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STABILITY CONSTANTS OF METAL COMPLEXES OF AMINO ACIDS† WITH CHARGED SIDE CHAINS —PART I: POSITIVELY CHARGED SIDE CHAINS‡

(Technical Report)

Prepared for publication by

O. YAMAUCHI and A. ODANI

Department of Chemistry, Faculty of Science, Nagoya University, Nagoya, 464-01 Japan

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†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**

Stability constants of metal complexes of amino acids with charged side chains—Part I: Positively charged side chains (Technical Report)
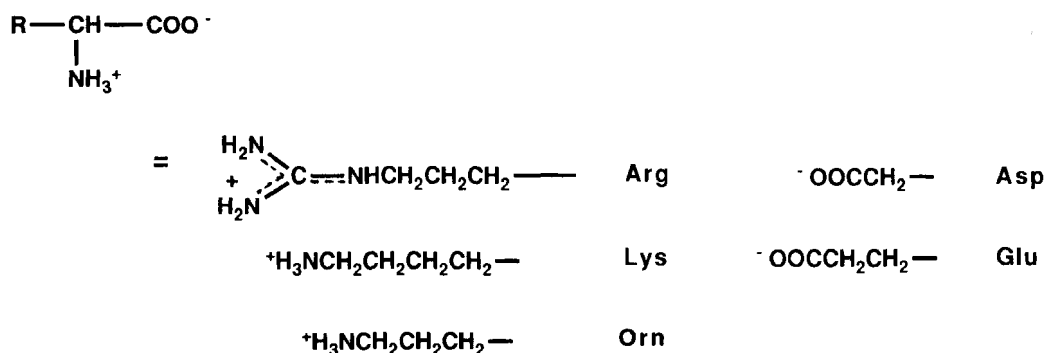
Synopsis: The stability constants of the proton and metal complexes of basic α-amino acids, arginine, lysine, and ornithine, have been collected and critically evaluated on the basis of the considerations of the factors affecting the stability constant determinations, such as experimental methods, conditions of measurements, purity of reactants, calibration of the apparatus, and methods of calculation. In the presence of the side chain basic group, metal complex formation normally occurs through the glycine-like mode of coordination by the amino acids with the side chain group protonated, and deprotonation from the complexes often occurs in basic solution. The collected stability constants were evaluated as 'recommended', 'tentative', 'informative', 'doubtful', or 'rejected' according to the above criteria. The thermodynamic parameters reported for a limited number of complexes have also been collected and evaluated.

1. Introduction

Natural α-amino acids constituting proteins are largely divided into three groups according to the nature of the side chain group R at neutral pH:

   (i)   aliphatic amino acids
   (ii)   charged amino acids
   (iii) aromatic amino acids

Group (i) amino acids are further classified into nonpolar and uncharged polar species, and aromatic amino acids which involve an uncharged polar amino acid, e. g. tyrosine. Arginine, lysine, ornithine, aspartic acid, and glutamic acid belong to group (ii) since they possess positively or negatively charged side chains. Arginine (Arg), lysine (Lys), and ornithine (Orn, which is not found in proteins but is naturally occurring), are called basic amino acids, because they have a strongly basic group in addition to the α-amino group, and are positively charged over a wide pH range (<9). Aspartic acid (Asp) and glutamic acid (Glu), which have an additional carboxylate group at β- and γ-carbon atoms respectively, are called acidic amino acids, because the side group is deprotonated, and they are negatively charged in neutral-alkaline solution. At neutral pH the amino acids considered may be represented as follows:

$$R\text{---}CH\text{---}COO^-$$
$$\underset{NH_3^+}{|}$$

$$= \quad \underset{H_2N}{\overset{H_2N}{>}}\overset{+}{C}\text{---}NHCH_2CH_2CH_2\text{---} \quad\quad Arg \quad\quad\quad ^-OOCCH_2\text{---} \quad\quad Asp$$

$$^+H_3NCH_2CH_2CH_2CH_2\text{---} \quad\quad Lys \quad\quad\quad ^-OOCCH_2CH_2\text{---} \quad\quad Glu$$

$$^+H_3NCH_2CH_2CH_2\text{---} \quad\quad Orn$$

Part I of this critical survey deals with the stability constants of the proton and metal complexes of basic amino acids with a positively charged side chain at neutral pH. Surveys of the stability constants for glycine (91KS) and aromatic amino acids (84P) have been reported earlier from IUPAC, and more recently the surveys on aliphatic amino acids with a non-polar (93SK) and with an uncharged polar side chain (95B) have been completed. The IUPAC stability constant database (93PP) covers all significant stability constants and associated thermodynamic data published between 1974-1989.

1.1 Amino Acids as Metal Binding Ligands

Amino acids are important low molecular weight ligands in biological systems. Their involvement in Cu^{II} transport in blood has been reported (67NS,73E), and computer simulation of multimetal-multiligand equilibria as models for those in blood has been made (73PA,77ML,78BM,86BH). Acidic and basic amino acids can in principle bind to metal ions through the α-amino and two carboxylate groups and the α-amino, carboxylate, and ω-amino or guanidinium groups, respectively. However, the glycine-like coordination through the α-amino and α-carboxylate groups is most common among these amino acids at neutral pH (79EG,79M), and the side chains of Arg and Lys are not involved in metal binding under physiological conditions. A Lys-containing tripeptide glycylhistidyllysine (GHL) is reported to be a specifc Cu^{II} carrier in blood (81P). The protonated side chain of the lysyl residue is inferred to be the receptor binding site and not involved in metal ion binding (80PF).
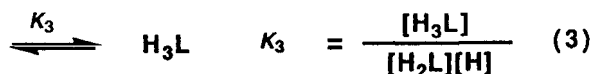
When incorporated into proteins, the side chain carboxylate groups of the aspartyl and glutamyl residues constitute the metal binding sites, e.g. in various zinc enzymes such as carboxypeptidases A and B and alkaline phosphatase (90VA) and in iron proteins such as hemerythrin (85SS,91HT). On the other hand, the side chains of the basic amino acids are not known to be metal binding sites in proteins. They are important as a positive charge carrier; the guanidinium group of Arg is involved in hydrogen bonding with the carboxylate group of peptide substrates in the carboxypeptidase A–peptide complex (70LR). A remarkable example showing the significance of the charged amino acid residues is seen in the specific DNA-protein binding by the 'zinc finger' domain of transcription factors, where Arg and Lys as well as Asp, Glu, and uncharged polar amino acids form a DNA-binding domain upon coordination of Zn^{II} through cysteinyl and histidyl residues (85MM). The DNA-protein binding has been shown to take place by electrostatic interactions or hydrogen bonds involving the side groups of charged amino acids (91PP).

1.2 Possible Forms of Charged Amino Acids and Their Metal Complexes in Aqueous Solution, and the Definition of Stability Constants
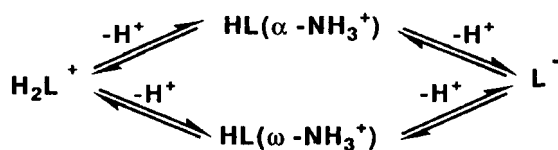
At pH 7-8 the basic amino acids (Arg, Lys, and Orn) are present in aqueous solution as monopositive ions with the protonated α-amino and ω-amino or guanidinium group and the deprotonated α-carboxylate group. For convenience the protonated ω-basic group is denoted as X^+ and the monopositive ion as H_2L^+:

$$X^+ \!\!-\!\!-\!\!CH\!\!-\!\!-\!\!COO^- \qquad (H_2L^+)$$
$$\underset{NH_3^+}{|}$$
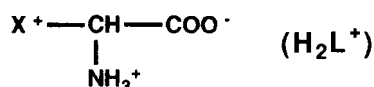
where L refers to the fully deprotonated form of the amino acid. The carboxylate group is protonated at low pH (<2), giving the fully protonated form, H_3L^{2+}, and at high pH (>10) the species HL and L^- become predominant. The protonation steps are described as follows (charges in metal complexes, equilibria, and equilibrium constants will be omitted hereafter for simplicity):

$$L + H \xrightleftharpoons{K_1} HL \qquad K_1 = \frac{[HL]}{[L][H]} \qquad (1)$$

$$HL + H \xrightleftharpoons{K_2} H_2L \qquad K_2 = \frac{[H_2L]}{[HL][H]} \qquad (2)$$

$$\xrightleftharpoons{K_3} H_3L \qquad K_3 = \frac{[H_3L]}{[H_2L][H]} \qquad (3)$$

In this formulation the equilibria are described as protonation reactions to give protonated amino acids and accordingly the equilibrium constants are stability constants. As is apparent from these equations, K_1, K_2, and K_3 are equal to the reciprocals of the respective acid dissociation constants (K_a). Since the K_1 and K_2 values of Lys and Orn are close to each other to within 2 log units, the following microscopic dissociations occur from the two amino groups (79M), and comparable steps are possible with Asp and Glu for the two carboxyl groups (79EG):

$$H_2L^+ \underset{-H^+}{\overset{-H^+}{\rightleftharpoons}} \begin{array}{c} HL(\alpha\text{-}NH_3^+) \\ HL(\omega\text{-}NH_3^+) \end{array} \underset{-H^+}{\overset{-H^+}{\rightleftharpoons}} L^-$$

The microscopic equilibria may be studied by methods such as nuclear magnetic resonance (NMR) spectroscopy (76SR,80SS), but because of the scarcity of the data, microscopic constants will not be discussed in this survey.

In weakly acid-weakly alkaline solution Arg, Lys, and Orn normally coordinate to a metal ion M through the α-amino and α-carboxylate groups with the side chain group protonated. For the majority of stability constants reported, the relevant complex formations are those between M and monoprotonated L, HL, and for convenience the successive stability constants treated in this survey are defined as follows:

$$M + HL \xrightleftharpoons{K_1'} M(HL)$$

$$M(HL) + HL \xrightleftharpoons{K_2'} M(HL)_2$$

$$\vdots$$

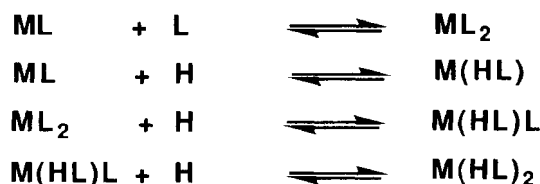$$M(HL)_{n-1} + HL \xrightleftharpoons{K_n'} M(HL)_n$$
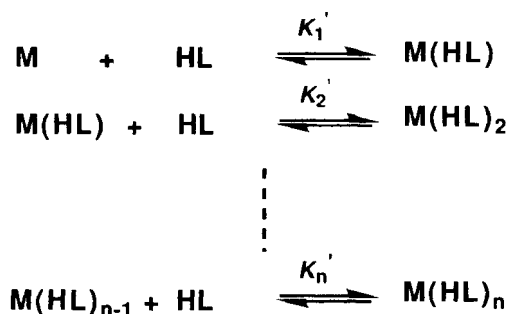
where $M(HL)$, $M(HL)_2$, etc. are protonated at the ω-basic group and release additional protons to give ML, $M(HL)L$, etc. The successive stability constants are related to the overall stability constants β as follows:

$$\beta = K_1' K_2' \cdots K_n'$$

When deprotonated complexes such as ML and $M(HL)L$ are formed, the relevant constants will be listed in the Tables with definition:

$$ML + L \rightleftharpoons ML_2$$

$$ML + H \rightleftharpoons M(HL)$$

$$ML_2 + H \rightleftharpoons M(HL)L$$

$$M(HL)L + H \rightleftharpoons M(HL)_2$$

The latter three equilibria correspond to the protonation of L's coordinated to M.

Stability constants K_n are related to the standard free energy change ΔG^0 by $\Delta G^0 = -RT \ln K_n$ at a constant pressure. Hence, the enthalpy change ΔH^0 can be determined not only by calorimetry but also from the temperature dependence of K_n values determined (e.g. by potentiometry) according to the van't Hoff equation:

$$\frac{d(\ln K)}{dT} = \frac{\Delta H^0}{RT^2}$$

The thermodynamic parameters obtained by the latter method are generally less accurate than those determined by calorimetry which measures directly the heat liberated upon complex formation. This is due to the experimental difficulty of determining the stability constants accurately over a wide range of temperature; the temperature variation of the constants is often small, and the temperature dependence of ΔH^0 which may not be negligible over the temperature range.

1.3 Criteria of Evaluation

Determination of stability constants depends on a number factors, the most important of which are the experimental conditions, the purity of materials used, experimental and computational methods, and the species considered in the computation. Therefore, the stability constants reported in the literature have been evaluated in this survey on the basis of the following considerations according to the guidelines presented by IUPAC (77B).

(1) Experimental methods

A number of methods are known for determining stability constants (87C). Because protons and metal ions compete for the donor groups of the amino acids, complex formation is investigated most accurately and conveniently by pH-metry, and for the acidic and basic amino acids surveyed most of the stability constants have been determined by this method. Various other electrochemical methods such as polarography and electrophoresis, methods such as spectrophotometry and NMR spectrometry which is effective for determining the microscopic constants, calorimetry, ion exchange technique, etc. have been used but rather infrequently.

The guidelines for determining stability constants by pH-metry have been published from IUPAC (82NT), and the experimental technique as well as the recommeded procedure for testing the potentiometric apparatus has also been described (87BO). Although high precision is attainable by pH-metry, reliable stability constants can only be obtained by the proper use of precision apparatus and proper data treatment. These problems, and other experimental methods and evaluation of data, have been treated in a monograph by Beck et al. (90BN).

(2) Conditions of measurements

Since temperature affects the equilibrium constants, it should be maintained constant. Although only stability constants expressed in terms of the activities of relevant species are thermodynamically meaningful, concentration or stoichiometric constants using concentration terms are useful for practical purpose because experiments can not be carried out at near infinite dilution. Most stability constants have been determined at constant ionic strength (I), usually with $I = 0.1$-1.0. It is then possible to compare the constants determined under similar conditions by different research groups. When determining concentration constant, ionic strength should be kept much higher than the concentrations of reacting species in order to keep the activity coefficients constant. The supporting electrolytes should be those which do not react with metal ions and complexes, or with the components of the filling solutions of electrodes.

Maintaining an inert atmosphere, e.g. N_2, during measurements is also important; metal ions and complexes formed may be oxidized by O_2, and carbon dioxide affects the pH values.

(3) Purity of reactants

Impure materials seriously affect the experimental data whether they are reactive or not, so that the chemicals used should be of analytical grade. Water, which is by far the most abundant reagent, should be thoroughly distilled and deionized. Reliability of the reported constants depends greatly on the purity of reactants, which may be a major reason for differences between reported values under similar conditions.

(4) Calibration of the apparatus

pH meters are probably the most frequently used apparatus, and their calibration is of prime importance for the reliability of the results. They are usually calibrated by standard buffer solutions such as NBS buffers (73B,84S). Calibration can also be done by using solutions of known hydrogen ion concentrations at a constant ionic strength. As described above in (2), measurements are usually made at a constant ionic strength, and the quantities of the species present are expressed in terms of concentration. However, the reading (pH_m) of the pH meter calibrated by standard buffer solutions and the liquid junction potential ΔE_j are related to the hydrogen ion activity a_H,

$$pa_H = pH_m + \Delta E_j,$$

so that the constants for proton complexes calculated from pH_m are therefore 'mixed' (M) constants and not 'concentration' (C) constants, e.g.

$$K_1^M = \frac{[HL]}{10^{-pH_m}[L]}$$

where the superscript M denotes that the constant is a mixed constant. It has to be mentioned, however, that only the hydrogen ion concentration, [H], can be used in the mass balance equation even when mixed ligand constants are calculated. There are several methods of converting the pH meter reading into [H] (87BO). At $I = 0.1$-0.5 the difference A defined as

$$A = pH_m - (-\log [H]/mol \ dm^{-3})$$

is in the range 0.02-0.07 (91SZ). In many reports in the literature, it is not clear whether the constants are concentration constants or mixed constants.

(5) Calculation of stability constants

Prior to treatment of experimental data by graphical methods or computer techniques, it is necessary to describe the complex formation by considering all possible species, and for this purpose the use of chemical and spectroscopic information supporting the presence of relevant species, and preferably their structures, is strongly recommended, especially when ligands have alternative donor groups. There are frequently used programs such as SCOGS (68S), MINIQUAD (74SV), and SUPERQUAD (85GS), which efficiently calculate stability constants from potentiometric data. A critical comparison of these programs has been made (86CT). Other programs including those for spectrophotometric data are also available (85L). It should be emphasized that erroneous use of computer programs may lead to false values and false conclusions. It is important, therefore, that the species and relevant stability constants obtained adequately describe the metal-ligand interactions under the experimental conditions.

All the literature values of proton and metal complexes were checked in terms of the above criteria. Agreement between values which were determined carefully under similar conditions by several research groups indicates that the values are reliable. The 'recommended' (R) value was obtained as the average of each set of reliable values under respective conditions. Stability constants for certain species have been described as 'tentative' (T) when they were carefully determined but there were no other reported values. Other values were evaluated informative (I) or doubtful (D) or were rejected (Rj) on the basis of the evaluation criteria. In spite of recent interest in mixed ligand complexes, the number of the stability constants reported for those complexes containing acidic and basic amino acids was too small to allow reasonable evaluation, and no attempt has been made to treat such systems critically.

1.4 Abbreviations Used in the Tables

The stability constants are expressed as stepwise constants, K_1, K_2, K_3, etc. in log units with standard deviations in parentheses whenever available, and constants for reactions such as protonation of metal complexes are listed after definition, e.g.

$$\frac{[\ M(HL)\ ]}{[ML][H]} = 8.90(4)$$

For the values determined in water, the 'Medium' column shows the ionic strength in mol dm^{-3} with the background electrolyte indicated in parentheses; 'var' refers to the medium without a constant ionic strength, and it was left blank when information is lacking. Solvents other than water are indicated by name and composition. The constants for proton complexes are classified as M (mixed) or C (concentration) whenever it was possible to identify the conditions. The amino acids investigated may be in the L-, D-, or DL-forms, and the constants for L-enantiomers and those not specified are shown without indicating the forms. The forms are shown before the constants only when D-enantiomers, both L- and D-enantiomers, or racemic mixtures were used.

Methods of determination are abbreviated as follows:
H: pH-metry (hydrogen electrode)
gl: pH-metry (glass electrode)
red: potentiometry (redox electrode)
pol: polarography
cal: calorimetry
nmr: NMR spectrometry
sp: spectrophotometry
elph: electrophoresis
ix: ion exchange
extr: solvent extraction
dis: distribution between two phases

In the cases where an additional method was used, it is indicated by '+' added to the method, e.g., gl+cal and gl+oth. The base dissociation constants, pK_b, reported for certain proton complexes were converted to the stability constants and are listed as K_n/K_w where K_w refers to the ion product of water.

2. Arginine (2-Amino-5-guanidinopentanoic acid, H_2L)

Arginine has a strongly basic guanidinium group at the δ-carbon which is protonated at pH<10 with very high log K_1 (>12.0) and is not involved in metal binding except in a few cases. In acid and weakly alkaline solution it behaves as a dibasic acid, where the two protons dissociate from the α-carboxylato and α-amino groups with the log K_3 and log K_2 values of about 2.0 and 9.0, respectively. A glycine-like coordination in complexes is denoted as M(HL), which on deprotonation of the guanidinium group gives the fully deprotonated complex ML.

2.1 Stability Constants of Proton Complexes

The literature values of the protonation constants of Arg are summarized in Table 1. Because of the measurements at high pH values where the linearity of the glass electrode response is unsatisfactory, it is rather difficult to give a reliable value of K_1 of Arg. Early data (30BH,35L) were obtained for 0.01-0.1 M Arg solutions or for unspecified solutions (30SA), whose concentration varied with addition of base, and other values (52A,53P,59DG,86HG) were obtained at low I values which were insufficient for maintaining a constant ionic background. Although the log K_2 and log K_3 values reported for 17-40 °C (60P) are within the reasonable range, no inert salt was used for the ionic background, and they were rejected.

Regarding the protonation of the guanidinium group, there is a wide discrepancy between the reported values; Noszal and Kassai-Tánczos (90NK) reported the macroscopic constant log K_1 to be 15 and the microscopic constants to be in the range 14.7-15.0 at 25.0 °C and $I = 1.0$. Other values for log K_1 are low in comparison with these, and the underestimation was ascribed to the lack of standard buffer solutions at high pH and errors in pH measurements with glass electrodes. The reported values thus range from 11.4 to 15 depending on the conditions, and not many stability constants are reported at 25 °C and $I = 0.1$. Four values of log K_1, 11.5 (70CM), 12.07 (76BP), 12.11 (78SY), and 11.58 (89AP), come into consideration, and comparison among the values and information from earlier values indicate that the values 11.5 and 11.58 are too low. The average of two careful determinations (76BP,78SY), i.e. 12.09(2), may be recommended, but from the above considerations it could still be too low. Therefore, it is better classified as tentative under the limited information available at present. There are only two log K_1 values (76PS,78BH) at higher ionic strengths; the values 12.28(6) (M(?), $I = 1.0$) and 13.80 ($I = 3.0$) were determined with reasonable care and may also be considered tentative together with the log K_2 and log K_3 values. The log K_2 values reported for 25 °C and $I = 0.1$ (70CM,76BP,78SY,83AD,89AP) were determined under well defined conditions and are in good agreement with each other except the value of 9.36 (70CM) for which an erroneous slope of electrode response is suspected. The average of the concentration constants (76BP,78SY,83AD), 9.02(4), is recommended. The mixed constants log K_2 and log K_3 (89AP) are well within the accepted range, but the log K_1 value of 11.58 is too low. The log K_3 values reported at 25 °C and $I = 0.1$ are 1.96 (76BP), 2.02 (83AD), and 2.22 (89AP), of which the first two from the same groups cited for log K_2 agree with each other and are averaged to give the recommended value of 1.99(3). Some determinations were made under physiological conditions at 37 °C and $I = 0.15$ (81A2,82NS); considering the temperature dependence of the constants (59DG,60P) and the difference between the concentration and mixed constants, agreement between the values from the two groups is satisfactory, and the averaged concentration constants log $K_2 = 8.79(2)$ and log $K_3 = 2.05(3)$ are recommended.

The stability constants reported for temperatures other than 25 °C and/or for higher ionic strengths (52LD,53TS,58P,75PT,76PS,78BH,85PN) vary considerably, and it is difficult to make any evaluation. The constants obtained in nonaqueous solution (88GK) and aqueous alcohol (85PN) are informative for studies in similar media.

Recommended and tentative values under various conditions are listed in Table 2.

2.2 Stability Constants of Metal Complexes

Arginine forms complexes with various metal ions normally by a glycine-like coordination with the side-chain guanidinium group protonated, e.g. M(HL), M(HL)$_2$, etc. The stability constants reported for Arg are listed in Table 3 in the alphabetical order of metal ions. While the constants for the 3d metal ions such as Cu^{II} and Zn^{II} have been reported by more than two groups of investigators, those for the typical metal ions and lanthanoid ions are too scarce for critical survey on comparative basis. The coordination by Arg at acid-neutral pH is essentially the same as that of glycine (Gly), so that the stability constants for Gly (91KS) often serve as references for the purpose of comparison.

The stability constants for Ag^I have been reported by three groups (59DG, 60P, 81PU). Although the values obtained at 0-50 °C (59DG) were determined at a low ionic strength (0.023) which is not sufficient for

TABLE 1.   Stability Constants of the Proton Complexes of Arginine (Literature Values)

Method	Temp. / °C	Medium / mol dm^{-3}	Type of constant	Log of equilibrium constant, remark	Ref
H	17	0.1 (Arg)	M	$K_1 > 13.2$, K_2 9.29, K_3 2.17	30BH
H	23	0.1 (Arg)	M	K_1 13.2, K_2 9.09, K_3 2.18	30BH
H	25		M	K_1 12.48, K_2/K_w 4.96, K_3/K_w 11.99	30SA
H	0		M	K_1 13.31, K_2/K_w 5.15, K_3/K_w 12.70	30SA
H	30	0.01 (Arg)	C	K_2 8.91	35L
H	25	➤ 0	C	K_2 9.012, K_3 1.807	40BS
gl	20	0.01 (Arg)	M	K_1 12.48, K_2 9.08, K_3 2.17	52A
gl	25	0.1 (NaCl)	M	K_2 9.07, K_3 2.10	52E
gl	25	1.0 (KNO$_3$)	M	K_2 9.04	52LD
gl	19	0.01 (Arg)	M	K_2 9.11	53P
gl	25.15	0.15(KNO$_3$)	M	K_2 9.11	53TS
gl	25	➤ 0	M	K_2 8.99	53TS
gl	20	1.0 (NaClO$_4$)	M	K_2 9.21, K_3 2.19	58P
gl	0	0.023	C	K_2 9.74	59DG
gl	10	0.023	C	K_2 9.41	59DG
gl	20	0.023	C	K_2 9.13	59DG
gl	30	0.023	C	K_2 8.87	59DG
gl	40	0.023	C	K_2 8.65	59DG
gl	50	0.023	C	K_2 8.46	59DG
gl	5-55	0.024	C	K_2 -434.9/T+12.654-0.023694T	59DG
gl	17	0.05 (Arg)	?	K_2 9.27, K_3 1.98	60P
gl	25	0.05 (Arg)	?	K_2 9.05, K_3 1.98	60P
gl	30	0.05 (Arg)	?	K_2 8.92, K_3 1.97	60P
gl	35	0.05 (Arg)	?	K_2 8.80, K_3 1.97	60P
gl	40	0.05 (Arg)	?	K_2 8.67, K_3 1.97	60P
gl	25	0.1(NaClO$_4$)	C	K_1 12.48, K_2 9.03, K_3 2.11	68IC
gl	25	0.1 (KNO$_3$)	C	K_1 11.5, K_2 9.36	70CM
gl	25	0.15(NaClO$_4$)	M?	K_2 8.92(2), K_3 2.02(2)	75PT
gl	25	0.1 (KNO$_3$)	C	K_1 12.07(2), K_2 9.02(2), K_3 1.96(1)	76BP
gl	25	1.0 (KNO$_3$)	?	K_1 12.28(6), K_2 9.27(1), K_3 2.21(1)	76PS
gl	25	3.0 (NaClO$_4$)	C	$K1$ 13.80, K_2 9.83, K_3 2.76	78BH
gl	25	0.1 (KNO$_3$)	C	K_1 12.11(1), K_2 9.07(1)	78SY
gl	37	0.15(NaClO$_4$)	C	K_2 8.781(3), K_3 2.024(1)	81A2
nmr	27	0.2(Arg)	M	K_2 8.9(1), K_3 2.2(1)	81PB
gl	30	0.1(KNO$_3$)	?	K_1 10.70(7), K_2 8.52(4), K_3 1.07(3)	81PU
gl	37	0.15(NaClO$_4$)	M	K_1 11.43(5), K_2 8.79(2), K_3 2.08(3)	82NS
gl	25	0.1 (KNO$_3$)	C	K_2 8.97(2), K_3 2.02(3)	83AD
pol	30	0.5 (KNO$_3$)	M?	K_2 9.05	85PN
		0.5 (KNO$_3$) 20%methanol	M?	K_2 9.20	
		0.5 (KNO$_3$) 40%methanol	M?	K_2 9.35	
		0.5 (KNO$_3$) 20%ethanol	M?	K_2 9.20	
		0.5 (KNO$_3$) 40%ethanol	M?	K_2 9.65	
elph	25		M	K_2 8.919	86HG
elph	35	0.1(H/NaClO$_4$)	M	K_1 12.00, K_2 9.00, K_3 2.00	88BY
gl	25	acetic acid	M	$K_{2(?)}$ 0.76	88GK
gl	25	90%CH$_3$CN -CH$_3$COOH	M	$K_{1(?)}$ 2.24, $K_{2(?)}$ 0.48	88GK

TABLE 1. (continued)

Method	Temp. / °C	Medium / mol dm^{-3}	Type of constant	Log of equilibrium constant, remark	Ref
gl	25	0.1 (NaNO$_3$)	M	K_1 11.58(2), K_2 8.98(2), K_3 2.22(2)	89AP
gl	25	0.3 (KCl)	C	K_2 9.28, K_3 2.20	90NK
		0.5 (KCl)	C	K_2 9.25, K_3 2.23	
		1.0 (KCl)	C	K_2 9.30, K_3 2.18	
		1.5 (KCl)	C	K_2 9.36, K_3 2.20	
		2.0 (KCl)	C	K_1 15, K_2 9.30, K_3 2.17	

TABLE 2. Recommended (R) and Tentative (T) Values of the Protonation Constants of Arginine*

Type of Constant	Medium / mol dm^{-3}	Temp. / °C	log K_1	log K_2	log K_3	Evaluation
C	0.1 (KNO$_3$)	25	12.09±0.02			T
M	0.1 (KNO$_3$)	25		9.02±0.04	1.99±0.03	R
C	0.15(NaClO$_4$)	37		8.79±0.02	2.05±0.03	R
M(?)	1.0 (KNO$_3$)	25	12.28±0.06	9.27±0.01	2.21±0.01	T
C	3.0 (NaClO$_4$)	25	13.80	9.83	2.76	T

* The standard deviations refer to the variances among the values averaged and are not a measure of precision.

maintaining a constant background, they are comparable with those for Gly (91KS) and the effect of I may be small because there is no changes in the charge upon complex formation. These values are therefore considered as informative. The other values were obtained at I unspecified and 17°C and at I = 0.1 and 30 °C. However, the sequence log K_1 > log K_2 is contrary to the other values and seems doubtful, and the constants for Ag(H$_2$L), Ag(H$_2$L)$_2$, AgL, and AgL$_2$ which are formed at low and high pH, respectively, are also doubtful, because the values for the former two species are irregular and the latter two are considered to suffer from serious errors in pH measurements at very high pH.

There is only a single constant for Al^{III} (60P), Be^{II} (53P), Cr^{III} (63KM), Ga^{III} (78BH), Pb^{II} (60P), Y^{III} (70RP) and the lanthanoids Dy^{III}, Eu^{III}, Nd^{III}, Pr^{III}, Sm^{III}, and Tb^{III} (81PB), and no comparison is possible. The log K_1K_2 value for Be^{II} is rejected, because hydrolysis of Be^{II} should have been taken into consideration in the calculation of constants and the ionic strength is insufficient. The values for the lanthanoids (0.9-1.7) which were determined by an NMR spectroscopic method (81PB) are much smaller than the K_1 values of the corresponding Gly complexes (91KS), and from the experimental conditions they are considered to refer to conditional stability constants at pD 4.5 where formation of M(H$_2$L) from M and H$_2$L is the predominant process. Therefore, they are merely regarded as being informative. For Ce^{III} a potentiometric study is reported (70RP), and the value is classified as tentative. The constants for Al^{III} and other metal ions from 60P are rejected due to the absence of constant ionic strengths, while those for Cr^{III} (63KM) are doubtful because the slow reaction between Cr^{III} and Arg might have not reached completion under the conditions employed. The log K_1 value reported for Y^{III} (70RP) may be too low, but no comparison is possible. There are two sets of values for Ca^{II} (66H,70CM), but the definition of stability constants in 66H is not clear from the description, and they are rejected. The Cd^{II} complexes were studied by three groups (53P,60P,79PG). The value determined under insufficient ionic strength (53P) is rejected. Log K_1 of 5.00 (79PG) appears to be too high when compared with the other results. On the other hand, no evaluation can be made for the constants for Hg^{II} complexes (53P,70CM,73LB,83HD), which differ from each other by several orders of magnitude. When Hg^{II} is used as HgCl$_2$ as in 70CM, mixed complexes containing Cl$^-$ and Hg^{II} could be present. The values from 73LB appear to be comparable with those for the

TABLE 3. Stability Constants for the Metal Complexes of Arginine (Literature Values)*

Metal Method	Temp. / °C	Medium / mol dm^{-3}	Evaluation	Log of equilibrium constant, remark	Ref
Ag^I					
gl	0	0.023	I	K_1' 3.65, K_2' 4.18	59DG
	10	0.023	I	K_1' 3.36, K_2' 4.03	59DG
	20	0.023	I	K_1' 3.37, K_2' 3.71	59DG
	30	0.023	I	K_1' 3.04, K_2' 3.62	59DG
	40	0.023	I	K_1' 3.02, K_2' 3.32	59DG
	50	0.023	I	K_1' 2.91, K_2' 3.36	59DG
			I	K_1' 3855.2/T-18.452+0.029208T	59DG
			I	K_1' 4898.35/T-23.905+0.037321T	59DG
gl	17		Rj	K_1' 4.12, K_2' 3.95	60P
gl	30	0.1	D	K_1' 3.18(7), K_2' 2.71(1)	81PU
			D	[M(H$_2$L)]/[M][H$_2$L] 0.36(6)	
			D	[M(H$_2$L)$_2$]/[M(H$_2$L)][H$_2$L] 2.11(2)	
			D	[ML]/[M][L] 4.72(4)	
			D	[ML$_2$]/[ML][L] 2.22(1)	
Al^{III}					
gl	17		Rj	K_1' 6.67, K_2' 6.38	60P
	25		Rj	K_1' 6.63, K_2' 6.23	60P
Be^{II}					
gl	19	0.005 BeSO$_4$	Rj	$K_1'{\cdot}K_2'$ 12.4	53P
Ca^{II}					
gl	25	0.7 (KCl)	Rj	K_1' 0.61	66H
	37	0.7 (KCl)	Rj	K_1' 0.61	66H
gl	25	0.1 (KNO$_3$)	I	K_1' 2.21	70CM
Cd^{II}					
gl	19	0.005 CdSO$_4$	Rj	$K_1'{\cdot}K_2'$ 6.7	53P
gl	17		Rj	K_1' 3.31, K_2' 3.30	60P
	25		Rj	K_1' 3.27, K_2' 3.18	60P
	30		Rj	K_1' 3.25, K_2' 3.11	60P
	35		Rj	K_1' 3.22, K_2' 3.03	60P
	40		D	K_1' 3.19, K_2' 2.96	60P
pol	30	1 (NaClO$_4$)	D	K_1' 5.00, K_2' 2.39, K_3' 2.00	79PG
Ce^{III}					
gl	20	0.1(KCl)	T	K_1' 2.7	70RP
nmr	27	0.2	I	K_1' 1.2(3)	81PB
Co^{II}					
gl	20	0.01	I	$K_1'{\cdot}K_2'$ 7.40	52A
gl	25	0.15(KNO$_3$)	T	K_1' 3.87, K_2' 3.20, K_3' 2.08	53TS
gl	17		Rj	K_1' 3.79, K_2' 3.10, K_3' 2.10	60P
	30		Rj	K_1' 3.73	60P
	35		Rj	K_1' 3.70	60P
	40		Rj	K_1' 3.68, K_2' 2.95, K_3' 2.00	60P
gl	25	0.1 (KNO$_3$)	T	K_1' 4.02, K_2' 3.22	70CM
gl	25	0.1 (KNO$_3$)	T	K_1' 3.855(8), K_2' 3.06(2), K_3' 2.41(9) 76B	
ix	-15?	0.5 (Na-/HClO$_4$)	Rj	K_1' 3.2(3), K_2' 0.3(3)	87MG
Cr^{III}					
gl	25	~0.5 (KCl)	D	K_1' 8.0, K_2' 6.1, K_3' 5.2	63KM

TABLE 3. (continued)

Metal Method	Temp. / °C	Medium / mol dm^{-3}	Evaluation	Log of equilibrium constant, remark	Ref
Cu^{II}					
gl	20	0.01	I	$K_1' \cdot K_2'$ 13.90	52A
pol	25	0.06(KH$_2$PO$_4$)	I	$K_1' \cdot K_2'$ 13.74	52LD
gl	17		Rj	K_1' 7.53, K_2' 6.54	60P
	25		Rj	K_1' 7.34, K_2' 6.42	60P
	30		Rj	K_1' 7.23, K_2' 6.32	60P
	35		Rj	K_1' 7.12, K_2' 6.23	60P
	40		Rj	K_1' 7.02, K_2' 6.14	60P
gl	25	0.1 (KNO$_3$)	I	K_1' 7.93, K_2' 6.64	70CM
gl	25	0.1 (KNO$_3$)	I	[M(HL)] / [MLH(OH)][H] 7.5	70CM
			T	[ML] / [M][L] 11.9	
			T	[ML(HL)] / [ML$_2$][H] 11	
gl	25	0.15(NaClO$_4$)	T	K_1' 7.49(6), K_2' 6.10(2)	75PT
gl	25	0.1 (KNO$_3$)	R	K_1' 7.555(4), K_2' 6.452(5)	76BP
sp	25	1 (KNO$_3$)	T	K_1' 7.84 (1), K_2' 6.57 (1)	76PS
			T	[ML(HL)] / [ML$_2$][H] 12.88(1)	
			T	[M(HL)$_2$] / [ML(HL)][H] 12.07(1)	
gl	25	0.1 (KNO$_3$)	T	K_1' 7.44(6), K_2' 6.25(8)	78SY
gl	37	0.15(NaClO$_4$)	D	K_1' 7.71(17), K_2' 7.54(13)	82NS
gl	25	0.1 (KNO$_3$)	T	K_1' 7.49(1), K_2' 6.34(1)	83AD
pol	30	0.5 (KNO$_3$)	D	K_1' 9.30, K_2' 3.45	85PN
		0.5 (KNO$_3$) 20%methanol	D	K_1' 9.48, K_2' 3.60	
		0.5 (KNO$_3$) 40%methanol	D	K_1' 10.30, K_2' 3.35	
		0.5 (KNO$_3$) 20%ethanol	D	K_1' 9.70, K_2' 3.73	
		0.5 (KNO$_3$) 40%ethanol	D	K_1' 10.85, K_2' 3.06	
gl	25	0.1 (KNO$_3$)	T	K_1' 7.49, K_2' 6.34	86DA
ix	-15?	0.5 (Na-/HClO$_4$)	Rj	K_1' 5.4(4), K_2' -0.1(4)	87MG
gl	25	0.1 (NaNO$_3$)	T	K_1' 7.44(1), K_2' 6.39(1)	89AP
Dy^{III}					
nmr	27	0.2	I	K_1' 1.7(3)	81PB
Eu^{III}					
nmr	27	0.2	I	K_1' 0.9(3)	81PB
Fe^{II}					
gl	20	0.01	I	K_1' 3.20	52A
gl	17		Rj	K_1' 3.29	60P
	25		Rj	K_1' 2.86	60P
ix	-15?	0.5(Na-/HClO$_4$)	Rj	K_1' 3.0(3), K_2' 0.3(3)	87MG
Fe^{III}					
red	20	1.0 (NaClO$_4$)	I	K_1' 8.7	58P
gl	25		Rj	K_1' 7.67, K_2' 7.53	60P
Ga^{III}					
gl	25	3.0 (NaClO$_4$)	I	K_1' 8.60	78BH
			I	[M(HL)] / [ML][H] 11.4	
			I	[M(H$_2$L)] / [M(HL)][H] 6.7	

TABLE 3. (continued)

Metal Method	Temp. / °C	Medium / mol dm^{-3}	Evaluation	Log of equilibrium constant, remark	Ref
Hg^{II}					
gl	19	0.005 (Hg(NO$_3$)$_2$)	D	$K_1' \cdot K_2'$ 17.4	53P
gl	25	0.1 (KNO$_3$)	D	K_1' 5.34, K_2' 4.87	70CM
emf	25	0.1 (NaNO$_3$)	I	K_1' 11.5, K_2' 7.3	73LB
ix	25	0.125(Na$_2$SO$_4$) 0.02856M acetate+ diethyl barbiturate	D	K_1' 3.65	83HD
Mg^{II}					
gl	25		I	K_1' 1.30	60P
gl	25	0.1 (KNO$_3$)	T	K_1' 2.21	70CM
Mn^{II}					
gl	20	0.01	Rj	K_1' 2.00	52A
gl	25		Rj	K_1' 2.64, K_2' 1.94	60P
	40		Rj	K_1' 2.60, K_2' 1.90	60P
gl	25	0.1 (KNO$_3$)	T	K_1' 2.55	70CM
ix	-15?	0.5(Na-/HClO$_4$)	Rj	K_1' 2.7(3), K_2' 0.1(3)	87MG
Nd^{III}					
nmr	27	0.2	I	K_1' 1.2(3)	81PB
Ni^{II}					
gl	20	0.01	I	$K_1' \cdot K_2'$ 9.2	52A
gl	17		Rj	K_1' 4.98, K_2' 4.32, K_3' 3.21	60P
	25		Rj	K_1' 4.92, K_2' 4.20, K_3' 3.08	60P
	30		Rj	K_1' 4.86, K_2' 4.14, K_3' 3.03	60P
	35		Rj	K_1' 4.83, K_2' 4.10, K_3' 2.93	60P
	40		Rj	K_1' 4.77, K_2' 4.04, K_3' 2.85	60P
gl	25	0.1 (KNO$_3$)	T	K_1' 5.18, K_2' 4.31	70CM
gl	25	0.1 (KNO$_3$)	R	K_1' 4.99(1), K_2' 4.02(1), K_3' 3.16(2) [M(HL)$_3$] / [ML(HL)$_2$][H] 10.76(2)	76BP
ix	-15?	0.5 (Na-/HClO$_4$)	Rj	K_1' 4.0(3), K_2' 0.5(3)	87MG
Pb^{II}					
gl	17		Rj	K_1' 4.65, K_2' 4.03	60P
	25		Rj	K_1' 4.06, K_2' 3.36	60P
	40		Rj	K_1' 3.89, K_2' 3.19	60P
Pr^{III}					
nmr	27	0.2	I	K_1' 1.3(3)	81PB
Sm^{III}					
nmr	27	0.2	I	K_1' 1.2(3)	81PB
Tb^{III}					
nmr	27	0.2	I	K_1' 1.3(3)	81PB
Y^{III}					
gl	20	0.1 (KCl)	I	K_1' 3.2	70RP
Zn^{II}					
gl	20	0.01	I	$K_1' \cdot K_2'$ 7.8	52A
gl	19	0.005 ZnSO$_4$	Rj	$K_1' \cdot K_2'$ 8.0	53P

TABLE 3. (continued)

Metal Method	Temp. / °C	Medium / mol dm^{-3}	Evaluation	Log of equilibrium constant, remark	Ref
gl	17		Rj	K_1' 4.20, K_2' 3.99	60P
	25		Rj	K_1' 4.19, K_2' 3.93	60P
	35		Rj	K_1' 4.16, K_2' 3.84	60P
	40		Rj	K_1' 4.14, K_2' 3.81	60P
gl	25	0.1 (KNO$_3$)	T	K_1' 4.11, K_2' 3.96	70CM
gl	37	0.15(NaClO$_4$)	T	K_1' 4.074(5), K_2' 3.809(6)	81A2
ix	-15?	0.5(Na-/HClO$_4$)	Rj	K_1' 3.5(3)	87MG

* K_n' refers to the successive stability constant for M(HL)$_n$.

Gly complexes (91KS). The log K_1 value from 83HD is not reliable because only ML was considered at pH 7.8.

The 3d metal ions Co^{II}, Cu^{II}, Fe^{II}, Fe^{III}, Mn^{II}, Ni^{II}, and Zn^{II} have been investigated in addition to Cr^{III} mentioned above. In the titration of Co^{II}, care should be taken to avoid aerobic oxidation to Co^{III} whose solution chemical properties are very different. The value determined at a low ionic strength (52A) is taken as informative. Those at I = 0.15 (53TS) and 0.1 (70CM,76BP) are within a relatively narrow range, but the values in 76BP have been determined with care and seem to be reliable. Because of the high log K_2 value of the proton complex in 70CM, the constants reported there are shifted to higher values. Two close sets of values (53TS,76BP) are averaged to give the constants at I = 0.1-0.15 (log K_1 = 3.86; log K_2 = 3.12; log K_3 = 2.25). The ion exchange method is not so precise as potentiometry, and since log K_2 of 0.3 at -15 °C (?) is definitely too low, this set of constants was rejected. Cu^{II} is by far the most studied of all Arg complexes. Of the values determined at I = 0.1-0.15 (70CM,75PT,76BP,78SY,83AD,86DA), those in 70CM are too high and this set was eliminated from comparison for the same reasons as described for Co^{II}. The same values are reported in 86DA as in 83AD, but it is not clear whether the equilibria were reinvestigated. These two sets of values are therefore better taken to have the same origin. The log K_1 and log K_2 values in 75PT, 76BP, 78SY, 83AD, and 89AP are in the range 7.44-7.555 and 6.10-6.45, respectively, which are averaged to give 7.48(4) and 6.31(12). Formation of deprotonated complexes ML(HL) are reported in 70CM and 76PS under different conditions and taken as informative or tentative. The value of 7.5 reported for protonation of ML in 70CM is too low for the guanidinium group and is therefore inferred to be due to protonation of the hydroxo complex M(LH)(OH). The earlier determinations (52A, 52LD) are regarded as informative because of the conditions employed. The data from 82NS are doubtful, because the experimental procedures are not described in detail and log K_2 is too high. The same conclusion is reached for the constants determined by the polarographic method in water and in water-alcohol mixture (85PN). For the same reason as given for Co^{II} the low values from 87MG are rejected. No reliable data are available for Fe^{II}, and the two sets of data for Fe^{III} are only informative in the absence of any other data for comparison. For Mn^{II}, the reported values are either rejected or informative, because the values are at variances and too low (52A, 87MG). The only remaining value of 2.55 (70CM) may be taken as informative. Ni^{II} forms a tris-complex M(HL)$_3$ with Arg (60P, 76BP). The values obtained at 25 °C and I = 0.1 (70CM, 76BP) may be compared, but those from 76BP are carefully determined and reliable. The other determination (52A) is' informative and the data from 87MG are rejected for the same reason as described above. Zn^{II} has been studied by several groups, but the value from 53P is rejected due to the low background concentration, and that from 52A is informative. Two sets of constants determined under different conditions (70CM, 81A2) are considered reliable from the experimental procedures except the high K_2 for the proton complex in 70CM, and in the absence of other comparable data they are classified as tentative.

3. Lysine (2,6-Diaminohexanoic acid, H$_2$L)

Lysine is also a basic amino acid giving rise to proteins with an additional amino group at the ε-carbon. The log K_1 value (~11) of the proton complexes is a little lower than that of Arg but is high enough to maintain the positive charge in proteins. Lys is a dibasic acid in acid-neutral solution, as is Arg, but the ε-

amino group of metal-coordinated Lys such as in $M(HL)_2$ dissociates to give $ML(HL)$ and ML_2 at pH > 9. Fully deprotonated Lys, L, coordinates to metal ions essentially as a substituted Gly (79M).

3.1 Stability Constants of Proton Complexes

Protonation steps for Lys at the ε- and α-amino groups are not completely separated. In terms of the first and second protonations, Lys with the deprotonated α-amino and protonated ε-amino groups predominates over Lys with the protonated α-amino and deprotonated ε-amino groups (79M). The stability constants of the proton complexes of Lys hitherto reported are summarized in Table 4. Early data (30SA,35L,52A,53P) were eliminated from evaluation because of insufficient background salt concentrations and lack of information.

At I = 0.1-0.2 and 25 °C the values from 52E, 76BP, 78GF, 78SY, 81FG, 84DA (86DA), and 89RV reasonably agree with each other and seem to be reliable from the experimental procedures of determination. These seven sets of data are averaged to give log K_1 = 10.71(8) and log K_2 = 9.19(9), and the average of six sets of data for log K_3 is 2.16(3). Satisfactory agreement of the constants for the L- and D-enantiomers has been shown in 52E. In this connection the DL-form was reported to have a slightly lower K_1 and K_2 values (65NC). Among the constants at higher ionic strengths those at I = 0.2-0.5 (89RV), I = 1.0 (75NM), and I = 3.0 (78BH) seem to be reliable, but in the absence of other data, they were evaluated as tentative. The only values under physiological conditions of I = 0.15 and 37 °C (81A1) were determined carefully and for the same reason are evaluated as tentative. On the other hand, a number of mixed stability constants were determined by potentiometry (32G,52LD,71SL,73BJ,80KH,80SG,88GK). There is no satisfactory agreement between the values of 32G and 72HM (I = 0.1, 25 °C), and the values from 68H are too low. The mixed constants of 71SL and 73BJ (I = 1.0, 25 °C) agree well with each other, but they are lower than the concentration constants determined under the same conditions (75NM). The overlapping protonation steps relevant to K_1 and K_2 should be separated by calculation by an appropriate method. Therefore, the data which involve only the K_2 value (52LD,79FM,80SG,84PB,86FD,86HG,88GK) should suffer from serious errors and are doubtful. The values from 80KH are much lower than the others. The stability determinations in acetic acid and 90 %CH_3CN-CH_3COOH (88GK) are merely informative.

The NMR spectral methods give information on the microscopic equilibria, and the microscopic constants (76SR) and the ratio of the ω-protonated to the α-protonated species (80SS) are informative. However, the pH meter reading in D_2O was not corrected in these and other (80IO,83NT) NMR experiments, and the results should be used with caution.

Recommended and tentative values under various conditions are summarized in Table 5.

TABLE 4.   Stability Constants of the Proton Complexes of Lysine (Literature Values)

Method	Temp. / °C	Medium / mol dm^{-3}	Type of constant	Log of equilibrium constant, remark	Ref
H	25	var?	M	K_1 10.53, K_2/K_w 5.05, K_3/K_w 11.82	30SA
H	0	var?	M	K_1 11.31, K_2/K_w 5.13, K_3/K_w 12.74	30SA
H	25	0.1(H-/Na Cl)	M	K_1 10.53, K_2 8.94, K_3 2.17	32G
H	30	0.01(Lys)	C	K_1 10.56, K_2 9.11	35L
gl	20	0.01(Lys)	M	K_1 10.72, K_2 9.18, K_3 2.18	52A
gl	25	0.1 (NaCl)	C	L-form K_1 10.79, K_2 9.18, K_3 2.16	52E
			C	D-form K_1 10.81, K_2 9.16, K_3 2.15	
gl	25	1.0 (KNO$_3$)	M?	K_2 8.95	52LD
gl	20	0.01(Lys)	M	DL-form K_2 9.03	53P
gl	25	0.1 (NaClO$_4$)	C	DL-form K_1 10.54, K_2 9.06	65NC
gl	20	0.1 (KNO$_3$)	M	K_1 10.47, K_2 9.13	68HL
gl	25	1.0 (KNO$_3$)	M	K_1 10.56, K_2 9.05, K_3 2.23	71SM
gl	25	0.1 (KCl)	M	K_1 10.902, K_2 9.116	72HM
	37	0.1 (KCl)	M	K_1 10.546, K_2 8.801	
	50	0.1 (KCl)	M	K_1 10.162, K_2 8.510	
gl	25	1.0 (NaNO$_3$)	M	K_1 10.53, K_2 8.95, K_3 2.18	73BJ
gl	25	1.0 (NaClO$_4$)	C	K_1 10.965(4), K_2 9.476(4), K_3 2.42(1)	75NM

TABLE 4. (continued)

Method	Temp. / °C	Medium / mol dm^{-3}	Type of constant	Log of equilibrium constant, remark	Ref
gl	25	0.1 (KNO$_3$)	C	K_1 10.669(1), K_2 9.139(1), K_3 2.20(1)	76BP
nmr	25	var (0.2-0.4)	M	K_1 10.82, K_2 9.27	76SR
				microscopic constant:	
				[H$_2$L] / [(HL)(α-NH$_2$)][H] 9.31	
				[H$_2$L] / [(HL)(ω-NH$_2$)][H] 10.30	
				[(HL)(α-NH$_2$)] / [L][H] 10.78	
				[(HL)(ω-NH$_2$)] / [L][H] 9.79	
gl	25	3.0 (NaClO$_4$)	C	K_1 11.58, K_2 9.96, K_3 2.77	78BH
gl+cal	25	0.1 (KCl)	C	K_1 10.66, K_2 9.20, K_3 2.15	78GF
gl	25	0.1 (KNO$_3$)	C	K_1 10.85(1), K_2 9.14(1)	78SY
gl	25	50%EtOH-H$_2$O		K_2 9.02	79FM
nmr	27	1(NaCl)D$_2$O	M	K_1 10.91, K_2 9.31	80IO
gl	35	0.1 (KNO$_3$)	M?	K_1 9.36, K_2 8.13	80KH
gl	30	1.0 (KNO$_3$)	M	K_2 8.95	80SG
nmr	40	var D$_2$O	M	K_1 11.17, K_2 9.38, K_3 1.87	80SS
		10~20%Lys	M	microscopic constant:	
				[(HL)(ω-NH$_2$)] / [(HL)(α-NH$_2$)] 0.83	
gl	37	0.15(NaClO$_4$)	C	K_1 10.296(2), K_2 8.887(1), K_3 2.147(3)	81A1
gl+cal	25	0.2 (KCl)	C	K_1 10.66, K_2 9.20, K_3 2.15	81FG
nmr	25	var	M	K_1 11.55, K_2 9.6, K_3 2.25	83NT
gl	25	0.1 (KNO$_3$)	C	K_1 10.60(2), K_2 9.10(2), K_3 2.10(4)	84DA
gl	25	0.1 (KNO$_3$)	C	K_2 9.06	84PB
gl	25	0.1 (KNO$_3$)	C	K_2 9.10, K_3 2.10	86DA
	25			K_2 9.18	86FD
elph	25		M	K_2 9.127	86HG
gl	25	acetic acid	M	$K_{2(?)}$ 0.78	88GK
gl	25	90%CH$_3$CN -CH$_3$COOH	M	$K_{1(?)}$ 2.37, $K_{2(?)}$ 0.59	88GK
gl	25	0.5(KNO$_3$)	C	K_1 11.21(2), K_2 9.49(3), K_3 2.53(4)	89RV
	25	0.3(KNO$_3$)	C	K_1 10.89(1), K_2 9.43(3), K_3 2.31(3)	
	25	0.2(KNO$_3$)	C	K_1 10.72(2), K_2 9.40(3), K_3 2.20(2)	
	25	0.1(KNO$_3$)	C	K_1 10.75(2), K_2 9.39(3), K_3 2.17(3)	
	25	0.05(KNO$_3$)	C	K_1 10.77(2), K_2 9.39(3), K_3 2.17(2)	
	25	0.025(KNO$_3$)	C	K_1 10.80(1), K_2 9.41(2), K_3 2.17(2)	

TABLE 5. Recommended (R) and Tentative (T) Values of the Protonation Constants of Lysine*

Type of Constant	Medium / mol dm^{-3}	Temp. / °C	log K_1	log K_2	log K_3	Evaluation
C	0.1-0.2	25	10.71±0.08	9.19±0.09	2.16±0.03	R
C	0.3	25	10.89±0.01	9.43±0.03	2.31±0.03	T
C	0.5	25	11.21±0.02	9.49±0.03	2.53±0.04	T
C	1.0	25	10.97±0.01	9.47±0.01	2.42±0.01	T
C	0.15	37	10.30±0.01	8.89±0.01	2.15±0.01	T

* The standard deviations refer to the variances among the values averaged and are not a measure of precision.

3.2 Stability Constants of Metal Complexes

Lysine binds metal ions through the α-amino and α-carboxylate groups in the glycine mode to form complexes of monoprotonated Lys, $M(HL)_n$, in acid-neutral solution. As compared with the guanidinium group of Arg, the ε-ammonium group is *ca.* 10-times more easily deprotonated but is not involved in metal binding in solution, because chelation through the two amino groups would result in an unstable eight-membered ring. The stability constants for Lys complexes are shown in Table 6 in alphabetical order.

Each of the typical metal ions Al^{III} (80KH), Ba^{II} (89S), Be^{II} (53P), Ca^{II} (66H), Ga^{III} (80KH), and Sb^{III} (86JS) has been studied by only one group, and the data are very limited. The stability constant for Ba^{II} is rejected because of low precision and lack of essential data on experimental conditions. As described in the Arg section, hydrolysis should be taken into account for calculation of the constants for Be^{II}, and the same is true for Al^{III}. For this reason, and because of the insufficient ionic strength, the value for Be^{II} is rejected. The values for Al^{III} and Ga^{III} are from the same source (80KH), where the constants for the proton complexes are too low (*vide supra*), and the protonation constants for the metal complexes are doubtful due to hydrolysis occurring in the pH range studied. The data on Ca^{II} (66H) show no temperature dependence, and it is doubtful if the value refers to the N,O-chelation and if such a weak complex can be studied by potentiometry. In this connection the values reported for Sr^{II} by 86JS and 89S are unreasonably large as compared

TABLE 6. Stability Constants for the Metal complexes of Lysine (Literature Values)*

Metal Method	Temp. / °C	Medium / mol dm⁻³	Evaluation	Log of equilibrium constant, remark		Ref
Al^{III}						
gl	35	0.1 (KNO₃)	D	K_1' 6.13(3)		80KH
				[M(HL)] / [ML][H] 7.44(1)		
Ba^{II}						
gl		0.1 BaCl₂	Rj	K_1' 7.664		89S
Be^{II}						
gl	20	0.005 BeSO₄	Rj	$K_1' \cdot K_2'$ 11.4		53P
Ca^{II}						
gl	25	0.7 (KCl)	D	K_1' 0.72		66H
	37	0.7 (KCl)	D	K_1' 0.72		66H
Cd^{II}						
gl	20	0.005 CdSO₄	Rj	$K_1' \cdot K_2'$ 5.8		53P
gl	20	0.1(NaClO₄)	Rj	K_1' 7.80		83S
	30	0.1(NaClO₄)	Rj	K_1' 7.60		
	40	0.1(NaClO₄)	Rj	K_1' 6.90		
pol	30	1.0 (KNO₃)	I	K_1' 3.70, K_2' 3.20, K_3' 2.05	86CG	
Ce^{III}						
gl	20	0.1 (KCl)	T	K_1' 2.6		70RP
nmr	27	0.2	I	K_1' 1.2(3)		81PB
Co^{II}						
gl	20	var	I	$K_1' \cdot K_2'$ 6.8		52A
gl	25	1.0(KNO₃)	T	K_1' 3.62, K_2' 3.06		71SL
gl	25	0.1(KNO₃)	R	K_1' 3.836(4), K_2' 3.232(8), K_3' 2.38(5)		
						76BP
			T	[M(HL)₃] / [ML(HL)₂][H] 9.9(1)		
			T	[M(HL)₂] / [ML(HL)][H] 9.91(4)		
			T	[M(HL)] / [ML][H] 6.05(2)		
Cr^{III}						
gl	25	~0.5 (KCl)	D	DL-form K_1' 8.1, K_2' 6.2, K_3' 5.3		63KM

TABLE 6. (continued)

Metal Method	Temp. / °C	Medium / mol dm^{-3}	Evaluation	Log of equilibrium constant, remark		Ref
Cu^{II}						
gl	20	var	I	$K_1' \cdot K_2'$ 13.7		52A
pol	25	0.1	I	$K_1' \cdot K_2'$ 13.6	52LD	
gl	25	0.1(NaClO$_4$)	I	DL-form $K_1' \cdot K_2'$ 13.90	65NC	
gl	25	1.0(NaClO$_4$)	T	K_1' 8.080(8), K_2' 6.841(5)	75NM	
			T	[M(HL)$_2$] / [ML(HL)][H] 10.361(5)		
			T	[ML(HL)] / [ML$_2$][H] 10.84(1)		
gl	20	0.1 (KNO$_3$)	I	K_1' 7.56, K_2' 6.46		68HL
gl	25	0.1 (KNO$_3$)	R	K_1' 7.62(2), K_2' 6.49(2)		76BP
			R	[M(HL)$_2$] / [ML(HL)][H] 9.93(2)		
			R	[ML(HL)] / [ML$_2$][H] 10.47(2)		
gl+cal	25	0.1 (KCl)	R	K_1' 7.61, K_2' 6.41		78GF
			T	[M(HL)$_2$] / [ML(HL)][H] 10.361(5)		
			T	[ML(HL)] / [ML$_2$][H] 10.84(1)		
gl	25	0.1 (KNO$_3$)	R	K_1' 7.62(1), K_2' 6.32(1)		78SY
			R	[M(HL)$_2$] / [ML(HL)][H] 10.08		
			R	[ML(HL)] / [ML$_2$][H] 10.51		
gl	30	1.0 (KNO$_3$)	D	K_1' 7.40, K_2' 6.30		80SG
gl	37	0.15(NaClO$_4$)	I	K_1' 7.69(1), K_2' 6.52(2)	81BK	
			I	[M(HL)$_2$] / [ML(HL)][H] 9.17(4)		
			I	[M(HL)] / [ML][H] 7.14(7)		
			Rj	[M(H$_2$L)] / [M(HL)][H] 2.66(5)		
gl	25	0.1 (KNO$_3$)	R	K_1' 7.60(2), K_2' 6.53(3)		84DA
			R	[M(HL)$_2$] / [ML(HL)][H] 9.79(5)		
			R	[ML(HL)] / [ML$_2$][H] 10.41(9)		
gl	25	0.1 (KNO$_3$)	R	K_1' 7.65(4), K_2' 6.44(4)		84PB
gl	25	0.1 (KNO$_3$)	R	K_1' 7.60, K_2' 6.41		86DA
			I	[M(HL)$_2$] / [ML$_2$][H]^2 20.2		
pol	30	1.0 (KNO$_3$)	D	K_1' 7.40, K_2' 6.30		88SK
Fe^{II}						
gl	20	var	I	K_1' 4.5		52A
gl	15	1.0 (KNO$_3$ or KCl)	Rj	K_1' 5.76 , K_2' 2.87		86JS
	30	1.0 (KNO$_3$ or KCl)	Rj	K_1' 5.14 , K_2' 2.65		
Ga^{III}						
gl	35	0.1 (KNO$_3$)	D	K_1' 6.56(4)	80KH	
			D	[M(HL)] / [M(HL)(OH)][H] 6.51(1)		
Hg^{II}						
gl	20	0.1(NaClO$_4$)	Rj	K_1' 8.00, K_2' 5.95		83S
	30	0.1(NaClO$_4$)	Rj	K_1' 7.94, K_2' 5.80		
	40	0.1(NaClO$_4$)	Rj	K_1' 7.35, K_2' 5.28		
Mn^{II}						
gl	20		Rj	K_1' 2.18		52A
Ni^{II}						
gl	20	var	I	$K_1' \cdot K_2'$ 8.8		52A
gl	25	1.0(NaNO$_3$)	D	K_1' 5.47, K_2' 3.53, K_3' 1.98		73BJ
gl	25	0.1(KNO$_3$)	R	K_1' 4.931(8), K_2' 4.22(1), K_3' 2.89(2)		76BP

TABLE 6. (continued)

Metal Method	Temp. / °C	Medium / mol dm^{-3}	Evaluation	Log of equilibrium constant, remark	Ref
			I	$[M(HL)_3] / [ML(HL)_2][H]$ 9.79(3)	
			I	$[M(HL)_2] / [ML(HL)][H]$ 10.06(5)	
			I	$[M(HL)] / [ML][H]$ 9.85(7)	
			I	$[ML(HL)] / [ML_2][H]$ 10.09(1)	
gl+cal	25	0.2 (KCl)	R	K_1' 4.84, K_2' 4.06, K_3' 2.79	81FG
			I	$[M(HL)_3] / [ML(HL)_2][H]$ 10.12	
			I	$[ML(HL)_2] / [ML_2(HL)][H]$ 10.37	
			I	$[ML_2(HL)] / [ML_3][H]$ 10.87	
			I	$[M(HL)_2] / [ML(HL)][H]$ 9.84	
Sr^{II}					
gl	15	1.0 (KNO$_3$ or KCl)	Rj	K_1' 5.25 , K_2' 2.99	86JS
	30	1.0 (KNO$_3$ or KCl)	Rj	K_1' 5.16 ?, K_2' 2.73	
gl			Rj	K_1' 7.968	89S
Sb^{III}					
gl	15	1.0 (KNO$_3$ or KCl)	D	K_1' 3.08 , K_2' 2.86	86JS
	30	1.0 (KNO$_3$ or KCl)	D	K_1' 2.35 , K_2' 3.20	
Th^{IV}					
gl	20	0.1(NaClO$_4$)	D	K_2' 8.50, K_3' 8.20, K_4' 5.00	86S
	30	0.1(NaClO$_4$)	D	K_2' 8.52, K_3' 8.25, K_4' 5.69	
	40	0.1(NaClO$_4$)	D	K_2' 8.60, K_3' 8.29, K_4' 5.99	
UO$_2$^{II}					
gl	20	0.1(NaClO$_4$)	D	K_1' 7.90, K_2' 7.00	86S
	30	0.1(NaClO$_4$)	D	K_1' 7.80, K_2' 6.90	
	40	0.1(NaClO$_4$)	D	K_1' 7.71, K_2' 6.00	
Y^{III}					
gl	20	0.1 (KCl)	I	K_1' 3.1	70RP
Zn^{II}					
gl	20	var	I	$K_1' \cdot K_2'$ 7.6	52A
gl	20	0.005 ZnSO$_4$	Rj	$K_1' \cdot K_2'$ 7.3	53P
gl	37	0.15(NaClO$_4$)	T	K_1' 4.09(1), K_2' 3.83(1)	81A1
			T	$[M(HL)_2] / [ML(HL)][H]$ 8.66(3)	
gl+cal	25	0.2 (KCl)	T	K_1' 4.06, K_2' 3.47	81FG
			T	$[M(HL)_2] / [ML(HL)][H]$ 9.15	
			T	$[M(HL)] / [ML$ or $M(HL)(OH)][H]$ 8.40	
gl	20	0.1(NaClO$_4$)	Rj	K_1' 8.92, K_2' 4.50	83S
	30	0.1(NaClO$_4$)	Rj	K_1' 8.40, K_2' 4.2	
	40	0.1(NaClO$_4$)	Rj	K_1' 7.40, K_2' 3.80	

* K_n' refers to the successive stability constant for M(HL)$_n$.

with the values for some 3d metal ions and should therefore be rejected. These results, and the erroneous calculation of thermodynamic parameters in 86JS, made the reliability of the constants for Fe^{II}, Sb^{III}, Th^{IV}, and UO_2^{II} from the same source doubtful, and the values for Fe^{II} which are higher than those for Gly (91KS) were rejected. Although no objective evaluation is possible with the constants for Hg^{II}, the precision of experiments by 83S does not warrant the claimed accuracy and that for Zn^{II}, and both were rejected. Ce^{III} was studied by two groups (70RP,81PB), but their evaluation is the same as with the Arg complex.

Among the 3d metal ions reported, Cu^{II} is the most extensively studied. The overall constants (52A,52LD,65NC) are classified as informative in the presence of many other data. The constants determined at $I = 0.1$ and 25 °C (76BP,78GF,78SY,84DA,84PB,86DA) are in good agreement and are taken to be reliable. They were averaged to give $\log K_1 = 7.62(2)$ and $\log K_2 = 6.43(7)$. Protonation of ML_2 has been described in the reliable data from three groups (76BP,78SY,84DA), the averages being 10.49(7) and 9.95(12) for the first and second protonation constants, respectively. Of the values determined under other conditions, those at $I = 1.0$ and 25 °C (75N) and at $I = 1.0$ and 30 °C (80SG,88SK) may be compared. There are differences of 0.5-0.7 log unit between the two sets of data. The former set was carefully determined and includes K_1, K_2, and the protonation constants with variances. They are therefore classified as tentative. The $\log K_1$ and $\log K_2$ values from 80SG and 88SK were evaluated as doubtful, because both values are lower than those of 75NM and are exactly the same in spite of the different methods of determination, and no description on the protonation constants was made. The constants determined under physiological conditions (I = 0.15 and 37 °C) were carefully determined (81BK), but due to lack of other data they could not be evaluated comparatively. Here the protonation constant for ML(HL) is much lower than that at $I = 0.1$ and 25 °C, and the value for ML of 7.14(7) is probably due to protonation of ML(OH). Formation of $M(H_2L)$ is hardly conceivable for Cu^{II} having a high affinity for N donors and is accordingly rejected. Three sets of data (52A,71SL,76BP) at different conditions have been reported for Co^{II}, but no comparison can be made due to the different experimental conditions. However, the values from 76BP including K_1, K_2, and the protonation constants were determined with care, and therefore evaluated as recommended, while those from 71SL are classified as tentative. With Cr^{III} the reported values are again doubtful because of the slow reaction, and the difficulty of maintaining the pH meter stability over a long period of time. There is no reliable value for Fe^{II} and Mn^{II}.

Ni^{II} can form up to the tris complex, and the Lys complexes were studied in detail. The values from 76BP and 81FG were well determined, and the $\log K_1$, $\log K_2$, and $\log K_3$ values were averaged to be 4.89(5), 4.14(8), 2.84(5), respectively, as recommended values. The protonation reactions of ML_3 etc. occur in a narrow pH range, so that analysis of the equilibria leaves some ambiguities. The reported constants for them were accordingly classified as informative. The equilibria of Zn^{II} complexes were studied by several groups (52A,53P,81A1,81FG,83S), but the data from 52A, 53P and 83S were eliminated for reasons described earlier. The $\log K_1$ and $\log K_2$ values at $I = 0.2$ and 25 °C (81FG) and $I = 0.15$ and 37 °C (81A1) seem to be reliable and are classified tentative in the absence of comparable data. The difference between the $\log K_2$ values of 0.36 is rather large for the temperature difference of 12 °C. Lastly, the constant for Y^{III} can not be evaluated due to lack of information.

4. Ornithine (2,5-Diaminopentanoic acid, H_2L)

Ornithine is not a constituent of proteins but is involved in the urea cycle forming urea in terrestrial vertebrates. It has two amino groups at the α- and δ-carbons, whose basicity is nearly comparable with that of Lys. Unlike Lys, however, it forms a chelate with a metal ion by coordinating through the two amino groups upon deprotonation from $M(HL)_n$ in alkaline solution.

4.1 Stability Constants of Proton Complexes

Protonation of the amino groups of Orn occurs predominantly at the δ-amino group as described for Lys, so that the microscopic equilibrium is shifted toward the form with the deprotonated α-amino and protonated δ-amino groups in weakly alkaline solution (79M). Table 7 shows the stability constants of the proton complexes of Orn. As with Arg and Lys, the stability constants determined at an insufficient ionic strength (52A,53P,54R) were eliminated from evaluation. The ionic strength of 0.02 in 75S may be too low, and the results were classified as informative. There are five sets of data obtained at $I = 0.1$-0.2 and 25 °C (32G,70CM,72HM,76BP,81FG(82FH), 84DA), two of which are mixed constants (32G,72HM) and the averaged values may be reliable. However, the difference due to concentration and mixed constants is not straightforward, and in the absence of additional data these are classified as tentative. The remainder are concentration constants, which are similar to each other and are regarded as reliable. The averages of $\log K_1$, $\log K_2$, and $\log K_3$, 10.56(9), 8.82(9), and 1.92(13), respectively, are recommended. There are only three

sets of data at $I = 1.0$. Those at 25 °C (58P) and 20 °C (59P) are both mixed constants; the value from the latter was evaluated as informative because it lacks the K_1 and K_2 values, whereas the former values, as well as the concentration constants from 70CM, may be classified as tentative. The only values determined at $I = 0.15$ and 37 °C (81NS) for the DL-form seem reliable, but due to lack of other information they are evaluated as tentative. Results from measurements in organic solvents (88GK), and log K_2 from electrophoresis (86HG), are merely informative.

Table 8 lists the recommended and tentative values under various conditions.

TABLE 7.   Stability Constants of the Proton Complexes of Ornithine (Literature Values)

Method	Temp / °C	Medium / mol dm^{-3}	Type of constant	Log of equilibrium constant, remark		Ref
H	25	0.1(H/Na Cl)	M	K_1 10.76, K_2 8.65, K_3 1.94		32G
H	25	→ 0	C	K_1 10.755, K_2 8.690, K_3 1.705		40BS
gl	20	0.01(Orn)	M	K_1 10.73, K_2 8.62, K_3 1.94		52A
gl	20	0.01(Orn)	M	K_1 10.73, K_2 8.75		53P
gl	25	var		K_1 10.67, K_2 8.65, K_3 1.98		54R
gl	25	1.0(NaClO$_4$)	M	K_1 10.59, K_2 8.93, K_3 2.11		58P
gl	20	1 (KCl)	M	K_2 8.93		59P
gl	25	0.1 (KNO$_3$)	C	K_1 10.73, K_2 8.98	70CM	
		1.0 (KNO$_3$)	C	K_1 10.46, K_2 8.58		
gl	25	0.1 (KCl)	M	K_1 10.770, K_2 8.739	72HM	
gl	25	0.02(NaCl)	C	K_1 10.506(12), K_2 8.70(1)		75SP
gl	25	0.1 (KNO$_3$)	C	K_1 10.521(1), K_2 8.752(1), K_3 1.75(1)		76BP
gl	25	0.2 (KCl)	C	L/D-form K_1 10.52, K_2 8.83, K_3 2.07		81FG
gl	37	0.15(NaClO$_4$)	C	DL-form		81NS
				K_1 10.22(1), K_2 8.63(2), K_3 2.14(4)		
gl	25	0.2 (KCl)	C	L/D-form K_1 10.52, K_2 8.83, K_3 2.07		82FH
gl	25	0.1 (KNO$_3$)	C	K_1 10.48(2), K_2 8.73(2), K_3 1.94(4)		84DA
elph	25		M	K_2 8.712		86HG
gl	25	acetic acid	M	$K_{2(?)}$ 0.69		88GK
gl	25	90%CH$_3$CN -CH$_3$COOH	M	$K_{1(?)}$ 2.29, $K_{2(?)}$ 0.32		88GK

TABLE 8.   Recommended (R) and Tentative (T) Values of the Protonation Constants of Ornithine[*1]

Type of Constant	Medium / mol dm^{-3}	Temp. / °C	log K_1	log K_2	log K_3	Evaluation
C	0.1-0.2	25	10.56±0.09	8.82±0.09	1.92±0.13	R
M	0.1	25	10.77±0.01	8.69±0.05		T
C	1.0	25	10.46	8.58		T
M	1.0	25	10.59	8.93	2.11	T
C	0.15	37	10.22±0.01	8.63±0.02	2.14±0.04	T[*2]

[*1] The standard deviations refer to the variances among the values averaged and are not a measure of precision.
[*2] DL-Ornithine.

4.2 Stability Constants of Metal Complexes

When the δ-amino group is deprotonated, Orn readily forms a seven-membered chelate ring through the two amino groups. Structural changes due to conversion of the glycine mode of coordination to the above Orn mode occurs e.g. with Cu^{II} when the pH of the solution is raised above 9. The stability constants of Orn complexes are listed in Table 9.

Be^{II} (53P), Ca^{II} (70CM), Hg^{II} (70CM), In^{III} (81SB), Mg^{II} (70CM), and Pb^{II} (81SB) are the typical metal ions investigated. The overall constant reported to Be^{II} was again rejected because serious errors are suspected when hydrolysis of Be^{II} was not considered. The values for Mg^{II}, Ca^{II}, and Hg^{II} (70CM) are regarded as informative in the absence of relevant data for comparison. Polarographic determinations of the stability constants for In^{III} and Pb^{II} were made by the same group (81SB). However, the pH of the solution and the protonation constants of Orn are lacking, and the order of the magnitudes of the constants, which is normally $K_1 > K_2 > \cdots$ is irregular. Under these circumstances, the values for In^{III} and Pb^{II} were rejected.

The 3d metal ions Co^{II}, Cu^{II}, Ni^{II}, and Zn^{II} have been studied by more than four groups. For Co^{II} the values at variable ionic strength (52A,54R) are regarded merely as informative. Those determined at $I = 0.02$ and 25 °C (75SP) are classified as informative due to the low ionic strength used. Among the values reported for Co^{II}, those at $I = 0.1$ and 25 °C (76BP) are considered reliable from the precision of measurements and by comparison with the Gly complex. Similar data (70CM) support the validity of the values from 76BP. The log K_1 and log K_2 values were therefore recommended, while the protonation constants for ML_2 etc. are regarded as tentative due to lack of sufficient data. The constants for Cu^{II} at $I = 0.1-0.2$ and 25 °C have been reported by 70CM, 76BP, 78SY, and 82FH. Log K_1 and the protonation constant of ML_2 from 70CM are too high in comparison with the others, and in addition the protonation constant for ML probably corresponds to the protonation of ML(OH). The data for $I = 1.0$ of 70CM are informative. The three carefully determined sets of data (76BP, 78SY, 82FH) are close to each other and are recommended, the averages being log $K_1 = 7.37(6)$ and log $K_2 = 6.15(3)$. Analysis of the protonation steps in 78SY and 82FH gave acceptable protonation constants, but the agreement was unsatisfactory, and these are therefore classified as tentative. Under physiological conditions ($I = 0.15$ and 37 °C), Cu^{II} complexes of DL-Orn were reported to have similar stabilities to those described above, but the protonation constant was much lower. For this reason this set of data was classified as informative from limited information.

The complexes of Ni^{II} can assume various forms, such as M(HL), M(HL)$_2$, M(HL)$_3$, and ML(HL)$_2$. Two groups (76BP,81FG) described the protonation and complexation reactions in detail. Since the values from both groups agree well with each other, they are evaluated as recommended except for some protonation constants. There are a variety of stability constants for Zn^{II}. Determination at low (53P) and variable (52A,54R) ionic strengths were rejected or classified as informative. By comparison with other measurements, the values reported in 81FG seem reliable for $I = 0.1-0.2$ and 25 °C, and those from 70CM are regarded as tentative. Zn^{II} was also studied at $I = 0.15$ and 37 °C for equilibria in blood serum, but again in the absence of data for comparison the values were taken to be informative. The data available for Fe^{II}, Fe^{III}, and Mn^{II} are so scarce that evaluation is almost meaningless; they are at best tentative.

Of the available constants for Cd^{II}, the overall constant (53P) is rejected due to the low ionic strength, and the other values are merely informative.

TABLE 9. Stability Constants for the Metal Complexes of Ornithine (Literature Values)*

Metal Method	Temp. / °C	Medium / mol dm^{-3}	Evaluation	Log of equilibrium constant, remark	Ref
Be^{II}					
gl	20	0.005 BeSO$_4$	Rj	$K_1' \cdot K_2'$ 11.7	53P
Ca^{II}					
gl	25	0.1 (KNO$_3$)	I	K_1' 1.52	70CM
		1.0 (KNO$_3$)	I	K_1' 1.68	
Cd^{II}					
gl	20	0.005 CdSO$_4$	Rj	$K_1' \cdot K_2'$ 6.1	53P
gl	25	var	I	K_1' 3.70, K_2' 2.70	54R

TABLE 9. (continued)

Metal Method	Temp. / °C	Medium / mol dm^{-3}	Evaluation	Log of equilibrium constant, remark	Ref
gl	25	1.0	I	K_1' 3.41, K_2' 2.41	54R
Co^{II}					
gl	20	var	I	$K_1' \cdot K_2'$ 6.3	52A
gl	25	var	I	K_1' 4.02, K_2' 2.90	54R
gl	25	0.1 (KNO$_3$)	T	K_1' 3.54, K_2' 3.33	70CM
			T	[M(HL)] / [ML][H] 9.0	
		1.0 (KNO$_3$)	T	K_1' 3.52, K_2' 2.80	
gl	25	0.02(NaCl)	I	K_1' 3.48(6), K_2' 2.96(6)	75SP
			I	[M(HL)] / [ML][H] 10.1(1)	
gl	25	0.1 (KNO$_3$)	R	K_1' 3.647(5), K_2' 3.087(8)	76BP
			T	[M(HL)$_2$] / [ML(HL)][H] 9.13(1)	
			T	[M(HL)] / [ML][H] 9.16(1)	
			T	[ML(HL)] / [ML$_2$][H] 10.16(1)	
Cu^{II}					
gl	20	var	I	$K_1' \cdot K_2'$ 13.0	52A
gl	25	var	D	K_1' 6.90, K_2' 5.55	54R
sp	25		Rj	K_2' 4.57	54R
gl	25	0.1 (KNO$_3$)	T	K_1' 7.87, K_2' 6.18	70CM
			D	[M(HL)] / [ML][H] 7.1	
			D	[M(HL)$_2$] / [ML(HL)][H] 8.53	
			D	[ML(HL)] / [ML$_2$][H] 11.06	
		1.0 (KNO$_3$)	I	K_1' 7.17, K_2' 6.14	
gl	25	0.1 (KNO$_3$)	R	K_1' 7.291(1), K_2' 6.115(1)	76BP
gl	25	0.1 (KNO$_3$)	R	K_1' 7.43(1), K_2' 6.18(1)	78SY
			R	[M(HL)$_2$] / [ML(HL)][H] 8.92	
			T	[ML(HL)] / [ML$_2$][H] 10.02	
gl	37	0.15(NaClO$_4$)	I	DL-form K_1' 7.45(2), K_2' 6.43(3)	81NS
			I	[M(HL)$_2$] / [ML(HL)][H] 8.20(6)	
gl	25	0.2 (KCl)	R	L/D-form K_1' 7.40, K_2' 6.16	82FH
			R	[M(HL)$_2$] / [ML(HL)][H] 9.20	
			T	[ML(HL)] / [ML$_2$][H] 9.57	
Fe^{II}					
gl	20	var	I	K_1' 5.0	52A
gl	20	1.0 (KCl)	T	K_1' 3.09	59P
Fe^{III}					
gl	20	1.0 (NaClO$_4$)	I	K_1' 8.7	58P
Hg^{II}					
gl	25	0.1 (KNO$_3$)	I	K_1' 4.83, K_2' 4.32	70CM
		1.0 (KNO$_3$)	I	K_1' 4.52, K_2' 3.29	
In^{III}					
pol	30	0.1 (NaClO$_4$)	Rj	DL-form K_1' 1.78, K_2' 1.56, K_3' 1.86	81SB
	40	0.1 (NaClO$_4$)	Rj	DL-form K_1' 1.30, K_2' 2.08, K_3' 1.69	
Mg^{II}					
gl	25	0.1 (KNO$_3$)	T	K_1' 1.54	70CM
		1.0 (KNO$_3$)	T	K_1' 1.71	

TABLE 9. (continued)

Metal Method	Temp. / °C	Medium / mol dm⁻³	Evaluation	Log of equilibrium constant, remark	Ref
Mn^{II}					
gl	20	var	Rj	K_1' <2	52A
gl	25	0.1 (KNO$_3$)	D	K_1' 1.60	70CM
Ni^{II}					
gl	20	var	I	$K_1' \cdot K_2'$ 8.3	52A
gl	25	var	I	K_1' 4.85, K_2' 3.89	54R
gl	25	0.1 (KNO$_3$)	D	K_1' 4.72, K_2' 4.34	70CM
			D	[M(HL)] / [ML][H] 8.69	
			T	[M(HL)$_2$] / [ML(HL)][H] 8.10	
			Rj	[ML(HL)] / [ML$_2$][H] 10.49	
		1.0 (KNO$_3$)	I	K_1' 4.44, K_2' 3.68	
gl	25	0.1 (KNO$_3$)	R	K_1' 4.734(8), K_2' 4.00(1), K_3' 2.99(4)	76BP
			R	[M(HL)$_3$] / [M(HL)$_2$L][H] 9.20(7)	
			T	[M(HL)$_2$L] / [M(HL)L$_2$][H] 9.56(9)	
			T	[M(HL)L$_2$] / [ML$_3$][H] 10.17(4)	
			R	[M(HL)$_2$] / [ML(HL)][H] 8.32(1)	
			R	[ML(HL)] / [ML$_2$][H] 9.43(1)	
			R	[M(HL)] / [ML][H] 8.142(9)	
gl	25	0.2 (KCl)	R	K_1' 4.52, K_2' 3.79, K_3' 2.84	81FG
			R	[M(HL)$_3$] / [M(HL)$_2$L][H] 9.26	
			R	[M(HL)$_2$] / [ML(HL)][H] 8.40	
			R	[ML(HL)] / [ML$_2$][H] 9.27	
			R	[M(HL)] / [ML][H] 8.21	
Pb^{II}					
pol	30	0.1(NaClO$_4$)	Rj	DL-form K_1' 3.0, K_2' 1.74, K_3' 1.62, K_4' 1.21	81SB
	40	0.1(NaClO$_4$)	Rj	DL-form K_1' 3.0, K_2' 1.60, K_3' 1.60, K_4' 1.36	
Zn^{II}					
gl	20	var	I	$K_1' \cdot K_2'$ 6.9	52A
gl	20	0.005 ZnSO$_4$	Rj	$K_1' \cdot K_2'$ 7.6	53P
gl	25	var	I	K_1' 4.10, K_2' 3.20	54R
gl	25	0.1 (KNO$_3$)	T	K_1' 3.77, K_2' 2.67	70CM
		1.0 (KNO$_3$)	T	K_1' 3.60	
gl	37	0.15(NaClO$_4$)	I	K_1' 4.34(2), K_2' 3.05(11)	86NP
			I	[M(HL)] / [ML or M(HL)(OH)][H] 7.87(3)	
gl	25	0.2 (KCl)	R	K_1' 3.73, K_2' 3.08	81FG
			T	[M(HL)$_2$] / [ML(HL)][H] 8.54	
			T	[M(HL)] / [ML or M(HL)(OH)][H] 8.08	

* K_n' refers to the successive stability constant for M(HL)$_n$.

5. Thermodynamic Parameters of Proton and Metal Complexes

Investigations aiming at thermodynamic parameters are very rare among the equilibrium studies on basic amino acid complexes. Arg was studied only for the proton and Ag^I complexes, and Orn for In^{III}, Ni^{II}, and Pb^{II} complexes, by the temperature dependence of equilibrium constants. A number of measurements have been done on the proton and metal complexes of Lys both by calorimetry and by the temperature

dependence. The literature values of ΔH_n° and ΔS_n° and $\Delta H_n^{'\circ}$ and $\Delta S_n^{'\circ}$ for K_n and K_n', respectively, are listed in Table 10.

The reliability of the thermodynamic parameters is evaluated by the stability constants which have already been classified in the preceding sections, and Table 10 shows the reported parameters and the results of the evaluation. Because of the limited number of reported and recommended values, it is difficult to make a comparative study. The values for Arg are either informative or doubtful due to the low background salt concentration. The parameters for the proton complex of Lys were obtained by two groups (72HM,78GF) by potentiometry and calorimetry, but the signs of the derived entropy terms are opposite. Although reliable values were reported for the Cu^{II} and Ni^{II} complexes of Lys and the Ni^{II} complex of Orn, the data for the Cd^{II}, Fe^{II}, Hg^{II}, Sr^{II}, Sb^{III}, Th^{IV}, UO_2^{II}, and Zn^{II} complexes of Lys, and the In^{III} and Pb^{II} complexes of Orn are not reliable, because their stability constants themselves were rejected due to low precision or errors.

Studies on thermodynamic parameters are strongly recommended because of their importance in understanding the nature of the metal-ligand bonding and the interactions of complexes with molecular surroundings.

TABLE 10. Thermodynamic Parameters of the Proton and Metal Complexes of Basic Amino Acids (Arginine, Lysine, and Ornithine) (Literature Values)*

Amino Acid

Metal Method	Temp. °C	Medium	Evaluation	Thermodynamic parameters, remark ΔH° / kJ mol^{-1} ΔS° / kJ mol^{-1}	Ref
Arg					
H$^+$					
gl	5~55	0.023	I	ΔH_2° -43(3), ΔS_2° 28(9)	59DG
Ag^I					
gl	0~50	0.023	D	$\Delta H_1^{'\circ}$ -24(4), $\Delta S_1^{'\circ}$ -20(12)	59DG
			D	$\Delta H_2^{'\circ}$ -30(4), $\Delta S_2^{'\circ}$ 32(12)	
Lys					
H$^+$					
gl	25~50	0.1 (KCl)	D	ΔH_1° −54.6(2.1), ΔS_1° −26	72HM
			D	ΔH_2° −44.7(1.8), ΔS_2° −25	
gl+cal	25	0.1 (KCl)	R	ΔH_1° -53.55, ΔS_1° 24	78GF
			R	ΔH_2° -47.3, ΔS_2° 17	
			R	ΔH_3° -2.1, ΔS_2° 34	
Cd^{II}					
gl	20~40		Rj	K_2'/K_1' ΔH° -122.4 ΔS° -62.0	83S
Cu^{II}					
gl+cal	25	0.1 (KCl)	R	$\Delta H_1^{'\circ}$ -25.9, $\Delta S_1^{'\circ}$ 59	78GF
			R	$\Delta H_2^{'\circ}$ -51.4, $\Delta S_2^{'\circ}$ 96	
			R	$[M(HL)_2]/[ML(HL)][H]$ ΔH° 53.2, ΔS° -7	
			R	$[ML(HL)]/[ML_2][H]$ ΔH° 54.1,ΔS° -19	
Fe^{II}					
gl	15,30	1.0 (KNO$_3$ or KCl)	Rj	$\Delta H_1^{'\circ}$ -95.6?, $\Delta S_1^{'\circ}$ -240?	86JS
Hg^{II}					
gl	20~40		Rj	K_2'/K_1' ΔH° -205.0 ΔS° -99.0	83S

TABLE 10. (continued)

Amino Acid

Metal Method	Temp. °C	Medium	Evaluation	Thermodynamic parameters, remark $\Delta H°$ / kJ mol^{-1} $\Delta S°$ / kJ mol^{-1}	Ref
Ni^{II}					
gl+cal	25	0.2 (KCl)	R	$\Delta H_1^{'°}$ 18.8, $\Delta S_1^{'°}$ 32	81FG
			R	$\Delta H_2^{'°}$ 24.9, $\Delta S_2^{'°}$ -9	
			R	$\Delta H_3^{'°}$ 10.9, $\Delta S_3^{'°}$ 16	
Sr^{II}					
gl	15,30	1.0 (KNO$_3$ or KCl)	Rj	$\Delta H_1^{'°}$ 10.4, $\Delta S_1^{'°}$ 138	86JS
Sb^{III}					
gl	15	1.0 (KNO$_3$ or KCl)	Rj	$\Delta H_1^{'°}$ 8.9, $\Delta S_1^{'°}$ 192	86JS
Th^{IV}					
gl	20~40		Rj	$\Delta H_1^{'°}\Delta H_2^{'°}$ 5.86 $\Delta S^{'°}$ 43.7	86S
UO$_2$^{II}					
gl	20~40		Rj	$\Delta H_1^{'°}\Delta H_2^{'°}$ $\Delta H^{'°}$ -4.78 $\Delta S^{'°}$ -7.63	86S
Zn^{II}					
gl	20~40		Rj	K_2'/K_1' $\Delta H^{'°}$ -241.2 $\Delta S^{'°}$ -132.3	83S

Orn

Metal Method	Temp. °C	Medium	Evaluation	Thermodynamic parameters, remark	Ref
In^{III}					
pol	30,40	0.1(NaClO$_4$)	Rj	DL-form $\Delta H_1^{'°}$ -85.9, $\Delta S_1^{'°}$ -25	81SB
			Rj	$\Delta H_2^{'°}$ 6.8, $\Delta S_2^{'°}$ 86	
			Rj	$\Delta H_3^{'°}$ -22.8, $\Delta S_3^{'°}$ 23	
Ni^{II}					
gl	25	0.2 (KCl)	R	$\Delta H_1(Ni)^{'°}/\Delta H_1(H)°$ 20.2, $\Delta S_1(Ni)^{'°}/\Delta S_1(H)°$ 18	81FG
			R	$\Delta H_2(Ni)^{'°}/2\Delta H_1(H)°$ 16.2, $\Delta S_1(Ni)^{'°}/\Delta S_1(H)°$ 19	
			R	[M(HL)$_2$] / [ML(HL)][H] $\Delta H°$ 6.7, $\Delta S°$ 17	
			R	[M(HL)] / [ML][H] $\Delta H°$?, $\Delta S°$ 32	
			R	[ML(HL)] / [ML$_2$][H] $\Delta H°$ 13.3, $\Delta S°$ 20	
Pb^{II}					
pol	30,40	0.1(NaClO$_4$)	Rj	DL-form $\Delta H_1^{'°}$ 0.0, $\Delta S_1^{'°}$ 57	81SB
			Rj	$\Delta H_2^{'°}$ -24.9, $\Delta S_2^{'°}$ 8	
			Rj	$\Delta H_3^{'°}$ -28.4, $\Delta S_3^{'°}$ 27	
			Rj	$\Delta H_4^{'°}$ 5.5, $\Delta S_4^{'°}$ 161	

* $\Delta H_n^{'°}$ and $\Delta S_n^{'°}$ are the enthalpy and entropy changes, respectively, for the successive formation of M(HL)$_n$.

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