Neumann and Sass-Kortsak (67NS) tends to definitely substantiate the results obtained in ref. 84BB. The nonexistence of the MLH and MLXH species mentioned by Hallman et al. has even been independently confirmed (81W).

It is finally worth noting that no determination of any thermodynamic quantity relative to complex formation equilibria with cystine was found in the literature.

Table 3-1. Protonation Constants of Cystine

Type of constants	Medium (mol dm^{-3})	Temp. (°C)	log K_1	log K_2	log K_3	log K_4	Ref.
-	-	25	9.85	7.86	2.21	1.60	26S
Mixed	0.02	30	9.02	7.48	1.70	<1.0	27CK
Thermo	0.01-0.11	25	10.25	8.00	2.05	1.04	37BE
-	0.1	35	8.71	8.02	-	-	39GK
Mixed	0.15 $NaClO_4$	20	8.80	8.03	-	-	63HP
Mixed	0.15 KNO_3	37	8.69	7.95	(1.7)	-	71HP
Stoichio	0.15 $NaClO_4$	37	8.71	7.93	2.38	-	80AM
Stoichio	0.15 $NaClO_4$	37	8.596	7.855	2.090	1.360	81BK
Stoichio	0.15 NaCl	37	8.602	7.754	2.051	1.636	82HA
Stoichio	0.15 NaCl	37	8.604	7.752	2.054	1.62	85CF

Table 3-2. Recommended Values for Protonation Constants of Cystine

Type of constants	Medium (mol dm^{-3})	Temp. (°C)	log K_1	log K_2	log K_3	log K_4	Ref.
Stoichio (R)	0.15	37	8.60 (±0.01)	7.84 (±0.09)	2.07 (±0.02)	1.5 (±0.15)	71HP, 80AM, 81BK, 82HA, 85CF

Table 3-3. Overall Formation Constants for L-Cystine Metal Complexes

Metal ion	Method	Medium (mol dm^{-3})	Temp. (°C)	Complex	log β	Ref.
Cu^{2+}	Gl.	0.15 $NaClO_4$	20	M(LH)	7.00	63HP
				[MLH	15.80]	
				$M_2L_2(H)$	21.33	
				$[M_2L_2H$	30.13]	
				$M(LH)_2$	13.72	
				$[ML_2H_2$	31.32]	
				$M_2(LH)_2L$	28.05	
				$[M_2L_3H_2$	45.65]	
				M_2L	14.00	
				M_2L_2	28.05	
				[MLH	15.80]	
				$[M_2L_2H$	30.13]	
				$[ML_2H_2$	31.32]	
				$[M_2L_3H_2$	45.65]	
				M_2L	14.00	
				M_2L_2	28.05	
	Gl.	0.15 KNO_3	37	MLH	16.20	71HP
				M_2L_2	28.07	
	Gl.	0.15 $NaClO_4$	37	MLH	16.081	81BK
				M_2L	14.860	
				M_2L_2	28.241	
	Gl.	0.15 NaCl	37	ML	8.22	82HA
	(by reference to NTA)					
	Gl.	0.15 NaCl	37	MLH	15.788	85CF
				M_2L	14.61	
				M_2L_2	27.803	
$C_6H_5Hg^{II}$						
	Solv. ext.	1.0	25	ML_2	8.77	88KS
Ni^{2+}	Gl.	0.15 NaCl	37	MLH	13.51	85CF
				M_2L	10.21	
				M_2L_2	17.54	
				ML_2	11.73	
Zn^{2+}	Gl.	0.15 NaCl	37?	M(LH)	4.64	72GH
				$M(LH)_2$	8.62	
	Gl.	0.15 $NaClO_4$	37	M_2L	10.07	80AM
	Gl.	0.15 NaCl	37	ML	6.688	82HA
	(by reference to histidine)			MLH	12.802	
	Gl.	0.15 NaCl	37	ML	6.65	85CF
				MLH	12.89	

(Gl. = glass electrode potentiometry [as exclusive or main method])

NB: These constants have been mistakenly cited under the cysteine heading in ref. 71SM. Moreover, the M(LH) and $M(LH)_2$ constants above have only been mentioned in ref. 74MS, and wrongly attributed to ML and ML_2. Overall constants in square brackets have been calculated from protonation constants in Table 3-1.

Table 3-4. Recommended (R) and Tentative (T) Overall Formation Constants for L-Cystine Metal Complexes

Metal ion		Medium (mol dm^{-3})	Temp. (°C)	Complex	log β	Ref.
Cu^{2+}	(R)	0.15 $NaClO_4$	37	MLH	16.14 (±0.06)	71HP, 81BK
				M_2L	14.86	81BK
				M_2L_2	28.16 (±0.09)	71HP, 81BK
	(T)	0.15 NaCl	37	MLH	15.79	85CF
				M_2L	14.61	
				M_2L_2	27.80	
Zn^{2+}	(T)	0.15 NaCl	37	ML	6.67 (±0.02)	82HA, 85CF
				MLH	12.85 (±0.05)	

Table 3-5. Overall Formation Constants for Mixed-Ligand Complexes Involving L-Cystine

Metal ion	Method	Medium (mol dm^{-3})	Temp. (°C)	Extra ligand (X)	Complex	log β	Ref.
Cu^{2+}	Gl.	0.15 KNO_3	37	L-Histidine	MLX	18.51	71HP
					MLXH	25.80	
					$MLXH_2$	30.69	
					MLX_2H	39.15	
	Gl.	0.15 $NaClO_4$	37	Histamine	no ternary complex in evidence		81BK
	Gl.	0.15 $NaClO_4$	37	L-Histidine	$MLXH_2$	30.437	84BB
Fe^{2+}	Kin.	0.1 $LiClO_4$	25	Cyanide	$(MX_5)L$	4.43	82TB
Fe^{3+}	Kin.	0.1 $LiClO_4$	25	Cyanide	$(MX_5)L$	4.76	82TB
Tb^{3+}	Sp.	-	-	EDTA	(MX)L	1.27	85SB
Zn^{2+}	Gl.	0.15 KNO_3	37	L-Histidine	MLX	11.62	71HP
					MLXH	19.55	
					$MLXH_2$	26.35	

(Gl. = glass electrode potentiometry [as exclusive or main method];
Sp. = spectrophotometry; Kin. = kinetics)

4. METHIONINE - $H_3CSCH_2CH_2CH[NH_2]CO_2H$ (2-amino-4-(methylthio)butanoic acid, LH)

Methionine displays virtually the same two protonation sites as simple glycine-like amino acids in aqueous media since its ether sulphur undergoes protonation in strongly acidic solutions (72BL). Nevertheless, the large electron-withdrawing effect of the thioether group (75IP) renders these two protons significantly more acidic than those of the above reference ligands. Methionine metal complexes are thus expected to be less stable than those of glycine-like amino acids unless chelation through the sulphur atom can bring some compensation.

As can be anticipated from the above, many efforts have been spent to test the involvement of the thioether function of methionine in metal coordination. As already stated in the Introduction, few metal ions except those definitely classified as soft can actually bind to the sulphur atom (74MG, 79M, 86M, 87L). In this respect, the Ag^+-methionine system has often been used as a reference for investigating the binding capacities of other ligands (75IP, 81PS, 84TS, 87SP). Within the same context, the influence of stereoselectivity on the formation of metal methionine complexes has also been assessed: no conclusive evidence was found for silver (75IP), but a small stereoselective effect has been observed for nickel, supporting the existence of a weak interaction between Ni^{2+} and the thioether sulphur atom (76SP).

4-1. Protonation constants of methionine

Investigations into the possible role of the soft thioether group of methionine and similar bioligands in metal coordination necessitated the determination of formation constants of many complexes involving this amino acid. Since proton-ligand equilibria commonly serve as a reference in such studies, it is thus no surprise that methionine protonation constants available in the literature are relatively abundant (Table 4-1), some of them being quite reliable.

For example, many stoichiometric constants have been determined at 25 °C in 0.1 mol dm^{-3} aqueous potassium nitrate (64LM, 75IP, 77BP, 81PS, 82NM). Except for the values found in 82NM - also published as apparently original data in two other articles (82NMa, 83NM)- which differ markedly from those obtained by previous authors, the corresponding results are very close to one another, and a recommended average has been calculated. Following criteria defined in the Introduction of this review, mixed or presumably mixed constants determined under the same conditions in $NaClO_4$ (84MCa, 86MC, 86MCa) have been discarded.

Among the remainder, the experimental conditions reported are so diverse that it is almost impossible to establish useful correlations likely to help select particular values. Nevertheless, given the specific conditions used and the previous inclusion of results by the same authors in Table 2-2, the stoichiometric constants determined in 3 mol dm^{-3} sodium perchlorate (76BH) have been proposed as tentative. Likewise, average stoichiometric values relative to the physiological medium (71HP, 84BP) have also been proposed as tentative: subtracting from the mixed constants reported in 71HP the 0.12 difference applicable between mixed and stoichiometric reference scales for I=0.15 mol dm^{-3} (see section 2-1) does indeed yield values (8.79, 2.135) which are almost identical with those obtained in 84BP (8.779, 2.170). Recommended and tentative values for the protonation constants of methionine are to be found in Table 4-2.

4-2. Thermodynamic quantities for the protonation of methionine

Among the thermodynamic quantities available for the protonation of methionine, fair agreement may be observed between the values deduced from potentiometric determinations at different temperatures in water (57PQ, 60Pc) and the results obtained by direct calorimetry (89RF). This attests to the good quality of the former. Corresponding values can be seen in Table 4-3, from which results reported in 88MA have been discarded as being too far from the others.

4-3. Metal complex formation constants

Although methionine displays only two accessible protonation steps in aqueous solution, it possesses three potential donor sites, namely the COO^-, NH_2 and thioether groups, which may alternately

participate in metal coordination depending on the individual character of the cation involved. Since few metal ions are in fact capable of accommodating more than two of these three different sites simultaneously, methionine is expected to form tris-complexes rather easily. This may effectively be observed in Table 4-4 where all stability constants for metal binary complexes involving methionine have been reported.

As outlined above, advantage was taken of the typical properties of the Ag^+ ion as soft acceptor to use it as a reference to test the potential capacity of the thioether group of methionine towards metal coordination. Among available data relative to the silver(I)-methionine system, some do not result from sufficiently modern calculation techniques to be selected (67AM, 77PU). More surprising, however, is the discrepancy observed between the ML constant values found by the other three groups of authors (64LM, 81PS, 84TS), though it might indirectly reflect the striking variations seen in the sets of complexes characterised. For example, ML was the only species mentioned in 64LM, and though the possibility of dimeric complexes was evoked in 81PS, no quantitative information was researched in view of the practical difficulties which had to be overcome. The latest results obtained by Tombeux et al. using both glass and silver electrodes (84TS) finally appear as the most complete and reliable, although they cannot be officially recommended until they have been independently reproduced. In the latter study (84TS), the noninvolvement of the carboxylate function in silver(I) coordination previously indicated by NMR data (81PS) was confirmed, the sulphur atom acting as exclusive donor group in $M(LH_2)_n$ and $M(LH)_n$ species and in conjunction with the N atom in ML_n ones, but the $M_2(LH)_2$ species suggested by Pettit et al. (81PS) was not found.

With respect to the above, much better agreement is observed concerning cadmium(II)-methionine equilibria investigated at 25 °C in 0.1 mol dm^{-3} KNO_3 (64LM, 75IP, 82NMa); recommended constants have thus been calculated for both ML and ML_2 species. Unfortunately, none of the above studies provides any information on the ML_3 complex which was characterised by four other groups under different conditions (64J, 82RB, 84MR, 86SV), and whose existence tends to confirm the classification of the Cd^{2+} ion as borderline (79M). By comparison of the latter results with the above recommended constants, we have selected data reported in 86SV as tentative. They do indeed appear as the most reliable among those giving a complete description of the system.

Fair agreement is also observed for the constants of the ML and ML_2 complexes of Co^{2+} determined at 25 °C in 0.1 mol dm^{-3} KNO_3 (64LM, 75IP, 82NMa), and recommended values have been calculated.

For copper(II), four groups of authors (64LM, 75IP, 77BP, 82NMa) have used the same experimental conditions, and corresponding results are most satisfactory. The different constants found for the ML complex are particularly close to one another, and apart from that reported in 64LM, the values proposed for the ML_2 constant are also quite reproducible. Recommended values have thus been calculated. In contrast, no agreement is observed between data relative to physiological conditions (71HP, 84BP) on which new investigations are therefore advisable.

Surprisingly, the constants available for Hg^{2+} complexes are extremely different from one group of authors to another (64LM, 66TA, 83HD, 73VB). By reference to the apparent reliability of the results published in 64LM, which are amongst those selected for Cd^{2+}, Co^{2+} and Cu^{2+} complexes and undoubtedly appear as the most reliable on experimental as well as computational criteria, one is tempted to choose these as the only acceptable values in the present case. In particular, the assumption made by Van der Linden and Beers (73VB) that their mercury electrode gave a Nernstian response since it did so in the presence of DTPA, CDTA and EGTA may well not be valid considering the fact that mercury(II) complexes of such ligands are by more than ten orders of magnitude more stable than those of amino acids (71SM, 74MS, 82MS, 89SM).

The situation with Mn^{2+} complexes is quite similar to that seen above in that results published in 64LM appear as the only acceptable ones. It would now be desirable that these constants as well as those relative to the complexes of the previous metals be tested on the basis of new calibration and calculation standards.

In spite of the apparent plethora of results available for nickel, relatively few constants actually offer a real basis for comparison. This essentially stems from the large number of determinations made

under different conditions of solvent or temperature (57P, 60P, 60Pa, 60Pb, 60Pc). The ML constant given by 64LM for 25 °C and 0.1 mol dm^{-3} KNO_3 is this time slightly at variance with those obtained by other authors (75IP, 76SP, 82NMa), and the fact that reference 82NMa reports values surprisingly identical with those published in 76SP without even mentioning this reference (!) does not help either. Nevertheless, average recommended constants have been calculated.

Once again, by reference to their recognized reliability regarding the above mentioned systems, Lenz and Martell's constants for lead complexes (64LM) are to be considered as acceptable. In contrast, no leading group can be selected for UO_2^{+}-methionine equilibria, and the values collected are too distant from one another to permit any reasonable comparison.

For the zinc(II)-methionine system, the three groups operating under the same experimental conditions 25 °C and 0.1 mol dm^{-3} KNO_3 (64LM, 75IP, 82NMa) again report very similar results from which recommended constants have been estimated. The only data applicable to the physiological medium have been published by Hallman et al. (71HP).

All recommended and tentative values are shown in Table 4-5. With few exceptions, individual data of Table 4-4 not considered for this selection often represent orders of magnitude only, and many of these would deserve more attentive investigations. Given that stability variations due to stereospecific effects are usually well within the reproducibility range, it is also noteworthy that formation constants relative to DL-methionine (64LM) have been indiscriminately considered in the calculations of constants in Table 4-5 when necessary.

Mixed-ligand complex formation constants involving methionine are reported in Table 4-6. Concerning coordination with other amino acids, no stereospecific effect has been detected whenever investigated (73BJ, 77BP). Determinations corresponding to physiological conditions are restricted to the copper(II)-histidine-methionine system (84BP) only. This is hardly surprising given the relatively low importance of methionine as a ligand for essential metal ions in vivo.

4-4. Thermodynamic quantities for metal complex formation with methionine

Determinations of enthalpies relative to methionine metal coordination are very few, and concern Mn^{2+}, Ni^{2+} and UO_2^{2+} ions only. The great majority of values reported in Table 4-7 have been deduced from potentiometric measurements using the van't Hoff isochore. The temperature interval used is indicated, and when not available in the referenced article, entropies have been calculated at 25 °C (values in brackets). The limited reliability of such data is attested by the poor reproducibility of the values found for manganese(II) under almost identical experimental conditions (71SS, 73BS). Results relative to the dimethyltin(IV) complex formation have not even been mentioned (88SS). The only quantities to be considered as reliable are those determined calorimetrically, on which the evidence of the stereospecific effect in the nickel(II)-methionine system was based (76SP).

Table 4-1. Protonation Constants of Methionine

Type of constants	Medium (mol dm^{-3})	Temp. (°C)	log K_1	log K_2	Ref.
Thermo	~ 0.01	20	9.34	2.20	50A
Thermo	~ 0.01	18	9.31	-	53P
Mixed(?)	0.15 KNO_3	25	9.10	-	55LM
Thermo	~ 0.05	10	9.73	2.13	57PQ, 60Pa
		15	9.58	2.13	60Pc
		25	9.28	2.125	57PQ, 60Pa
		30	9.15	2.125	
		40	8.92	2.12	
Mixed	1.0 $NaClO_4$	20	9.13	2.26	58P
Mixed(?)	1.0 KCl	20	9.13	-	59P
Thermo	~ 0.05	10	10.10	3.17	60Pc
	44.6% dioxane	15	9.99	3.14	
		25	9.75	3.09	
		30	9.66	3.04	
		40	9.42	3.01	
Thermo	~ 0.05	10	10.60	3.52	60Pc
	59.7% dioxane	15	10.46	3.52	
		25	10.19	3.51	
		30	10.07	3.50	
		40	9.84	3.49	
Thermo	~ 0.05	15	11.05	3.94	60Pc
	69.0% dioxane	25	10.83	3.88	
		30	10.72	3.84	
		40	10.51	3.77	
Mixed	0.15 $NaClO_4$	20	9.20	2.17	63HP
Mixed	0.15 KCl	30	9.08	-	64FW
Stoichio	0.10 KNO_3	25	9.04	-	64LM
Mixed (pol.)	0.6	25	9.15	-	67AM
Mixed	0.15 KNO_3	37	8.91	2.25_5	71HP
Mixed(?)	0.1 KCl	25	9.17	2.24	71SS
		35	9.02	2.09	
		45	8.55	1.62	
Mixed(?)	1.0 $NaNO_3$	25	9.21	2.28	73BJ
Mixed(?)	0.1 KNO_3	20	9.25	-	73BS
		30	9.01	-	
		40	8.78	-	
		50	8.54	-	
		60	8.30	-	
Mixed	0.1 KCl	20	9.3	-	74PN
Stoichio	0.1 KNO_3	25	9.052	2.151	75IP
Stoichio	3.0 $NaClO_4$	25	9.69	2.70	76BH
Stoichio	0.1 KNO_3	25	9.058	2.153	77BP, 81PS
Mixed	0.1 KNO_3	30	9.42	1.85	77PU
Thermo	~0	30	9.30	1.85	77PU, 81PU
Stoichio(?)	0.5 KNO_3	25	9.22	2.25	78L
Stoichio	1.0 $NaClO_4$	25	9.04	2.18	81JI
Mixed(?)	0.1 $NaClO_4$	25	9.15	2.32	81MC, 84MCb

cont'd

Table 4-1. Protonation Constants of Methionine (continued)

Type of constants	Medium (mol dm^{-3})	Temp. (°C)	log K_1	log K_2	Ref.
Thermo	~0	25	9.20	2.29	82DD
	8.0% propane-2-ol	25	9.20	2.37	
	16.3% propane-2-ol	25	9.17	2.46	
	25.1% propane-2-ol	25	9.17	2.61	
	34.3% propane-2-ol	25	9.19	2.76	
	43.9% propane-2-ol	25	9.20	2.95	
	54.0% propane-2-ol	25	9.23	3.06	
	64.6% propane-2-ol	25	9.27	3.29	
	75.8% propane-2-ol	25	9.30	3.47	
Stoichio	0.1 KNO_3	25	8.921	2.35	82NM, 82NMa, 83NM
Stoichio	0.15 $NaClO_4$	37	8.779	2.170	84BP
Mixed	0.5 $NaClO_4$	25	9.15	2.32	84MC
Mixed	0.1 $NaClO_4$	25	9.12	2.30	84MCa
Stoichio	0.5 KNO_3	25	9.089	2.199	84TS
Mixed(?)	0.1 KNO_3	25	9.13	-	85MK
Mixed(?)	0.1 $NaClO_4$	25	9.150	2.321	86MC, 86MCa
Thermo	~0	25	9.20	2.29	86PD
	8.0% t-BuOH	25	9.18	2.43	
	16.4% t-BuOH	25	9.17	2.57	
	25.0% t-BuOH	25	9.16	2.64	
	34.2% t-BuOH	25	9.19	2.73	
	43.8% t-BuOH	25	9.26	2.77	
	54.0% t-BuOH	25	9.34	2.89	
	64.5% t-BuOH	25	9.44	3.02	
	75.8% t-BuOH	25	9.53	3.39	
Stoichio(?)	0.2 KNO_3	25	9.06	2.18	86SV
Mixed(?)	0.15 KNO_3	25	9.12	-	87CJ
Thermo	~0	25	9.02	2.29	87CL
	10% methanol	25	9.01	2.33	
	20% methanol	25	8.98	2.42	
	30% methanol	25	8.98	2.60	
	40% methanol	25	9.00	2.75	
	50% methanol	25	9.02	2.90	
	60% methanol	25	9.05	3.00	
	70% methanol	25	9.08	3.20	
	80% methanol	25	9.11	3.50	
	10% ethanol	25	9.15	2.36	
	20% ethanol	25	9.14	2.40	
	30% ethanol	25	9.14	2.61	
	40% ethanol	25	9.15	2.76	
	50% ethanol	25	9.18	2.92	
	60% ethanol	25	-	2.98	
	70% ethanol	25	-	3.20	
	80% ethanol	25	-	3.45	
Stoichio	0.2 KNO_3	25	8.75	2.08	87PS
Stoichio	0.2 KCl	25	9.12	2.22	87SP
Mixed	0.1 NaCl	20	10.44	3.22	88SS
	75% dioxane	30	10.14	3.16	
		40	9.32	3.05	
Mixed	0.1 KNO_3	25	9.09	-	89S
Mixed(?)	0.5 KCl	25	-	2.15	89YW

N.B. Other reference consulted but rejected: 74PN

Table 4-2. Recommended (R) and Tentative (T) Values for Protonation Constants of Methionine

Type of constants	Medium (mol dm^{-3})	Temp. (°C)	log K_1	log K_2	Ref.
Stoichio (R)	0.1 KNO_3	25	9.05 (±0.01)	2.15 (±0.01)	64LM, 75IP, 77BP, 81PS
Stoichio (T)	3.0 $NaClO_4$	25	9.69	2.70	76BH
Stoichio (T)	0.15	37	8.78 (±0.01)	2.16 (±0.02)	71HP, 84BP

Table 4-3. Thermodynamic Quantities for Methionine Protonation Equilibria

Method	Medium (mol dm^{-3})	Temp. (°C)	$\Delta H°_1$ (kJ mol^{-1})	$\Delta H°_2$ (kJ mol^{-1})	$\Delta S°_1$ (J K^{-1} mol^{-1})	$\Delta S°_2$ (J K^{-1} mol^{-1})	Ref.
Pot.	~ 0.05	10-40	-43.5	-0.6	31.4	38.9	57PQ, 60Pc
Pot.	~ 0.05 44.6% dioxane	10-40	-38.9	-14.6	55.2	9.6	60Pc
	~ 0.05 59.7% dioxane	10-40	-42.2	-2.7	53.6	58.2	
	~ 0.05 69.0% dioxane	15-40	-37.7	-12.8	81.2	31.4	
Cal.	~0	20	-42.8	-	-	-	71MB
Cal.	~0	25	-44.1	-2.6	28.5	34.9	89RF, 89R
Cal.	0.5 KCl	25	-	-3.87	-	28.2	89YW

(Pot. = potentiometry; Cal. = calorimetry)

Table 4-4. Overall Formation Constants for L-Methionine Metal Complexes

Metal ion	Method	Medium (mol dm^{-3})	Temp. (°C)	Complex	log β	Ref.
Ag^+	Gl. (DL-)	0.1 KNO_3	25	ML	3.17	64LM
	Gl.	0.6	25	ML	6.45(!)	67AM
	Ag el.	0.1 KNO_3	30	ML	4.9	77PU
				ML_2	7.60	
				M(LH)	3.29	
				$M(LH)_2$	5.38	
		~0	30	ML	5.14	77PU, 81PU
				ML_2	7.84	
				M(LH)	3.29	
				$M(LH)_2$	5.38	
	Gl.	0.1 KNO_3	25	ML	5.22	81PS
				MLH	12.22 (12.36)	
				ML_2H_2	24.60 (23.80)	
	Gl. (DL-)	0.5 KNO_3	25	ML	4.8	84TS
				ML_2	7.88	
				M_2L	7.46	
				M_2L_2	13.49	
				M(LH)	3.37	
				$M(LH)_2$	5.88	
				ML(LH)	7.38	
				$M(LH_2)$	3.11	
				$M(LH_2)_2$	5.40	
				$M(LH)(LH_2)$	5.88	
Au^{3+}	Gl. (DL-)	~ 0.02	25	ML	7.23	74FA
				ML_2	10.19	
Be^{2+}	Gl. (DL-)	0.015	18	ML_2	12.0	53P
Ca^{2+}	Ion exch. (pH 7.2)	0.16	25	ML	-0.66	54S
Cd^{2+}	Gl. (DL-)	0.015	18	ML_2	7.1	53P
	Gl.	0.15 KNO_3	25	ML	3.88	55LM
				ML_2	6.99	
	Paper electrophor.	0.1 KNO_3	20	ML	5.4	64J
				ML_2	8.7	
				ML_3	10.8	
	Gl. (DL-)	0.1 KNO_3	25	ML	3.67	64LM
				ML_2	7.03	
	Gl.	0.1 KNO_3	25	ML	3.70	75IP
				ML_2	6.97	
	Pol.	1.0 KNO_3	30	ML	3.81	77RN
				ML_2	6.24	
				ML_3	8.32	
	Gl.	0.1 KNO_3	25	ML	3.71	82NMa
				ML_2	6.99	
	(D-)			ML	3.71	
				ML_2	6.966	
	(DL-)			ML	3.70	
				ML_2	6.97	

cont'd

Table 4-4. Overall Formation Constants for L-Methionine Metal Complexes (continued)

Metal ion	Method	Medium (mol dm^{-3})	Temp. (°C)	Complex	log β	Ref.
	Pol. (DL-)	1.0 KNO_3	30?	ML	3.80	82RB
				ML_2	6.35	
				ML_3	8.19	
	Gl.	0.2	30	ML	4.04	84J, 84Ja
				ML_2	7.19	86J
	Pol.	-	25	ML	3.81	84MR
				ML_2	6.99	
				ML_3	8.10	
	Gl.	0.2 KNO_3	25	ML	3.65	86SV
				ML_2	6.76	
				ML_3	9.08	
	Gl.	0.2 KNO_3	35	ML	3.63	89KS, 89KV
				ML_2	6.51	
	Gl.	0.2 $NaClO_4$	27	ML	4.30	88PP
				ML_2	8.34	
Ce^{3+}	Gl.	0.1 KCl	20	ML	4.4	70RP
Co^{2+}	Gl. (DL-)	~ 0.01	20	ML_2	7.9	50A
	Paper electrophor.	0.1 KNO_3	20	ML	4.5	64J
				ML_2	7.6	
				ML_3	9.5	
	Gl. (DL-)	0.1 KNO_3	25	ML	4.12	64LM
				ML_2	7.56	
	Gl.	0.1 KNO_3	25	ML	4.16	75IP
				ML_2	7.60	
	Gl.	0.1 KNO_3	25	ML	4.154	82NMa
				ML_2	7.583	
	(D-)			ML	4.152	
				ML_2	7.592	
	(DL-)			ML	4.158	
				ML_2	7.597	
	Gl.	0.15 KNO_3	25	ML	4.16	87CJ
				ML_2	7.62	
	Gl.	0.2 KNO_3	35	ML	3.98	89KS, 89KV
				ML_2	7.50	
Cr^{2+}	Gl. (DL-)	~ 0.015	25	ML_2	7.30	70FMa
Cr^{3+}	Gl.	0.4 KCl	25	ML	8.3	63KM
				ML_2	14.5	
				ML_3	19.8	
	Gl. (DL-)	0.1 $NaClO_4$	25	ML	7.91	81MC
				ML_2	14.85	
				ML_3	21.28	
	Sp. (DL-)	0.1 $NaClO_4$	25	ML	7.45	81MC, 84MCb
				ML_2	13.90 (or 13.99?)	
				ML_3	19.89 (or 19.98?)	

cont'd

Table 4-4. Overall Formation Constants for L-Methionine Metal Complexes (continued)

Metal ion	Method	Medium (mol dm^{-3})	Temp. (°C)	Complex	log β	Ref.
	Gl. (DL-)	0.1 $NaClO_4$	25	ML	8.35	86MC, 86MCa
				MLH	11.41	
				ML_2	15.52	
Cu^+	Sp.	1.0	20	ML	10.09	78BK
Cu^{2+}	Gl. (DL-)	~ 0.01	20	ML_2	14.7	50A
	Pol.	~ 0.02	25	ML_2	14.75	54LD
	Gl.	0.15 $NaClO_4$	20	ML	8.00	63HP
				ML_2	15.23	
	Paper electrophor.	0.1 KNO_3	20	ML	8.1	64J
				ML_2	14.8	
	Gl. (DL-)	0.1 KNO_3	25	ML	7.87	64LM
				ML_2	14.72	
	Pol. (DL-)	orthophosphate buffer (pH 7.4)	25	ML_2	9.25	65PP
	Gl.	0.15 KNO_3	37	ML	7.67	71HP
				ML_2	14.08	
	Gl.	0.1 KNO_3	25	ML	7.85	75IP
				ML_2	14.51	
	Gl.	0.1 KNO_3	25	ML	7.849	77BP
				ML_2	14.529	
	Gl.	0.1 KNO_3	25	ML	7.850	82NMa
				ML_2	14.521	
	(D-)			ML	7.844	
				ML_2	14.537	
	(DL-)			ML	7.850	
				ML_2	14.511	
	Gl.	0.15 $NaClO_4$	37	ML	7.490	84BP
				ML_2	13.696	
	Gl.	0.2 KNO_3	25	ML	7.70	87PS
				ML_2	14.31	
	Gl.	0.2 KCl	25	ML	7.76	87SP
				ML_2	14.29	
	Gl.	0.2 KNO_3	35	ML	7.70	89PV
Dy^{3+}	Gl.	0.1 KCl	20	ML	4.5	74PN
Fe^{2+}	Gl. (DL-)	~ 0.01	20	ML_2	6.7	50A
	Gl.	1.0 KCl	20	ML	3.24	59P
Fe^{3+}	Gl.	1.0 $NaClO_4$	20	ML	9.1	58P
Ga^{3+}	Gl.	3.0 $NaClO_4$	25	ML	8.9	76BH
				M(LH)	1.8	
Gd^{3+}	Gl.	0.1 KCl	20	ML	4.6	74PN
Hg^{2+}	Gl. (DL-)	0.1 KNO_3	25	ML	6.52	64LM
				ML_2	11.45	
	Pol.	0.6 KNO_3	25	ML_2	17.62(!)	66TA
	Ion exch. (pH 7.8)	0.375	25	ML	3.37(!)	83HD
	Gl.	0.1 $NaNO_3$	25	ML	12.8(!)	73VB

cont'd

Table 4-4. Overall Formation Constants for L-Methionine Metal Complexes (continued)

Metal ion	Method	Medium (mol dm^{-3})	Temp. (°C)	Complex	log β	Ref.
	(Hg el.)			ML_2	19.5(!)	
				ML_2H	24.6(!)	
				ML_2H_2	27.3(!)	
CH_3Hg^{II}						
	PMR	-	-	ML	7.40	75FR
				M(LH)	1.94	
	Gl.	1.0 $NaNO_3$	25	ML	7.17	81JI
$C_6H_5Hg^{II}$						
	Solv. ext.	1.0	25	ML	8.42	88KS
In^{3+}	Gl. (DL-)	~ 0.02	24	ML	7.75	76KF
				ML_2	15.17	
	Pol.	0.1 $NaClO_4$	30	ML	6.76	80JK
				ML_2	14.38	
La^{3+}	Gl.	0.1 KCl	20	ML	4.6	74PN
Mn^{2+}	Paper electrophor.	0.1 KNO_3	20	ML	3.2	64J
				ML_2	(4.7)	
	Gl. (DL-)	0.1 KNO_3	25	ML	2.77	64LM
				ML_2	4.57	
	Gl. (DL-)	0.1 KCl	25	ML	2.89	71SS
			35	ML	2.85	
			45	ML	2.78	
	Gl.	0.1 KNO_3	20	ML	2.87	73BS
				ML_2	4.92	
			30	ML	2.81	
				ML_2	4.87	
			40	ML	2.79	
				ML_2	4.83	
			50	ML	2.75	
				ML_2	4.78	
			60	ML	2.72	
				ML_2	4.75	
Ni^{2+}	Gl. (DL-)	-	19	ML	5.59	56PC
				ML_2	10.30	
				ML_3	13.12	
	Gl.	-	10	ML	5.77	57P, 60P, 60Pa, 60Pb
				ML_2	10.64	
				ML_3	13.44	
			15	ML	5.70	
				ML_2	10.48	
				ML_3	13.21	
			18.5	ML	5.71	
				ML_2	10.36	
				ML_3	13.03	
			22	ML	5.67	
				ML_2	10.26	
				ML_3	12.82	

cont'd

Table 4-4. Overall Formation Constants for L-Methionine Metal Complexes (continued)

Metal ion	Method	Medium (mol dm^{-3})	Temp. (°C)	Complex	log β	Ref.
			25	ML	5.56	
				ML_2	10.19	
				ML_3	12.82	
			30	ML	5.46	
				ML_2	10.05	
				ML_3	12.50	
			40	ML	5.39	
				ML_2	9.87	
				ML_3	12.24	
	Gl.	44.6% dioxane	25	ML	6.84	60P, 60Pc
				ML_2	12.75	
				ML_3	16.69	
			30	ML	6.81	
				ML_2	12.66	
				ML_3	16.53	
			40	ML	6.70	
				ML_2	12.40	
				ML_3	16.14	
	Gl.	59.7% dioxane	10	ML	7.41	60P, 60Pc
				ML_2	14.12	
			15	ML	7.36	
				ML_2	14.02	
			25	ML	7.30	
				ML_2	13.85	
			30	ML	7.25	
				ML_2	13.74	
				ML_3	19.42	
			40	ML	7.21	
				ML_2	13.62	
				ML_3	19.17	
	Gl.	69% dioxane	15	ML	8.48	60P, 60Pc
				ML_2	15.61	
				ML_3	20.40	
			30	ML	8.43	
				ML_2	15.52	
			40	ML	8.39	
				ML_2	15.25	
				ML_3	19.44	
	Paper electrophor.	0.1 KNO_3	20	ML	5.7	64J
				ML_2	9.4	
				ML_3	11.7	
	Gl. (DL-)	0.1 KNO_3	25	ML	5.19	64LM
				ML_2	9.84	
	Gl.	1.0 $NaNO_3$	25	ML	5.41	73BJ
				ML_2	10.81	
				ML_3	13.43	
	Gl.	0.1 KNO_3	25	ML	5.34	75IP
				ML_2	9.90	
	Gl.	0.1 KNO_3	25	ML	5.318	76SP
				ML_2	9.894	
	(D-)			ML	5.330	
				ML_2	9.892	

cont'd

Table 4-4. Overall Formation Constants for L-Methionine Metal Complexes (continued)

Metal ion	Method	Medium (mol dm^{-3})	Temp. (°C)	Complex	log β	Ref.
	(DL-)			ML	5.340	
				ML_2	9.990	
	Gl.	0.1 KNO_3	25	ML	5.318	82NMa
				ML_2	9.894	
	(D-)			ML	5.330	
				ML_2	9.892	
	(DL-)			ML	5.34	
				ML_2	9.990	
	Gl. (DL-)	0.5 $NaClO_4$	25	ML	5.10	84MC
				ML_2	9.88	
	Gl. (DL-)	0.1 $NaClO_4$	25	ML	5.08	84MCa
				ML_2	9.65	
	Gl.	0.2 KCl	25	ML	5.23	87SP
				ML_2	9.71	
				ML_3	12.60	
	Gl.	0.2 KNO_3	35	ML	5.32	89KS, 89KV
				ML_2	9.66	
	Gl.	0.2 $NaClO_4$	27	ML	5.60	88PP
				ML_2	10.41	
Os^{4+}	Gl. (DL-)	~ 0.02	28	ML_2	6.06	74FAa
Pb^{2+}	Gl.	0.15 KNO_3	25	ML	4.40	55LM
	Gl. (DL-)	0.1 KNO_3	25	ML	4.38	64LM
				ML_2	8.62	
Pd^{2+}	Gl. (DL-)	~ 0.02	27	ML_2	16.97	73FA
Rh^{3+}	Gl. (DL-)	~ 0.02	25	ML	6.69	74FAb
				ML_2	9.38	
Sm^{3+}	Gl.	0.1 KCl	20	ML	4.6	74PN
$(CH_3)_2Sn^{IV}$						
	Gl. (DL-)	0.1 NaCl	20	ML	7.73	88SS
		75% dioxane	30	ML	7.22	
			40	ML	7.01	
Sr^{2+}	Sol.	-	20	ML	2.29	75S
Th^{4+}	Gl.	0.1 KNO_3	25	ML	6.88	82NMa, 83NM
				ML_2	13.58	
	(D-)			ML	6.82	
				ML_2	13.48	
	(DL-)			ML	6.79	
				ML_2	13.42	
UO_2^{2+}	Gl. (DL-)	0.1 KCl	25	ML	6.52	71SS
				ML_2	11.88	
			35	ML	6.35	
				ML_2	11.55	
			45	ML	6.14	
				ML_2	11.24	

cont'd

Table 4-4. Overall Formation Constants for L-Methionine Metal Complexes (continued)

Metal ion	Method	Medium (mol dm^{-3})	Temp. (°C)	Complex	log β	Ref.
	Gl.	0.1 $NaClO_4$	30	ML	7.65	73RS
				ML_2	13.95	
	Gl.	0.1 KNO_3	25	ML	6.39	82NM, 82NMa, 83NM
				ML_2	13.29	
	(D-)			ML	6.41	
				ML_2	13.38	
	(DL-)			ML	6.43	
				ML_2	13.42	
Y^{3+}	Gl.	0.1 KCl	25	ML	4.6	70RP
	Gl.	0.1 KCl	20	ML	4.5	74PN
Yb^{3+}	Gl.	0.1 KCl	20	ML	4.6	74PN
Zn^{2+}	Gl. (DL-)	0.015	18	ML_2	8.3	53P
	Gl.	0.15 KNO_3	25	ML	4.38	55LM
				ML_2	8.47	
	Pol. (DL-)	-	25	ML_2	8.3	59MH
	Paper electrophor.	0.1 KNO_3	20	ML	4.9	64J
				ML_2	8.5	
				ML_3	(11.7)	
	Gl. (DL-)	0.1 KNO_3	25	ML	4.37	64LM
				ML_2	8.33	
	Gl.	0.15 KNO_3	37	ML	4.22	71HP
				ML_2	6.93	
	Gl.	0.1 KNO_3	25	ML	4.39	75IP
				ML_2	8.38	
	Gl.	0.1 KNO_3	25	ML	4.38	82NMa
				ML_2	8.33	
	(D-)			ML	4.38	
				ML_2	8.32	
	(DL-)			ML	4.39	
				ML_2	8.38	
	Gl.	0.2	30	ML	4.69	84J, 84Ja
				ML_2	8.65	86J
	Gl.	0.1 KNO_3	25	ML	4.45	85MK
	Gl.	0.2 KNO_3	35	ML	4.37	89KS, 89KV
				ML_2	7.93	
	Gl.	0.2 $NaClO_4$	27	ML	4.69	88PP
				ML_2	8.64	

(Gl. = glass electrode potentiometry [as exclusive or main method]; Pol. = polarography; Sp. = spectrophotometry; Sol. = solubility)

Table 4-5. Recommended (R) and Tentative (T) Overall Formation Constants for L-Methionine Metal Complexes

Metal ion		Medium (mol dm^{-3})	Temp. (°C)	Complex	log β	Ref.
Cd^{2+}	(R)	0.1 KNO_3	25	ML	3.69 (±0.02)	64LM, 75IP, 82NMa
				ML_2	7.00 (±0.03)	
	(T)	0.2 KNO_3	25	ML	3.65	86SV
				ML_2	6.76	
				ML_3	9.08	
Co^{2+}	(R)	0.1 KNO_3	25	ML	4.14 (±0.02)	64LM, 75IP, 82NMa
				ML_2	7.28 (±0.02)	
Cu^{2+}	(R)	0.1 KNO_3	25	ML	7.85 (±0.02)	64LM, 75IP,77BP,
				ML_2	14.52 (±0.01)	82NMa
Ni^{2+}	(R)	0.1 KNO_3	25	ML	5.33 (±0.01)	75IP, 76SP
				ML_2	9.90 (±0.01)	
Zn^{2+}	(R)	0.1 KNO_3	25	ML	4.38 (±0.01)	64LM, 75IP, 82NMa
				ML_2	8.35 (±0.03)	

Table 4-6. Constants for Mixed-ligand Complexes Involving L-Methionine

Metal ion	Method	Medium (mol dm^{-3})	Temp. (°C)	Extra ligand (X)	Complex	log β	Ref.
Cd^{2+}	Gl.	0.2	30	NTA	(MX)L	3.14	82J
	Pol.	1.0 KNO_3	30?	Glycine	MLX	6.00	82RB
					ML_2X	9.10	
					MLX_2	9.50	
	Gl.	0.2	30	Iminodiacetate	(MX)L	3.20	84J
	Gl.	0.2	30	Iminodiacetate	(MX)L	3.1±0.1	86J
	Gl.	0.2	30	2,2'-Bipyridyl	(MX)L	3.89	84Ja
	Pol.	-	25	Ethylenediamine	MLX	9.52	84MR
					ML_2X	10.82	
					MLX_2	12.00	
	Gl.	0.2 $NaClO_4$	27	Di-2-pyridylamine	(MX)L	3.85	88PP
	Gl.	0.2 KNO_3	35	Bis(imidazol-2-yl)methane	(MX)L	3.09	89KV
Co^{2+}	Gl.	0.15 KNO_3	25	Iminodiacetic acid	MLX	10.53	87CJ
	Gl.	0.2 KNO_3	35	Bis(imidazol-2-yl)methane	(MX)L	3.57	89KV
	Gl.	0.1 KNO_3	25	ATP	(MX)L	4.05	89MA
Cr^{3+}	Gl. (DL-)	0.1 $NaClO_4$	25	L-Aspartate	MLX	19.75	86MC
					MLXH	23.90	
	Gl. (DL-)	0.1 $NaClO_4$	25	L-Glutamate	MLX	18.75	86MCa
					MLXH	22.68	
				DL-α-Amino-n-butyrate	MLX	16.25	
					MLXH	20.06	
				L-Serine	MLX	15.72	
					MLXH	19.64	
				L-Threonine	MLX	15.52	
					MLXH	19.35	
Cu^{+}	Sp.	1.0	20	Chloride	MLX	14.49	78BK

cont'd

Table 4-6. Constants for Mixed-ligand Complexes Involving L-Methionine (continued)

Metal ion	Method	Medium (mol dm^{-3})	Temp. (°C)	Extra ligand (X)	Complex	log β	Ref.
Cu^{2+}	Gl.	0.1 KNO_3	25	L- or D-Histidine	MLX	17.271	77BP
	Sp.	0.5 $NaClO_4$	-	Salicylic acid	MLX	18.30	77MG
				5-sulfo-salicylic acid	MLX	16.17	
	Gl.	0.15 $NaClO_4$	37	L-Histidine	MLX	16.731	84BP
	Gl.	0.2 KNO_3	25	2,2'-Bipyridyl	(MXL)	7.19	87PS
	Gl.	0.2 KNO_3	35	2,2'-Bipyridyl	(MX)L	7.19	88PS
				Bis(imidazol-2-yl)methane	(MX)L	7.10	
	Gl.	0.2 KNO_3	35	Imidazole	(MX)L	7.16	89PV
					$(MX_2)L$	6.93	
	Gl.	0.1 KNO_3	25	Diethylene-triamine	(MX)L	3.90	89SH
Fe^{2+}	Kin.	0.1 $LiClO_4$	25	Cyanide	$(MX_5)L$	6.08	82TB
Fe^{3+}	Kin.	0.1 $LiClO_4$	25	Cyanide	$(MX_5)L$	2.61	82TB
In^{3+}	Pol.	0.1 $NaClO_4$	30	L-Glutamine	MLX	14.28	80JK
	Pol.	0.1 $NaClO_4$	30	L-Glutamic acid	MLX	16.78	86Ja
Nd^{3+}	Gl.	0.2 $NaClO_4$	40	Hydroxyquinoline	(ML)X	6.52	88AG
			50			6.18	
Ni^{2+}	Gl.	1.0 $NaNO_3$	25	Histidine	MLX	13.40	73BJ
				Aspartate	MLX	11.95	
				Lysine	MLX	10.00	
	Gl. (DL-)	0.5 $NaClO_4$	25	DL-Ethionine	MLX	9.50	84MC
					MLXH	12.07	
	Gl.	0.2 $NaClO_4$	27	Di-2-pyridylamine	(MX)L	5.38	88PP
	Gl.	0.1 KNO_3	25	ATP	(MX)L	4.90	89MA
	Gl.	0.2 KNO_3	35	Bis(imidazol-2-yl)methane	(MX)L	4.72	89KV
Pd^{2+}	Gl.	0.5 KNO_3	25	Ethylenediamine	(MX)L	9.14	78L
					(MX)LH	0.74	
Pr^{3+}	Gl.	0.2 $NaClO_4$	30	Hydroxyquinoline	(ML)X	7.04	88AG
			40			6.17	
			50			5.92	
Pt^{2+}	Gl.	-	-	cis-Diammine	(MX)L	8.70	82XL
	Sp.	-	-			8.60	
Tb^{3+}	Sp.	-	-	EDTA	(MX)L	1.56	85SB
Zn^{2+}	Gl.	-	-	ATP	(MX)L	3.72	80MS
	Gl.	0.2	30	NTA	(MX)L	3.27	82J
	Gl.	0.2	30	Iminodiacetate	(MX)L	3.59	84J
	Gl.	0.2	30	2,2'-Bipyridyl	(MX)L	4.59	84Ja
	Gl.	0.1 KNO_3	25	ATP	(MX)L	3.56	85MK
					(MLX)OH	4.29	
	Gl.	0.2	30	Iminodiacetate	(MX)L	3.5±0.1	86J
	Gl.	0.2 $NaClO_4$	27	Di-2-pyridylamine	(MX)L	4.54	88PP
	Gl.	0.2 KNO_3	35	Bis(imidazol-2-yl)methane	(MX)L	3.81	89KV
	Gl.	0.1 KNO_3	25	NTA	(MX)L	2.94	89S

(Gl. = glass electrode potentiometry [as exclusive or main method]; Pol. = polarography; Sp. = spectrophotometry; Kin. = kinetics)

Table 4-7. Overall Thermodynamic Quantities for L-Methionine Metal Complex Equilibria

Metal ion	Method	Medium (mol dm^{-3})	Temp. (°C)	Complex	ΔH° (kJ mol^{-1})	ΔS° (J K^{-1} mol^{-1})	Ref.
Mn^{2+}	Pot.	0.1 KCl	25 (25-45)	ML	-9.9	(22.1)	71SS
	Pot.	0.1 KNO_3	25 (20-60)	ML ML_2	-7.1 -7.9	29.3 66.9	73BS
Ni^{2+}	Pot.	-	25 (10-40)	ML ML_2 ML_3	-21.6 -43.3 -70.1	33.9 50.2 10.5	57P, 60Pa, 60Pb, 60Pc
		44.6% dioxane	25 (25-40)	ML ML_2 ML_3	-16.7 -41.8 -64.8	74.9 103.8 102.1	60Pc
		59.7% dioxane	25 (10-40)	ML ML_2	-12.6 -29.7	97.5 28.0	60Pc
	Cal.	0.1 KNO_3	25	ML ML_2	-13.1 -35.17	(57.9) (73.3)	76SP
	(D-)			ML ML_2	-13.2 -35.13	(57.8) (71.7)	
	(DL-)			ML ML_2	-13.3 -36.09	(57.7) (70.3)	
UO_2^{2+}	Pot.	0.1 KCl	25 (25-45)	ML ML_2	-34.5 -58.0	(9.2) (32.9)	71SS

(Pot. = potentiometry; Cal. = calorimetry)

5. SERINE - $HOCH_2CH[NH_2]CO_2H$ (2-amino-3-hydroxypropanoic acid, LH)

In aqueous solution, the dissociation of the hydroxy group of serine occurs well beyond the basic limit of the pH range accessible to glass electrode measurements. As far as protonation equilibria are concerned, serine thus virtually behaves in a glycine-like manner apart from the lesser stability of its protonated forms with respect to alanine due to the electron-withdrawing effect of the -OH substituent. Proton dissociation of the latter may, however, be made easier by metal coordination in some specific cases such as in the presence of copper(II) (73GM, 87KS).

Among all studies carried out on the potential role of functional side chain groups in the metal coordination of substituted amino acids, many have been devoted to the hydroxy group of serine (67SS, 68RM, 70LB, 72GM, 72GMa, 72IN, 76PS, 79M, 87KS). Although these have often resulted in controversial interpretations, the relatively large number of complex stability constants determined on this occasion offers a sound basis of data for the comparisons of the present evaluation.

Concerning the particular point raised above, conclusions originally drawn from incomplete or imprecise thermodynamic quantities (mainly derived from the van't Hoff equation) led some to argue in favour of the involvement of the lateral hydroxy group of serine in metal coordination (67SS, 68RM, 72GM, 72GMa, 76PS), others against it (70LB, 72IN). However, the small but significant stereoselectivity characterised using complete and precise (calorimetrically determined) enthalpies relative to copper(II)-serine interactions (76PS) put an end to this discussion by definitely confirming this involvement. So did the discovery of the participation of the hydroxy group in the complexation of copper(II) by the serine zwitterion (76PS). The only question remaining was whether it was associated to the inner (72GMa) or the outer coordination sphere (68RM, 76PS). This point has been clarified in a more recent study which suggests that the -OH group hydrogen-bonded to an axially coordinated water molecule at acidic pH enters the inner coordination sphere of copper(II) on deprotonation (81SH).

In this debate, crystal structure determinations indicated that nickel(II) (69VH), copper(II) (69VF) and zinc(II) (70VN) coordinated with serine in a glycine-like manner. Except for the structure assigned to $Cu(Ser)_2$, which was effectively in line with the indirect binding of the hydroxy group -later shown to take place through a hydrogen bond on thermodynamic grounds (76PS)-, this case once more illustrates how misleading it can be to infer conclusions regarding metal coordination in solution from solid state considerations (88LD).

5-1. Protonation constants of serine

As stated above, numerous investigations have been carried out on the formation of metal serine complexes in which protonation equilibria were used as a reference. The number of data available for the present evaluation is thus relatively important. Unfortunately however, most of these refer to distinct experimental conditions or are poorly reproducible (Table 5-1), so that comparisons are more difficult than expected.

For example, all available data at 25 °C and 0.05 mol dm^{-3} KCl have been obtained by a single group of authors (70GN, 71GN, 72GM, 72GMa, 72GS) under standard conditions not well defined. Moreover, the above articles do not necessarily refer to different works; as is frequently the case with this group, references 71GN and 72GMa seem to be English versions of 70GN and 72GM, respectively. Derived averages introduced in Table 5-2 are thus only tentative.

Of some fifteen independent studies performed at 25 °C with an ionic strength of 0.1 mol dm^{-3} in aqueous medium, only six (70HM, 74KU, 76PS, 77BP, 82NM/83NM, 86MCa) report constants defined on the stoichiometric scale, and the dispersion of these is such that corresponding averages are $\log K_1 = 9.12 \pm 0.14$ and $\log K_2 = 2.12 \pm 0.23$. Nevertheless, considering mixed constants (65PG, 72IN, 75HV, 81L, 86MCa, 89S) and reducing them by the 0.11 variation applicable to the appropriate ionic strength (74MS, 82MS, 89SM) leads, after discarding the most extreme values, to more acceptable averages which are considered as tentative (Table 5-2). It is worth noting in this respect that Sillén and Martell's tables (71SM) wrongly report 9.83 in place of 9.17 for the constant obtained in 65PG, this mistake being copied in 73W.

The situation is not more favourable for the stoichiometric constants determined at 25 °C at an ionic strength of 1.0 mol dm^{-3} (73GM, 81JI), and correction of the mixed values (79FD, 86FA) does not significantly improve it. No average has thus been calculated. The agreement among constants

referring to 25 °C and 3.0 mol dm^{-3} ionic strength (73W, 76BH, 78VV, 85BP) is not much more satisfactory, and corresponding averages have been proposed as only tentative.

Fortunately, protonation constants determined at 37 °C are much more reliable. Indeed, if we correct the mixed constants proposed in references 67PS and 67S by the appropriate 0.12 increment to turn them into stoichiometric values (74MS, 82MS, 89SM), one obtains respectively $\log K_1 = 8.721$ and $\log K_2 = 2.06$, and $\log K_1 = 8.719$ and $\log K_2 = 2.06$, which almost exactly corresponds to the constants reported in 82BK (8.712 and 2.081). The more recent pairs of values obtained in 91DB and 93BA under identical conditions (Table 5-1) also compare favorably with these, and a recommended value has thus been calculated (Table 5-2).

5-2. Thermodynamic quantities for the protonation of serine

Almost all enthalpic determinations relative to the protonation of serine have been made using the calorimetric technique (Table 5-3). Corresponding results are thus reliable a priori. In particular, formation enthalpies for the first protonation step reported in refs. 72IN and 76PS are surprisingly close compared to the related constants (Table 5-1). As well, no apparent difference is noticeable in derived entropies. This similarity stems from the distinct standard states to which formation constants refer, and if these are made identical (see above), corresponding entropies actually differ by more than 2 units.

5-3. Metal complex formation constants

Formation constants for the binary metal complexes of serine are collected in Table 5-4. Once again, the most striking feature is the large diversity of the experimental conditions used, and except for copper(II) and to a lesser extent nickel(II) and zinc(II), it seems at first sight very difficult to extract reliable averages from the available data.

The first illustration of this is given by the cadmium(II)-serine system for which the experimental conditions are so diverse that no comparison is allowed. Corresponding constants are thus left to the responsibility of the involved authors. A majority of these have characterised the existence of a tris-complex. Accordingly, ML_2 constants reported by other groups may be significantly affected by the missing equilibrium and should thus be taken with caution (75HV, 84SC).

A comparable situation is encountered with cobalt(II), for which results cited under refs. 73W for 3 mol dm^{-3} at 25 °C and 67S for 0.15 mol dm^{-3} at 37 °C should be considered as the most reliable a priori and have been accepted as tentative.

The number of constants available for the copper(II)-serine system is exceptionally large, a situation that stems mainly from the interest raised by the possible chelation of copper(II) through the lateral hydroxy group of the ligand, from the facilities offered by Cu^{2+} ion properties to investigate it, and from the biological relevance of copper.

Within the general diversity of the experimental conditions reported, three standard states have been used by two groups of authors at least: 0.05 mol dm^{-3} KCl or KNO_3 (64S, 70GN, 71GN, 72GM, 72GMa, 72GS) and 0.1 mol dm^{-3} KNO_3 or $NaClO_4$ (64S, 72IN, 76PS, 77BP, 81SH, 84BP, 88LG) at 25 °C, and 0.15 mol dm^{-3} $NaClO_4$ or KNO_3 at 37 °C (67PS, 67S, 82BK).

For the data in 0.05 mol dm^{-3} KCl or KNO_3 at 25 °C, only ML and ML_2 have been mentioned, and since (i) MLH (76PS, 82BK) as well as hydroxo[1] species (73GM, 82BK, 87KS) have later been characterised, (ii) MLH has been shown to display an anomalously high stability claimed to result from the participation of the hydroxy group in chelate formation (76PS), the corresponding constants may be altered. In the same manner, the ML_3 species mentioned in 80RR has probably been mistaken for a hydroxo complex. If we nevertheless compare the constants relative to the above conditions, the values found by the same group of authors (70GN, 71GN, 72GM, 72GMa, 72GS) are identical for ML and very similar for ML_2. They are thus to be considered as much more reliable than those reported in 64S whose difference is too large to be interpreted in terms of distinct background electrolytes. Accordingly, average constants derived from the five above references have been proposed as tentative.

[1]The term hydroxo is used here in its most general sense, materializing in fact the loss of a proton regardless of its actual origin. Whether the complex really results from the dissociation of a water molecule or from that of the -OH group of the amino acid is equivalent from the numerical point of view.

In 0.1 mol dm^{-3} KNO_3 at 25 °C, comparable results have been obtained for ML and ML_2 by the authors of refs. 72IN on the one hand and 76PS (and 77BP) on the other hand in spite of the discrepancy affecting their protonation constants.[2] In 76PS, the fact that MLH has also been characterised should logically interfere with the constants of the above species, but this influence has been overlooked in the present case since the MLH constant has been calculated from separate titrations and refinements. The proposed averages, which also take into account the results in 88LG, should nevertheless be considered as tentative only. The constants found in 64S have this time been rejected as very different from those determined in 72IN, 76PS and 77BP, though relating to the same ionic background.

A particular problem was met with the formation of copper(II)-serine complexes under biological conditions. In spite of the excellent agreement of parent protonation constants (see above), a clear discrepancy was noted between complex formation constants reported in 67PS and 67S, and in 82BK (present author involved). As a matter of fact, the ML complex in the latter reference was found to be about three times more stable than that in 67PS and 67S. The high value of the ML constant was all the more surprising as it was also higher than all those obtained at lower temperatures under similar conditions of ionic strength, while the enthalpy of the corresponding equilibrium is known to be negative (70LB, 72IN). The fact that MLH (as well as ML_2H_{-1}) was characterised along with ML and ML_2 might be at the origin of this effect, but this interpretation proved insufficient. Indeed, while ignoring MLH in the pertinent calculations did effectively reduce the ML constant to 7.92, the latter value still looked too high and neglecting ML_2H_{-1} did not change it further. Given the lack of other data under physiological conditions, reinvestigating the copper(II)-serine system was advisable. This has been done recently (93BA).

From comparisons with the copper(II)-threonine system (see next chapter), the constant calculated in 82BK for the ML copper(II)-serine complex was expected to be overvalued by about 0.3 log units. The value obtained in 93BA is effectively 0.29 lower. Incidentally, this indicates at the same time that the values determined in 67PS and 67S were undervalued, which presumably stems from the fact that no account was taken of MLH (see above). Finally, the results found in 93BA appear as the most reliable and have thus been proposed as tentative.

For Fe^{2+} and Mn^{2+} coordination equilibria, no average constant can be proposed given the paucity of the data available. By reference to the above examinations, the results in 73W should be taken as the most reliable.

Although the number of data relative to nickel(II) is appreciably larger, no result has been independently tested under identical experimental conditions and hence no average can be calculated. From the above considerations, refs. 73W and 76PS seem to offer the best standard of quality in the present case. Corresponding constants have thus been accepted as tentative. In the latter reference, it is to be noted that its Table I reports for ML a value of 5.137 for L-serine but a value of 5.320 for DL-serine while both are considered to be identical. By comparison with values relative to threonine in the same reference, 5.137 has been transcribed into the more logical 5.317(?) in Table 5-4.

The situation with lead(II) is still more complicated since available results not only refer to different experimental conditions, but also differ as to the stoichiometry of the complexes formed (73CT, 79KC). No selection can thus be proposed.

The case of zinc(II) is a priori more favourable, because three sets of experimental conditions have been investigated, each of these by at least two groups of authors: 0.05 mol dm^{-3} KNO_3 or KCl (64S, 72GM, 72GMa) and 0.2 mol dm^{-3} KCl or $NaNO_3$ (68RM, 81G) at 25 °C, and 0.15 mol dm^{-3} KNO_3 or $NaClO_4$ at 37 °C (67S, 69PS, 82BK). No conclusion can be drawn from the first results (64S, 72GM, 72GMa) since they refer to ML and ML_2 complexes only while additional species have been shown to exist (67S, 69PS, 73W, 79SS, 81G, 82BK), but a comparison of all the data available for this

[2]This is an example among others that protonation constants may be imprecise in absolute terms without the precision of metal complex formation constants determined with respect to them being significantly affected, provided measurements made in the presence of metal express differences relative to the same internal reference (see introduction). Of course, this does not imply that determinations of metal complex formation constants do not depend on protonation constants, and differences between the protonation constants used for the calculations and those to which measurements implicitely refer are directly reflected in the values obtained, hence the necessity to redefine new protonation references every time formation

system indicates that the constants in 72GM and 72GMa should definitely be preferred in case of necessity.

For the second set of conditions, the results obtained in 68RM would seem reliable if ML and ML_2 were the sole species formed (the corresponding constants are very close to those cited for 30 °C in 81RSa and 81RSb), but more recent works (81G, 82BK) clearly show that it is not so. On the other hand, the ML and ML_2 constants reported in 81G seem too low relative to the values obtained at 37 °C with a 0.15 mol dm^{-3} ionic strength (67S, 69PS, 82BK), at 40 °C in 0.2 mol dm^{-3} KNO_3 (68RM) and at 35 °C in 0.05 mol dm^{-3} KCl (72GM, 72GMa). No definite value can thus be selected at 25 °C.

Under physiological conditions, perfect agreement is observed between ML and (to a lesser extent) ML_2 constants found in 67S and 69PS on the one hand, and in 82BK on the other hand. However, the results in 82BK seem more reliable since (i) hydroxo species have also been characterised in 81G, (ii) the ML_3 complex proposed in 67S and 69PS was tested and proved nonexistent in 82BK. Average values of ML and ML_2 constants have been recommended, $\beta_{ML_2H_{-1}}$ from 82BK being accepted as tentative.

All constants selected for metal serine complexes are shown in Table 5-5. Constants for complex equilibria reported in Table 5-4 but not mentioned in the above discussion should usually be considered accurate to orders of magnitude only.

Numerous mixed-ligand complex formation constants involving serine have been determined (Table 5-6). Nevertheless, sound bases of comparison are extremely scarce. For example, the copper(II)-serine-histidine system has been investigated by two groups of authors in 0.1 mol dm^{-3} KNO_3 at 25 °C (77BP, 79YS) but the average calculated for the MLX constant (17.15 ± 0.06) can only be considered as tentative since other ternary species have been characterised since then (86BH, 93BA). Among the constants obtained in these studies performed under physiological conditions, the values reported in reference 86BH should logically be rejected since they result from the erroneous binary copper(II)-serine values calculated in 82BK (see above). Those found in 93BA should thus be preferred.

No better agreement is observed between results relative to MLX in the copper(II)-serine-histamine system under physiological conditions (67PS, 82BK). This, which might a priori stem from the additional characterisation of MLXH and $MLXH_{-1}$ in 82BK, is more probably attributable to the erroneous copper(II)-serine binary constants (see above).

More surprising, however, is the discrepancy observed between the results obtained by the same two groups of authors on the zinc(II)-serine-histamine system (69PS, 82BK) while parent ML and ML_2 zinc(II)-serine constants have been found almost identical (see Table 5-4). The discrepancy presumably arises from the presence of ML_2X and MLX_2 species in the SCOGS refinement carried out in 69PS.

5-4. Thermodynamic quantities for metal complex formation with serine

The number of available thermodynamic quantities for metal serine interactions is appreciably large, especially as far as copper(II), nickel(II) and zinc(II) are concerned (Table 5-7). In particular, parallel enthalpic determinations by potentiometry and calorimetry relative to the formation of cobalt(II), copper(II), nickel(II) and zinc(II) complexes stress the limits to be expected from the application of the van't Hoff isochore (72GM, 72GMa).

Within calorimetric results, excellent agreement is observed between those obtained for copper(II) in 70LB and 72IN (and even 72GM and 72GMa) under relatively close experimental conditions. It is also the case for nickel, although to a lesser extent (70LB, 72GM, 72GMa). Unfortunately, no such comparison is possible for zinc(II).

Let us finally note that studies on copper(II)-serine interactions are so numerous that calorimetric measurements have even been made on ternary equilibria involving alanine, glycine, valine (72IN), and N-acetyl-glycine (88LG). Corresponding results are to be found in Table 5-8.

Table 5-1. Protonation Constants of Serine

Type of constants	Medium (mol dm^{-3})	Temp. (°C)	log K_1	log K_2	Ref.
Thermo	→0	1	9.880	2.296	42SG
		12.5	9.542	2.232	
		25	9.208	2.186	
		37.5	8.904	2.154	
		50	8.628	2.132	
Thermo	~0.01	20	9.24	2.20	50A
Mixed	0.06 KH_2PO_4	25	9.14	-	52LD
Thermo	~0.01	20	9.34	-	53P
Mixed	1.0 $NaClO_4$	20	9.12	2.26	58P
Stoichio	0.15 KCl	25	9.02	2.12	59FO
Mixed(?)	1.0 KCl	20	9.12	-	59P
Thermo	~0.05	10	9.57	2.27	60Pa
		19.5	9.35	2.23	
		25	9.15	2.21	
		30	9.02	2.19	
		40	8.78	2.17	
Mixed	0.1 $NaNO_3$	25	9.17	-	65PG
Mixed	0.6	25	9.24	-	67AM
Mixed	0.15 KNO_3	37	8.841	2.180	67PS, 68PSa
Mixed	0.15 KNO_3	37	8.839	2.180	67S
?	0.2 KNO_3	15	9.34	2.30	68RM
		25	9.12	2.29	
		40	8.78	2.27	
Mixed(?)	0.1 KCl	22	9.21	-	68RP
Stoichio(?)	0.05 KCl	25	9.10	2.15	70GN, 71GN
Stoichio	0.1 KCl	25	9.260	-	70HM
		37	8.977	-	
		50	8.685	-	
Mixed(?)	0.16 KNO_3	25	9.18	-	70LB
Stoichio(?)	0.05KCl	20	9.23	2.14	72GM, 72GMa
		25	9.10	2.15	
		30	8.97	2.18	
		35	8.83	2.22	
Stoichio(?)	0.05 KCl	25	9.08	2.17	72GS
Mixed	0.1 KNO_3	25	9.15	2.55	72IN
	0.2 KNO_3	25	9.12	2.29	
Mixed(?)	0.1 KNO_3	20	9.18	-	73BS
		30	8.95	-	
		40	8.78	-	
		50	8.57	-	
		60	8.38	-	
Stoichio	1.0 $NaClO_4$	25	9.18	2.27	73GM
Stoichio	0.15 NaCl	25	8.954	2.209	73KS, 77S
Mixed(?)	0.5	25	8.99	2.24	73SK
Stoichio	3.0 $NaClO_4$	25	9.574	2.559	73W
Mixed	0.5 KNO_3	20	9.26	2.80	74KH
Stoichio(?)	0.1 $LiClO_4$	25	9.01	2.12	74KU
Mixed	0.1 KCl	20	9.0	-	74PN
Mixed(?)	0.1 KNO_3	25	9.14	-	75HV
	0.5 KNO_3	25	9.06	-	
Stoichio	3.0 $NaClO_4$	25	9.61	2.60	76BH
Stoichio	0.1 KNO_3	25	9.074	1.95	76PS
Stoichio	0.1 KNO_3	25	9.073	1.951	77BP

cont'd

Table 5-1. Protonation Constants of Serine (continued)

Type of constants	Medium (mol dm^{-3})	Temp. (°C)	log K_1	log K_2	Ref.
Thermo	→0	25	1.09		78KA
	100% formic acid				
Stoichio(?)	3.0 KCl	25	9.452	2.405	78VV
Mixed(?)	1.0 KCl	25	9.15	-	79FD
Thermo	~0	25	8.98	-	79FM
	50% ethanol				
Thermo	~0	25	9.04		80KT
	formic acid: ethyl methyl ketone (1:24				
Stoichio	0.1 KNO_3	25	9.16	2.44	80YT
	20% dioxane				
Stoichio	0.1	20	9.07	2.13	81CD
	0.1	20	7.67	-	
	100% trifluoroethanol				
Thermo	~0	25	9.15	-	81FP
Stoichio	1.0 $NaNO_3$	25	8.97	2.19	81JI
Mixed(?)	0.1 KNO_3	25	9.17	2.27	81L
Mixed	0.25 KNO_3	30	8.81	2.17	81RK
Mixed	0.2 $NaNO_3$	30	8.95	2.25	81RSa, 81RSb
Stoichio	0.15 $NaClO_4$	37	8.712	2.081	82BK
Thermo	~0	25	8.97	2.22	82DD
	8.0% propan-2-ol	25	8.96	2.33	
	16.3% propan-2-ol	25	8.99	2.43	
	25.1% propan-2-ol	25	8.99	2.55	
	34.3% propan-2-ol	25	8.99	2.65	
	43.9% propan-2-ol	25	9.04	2.72	
	54.0% propan-2-ol	25	9.06	2.82	
	64.6% propan-2-ol	25	9.07	2.90	
	75.8% propan-2-ol	25	9.09	3.11	
Stoichio	0.1 KNO_3	25	9.16	2.349	82NM, 83NM
Stoichio	0.25 NaCl	25	9.03	2.173	84AO
Mixed	1.0 KNO_3	30	9.10	-	84CG
Mixed	0.5 KNO_3	30	9.18	2.21	84KB
Mixed	0.1	35	9.0	2.1	84SY, 85SY
Stoichio	3.0 NaCl	25	9.50	2.45	85BP
Mixed(?)	0.1 KNO_3	25	9.05	-	85MK
Mixed	0.1 KNO_3	27	9.18	-	85MS
	50% methanol				
Mixed(?)	0.7 $NaClO_4$	20	8.98	-	85SC
Mixed(?)	0.15 NaCl	20	9.18	-	85VD
Mixed(?)	1.0 KCl	25	9.24	-	86FA
Stoichio	0.1 $NaClO_4$	25	9.171	2.211	86MCa
Mixed(?)	0.7 $NaClO_4$	25	8.98	-	86CS
Mixed	0.2 KCl	25	9.38	2.44	86KD
Thermo	~0	25	8.97	2.22	86PD
	8.0% t-BuOH	25	9.16	2.40	
	16.4% t-BuOH	25	9.20	2.52	
	25.0% t-BuOH	25	9.22	2.57	
	34.2% t-BuOH	25	9.24	2.61	
	43.8% t-BuOH	25	9.28	2.63	
	54.0% t-BuOH	25	9.32	2.73	
	64.5% t-BuOH	25	9.38	2.87	
	75.8% t-BuOH	25	9.38	3.18	

cont'd

Table 5-1. Protonation Constants of Serine (continued)

Type of constants	Medium (mol dm^{-3})	Temp. (°C)	log K_1	log K_2	Ref.
Stoichio(?)	0.2 KNO_3	25	9.04	2.25	86SV
Mixed(?)	0.15 KNO_3	25	9.14	-	87CJ
Thermo	~0	25	8.99	2.23	87CL
	10% methanol	25	8.97	2.29	
	20% methanol	25	8.97	2.39	
	30% methanol	25	9.00	2.51	
	40% methanol	25	9.00	2.68	
	50% methanol	25	9.04	2.82	
	60% methanol	25	9.08	3.96	
	70% methanol	25	9.10	3.19	
	80% methanol	25	9.11	3.51	
	10% ethanol	25	9.00	2.29	
	20% ethanol	25	8.99	2.39	
	30% ethanol	25	9.00	2.53	
	40% ethanol	25	9.02	2.67	
	50% ethanol	25	9.05	2.83	
	60% ethanol	25	-	2.91	
	70% ethanol	25	-	3.10	
	80% ethanol	25	-	3.37	
Stoichio	0.2 KCl	25	9.04	2.13	87KS
Mixed	0.1 NaCl	25	9.24	-	87SM
?	0.1 $NaClO_4$	25	9.02	2.29	88LG
Mixed	2.25 $NaNO_3$	25	9.274	2.322	89CV
Thermo	0	25	9.32	-	89JA
	20% ethanol	25	9.27	-	
	40% ethanol	25	9.30	-	
	60% ethanol	25	9.40	-	
	80% ethanol	25	9.71	-	
Mixed	0.1 KNO_3	25	9.15	-	89S,90S
Stoichio	0.15 NaCl	37	8.708	2.107	91DB
Stoichio	0.15 $NaClO_4$	37	8.728	2.158	93BA

Table 5-2. Recommended (R) and Tentative (T) Values for Protonation Constants of Serine

Type of constants	Medium (mol dm^{-3})	Temp. (°C)	log K_1	log K_2	Ref.
Stoichio? (T)	0.05 KCl	25	9.09 (±0.01)	2.16 (±0.01)	70GN, 71GN, 72GM, 72GMa, 72GS
Stoichio (T)	0.1 KNO_3	25	9.05 (±0.04	2.1 (±0.2)	65PG, 72IN, 74KU, 75HV, 76PS, 77BP, 81L, 86MCa, 89S
Stoichio (T)	3.0 $NaClO_4$	25	9.53 (±0.08)	2.5 (±0.1)	73W, 76BH, 78VV, 85BP
Stoichio (R)	0.15	37	8.72 (±0.01)	2.09 (±0.07)	67PS, 67S, 82BK, 91DB, 93BA

Table 5-3. Thermodynamic Quantities for Serine Protonation Equilibria

Method	Medium (mol dm^{-3})	Temp. (°C)	$\Delta H°_1$ (kJ mol^{-1})	$\Delta H°_2$	$\Delta S°_1$ (J K^{-1} mol^{-1})	$\Delta S°_2$	Ref.
Pot.	→0	1	-43.72	-8.29	29.4	13.8	42SG
		12.5	-43.89	-7.20	29.1	17.6	
		25	-43.53	-5.71	30.1	22.6	
		37.5	-42.68	-3.90	33.0	28.4	
		50	-41.17	-1.72	38.1	35.5	
Pot.	0.1 KCl	25	-42.42	-	35.1	-	70HM
Cal.	0.16 KNO_3	25	-42.05	-	34.7	-	70LB
Cal.	~0	20	-41.5	-	-	-	71MB
Cal.	0.05 KCl	25	-42.68	-5.02	33.9	24.3	72GM, 72GMa
Cal.	0.1 KNO_3	25	-43.76	-	28.3	-	72IN
Cal.	0.1 KNO_3	25	-43.28	-	28.5	-	76PS
Cal.	0.2 KCl	25	-43.6	-1.9	26.9	34.3	87KS
Cal.	~0	25	-40.6	-1.34	40.0	37.3	87RF, 89R, 89RM
Cal.	0.1 $NaClO_4$	25	-45.5	-3.99	20.1	30.5	88LG

(Pot. = potentiometry; Cal. = calorimetry)

Table 5-4. Overall Formation Constants for L-Serine Metal Complexes

Metal ion	Method	Medium (mol dm^{-3})	Temp. (°C)	Complex	log β	Ref.
Ag^+	Pol.	0.6	25	ML	3.40	67AM
				ML_2	6.67	
	Ag el. (DL-)	0.1 (KNO_3	25	ML	4.1	81UP
				MLH	7.4	
				MLH_2	9.9 (?)	
Al^{3+}	Gl.	0.15 NaCl	37	ML	5.97	91DB
Au^{3+}	Gl. (DL-)	~ 0.02	25	ML	6.54	74FA
				ML_2	9.34	
Be^{2+}	Gl. (DL-)	0.015	20	ML_2	12.1	53P
Ca^{2+}	Sol.	→0	25	ML	1.43	50DW
	Ion exch.	0.16 (pH 7.2)	25	ML	~0.5	54S
	Gl.	3.0 NaCl	25	ML	1.00	85BP
Cd^{2+}	Gl. (DL-)	0.015	20	ML_2	7.4	53P
	Gl.	3.0 $NaClO_4$	25	ML	4.154	74WW
				ML_2	7.863	
				ML_3	10.221	
	Gl.	0.1 KNO_3	25	ML	4.0	75HV
				ML_2	7.2	
	Pol. (DL-)	1.0 $NaClO_4$	30	ML	4.69	79PG
				ML_2	6.77	
				ML_3	8.85	
	Pol. (DL-)	0.5 KNO_3	25	ML	4.00	79SGa
				ML_2	7.15	
				ML_3	9.22	
		15% DMF(v/v)	ML	4.08		
				ML_2	7.62	
				ML_3	9.71	
		15% DMSO(v/v)	ML	4.30		
				ML_2	7.90	
				ML_3	9.98	
	Pol.	1.0 KNO_3	30	ML	4.10	82CG,
				ML_2	7.10	84CG
				ML_3	9.08	
	Gl.	0.2	30	ML	3.95	84J, 84Ja
				ML_2	7.25	86J
	Gl.	0.7 $NaClO_4$	20	ML	3.731	84SC
				ML_2	7.091	
	Pol.	0.7 $NaClO_4$	20	ML	3.45	
				ML_2	6.80	
	Pol.	0.5 KNO_3	30	ML	4.78	84KB
				ML_2	7.29	
				ML_3	9.45	
		20% methanol	30	ML	5.00	
				ML_2	7.89	
				ML_3	10.18	
		40% methanol	30	ML	5.35	
				ML_2	7.95	
				ML_3	10.45	

cont'd

Table 5-4. Overall Formation Constants for L-Serine Metal Complexes (continued)

Metal ion	Method	Medium (mol dm^{-3})	Temp. (°C)	Complex	log β	Ref.
		40% ethanol	30	ML	4.78	
				ML_2	8.20	
				ML_3	11.74	
		20% aceto-nitrile	30	ML	4.61	
				ML_2	7.30	
				ML_3	9.56	
		40% aceto-nitrile	30	ML	4.78	
				ML_2	7.40	
				ML_3	10.30	
	Pol.	1.0 KNO_3 (pH 8-9)	30	ML	4.00	85KC
				ML_2	7.10	86KC
				ML_3	9.30	
	Gl.	0.7 $NaClO_4$	20	ML	3.728	85SC
				ML_2	7.02	
				MLH_{-1}	-5.83	
	DPP			ML	3.45	
				ML_2	6.80	
	Gl.	0.2 KNO_3	25	ML	3.77	86SV
				ML_2	7.03	
				ML_3	9.33	
	Gl.	0.2 $NaClO_4$	27	ML	3.95	88PP
				ML_2	7.25	
	Gl.	0.2 KNO_3	35	ML	3.78	89KS, 89KV
				ML_2	6.80	
Ce^{3+}	Gl.	0.1 KCl	22	ML	3.4	68RP
Co^{2+}	Gl. (DL-)	~ 0.01	20	ML_2	8.0	50A
	Gl. (DL-)	→0	25	ML	4.90	64S
				ML_2	9.10	
		0.01 KNO_3	25	ML	4.84	
				ML_2	8.98	
		0.02 KNO_3	25	ML	4.74	
				ML_2	8.86	
		0.05 KNO_3	25	ML	4.47	
				ML_2	8.25	
	Gl.	0.15 KNO_3	37	ML	4.20	67S, 69PS
				ML_2	7.56	
				ML_3	9.81	
	Gl. (DL-)	0.2 KNO_3	15	ML	4.37	68RM
				ML_2	7.75	
			25	ML	4.33	
				ML_2	7.66	
			40	ML	4.25	
				ML_2	7.51	
	Gl.	0.05 KCl	20	ML	4.42	72GM, 72GMa
				ML_2	8.08	
			25	ML	4.38	
				ML_2	8.00	
			30	ML	4.34	
				ML_2	7.92	
			35	ML	4.30	
				ML_2	7.84	

cont'd

Table 5-4. Overall Formation Constants for L-Serine Metal Complexes (continued)

Metal ion	Method	Medium (mol dm^{-3})	Temp. (°C)	Complex	log β	Ref.
	Gl.	3.0 $NaClO_4$	25	ML	4.584	73W
				ML_2	8.568	
				ML_3	11.554	
	Gl.	3.0 NaCl	25	ML	4.32	85BP
				ML_2	7.90	
				ML_3	10.2	
	Gl.	0.15 KNO_3	25	ML	4.36	87CJ
				ML_2	8.00	
	Gl.	0.2 KNO_3	35	ML	4.19	89KS, 89KV
				ML_2	7.71	
Cr^{2+}	Gl. (DL-)	~ 0.015	25(?)	ML	7.21	70FM
Cr^{3+}	Gl.	0.4 KCl	25	ML	8.0	63KM
				ML_2	14.2	
				ML_3	19.4	
	Gl.	0.1 $NaClO_4$	25	ML	8.31	86MCa
				ML_2	11.27	
				ML_3	15.44	
Cu^{2+}	Gl. (DL-)	~ 0.01	20	ML_2	14.6	50A
	Pol.	0.06 KH_2PO_4	25	ML_2	14.54	52LD
	Gl. (DL-)	→0	25	ML	8.40	64S
				ML_2	14.50	
		0.01 KNO_3	25	ML	8.20	
				ML_2	14.26	
		0.02 KNO_3	25	ML	8.00	
				ML_2	14.02	
		0.05 KNO_3	25	ML	7.65	
				ML_2	13.50	
		0.10 KNO_3	25	ML	7.57	
				ML_2	13.32	
	Gl.	0.15 $NaClO_4$	37	ML	7.57	67PS
				ML_2	14.02	
	Gl.	0.15 KNO_3	37	ML	7.56	67S
				ML_2	14.01	
	Gl. (DL-)	0.2 KNO_3	15	ML	8.02	68RM
				ML_2	14.64	
			25	ML	7.89	
				ML_2	14.40	
			40	ML	7.73	
				ML_2	14.06	
	Gl.	0.05 KCl	25	ML	7.93	70GN, 71GN
				ML_2	14.67	
	Gl. (DL-)	0.16 KNO_3	25	ML	7.85	70LB
				ML_2	14.50	
	Gl.	0.05 KCl	20	ML	7.97	72GM, 72GMa
				ML_2	14.62	
			25	ML	7.93	
				ML_2	14.48	
			30	ML	7.88	
				ML_2	14.37	
			35	ML	7.80	
				ML_2	14.19	

cont'd

Table 5-4. Overall Formation Constants for L-Serine Metal Complexes (continued)

Metal ion	Method	Medium (mol dm^{-3})	Temp. (°C)	Complex	log β	Ref.
	Gl.	0.05 KCl	25	ML	7.93	72GS
				ML_2	14.57	
	Gl.	0.1 KNO_3	25	ML	7.92	72IN
				ML_2	14.57	
	Gl.	1.0 $NaClO_4$	25	ML	7.95	73GM
				ML_2	14.68	
				ML_2H_{-1}	4.43	
				ML_2H_{-2}	-6.83	
	Gl.	0.15 NaCl	25	ML	8.010	73KS, 77S
				ML_2	14.585	
				ML_2H_{-1}	4.772	
				ML_2H_{-2}	-6.18	
	Gl.	3.0 $NaClO_4$	25	ML	8.950	73W
				ML_2	16.230	
	Gl.	0.1 KNO_3	25	ML	7.858	76PS
				ML_2	14.428	
				MLH	11.41	
	(DL-)			ML	7.862	
				ML_2	14.437	
	Gl.	0.1 KNO_3	25	ML	7.858	77BP
				ML_2	14.428	
	Sp.	~0	25	ML	7.77	79FM
		50% ethanol		ML_2	14.67	
	Pol. (DL-)	0.5 KNO_3	25	ML	7.88	79SS
				ML_2	15.50	
			35	ML	7.75	
				ML_2	15.18	
	Gl.	0.1 $NaClO_4$	30	ML	7.85	80AS
				ML_2	14.43	
	Pol. (DL-)	0.1 $NaClO_4$	30	ML_2	14.8(4)	80RR
				ML_3	18.26	
	Gl.	0.1 KNO_3	25	ML	8.14	80YT
		20% dioxane		ML_2	14.98	
	Gl.	~0	25	ML	8.66	81FP
	Gl.	0.25 KNO_3	30	ML	7.56	81RK
				ML_2	14.01	
	Gl.	0.2 $NaNO_3$	30	ML	7.84	81RSa, 81RSb
				ML_2	14.31	
	Gl.	0.1 KNO_3	25	ML	7.92	81SH
				ML_2	14.73	
				ML_2H_{-1}	4.37	
				ML_2H_{-2}	-6.77	
	Gl.	0.15 $NaClO_4$	37	ML	8.034	82BK
				ML_2	14.366	
				MLH	10.645	
				ML_2H_{-1}	4.832	
	Gl.	0.25 NaCl	25	ML	7.781	84AO
				ML_2	14.295	
				ML_2H_{-1}	4.375	
				ML_2H_{-2}	-6.525	
	Cu(Hg) el.	0.1 KNO_3	25	ML	8.11	84PB
				ML_2	14.69	

cont'd

Table 5-4. Overall Formation Constants for L-Serine Metal Complexes (continued)

Metal ion	Method	Medium (mol dm^{-3})	Temp. (°C)	Complex	log β	Ref.
	Gl.	0.2 KCl	25	ML	7.81	87KS
				ML_2	14.24	
				ML_2H_{-1}	4.09	
				ML_2H_{-2}	-7.06	
	Gl.	0.1 $NaClO_4$	25	ML	7.95	88LG
				ML_2	14.52	
	Pol.	1.0 KNO_3	30	ML	7.80	88SKa
				ML_2	14.10	
	Gl.	0.15 $NaClO_4$	37	ML	7.748	93BA
				ML_2	14.083	
				MLH	10.030	
				ML_2H_{-1}	4.285	
Dy^{3+}	Gl.	0.1 KCl	20	ML	3.4	74PN
Er^{3+}	Gl.	0.1 $NaNO_3$	25	ML	3.89	65PG
Fe^{2+}	Gl. (DL-)	~ 0.01	20	ML_2	7.0	50A
	Gl.	1.0 KCl	20	ML	3.43	59P
	Estim.	→0	25	ML	7.7	64S
	Gl. (DL-)	0.2 KNO_3	15	ML	3.67	68RM
				ML_2	6.45	
			40	ML	3.62	
				ML_2	6.36	
	Gl.	3.0 $NaClO_4$	25	ML	4.299	73W
				ML_2	7.377	
				ML_3	10.299	
Fe^{3+}	Gl.	1.0 $NaClO_4$	20	ML	9.2	58P
	Ox. Pot.	1.0 $NaNO_3$	25	ML_2H	18.78	88SP
				ML_2H_2	22.06	
Ga^{3+}	Gl.	3.0 $NaClO_4$	25	ML	9.0	76BH
				M(LH)	1.8	
Gd^{3+}	Gl.	0.1 $NaNO_3$	25	ML	3.59	65PG
	Gl.	0.1 KCl	20	ML	3.2	74PN
$HfOCl_2$	Color.	-	25	ML	1.25	71KP
Hg^{2+}	Gl. (DL-)	0.015	20	ML_2	17.5	53P
	Pol.	0.5 KNO_3	25	ML_2	17.34	66TA
	Hg el.	0.1 $NaNO_3$	25	ML	11.7	73VB
				ML_2	19.1	
	Ion exch.	0.375 (pH 7.8)	25	ML	4.53(!)	83HD
CH_3Hg^{II}						
	Gl.	1.0 $NaNO_3$	25	ML	6.93	81JI
Ho^{3+}	Gl.	0.1 $NaNO_3$	25	ML	4.00	65PG
In^{3+}	Gl. (DL-)	~ 0.02	24	ML	7.53	76KF
				ML_2	14.58	
La^{3+}	Gl.	0.1 KCl	20	ML	3.0	74PN

cont'd

Table 5-4. Overall Formation Constants for L-Serine Metal Complexes (continued)

Metal ion	Method	Medium (mol dm^{-3})	Temp. (°C)	Complex	log β	Ref.
Lu^{3+}	Gl.	0.1 $NaNO_3$	25	ML	3.92	65PG
Mg^{2+}	Gl.	3.0 NaCl	25	ML	1.03	85BP
	Gl. (DL-)	0.15 NaCl	20	ML	1.47	85VD
Mn^{2+}	Estim.	→0	25	ML	3.4	64S
	(DL-)			ML_2	6.7	
	Gl.	0.15 $NaClO_4$	37	ML	2.32	67S
	Gl. (DL-)	0.2 KNO_3	15	ML	2.51	68RM
				ML_2	4.00	
			40	ML	2.48	
				ML_2	3.95	
	Gl.	0.1 KNO_3	20	ML	3.91	73BS
				ML_2	6.31	
			30	ML	3.87	
				ML_2	6.27	
			40	ML	3.81	
				ML_2	6.22	
			50	ML	3.77	
				ML_2	6.18	
			60	ML	3.72	
				ML_2	6.15	
	Gl.	3.0 $NaClO_4$	25	ML	2.893	73W
				ML_2	4.791	
	Gl. (DL-)	0.15 NaCl	20	ML	2.38	85VD
Nd^{3+}	Gl.	0.2 KCl	25	ML	0.99	73SY
	NMR	0.2 KCl	25	ML	1.10	
Ni^{2+}	Gl. (DL-)	-	20	ML	5.44	56PC
				ML_2	10.06	
				ML_3	13.17	
	Gl.	-	10	ML	5.66	57P, 60P, 60Pa, 60Pb
				ML_2	10.37	
				ML_3	13.68	
			19.5	ML	5.58	
				ML_2	10.12	
				ML_3	13.20	
			25	ML	5.48	
				ML_2	9.94	
				ML_3	12.97	
			30	ML	5.44	
				ML_2	9.82	
				ML_3	12.79	
			40	ML	5.27	
				ML_2	9.57	
				ML_3	12.34	
	Estim.	~0	25	ML	6.0	64S
	(DL-)			ML_2	10.6	
	Gl.	0.15 KNO_3	37	ML	5.21	67S, 68PSa
				ML_2	9.59	
				ML_3	12.49	

cont'd

Table 5-4. Overall Formation Constants for L-Serine Metal Complexes (continued)

Metal ion	Method	Medium (mol dm^{-3})	Temp. (°C)	Complex	log β	Ref.
	Gl. (DL-)	0.2 KNO_3	15	ML	5.50	68RM
				ML_2	9.94	
			25	ML	5.42	
				ML_2	9.76	
			40	ML	5.28	
				ML_2	9.47	
	Gl. (DL-)	0.16 KNO_3	25	ML	5.45	70LB
				ML_2	9.98	
				ML_3	13.52	
	Gl.	0.05 KCl	20	ML	5.48	72GM, 72GMA
				ML_2	10.07	
			25	ML	5.43	
				ML_2	9.96	
			30	ML	5.40	
				ML_2	9.87	
			35	ML	5.30	
				ML_2	9.71	
	Gl.	0.05 KCl	25	ML	5.43	72GS
				ML_2	9.96	
	Gl.	3.0 $NaClO_4$	25	ML	5.626	73W
				ML_2	10.621	
				ML_3	14.178	
	Gl.	0.1 KNO_3	25	ML	5.317(?)	76PS
				ML_2	9.743	
				ML_3	12.73	
	(DL-)			ML	5.320	
				ML_2	9.755	
				ML_3	12.68	
	Gl.	0.2 $NaNO_3$	30	ML	5.40	81RSa, 81RSb
				ML_2	9.68	
	Gl.	1.0 KCl	25	ML	5.42	83FA
				ML_2	9.76	
	Gl.	3.0 NaCl	25	ML	5.34	85BP
				ML_2	9.94	
				ML_3	13.02	
	Gl.	0.2 $NaClO_4$	27	ML	5.69	88PP
				ML_2	10.45	
	Gl.	0.2 KNO_3	35	ML	5.42	89KS, 89KV
				ML_2	9.76	
Os^{4+}	Gl. (DL-)	~ 0.02	28	ML	5.60	74FAa
Pb^{2+}	Gl.	0.15 KNO_3	37	ML	4.41	67S
				ML_2	7.51	
	Gl.	3.0 $NaClO_4$	25	ML	5.054	73CT
				ML_2	8.265	
				ML_3	9.957	
	Gl.	1.0 $NaClO_4$	25	ML	4.86	79KC
				MLH	11.00	
				MLH_{-1}	-3.15	
	Pol. (DL-)	0.5 KNO_3	25	ML	4.48	79SGa
				ML_2	8.00	
				ML_3	10.69	

cont'd

Table 5-4. Overall Formation Constants for L-Serine Metal Complexes (continued)

Metal ion	Method	Medium (mol dm^{-3})	Temp. (°C)	Complex	log β	Ref.
		15% DMF(v/v)		ML	4.78	
				ML_2	8.48	
				ML_3	10.91	
		15% DMSO(v/v)		ML	5.18	
				ML_2	8.81	
				ML_3	11.25	
	Pol.	0.7 $NaClO_4$	25	ML	4.71	86CS
				ML_2	7.88	
	Pol.	1.0 KNO_3	30	ML	4.80	89SC
				ML_2	7.90	
Pd^{2+}	Gl. (DL-)	0.5 KNO_3	20	ML	9.7	74KH
				ML_2	18.8	
	Gl. (DL-)	~ 0.02	27	ML	16.88	73FA
	Gl.	0.1 NaCl	25	ML	8.66	87SM
Pu^{3+}	Ion-exch.	1.0 KCl	18	ML	3.42	73RK
Rh^{3+}	Gl. (DL-)	~ 0.02	25	ML	6.92	74FAb
				ML_2	9.95	
Sm^{3+}	Gl.	0.1 KCl	20	ML	3.4	74PN
Sr^{2+}	Ion exch.	0.16 (pH 7.2)	25	ML	~0.4	54S
	Sol.	-	20	ML	2.69	75S
Tb^{3+}	Gl.	0.1 $NaNO_3$	25	ML	3.77	65PG
Th^{4+}	Gl.	0.5	25	ML	8.07	73SK
	Ion exch.	0.5	20	ML	8.10	80S
	Gl. (D-)	0.1 KNO_3	25	ML	8.25	83NM
				ML_2	16.75	
Ti^{3+}	Gl. (DL-)	~ 0.02	25?	ML	7.54	70FMb
Tl^{+}	Gl.	0.1 $LiClO_4$	25	ML	1.53	74KU
U^{4+}	Sp.	0.5	20	ML	9.70	74SK
UO_2^{2+}	Solv. extr.	0.45 NaCl	25	M(LH)	0.87	57LW
	Gl. (DL-)	~ 0.02	25?	ML	6.86	70FMb
	Gl.	0.1 $NaClO_4$	30	ML	7.60	73RS
				ML_2	14.75	
	Gl.	0.5	25	ML	6.04	73SKa
	Sp.	0.5	25	ML	5.90	
	Gl. (D-)	0.1 KNO_3	25	ML	8.66	82NM, 83NM
				ML_2	14.66	
	Gl. (DL-)	0.1 KNO_3 50% methanol	27	ML	7.92	85MS
V^{3+}	Gl.	0.2 KCl	25	ML	11.82	86KD

cont'd

Table 5-4. Overall Formation Constants for L-Serine Metal Complexes (continued)

Metal ion	Method	Medium (mol dm^{-3})	Temp. (°C)	Complex	log β	Ref.
VO^{2+}	Gl. (DL-)	~ 0.02	25?	ML	7.54	70FMb
	Gl.	2.25 $NaNO_3$	25	MLH	10.37	89CV
				ML	6.38	
				ML_2H_2	19.9	
				ML_2H	16.44	
				ML_2	11.70	
				$M_2L_2H_{-2}$	4.99	
				ML_2H_{-1}	4.45	
				$M_2L_2H_{-3}$	-1.23	
				ML_2H_{-2}	-5.0	
				MLH_{-2}	-6.0	
				MLH_{-3}	-18.0	
Y^{3+}	Gl.	0.1 $NaNO_3$	25	ML	3.49	65PG
	Gl.	0.1 KCl	22	ML	3.5	68RP
	Gl.	0.1 KCl	20	ML	3.3	74PN
Yb^{3+}	Gl.	0.1 $NaNO_3$	25	ML	3.92	65PG
	Gl.	0.1 KCl	20	ML	3.7	74PN
Zn^{2+}	Gl. (DL-)	0.015	20	ML_2	8.6	53P
	Gl. (DL-)	→0	25	ML	5.30	64S
				ML_2	9.75	
		0.01 KNO_3	25	ML	5.22	
				ML_2	9.68	
		0.02 KNO_3	25	ML	5.19	
				ML_2	9.64	
		0.05 KNO_3	25	ML	5.08	
				ML_2	9.48	
		0.10 KNO_3	25	ML	4.94	
				ML_2	9.22	
	Gl.	0.15 KNO_3	37	ML	4.47	67S, 69PS
				ML_2	8.31	
				ML_3	10.56	
	Gl. (DL-)	0.2 KNO_3	15	ML	4.71	68RM
				ML_2	8.48	
			25	ML	4.66	
				ML_2	8.38	
			40	ML	4.58	
				ML_2	8.22	
	Gl.	0.15 NaCl	37?	ML	4.62	72GH
				ML_2	8.48	
	Gl.	0.05 KCl	20	ML	4.69	72GM, 72GMa
				ML_2	8.76	
			25	ML	4.65	
				ML_2	8.68	
			30	ML	4.61	
				ML_2	8.61	
			35	ML	4.58	
				ML_2	8.54	
	Gl.	3.0 $NaClO_4$	25	ML	4.898	73W
				ML_2	9.279	
				ML_3	11.909	
	Pol. (DL-)	0.5 KNO_3	25	ML	4.60	79SS
				ML_2	8.30	
				ML_3	11.00	
			35	ML	4.52	
				ML_2	8.13	
				ML_3	10.77	

cont'd

Table 5-4. Overall Formation Constants for L-Serine Metal Complexes (continued)

Metal ion	Method	Medium (mol dm^{-3})	Temp. (°C)	Complex	log β	Ref.
	Gl.	0.2 KCl	25	ML	4.45	81G
				ML_2	8.16	
				MLH_{-1}	-3.73	
				ML_2H_{-1}	-2.4	
	Gl.	0.2 $NaNO_3$	30	ML	4.68	81RSa, 81RSb
				ML_2	8.39	
	Gl.	0.15 $NaClO_4$	37	ML	4.475	82BK
				ML_2	8.262	
				ML_2H_{-1}	-1.140	
	Gl.	0.2	30	ML	5.06	84J, 84Ja
				ML_2	9.16	86J
	Gl.	0.1 KNO_3	25	ML	4.62	85MK
	Gl.	0.2 $NaClO_4$	27	ML	5.06	88PP
				ML_2	9.17	
	Gl.	0.2 KNO_3	35	ML	4.66	89KS, 89KV
				ML_2	8.49	

(Gl. = glass electrode potentiometry [as exclusive or main method]; Pol. = polarography; Sp. = spectrophotometry; Sol. = solubility; DPP = differential pulse polarography)

Table 5-5. Recommended (R) and Tentative (T) Overall Formation Constants for L-Serine Metal Complexes

Metal ion		Medium (mol dm^{-3})	Temp. (°C)	Complex	log β	Ref.
Co^{2+}	(T)	3.0 $NaClO_4$	25	ML	4.58	73W
				ML_2	8.57	
				ML_3	11.55	
Cu^{2+}	(T)	0.05 KCl	25	ML	7.93 (±0.01)	71GN, 70GN, 72GM,
				ML_2	14.57 (±0.10)	72GMa, 72GS
	(T)	0.1	25	ML	7.90 (±0.05)	72IN, 76PS, 77BP, 88LG
				ML_2	14.49 (±0.08)	
	(T)	0.15 $NaClO_4$	37	ML	7.75	93BA
				ML_2	14.08	
				MLH	10.03	
				ML_2H_{-1}	4.28	
Ni^{2+}	(T)	0.1 KNO_3	25	ML	5.32	76PS
				ML_2	9.74	
				ML_3	12.7	
	(T)	3.0 $NaClO_4$	25	ML	5.63	73W
				ML_2	10.62	
				ML_3	14.2	
Zn^{2+}	(T)	0.2 KCl	25	ML	4.45	81G
				ML_2	8.16	
				MLH_{-1}	-3.73	
				ML_2H_{-1}	-2.4	
	(R)	0.15 $NaClO_4$	37	ML	4.47 (±0.01)	67S, 69PS, 82BK
				ML_2	8.29 (±0.03)	
	(T)			ML_2H_{-1}	-1.14	

Table 5-6. Constants for Mixed-ligand Complexes Involving L-Serine

Metal ion	Method	Medium (mol dm^{-3})	Temp. (°C)	Extra ligand (X)	Complex	log β	Ref.
Cd^{2+}	Gl.	0.2 $NaNO_3$	30	Diethylene-triamine	MLX	11.55	81RS
	Pol.	1.0 KNO_3	30	Malonic acid	MLX	5.45	82CG
					MLX_2	6.69	
					ML_2X	7.69	
	Gl.	0.2	30	NTA	(MX)L	3.21	82J
	Pol.	1.0 KNO_3	30	N-(2-Hydroxy-ethyl)ethylene-diamine	MLX	9.02	84CG
					ML_2X	11.20	
					MLX_2	12.18	
	Gl.	0.2	30	Iminodiacetic acid	(MX)L	3.05	84J
	Gl.	0.2	30	2,2'-Bipyridyl	(MX)L	3.76	84Ja
	Pol.	1.0 KNO_3 (pH 8-9)	30	Pyridoxine	MLX	5.05	85KC
					ML_2X	7.98	
					MLX_2	6.00	
	Pol.	1.0 KNO_3 (pH 8.5)	30	Ascorbic acid	MLX	4.99	86KC
					ML_2X	7.52	
					MLX_2	5.20	
	Gl.	0.2	30	Iminodiacetic acid	(MX)L	3.0±0.1	86J
	Gl.	0.2 $NaClO_4$	27	Di-2-pyridylamine	(MX)L	3.76	88PP
	Gl.	0.2 KNO_3	35	Bis(imidazol-2-yl)methane	(MX)L	3.21	89KV
	Gl.	0.1 KNO_3	25	NTA	(MX)L	3.22	90S
Co^{2+}	Gl.	0.1 $NaClO_4$	25	NTA	(MX)L	3.18	68IC
	Gl.	0.15 KNO_3	37	Ethylene-diamine	MLX	9.04	69PS
					ML_2X	11.18	
					MLX_2	11.87	
				Histamine	MLX	8.61	
					MLX_2	11.01	
	Gl.	1.0 KCl	25	Ascorbic acid	(ML)XH	0.66	86FA
					$(ML_2)XH$	-0.18	
					MLX	3.00	
					ML_2X	3.07	
	Sp.	-	25	Gluconic acid	(ML)XH	1.01	86FD
				Pangamic acid	(ML)XH	1.00	
	Gl.	0.15 KNO_3	25	Iminodiacetic acid	MLX	10.52	87CJ
	Gl.	0.2 KNO_3	35	Bis(imidazol-2-yl)methane	(MX)L	3.71	89KV
	Gl.	0.1 KNO_3	25	ATP	(MX)L	4.20	89MA
Cr^{3+}	Gl.	0.1 $NaClO_4$	25	DL-Methionine	MLX	15.72	86MCa
					MLXH	19.64	
				DL-Ethionine	MLX	15.80	
					MLXH	19.82	
Cu^{2+}	Gl.	0.15 $NaClO_4$	37	Ethylene-diamine	MLX	16.87	67PS
				Histamine	MLX	16.27	
				Salicylic acid	MLX	16.55	
	Gl.	0.1 $NaClO_4$	25	NTA	(MX)L	5.01	68IC

cont'd

Table 5-6. Constants for Mixed-ligand Complexes Involving L-Serine (continued)

Metal ion	Method	Medium (mol dm^{-3})	Temp. (°C)	Extra ligand (X)	Complex	log β	Ref.
	Gl.	0.05 KCl	25	Alanine	MLX	15.12	72GS
				α-Amino-butyric acid	MLX	15.06	
				Glycine	MLX	15.10	
				Norvaline	MLX	15.13	
				Phenylalanine	MLX	15.00	
				Threonine	MLX	14.95	
				Tyrosine	MLX	14.96	
	Gl.	0.1 KNO_3	25	α-Alanine	MLX	14.91	72IN
				Glycine	MLX	14.66	
				Valine	MLX	14.84	
	Gl.	0.15 NaCl	25	L-Histidine	MLX	17.540	73KS,
					MLXH	21.703	77S
					$MLXH_{-1}$	6.90	
	Gl.	0.24 KCl	25	*p*-Amino-benzoic acid	MLX	10.38	74FL
				Riboflavin	MLX	14.94	
	Gl.	0.2 KCl	25	L-Asparagine	MLX	14.62	75GN
	Gl.	0.1 KNO_3	25	L- or D- Histidine	MLX	17.20	77BP
	Gl.	0.2 KCl	25	Glycylglycine	$MLXH_{-1}$	4.94	77NG
				Glycyl-DL-α-alanine	$MLXH_{-1}$	5.07	
				DL-α-Alanyl-DL-α-alanine	$MLXH_{-1}$	4.86	
	Sp.	0.5 $NaClO_4$ (pH 5)	25?	2,4-Dihydroxy-benzoic acid	$MLXH_2$	19.26	78MG, 78MGa
	Sp.	~0 50% ethanol	25	Acetoacetic ester	MLX	14.81	79FM
	Gl.	0.1 KNO_3	25	L-Histidine	MLX	17.09	79YS
	Gl.	0.1 $NaClO_4$	30	Glycylsarcosine	MLX	19.07	80AS
	Gl.	0.25 KNO_3	30	Lactic acid	MLX	10.02	80RK
	Sp.	0.25 KNO_3	30		MLX	9.76	
	Sp.	0.25 KNO_3	30	Oxalic acid	MLX	11.99	80RKa
	Gl.	0.1 KNO_3 (20% dioxane)	25	L-Histidine	MLX	17.51	80YT
				D-Histidine	MLX	17.54	
	Gl.	~0	25	Thymine	MLX	13.31	81FP
	Pol.	0.25 KNO_3	30	Malonic acid	MLX	11.41	81RK
	Gl.	0.2 $NaNO_3$	30	Diethylene-triamine	MLX	19.89	81RS
				Dipropylene-triamine	MLX	17.55	
	Gl.	0.2 $NaNO_3$	30	Iminodiacetic acid	MLX	15.86	81RSa
	Gl.	0.2 $NaNO_3$	30	DL-Aspartic acid	MLX	15.30	81RSb
	Gl.	0.15 $NaClO_4$	37	Histamine	MLX	16.776	82BK
					MLXH	20.630	
					$MLXH_{-1}$	6.665	
	Gl.	0.1 $NaClO_4$	30	Glycyl-L-phenylalanine	$MLXH_{-1}$	5.47	82S
	Gl. (DL-)	0.1 $NaClO_4$	30	Glycyl-DL-serine	$MLXH_{-1}$	4.78	83S
	Sp.	0.15 NaCl	20	Orotic acid	MLX	15.85	83VD
	Gl.	0.1 KNO_3	25	NTA	(MX)L	4.96	84PB

cont'd

Table 5-6. Constants for Mixed-ligand Complexes Involving L-Serine (continued)

Metal ion	Method	Medium (mol dm^{-3})	Temp. (°C)	Extra ligand (X)	Complex	log β	Ref.
	Gl.	0.2 $NaNO_3$	30	Thiodiglycolic acid	MLX	11.35	84RS
	Sp.	0.6 $NaNO_3$	30	Thiodiglycolic acid	MLX	11.24	
	Gl.	0.1 $NaClO_4$	30	Alanyl-L-phenylalanine	$MLXH_{-1}$	4.60	84S
	Gl.	0.15 $NaClO_4$	37	EDTA	MLX MLXH	20.6 29.3	85AM
	Sp. Gl.	-	25	Gluconic acid	(ML)XH [MLX][H]/[ML][XH]	1.73 4.12	85FD, 86FD
	Sp. Gl.			Pangamic acid	(ML)XH [MLX][H]/[ML][XH]	1.84 3.72	
	Gl.	0.5 $NaClO_4$	25	5-Nitro-salicylic acid	MLX	15.46	85MG
	Gl.	0.1 $NaClO_4$	30	Glycyl-L-Asparagine	$MLXH_{-1}$	10.57	86AJ
	Gl.	0.15 $NaClO_4$	37	L-Histidine	MLX MLXH $MLXH_{-1}$	17.126 21.003 6.786	86BH
	Gl.	0.1 $NaClO_4$	25	DL-α-Alanyl-DL-methionine	(ML)X (?)	5.41	88JA
				DL-Alanyl-DL-norvaline	(ML)X (?)	5.86	
	Gl.	0.1 $NaClO_4$	25	N-Acetylglycine	MLX	10.30	88LG
	Pol.	1.0 KNO_3	30	Pyridoxine	MLX	9.07	88SKa
	Sp.	-	25?	Butyric acid	(ML)X	1.44	89DF
				γ-hydroxybutyric acid	(ML)X	1.25	
				Pantoic acid	(ML)X	1.17	
	Gl.	0.1 KNO_3	25	Diethylene-triamine	(MX)L	4.07	89SH
	Gl.	0.15 $NaClO_4$	37	L-Histidine MLXH $MLXH_{-1}$ ML_2X ML_2XH	MLX 20.873 6.852 19.971 28.446	16.972	93BA
Fe^{2+}	Kin.	0.1 $LiClO_4$	25	Cyanide	$(MX_5)L$	3.32	82TB
Fe^{3+}	Sp.	0.5 $NaClO_4$ (pH 4)	-	5-Nitro-salicylic acid	ML_3X	19.62	81MG
	Kin.	0.1 $LiClO_4$	25	Cyanide	$(MX_5)L$	3.58	82TB
Mg^{2+}	Gl. (DL-)	0.15 NaCl	20	Orotic acid	MLX	5.55	85VD
Mn^{2+}	Gl.	0.1 $NaClO_4$	25	NTA	(MX)L	1.28	68IC
	Gl. (DL-)	0.15 NaCl	20	Orotic acid	MLX	6.90	85VD
Ni^{2+}	Gl.	0.1 $NaClO_4$	25	NTA	(MX)L	4.14	68IC
	Gl.	0.15 KNO_3	37	Ethylene-diamine	MLX MLX_2 ML_2X	11.78 16.08 14.58	68PSa

cont'd

Table 5-6. Constants for Mixed-ligand Complexes Involving L-Serine (continued)

Metal ion	Method	Medium (mol dm^{-3})	Temp. (°C)	Extra ligand (X)	Complex	log β	Ref.
				Histamine	MLX	10.99	
					MLX_2	14.19	
					ML_2X	13.69	
	Gl.	0.05 KCl	25	Alanine	MLX	10.29	72GS
				α-Amino-butyric acid	MLX	10.21	
				Glycine	MLX	10.63	
				Norleucine	MLX	10.21	
				Norvaline	MLX	10.27	
				Phenylalanine	MLX	10.07	
				Threonine	MLX	10.34	
				Tyrosine	MLX	10.03	
	Gl.	1.0 KNO_3	25	*N*-Carboxymethyl-β-(2-pyridyl)-L-α-alanine	(MX)L	2.71	77BR
	(D-)				(MX)L	2.92	
	Sp.	1.0 KCl	25	Ascorbic acid	(MX)L	0.48	79FD
					(MX)LH	7.88	
	Gl.	0.2 $NaNO_3$	30	Diethylene-triamine	MLX	15.31	81RS
				Dipropylene-triamine	MLX	12.84	
	Gl.	0.2 $NaNO_3$	30	Iminodiacetic acid	MLX	12.58	81RSa
	Gl.	0.2 $NaNO_3$	30	Aspartic acid	MLX	11.46	81RSb
	Gl.	1.0 KCl	25	Aspartic acid	(ML)X	3.67	83FA
					$(ML_2)X$	3.35	
	Sp.				(ML)XH	0.48	
					$(ML_2)XH$	0.24	
	Sp.	-	25	Gluconic acid	(ML)XH	1.19	86FD
				Pangamic acid	(ML)XH	1.01	
	Gl.	0.2 $NaClO_4$	27	Di-2-pyridylamine	(MX)L	5.21	88PP
	Gl.	0.2 KNO_3	35	Bis(imidazol-2-yl)methane	(MX)L	4.88	89KV
	Gl.	0.1 KNO_3	25	ATP	(MX)L	4.94	89MA
Pb^{2+}	Gl.	0.1 $NaClO_4$	25	NTA	(MX)L	1.15	68IC
	Pol.	1.0 KNO_3	30	Pyridoxine	MLX	5.43	89SC
Pd^{2+}	Gl.	0.1 KNO_3	25	Ethylenediamine	(MX)L	11.01	81L
					$(MXL)H_{-1}$	-8.51	
	Gl.	0.1 NaCl	25	Diethylene-triamine	(MX)L	5.10	87SM
Tb^{3+}	Sp.	-	-	EDTA	(MX)L	2.57	85SB
UO_2^{2+}							
	Gl. (DL-)	0.1 KNO_3 50% methanol	27	2-Hydroxy-1-naphthaldehyde	MLX	13.31	85MS
Zn^{2+}	Gl.	0.1 $NaClO_4$	25	NTA	(MX)L	3.18	68IC
	Gl.	0.15 KNO_3	37	Ethylene-diamine	MLX	9.86	69PS
					ML_2X	12.47	
					MLX_2	12.96	

cont'd

Table 5-6. Constants for Mixed-ligand Complexes Involving L-Serine (continued)

Metal ion	Method	Medium (mol dm^{-3})	Temp. (°C)	Extra ligand (X)	Complex	log β	Ref.
				Histamine	MLX	9.67	
					ML_2X	12.18	
					MLX_2	13.04	
	Gl.	0.2 KCl	25	L-Histidine	MLX	10.14	81G
	Gl.	0.2 $NaNO_3$	30	Diethylene-triamine	MLX	13.37	81RS
	Gl.	0.2 $NaNO_3$	30	Iminodiacetic acid	MLX	10.56	81RSa
	Gl.	0.2 $NaNO_3$	30	Aspartic acid	MLX	9.68	81RSb
	Gl.	0.15 $NaClO_4$	37	Histamine	MLX	9.257	82BK
	Gl.	0.2	30	NTA	(MX)L	3.37	82J
	Gl.	0.2	30	Iminodiacetic acid	(MX)L	4.00	84J
	Gl.	0.2	30	2,2'-Bipyridyl	(MX)L	4.79	84Ja
	Gl.	0.1 KNO_3	25	ATP	(MX)L	3.84	85MK
					(MLX)OH	4.23	
	Gl.	0.2	30	Iminodiacetic acid	(MX)L	4.0±0.1	86J
	Gl.	0.2 $NaClO_4$	27	Di-2-pyridylamine	(MX)L	4.71	88PP
	Gl.	0.2 KNO_3	35	Bis(imidazol-2-yl)methane	(MX)L	4.13	89KV
	Gl.	0.1 KNO_3	25	NTA	(MX)L	2.99	89S

(Gl. = glass electrode potentiometry [as exclusive or main method]; Pol. = polarography; Sp. = spectrophotometry; Kin. = kinetics)

Table 5-7. Overall Thermodynamic Quantities for L-Serine Metal Complex Equilibria

Metal ion	Method	Medium (mol dm^{-3})	Temp. (°C)	Complex	ΔH° (kJ mol^{-1})	ΔS° (J K^{-1} mol^{-1})	Ref.
Co^{2+}	Pot. (DL-)	0.2 KNO_3	25	ML_2	-16.7	92.0	68RM
	Pot.	0.05 KCl	25	ML	-13.22	41.8	72GM, 72GMa
				ML_2	-25.94	66.9	
	Cal.	0.05 KCl	25	ML	-11.30	46.0	
				ML_2	-20.50	83.7	
Cu^{2+}	Cal. (DL-)	0.1 KNO_3	21.9	ML_2	-59.0	79.5	67SS
	Pot. (DL-)	0.2 KNO_3	25	ML_2	-40.2	142.2	68RM
	Cal.	0.05 KCl	25	ML	-23.01	75.3	70GN
				ML_2	-49.37	113.0	
	Cal. (DL-)	0.16 KNO_3	25	ML	-23.05	73.2	70LB
				ML_2	-48.70	114.2	
	Cal.	0.05 KCl	25	ML	-28.45	54.4	71GN
				ML_2	-51.46	121.3	
	Pot.	0.05 KCl	25	ML	-17.99	92.0	72GM, 72GMa
				ML_2	-46.86	121.3	
	Cal.	0.05 KCl	25	ML	-23.01	75.3	
				ML_2	-49.37	112.9	
	Cal.	0.1 KNO_3	25	ML	-23.01	74.5	72IN
				ML_2	-48.53	116.3	
	Cal.	0.1 $NaClO_4$	24	ML_2	-54.39	-	72ST
	Cal. (DL-)	0.1 KNO_3	25	ML_2	-53.59	96.3	76PS
				ML_2	-52.76	98.9	
	Pol.	0.5 KNO_3	25	ML	-22.84	74.2	79SS
				ML_2	-56.23	108.0	

cont'd

Table 5-7. Overall Thermodynamic Quantities for L-Serine Metal Complex Equilibria (continued)

Metal ion	Method	Medium (mol dm^{-3})	Temp. (°C)	Complex	ΔH° (kJ mol^{-1})	ΔS° (J K^{-1} mol^{-1})	Ref.
Cu^{2+}	Cal.	0.2 KCl	25	ML	-22.6	74	87KS
				ML_2	-52.1	98	
				ML_2H_{-1}	-19.7	12	
				ML_2H_{-2}	-0.6	-137	
	Cal.	0.1 $NaClO_4$	25	ML	-26.1	65	88LG
				ML_2	-53.4	99	
Fe^{2+}	Pot. (DL-)	0.2 KNO_3	25	ML_2	-6.3	100.4	68RM
Mn^{2+}	Pot. (DL-)	0.2 KNO_3	25	ML_2	-3.3	62.8	68RM
	Pot.	0.1 KNO_3	(20-60)	ML	-8.8	46.0	73BS
				ML_2	-7.5	92.0	
Ni^{2+}	Pot.	-	(10-40)	ML	-21.8	32.6	57P, 60Pa, 60Pb
				ML_2	-45.6	39.3	
				ML_3	-71.8	9.2	
	Cal. (DL-)	0.1 KNO_3	22	ML_2	-33.5	79.5	67SS
	Pot. (DL-)	0.2 KNO_3	25	ML_2	-32.6	79.5	68RM
	Cal. (DL-)	0.16 KNO_3	25	ML	-15.73	51.5	70LB
				ML_2	-33.60	78.2	
				ML_3	-55.69	72.0	
	Pot.	0.05 KCl	25	ML	-14.22	58.6	72GM, 72GMa
				ML_2	-33.47	79.5	
	Cal.	0.05 KCl	25	ML	-15.90	50.2	
				ML_2	-35.14	75.3	
Zn^{2+}	Cal. (DL-)	0.1 KNO_3	22	ML_2	(-28.0)		67SS
	Pot. (DL-)	0.2 KNO_3	25	ML_2	-18.0	100.4	68RM
	Pot.	0.05 KCl	25	ML	-12.55	46.0	72GM, 72GMa
				ML_2	-25.52	83.7	
	Cal.	0.05 KCl	25	ML	-9.62	54.4	
				ML_2	-20.50	96.2	
	Pol.	0.5 KNO_3	25	ML	-14.06	40.9	79SS
				ML_2	-29.87	58.7	
				ML_3	-40.42	75.0	

(Pot. = potentiometry; Cal. = calorimetry)

Table 5-8. Thermodynamic Quantities for Mixed-ligand Complexes Involving L-Serine

Metal ion	Method	Medium (mol dm^{-3})	Temp. (°C)	Extra ligand (X)	Complex	ΔH° (kJ mol^{-1})	ΔS° (J K^{-1} mol^{-1})	Ref.
Cu^{2+}	Cal.	0.1 KNO_3	25	α-Alanine	MLX	-48.95	121.3	72IN
					(MX)L	-25.52	43.9	
					(ML)X	-25.94	46.9	
				Glycine	MLX	-48.95	116.3	
					(MX)L	-23.85	43.5	
					(ML)X	-25.94	42.2	
				Valine	MLX	-48.74	120.5	
					(MX)L	-25.48	43.1	
					(ML)X	-25.73	46.0	
	Cal.	0.1 $NaClO_4$	25	N-Acetyl-glycine	MLX	-24.2	116	88LG

(Cal. = calorimetry)

6. THREONINE - $CH_3CH[OH]CH[NH_2]CO_2H$ (2-amino-3-hydroxybutanoic acid, LH)

Like serine, threonine contains a hydroxy group whose dissociation in aqueous solution takes place well beyond the basic limit of the pH range commonly investigated. Threonine is thus usually considered a glycine-like monoacid. However, the involvement of the oxygen atom of its hydroxy group in metal chelation can make it lose its proton at more accessible pH values (69FM, 73GM, 84AO).

As with serine, many of the investigations on threonine metal complex equilibria have been undertaken to test the possible participation of the side-chain hydroxy group in chelation (68RM, 69FM, 70LB, 72GM, 76PS, 79M). Since stereoselective effects may accompany metal coordination of tridentate amino acids, a few studies were also devoted to that problem. Contrary to what was observed with serine, no significant stereoselective effect was detected in the formation of ML_2 copper(II)-threonine complexes on the basis of enthalpy determinations (76PS). Nevertheless, a slight effect of this kind was characterised in the formation of ML_2H_{-2} following deprotonation of the hydroxyl group (84AO).

6-1. Protonation constants of threonine

Among the relatively numerous determinations of threonine protonation constants, most are difficult to evaluate given the diversity of the experimental conditions used. Nevertheless, average values derived from the three sets of constants successively reported by the same group of authors in 0.05 mol dm^{-3} KCl at 25 °C (70GN, 71GN, 72GM, 72GMa, 72GS, with 71GN and 72GM reporting the same results as 70GN and 72GMa, respectively - see Chapter 5) are proposed as tentative.

Acceptable agreement has also been observed between the results found in refs. 69FM, 76PS, 77BP, 77DO and 83NM relative to 0.1 mol dm^{-3} KNO_3 at 25 °C, and corresponding averages are recommended in spite of the poor reproducibility of the more acidic constant. These averages almost exactly coincide with the values published in 88LG for which no experimental information has unfortunately been given, but which seem to be considered as stoichiometric. They are also relatively close to those of 81IS, 82KP and 84SP determined under the same experimental conditions except for the nature of the background electrolyte. It should also be noted that for reasons developed in preceding chapters, values reported in 86MCa have been excluded from this evaluation.

Under physiological conditions, if we once more apply the difference of 0.12 (74MS, 82MS, 89SM) between the distinct standard states used in references 67S and 82KB, excellent accordance is obtained. Recommended stoichiometric averages are thus proposed. All recommended and tentative protonation constants are to be found in Table 6-1.

6-2. Thermodynamic quantities for the protonation of threonine

All determinations of thermodynamic quantities for threonine protonation except two have been made calorimetrically (Table 6-3). Fairly good agreement is observed between enthalpies obtained in 64IC and 72GM under relatively close experimental conditions. More generally, all values relative to the first protonation step lie within acceptable limits of variation. The most amazing observation about these data is the precision of the enthalpies and entropies for both protonation steps derived from potentiometric determinations in 42SG, which compare well with values determined up to 30 years later with modern calorimetric techniques (64IC, 72GM).

6-3. Metal complex formation constants

Overall formation constants relative to threonine metal complexes are collected in Table 6-4. Experimental conditions used for studying cadmium(II) equilibria are too different to allow any quantitative comparison. The situation is basically similar for cobalt(II), but from other examinations made in the present evaluation, results reported by references 67S, 68RM, 72GM and 82KP are to be recommended.

As was the case for serine (cf Chapter 5), copper(II) complex determinations are the most numerous, and results contained in Table 6-4 call for a few remarks.

First of all, in contrast with Pettit and Swash's study which only reports the existence of MLH in addition to ML and ML_2 (76PS), all thorough investigations on copper(II)-threonine interactions concur in establishing the existence of hydroxo complexes: MLH_{-1} (82KB), ML_2H_{-1} (69FM, 73GM,

77DO, 82KB, 82KP), and ML_2H_{-2} (69FM, 73GM, 77DO, 82KP). This is reminiscent of the situation encountered with the copper(II)-serine system: except for refs. 76PS and 82BK, no mention was made of MLH whereas both ML_2H_{-1} (73GM, 82BK, 87KS) and ML_2H_{-2} (73GM, 87KS) were characterised. Such discrepancies may arise from the extent of the pH interval investigated (pH < 8.5 in 76PS) as well as from the frequent difficulty in ascertaining the formation of acidic complexes of glycine-like amino acids (76PS, 86BH). In any event, since hydroxo species reach noticeable levels at high pH only, neglecting them in the calculations should not significantly affect the values of ML and even ML_2 constants. All data relative to these two complexes are thus worth comparing.

In particular, the sets of constants relative to 0.1 mol dm^{-3} KNO_3 (69FM, 76PS, 77BP, 77DO), $NaNO_3$ (82KP) or $NaClO_4$ (88LG) at 25 °C are quite comparable, and average values have been recommended for KNO_3 (Table 6-5). The reliability of these values is confirmed by the close similarity of those found by Sarkar (77S) using a slightly different ionic strength (0.15 NaCl).

Of the three results successively produced by the same group of authors in 0.05 mol dm^{-3} KCl (70GN, 71GN, 72GM, 72GMa, 72GS), the first (70GN, 71GN) has been discarded as too distant from the latter two, and average constants from these have been proposed as tentative.

If we now compare the constant of the ML copper(II)-threonine complex to that of its serine homologue in works common to the same groups of authors (67S, 68RM, 70LB, 70GN, 71GN, 72GM, 72GMa, 72GS, 73GM, 76PS, 77BP, 82KB), one may notice a systematic increase in stability from serine to threonine which varies from 0.04 (93BA at 37 °C) to 0.14 (68RM at 25 °C). Three sets of results only are at variance with this observation: 67S (-0.02, which tends to indicate that the constant of threonine is too low; indeed, this unexpected decrease cannot be due to a too high constant of serine since that constant has been shown to be underevaluated in the preceding chapter), 70GN and 71GN (-0.03, which justifies its above rejection) and 82KB (-0.23). In the latter reference at 37 °C (present author involved), the above comparisons led to the conclusion that its copper(II)-serine ML constant should be overvalued by about 0.3 log units. This was recently confirmed and corrected (93BA - see Chapter 5). Similarly, it seems that all constants obtained in 67S on the copper(II)-threonine system under physiological conditions are appreciably too low (see above). Finally, given that the ML copper(II)-threonine constant in 82KB (7.79) is of the order of magnitude of that reported at 40 °C in 68RM (7.87), the data on this system in 82KB should be regarded as the most reliable.

The only other two metals for which the number of determinations is sufficiently high to allow reasonable comparisons are nickel(II) and zinc(II). For nickel(II), no average constant can, in principle, be calculated since all determinations refer to different experimental conditions. However, all the constants obtained in KNO_3 from 0.1 to 0.2 mol dm^{-3} at 25 °C display such a good homogeneity (68RM, 70LB, 76PS) that a tentative average of ML and ML_2 constants is proposed for the corresponding interval of ionic strengths (Table 6-5).

For zinc(II), the constants obtained by Gergely (81G) for zinc(II) L-threonine, zinc(II) D-threonine, and zinc(II) L/D-threonine complexes may be considered as fairly reproducible since there is most probably no stereoselective effect in these systems. However, any average derived from such data determined by the same author under presumably identical technical conditions would have no significance, and the results reported in 68RM on the same system are too distant to allow such a calculation.

By contrast, the results obtained in 67S and 80KB under physiological conditions are more comparable, at least as far as the ML constant is concerned. There is indeed no agreement about the stoichiometry of other species, but since ML_2H_{-1} has been definitely characterised at the expense of ML_3 on a graphical basis (80KB), the constants appearing in the latter reference are worth selecting as tentative.

Constant determinations for mixed-ligand complexes are fairly numerous. In particular, the copper(II)-threonine-histidine system has been investigated by three groups of authors in 0.1 mol dm^{-3} KNO_3 at 25 °C (69FM, 77BP, 79YS). The former two found a similar value for MLX, but their agreement stops there since the constant they calculated for MLXH differs by about half a log unit. Furthermore, Brookes and Pettit (77BP) failed to characterise the $MLXH_{-1}$ species reported in 69FM (as well as in 77S and 84BB under different experimental conditions). As was discussed above, the absence of this complex in the refinement may not entail serious bias in the MLX constant, but it may be of some importance for speciation calculations relative to this system (see introduction). The third

group of authors (79YS) only characterised the MLX species, and found a very low constant which compares better to the value corresponding to physiological conditions (84BB) than to those of the two former studies (69FM, 77BP); it has thus been discarded. Finally, average constants for MLX and MLXH calculated from 69FM and 77BP (respectively, 17.51 ± 0.05 and 21.65 ± 0.25) can be proposed as tentative along with the $MLXH_{-1}$ one taken from 69FM (7.0). It is noteworthy that the values determined by Sarkar in 0.15 mol dm^{-3} NaCl at 25 °C (77S) fall within the limits of error of the above results, and lend more support to 69FM than to 77BP.

Under physiological conditions, comparisons of the MLX, MLXH and $MLXH_{-1}$ constants calculated in 84BB with the values obtained in 77S (and 69FM) at 25 °C show that the former can be considered as reliable.

Due to the lack of data, no other direct comparison is possible concerning mixed-ligand complexes involving threonine. However, a qualitative evaluation is allowed for the zinc(II)-threonine-histidine system. In the study reporting results obtained under physiological conditions (81ABa), it was pointed out that the poor stability observed for the MLX species presumably arose from "antagonistic interactions of the carboxy group of histidinate and the hydroxy group of threoninate". This stereoselective effect was later investigated and confirmed by Gergely (81G), which indirectly gives credit to the two corresponding sets of constants (81ABa, 81G).

6-4. Thermodynamic quantities for metal complex formation with threonine

Among the systems on which thermodynamic quantities have been determined, copper(II)-threonine has been the most investigated. Concerning this system, it is somewhat surprising that very close results have been found in 70LB and 70GN/71GN/72GM/72GMa for different ionic strengths whereas the values obtained under identical experimental conditions (76PS, 78IS, 88LG) differ to a significant extent. Of the latter three sets of data, the values reported in 78IS are not expected to be very reliable since their cobalt(II) counterparts differ from the results of 72GM/72GMa by almost equal amounts. The data mentioned in 88LG for which copper(II)-serine determinations were at variance with other reproducible results (see Chapter 5) appear to be similar. Thus, the existence of a discrepancy between the thermodynamic quantities relative to ML_2 in 76PS and those in 78IS and 88LG is not a surprise, but the important difference between these values and those found in 70LB and 70GN/71GN seems more difficult to explain.

Table 6-1. Protonation Constants of Threonine

Type of constants	Medium (mol dm^{-3})	Temp. (°C)	log K_1	log K_2	Ref.
Thermo	→0	1	9.748	2.200	42SG
		12.5	9.420	2.132	
		25	9.100	2.088	
		37.5	8.812	2.070	
		50	8.548	2.055	
Mixed	0.06 KH_2PO_4	25	9.00	-	52LD
Thermo	~0.01	20	9.12	-	53P
Mixed	1.0 $NaClO_4$	20	8.86	2.24	58P
Mixed(?)	1.0 KCl	20	8.86	-	59P
Thermo	→0	20	9.26	2.21	64IC
		30	9.01	2.14	
Mixed	0.1 KCl	20	9.16	2.29	64KW
Mixed	0.15 KNO_3	37	8.709	2.20	67S
?	0.2 KNO_3	15	9.26	2.32	68RM
		25	9.03	2.32	
		40	8.71	2.30	
Stoichio	0.1 KNO_3	25	8.95	2.21	69FM
Mixed(?)	0.16 KNO_3	25	9.07	-	70LB
Stoichio(?)	0.05 KCl	25	8.98	2.12	71GN
Stoichio(?)	0.05 KCl	20	9.11	2.26	72GM, 72GMa
		25	8.98	2.24	
		30	8.82	2.14	
		35	8.71	2.10	
Stoichio(?)	0.05 KCl	25	8.98	2.17	72GS
Stoichio	1.0 $NaClO_4$	25	9.11	2.30	73GM
Mixed	0.05 KCl	25	9.10	2.20	73SC
		45	8.75	2.15	
	0.15 KCl	25	9.07	2.17	
		45	8.70	2.13	
	0.25 KCl	25	9.03	2.15	
		45	8.60	2.11	
Mixed(?)	0.5	25	8.92	2.21	73SK
Mixed	0.5 KNO_3	20	9.14	2.75	74KH
Mixed	0.1 KCl	20	8.7	-	74PN
Mixed(?)	0.1 KNO_3	25	9.00	-	75HV
	0.5 KNO_3	25	8.98	-	
Stoichio	0.1 KNO_3	25	8.974	1.98	76PS
Stoichio	0.1 KNO_3	25	8.974	1.979	77BP
Stoichio	0.1 KNO_3	25	8.93	2.20	77DO
Stoichio	0.15 NaCl	25	8.954	2.209	77S
Thermo	→0	25	2.25		78KA
	100% formic acid				
Stoichio(?)	3.0 KCl	25	9.346	2.406	78VV
Thermo	~0	25	10.08		80KT
	formic acid: ethyl methyl ketone (1:24)				
	acetic acid: ethyl methyl ketone (1:8)		10.73		
Mixed	0.1 KNO_3	35	9.52(?)	-	80TH
Stoichio	0.1 KNO_3 20% dioxane	25	9.07	2.50	80YT

cont'd

Table 6-1. Protonation Constants of Threonine (continued)

Type of constants	Medium (mol dm^{-3})	Temp. (°C)	log K_1	log K_2	Ref.
Stoichio	0.1	20	8.98	2.21	81CD
	0.1 100% trifluoro-ethanol	20	7.50	-	
Stoichio	0.1 $NaNO_3$	25	8.980	2.098	81IS
Mixed(?)	0.1 KNO_3	25	9.07	2.25	81L
Mixed(?)	0.1	30	9.20	-	81R
Stoichio	0.15 $NaClO_4$	37	8.573	2.148	82KB
Thermo	~0	25	9.00	2.21	82DD
	8.0% propan-2-ol	25	8.98	2.30	
	16.3% propan-2-ol	25	9.02	2.40	
	25.1% propan-2-ol	25	9.02	2.52	
	34.3% propan-2-ol	25	9.03	2.59	
	43.9% propan-2-ol	25	8.95	2.73	
	54.0% propan-2-ol	25	9.02	2.87	
	64.6% propan-2-ol	25	9.04	3.00	
	75.8% propan-2-ol	25	9.04	3.19	
Stoichio	0.1 $NaNO_3$	25	8.89	2.20	82KP
Stoichio	0.1 KNO_3	25	9.035	2.480	83NM
Stoichio	0.25 NaCl	25	8.92	2.174	84AO
Mixed	1.0 KNO_3	30	9.12	-	84CG
Stoichio(?)	0.1 $NaClO_4$	25	8.96	2.26	84SP
		35	8.71	2.22	
		45	8.47	2.17	
	20% DMSO	35	8.82	2.37	
	20% DMF	35	8.76	2.31	
	20% acetonitrile	35	8.72	2.28	
	20% propan-2-ol	35	8.67	2.17	
	20% ethanol	35	8.64	2.14	
	20% methanol	35	8.59	2.09	
	20% acetone	35	8.44	2.06	
	0.25 $NaClO_4$	35	8.84	2.24	
	0.5 $NaClO_4$	35	8.89	2.28	
	1.0 $NaClO_4$	35	8.98	2.33	
Mixed	0.1	35	8.9	2.2	84SY, 85SY
Mixed(?)	0.1 KNO_3	25	9.07	-	85MK
Mixed	0.1 KNO_3 50% methanol	27	9.04	-	85MS
Mixed(?)	0.15 NaCl	20	9.08	-	85VD
Mixed	0.2 KCl	25	9.12	2.30	86KD
Stoichio	0.1 $NaClO_4$	25	9.103	2.162	86MCa
Thermo	~0	25	9.00	2.21	86PD
	8.0% t-BuOH	25	9.16	2.26	
	16.4% t-BuOH	25	9.21	2.40	
	25.0% t-BuOH	25	9.27	2.44	
	34.2% t-BuOH	25	9.31	2.51	
	43.8% t-BuOH	25	9.34	2.57	
	54.0% t-BuOH	25	9.40	2.62	
	64.5% t-BuOH	25	9.46	2.79	
	75.8% t-BuOH	25	9.47	3.08	

cont'd

Table 6-1. Protonation Constants of Threonine (continued)

Type of constants	Medium (mol dm^{-3})	Temp. (°C)	log K_1	log K_2	Ref.
Thermo	~0	25	8.99	2.21	87CL
	10% methanol	25	8.94	2.29	
	20% methanol	25	8.97	2.38	
	30% methanol	25	8.99	2.56	
	40% methanol	25	8.97	2.72	
	50% methanol	25	8.92	-	
	60% methanol	25	9.00	2.95	
	70% methanol	25	9.02	3.20	
	80% methanol	25	9.01	3.54	
	10% ethanol	25	9.10	2.32	
	20% ethanol	25	9.09	2.39	
	30% ethanol	25	9.08	2.55	
	40% ethanol	25	9.11	2.68	
	50% ethanol	25	9.15	2.83	
	60% ethanol	25	-	2.93	
	70% ethanol	25	-	3.08	
	80% ethanol	25	-	3.37	
Stoichio(?)	0.1	20	8.99	2.13	87MT
Mixed	0.1 NaCl	25	8.72	-	87SM
Stoichio(?)	0.1 $NaClO_4$	25	8.98	2.20	88LG
Mixed	2.25 $NaNO_3$	25	9.187	2.326	89CV
Stoichio	0.15 NaCl	37	8.610	2.123	91DB

Table 6-2. Recommended (R) and Tentative (T) Values for Protonation Constants of Threonine

Type of constants	Medium (mol dm^{-3})	Temp. (°C)	log K_1	log K_2	Ref.
Stoichio? (T)	0.05KCl	25	8.98 (±0.01)	2.18 (±0.06)	71GN, 72GM, 72GS
Stoichio (R)	0.1KNO_3	25	8.97 (±0.06)	2.2 (±0.3)	69FM, 76PS, 77BP, 77DO, 83NM
Stoichio (R)	0.15	37	8.59 (±0.02)	2.12 (±0.04)	67S, 82KB, 91DB

Table 6-3. Thermodynamic Quantities for Threonine Protonation Equilibria

Method	Medium (mol dm^{-3})	Temp. (°C)	$\Delta H°_1$ (kJ mol^{-1})	$\Delta H°_2$ (kJ mol^{-1})	$\Delta S°_1$ (J K^{-1} mol^{-1})	$\Delta S°_2$ (J K^{-1} mol^{-1})	Ref.
Pot.	→0	1	-42.15	-7.63	33.5	14.2	42SG
		12.5	-42.20	-6.48	32.6	18.4	
		25	-41.67	-4.94	34.3	23.4	
		37.5	-40.63	-3.04	37.7	29.7	
		50	-38.99	-0.80	43.1	36.8	
Cal.	→0	25	-42.00	-5.69	33.5	20.9	64IC
Cal.	0.16 KNO_3	25	-40.92	-	36.4	-	70LB
Cal.	~0	20	-40.8	-	-	-	71MB
Cal.	0.05 KCl	25	-41.84	-5.02	31.6	26.0	72GM, 72GMa
Cal.	0.1 KNO_3	25	-42.24	-	30.2	-	76PS
Cal.	0.1 KNO_3	25	-41.6	-	-	-	78IS
Pot.	0.1 $NaClO_4$	35	-45.86	-9.54	17.4	11.1	84SP
Cal.	~0	25	-41.1	-1.55	36.4	34.9	87RF, 89R, 89RM
Cal.	0.1 $NaClO_4$	25	-43.9	-3.99	24.7	28.7	88LG

(Pot. = potentiometry; Cal. = calorimetry)

Table 6-4. Overall Formation Constants for L-Threonine Metal Complexes

Metal ion	Method	Medium (mol dm^{-3})	Temp. (°C)	Complex	log β	Ref.
Al^{3+}	Gl.	0.15 NaCl	37	ML	5.71	91DB
Au^{3+}	Gl. (DL-)	~ 0.02	25	ML	6.74	74FA
				ML_2	10.19	
Be^{2+}	Gl. (DL-)	0.015	20	ML_2	11.9	53P
Cd^{2+}	Gl. (DL-)	0.015	20	ML_2	7.2	53P
	Pol.	0.5 KNO_3	20	ML	6.3	73RG
		20% DMF		ML	8.44	
		20% DMSO		ML	8.33	
	Gl.	0.1 KNO_3	25	ML	3.9	75HV
				ML_2	7.1	
	Pol.	1.0 KNO_3	30	ML	4.06	84CG
				ML_2	7.06	
				ML_3	9.02	
	Pol.	1.0 KNO_3 (pH 8-9)	30	ML	4.00	85KC, 86KC
				ML_2	6.70	
				ML_3	9.10	
	Gl.	0.2 KNO_3	35	ML	3.89	89KS, 89KV
				ML_2	7.17	
	Gl.	0.2 $NaClO_4$	27	ML	4.02	88PP
				ML_2	7.22	
Ce^{3+}	Gl.	0.1 KCl	20	ML	3.7	70RP
Co^{2+}	Gl.	0.1 KCl	20	ML	4.58	64KW
	Gl.	0.15 KNO_3	37	ML	4.16	67S
				ML_2	7.45	
				ML_3	8.82	
	Gl. (DL-)	0.2 KNO_3	15	ML	4.50	68RM
				ML_2	7.98	
			25	ML	4.43	
				ML_2	7.84	
			40	ML	4.37	
				ML_2	7.72	
	Gl.	0.05 KCl	20	ML	4.39	72GM, 72GMa
				ML_2	8.03	
			25	ML	4.38	
				ML_2	8.01	
			30	ML	4.35	
				ML_2	7.92	
			35	ML	4.33	
				ML_2	7.83	
	Gl.	0.1 $NaNO_3$	25	ML	4.25	78IS, 81IS
				ML_2	8.18	
	Gl.	0.1 $NaNO_3$	25	ML	4.298	82KP
				ML_2	7.762	
				ML_2H_{-1}	-1.94	
	Gl.	0.2	30	ML	4.02	84J, 84Ja, 86J
				ML_2	7.22	
	Gl.	0.1	20	ML	4.31	87MT
				ML_2	7.16	
	Gl.	0.2 KNO_3	35	ML	4.13	89KS, 89KV
				ML_2	7.91	

cont'd

Table 6-4. Overall Formation Constants for L-Threonine Metal Complexes (continued)

Metal ion	Method	Medium (mol dm^{-3})	Temp. (°C)	Complex	log β	Ref.
Cr^{3+}	Gl.	0.1 $NaClO_4$	25	ML	8.17	86MCa
				ML_2	11.04	
				ML_3	15.30	
Cu^{2+}	Pol.	0.06 KH_2PO_4	25	ML_2	14.54	52LD
	Gl.	→0	20	ML	8.44	64IC
				ML_2	15.40	
			30	ML	8.41	
				ML_2	15.32	
	Gl.	0.1 KCl	20	ML	8.34	64KW
				ML_2	15.32	
	Gl.	0.15 KNO_3	37	ML	7.55	67S
				ML_2	14.01	
	Gl. (DL-)	0.2 KNO_3	15	ML	8.20	68RM
				ML_2	14.94	
			25	ML	8.06	
				ML_2	14.69	
			40	ML	7.87	
				ML_2	14.34	
	Gl.	0.1 KNO_3	25	ML	8.00	69FM
				ML_2	14.71	
				ML_2H_{-1}	4.78	
				ML_2H_{-2}	-6.14	
	Sp. (DL-)	1.0 $NaClO_4$	22	ML	7.85	70JP
				ML_2	14.71	
	Gl.			ML_2H_{-1}	4.82	
				ML_2H_{-2}	-6.37	
	Gl. (DL-)	0.16 KNO_3	25	ML	7.95	70LB
				ML_2	14.69	
	Gl.	0.05 KCl	25	ML	7.90	71GN
				ML_2	14.50	
	Gl.	0.05 KCl	20	ML	8.10	72GM, 72GMa
				ML_2	14.89	
			25	ML	8.02	
				ML_2	14.72	
			30	ML	7.95	
				ML_2	14.56	
			35	ML	7.88	
				ML_2	14.40	
	Gl.	0.05 KCl	25	ML	8.03	72GS
				ML_2	14.77	
	Gl.	1.0 $NaClO_4$	25	ML	8.06	73GM
				ML_2	14.92	
				ML_2H_{-1}	4.88	
				ML_2H_{-2}	-6.17	
	Gl.	3.0 $NaClO_4$	25	ML	8.597	75BW
				ML_2	16.031	
	Gl.	0.1 KNO_3	25	ML	7.947	76PS
				ML_2	14.613	
				MLH	11.54	
	(DL-)			ML	7.940	
				ML_2	14.601	
	Gl.	0.1 KNO_3	25	ML	7.946	77BP
				ML_2	14.612	

cont'd

Table 6-4. Overall Formation Constants for L-Threonine Metal Complexes (continued)

Metal ion	Method	Medium (mol dm^{-3})	Temp. (°C)	Complex	log β	Ref.
	Gl. (DL-)	0.1 KNO_3	25	ML	7.99	77DO
				ML_2	14.68	
				ML_2H_{-1}	4.84	
				ML_2H_{-2}	-5.94	
	Gl.	0.15 NaCl	25	ML	8.006	77S
				ML_2	14.688	
				ML_2H_{-1}	4.750	
				ML_2H_{-2}	-6.17	
	Gl.	0.1 $NaNO_3$	25	ML	8.05	78IS, 81IS
				ML_2	14.94	
	Gl.	0.1 $NaClO_4$	30	ML	7.95	80AS
				ML_2	14.62	
	Pol. (DL-)	0.1 $NaClO_4$	30	ML_2	14.90	80RR
				ML_3	18.68	
	Pol.	-	-	ML	7.80	80SG
				ML_2	14.15	
	Gl.	0.1 KNO_3 20% dioxane	25	ML	8.28	80YT
				ML_2	15.21	
	Gl.	0.1	30	ML_2	14.77	81R
				ML_3	18.07	
	Gl.	0.15 $NaClO_4$	37	ML	7.789	82KB
				ML_2	14.299	
				MLH_{-1}	1.599	
				ML_2H_{-1}	4.693	
	Gl.	0.1 $NaNO_3$	25	ML	7.893	82KP
				ML_2	14.538	
				ML_2H_{-1}	4.79	
				ML_2H_{-2}	-5.78	
	Gl.	0.25 NaCl	25	ML	7.888	84AO
				ML_2	14.504	
				ML_2H_{-1}	4.684	
				ML_2H_{-2}	-6.096	
	Gl.	0.1	20	ML	8.26	87MT
				ML_2	14.54	
	Gl.	0.1 $NaClO_4$	25	ML	8.02	88LG
				ML_2	14.68	
	Pol.	1.0 KNO_3	30	ML	7.80	88SKa
				ML_2	14.15	
Dy^{3+}	Gl.	0.1 KCl	20	ML	3.3	74PN
Fe^{2+}	Gl.	1.0 KCl	20	ML	3.30	59P
	Estim.	→0	25	ML	7.7	64S
	Gl. (DL-)	0.2 KNO_3	15	ML	3.76	68RM
				ML_2	6.62	
			40	ML	3.69	
				ML_2	6.50	
Fe^{3+}	Gl.	1.0 $NaClO_4$	20	ML	8.6	58P
	Ox. Pot.	1.0 $NaNO_3$	25	ML_2H	18.66	88SP
				ML_2H_2	21.32	
Gd^{3+}	Gl.	0.1 KCl	20	ML	3.1	74PN

cont'd

Table 6-4. Overall Formation Constants for L-Threonine Metal Complexes (continued)

Metal ion	Method	Medium (mol dm^{-3})	Temp. (°C)	Complex	log β	Ref.
Hg^{2+}	Gl. (DL-)	0.015	20	ML_2	17.5	53P
	Gl.	0.1 $NaNO_3$	25	ML	11.7	73VB
	(Hg el.)			ML_2	18.7	
La^{3+}	Gl.	0.1 KCl	20	ML	2.8	74PN
	Gl.	0.05 KCl	25	ML	4.05	75SC
				ML_2	7.05	
		0.15 KCl	25	ML	3.72	
				ML_2	6.68	
		0.25 KCl	25	ML	3.55	
				ML_2	6.40	
		0.05 KCl	45	ML	3.70	
				ML_2	6.65	
		0.15 KCl	45	ML	3.57	
				ML_2	6.40	
		0.25 KCl	45	ML	3.42	
				ML_2	5.95	
Mg^{2+}	Gl. (DL-)	0.15 NaCl	20	ML	1.45	85VD
Mn^{2+}	Gl.	0.15 $NaClO_4$	37	ML	2.07	67S
	Gl. (DL-)	0.2 KNO_3	15	ML	2.59	68RM
				ML_2	3.98	
			40	ML	2.56	
				ML_2	3.93	
	Gl. (DL-)	0.15 NaCl	20	ML	2.17	85VD
Nd^{3+}	NMR	0.2 KCl	25	ML	0.88	73SY
Ni^{2+}	Gl.	0.1 KCl	20	ML	5.66	64KW
				ML_2	10.20	
	Gl.	0.15 KNO_3	37	ML	5.15	67S
				ML_2	9.37	
				ML_3	11.84	
	Gl. (DL-)	0.2 KNO_3	15	ML	5.62	68RM
				ML_2	10.17	
			25	ML	5.51	
				ML_2	9.94	
			40	ML	5.38	
				ML_2	9.68	
	Gl. (DL-)	0.16 KNO_3	25	ML	5.46	70LB
				ML_2	9.97	
				ML_3	13.42	
	Gl.	0.05 KCl	20	ML	5.52	72GM, 72GMa
				ML_2	10.11	
			25	ML	5.42	
				ML_2	9.95	
			30	ML	5.41	
				ML_2	9.89	
			35	ML	5.38	
				ML_2	9.82	
	Gl.	0.05 KCl	25	ML	5.50	72GS
				ML_2	9.98	

cont'd

Table 6-4. Overall Formation Constants for L-Threonine Metal Complexes (continued)

Metal ion	Method	Medium (mol dm^{-3})	Temp. (°C)	Complex	log β	Ref.
	Gl.	0.1 KNO_3	25	ML	5.467	76PS
				ML_2	10.040	
				ML_3	13.18	
	(DL-)			ML	5.45	
				ML_2	10.02	
				ML_3	13.13	
	Gl.	0.1	20	ML	5.59	87MT
				ML_2	10.30	
	Gl.	0.2 KNO_3	35	ML	5.52	89KS, 89KV
				ML_2	9.80	
	Gl.	0.2 $NaClO_4$	27	ML	5.96	88PP
				ML_2	10.89	
Os^{4+}	Gl. (DL-)	~ 0.02	28	ML	5.60	74FAa
Pb^{2+}	Gl.	0.15 KNO_3	37	ML	4.43	67S
				ML_2	7.20	
	Pol.	0.5 KNO_3	20	ML	2.61	73RG
		20% DMF		ML	2.75	
		20% DMSO		ML	2.92	
	Pol.	1.0 KNO_3	30	ML	4.74	89SC
				ML_2	7.80	
Pd^{2+}	Gl. (DL-)	0.5 KNO_3	20	ML	9.4	74KH
				ML_2	18.6	
Rh^{3+}	Gl. (DL-)	~ 0.02	25	ML	6.86	74FAb
				ML_2	9.88	
Sm^{3+}	Gl.	0.1 KCl	20	ML	3.1	74PN
Th^{4+}	Gl.	0.5	25	ML	7.97	73SK
	Ion exch.	0.5	20	ML	8.00	80S
	Gl. (DL-)	0.1 KNO_3	25	ML	7.21	83NM
				ML_2	14.01	
Tl^{+}	Pol.	0.1 $NaClO_4$	25	ML	0.90	86SP
				ML_2	1.95	
U^{4+}	Sp.	0.5	20	ML	9.72	74SK
UO_2^{2+}	Gl.	0.1 $NaClO_4$	30	ML	7.30	73RS
				ML_2	14.20	
	Gl.	0.05 KCl	25	ML	6.35	73SC
				ML_2	12.50	
			45	ML	6.12	
				ML_2	12.04	
		0.15 KCl	25	ML	6.30	
				ML_2	12.40	
			45	ML	6.08	
				ML_2	11.90	
		0.25 KCl	25	ML	6.22	
				ML_2	12.26	
			45	ML	5.95	
				ML_2	11.65	

cont'd

Table 6-4. Overall Formation Constants for L-Threonine Metal Complexes (continued)

Metal ion	Method	Medium (mol dm^{-3})	Temp. (°C)	Complex	log β	Ref.
	Gl.	0.5	25	ML	6.00	73SKa
	Sp.	0.5	25	ML	5.95	
	Gl. (DL-)	0.1 KNO_3	25	ML	6.65	83NM
				ML_2	12.08	
	Gl. (DL-)	0.1 KNO_3 50% methanol	27	ML	8.53	85MS
VO^{2+}	Gl.	2.25 $NaNO_3$	25	MLH	10.30	89CV
				ML	6.41	
				ML_2H_2	20.0	
				ML_2H	16.43	
				ML_2	11.93	
				$M_2L_2H_{-2}$	4.98	
				ML_2H_{-1}	4.80	
				$M_2L_2H_{-3}$	-1.35	
				ML_2H_{-2}	-4.8	
				MLH_{-2}	-6.0	
				MLH_{-3}	-18.0	
Y^{3+}	Gl.	0.1 KCl	20	ML	3.7	70RP
	Gl.	0.1 KCl	20	ML	3.0	74PN
Yb^{3+}	Gl.	0.1 KCl	20	ML	3.5	74PN
Zn^{2+}	Gl. (DL-)	0.015	20	ML_2	8.6	53P
	Gl.	0.1 KCl	20	ML	4.87	64KW
	Gl.	0.15 KNO_3	37	ML	4.43	67S
				ML_2	8.14	
				ML_3	10.09	
	Gl. (DL-)	0.2 KNO_3	15	ML	4.79	68RM
				ML_2	8.62	
			25	ML	4.74	
				ML_2	8.51	
			40	ML	4.67	
				ML_2	8.35	
	Gl.	0.15 NaCl	37?	ML	4.72	72GH
				ML_2	8.68	
	Gl.	0.05 KCl	20	ML	4.71	72GM, 72GMa
				ML_2	8.73	
			25	ML	4.67	
				ML_2	8.66	
			30	ML	4.64	
				ML_2	8.59	
			35	ML	4.60	
				ML_2	8.52	
	Gl.	0.15 $NaClO_4$	37	ML	4.467	80KB
				ML_2	8.279	
				ML_2H_{-1}	-1.159	
	Gl.	0.2 KCl	25	ML	4.53	81G
				ML_2	8.38	
				MLH_{-1}	-4.09	
				ML_2H_{-1}	-1.5	

cont'd

Table 6-4. Overall Formation Constants for L-Threonine Metal Complexes (continued)

Metal ion	Method	Medium (mol dm^{-3})	Temp. (°C)	Complex	log β	Ref.
	(D-)			ML	4.54	
				ML_2	8.40	
				MLH_{-1}	-4.0	
				ML_2H_{-1}	-1.5	
	(DL-)			ML	4.54	
				ML_2	8.45	
				MLH_{-1}	-4.2	
				ML_2H_{-1}	-1.4	
	Gl.	0.2	30	ML	5.16	84J, 84Ja
				ML_2	9.35	86J
	Gl.	0.1 KNO_3	25	ML	4.66	85MK
	Gl.	0.2 KNO_3	35	ML	4.69	89KS, 89KV
				ML_2	8.53	
	Gl.	0.2 $NaClO_4$	27	ML	5.16	88PP
				ML_2	9.35	

(Gl. = glass electrode potentiometry [as exclusive or main method]; Pol. = polarography; Sp. = spectrophotometry)

Table 6-5. Recommended (R) and Tentative (T) Overall Formation Constants for L-Threonine Metal Complexes

Metal ion		Medium (mol dm^{-3})	Temp. (°C)	Complex	log β	Ref.
Cu^{2+}	(T)	0.05 KCl	25	ML	8.02 (±0.01)	71GN, 72GM, 72GMa,
				ML_2	14.75 (±0.03)	72GS
	(R)	0.1 KNO_3	25	ML	7.98 (±0.04)	69FM, 76PS, 77BP, 77DO
				ML_2	14.66 (±0.05)	88LG
				ML_2H_{-1}	4.81 (±0.03)	
				ML_2H_{-2}	-6.04 (±0.10)	
	(T)	0.15 $NaClO_4$	37	ML	7.79	82KB
				ML_2	14.30	
				MLH_{-1}	1.60	
				ML_2H_{-1}	4.69	
Ni^{2+}	(T)	0.1-0.2 KNO_3	25	ML	5.47 (±0.04)	68RM, 70LB, 76PS
				ML_2	9.99 (±0.03)	
Zn^{2+}	(T)	0.15 $NaClO_4$	37	ML	4.47	80KB
				ML_2	8.28	
				ML_2H_{-1}	-1.16	

Table 6-6. Constants for Mixed-ligand Complexes Involving L-Threonine

Metal ion	Method	Medium (mol dm^{-3})	Temp. (°C)	Extra ligand (X)	Complex	log β	Ref.
Al^{3+}	Gl.	0.1 KNO_3	35	Tripolyphosphate	MLX	7.55	80TH
Cd^{2+}	Gl.	0.2	30	NTA	(MX)L	3.32	82J
	Pol.	1.0 KNO_3	30	N-(2-Hydroxy-ethyl)ethylene-diamine	MLX ML_2X MLX_2	9.00 11.16 12.20	84CG
	Gl.	0.2	30	Iminodiacetic acid	(MX)L	3.25	84J
	Gl.	0.2	30	2,2'-Bipyridyl	(MX)L	3.86	84Ja
	Pol.	1.0 KNO_3 (pH 8-9)	30	Pyridoxine	MLX ML_2X MLX_2	5.00 7.75 5.80	85KC
	Pol.	1.0 KNO_3 (pH 8.5)	30	Ascorbic acid	MLX ML_2X MLX_2	4.80 7.35 5.11	86KC
	Gl.	0.2	30	Iminodiacetic acid	(MX)L	3.2±0.1	86J
	Gl.	0.2 $NaClO_4$	27	Di-2-pyridylamine	(MX)L	3.72	88PP
	Gl.	0.2 KNO_3	35	Bis(imidazol-2-yl)methane	(MX)L	3.38	89KV
Co^{2+}	Gl.	0.2 KNO_3	35	Bis(imidazol-2-yl)methane	(MX)L	3.64	89KV
	Gl.	0.1 KNO_3	25	ATP	(MX)L	4.00	89MA
Cr^{3+}	Gl.	0.1 $NaClO_4$	25	DL-Methionine	MLX MLXH	15.52 19.35	86MCa
				DL-Ethionine	MLX MLXH	15.62 19.53	
Cu^{2+}	Gl.	0.1 KNO_3	25	L- or D-Histidine	MLX MLXH $MLXH_{-1}$	17.56 21.90 7.00	69FM
	Gl.	0.05 KCl	25	α-Amino-butyric acid	MLX	15.16	72GS
				Alanine	MLX	15.23	
				Glycine	MLX	15.24	
				Norvaline	MLX	15.09	
				Phenylalanine	MLX	15.00	
				Serine	MLX	14.95	
				Tyrosine	MLX	15.06	
	Gl.	0.1 KNO_3	25	N-Carboxymethyl-L-isoleucine	(MX)L	5.30	73SA
	(D-)				(MX)L	5.17	
				N-Carboxymethyl-L-serine	(MX)L	5.27	
	(D-)				(MX)L	5.25	
				N-Carboxymethyl-L-valine	(MX)L	5.14	

cont'd

Table 6-6. Constants for Mixed-ligand Complexes Involving L-Threonine (continued)

Metal ion	Method	Medium (mol dm^{-3})	Temp. (°C)	Extra ligand (X)	Complex	log β	Ref.
	(D-)				(MX)L	5.07	
				N-Benzyl-N-carboxymethyl-L-alanine	(MX)L	5.53	
	(D-)				(MX)L	5.28	
				N-Benzyl-N-carboxymethyl-L-leucine	(MX)L	5.28	
	(D-)				(MX)L	5.09	
	Gl.	3.0 $NaClO_4$	25	L-Asparagine	MLX	16.471	75BW
				L-Histidine	MLX	18.613	
					MLXH	23.426	
	Gl.	0.1 KNO_3	25	L- or D-Histidine	MLX	17.464	77BP
					MLXH	21.43	
	Gl. (DL-)	0.1 KNO_3	25	Glycine	MLX	15.17	77DO
					$MLXH_{-1}$	5.29	
				Sarcosine	MLX	14.70	
					$MLXH_{-1}$	4.68	
	Sp.	0.5 $NaClO_4$	-	Salicylic acid	MLX	18.34	77MG,
				5-sulfo-salicylic acid	MLX	16.22	78MGa
	Gl.	0.2 KCl	25	Glycylglycine	$MLXH_{-1}$	4.95	77NG
				Glycyl-DL-α-alanine	$MLXH_{-1}$	4.98	
				DL-α-Alanyl-DL-α-alanine	$MLXH_{-1}$	4.81	
	Gl.	0.15 NaCl	25	L-Histidine	MLX	17.55	77S
					MLXH	21.831	
					$MLXH_{-1}$	6.96	
	Sp.	0.5 $NaClO_4$ (pH 5)	25?	2,4-Dihydroxy-benzoic acid	$MLXH_2$	20.92	78MG
	Gl.	0.1 KNO_3	25	L-Histidine	MLX	17.08	79YS
	Gl.	0.1 $NaClO_4$	30	Glycylsarcosine	MLX	19.45	80AS
	Pol.	-	-	Malonic acid	MLX	11.50	80SG
				Oxalic acid	MLX	12.10	
	Gl.	0.1 KNO_3 (20% dioxane)	25	L-Histidine	MLX	17.57	80YT
				D-Histidine	MLX	17.59	
	Gl.	0.1	30	Glycine	MLX	15.71	81R
					ML_2X	19.78	
					MLX_2	19.01	
				Phenylalanine	MLX	15.36	
					ML_2X	19.01	
					MLX_2	18.30	
	Gl.	0.15 $NaClO_4$	37	Histamine	MLX	16.433	82KB
					MLXH	20.360	
					$MLXH_{-1}$	6.464	
	Gl.	0.1 $NaClO_4$	30	Glycyl-L-phenylalanine	$MLXH_{-1}$	5.34	82S
	Gl.	0.1 $NaClO_4$	30	Glycyl-DL-serine	$MLXH_{-1}$	4.73	83S
	Gl.	0.15 $NaClO_4$	37	L-histidine	MLX	17.030	84BB
					MLXH	20.656	
					$MLXH_{-1}$	6.818	

cont'd

Table 6-6. Constants for Mixed-ligand Complexes Involving L-Threonine (continued)

Metal ion	Method	Medium (mol dm^{-3})	Temp. (°C)	Extra ligand (X)	Complex	log β	Ref.
	Gl.	0.1 $NaClO_4$	30	Alanyl-L-phenylalanine	$MLXH_{-1}$	4.40	84S
	Gl.	0.1 $NaClO_4$	30	Glycyl-L-asparagine	$MLXH_{-1}$	10.98	86AJ
	Gl.	0.1 $NaClO_4$	25	DL-α-Alanyl-DL-methionine	(ML)X (?)	5.37	88JA
				DL-Alanyl-DL-norvaline	(ML)X (?)	5.90	
	Gl.	0.1 $NaClO_4$	25	N-Acetyl-glycine	MLX	10.35	88LG
	Pol.	1.0 KNO_3	30	Pyridoxine	MLX	9.28	88SKa
	Gl.	0.1 KNO_3	25	Diethylene-triamine	(MX)L	3.60	89SH
Mg^{2+}	Gl. (DL-)	0.15 NaCl	20	Orotic acid	MLX	5.36	85VD
Ga^{3+}	Gl.	0.1 KNO_3	35	Tripolyphosphate	ML	7.21	80TH
Mn^{2+}	Gl. (DL-)	0.15 NaCl	20	Orotic acid	MLX	6.64	85VD
Ni^{2+}	Gl.	0.05 KCl	25	α-Amino-butyric acid	MLX	10.27	72GS
				Alanine	MLX	10.37	
				Glycine	MLX	10.70	
				Norleucine	MLX	10.30	
				Norvaline	MLX	10.29	
				Phenylalanine	MLX	10.09	
				Serine	MLX	10.34	
				Tyrosine	MLX	10.14	
	Gl.	0.2 $NaClO_4$	27	Di-2-pyridylamine	(MX)L	5.35	88PP
	Gl.	0.2 KNO_3	35	Bis(imidazol-2-yl)methane	(MX)L	4.94	89KV
	Gl.	0.1 KNO_3	25	ATP	(MX)L	4.30	89MA
Pb^{2+}	Pol.	1.0 KNO_3	30	Pyridoxine	MLX	5.39	89SC
Pd^{2+}	Gl.	0.1 KNO_3	25	Ethylenediamine	(MX)L	10.96	81L
					$(MXL)H_{-1}$	-8.05	
	Gl.	0.1 NaCl	25	Diethylene-triamine	(MX)L	4.15	87SM
Tb^{3+}	Sp.	-	-	EDTA	(MX)L	2.48	85SB
UO_2^{2+}							
	Gl. (DL-)	0.1 KNO_3 50% methanol	27	2-Hydroxy-1-naphtaldehyde	MLX	13.08	85MS
Zn^{2+}	Gl.	0.15 $NaClO_4$	37	Histamine	MLX	9.311	80KB
	Gl.	0.15 $NaClO_4$	37	L-Histidine	MLX	9.863	81ABa
	Gl. (D-)	0.2 KCl	25	L-Histidine	MLX	10.10	81G
					MLX	10.48	
	Gl.	0.15 $NaClO_4$	37	Citrate	M_2LXH_{-2}	-2.299	82BB

cont'd

Table 6-6. Constants for Mixed-ligand Complexes Involving L-Threonine (continued)

Metal ion	Method	Medium (mol dm^{-3})	Temp. (°C)	Extra ligand (X)	Complex	log β	Ref.
	Gl.	0.2	30	NTA	(MX)L	3.40	82J
	Gl.	0.2	30	Iminodiacetic acid	(MX)L	4.08	84J
	Gl.	0.2	30	2,2'-Bipyridyl	(MX)L	4.89	84Ja
	Gl.	0.1 KNO_3	25	ATP	(MX)L (MLX)OH	3.80 4.39	85MK
	Gl.	0.2	30	Iminodiacetic acid	(MX)L	4.0±0.1	86J
	Gl.	0.2 $NaClO_4$	27	Di-2-pyridylamine	(MX)L	4.85	88PP
	Gl.	0.2 KNO_3	35	Bis(imidazol-2-yl)methane	(MX)L	4.21	89KV

(Gl. = glass electrode potentiometry [as exclusive or main method]; Pol. = polarography; Sp. = spectrophotometry)

Table 6-7. Overall Thermodynamic Quantities for L-Threonine Metal Complex Equilibria

Metal ion	Method	Medium (mol dm^{-3})	Temp. (°C)	Complex	ΔH° (kJ mol^{-1})	ΔS° (J K^{-1} mol^{-1})	Ref.
Co^{2+}	Pot. (DL-)	0.2 KNO_3	25	ML_2	-18.0	92.0	68RM
	Pot.	0.05 KCl	25	ML	-7.53	58.6	72GM, 72GMa
				ML_2	-24.69	71.1	
	Cal.	0.05 KCl	25	ML	-4.60	66.9	
				ML_2	-23.01	75.3	
	Cal. (L- or DL-)	0.1 KNO_3	25	ML	-10.8	45	78IS
				ML_2	-18.9	93	
Cu^{2+}	Cal.	→0	25	ML	-22.2	87.9	64IC
				ML_2	-47.7	133.9	
	Pot. (DL-)	0.2 KNO_3	25	ML_2	-44.4	142.2	68RM
	Cal. (DL-)	0.16 KNO_3	25	ML	-23.26	74.0	70LB
				ML_2	-48.74	117.6	
	Cal.	0.05 KCl	25	ML	-23.01	75.3	71GN
				ML_2	-48.53	117.1	
	Pot.	0.05 KCl	25	ML	-25.52	66.9	72GM, 72GMa
				ML_2	-53.55	100.4	
	Cal.	0.05 KCl	25	ML	-23.01	75.3	
				ML_2	-48.53	117.1	
	Cal.	3.0 $NaClO_4$	25	ML	-18.0	104.2	75BW
				ML_2	-47.0	149.4	
	Cal. (DL-)	0.1 KNO_3	25	ML_2	-53.13	101.3	76PS
				ML_2	-52.91	102.0	
	Cal. (L- or DL-)	0.1 KNO_3	25	ML	-25.6	68	78IS
				ML_2	-46.3	130	
	Cal.	0.1 $NaClO_4$	25	ML	-27.5	61	88LG
				ML_2	-55.5	95	
Fe^{2+}	Pot. (DL-)	0.2 KNO_3	25	ML_2	-8.4	96.2	68RM
La^{3+}	Pot.	0.05 KCl	25	ML	-31.8	-29.3	75SC
				ML_2	-36.3	13.0	

cont'd

Table 6-7. Overall Thermodynamic Quantities for L-Threonine Metal Complex Equilibria (continued)

Metal ion	Method	Medium (mol dm^{-3})	Temp. (°C)	Complex	ΔH° (kJ mol^{-1})	ΔS° (J K^{-1} mol^{-1})	Ref.
Mn^{2+}	Pot. (DL-)	0.2 KNO_3	25	ML_2	-3.3	62.8	68RM
Ni^{2+}	Pot.	-	(10-40)	ML	-21.8	32.6	57P, 60Pa, 60Pb
				ML_2	-45.6	39.3	
				ML_3	-71.8	9.2	
	Pot. (DL-)	0.2 KNO_3	25	ML_2	-33.9	79.5	68RM
	Cal. (DL-)	0.16 KNO_3	25	ML	-15.94	51.0	70LB
				ML_2	-34.18	76.1	
				ML_3	-55.94	69.5	
	Pot.	0.05 KCl	25	ML	-14.22	54.4	72GM, 72GMa
				ML_2	-32.22	83.7	
	Cal.	0.05 KCl	25	ML	-13.39	58.6	
				ML_2	-35.56	71.1	
UO_2^{2+}							
	Pot.	0.05 KCl	25	ML	-20.88	51.5	73SC
				ML_2	-41.76	99.2	
Zn^{2+}	Pot. (DL-)	0.2 KNO_3	25	ML_2	-18.8	100.4	68RM
	Pot.	0.05 KCl	25	ML	-12.13	50.2	72GM, 72GMa
				ML_2	-23.01	87.9	
	Cal.	0.05 KCl	25	ML	-10.46	54.4	
				ML_2	-22.17	92.0	

(Pot. = potentiometry; Cal. = calorimetry)

Table 6-8. Thermodynamic Quantities for Mixed-ligand Complexes Involving L-Threonine

Metal ion	Method	Medium (mol dm^{-3})	Temp. (°C)	Extra ligand (X)	Complex	ΔH° (kJ mol^{-1})	ΔS° (J K^{-1} mol^{-1})	Ref.
Cu^{2+}	Cal.	3.0 $NaClO_4$	25	L-Aspa-ragine	MLX	-50.0	147.7	75BW
				L-Histidine	MLX	-67.4	130.3	
					MLXH	-103.5	101.3	
	Cal.	0.1 $NaClO_4$	25	N-Acetyl-glycine	MLX	-25.2	114	88LG

(Cal. = calorimetry)

7. ASPARAGINE - $H_2NCOCH_2CH[NH_2]CO_2H$ (2-aminobutanedioic acid 4-amide, LH)

Like the -OH group of serine and threonine, the amide group of asparagine releases a proton well above the limit of pH attainable with a glass electrode in aqueous solution. Even at high ligand concentrations, no dissociation can be detected (75GN). In the presence of metal ions however, the amide group can deprotonate and participate in the coordination process (75GN). Thus, contrary to glutamine whose potential chelate ring displays a less favourable size (see introduction), asparagine can act as a tridentate ligand and give rise to hydroxo complexes with copper(II) (75GN, 86BH). Like the unionized hydroxyl group of serine (76PS), the amide group of asparagine also interacts as such with the carboxylate oxygen of histidine in the corresponding mixed-ligand copper(II) species. However, this does not induce any stereoselective effect around the central metal ion (70BP, 71BP, 79YS).

7-1. Protonation constants of asparagine

Comparatively to serine and threonine, the number of determinations devoted to proton-asparagine interactions is significantly smaller (Table 7-1), which makes data selection more difficult. The constants found by 65RW and 73TS are the only ones determined under identical experimental conditions (25 °C, 0.1 mol dm^{-3}). Fortunately they are quite reproducible and if we assume, as Martell and Smith apparently did (82MS, 89SM), that those in 73TS can be classified as stoichiometric, average values can be calculated (Table 7-2). These values seem all the more reliable as they are almost equivalent to those found by Gergely et al. in 0.2 mol dm^{-3} aqueous KCl at the same temperature (75GN). They are thus recommended.

Apart from this example, the number of determinations is insufficient to allow the calculation of any recommended average. Nevertheless, the constants obtained in refs. 72GW, 75GN, 81JI and 86BH appear sufficiently reliable to be proposed as tentative for the corresponding experimental conditions.

7-2. Thermodynamic quantities for the protonation of asparagine

Determinations of thermodynamic quantities for proton-asparagine interactions are relatively scarce. Nevertheless, the four sets of data obtained from direct calorimetric measurements can be considered as reliable (Table 7-3). In comparison, the values deduced from the van't Hoff equation within the 25-45 °C interval (85SS) should be regarded with caution, especially those relative to the first protonation step.

7-3. Metal complex formation constants

Formation constants for the binary metal complexes of asparagine are collected in Table 7-4. From a general point of view, the number of independent determinations for each metal ion is appreciably smaller than for previous amino acids, which makes the evaluation of the corresponding constants less easy. Complexes of cadmium(II), copper(II) and nickel(II) are the only ones to have been investigated by several groups of authors. In addition, most of the data available refer to distinct experimental conditions.

For cadmium(II) for example, all determinations have been made at different temperatures or under different conditions of ionic strength except for the two relative to 3.0 mol dm^{-3} at 25 °C (74WW, 81M). Unfortunately, corresponding constants are too distant to offer a sound basis of comparison. It seems unlikely that such a discrepancy can be due to the different nature of the background electrolytes used, the more so as protonation constants from the same groups of authors (72GW, 81M) already differed considerably, the one from reference 81M being much too low for that ionic strength. Because of this and also from comparisons made in preceding chapters, the values obtained by Walker and Williams (74WW) are to be preferred and have thus been proposed as tentative.

The experimental conditions under which copper(II) complexes have been investigated are extremely diverse, and no direct comparison is possible. The most complete results refer to physiological conditions (86BH), but other data can also be considered as reliable (65RW, 74BW, 75GN). All of these can be taken as tentative.

Similarly, constants for cobalt(II) and nickel(II) complexes reported in refs. 65RW and 74BW can also be selected as tentative, as is also the case for zinc(II) complexes in 74BW. All these values can be

found in Table 7-5.

For mixed-ligand complexes (Table 7-6), few data are available except for copper(II), for which the results obtained in refs. 75BW, 79YS and 86BH are to be considered as the most reliable.

7-4. Thermodynamic quantities for metal complex formation with asparagine

The number of studies devoted to determinations of thermodynamic quantities is relatively limited. Nevertheless, all values derived from direct calorimetric measurements, reported in Tables 7-7 and 7-8, are worth recommending since they have been obtained by authors whose results have regularly been selected in previous evaluations.

A series of data deduced from the van't Hoff equation have also been mentioned in Table 7-7. These have been obtained by a same group of authors under identical experimental conditions, and may provide a useful basis for comparison within the lanthanide series (86SS). Other values relative to cerium(III) (86K), also obtained from potentiometric determinations, have been rejected as too imprecise.

Table 7-1. Protonation Constants of Asparagine

Type of constants	Medium (mol dm^{-3})	Temp. (°C)	log K_1	log K_2	Ref.
Thermo	~0.01	20	8.85	2.14	50A
Thermo	~0.01	15	9.13	-	53P
Mixed	0.15 KNO_3	25.15	8.84	-	53TS
Mixed	0.15	25	8.71	-	58LD
Mixed	1.0 $NaClO_4$	20	8.79	2.09	58P
Mixed(?)	1.0 KCl	20	8.79	-	59P
Mixed	0.15 KCl	30	8.72	-	64FW
Mixed(?)	1.0 KNO_3	30	8.88	-	64RS
Stoichio	0.1 KNO_3	25	8.72	2.14	65RW
Mixed	0.6	25	9.04	-	67AM
Stoichio	3.0 $NaClO_4$	25	9.303	2.586	72GW
Stoichio(?)	0.1 $NaClO_4$	25	8.70	2.16	73TS
Stoichio	0.2 KCl	25	8.74	2.14	75GN
Mixed	0.5 KNO_3	25	8.79	2.26	77La
Stoichio(?)	3.0 $LiClO_4$	25	8.83	-	77M, 81M
Stoichio	0.2 $NaClO_4$	30	8.555	2.085	77MS, 78MS
Mixed	0.1 $NaClO_4$	31	8.725	2.140	77RR
Thermo	→0 100% formic acid	25	1.42		78KA
Thermo	~0 50% ethanol	25	8.76	-	79FM
Thermo	~0 formic acid: ethyl methyl ketone (1:24) acetic acid: ethyl methyl ketone (1:8)	25 9.87	9.52		80KT

cont'd

Table 7-1. Protonation Constants of Asparagine (continued)

Type of constants	Medium (mol dm^{-3})	Temp. (°C)	log K_1	log K_2	Ref.
Stoichio	0.1 KNO_3 20% dioxane	25	8.89	2.46	80YT
Stoichio	0.1	20	8.76	2.40	81CD
	0.1 100% trifluoro-ethanol	20	7.08	-	
Stoichio	1.0 $NaNO_3$	25	8.69	2.15	81JI
Thermo	~0	30	9.01	2.02	81PU
Thermo	~0	25	8.69	2.28	82DD
	8.0% propan-2-ol	25	8.68	2.40	
	16.3% propan-2-ol	25	8.68	2.51	
	25.1% propan-2-ol	25	8.67	2.65	
	34.3% propan-2-ol	25	8.69	2.78	
	43.9% propan-2-ol	25	8.76	2.92	
	54.0% propan-2-ol	25	8.78	3.07	
	64.6% propan-2-ol	25	8.85	3.30	
	75.8% propan-2-ol	25	8.91	3.46	
Mixed(?)	0.1 $NaClO_4$	21	8.91	2.01	83LW
Mixed(?)	0.1 $NaClO_4$	25	8.79	2.18	85SS
		35	8.64	2.15	
		45	8.52	2.12	
	0.2 $NaClO_4$	35	8.60	2.10	
	0.5 $NaClO_4$	35	8.52	2.06	
	1.0 $NaClO_4$	35	8.45	2.00	
	0.1 $NaClO_4$	35			
	20.0% DMSO		8.74	2.29	
	20% DMF		8.68	2.25	
	20.0% acetonitrile		8.61	2.19	
	20.0% methanol		8.58	2.14	
	20.0% ethanol		8.53	2.09	
	20.0% propan-2-ol		8.49	2.03	
Mixed(?)	0.1	35	8.73	2.10	85SYa
Stoichio	0.15 $NaClO_4$	37	8.458	2.151	86BH
Thermo	~0	25	8.70	2.29	87CL
	10% methanol	25	8.66	2.35	
	20% methanol	25	8.67	2.44	
	30% methanol	25	8.66	2.59	
	40% methanol	25	8.68	2.74	
	50% methanol	25	8.74	2.88	
	60% methanol	25	8.78	2.94	
	70% methanol	25	8.85	3.16	
	80% methanol	25	8.90	3.42	
	10% ethanol	25	8.67	2.37	
	20% ethanol	25	8.67	2.46	
	30% ethanol	25	8.66	2.61	
	40% ethanol	25	8.68	2.73	
	50% ethanol	25	8.75	2.86	
	60% ethanol	25	-	2.98	
	70% ethanol	25	-	3.07	
	80% ethanol	25	-	3.27	
Mixed(?)	0.15 KNO_3	25	8.82	-	87CJ
Mixed(?)	0.2 KCl	25	8.73	2.27	88KD
Mixed(?)	1.0 KNO_3	25	8.80	2.02	89KN, 89NK

Table 7-2. Recommended (R) and Tentative (T) Values for Protonation Constants of Asparagine

Type of constants	Medium (mol dm^{-3})	Temp. (°C)	log K_1	log K_2	Ref.
Stoichio? (T)	0.05 KCl	25	8.98 (±0.01)	2.18 (±0.06)	71GN, 72GM, 72GS
Stoichio (R)	0.05 KCl	25	8.71 (±0.01)	2.15 (±0.01)	65RW, 73TS
Stoichio (T)	3.0 $NaClO_4$	25	9.30	2.59	72GW
Stoichio (T)	0.2 KCl	25	8.74	2.14	75GN
Stoichio (T)	1.0 $NaNO_3$	25	8.69	2.15	81JI
Stoichio (T)	0.15 $NaClO_4$	37	8.46	2.15	86BH

Table 7-3. Thermodynamic Quantities for Asparagine Protonation Equilibria

Method	Medium (mol dm^{-3})	Temp. (°C)	$\Delta H°_1$ (kJ mol^{-1})	$\Delta H°_2$	$\Delta S°_1$ (J K^{-1} mol^{-1})	$\Delta S°_2$	Ref.
Cal.	0.1 KNO_3	25	-40.79	-	-	-	71BP
Cal.	3.0 $NaClO_4$	25	-50.5	-5.10	8.9	32.4	72GW, 74BW
Cal.	0.2 KCl	25	-41.4	-4.72	28.0	25.0	75GN
Cal.	~0	25	-41.2	-3.10	16.4	28.3	89RF, 89R
Pot.	0.1 $NaClO_4$	35	-25.8	-5.9	81.7	22.0	85SS

(Pot. = potentiometry; Cal. = calorimetry)

Table 7-4. Overall Formation Constants for L-Asparagine Metal Complexes

Metal ion	Method	Medium (mol dm^{-3})	Temp. (°C)	Complex	log β	Ref.
Ag^{+}	Pol.	0.6	25	ML	3.30	67AM
				ML_2	6.45	
	Ag el.	~0	30	ML	3.64	81PU
				ML_2	6.64	
Al^{3+}	Gl.	0.1 $NaClO_4$	25	ML	~6.65	73TSb
				ML_2	10.30	
Au^{3+}	Gl.	~ 0.02	25	ML	6.18	74FA
				ML_2	9.28	
	Gl.	0.1 $NaClO_4$	25	ML	8.88	74TS
				ML_2	17.02	
				ML_3	24.62	
Be^{2+}	Gl. (DL-)	0.015	15	ML_2	11.7	53P
	Gl.	0.1 $NaClO_4$	25	ML	~5.87	73TSb
				ML_2	10.70	
Bi^{3+}	Gl.	0.1 $NaClO_4$	25	ML	9.76	74TS
				ML_2	18.64	
Cd^{2+}	Gl.	~ 0.01	20	ML	3.87	50A
				ML_2	6.77	
	Gl. (DL-)	0.015	15	ML_2	7.1	53P
	Pol.	1.0	30	ML_3	8.60	62RS
	Pol.	1.0 KNO_3	30	ML_2	6.90	64RS
				ML_3	8.58	
				$ML_3(OH)$	9.22	
	Gl.	3.0 $NaClO_4$	25	ML	4.071	74WW
				ML_2	7.581	
				ML_3	9.610	
	Gl.	3.0 $LiClO_4$	25	ML	3.89	81M, 82MH
				ML_2	7.06	
	Pol.	0.5 KNO_3	20	ML	4.81	84GN
				ML_2	7.86	
				ML_3	9.50	
			30	ML	4.38	
				ML_2	6.90	
				ML_3	8.78	
			30	ML	3.93	
				ML_2	6.70	
				ML_3	8.40	
	Pol.	0.1 KNO_3	25	ML_2	6.26	86SSa
			35	ML_2	5.92	
			45	ML_2	5.58	
	Pol.	1.0 KNO_3	25	ML	4.07	89KN, 89NK
				ML_2	7.18	
				ML_3	9.10	
Ce^{3+}	Gl.	0.1 $NaClO_4$	25	ML	~3.80	73TSa
				ML_2	7.17	
	Gl.	0.2 $NaClO_4$	30	ML	3.775	77MS, 78MS

cont'd

Table 7-4. Overall Formation Constants for L-Asparagine Metal Complexes (continued)

Metal ion	Method	Medium (mol dm^{-3})	Temp. (°C)	Complex	log β	Ref.
	Pol.	1.0 KCl	25	ML	3.52	86K
			35	ML	3.00	
			45	ML	2.60	
	Gl.	0.1 KNO_3	25	ML	3.85	86SS
				ML_2	7.25	
			35	ML	3.99	
				ML_2	7.52	
			45	ML	4.17	
				ML_2	7.87	
Co^{2+}	Gl.	~ 0.01	20	ML_2	8.4	50A
	Gl.	0.15 KNO_3	25.15	ML	4.55	53TS
				ML_2	8.13	
				ML_3	9.96	
	Gl.	0.1 KNO_3	25	ML	4.45	65RW
				ML_2	7.99	
	(DL-)			ML	4.51	
				ML_2	8.01	
	Gl.	3.0 $NaClO_4$	25	ML	4.903	74BW
				ML_2	9.029	
				ML_3	11.855	
	Gl.	0.15 KNO_3	25	ML	4.51	87CJ
				ML_2	8.01	
Cr^{2+}	Gl.	~ 0.015	25(?)	ML	6.97	70FM
Cr^{3+}	Gl.	0.4 KCl	25	ML	7.7	63KM
				ML_2	13.6	
				ML_3	18.5	
Cu^{2+}	Gl.	~ 0.01	20	ML_2	14.9	50A
	Gl.	0.15	25	ML	7.78	58LD
	(D-, L-, or DL-)			ML_2	14.13	
	Gl. (DL-)	0.1 KCl	25	$[ML_2]/[ML]$	6.45	59B
					6.24	
	Gl.	0.1 KNO_3	25	ML	7.90	65RW
				ML_2	14.45	
	(DL-)			ML	7.86	
				ML_2	14.42	
	Gl.	3.0 $NaClO_4$	25	ML	8.677	74BW
				ML_2	16.052	
	Gl.	0.2 KCl	25	ML	7.79	75GN
				ML_2	14.29	
				ML_2H_{-1}	3.84	
				ML_2H_{-2}	-8.16	
	Sp. (D-)	~0 (50% ethanol)	25	ML	8.12	79FM
				ML_2	14.92	
	Gl.	0.1 $NaClO_4$	30	ML	7.805	80AS
				ML_2	14.36	
	Gl.	0.1 KNO_3	25	ML	8.20	80YT
		20% dioxane		ML_2	14.95	
	Gl.	0.1 $NaClO_4$	21	ML	7.69	83LW
				ML_2	14.38	
				MLH_{-1}	2.33	

cont'd

Table 7-4. Overall Formation Constants for L-Asparagine Metal Complexes (continued)

Metal ion	Method	Medium (mol dm^{-3})	Temp. (°C)	Complex	log β	Ref.
	Gl.	0.2 $NaClO_4$ (pH 6)	25	ML	7.50	84KW
				ML_2	13.50	
	Gl.	0.15 $NaClO_4$	37	ML	7.714	86BH
				ML_2	14.210	
				ML_2H	17.417	
				ML_2H_2	20.186	
				MLH_{-1}	0.675	
				ML_2H_{-1}	3.941	
Dy^{3+}	Gl.	0.1 KNO_3	25	ML	4.53	86SS
				ML_2	8.58	
			35	ML	4.70	
				ML_2	8.88	
			45	ML	4.86	
				ML_2	9.23	
Fe^{2+}	Gl.	~ 0.01	20	ML_2	6.5	50A
	Gl.	1.0 KCl	20	ML	3.40	59P
	Gl.	3.0 $NaClO_4$	25	ML	4.366	74BW
				ML_2	7.569	
				ML_3	10.259	
Fe^{3+}	Gl.	1.0 $NaClO_4$	20	ML	8.6	58P
Ga^{3+}	Gl.	0.1 KNO_3	22	ML	11.17	68ZK
Gd^{3+}	Gl.	0.1 KNO_3	25	ML	4.33	86SS
				ML_2	8.19	
			35	ML	4.48	
				ML_2	8.48	
			45	ML	4.66	
				ML_2	8.84	
Hg^{2+}	Hg el.	0.1 $NaNO_3$	25	ML	11.4	73VB
				ML_2	18.6	
CH_3Hg^{II}	Gl.	1.0 $NaNO_3$	25	ML	6.32	81JI
In^{3+}	Gl.	0.1 $NaClO_4$	25	ML	~7.45	73TSb
				ML_2	14.55	
	Gl.	~ 0.02	24	ML	7.17	76KF
				ML_2	14.38	
La^{3+}	Gl.	0.1 $NaClO_4$	25	ML	~3.50	73TSa
				ML_2	6.55	
	Gl.	0.2 $NaClO_4$	30	ML	3.525	77MS, 78MS
	Gl.	0.1 KNO_3	25	ML	3.75	86SS
				ML_2	7.07	
			35	ML	3.89	
				ML_2	7.34	
			45	ML	4.04	
				ML_2	7.67	

cont'd

Table 7-4. Overall Formation Constants for L-Asparagine Metal Complexes (continued)

Metal ion	Method	Medium (mol dm^{-3})	Temp. (°C)	Complex	log β	Ref.
Mg^{2+}	Gl.	~ 0.01	20	ML_2	4	50A
Mn^{2+}	Gl.	~ 0.01	20	ML_2	4.5	50A
	Gl.	3.0 $NaClO_4$	25	ML	3.102	74BW
				ML_2	5.222	
Mo^{VI}	Gl.	0.1 $NaClO_4$	25	ML	8.06	73TS
				ML_2	15.29	
				ML_3	18.74	
Nd^{3+}	Gl.	0.1 $NaClO_4$	25	ML	~4.15	73TSa
				ML_2	7.85	
	Gl.	0.2 $NaClO_4$	30	ML	4.260	77MS, 78MS
	Gl.	0.1 KNO_3	25	ML	4.14	86SS
				ML_2	7.81	
			35	ML	4.28	
				ML_2	8.09	
			45	ML	4.46	
				ML_2	8.44	
Ni^{2+}	Gl.	~ 0.01	20	ML_2	10.6	50A
	Gl.	0.15	25	ML	5.58	58LD
				ML_2	9.96	
	Gl.	0.1 KNO_3	25	ML	5.64	65RW
				ML_2	10.20	
	(DL-)			ML	5.68	
				ML_2	10.23	
	Gl.	3.0 $NaClO_4$	25	ML	6.152	74BW
				ML_2	11.163	
				ML_3	14.545	
Os^{4+}	Gl.	~ 0.02	28	ML	5.17	74FAa
Pb^{2+}	Gl.	3.0 $NaClO_4$	25	ML	4.914	73CT
				ML_2	7.815	
				ML_3	8.815	
	Pol.	0.1 KNO_3	25	ML_2	6.42	86SSa
			35	ML_2	6.09	
			45	ML_2	5.75	
Pd^{2+}	Gl.	~ 0.02	27	ML_2	15.11	73FA
	Gl.	3.0 $NaClO_4$	25	MLH	12.11	74GW
				MLH_{-1}	9.1	
	Gl.	0.1 $NaClO_4$	25	ML	9.15	74TS
				ML_2	17.65	
Pr^{3+}	Gl.	0.1 $NaClO_4$	25	ML	~4.05	73TSa
				ML_2	7.65	
	Gl.	0.2 $NaClO_4$	30	ML	4.085	77MS, 78MS
	Gl.	0.1 KNO_3	25	ML	4.05	86SS
				ML_2	7.60	
			35	ML	4.18	
				ML_2	7.90	
			45	ML	4.36	
				ML_2	8.25	

cont'd

Table 7-4. Overall Formation Constants for L-Asparagine Metal Complexes (continued)

Metal ion	Method	Medium (mol dm^{-3})	Temp. (°C)	Complex	log β	Ref.
Pt^{4+}	Gl.	0.1 $NaClO_4$	25	ML	7.98	74TS
				ML_2	11.50	
Rh^{3+}	Gl.	~ 0.02	25	ML	6.86	74FAb
				ML_2	9.73	
Sc^{3+}	Gl.	0.2 $NaClO_4$	30	ML	7.083	77MS, 78MS
Sm^{3+}	Gl.	0.1 KNO_3	25	ML	4.24	86SS
				ML_2	8.00	
			35	ML	4.38	
				ML_2	8.29	
			45	ML	4.56	
				ML_2	8.64	
Sr^{2+}	Ion exch.	0.16 (pH 7.2)	25	ML	-0.43	54S
Tb^{3+}	Gl.	0.1 KNO_3	25	ML	4.43	86SS
				ML_2	8.38	
			35	ML	4.59	
				ML_2	8.69	
			45	ML	4.70	
				ML_2	8.98	
Ti^{3+}	Gl.	~ 0.02	25?	ML	6.95	70FMb
UO_2^{2}	Gl.	~ 0.02	25?	ML	6.88	70FMb
	Gl.	0.1 $NaClO_4$	31	ML	7.23	77RR
V^{3+}	Gl.	0.2 KCl	20	ML	8.08	88KD
				ML_2	15.33	
VO^{2+}	Gl.	~ 0.02	25?	ML	7.25	70FMb
	Gl.	0.1 $NaClO_4$	25	ML	~7.50	73TS
				ML_2	14.50	
				ML_3	18.54	
W^{VI}	Gl.	0.1 $NaClO_4$	25	ML	5.84	73TS
				ML_2	10.95	
				ML_3	14.25	
Y^{3+}	Gl.	0.1 $NaClO_4$	25	ML	~4.25	73TSa
				ML_2	8.08	
	Gl.	0.2 $NaClO_4$	30	ML	4.425	77MS, 78MS
	Gl.	0.1 KNO_3	25	ML	4.63	86SS
				ML_2	8.78	
			35	ML	4.78	
				ML_2	9.07	
			45	ML	4.96	
				ML_2	9.43	

cont'd

Table 7-4. Overall Formation Constants for L-Asparagine Metal Complexes (continued)

Metal ion	Method	Medium (mol dm^{-3})	Temp. (°C)	Complex	log β	Ref.
Zn^{2+}	Gl.	~ 0.01	20	ML_2	8.7	50A
	Gl. (DL-)	0.015	15	ML_2	8.5	53P
	Gl.	3.0 $NaClO_4$	25	ML	5.070	74BW
				ML_2	9.426	
				ML_3	12.300	
	Gl.	0.1 $NaClO_4$	21	ML	4.52	83LW
				ML_2	7.86	

(Gl. = glass electrode potentiometry [as exclusive or main method]; Pol. = polarography; Sp. = spectrophotometry)

Table 7-5. Recommended (R) and Tentative (T) Overall Formation Constants for L-Asparagine Metal Complexes

Metal ion		Medium (mol dm^{-3})	Temp. (°C)	Complex	log β	Ref.
Cd^{2+}	(T)	3.0 $NaClO_4$	25	ML	4.07	74WW
				ML_2	7.58	
				ML_3	9.61	
Co^{2+}	(T)	0.1 KNO_3	25	ML	4.45	65RW
				ML_2	7.99	
	(T)	3.0 $NaClO_4$	25	ML	4.90	74BW
				ML_2	9.03	
				ML_3	11.86	
Cu^{2+}	(T)	0.1 KNO_3	25	ML	7.90	65RW
				ML_2	14.45	
	(T)	3.0 $NaClO_4$	25	ML	8.68	74BW
				ML_2	16.05	
	(T)	0.2 KCl	25	ML	7.79	75GN
				ML_2	14.29	
				ML_2H_{-1}	3.84	
				ML_2H_{-2}	-8.16	
	(T)	0.15 $NaClO_4$	37	ML	7.71	86BH
				ML_2	14.21	
				ML_2H	17.42	
				ML_2H_2	20.19	
				MLH_{-1}	0.68	
				ML_2H_{-1}	3.94	
Ni^{2+}	(T)	0.1 KNO_3	25	ML	5.64	65RW
				ML_2	10.20	
	(T)	3.0 $NaClO_4$	25	ML	6.15	74BW
				ML_2	11.16	
				ML_3	14.54	
Zn^{2+}	(T)	3.0 $NaClO_4$	25	ML	5.07	74BW
				ML_2	9.43	
				ML_3	12.30	

Table 7-6. Constants for Mixed-ligand Complexes Involving L-Asparagine

Metal ion	Method	Medium (mol dm^{-3})	Temp. (°C)	Extra ligand (X)	Complex	log β	Ref.
Cd^{2+}	Pol.	1.0 KNO_3	30	Carbonate	ML_2X	8.14	64RS
				Ammonia	ML_2X_2	9.08	
	Pol.	1.0 KNO_3	25	Formate	MLX	5.95	89KN
					MLX_2	7.94	
					ML_2X	8.30	
	Pol.	1.0 KNO_3	25	Acetate	MLX	6.08	89NK
					MLX_2	8.12	
					ML_2X	8.48	
Ce^{3+}	Gl.	0.2 $NaClO_4$	30	EDTA	(MX)L	3.28	78MS
Co^{2+}	Gl.	0.15 KNO_3	25	Iminodiacetic acid	MLX	10.36	87CJ
Cu^{2+}	Gl.	3.0 $NaClO_4$	25	L-Histidine	MLX	18.597	75BW
					MLXH	23.326	
				L-Threonine	MLX	16.471	
	Gl.	0.2 KCl	25	Glycine	MLX	14.91	75GN
				L-Serine	MLX	14.62	
	Gl.	0.2 KCl	25	Glycyl-glycine	$MLXH_{-1}$	4.92	77NG
				Glycyl-DL-α-alanine	$MLXH_{-1}$	4.93	
				DL-α-Alanyl-DL-α-alanine	$MLXH_{-1}$	4.45	
	Gl. (D-)	~0 (50% ethanol)	25	Acetoacetic ester	MLX	15.41	79FM
	Gl. (D-)	0.1 KNO_3	25	L-Histidine	MLX	17.03	79YS
					MLX	17.04	
	Gl.	0.1 $NaClO_4$	30	Glycyl-sarcosine	MLX	19.02	80AS
	Gl.	0.1 KNO_3 (20% dioxane)	25	L-Histidine	MLX	17.53	80YT
				D-Histidine	MLX	17.54	
	Gl.	0.1 $NaClO_4$	30	Glycyl-L-phenylalanine	$MLXH_{-1}$	5.29	82S
	Gl.	0.1 $NaClO_4$	30	Glycyl-DL-serine	$MLXH_{-1}$	4.73	83S
	Gl.	0.1 $NaClO_4$	30	Alanyl-L-phenylalanine	$MLXH_{-1}$	4.28	84S
	Gl.	0.1 $NaClO_4$	30	Glycyl-L-asparagine	$MLXH_{-1}$	10.85	86AJ
	Gl.	0.15 $NaClO_4$	37	L-Histidine	MLX	16.756	86BH
					MLXH	20.057	
					$MLXH_{-1}$	5.702	
	Gl.	0.1 $NaClO_4$	25	DL-α-Alanyl-DL-methionine	(ML)X (?)	5.58	88JA
				DL-Alanyl-DL-norvaline	(ML)X (?)	5.77	
La^{3+}	Gl.	0.2 $NaClO_4$	30	EDTA	(MX)L	3.25	78MS
Nd^{3+}	Gl.	0.2 $NaClO_4$	30	EDTA	(MX)L	3.35	78MS

cont'd

Table 7-6. Constants for Mixed-ligand Complexes Involving L-Asparagine (continued)

Metal ion	Method	Medium (mol dm^{-3})	Temp. (°C)	Extra ligand (X)	Complex	log β	Ref.
Ni^{2+}	Gl.	3.0 $NaClO_4$	25	Chloride	MLX ML_2X $MLXH_{-1}$	6.1 11.7 11.64	74GW
Pd^{2+}	Gl.	3.0 $NaClO_4$	25	Chloride	MLXH $MLXH_{-1}$	18.29 17.0	74GW
	Gl.	0.1 KNO_3	25	Ethylenediamine	(MX)L (MLX)H	10.46 6.46	77La
Pr^{3+}	Gl.	0.2 $NaClO_4$	30	EDTA	(MX)L	3.30	78MS
Sc^{3+}	Gl.	0.2 $NaClO_4$	30	EDTA	(MX)L	3.38	78MS
Tb^{3+}	Sp.	-	-	EDTA	(MX)L	3.09	85SB
Y^{3+}	Gl.	0.2 $NaClO_4$	30	EDTA	(MX)L	3.35	78MS

(Gl. = glass electrode potentiometry [as exclusive or main method]; Pol. = polarography; Sp. = spectrophotometry)

Table 7-7. Overall Thermodynamic Quantities for L-Asparagine Metal Complex Equilibria

Metal ion	Method	Medium (mol dm^{-3})	Temp. (°C)	Complex	ΔH° (kJ mol^{-1})	ΔS° (J K^{-1} mol^{-1})	Ref.
Cd^{2+}	Pol.	0.1 KNO_3	35	ML_2	-61.7	-87.1	86SSa
Ce^{3+}	Pot.	0.1 KNO_3	35	ML_2	55.7	322.3	86SS
Co^{2+}	Cal.	3.0 $NaClO_4$	25	ML	-11.95	53.8	74BW
				ML_2	-26.71	83.3	
				ML_3	-36.40	104.8	
Cu^{2+}	Cal. (DL-)	0.1 KNO_3	25	ML_2	-47.50	117	70BP, 71BP
				ML_2	-47.16	118	
	Cal.	3.0 $NaClO_4$	25	ML	-27.5	73.9	74BW
				ML_2	-61.5	97.7	
	Cal.	0.2 KCl	25	ML	-26.3	60.6	75GN
				ML_2	-53.9	92.4	
Dy^{3+}	Pot.	0.1 KNO_3	35	ML_2	65.4	377.6	86SS
Gd^{3+}	Pot.	0.1 KNO_3	35	ML_2	58.2	349.7	86SS
La^{3+}	Pot.	0.1 KNO_3	35	ML_2	45.7	288.0	86SS
Nd^{3+}	Pot.	0.1 KNO_3	35	ML_2	56.5	336.2	86SS
Mn^{2+}	Cal.	3.0 $NaClO_4$	25	ML	-7.26	35.0	74BW
				ML_2	-14.23	52.2	
Ni^{2+}	Cal.	3.0 $NaClO_4$	25	ML	-17.11	60.4	74BW
				ML_2	-43.45	67.9	
				ML_3	-63.50	65.5	
Pb^{2+}	Pol.	0.1 KNO_3	35	ML_2	-60.8	-81.0	86SSa
Pr^{3+}	Pot.	0.1 KNO_3	35	ML_2	50.1	310.8	86SS
Sm^{3+}	Pot.	0.1 KNO_3	35	ML_2	54.6	326.2	86SS
Tb^{3+}	Pot.	0.1 KNO_3	35	ML_2	56.2	347.2	86SS
Y^{3+}	Pot.	0.1 KNO_3	35	ML_2	71.9	405.8	86SS
Zn^{2+}	Cal.	3.0 $NaClO_4$	25	ML	-10.44	62.1	74BW
				ML_2	-23.17	102.7	
				ML_3	-27.55	143.0	

(Pol. = polarography; Pot. = potentiometry; Cal. = calorimetry)

Table 7-8. Thermodynamic Quantities for Mixed-ligand Complexes Involving L-Asparagine

Metal ion	Method	Medium (mol dm^{-3})	Temp. (°C)	Extra ligand (X)	Complex	ΔH° (kJ mol^{-1})	ΔS° (J K^{-1} mol^{-1})	Ref.
Cu^{2+}	Cal.	3.0 $NaClO_4$	25	L-Histidine	MLX	-67.5	129.7	75BW
					MLXH	-88.2	150.7	
				L-Threonine	MLX	-50.0	147.7	

(Cal. = calorimetry)

8. GLUTAMINE - $H_2NCOCH_2CH_2CH[NH_2]CO_2H$ (2-amino-4-carbamoylbutanoic acid, LH)

Formally, glutamine contains three electron-donating centres. However, its amide group, like that of asparagine, dissociates at a pH near the limit of the ionic product of water and the dissociation cannot be detected in aqueous solution (75GN). Thus, the only measurable effect of adding a $-CH_2$ group to the asparagine skeleton in respect of the proton interactions of these two amino acids is the increased stability of the protonated forms of the glycine-like donors of glutamine. This effect, almost totally entropic in nature, has been attributed to the larger perturbation brought about by the proton approach in the solvation shell of the more hydrophobic glutamine molecule (74BW).

For metal complexation, attempts have been made to characterise a possible participation of the amide group in the coordination of several metal ions (79M). However, given the unfavourable size of the chelate ring potentially involved, glutamine displays only a very weak tridentate capability with cobalt(II) and nickel(II) (79M) and exclusively behaves as a bidentate ligand with copper(II) (75GN). This is in line with the fact that the formation of copper(II)-glutamine complexes is not accompanied by any stereoselective effect (65RW).

8-1. Protonation constants of glutamine

Glutamine protonation constants available in the literature are collected in Table 8-1. Although still more limited in number than those for asparagine, these data provide an acceptable basis for the present evaluation. Some of them are proposed as tentative, and recommended averages have been calculated for physiological conditions (Table 8-2).

Contrary to what was observed with asparagine, stoichiometric protonation constants determined in refs. 65RW and 73TS (25 °C and I=0.1 mol dm^{-3}) do not coincide. Nevertheless, one of these sets has been selected on the basis of the following considerations. For asparagine, the average values calculated from the two references above are very close to the constants determined by Gergely et al. (75GN) at 25 °C in 0.2 mol dm^{-3} KCl. This was taken as a criterion of reliability (see previous chapter) since constants determined in a 0.1 mol dm^{-3} ionic background are theoretically expected to be equal or slightly higher than those measured at I=0.2 mol dm^{-3}. In the present case, only the constants obtained in ref. 65RW are close to the values determined in 75GN. They are thus proposed as tentative together with those from 75GN.

By reference to the discrimination made between asparagine constants reported in 72GW and 81M, values relative to glutamine determined in 73W at 25 °C in 3.0 mol dm^{-3} ionic strength are taken as tentative while the only constant available in 81M was rejected.

The stoichiometric constants determined under physiological conditions (82KB, 85CF) are quite reproducible, and corresponding averages have been recommended. Moreover, if we apply the usual 0.12 correction (74MS, 82MS, 89SM) to the mixed constant determined by Hallman et al. (71HP), the resulting log K_1 (8.71) is quite close to the above average (8.69). In contrast, the corrected log K_2 (2.03) is comparatively much lower than its recommended value (2.19).

8-2. Thermodynamic quantities for the protonation of glutamine

The three sets of data available for glutamine protonation (Table 8-3) have been obtained from direct calorimetric measurements. They can thus be taken as reliable.

8-3. Metal complex formation constants

Formation constants for metal complexes of glutamine are collected in Table 8-4. Many metal ions have been investigated, but the number of independent determinations for each of these is rather limited and rarely offers a sound basis of evaluation.

For cadmium(II) complexes, for example, only two studies refer to comparable experimental conditions (74WW, 81M) and their results differ to a considerable extent. As already noticed for asparagine, it seems unlikely that such a discrepancy can originate in the different nature of the background electrolyte, and in accordance with previous comparisons on data from the same authors, the constants determined in 74WW have been chosen as tentative. Still, this selection has been limited to the ML and ML_2 species since the group of authors involved did not confirm the existence of ML_3 in a subsequent study where MLH_{-1} was characterised instead (85CF). Only the ML and ML_2 constants

determined under physiological conditions in the latter investigation have thus been accepted as tentative (85CF).

By reference to considerations developed for asparagine, constants relative to cobalt(II) complexes determined in 65RW and 73W can be considered as reliable and have then been proposed as tentative.

For copper(II), four sets of constants have been determined under similar experimental conditions (65RW, 75GN, 73KS-77S, 84KW). The lower values found in 75GN with respect to 65RW are certainly attributable to the competitive influence of the chloride ion rather than to the higher ionic strength, and both sets can a priori be accepted as tentative along with log β_{ML} from 84KW. As for the third set however, the constants, especially β_{ML_2}, seem too high and have not been selected. This is all the more surprising as their homologues for threonine and, to a lesser extent, serine, conformed quite well to values determined at 0.1 and 0.2 mol dm^{-3} ionic strengths (see preceding chapters).

The evaluation of the constants of copper(II) complexes corresponding to physiological conditions is more straightforward since the values obtained by two (82KB, 85CF) of the three groups involved are almost identical. Average values have thus been recommended (Table 8-5). Exceptionally, values from 71HP, obviously too low, should be rejected. Precision in the determination of these constants is especially important since glutamine is the second most important l.m.m. ligand of copper(II) (after histidine) in blood plasma (86BH).

Three studies relative to nickel(II)-glutamine complexes have been performed under different experimental conditions by groups of authors regularly selected in the above evaluations (65RW, 73W, 85CF). Corresponding constants have thus been accepted as tentative.

Also by reference to above evaluations, formation constants of zinc(II) complexes determined by Williams at 25 °C in 3.0 mol dm^{-3} $NaClO_4$ (73W) have been accepted as tentative. Data from three independent groups are available for physiological conditions (71HP, 80KB, 85CF), but the agreement is relatively poor. Accordingly, the average values calculated from these have only been proposed as tentative.

Determinations relative to mixed-ligand complexes are limited. About half of these refer to physiological conditions, which appears logical considering the important role of glutamine as a ligand in vivo. This is especially true for copper(II), whose neutral mixed-ligand complex with histidine and glutamine has recently been recognized as the main species of its l.m.m. fraction in blood plasma (86BH). No comparative study of the corresponding data is allowed, but given the frequent selection of the authors involved in preceding evaluations, all constants from 86BH can be considered as reliable.

For the copper(II)-histidine-glutamine species evoked above, its two constants determined at 25 °C (73KS-77S, 79YS) are obviously too different for the similar ionic strengths used. The value reported by Yamauchi et al. (79YS) has been calculated with protonation and binary complex constants taken from the literature, which is far from being recommended (see introduction). Moreover, the copper(II)-histidine-threonine constant determined in that study (79YS) has already been discarded as being far too low compared to others obtained under similar conditions (see Chapter 6). By contrast, the value of the copper(II)-histidine-threonine constant reported in ref. 77S has been found to fall within the limits of error of the average relative to the 0.1 mol dm^{-3} ionic strength at 25 °C (see Chapter 6), which would tend to support the present copper(II)-histidine-glutamine constant by the same author. However, since doubt has been cast on the constants of the parent copper(II)-glutamine system (see above), it is impossible to conclude in favour of either of these two works.

8-4. Thermodynamic quantities for metal complex formation with glutamine

The few thermodynamic quantities available in the literature concerning copper(II)- and nickel(II)-glutamine complexes (Table 8-7) have been obtained from direct calorimetric measurements and by authors frequently selected in the above evaluations. Corresponding values can thus logically be considered as reliable. By contrast, those relative to cerium deduced from the van't Hoff equation (86K) have been rejected as too imprecise.

Table 8-1. Protonation Constants of Glutamine

Type of constants	Medium (mol dm^{-3})	Temp. (°C)	log K_1	log K_2	Ref.
Thermo	~0.01	15	9.34	-	53P
Stoichio	0.1 KNO_3	25	9.01	2.17	65RW
Mixed	0.15 KNO_3	37	8.83	2.15	71HP
-	-	25	9.13	2.17	72JB
Stoichio(?)	0.1 $NaClO_4$	25	8.91	2.21	73TS
Stoichio	3.0 $NaClO_4$	25	9.640	2.721	73W
Mixed(?)	0.1 KNO_3	35	9.10	2.25	74SC
		45	8.80	2.15	
	0.2 KNO_3	35	9.08	2.23	
	0.3 KNO_3	35	9.06	2.20	
Stoichio	0.2 KCl	25	9.00	2.15	75GN
Thermo	~0	25			77CL
	10% methanol	25	-	2.47	
	20% methanol	25	-	2.55	
	30% methanol	25	-	2.62	
	40% methanol	25	-	2.84	
	50% methanol	25	-	3.14	
	60% methanol	25	-	3.40	
	70% methanol	25	-	3.52	
	80% methanol	25	9.20	3.68	
	10% ethanol	25	-	2.50	
	20% ethanol	25	-	2.60	
	30% ethanol	25	-	2.70	
	40% ethanol	25	-	2.90	
	50% ethanol	25	-	3.15	
	60% ethanol	25	-	3.35	
	70% ethanol	25	-	3.55	
	80% ethanol	25	9.22	3.85	
Mixed	0.5 KNO_3	25	9.09	2.29	77La
Stoichio(?)	3.0 $LiClO_4$	25	9.19	-	77M, 81M
Stoichio	0.2 $NaClO_4$	30	8.515	2.210	77MS, 78MS
Stoichio	0.15 NaCl	25	8.970	2.390	73KS, 77S
Stoichio	0.1 KNO_3 20% dioxane	25	9.14	2.45	80YT
Thermo	~0	25	9.08	2.16	82DD
	8.0% propan-2-ol	25	9.08	2.40	
	16.3% propan-2-ol	25	9.08	2.51	
	25.1% propan-2-ol	25	9.08	2.64	
	34.3% propan-2-ol	25	9.11	2.78	
	43.9% propan-2-ol	25	9.18	2.91	
	54.0% propan-2-ol	25	9.23	3.09	
	64.6% propan-2-ol	25	9.26	3.56	
	75.8% propan-2-ol	25	9.27	3.70	
Stoichio	0.15 $NaClO_4$	37	8.680	2.184	82KB
Stoichio	0.15 NaCl	37	8.697	2.202	85CF
Mixed(?)	0.7 $NaClO_4$	25	9.031	-	85SC
Mixed(?)	0.1	35	9.10	2.15	85SYa

cont'd

Table 8-1. Protonation Constants of Glutamine (continued)

Type of constants	Medium (mol dm^{-3})	Temp. (°C)	log K_1	log K_2	Ref.
Thermo	~0	25	9.08	2.16	86PD
	8.0% t-BuOH	25	9.11	2.28	
	16.4% t-BuOH	25	9.10	2.40	
	25.0% t-BuOH	25	9.13	2.44	
	34.2% t-BuOH	25	9.16	2.52	
	43.8% t-BuOH	25	9.21	2.56	
	54.0% t-BuOH	25	9.28	2.65	
	64.5% t-BuOH	25	9.40	2.78	
	75.8% t-BuOH	25	9.48	3.00	
Mixed(?)	0.2 KCl	25	8.94	2.33	88KD
Mixed(?)	1.0 KNO_3	25	9.13	2.17	89KN, 89NK

Table 8-2. Recommended (R) and Tentative (T) Values for Protonation Constants of Glutamine

Type of constants	Medium (mol dm^{-3})	Temp. (°C)	log K_1	log K_2	Ref.
Stoichio (T)	0.1 KNO_3	25	9.01	2.17	65RW
Stoichio (T)	0.2 KCl	25	9.00	2.15	75GN
Stoichio (T)	3.0 $NaClO_4$	25	9.64	2.72	73W
Stoichio (R)	0.15	37	8.69 (±0.01)	2.19 (±0.01)	82KB, 85CF

Table 8-3. Thermodynamic Quantities for Glutamine Protonation Equilibria

Method	Medium (mol dm^{-3})	Temp. (°C)	$\Delta H°_1$ (kJ mol^{-1})	$\Delta H°_2$	$\Delta S°_1$ (J K^{-1} mol^{-1})	$\Delta S°_2$	Ref.
Cal.	3.0 $NaClO_4$	25	-50.86	-4.42	14.0	37.4	74BW
Cal.	0.2 KCl	25	-41.6	-3.43	31.8	29.6	75GN
Cal.	~0	25	-40.8	-2.80	38.1	32.1	89RF, 89R

(Cal. = calorimetry)

Table 8-4. Overall Formation Constants for L-Glutamine Metal Complexes

Metal ion	Method	Medium (mol dm^{-3})	Temp. (°C)	Complex	log β	Ref.
Al^{3+}	Gl.	0.1 $NaClO_4$	25	ML	~6.59	73TSb
				ML_2	10.25	
Be^{2+}	Gl.	0.015	15	ML_2	12.4	53P
	Gl.	0.1 $NaClO_4$	25	ML	~5.80	73TSb
				ML_2	10.36	
Bi^{3+}	Gl.	0.1 $NaClO_4$	25	ML	9.81	74TS
				ML_2	17.25	
Ca^{2+}	Ion exch.	0.16 (pH 7.2)	25	ML	0.18	54S
Cd^{2+}	Gl.	0.015	15	ML_2	7.4	53P
	Gl.	3.0 $NaClO_4$	25	ML	4.099	74WW
				ML_2	7.664	
				ML_3	9.999	
	Gl.	3.0 $LiClO_4$	25	ML	3.83	81M, 82MH
				ML_2	6.95	
	Gl.	0.15 NaCl	37	ML	3.168	85CF
				ML_2	5.694	
				MLH_{-1}	-6.58	
	Gl.	0.7 $NaClO_4$	25	ML	3.62	85SC
				ML_2	6.66	
	Pol.	1.0 KNO_3	25	ML	4.00	89KN, 89NK
				ML_2	7.04	
				ML_3	8.91	
Ce^{3+}	Gl.	0.1 $NaClO_4$	25	ML	~3.80	73TSa
				ML_2	7.15	
	Gl.	0.1 KNO_3	35	ML	4.77	74SC
				ML_2	8.80	
			45	ML	4.68	
				ML_2	8.68	
		0.2 KNO_3	35	ML	4.55	
				ML_2	8.40	
		0.3 KNO_3	35	ML	4.38	
				ML_2	8.11	
	Gl.	0.2 $NaClO_4$	30	ML	3.945	77MS, 78MS
	Pol.	1.0 KCl	25	ML	3.72	86K
			35	ML	3.15	
			45	ML	2.65	
Co^{2+}	Gl.	0.1 KNO_3	25	ML	4.03	65RW
				ML_2	7.29	
	(DL-)			ML	4.05	
				ML_2	7.35	
	Gl.	3.0 $NaClO_4$	25	ML	4.518	73W
				ML_2	8.361	
				ML_3	11.405	
Cu^{2+}	Gl.	0.1 KNO_3	25	ML	7.75	65RW
				ML_2	14.25	
	(DL-)			ML	7.74	
				ML_2	14.20	

cont'd

Table 8-4. Overall Formation Constants for L-Glutamine Metal Complexes (continued)

Metal ion	Method	Medium (mol dm^{-3})	Temp. (°C)	Complex	log β	Ref.
	Gl.	0.15 KNO_3	37	ML	7.24	71HP
				ML_2	13.40	
	Gl.	0.15 NaCl	25	ML	7.765	73KS, 77S
				ML_2	14.613	
	Gl.	3.0 $NaClO_4$	25	ML	8.950	73W
				ML_2	16.230	
	Gl.	0.2 KCl	25	ML	7.62	75GN
				ML_2	14.00	
	Gl.	0.1 KNO_3 20% dioxane	25	ML	8.02	80YT
				ML_2	14.805	
	Gl.	0.15 $NaClO_4$	37	ML	7.475	82KB
				ML_2	13.586	
	Gl.	0.2 $NaClO_4$ (pH 6)	25	ML	7.62	84KW
				ML_2	13.77	
	Gl.	0.15 NaCl	37	ML	7.474	85CF
				ML_2	13.600	
				MLH_{-1}	-0.07	
Fe^{2+}	Gl.	3.0 $NaClO_4$	25	ML	4.432	73W
				ML_2	7.258	
				ML_3	10.401	
Hg^{2+}	Hg el.	0.1 $NaNO_3$	25	ML	11.5	73VB
				ML_2	18.7	
In^{3+}	Gl.	0.1 $NaClO_4$	25	ML	~7.45	73TSb
				ML_2	14.55	
	Pol.	0.1 $NaClO_4$	30	ML	6.65	80JK, 83JK
				ML_2	14.39	
La^{3+}	Gl.	0.1 $NaClO_4$	25	ML	~3.40	73TSa
				ML_2	6.45	
	Gl.	0.1 KNO_3	35	ML	3.48	74SC
			45	ML	4.10	
		0.2 KNO_3	35	ML	4.20	
		0.3 KNO_3	35	ML	3.88	
	Gl.	0.2 $NaClO_4$	30	ML	3.710	77MS, 78MS
Mn^{2+}	Gl.	3.0 $NaClO_4$	25	ML	2.863	73W
				ML_2	4.62	
Mo^{VI}	Gl.	0.1 $NaClO_4$	25	ML	7.90	73TS
				ML_2	14.83	
				ML_3	18.18	
Nd^{3+}	Gl.	0.1 $NaClO_4$	25	ML	~4.10	73TSa
				ML_2	7.78	
	Gl.	0.2 $NaClO_4$	30	ML	4.530	77MS, 78MS
Ni^{2+}	Gl.	0.1 KNO_3	25	ML	5.14	65RW
				ML_2	9.38	
	(DL-)			ML	5.17	
				ML_2	9.45	

cont'd

Table 8-4. Overall Formation Constants for L-Glutamine Metal Complexes (continued)

Metal ion	Method	Medium (mol dm^{-3})	Temp. (°C)	Complex	log β	Ref.
	Gl.	3.0 $NaClO_4$	25	ML	5.561	73W
				ML_2	10.282	
				ML_3	12.816	
	Gl.	0.15 NaCl	37	ML	4.979	85CF
				ML_2	9.015	
				ML_3	11.62	
				ML_2H_{-1}	-1.91	
Pb^{2+}	Pol.	0.6 $NaNO_3$	25	$ML_2(OH)$	10.16	69LC
	Gl.	3.0 $NaClO_4$	25	ML	4.697	73CT
				ML_2	8.364	
				ML_3	10.123	
Pd^{2+}	Gl.	0.1 $NaClO_4$	25	ML	9.10	74TS
				ML_2	17.45	
Pr^{3+}	Gl.	0.1 $NaClO_4$	25	ML	~4.00	73TSa
				ML_2	7.55	
	Gl.	0.2 $NaClO_4$	30	ML	4.275	77MS, 78MS
Pt^{4+}	Gl.	0.1 $NaClO_4$	25	ML	7.31	74TS
				ML_2	10.46	
Sc^{3+}	Gl.	0.2 $NaClO_4$	30	ML	7.405	77MS, 78MS
UO_2^{2+}	Gl.	0.1 KNO_3	35	ML	7.05	74SC
				ML_2	13.90	
			45	ML	7.00	
				ML_2	13.73	
		0.2 KNO_3	35	ML	6.99	
				ML_2	13.78	
		0.3 KNO_3	35	ML	6.95	
				ML_2	13.70	
V^{3+}	Gl.	0.2 KCl	25	ML	8.20	88KD
				ML_2	15.82	
VO^{2+}	Gl.	0.1 $NaClO_4$	25	ML	~7.40	73TS
				ML_2	14.45	
				ML_3	18.52	
W^{VI}	Gl.	0.1 $NaClO_4$	25	ML	5.76	73TS
				ML_2	10.85	
				ML_3	14.05	
Y^{3+}	Gl.	0.1 $NaClO_4$	25	ML	~4.20	73TSa
				ML_2	8.00	
	Gl.	0.1 KNO_3	35	ML	4.65	74SC
			45	ML	4.25	
		0.2 KNO_3	35	ML	4.51	
		0.3 KNO_3	35	ML	4.36	
	Gl.	0.2 $NaClO_4$	30	ML	4.720	77MS, 78MS

cont'd

Table 8-4. Overall Formation Constants for L-Glutamine Metal Complexes (continued)

Metal ion	Method	Medium (mol dm^{-3})	Temp. (°C)	Complex	log β	Ref.
Zn^{2+}	Gl.	0.015	15	ML_2	8.4	53P
	Gl.	0.15 KNO_3	37	ML	4.27	71HP
				ML_2	7.94	
	Gl.	0.15 NaCl	37?	ML	4.39	72GH
				ML_2	8.14	
	Gl.	3.0 $NaClO_4$	25	ML	4.826	73W
				ML_2	9.165	
				ML_3	11.843	
	Gl.	0.15 $NaClO_4$	37	ML	4.174	80KB
				ML_2	7.664	
				ML_2H_{-1}	-2.137	
	Gl.	0.15 NaCl	37	ML	4.215	85CF
				ML_2	7.808	
				ML_2H_{-1}	-1.35	

(Gl. = glass electrode potentiometry [as exclusive or main method]; Pol. = polarography)

Table 8-5. Recommended (R) and Tentative (T) Overall Formation Constants for L-Glutamine Metal Complexes

Metal ion		Medium (mol dm^{-3})	Temp. (°C)	Complex	log β	Ref.
Cd^{2+}	(T)	3.0 $NaClO_4$	25	ML	4.10	74WW
				ML_2	7.66	
		0.15 NaCl	37	ML	3.17	85CF
				ML_2	5.69	
Co^{2+}	(T)	0.1 KNO_3	25	ML	4.03	65RW
				ML_2	7.29	
	(T)	3.0 $NaClO_4$	25	ML	4.52	73W
				ML_2	8.36	
				ML_3	11.40	
Cu^{2+}	(T)	0.1 KNO_3	25	ML	7.75	65RW
				ML_2	14.25	
	(T)	0.2	25	ML	7.62	75GN, 84KW
	(T)	0.2 KCl	25	ML_2	14.0	75GN
	(R)	0.15	37	ML	7.47 (±0.01)	82KB, 85CF
				ML_2	13.59 (±0.01)	
Ni^{2+}	(T)	0.1 KNO_3	25	ML	5.14	65RW
				ML_2	9.38	
	(T)	3.0 $NaClO_4$	25	ML	5.56	73W
				ML_2	10.28	
				ML_3	12.82	
	(T)	0.15 NaCl	37	ML	4.98	85CF
				ML_2	9.02	
				ML_3	11.62	
				ML_2H_{-1}	-1.91	
Zn^{2+}	(T)	3.0 $NaClO_4$	25	ML	4.83	73W
				ML_2	9.17	
				ML_3	11.84	
	(T)	0.15	37	ML	4.22 (±0.05)	71HP, 80KB, 85CF
				ML_2	7.80 (±0.15)	

Table 8-6. Constants for Mixed-ligand Complexes Involving L-Glutamine

Metal ion	Method	Medium (mol dm^{-3})	Temp. (°C)	Extra ligand (X)	Complex	log β	Ref.
Cd^{2+}	Pol.	1.0 KNO_3	25	Formate	MLX	5.79	89KN
					MLX_2	7.71	
					ML_2X	8.07	
	Pol.	1.0 KNO_3	25	Acetate	MLX	5.92	89NK
					MLX_2	7.90	
					ML_2X	8.26	
Ce^{3+}	Gl.	0.2 $NaClO_4$	30	EDTA	(MX)L	3.32	78MS
Cu^{2+}	Gl.	0.2 KCl	25	Glycyl-glycine	MLXH-1	4.65	77NG
				Glycyl-DL-α-alanine	MLXH-1	4.69	
				DL-α-Alanyl-DL-α-alanine	MLXH-1	4.32	
	Gl.	0.15 NaCl	25	L-Histidine	MLX	17.624	73KS,
					MLXH	21.654	77S
	Gl.	0.1 KNO_3	25	L-Histidine	MLX	17.06	79YS
	Gl.	0.1 KNO_3 (20% dioxane)	25	L-Histidine	MLX	17.42	80YT
				D-Histidine	MLX	17.45	
	Gl.	0.15 $NaClO_4$	37	Histamine	MLX	15.971	82KB
					MLXH	20.112	
	Gl.	0.15 $NaClO_4$	37	L-Histidine	MLX	16.703	86BH
					MLXH	20.108	
					$MLXH_{-1}$	5.844	
In^{3+}	Pol.	0.1 $NaClO_4$	30	L-Histidine	MLX	16.37	83JK
La^{3+}	Gl.	0.2 $NaClO_4$	30	EDTA	(MX)L	3.27	78MS
Nd^{3+}	Gl.	0.2 $NaClO_4$	30	EDTA	(MX)L	3.36	78MS
Pd^{2+}	Gl.	0.1 KNO_3	25	Ethylenediamine	(MX)L	10.76	77La
					(MLX)H	9.03	
Pr^{3+}	Gl.	0.2 $NaClO_4$	30	EDTA	(MX)L	3.33	78MS
Sc^{3+}	Gl.	0.2 $NaClO_4$	30	EDTA	(MX)L	3.43	78MS
Tb^{3+}	Sp.	-	-	EDTA	(MX)L	1.62	85SB
Y^{3+}	Gl.	0.2 $NaClO_4$	30	EDTA	(MX)L	3.39	78MS
Zn^{2+}	Gl.	0.15 $NaClO_4$	37	Histamine	MLX	9.102	80KB
	Gl.	0.15 $NaClO_4$	37	Citrate	M_2LXH_{-2}	-2.815	82BB
	Gl.	0.15 NaCl	37	L-Cysteine	MLXH	19.66	85CF

(Gl. = glass electrode potentiometry [as exclusive or main method]; Pol. = polarography; Sp. = spectrophotometry)

Table 8-7. Overall Thermodynamic Quantities for L-Glutamine Metal Complex Equilibria

Metal ion	Method	Medium (mol dm^{-3})	Temp. (°C)	Complex	ΔH° (kJ mol^{-1})	ΔS° (J K^{-1} mol^{-1})	Ref.
Cu^{2+}	Cal.	3.0 $NaClO_4$	25	ML	-16.5	118.0	74BW
				ML_2	-42.5	174.3	
	Cal.	0.2 KCl	25	ML	-23.6	66.9	75GN
				ML_2	-49.1	103.3	
Ni^{2+}	Cal.	3.0 $NaClO_4$	25	ML	-13.28	61.9	74BW
				ML_2	-36.09	75.9	
				ML_3	-54.75	80.9	

(Cal. = calorimetry)

9. REFERENCES

26S K. Sano, *Biochem. Z.*, *168*, 14 (1926).

27CK R.K. Cannan and C.J.G. Knight, *Biochem. J.*, *21*, 1384 (1927).

37BE H. Borsook, E.L. Ellis and H.M. Huffman, *J. Biol. Chem.*, *117*, 281 (1937).

39GK J. D. Greenstein, F.W. Klemperer and J. Wyman, *J. Biol. Chem.*, *129*, 681 (1939).

42SG P.K. Smith, A.T. Gorham and E.R.B. Smith, *J. Biol. Chem.*, *144*, 737 (1942).

44RS L.K. Ryklan and C.L.A. Schmidt, *Arch. Biochem.*, *5*, 89 (1944).

50A A. Albert, *Biochem. J.*, *47*, 531 (1950).

50DW C.W. Davies and G.M. Waind, *J. Chem. Soc.*, 301 (1950).

51SK W. Stricks and I.M. Kolthoff, *J. Am. Chem. Soc.*, *73*, 4569 (1951).

51SKa W. Stricks and I.M. Kolthoff, *J. Am. Chem. Soc.*, *73*, 1723 (1951).

52A A. Albert, *Biochem. J.*, *50*, 690 (1952).

52K H. Kroll, *J. Am. Chem. Soc.*, *74*, 2034 (1952).

52LD N.C. Li and E. Doody, *J. Am. Chem. Soc.*, *74*, 4184 (1952).

53P D.J. Perkins, *Biochem. J.*, *55*, 649 (1953).

53SK W. Stricks and I.M. Kolthoff, *J. Am. Chem. Soc.*, *75*, 5673 (1953).

53TS C. Tanford and W.S. Shore, *J. Am. Chem. Soc.*, *75*, 816 (1953).

54LD N.C. Li and E. Doody, *J. Am. Chem. Soc.*, *76*, 221 (1954).

54S J. Schubert, *J. Am. Chem. Soc.*, *76*, 3442 (1954).

55BB R. Benesch and R.E Benesh, *J. Am. Chem. Soc.*, *77*, 3389 (1955).

55GN M.A. Grafius and J.B. Neilands, *J. Am. Chem. Soc.*, *77*, 3389 (1955).

55LM N.C. Li and R.A. Manning, *J. Am. Chem. Soc.*, *77*, 5225 (1955).

55TK N. Tanaka, I.M. Kolthoff and W. Striks, *J. Am. Chem. Soc.*, *77*, 1996 (1955).

56G G. Gorin, *J. Am. Chem. Soc.*, *78*, 767 (1956).

56PC S. Pelletier, J. Curchod and M. Quintin, *C. R. Hebd. Séances Acad. Sci.*, *243*, 1868 (1956).

56WM J.M. White, R.A. Manning and N.C. Li, *J. Am. Chem. Soc.*, *78*, 2367 (1956).

57LW N.C. Li, W.M. Westfall, A. Lindenbaum, J.M. White and J. Schubert, *J. Am. Chem. Soc.*, *79*, 5864 (1957).

57P S. Pelletier, *C. R. Hebd. Séances Acad. Sci.*, *245*, 160 (1957).

57PQ S. Pelletier and M. Quintin, *C. R. Hebd. Séances Acad. Sci.*, *244*, 894 (1957).

58LD N.C. Li, B.E. Doody and J.M. White, *J. Am. Chem. Soc.*, *80*, 5901 (1958).

58P D.D. Perrin, *J. Chem. Soc.*, 3125 (1958).

59B W.E. Bennett, *J. Am. Chem. Soc.*, *81*, 246 (1959).

59FO G. Fölsch and R. Österberg, *J. Biol. Chem.*, *234*, 2298 (1959).

59MH Y. Mashiko, N. Hosoya and M. Akimoto, *J. Electrochem. Soc. Japan*, *27*, E-33 (1959).

59P D.D. Perrin, *J. Chem. Soc.*, 290 (1959).

60P S. Pelletier, Diss., University of Paris (1960).

60Pa S. Pelletier, *J. Chim. Phys.*, *57*, 301 (1960).

60Pb S. Pelletier, *J. Chim. Phys.*, *57*, 306 (1960).

60Pc S. Pelletier, *J. Chim. Phys.*, *57*, 311 (1960).

61KP E.C. Knoblock and W.C. Purdy, *J. Electroanal. Chem.*, *2*, 493 (1961).

61RR F.J.C. Rossotti and H. Rossotti, 'The Determination of Stability Constants', Mc Graw-Hill, New York (1961).

61S R.B. Simpson, *J. Am. Chem. Soc.*, *83*, 4711 (1961).

62EE E.L. Elson and J.T. Edsall, *Biochem*, *1*, 1 (1962).

62RS G.N. Rao and R.S. Subrahmanya, *Current Sci.*, *31*, 55 (1962).

63HP C.J. Hawkins and D.D. Perrin, *Inorg. Chem.*, *2*, 843 (1963).

63KM A. Aziz Khan and W.U. Malik, *J. Indian Chem. Soc.*, *40*, 565 (1963).

63SC J.T. Spence and H.H.Y. Chang, *Inorg. Chem.*, *2*, 319 (1963).

64FW M. Friedman and J.S. Wall, *J. Am. Chem. Soc.*, *86*, 3735 (1964).

64IC R.M. Izatt, J.J. Christensen and V. Kothari, *Inorg. Chem.*, *3*, 1565 (1964).

64J V. Jokl, *J. Chromatogr.*, *14*, 71 (1964).

64KW H.-W. Krause, F.-W. Wilcke, H. Mix and W. Langenbeck, *Z. Phys. Chem.*, *225*, 342 (1964).

64LM G.R. Lenz and A.E. Martell, *Biochemistry*, *3*, 745 (1964).

64RS G.N. Rao and R.S. Subrahmanya, *Proc. Indian Acad. Sci.*, *60*, 165 (1964).

64S A.Y. Sychev, *Russ. J. Inorg. Chem.*, *9*, 1270 (1960).

64SM L.G. Sillén and A.E. Martell, 'Stability Constants of Metal-ion Complexes', The Chemical Society, Special Publication N°17, London (1964).

64WI D.P. Wrathall, R.M. Izatt and J.J. Christensen, *J. Am. Chem. Soc.*, *86*, 4779 (1964).

65CM H.L. Conley Jr and R.B. Martin, *J. Phys. Chem.*, *69*, 2923 (1965).

65D D.A. Doornbos, Thesis, University of Rijks, Groningen, Netherlands (1965).

65FC M. Friedman, J.F. Cavins and J.S. Wall, *J. Am. Chem. Soc.*, *87*, 3672 (1965).

65PG V.D. Panasyuk and V.A. Golub, *Russ. J. Inorg. Chem.*, *10*, 482 (1965).

65PP P.A. Pella and W.C. Purdy, *J. Electroanal. Chem.*, *10*, 51 (1965).

65RW J.H. Ritsma, G.A. Wiegers and F. Jellinek, *Recl. Trav. Chim. Pays-Bas*, *84*, 1577 (1965).

66TA V.F. Toropova and Y.M. Azizov, *Russ. J. Inorg. Chem.*, *11*, 288 (1966).

66SP I.H. Suffet and W.C. Purdy, *J. Electroanal. Chem.*, *11*, 302 (1966).

66WS K. Wallenfels and C. Streffer, *Biochem. Z.*, *346*, 119 (1966).

67AM Y.M. Azizov, A.M. Miftakhova and V.F. Toropova, *Russ. J. Inorg. Chem.*, *12*, 345 (1967).

67NS P.Z. Neumann and A. Sass-Kortsak, *J. Clin. Invest.*, *46*, 646 (1967).

67PS D.D. Perrin, I.G. Sayce and V.S. Sharma, *J. Chem. Soc. (A)*, 1755 (1967).

67S V.S. Sharma, *Biochim. Biophys. Acta*, *148*, 37 (1967).

67SS W.F. Stack and H.A. Skinner, *Trans. Faraday Soc.*, *63*, 1136 (1967).

68IC J. Israeli and M. Cecchetti, *Can. J. Chem.*, *46*, 3821 (1968).

68PO A.S. Prasad and D. Oberleas, *J. Lab. Clin. Med.*, *72*, 1006 (1968).

68PS D.D. Perrin and I.G. Sayce, *J. Chem. Soc. (A)*, 53 (1968).

68PSa D.D. Perrin and V.S. Sharma, *J. Chem. Soc. (A)*, 446 (1968).

68RM E.V. Raju and H.B. Mathur, *J. Inorg. Nucl. Chem.*, *30*, 2181 (1968).

68RP E.M. Rogozina, D.K. Popov and T.M. Ponikarova, *Radiokhim.*, *10*, 593 (1968); *Soviet Radiochem.*, *10*, 579 (1968).

68S I.G. Sayce, *Talanta*, *15*, 1397 (1968).

68ZK E.A. Zekharova and V.N. Kumok, *Zh. Obshch. Khim.*, *38*, 1922 (1968); *J. Gen. Chem. USSR*, *38*, 1868 (1968).

69CM E. Coates, C.G. Marsden and B. Rigg, *Trans. Faraday Soc.*, *65*, 863 (1969).

69CMa E. Coates, C.G. Marsden and B. Rigg, *Trans. Faraday Soc.*, *65*, 3032 (1969).

69CP C.W. Childs and D.D. Perrin, *J. Chem. Soc. (A)*, 1039 (1969).

69FM H.C. Freeman and R.-P. Martin, *J. Biol. Chem.*, *244*, 4823 (1969).

69LC T.-T. Lai and M.-C. Chen, *Talanta, 16*, 544 (1969).

69PS D.D. Perrin and V.S. Sharma, *J. Chem. Soc. (A)*, 2060 (1969).

69TS A.C.R. Thornton and H.A. Skinner, *Trans. Faraday Soc., 65*, 2044 (1969).

69VF D. van der Helm and W.A. Franks, *Acta Cryst., B25*, 451 (1969).

69VH D. van der Helm and M.B. Hossain, *Acta Cryst., B25*, 457 (1969).

70B M.T. Beck, 'Chemistry of Complex Equilibria', Van Nostrand Reinhold Co., London (1970).

70BP D.S. Barnes and L.D. Pettit, *Chem. Comm.*, 1000 (1970).

70FM O. Farooq, A.U. Malik and N. Ahmad, *J. Electroanal. Chem., 24*, 233 (1970).

70FMa O. Farooq, A.U. Malik and N. Ahmad, *J. Electroanal. Chem., 26*, 409 (1970).

70FMb O. Farooq, A.U. Malik, N. Ahmad and S.M.F. Rahman, *J. Electroanal. Chem., 24*, 46 (1970).

70GN A. Gergely, I. Nagypal and I. Sovago, *Magy. Kém. Foly., 76*, 550 (1970).

70HM R.W. Hay and P.J. Morris, *J. Chem. Soc. (B)*, 1577 (1970).

70JP T.J. Janjic, L.B. Pfendt and M.B. Celap, *Z. Anorg. Allg. Chem., 373*, 83 (1970).

70LB J.E. Letter Jr and J.E. Bauman Jr, *J. Am. Chem. Soc., 92*, 437 (1970).

70RP E.M. Rogozina and T.M. Ponikarova, *Zh. Obshch. Khim., 40*, 2357 (1970); *J. Gen. Chem. USSR, 40*, 2346 (1970).

70RS A. Raghavan and M. Santappa, *Curr. Sci., 39*, 302 (1970).

70VN D. van der Helm, A.F. Nicholas and C.G. Fisher, *Acta Cryst., B26*, 1172 (1970).

71BP D.S. Barnes and L.D. Pettit, *J. Inorg. Nucl. Chem., 33*, 2177 (1971).

71GN A. Gergely, I. Nagypal and I. Sovago, *Acta Chim. Acad. Sci. Hung., 67*, 241 (1971).

71HP P.S. Hallman, D.D. Perrin and A.E. Watt, *Biochem. J., 121*, 549 (1971).

71KP S.S. Kalinina, Z.N. Prozorovskaya, L.N. Komissarova and V.I. Spitsyn, *Russ. J. Inorg. Chem., 16*, 1357 (1971).

71MB M.A. Marini, R.L. Berger, D.P. Lam and C.J. Martin, *Anal. Biochem., 43*, 188 (1971).

71SM L.G. Sillén and A.E. Martell, 'Stability Constants of Metal-ion Complexes', Supplement N°1, The Chemical Society, Special Publication N°25, London (1971).

71SS B.S. Sekhon, P.P. Singh and S.L. Chopra, *Indian J. Chem., 9*, 485 (1971).

72BL P. Bonvicini, A. Levi, V. Lucchini and G. Scorrano, *J. Chem. Soc., Perkin Trans. II*, 2267 (1972).

72CB G. Carpeni, E. Boitard and R. Pilard, *J. Chim. Phys., 69*, 1445 (1972).

72GH E.L. Giroux and R.I. Henkin, *Biochim. Biophys. Acta, 273*, 64 (1972).

72GM A. Gergely, J. Mojzes and ZS. Kassai-Bazsa, *Magy Kém. Foly, 78*, 76 (1972).

72GMa A. Gergely, J. Mojzes and ZS. Kassai-Bazsa, *J. Inorg. Nucl. Chem., 34*, 1277 (1972).

72GP K. Garbett, G.W. Partridge and R.J.P. Williams, *Bioinorg. Chem., 1*, 309 (1972).

72GS A. Gergely, I. Sovago, I. Nagypal and R. Kiraly, *Inorg. Chim. Acta, 6*, 435 (1972).

72GW R.D. Graham, D.R. Williams and P.A. Yeo, *J. Chem. Soc., Perkin Trans. II*, 1876 (1972).

72IN T.P. I and G.H. Nancollas, *Inorg. Chem., 11*, 2414 (1972).

72JB G. Jung, E. Breitmaier and W. Voelter, *Eur. J. Biochem., 24*, 438 (1972).

72RJ J.H. Ritsma and F. Jellinek, *Recl. Trav. Chim. Pays-Bas, 91*, 923 (1972).

72ST H.A. Skinner and E.W. Tipping, *Rev. Chim. Min., 9*, 51 (1972).

73BJ J.R. Blackburn and M.M. Jones, *J. Inorg. Nucl. Chem., 35*, 1605 (1973).

73BL P. Bonvicini, A. Levi, V. Lucchini, G. Modena and G. Scorrano, *J. Am. Chem. Soc., 95*, 5960 (1973).

73BS L.P. Berezina, V.G. Samoilenko and A.I. Pozigun, *Russ. J. Inorg. Chem., 18*, 205 (1973).

73CT A.M. Corrie, M.L.D. Touche and D.R. Williams, *J. Chem. Soc., Dalton Trans.*, 2561 (1973).

73FA O. Farooq, N. Ahmad and A.U. Malik, *J. Electroanal. Chem.*, *48*, 475 (1973).

73GM P. Grenouillet, R-P. Martin, A. Rossi and M. Ptak, *Biochim. Biophys. Acta*, *322*, 185 (1973)

73H J.A. Happe, *J. Am. Chem. Soc.*, *95*, 6232 (1973).

73KS T.P.A. Kruck and B. Sarkar, *Can. J. Chem.*, *51*, 3555 (1973).

73PA D.D. Perrin and R.P. Agarwal, in 'Metal Ions in Biological Systems', Vol. 2, H. Sigel ed., Marcel Dekker, New York (1973), p. 167.

73RG P.C. Rawat and C.M. Gupta, *Indian J. Chem.*, *II*, 186 (1973).

73RK E.M. Rogozina, L.F. Konkina and D.K. Popov, *Radiokhim.*, *15*, 61 (1973); *Soviet Radiochem.*, *15*, 59 (1973).

73RS A. Raghavan and M. Santappa, *J. Inorg. Nucl. Chem.*, *35*, 3363 (1973).

73SA R.V. Snyder and R.J. Angelici, *J. Inorg. Nucl. Chem.*, *35*, 523 (1973).

73SC B.S. Sekhon and S.L. Chopra, *Thermochim. Acta*, *7*, 311 (1973).

73SR S.K. Srivastava, E.V. Raju and H.B. Mathur, *J. Inorg. Nucl. Chem.*, *35*, 253 (1973).

73SK G.M. Sergeev and I.A. Korshunov, *Radiokhim.*, *15*, 618 (1973); *Soviet Radiochem.*, *15*, 619 (1973).

73SKa G.M. Sergeev and I.A. Korshunov, *Radiokhim.*, *15*, 621 (1973); *Soviet Radiochem.*, *15*, 623 (1973).

73SY A.D. Sherry, C. Yoshida, E.R. Birnbaum and D.W. Darnall, *J. Am. Chem. Soc.*, *95*, 3011 (1973).

73TS R.C. Tewari and M.N. Srivastava, *Talanta*, *20*, 133 (1973).

73TSa R.C. Tewari and M.N. Srivastava, *J. Inorg. Nucl. Chem.*, *35*, 3044 (1973).

73TSb R.C. Tewari and M.N. Srivastava, *Indian J. Chem.*, *11*, 701 (1973).

73VB W.E. van der Linden and C. Beers, *Anal. Chim. Acta*, *68*, 143 (1973).

73W D.R. Williams, *J. Chem. Soc., Dalton Trans.*, 1064 (1973).

74BW A.C. Baxter and D.R. Williams, *J. Chem. Soc., Dalton Trans.*, 1117 (1974).

74FA O. Farooq and N. Ahmad, *J. Electroanal. Chem.*, *53*, 457 (1974).

74FAa O. Farooq and N. Ahmad, *J. Electroanal. Chem.*, *53*, 461 (1974).

74FAb O. Farooq and N. Ahmad, *J. Electroanal. Chem.*, *57*, 121 (1974).

74FL Y.D. Fridman and M.G. Levina, *Zh. Neorg. Khim.*, *19*, 2422 (1974); *Russ. J. Inorg. Chem.*, *19*, 1324 (1974).

74GW R.D. Graham and D.R. Williams, *J. Chem. Soc., Dalton Trans.*, 1123 (1974).

74KH V.J. Kollmann and E. Hoyer, *J. Prakt. Chem.*, *316*, 119 (1974).

74KU F.Y. Kul'ba, V.G. Ushakova and Y.B. Yakovlev, *Zh. Neorg. Khim.*, *19*, 1785 (1974); *Russ. J. Inorg. Chem.*, *19*, 972 (1974).

74MG D.B. Mc Cormick, R. Griesser and H. Sigel, in 'Metal Ion in Biological Systems', Vol. 1, H. Sigel ed., M. Dekker, New York (1974), p. 213.

74MS A.E. Martell and R.M. Smith, 'Critical Stability Constants', Vol. 1, Plenum Press, New York (1974).

74PN V.E. Plyushchev, G.V. Nadezhdina, G.S. Loseva, V.V. Mel'nikova and T.S. Parfenova, *Zh. Obshch. Khim.*, *44*, 2319 (1974); *J. Gen. Chem. USSR*, *44*, 2274 (1974).

74RM S. Ramamoorthy and P.G. Manning, *Inorg. Nucl. Chem. Letters*, *10*, 623 (1974).

74RMa S. Ramamoorthy and P.G. Manning, *J. Inorg. Nucl. Chem.*, *36*, 1671 (1974).

74SC B.S. Sekhon and S.L. Chopra, *Indian J. Chem.*, *12*, 1322 (1974).

74SK G.M. Sergeev and I.A. Korshunov, *Radiokhim.*, *16*, 783 (1974); *Soviet Radiochem.*, *16*, 767 (1974).

74TS R.C. Tewari and M.N. Srivastava, *Acta Chim. Acad. Sci. Hung.*, *83*, 259 (1974).

74WL D.B. Walters and D.E. Leyden, *Anal. Chim. Acta*, *72*, 275 (1974).

74WW M.D. Walker and D.R. Williams, *J. Chem. Soc., Dalton Trans.*, 1186 (1974).

75BW A.C. Baxter and D.R. Williams, *J. Chem. Soc., Dalton Trans.*, 1757 (1975).

75CM A.M. Corrie, G.K.R. Makar, M.L.D. Touche and D.R. Williams, *J. Chem. Soc., Dalton Trans.*, 1803 (1975).

75FR M.T. Fairhurst and D.L. Rabenstein, *Inorg. Chem.*, *14*, 1413 (1975).

75GN A. Gergely, I. Nagypal and E. Farkas, *J. Inorg. Nucl. Chem.*, *37*, 551 (1975).

75HV G.J.M. Heijne and W.E. van der Linden, *Talanta*, *22*, 923 (1975).

75IP M. Israeli and L.D. Pettit, *J. Inorg. Nucl. Chem.*, *37*, 999 (1975).

75RF D.L. Rabenstein and M.T. Fairhurst, *J. Am. Chem. Soc.*, *97*, 2086 (1975).

75RM S. Ramamoorthy and P.G. Manning, *J. Inorg. Nucl. Chem.*, *37*, 363 (1975).

75S T. Simeonova, *Nauchni Tr.- Plovdiv Univ.*, *13*, 61 (1975).

75SC B.S. Sekhon and S.L. Chopra, *Ann. Chim.*, *10*, 22 (1975).

75ZK G.D. Zegzhda, V.N. Kabanova and F.M. Tulyupa, *Zh. Neorg. Khim.*, *20*, 2325 (1975); *Russ. J. Inorg. Chem.*, *20*, 1289 (1975).

76BH P. Bianco, J. Haladjian and R. Pilard, *J. Electroanal. Chem.*, *72*, 341 (1976).

76CW A.M. Corrie, M.D. Walker and D.R. Williams, *J. Chem. Soc., Dalton Trans.*, 1012 (1976).

76CWa A.M. Corrie and D.R. Williams, *J. Chem. Soc., Dalton Trans.*, 1068 (1976).

76HS Y. Hojo, Y. Sugiura and H. Tanaka, *J. Inorg. Nucl. Chem.*, *38*, 641 (1976).

76KF B. Khan, O. Farooq and N. Ahmad, *J. Electroanal. Chem.*, *74*, 239 (1976).

76KS N. Kojima, Y. Sugiura and H. Tanaka, *Bull. Soc. Chim. Japan*, *49*, 3023 (1976).

76PS L.D. Pettit and J.L.M. Swash, *J. Chem. Soc., Dalton Trans.*, 2416 (1976).

76SP J.L.M. Swash and L.D. Pettit, *Inorg. Chim. Acta*, *19*, 19 (1976).

76ZN G.D. Zegzhda, S.I. Neikovskii and F.M. Tulyupa, *Koord. Khim.*, *2*, 162 (1976); *Soviet J. Coord. Chem.*, *2*, 124 (1976).

77B M.T. Beck, *Pure & Appl. Chem.*, *49*, 127 (1977).

77BP G. Brookes and L.D. Pettit, *J. Chem. Soc., Dalton Trans.*, 1918 (1977).

77BR S.A. Bedell, P.R. Rechani, R.J. Angelici and R. Nakon, *Inorg. Chem.*, *16*, 972 (1977).

77CL A.K. Chattopadhyay and S.C. Lahiri, *Indian J. Chem.*, *15A*, 930 (1977).

77DO P.G. Daniele and G. Ostacoli, *Ann. Chim.*, *67*, 311 (1977).

77L M. Lamache-Duhameaux, *J. Inorg. Nucl. Chem.*, *39*, 2081 (1977).

77La M.-C. Lim, *J. Chem. Soc., Dalton Trans.*, 1398 (1977).

77M H. Matsui, *Denki Kagaku Oyobi Kogyo Butsuri Kagaku*, *45*, 734 (1977).

77MG P.K. Migal, A.P. Gerbeleu and I.K. Gaidarzhi, *Zh. Neorg. Khim.*, *22*, 155 (1977).

77ML P.M. May, P.W. Linder and D.R. Williams, *J. Chem Soc., Dalton Trans.*, 588 (1977).

77MS S.D. Makhijani and S.P. Sangal, *J. Indian Chem. Soc., LIV*, 670 (1977).

77NG I. Nagypal and A. Gergely, *J. Chem. Soc., Dalton Trans.*, 1109 (1977).

77PU V.P. Poddymov and A.A. Ustinova, *Zh. Neorg. Khim.*, *22*, 1617 (1977); *Russ. J. Inorg. Chem.*, *22*, 877 (1977).

77RN J. Rangarajan, B.I. Nemade and R. Sundaresan, *Proc. Indian Acad. Sci.*, *85A*, 454 (1977).

77RR K. Rangaraj and V.V. Ramanujam, *J. Inorg. Nucl. Chem.*, *39*, 489 (1977).

77S B. Sarkar, *J. Indian Chem. Soc., LIV*, 117 (1977).

78BK G.A. Bagiyan, I.K. Koroleva and N.V. Soroka, *Zh. Neorg. Khim.*, *23*, 2422 (1978); *Russ. J. Inorg. Chem.*, *23*, 1337 (1978).

78BM G. Berthon, P.M. May and D.R. Williams, *J. Chem. Soc., Dalton Trans.*, 1433 (1978).

78IS N. Ivicic and V. Simeon, *Thermochim. Acta, 25*, 299 (1978).

78KA A.P. Kreshkov, N.S. Aldarova, A.M. Yarovenko, B.B. Tanganov, K.N. Shulunova, T.K. Batorova and T.E. Batlaeva, *Zh. Fiz. Khim., 52*, 456 (1978); *Russ. J. Phys. Chem., 52*, 255 (1978).

78L M.-C. Lim, *J. Chem. Soc., Dalton Trans.*, 726 (1978).

78MG P.K. Migal, A.P. Gerbeleu, P.G. Kalitina and T.K. Utkina, *Zh. Neorg. Khim., 23*, 1593 (1978); *Russ. J. Inorg. Chem., 23*, 878 (1978).

78MGa P.K. Migal, A.P. Gerbeleu and P.G. Kalitina, *Zh. Neorg. Khim., 23*, 1602 (1978); *Russ. J. Inorg. Chem., 23*, 882 (1978).

78MS S.D. Makhijani and S.P. Sangal, *Chem. Era*, 202 (1978).

78NM M. Niitsu, T. Manri and N. Iritani, *Bull. Chem. Soc. Japan, 51*, 2165 (1978).

78VV J. Vliegen and L.C. van Poucke, *Bull. Soc. Chim. Belg., 87*, 837 (1978).

79FD Y.D. Fridman, N.V. Dolgashova and T.Z. Zhusupbekov, *Zh. Neorg. Khim., 24*, 3325 (1979); *Russ. J. Inorg. Chem., 24*, 1852 (1979).

79FM Y.D. Fridman and L.Y. Mikhailyuk, *Koord. Khim., 5*, 972 (1979).

79GS A. Gergely and I. Sovago, in 'Metal Ions in Biological Systems', Vol. 9, H. Sigel ed., M. Dekker, New York (1979) p. 77.

79KC Y. Khayat, M. Cromer-Morin and J.P. Scharff, *J. Inorg. Nucl. Chem., 41*, 1496 (1979).

79M R.B. Martin, in 'Metal Ions in Biological Systems', Vol. 9, H. Sigel ed., M. Dekker, New York (1979) p. 1.

79PB L. Pillai, R.D. Boss and M.S. Greenberg, *J. Sol. Chem., 8*, 635 (1979).

79PG M.M. Palrecha and J.N. Gaur, *J. Electrochem. Soc. India, 28*, 233 (1979).

79PH L.D. Pettit and R.J.W. Hefford, in 'Metal Ions in Biological Systems', Vol. 9, H. Sigel ed., M. Dekker, New York (1979) p. 173.

79SG I. Sovago, A. Gergely, B. Harman and T. Kiss, *J. Inorg. Nucl. Chem., 41*, 1629 (1979).

79SGa N.P. Sachan and C.M. Gupta, *Indian J. Chem., 18A*, 82 (1979).

79SP H. Stünzi and D.D. Perrin, *J. Inorg. Biochem., 10*, 309 (1979).

79SS N.P. Sachan, S.K.Shah and C.M. Gupta, *Indian J. Chem., 17A*, 622 (1979).

79SSb C.F. Shaw III, G. Schmitz, H.O. Thompson and P. Witkiewicz, *J. Inorg. Biochem., 10*, 317 (1979).

79YS O. Yamauchi, T. Sakurai and A. Nakahara, *J. Am. Chem. Soc., 101*, 4164 (1979).

79ZJ T.D. Zucconi, G.E. Janauer, S. Donahe and C. Lewkowicz, *J. Pharm. Sci., 68*, 426 (1979).

79ZN G.D. Zegzhda, S.I. Neikovskii, F.M. Tulyupo and A.P. Tulya, *Koord. Khim., 5*, 632 (1979); *Soviet J. Coord. Chem., 5*, 494 (1979).

80AM G. Arena, S. Musumeci, E. Rizzarelli and S. Sammartano, *Transition Met. Chem., 5*, 297 (1980).

80AS B.R. Arbad, D.N. Shelke and D.V. Jahagirdar, *Inorg. Chim. Acta, 46*, L17 (1980).

80BM G. Berthon, C. Matuchansky and P.M. May, *J. Inorg. Biochem., 13*, 63 (1980).

80JK S.L. Jain and R.C. Kapoor, *Indian J. Chem., 19A*, 351 (1980).

80KB A. Kayali and G. Berthon, *J. Chem. Soc., Dalton Trans.*, 2374 (1980).

80KT A.P. Kreshkov, B.B. Tanganov, A.N. Yarovenko and T.K. Batorova, *Zh. Fiz. Khim., 54*, 105 (1980); *Russ. J. Phys. Chem., 54*, 56 (1980).

80MS K. Matsuda, C. Shirahige, M. Takahara and M. Maki, *Nihon Daigaku Seisankogakubu Hokoku, 13*, 73 (1980); CA 94:116414h (1981).

80RK V.V. Ramanujam and U. Krishnan, *J. Indian. Chem. Soc., LVII*, 359 (1980).

80RKa V.V. Ramanujam and U. Krishnan, *Indian. J. Chem., 19A*, 779 (1980).

80RR V.V. Ramanujam, K. Rengaraj and B. Sivasankar, *Indian J. Chem.*, *19A*, 240 (1980).

80S G.M. Sergeev, *Radiokhim.*, *22*, 701 (1980).

80SD C.L. Sharma and T.K. De, *J. Less-Common Metals*, *70*, 63 (1980).

80SG S.K. Shah and C.M. Gupta, *Talanta*, *27*, 823 (1980).

80TH M.M. Taqui Khan and A. Hussain, *Indian J. Chem.*, *19A*, 44 (1980).

80YT O. Yamauchi, T. Takara and T. Sakurai, *Bull. Chem. Soc. Japan*, *53*, 106 (1980).

81AB T. Alemdaroglu and G. Berthon, *Inorg. Chim. Acta*, *56*, 115 (1981).

81ABa T. Alemdaroglu and G. Berthon, *Inorg. Chim. Acta*, *56*, 51 (1981).

81ABb T. Alemdaroglu and G. Berthon, *Bioelectrochem. Bioenerg.*, *8*, 49 (1981).

81BC M.A. Basinger, J.S. Casas, M.M. Jones, A.D. Weaver and N.H. Weinstein, *J. Inorg. Nucl. Chem.*, *43*, 1419 (1981).

81BK M.J. Blais, A. Kayali and G. Berthon, *Inorg. Chim. Acta*, *56*, 5, (1981).

81BR S.J. Backs and D.L. Rabenstein, *Inorg. Chem.*, *20*, 410 (1981).

81CD B. Carré and J. Devinck, *Bull. Soc. Chim. Fr.*, I-309 (1981).

81FP Y.D. Fridman, Z.M. Pulatova and M.G. Levina, *Koord. Khim.*, *7*, 73 (1981).

81G A. Gergely, *Inorg. Chim. Acta*, *56*, L75 (1981).

81IS N. Ivicic and V. Simeon, *J. Inorg. Nucl. Chem.*, *43*, 2581 (1981).

81JI M. Jawaid and F. Ingman, *Talanta*, *28*, 137 (1981).

81L M.-C. Lim, *Inorg. Chem.*, *20*, 1377 (1981).

81M H. Matsui, *J. Inorg. Nucl. Chem.*, *43*, 2187 (1981).

81MC J. Maslowska and L. Chruscinski, *J. Inorg. Nucl. Chem.*, *43*, 3398 (1981).

81MG P.K. Migal, A.P. Gerbeleu and A.P. Tyunikova, *Zh. Neorg. Khim.*, *26*, 1826 (1981); *Russ. J. Inorg. Chem.*, *26*, 985 (1981).

81MW P.M. May and D.R. Williams, in 'Metal Ions in Biological Systems', Vol. 12, H. Sigel ed., M. Dekker, New York (1981) p. 283.

81PS L.D. Pettit, K.F. Siddiqui, H. Kozlowski and T. Kowalik, *Inorg. Chim. Acta*, *55*, 87 (1981).

81PU V.D. Poddymov and A.A. Ustinova, *Zh. Neorg. Khim.*, *26*, 1307 (1981); *Russ. J. Inorg. Chem.*, *26*, 702 (1981).

81R D. Reddy, *Indian J. Chem.*, *20A*, 1038 (1981).

81RK V.V. Ramanujam and U. Krishnan, *J. Indian. Chem. Soc.*, *LVIII*, 425 (1981).

81RR R.S. Reid and D.L. Rabenstein, *Can. J. Chem.*, *59*, 1505 (1981).

81RS V.V. Ramanujam and V.M. Selvarajan, *Indian J. Chem.*, *20A*, 633 (1981).

81RSa V.V. Ramanujam and V.M. Selvarajan, *J. Indian. Chem. Soc.*, *LVIII*, 125 (1981).

81RSb V.V. Ramanujam and V.M. Selvarajan, *J. Indian. Chem. Soc.*, *LVIII*, 1131 (1981).

81S B. Sarkar, in 'Metal Ions in Biological Systems', Vol. 12, H. Sigel ed., M. Dekker, New York (1981) p. 233.

81SH P. Sharrock and R. Haran, *J. Coord. Chem.*, *11*, 117 (1981).

81UP P. Utrilla Sanchez, L. Parra Bravo and P. Sanchez Batanero, *Analusis*, *9*, 455 (1981).

81W D.R. Williams, private communication.

82BB M.J. Blais and G. Berthon, *Inorg. Chim. Acta*, *67*, 109 (1982).

82BC Y. Bizri, M. Cromer-Morin and J.P. Scharff, *J. Chem. Res.*, *192* (1982).

82BK G. Berthon and A. Kayali, *Agents Actions*, *12*, 398 (1982).

82CG C.P.S. Chandel, C.M. Gupta and N.P. Sachan, *Chem. Scr.*, *20*, 229 (1982).

82DD B.P. Dey, S. Dutta and S.C. Lahiri, *Indian J. Chem.*, *21A*, 886 (1982).

82HA Z-X. Huang, H.S. Al-Falahi, A. Cole, J.R. Duffield, C. Furnival, D.C. Jones, P.M. May, G.L. Smith and D.R. Williams, *Polyhedron*, *1*, 153 (1982).

82J J.D. Joshi, *Indian J. Chem.*, *21A*, 446 (1982).

82KB A. Kayali and G. Berthon, *Polyhedron*, *1*, 371 (1982).

82KP Z. Kralj, N. Paulic, N. Raos and V. Simeon, *Croat. Chem. Acta*, *55*, 337 (1982).

82MH H. Matsui, Y. Hirabayashi and M. Furukawa, *Nagoya Kogyo Gijutsu Shikensho Hokoku*, *31*, 168 (1982).

82MS A.E. Martell and R.M. Smith, 'Critical Stability Constants', Vol. 5, Plenum Press, New York (1982).

82N A. Napoli, *Ann. Chim.*, *72*, 575 (1982).

82NA T. Nageswara Rao, G. Aravamudan and R. Narayan, *Electrochim. Acta*, *27*, 985 (1982).

82NM M. Nourmand and N. Meissami, *Polyhedron*, *1*, 537 (1982).

82NMa M. Nourmand and N. Meissami, *Radiochem. Radioanal. Letters*, *55*, 149 (1982).

82RB M. Ramaiah, B.G. Bhat and R. Sundaresan, *Proc. Indian Acad. Sci.*, *91*, 151 (1982).

82S D.N. Shelke, *J. Coord. Chem.*, *12*, 35 (1982).

82SD C.L. Sharma and T.K. De, *J. Indian Chem. Soc.*, *LIX*, 101 (1982).

82TB H.E. Toma, A.A. Batista and H.B. Gray, *J. Am. Chem. Soc.*, *104*, 7509 (1982).

82VN K. Venkatachalapathi, M.S. Nair, D. Ramaswamy and M. Santappa, *J. Chem. Soc., Dalton Trans.*, 291 (1982).

82WF D.R. Williams, C. Furnival and P.M. May, in J.R.J. Sorenson (ed.), 'Inflammatory Diseases and Copper', The Humana Press, Clifton, New Jersey, (1982), p. 45.

82XL S. Xu, X. Liu, G. Sun and K. Wang, *Fenzi Kexue Xuebao*, *2*, 19 (1982); CA 98:60708v (1983).

83AC A.P. Arnold and A.J. Canty, *Can. J. Chem.*, *61*, 1428 (1983).

83BA R.K. Boggess, J.R. Absher, S. Morelen, L.T. Taylor and J.W. Hughes, *Inorg. Chem.*, *22*, 1273 (1983).

83BV G.A. Bagiyan, A.K. Valeev, I.K. Koroleva and N.V. Soroka, *Zh. Neorg. Khim.*, *28*, 2016 (1983); *Russ. J. Inorg. Chem.*, *28*, 1142 (1983).

83DQ K.P. Dubey and M.A. Qazi, *Proc. Nat. Acad. Sci. India*, *53(A)*, 342 (1983).

83FA Ya.D. Fridman, S.V. Alikeeva, N.V. Dolgashova and T.G. Nemal'tseva, *Russ. J. Inorg. Chem.*, *28*, 836 (1983).

83HD D. Huljev, M. Dzajo, N. Kristic and P. Strohal, *Intern. J. Environ. Anal. Chem.*, *15*, 53 (1983).

83HS B. Harman and I. Sovago, *Inorg. Chim. Acta*, *80*, 75 (1983).

83HV T.U. Hoogenraad and C.J.A. van den Hamer, *Acta Neurol. Scand.*, *67*, 356 (1983).

83JK S.L. Jain and R.C. Kapoor, *Inorg. Chim. Acta*, *78*, 93 (1983).

83KP A. Kufelnicki and S. Petri, *Pol. J. Chem.*, *57*, 1129 (1983).

83LW L. Lomozik, A. Wojciechowska and M. Jaskolski, *Mon. Chem.*, *114*, 1185 (1983).

83NM M. Nourmand and N. Meissami, *J. Chem. Soc., Dalton Trans.*, 1529 (1983).

83S D.N. Shelke, *Inorg. Chim. Acta*, *80*, 255 (1983).

83VD N.N. Vlasova and N.K. Davidenko, *Koord. Khim.*, *9*, 1470 (1983).

83VK M. Vašák and J.H.R. Kägi, in 'Metal Ions in Biological Systems', Vol. 15, H. Sigel ed., M. Dekker, New York (1983) p. 213.

84AO N. Al-Ani and Å. Olin, *Chem. Scr.*, *23*, 161 (1984).

84BB G. Berthon, M.J. Blais, M. Piktas and K. Houngbossa, *J. Inorg. Biochem.*, *20*, 113 (1984).

84BP G. Berthon, M. Piktas and M.J. Blais, *Inorg. Chim. Acta*, *93*, 117 (1984).

84CG C.P.S. Chandel and C.M. Gupta, *Bull. Chem. Soc. Jpn.*, *57*, 2303 (1984).

84GN H.B. Gurav and B.I. Nemade, *J. Electrochem. Soc. India, 33*, 139 (1984).

84ID S. Iftekhar and K.P. Dubey, *J. Indian Chem. Soc., LXI*, 702 (1984).

84J J.D. Joshi, *J. Indian Chem. Soc., 61*, 257 (1984).

84Ja J.D. Joshi, *J. Indian Chem. Soc., 61*, 901 (1984).

84KB V.G. Kulkarni, P.K.Bhansali and B.I. Nemade, *J. Electrochem. Soc. India, 33*, 143 (1984).

84KW F. Karczinski, J. Wolinski and H. Lapkowska, *Chem. Anal. (Warsaw), 29*, 19 (1984).

84LT P.W. Linder, R.G. Torrington and D.R. Williams, 'Analysis Using Glass Electrodes', Open University Press, Milton Keynes, (1984).

84MC J. Maslowska and L. Chruscinski, *Polyhedron, 3*, 523 (1984).

84MCa J. Maslowska and L. Chruscinski, *Polyhedron, 3*, 1329 (1984).

84MCb J. Maslowska and L. Chruscinski, *Acta Univ. Lodz., 3*, 23 (1984).

84MM K. Murray and P.M. May, ESTA Users' Manual, UWIST, Cardiff (1984).

84MR V.R. Mundra, G.N. Rao and C.S.R. Murthy, *Pol. J. Chem., 58*, 53 (1984).

84P L.D. Pettit, *Pure & Appl. Chem., 56*, 247 (1984).

84PB J.M. Pingarron Carrazon, I. del Barrio Marcaida and L.M. Polo Diez, *Anal. Quim., 80*, 141 (1984).

84RS V.V. Ramanujam and V.M. Selvarajan, *Proc. Indian Acad. Sci. (Chem. Sci.), 93*, 1251 (1984).

84S D.N. Shelke, *Acta Cienc. Ind., Xc*, 97 (1984).

84SC M.L.S. Simoès Gonçalves and M.M. Correia Dos Santos, *J. Electroanal. Chem., 163*, 315 (1984).

84SP R.S. Saxena and R.D. Parikh, *Bull. Soc. Chim. Belg., 93*, 507 (1984).

84SY S. Singh, H.L. Yadava, P.C. Yadava and K.L. Yadava, *J. Electrochem. Soc. India, 33*, 249 (1984).

84TS J.J. Tombeux, J. Schaubroek, C.T. Huys, H.F. de Brabander and A.M. Goeminne, *Z. Anorg. Allg. Chem., 517*, 235 (1984).

85AM G. Arena, S. Musumeci, E. Rizzarelli and S. Sammartano, *Transition Met. Chem., 10*, 399 (1985).

85BC R. Benhallam, E. Collange and M.R. Pâris, *Bull. Soc. Chim. Fr.*, 1159 (1985).

85BP E. Bottari and R. Porto, *Ann. Chim., 75*, 393 (1985).

85CF A. Cole, C. Furnival, Z.X. Huang, D. Ceri Jones, P.M. May, G.L. Smith, J. Whittaker and D.R. Williams, *Inorg. Chim. Acta, 108*, 165 (1985).

85FD Y.D. Fridman, M.S. Dzhusueva and N.V. Dolgashova, *Zh. Neorg. Khim., 30*, 2286 (1985); *Russ. J. Inorg. Chem., 30*, 1299 (1985).

85KC R. Kumari, C.P.S. Chandel and C.M. Gupta, *J. Indian Chem. Soc., LXII*, 740 (1985).

85KR K.P. Kariya, M.M. Ranade and N.S. Bhave, *J. Indian Chem. Soc., LXII*, 187 (1985).

85MG P.K. Migal and A.P. Gerbeleu, *Metallkhelaty Ikh Svoistva*, 25 (1985); CA 107:122145z (1987).

85MK K. Matsuda, C. Kanai, M. Takahara and M. Maki, *Nippon Kagaku Kaishi, 4*, 698 (1985).

85MM K. Murray, P.M. May and D.R. Williams, *Talanta, 32*, 483 (1985).

85MMa P.M. May, K. Murray and D. Peaper, *Rev. Port. Quim., 27*, 312 (1985).

85MS B.V. Mrudula Rao, S.J. Swamy and P. Lingaiah, *Indian. J. Chem., 24A*, 887 (1985).

85S M.M. Shoukry, *Egypt. J. Chem., 28*, 443 (1985).

85SB L. Spaulding and H.G. Brittain, *Inorg. Chem., 24*, 3692 (1985).

85SC M.L.S. Simoes Gonçalves and M.M. Correia Dos Santos, *J. Electroanal. Chem., 187*, 333 (1985).

85SN C.L. Sharma and S.S. Narvi, *Thermochim. Acta, 90*, 1 (1985).

85SS K.K. Saxena, S. Sharma and R.S. Saxena, *Afinidad*, 91 (1985).

85SY S. Singh, H.L. Yadava, P.C. Yadava and K.L. Yadava, *J. Electrochem. Soc. India, 34*, 125 (1985).

85SYa R.K.P. Singh and K.L. Yadava, *J. Electrochem. Soc. India, 34*, 128 (1985).

85VD N.N. Vlasova and N.K. Davidenko, *Zh. Neorg. Khim., 30*, 1738 (1985); *Russ. J. Inorg. Chem., 30*, 988 (1985).

86AJ B.R. Arbad and D.V. Jahagirdar, *Indian J. Chem., 25A*, 253 (1986).

86BH G. Berthon, B. Hacht, M.J. Blais and P.M. May, *Inorg. Chim. Acta, 125*, 219 (1986).

86CS M.M. Correia Dos Santos and M.L.S. Simoès Gonçalves , *J. Electroanal. Chem., 208*, 137 (1986).

86FA Y.D. Fridman, S.V. Alideeva, N.V. Dolgashova and T.G. Nemal'tseva, *Zh. Neorg. Khim., 31*, 1232 (1986); *Russ. J. Inorg. Chem., 31*, 700 (1986).

86FD Y.D. Fridman, M.S. Dzhusueva and N.V. Dolgashova, *Zh. Neorg. Khim., 31*, 1459 (1986); *Russ. J. Inorg. Chem., 31*, 834 (1986).

86J J.D. Joshi, *J. Indian Chem. Soc., LXIII*, 929 (1986).

86Ja S.L. Jain, *J. Indian Chem. Soc., LXIII*, 805 (1986).

86K F. Khan, *J. Indian Chem. Soc., LXIII*, 340 (1986).

86KC R. Kumari, C.P.S. Chandel and C.M. Gupta, *Indian J. Chem., 25A*, 877 (1986).

86KD D. Kovala-Demertzi, M. Demertzis and J.M. Tsangaris, *Bull. Soc. Chim. Fr.*, 558 (1986).

86LS G. Lewis and C.F. Shaw III, *Inorg. Chem., 25*, 58 (1986).

86M R.B. Martin, in 'Metal Ions in Biological Systems', Vol. 20, H. Sigel ed., M. Dekker, New York, (1986) p. 21.

86MC J. Maslowska and L. Chruscinski, *Polyhedron, 5*, 1131 (1986).

86MCa J. Maslowska and L. Chruscinski, *Polyhedron, 5*, 1135 (1986).

86PD A. Pal, B.P. Dey and S.C. Lahiri, *Indian J. Chem., 25A*, 322 (1986).

86SP R.S. Saxena and R.D. Parikh, *Bull. Soc. Chim. Belg., 95*, 163 (1986).

86SS S. Sharma, K.K. Saxena and R.S. Saxena, *Bol. Soc. Chil. Quim., 31*, 7 (1986).

86SSa S. Sharma, K.K. Saxena and R.S. Saxena, *Trans. SAEST, 21*, 127 (1986).

86SV I. Sovago, K. Varnagy and A. Benyei, *Magy. Kém. Foly., 92*, 114 (1986).

87CJ F. Chunmei and Z. Jia, *Chem. J. Chin. Univ., 8*, 1 (1987).

87CL S.K. Chakravorty and S.C. Lahiri, *J. Indian Chem. Soc., LXIV*, 399 (1987).

87HO M.J. Hynes and M. O'Dowd, *J. Chem. Soc., Dalton Trans.*, 563 (1987).

87KS T. Kiss, C. Simon and Z. Vachter, *J. Coord. Chem., 16*, 225 (1987).

87L S. Laurie, in 'Comprehensive Coordination Chemistry', Vol. 2, G. Wilkinson ed., Pergamon Press, Oxford (1987) p. 739.

87MT A.K. Molodkin, E.V. Tarakanova and N.Ya. Esina, *Zh. Neorg. Khim., 32*, 2299 (1987); *Russ. J. Inorg. Chem., 32*, 1344 (1987).

87PS K. Prasad and M. Srinivas Mohan, *J. Coord. Chem., 16*, 1 (1987).

87RF F. Rodante and F. Fantauzzi, *Thermochim. Acta, 111*, 233 (1987).

87SB R.R. Sharma, B.L. Bhat and K.P. Dubey, *J. Indian Chem. Soc., LXIV*, 437 (1987).

87SM M.M. Shoukry, A.E. Mahgoub and W.M. Hosny, *Transition Met. Chem., 12*, 77 (1987).

87SP I. Sovago and G. Petöcz, *J. Chem. Soc., Dalton Trans.*, 1717 (1987).

88AG S.K. Agrawal and K.C. Gupta, *Indian J. Chem., 27A*, 1008 (1988).

88BA J. Benzakour, G. Antonetti and G. Ferroni, *Bull. Soc. Chim. Belg., 97*, 541 (1988).

88GG M. Garcia Bugarin, M.E. Garcia, G. Berthon, J.S. Casas and J. Sordo, *Polyhedron, 7*, 2487 (1988).

88JA D.V. Jahagirdar and B.R. Arbad, *Transition Met. Chem.*, *13*, 238 (1988).

88KD D. Kovala-Demertzi, M. Demertzis and J.M. Tsangaris, *Bull. Soc. Chim. Fr.*, 793 (1988).

88KS K. Kratzer and J. Stary, *J. Radioanal. Nucl. Chem. Letters*, *127*, 325 (1988).

88LD L. Lambs, B. Decock-Le Révérend, H. Kozlowski and G. Berthon, *Inorg. Chem.*, 27, 3001 (1988).

88LG H.-K. Lin, Z.-Z. Gu, X.-M. Chen and Y.-T. Chen, *Thermochim. Acta*, *123*, 201 (1988).

88M L. Magos, in 'Handbook on Toxicity of Inorganic Compounds', H.G. Seiler and H. Sigel eds., M. Dekker, New York (1988) p. 419.

88MA M.S. Masoud, B.A. Abdel-Nabby, E.M. Soliman and O.H. Abdel-Hamid, *Thermochim. Acta*, *128*, 75 (1988).

88PP M. Philip, M.N. Patel, M.P. Peerzada and J.D. Joshi, *J. Indian Chem. Soc.*, *LXV*, 871 (1988).

88PS K. Prasad, M. Srinivas Mohan and H.B. Bathina, *J. Coord. Chem.*, *17*, 63 (1988).

88SKI I. Sovago, T. Kiss, K. Varnagy and B. Decock-Le Révérend, *Polyhedron*, *7*, 1089 (1988).

88SKa R.K. Saxena, R. Kumari, C.P.S. Chandel and C.M. Gupta, *Trans. SAEST*, *23*, 93 (1988).

88SP V.I. Shcherbakova, O.B. Pankratova and G.B. Zhaiykova, *Vestn. Leningr. Univ. Ser.*, *4*, 97 (1988).

88SS K. Singh, G. Singh and V.D. Gupta, *Indian J. Chem.*, *27A*, 264 (1988).

89CV J. Costa Pessoa, L.F. Vilas Boas and R.D. Gillard, *Polyhedron*, *8*, 1173 (1989).

89CVa J. Costa Pessoa, L.F. Vilas Boas and R.D. Gillard, *Polyhedron*, *8*, 1745 (1989).

89DF M.S. Dzhusueva and Y.D. Fridman, *Zh. Neorg. Khim.*, *34*, 2839 (1989); *Russ. J. Inorg. Chem.*, *34*, 11 (1989).

89JA D.V. Jahagirdar, B.R. Arbad, T.K. Chondhekar and S.U. Pankanti, *Indian J. Chem.*, *28A*, 366 (1989).

89KN F. Khan and K. Nema, *J. Indian Chem. Soc.*, *66*, 17 (1989).

89KS A. Koteswar Rao and M. Srinivas Mohan, *Proc. Indian Acad. Sci. (Chem. Sci.)*, *101*, 1 (1989).

89KV A. Koteswar Rao, P. Venkataiah, M. Srinivas Mohan and H.B. Bathina, *J. Coord. Chem.*, *20*, 69 (1989).

89MA M.R. Mahmoud, H.A. Azab, M.M.A. Hamed and A.H. Mohamed, *Chem. Script.*, *29*, 17 (1989).

89NK K. Nema and F. Khan, *Chem. Script.*, *29*, 155 (1989).

89PV K. Prasad, P. Venkataiah and M. Srinivas Mohan, *Indian J. Chem.*, *28A*, 325 (1989).

89R F. Rodante, *Thermochim. Acta*, *149*, 157 (1989).

89RF F. Rodante and F. Fantauzzi, *Thermochim. Acta*, *144*, 275 (1989).

89RM F. Rodante, G. Marrosu and F. Fantauzzi, *Thermochim. Acta*, *141*, 297 (1989).

89S M.M. Shoukry, *Talanta*, *36*, 1151 (1989).

89SC R.K. Saxena, C.P.S. Chandel and C.M. Gupta, *Indian J. Chem.*, *28A*, 625 (1989).

89SH M.M. Shoukry and W.M. Hosny, *Transition Met. Chem.*, *14*, 69 (1989).

89SM R.M. Smith and A.E. Martell, 'Critical Stability Constants', Vol. 6, Plenum Press, New York (1989).

89WZ L. Wagner-Roos, H. Zahn, J.-M. Séquaris and P. Valenta, *Toxicol. Environ. Chem.*, *22*, 77 (1989).

89YW H. Yang, W. Wang and L. Peng, *Acta Phys.-Chim. Sin.*, *5*, 583 (1989).

90BB V. Brumas and G. Berthon, in 'Metal Ions in Biology and Medicine', P. Collery, L.A. Poirier, M. Manfait and J.C. Etienne eds., John Libbey Eurotext, Paris (1990) p. 5.

90S M. Shoukry, *Proc. Indian Acad. Sci. (Chem. Sci.)*, *102*, 19 (1990).

91DB S. Daydé and G. Berthon, unpublished results.

93BA V. Brumas, N. Alliey and G. Berthon, *J. Inorg. Biochem.*, *52*, 287 (1193).

ACKNOWLEDGEMENT

The author wishes to express his thanks to Prs S. Ishiguro, T. Kiss, S.H. Laurie, H. Ohtaki, L.D. Pettit and S. Sjöberg for reading the manuscript and making useful suggestions.
The author is also grateful to Prs Griepink, K. Izutsu, J. Lorimer and H. Ohtaki for their useful advice in the editing.