新型多氨-多酰氨配体和氨基酸的三元铜(Ⅱ)配合物

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合成 3 个多氨-多酰氨配体 1,12-二((α-羟甲基)苯基)-2,5,8,11-四氮杂十二烷-1,12-二酮($\mathbf{L}_1$),1,13-二((α-羟甲基)苯基)-2,5,9,12-四氮杂十三烷-1,13-二酮($\mathbf{L}_2$),1,15-二((α-羟甲基)苯基)2,5,8,11,14-五氮杂十五烷-1,15-二酮($\mathbf{L}_3$)。利用 pH 滴定分别在 5.0 ℃,15.0 ℃,25.0 ℃,35.0 ℃测定了铜(Ⅱ)与这 3 种配体在二氧六环/水(*V*/*V*,15/85)混合溶剂中配位的稳定常数,得到了热力学参数 $\Delta H_m^{\ominus}$ 和 $\Delta S_m^{\ominus}$。其结果显示了配体的质子化和金属配合物的形成受到焓变化的控制。此外,在 25.0 ℃测定了铜(II),配体 **L** 和氨基酸(AA)三元配合物的稳定常数,其中 **L**=$\mathbf{L}_1$,$\mathbf{L}_2$ 和 $\mathbf{L}_3$,AA=*L*-脯氨酸(Pro),*L*-异亮氨酸(Ile),*L*-缬氨酸(Val),甘氨酸(Gly),*L*-丝氨酸(Ser)。观察到在三元体系中存在着直线自由能关系(LFER)。

关键词: 多氨-酰氨配体　α-氨基酸　铜(Ⅱ)　三元配合物
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Ternary Copper(Ⅱ) Complexes of Novel Polyamino-polyamide Ligands and Amino-acids

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Three polyamino-polyamide ligands 1,12-bis((α-hydroxylmethyl)phenyl)-2,5,8,11-tetraazadodecane-1,12-dione ($\mathbf{L}_1$), 1,13-bis((α-hydroxylmethyl)phenyl)-2,5,9,12-tetraazatridecane-1,13- dione ($\mathbf{L}_2$), 1,15-bis ((α-hydroxylmethyl) phenyl)-2,5,8,11,14-pentaazapentadecane-1,15-dione ($\mathbf{L}_3$) have been synthesized. The stability constants of complexation of Cu(Ⅱ) with these three ligands in dioxane/water (*V*/*V*, 15/85) mixed solvent have been determined by pH titrations at 5.0 ℃, 15.0 ℃, 25.0 ℃ and 35.0 ℃ respectively. The thermodynamic parameters $\Delta H_m^{\ominus}$ and $\Delta S_m^{\ominus}$ were obtained. The result shows that both the protonation of the ligands and the formation of metal complexes are controlled by the change of enthalpy. In addition, the stability constants of ternary complexes of Cu(Ⅱ), **L** and α-amino-acid (AA) have been determined at 25.0 ℃, where **L** = $\mathbf{L}_1$, $\mathbf{L}_2$ and $\mathbf{L}_3$, AA = *L*-proline (Pro), *L*-isoleucine (Ile), *L*-valine (Val), glycine (Gly), *L*-serine (Ser), respectively. It is observed that linear free energy relationship (LFER) exists in the ternary systems.

Keywords: **polyamino-polyamido ligands** ***α*-amino acids** **copper(Ⅱ)** **ternary complexes**

0 Introduction

The coordination chemistry of amides[1] is of considerable interest because of the biological importance of these groups in peptides and proteins. Deprotonation of the amide group is well known to occur in the presence of various metal ions and the sites of coordination are generally considered to be the carbonyl

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oxygen atom prior to deprotonation and the amido nitrogen atom after deprotonation. The binding of carbonyl oxygen[2] or amide nitrogen[3] to metal ions has been proved directly from structure determination.

The function of amino-acids and peptides is, in part, the result of a perfectly coordination of the metal ion (s) and one or several functional groups, e.g. amines or amides. Closure of the five-membered chelate ring involving deprotonated peptide nitrogen provides strong metal binding and occurs at acidic or alkaline pH values only for Pd(Ⅱ), Cu(Ⅱ), Co(Ⅱ), Ni(Ⅱ)[4]. Whereas, it has been found that Zn(Ⅱ) ion normally does not promote peptide-nitrogen or amide nitrogen deprotonation[5].

Here, we report the investigation, by potentiometric means, of the coordination ability of three polyamino-polyamide ligands toward Cu(Ⅱ) in order to find out whether the electron- withdrawing effect of the Cu(Ⅱ) influences the deprotonation of amide nitrogen. Furthermore, through the determination of the stability constants of metal complexes with the second ligand, α-amino-acids, with particular interest in the amount of metal complexation at physiological pH, the selectivity of the metal complexes towards the various α-amino-acids was studied.

1 Experimental

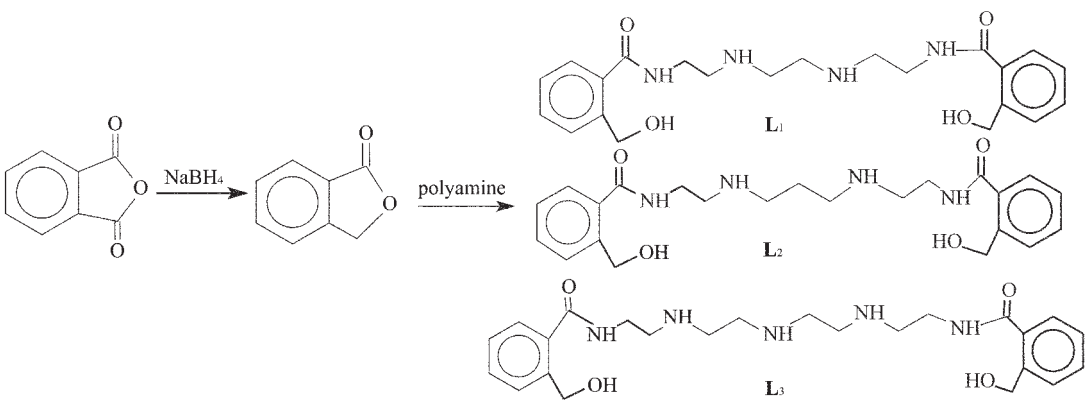
1.1 Physical Methods

Elemental analyses were obtained using a Parkin-Elmer 2400c CHN analyzer. ^{1}H NMR spectra were recorded on a Varian UNITY-plus instrument at 400 MHz and IR spectra on an Equinox 55FT spectrometer. Stability constants were measured on a Beckmen pH meter *Φ*-71 equipped with a type of 39841 combination electrode.

1.2 Chemicals

All reagents used were of reagent grade. KNO_3 was re-crystallized before use. Redistilled water was used for the preparation of all the solutions. The ionic strength was adjusted to I = 0.1mol·dm^{-3} KNO_3.

The ligands **L** were synthesized as below:



1,12-bis((α-hydroxylmethyl)phenyl)-2,5,8,11-tetraazadodecane-1,12-dione (**L**$_1$)

Phthalide[7] (m.p. 72~73 ℃)(3 g, 22.4 mmol) was put into a 50mL round-bottom flask and then 1, 4, 7, 10-tetraazadecane (1.61 g, 11.1 mmol) was added. The mixture was heated at 90 ℃ for 10 hours with continuing stirring. After cooling, the pale-yellow viscous oil was obtained, the white needle crystal was re-crystallized from alcohol/water(V/V: 20/80), yield being 3.75 g, 32%. IR (KBr pellet): 3402, 3268, 2852, 1483, 1445, 1238, 1640, 1598, 1113, 1039, 743, 795 cm^{-1}. ^{1}H NMR (DMSO-d_6): δ 7.38~7.42 (8H, m, C_6H_5), 4.56 (4H, s, $C_6H_5CH_2$), 2.49~2.65 (12H, m, NCH_2). Elemental Anal: Found for $C_{22}H_{30}N_4O_4\cdot 6H_2O$: C, 50.83%; N, 10.62%; H, 8.1%. Calculated: C, 50.57%; N, 10.73%, 8.54%.

L$_2$ and **L**$_3$ were obtained under the same condition as that of **L**$_1$ except replacing corresponding amine by 1,4,8,11-tetraazaundecane and 1,4,7,10,13-pentaazatridecane, respectively.

1,13-bis ((α-hydroxylmethyl)phenyl)-2,5,9,12-tetraazatridecane-1,13-dione(**L**$_2$) IR(KBr pellet): 3450, 3288, 2839, 1636, 1599, 1473, 1438, 1321, 1275, 1125, 1043, 795, 738 cm^{-1}. ^{1}H NMR (DMSO-d_6): (7.32~7.40 (8H, m, C_6H_5), 4.57(4H, s, $C_6H_5CH_2$), 2.49~3.36(14H, NCH_2, NCH_2CH_2). Elemental Anal: Found for $C_{23}H_{32}N_4O_4\cdot 6H_2O$: C, 51.57%; N, 10.59%; H, 8.26%. Calculated: C, 51.43%; N, 10.44%; H, 8.26%.

1,15-bis ((α-hydroxymethyl)phenyl)-2,5,8,11,14-pentaazapentadecane-1,15-dione(**L**$_3$) IR (KBr pellet): 3407, 3270, 2915, 2847, 1643, 1481, 1445, 1326, 1280, 1118, 1035, 810, 740 cm^{-1}. ^{1}H NMR (DMSO-d^6): δ 7.32~7.47(8H, m, C_6H_5), 4.57(4H, s, $C_6H_5CH_2$), 2.49~2.67(16H, m, NCH_2). Elemental Analysis: Found for $C_{24}H_{35}N_5O_4\cdot 7.5H_2O$: C, 47.57%; N, 11.68%; H, 8.61%. Calculated: C, 47.90%; N, 11.64%; H, 8.54%.

The preparation of the test solutions and the calibration of the electrode system were the same as described earlier[6]. All solutions (20 mL) were kept under nitrogen atmosphere at 5.0, 15.0, 25.0, 35.0±0.1 ℃, and at least three independent titrations were made for each system. The solutions used were dioxane/water (*V*/*V*, 15/85), and the concentrations of Cu(Ⅱ), **L**, AA (amino-acid) were 1×10^{-3} mol·dm^{-3} in the I = 0.1 mol·dm^{-3} (KNO_3). The calculation methods using the computer improved program (TITFIT)[6] were the same as described previously.

2 Results and Discussion

2.1 Protonation

The protonation constants of polyamino-polyamide ligands in mixed-solution were determined using potentiometric titrations at 5.0 ℃, 15.0 ℃, 25.0 ℃ and 35.0 ℃ respectively, and are shown in Table 1 according to equilibrium (**1**).

$$LH_{m-1}^{(m-1)+} + H^+ = LH_m^{m+} \quad K = [LH_m]^{m+}/[LH_{m-1}]^{(m-1)+}[H]^+ \quad (\mathbf{1})$$

It is observed that the first protonation constants of $\mathbf{L}_1$, $\mathbf{L}_2$ and $\mathbf{L}_3$ at 25 ℃ are 7.79, 8.45 and 8.09 respectively, and are lower than first protonation constant of an analogous diamino-diamide ligand (**L**′), 1, 5,8,12-tetraazadodecane-2,11-dione (with the protonation constants $\lg K_1'$=8.75, and $\lg K_2'$=5.74 at 25 ℃)[8]. That the first protonation constants of **L** are lower than that of **L**′ is attributed to two factors: (1) the steric effect of the two phenyls groups inhibits the attack of protons to nitrogen atoms of amino groups; (2) phenyl-amido groups of **L** decrease the electron density of nitrogen atoms of the amino groups stronger than amido groups of **L**′.

As shown in Table 1, both the first and second protonation constants of $\mathbf{L}_2$ are higher than those of $\mathbf{L}_1$, which can be attributed to the longer chain of ligand $\mathbf{L}_2$ and the much more extensive space to accommodate protons and then the lower electrostatic repulsion effect. However, as to the three-amino-groups containing ligand $\mathbf{L}_3$, the protonation constants are lager than ones of $\mathbf{L}_1$ due to the ability of electron-drawing of phenyl-amido groups being decreased by its longer chain.

With regard to a chemical reaction, the equilibrium constant has relationship with temperature T and

Table 1　Stepwise Protonation Constants (lg$K$), Standard Molar Enthalpy Change ($\Delta H_m^{\ominus}$) and Stand Molar Entropy Change ($\Delta S_m^{\ominus}$) of the Protonation of Ligands L at Different Temperatures

		5 ℃	15 ℃	25 ℃	35 ℃	$\Delta H_m^{\ominus}$ / (kJ·mol^{-1})	$\Delta S_m^{\ominus}$ / (J·mol^{-1}·K^{-1})
$\mathbf{L}_1$	lgK_1	8.98±0.03	8.15±0.08	7.79±0.04	7.14±0.03	−96.66±0.59	−176.72±1.14
	lgK_2	6.83±0.01	5.83±0.11	5.30±0.06	4.58±0.02	−119.74±0.17	−301.10±0.38
$\mathbf{L}_2$	lgK_1	9.53±0.04	8.99±0.05	8.45±0.05	7.68±0.07	−99.64±1.46	−174.50±6.01
	lgK_2	8.35±0.09	7.30±0.07	6.43 ± 0.02	5.46±0.04	−156.58±3.33	−403.01±10.30
$\mathbf{L}_3$	lgK_1	8.98±0.05	8.37±0.03	8.09±0.06	7.54±0.06	−75.53±0.96	−100.13±4.24
	lgK_2	7.62±0.02	6.94±0.03	6.18±0.11	5.28±0.01	−127.37±0.94	−310.52±4.03
	lgK_3	5.93±0.02	5.24±0.08	3.52±0.10	2.94±0.02	−175.45±0.48	−514.89±2.71

standard molar enthalpy change $\Delta H_m^{\ominus}$ and standard molar entropy change $\Delta S_m^{\ominus}$ is expressed as follow,

$$-RT\ln K=\Delta H_m^{\ominus}-T\Delta S_m^{\ominus} \quad \ln K= -\Delta H_m^{\ominus}/RT + \Delta S_m^{\ominus}/R \quad (2)$$

When plot $\ln K$ versus $1/T$, the values of $\Delta H_m^{\ominus}$ and $\Delta S_m^{\ominus}$ were obtained from the slope and the intercept. The negative value of $\Delta H_m^{\ominus}$ indicates that the process of protonation is an exothermic reaction. At the same time, the negative value of $\Delta S_m^{\ominus}$ indicates that the system becomes lager-order with the protonation of the nitrogen atoms.

2.2 Metal Complexes

The interaction of Cu(Ⅱ) with ligands (molar ratio 1:1) at 5.0 ℃, 15.0 ℃, 25.0 ℃ and 35.0 ℃ was also investigated using potentiometric titrations. The species distributed curve of $\mathbf{L}_2$ in the presence of equimolar Cu(Ⅱ) (Fig.1, 25 ℃) reveals that complexes forms at pH>3. The stability constants for the 1:1 Cu(Ⅱ) complex, according to equilibrium **3** are listed in Table 2.

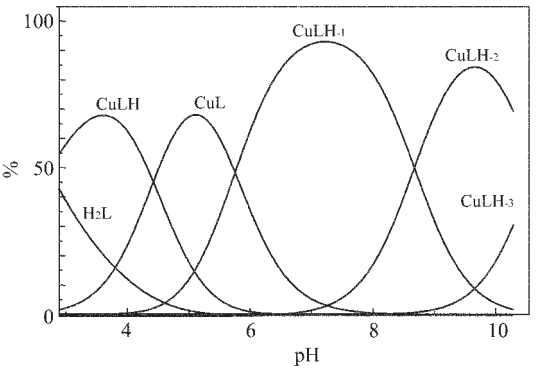


Fig.1 Species distribution curve for 1:1 Cu^{2+}-$\mathbf{L}_2$ complexes, $c(Cu^{2+})=c(\mathbf{L})=1\times10^{-3}$ mol·L^{-1}, t = 25 ℃

$$Cu^{2+}+L+mH^+=[CuLH_m]^{(m+2)+}$$

$$\beta=[CuLH_m]^{(m+2)+}/[Cu]^{2+}[L][H]^{m+} \quad (3)$$

All the ligands can coordinates with Cu(Ⅱ) to form metal complexes CuLH(111), CuL(110), $CuLH_{-1}$(11-1), $CuLH_{-2}$(11-2) and $CuLH_{-3}$(11-3). In species (11-1), (11-2) and (11-3), the negative values stand for the number of protons, released from amido group and/or from the metal-bound water or methylhydroxyl of **L**. As shown in Fig.1, complex CuLH begins to form at pH ca. 3 and has the maximum concentration at pH ca. 3.7, while CuL forms in the pH range 3~8 and

Table 2 Stability Constants of Complexes in the Cu(Ⅱ)/L Systems at Different Temperatures ($c(Cu^{2+}) = c(\mathbf{L}) = 1\times10^{-3}$ mol·dm^{-3}, I = 0.1 mol·dm^{-3} KNO_3)

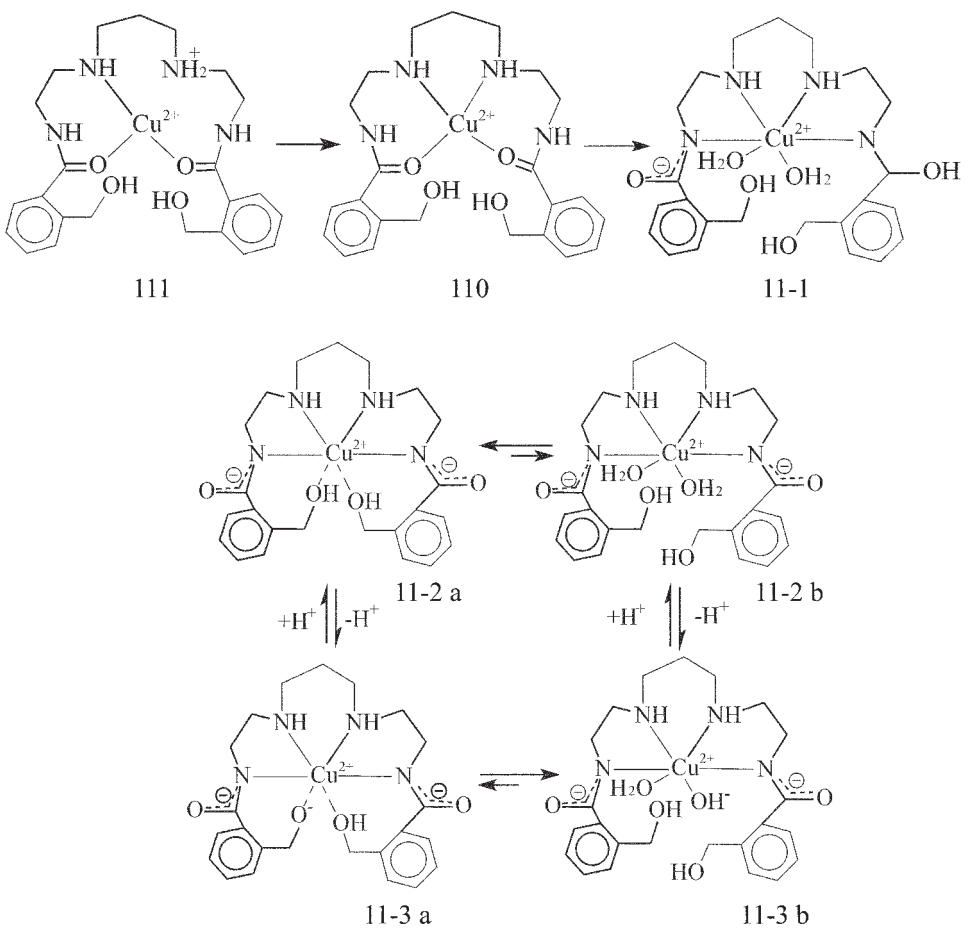
$Cu\mathbf{L}_1$	5 ℃	15 ℃	25 ℃	35 ℃	$\Delta H_m^{\ominus}$ / (kJ·mol^{-1})	$\Delta S_m^{\ominus}$ / (J·mol^{-1})
$\lg\beta_{111}$	15.22±0.07	14.26±0.05	13.12±0.08	12.74±0.05	−141.38±0.48	−218.03±0.45
$\lg\beta_{110}$	10.94±0.08	10.12±0.07	9.18±0.07	8.44±0.09	−138.53±0.46	−288.04±3.05
$\lg\beta_{11-1}$	4.43±0.03	3.68±0.04	2.05±0.12	1.39±0.05	−176.42±2.39	−547.29±9.29
$\lg\beta_{11-2}$	−2.79±0.04	−3.86±0.09	−4.93±0.06	−5.98±0.07	−174.55±2.39	−680.25±7.09
$\lg\beta_{11-3}$	−11.29±0.04	−12.54±0.04	−13.95±0.05	−14.62±0.03	−178.64±0.39	−891.69±1.61
$Cu\mathbf{L}_2$						
$\lg\beta_{111}$	17.39±0.02	16.53±0.06	16.01±0.05	14.58±0.08	−146.19±2.80	−190.56±10.57
$\lg\beta_{110}$	13.01±0.04	12.39±0.06	11.98±0.05	10.24±0.10	−141.80±2.75	−256.42±10.59
$\lg\beta_{11-1}$	8.15±0.08	7.38±0.07	6.77±0.09	6.25±0.02	−103.79±2.55	−217.85±7.49
$\lg\beta_{11-2}$	1.27±0.05	0.45±0.04	−0.31±0.04	−3.66±.0.06	−252.27±2.52	−872.43±8.35
$\lg\beta_{11-3}$	−7.96±0.07	−9.03±0.05	−9.97±0.06	−10.79±0.04	−154.96±1.31	−709.97±3.43
$Cu\mathbf{L}_3$						
$\lg\beta_{111}$	15.14±0.04	14.81±0.06	13.84±0.05	12.97±0.08	−122.08±1.79	−145.33±7.23
$\lg\beta_{110}$	10.35±0.06	9.76±0.06	9.37±0.10	9.37±0.10	−86.35±0.74	−112.78±1.35
$\lg\beta_{11-1}$	5.06±0.30	3.87±0.31	2.62±0.02	1.59±0.10	−191.44±2.89	−590.99±10.82
$\lg\beta_{11-2}$	−1.28±.0.13	−2.87±0.35	−4.19±0.09	−5.59±0.02	−235.34±2.08	−870.07±7.76
$\lg\beta_{11-3}$	−10.61±0.09	−11.98±0.42	−13.26±0.12	−14.40±0.11	−207.76±2.25	−950.13±0.41

reaches the maximum amount at pH ca. 5.2. With the increase of pH of the solution, species $CuLH_{-1}$, $CuLH_{-2}$ and $CuLH_{-3}$ form at pH 4, 6.5, 8.5 and reaches the peak at pH ca. 7, 9.5 and >10, respectively.

It is interesting to discuss the structures of metal complexes of polyamino-polyamide ligand, since the pH-dependent coordination of the CO-NH group by metal ion may occur through either carbonyl oxygen at low pH or deprotonated amido nitrogen at high pH[2,4].

As shown in Scheme 1, one nitrogen atom of $\mathbf{L}_2$ is bound to Cu(Ⅱ) while the other is protonated in complex CuLH. Since the complex CuLH exists in an acidic or slightly acidic solution, the carbonyl oxygen atoms are considered to be bound to Cu(Ⅱ). In species 110, both the two nitrogen atoms of amino group and two carboxyl oxygen atoms are involved in the coordination with Cu(Ⅱ). With regard to complex $CuLH_{-1}$, which exists in the pH range 4~10 and has a percentage concentration more than 90% at neutral pH, the binding sites of two of the oxygen atoms of carbonyl groups are replaced by two nitrogen atoms of amido groups, in which one is deprotonated.

For $CuLH_{-2}$ complex, either (11-2, a) or (11-2, b) can be assigned reasonably in aqueous solution. The coordination of hydroxyl group to Zn(Ⅱ) has been found by Kimura et al. in the binary system of a pendant macrocycle[9]. On the other hand, the chelate seven-member rings in (11-2 a) involves Cu(Ⅱ), amido nitrogen and alkoxide is not stable enough, and one or two water molecules can partially or completely displace the coordination of alkoxide and leading to the conformation (11-2 b). Similarly, both (11-3 a) and (11-3 b) are proposed for the tri-deprotonated species. For 11-3 b the OH^- in the water takes part in the complexation process. For 11-3 a the deprotonated alkoxide group can bind Cu(Ⅱ) since the electronic density of the oxygen atom of the alkoxyl group decreases significantly due to the strong inductive effect



Scheme 1

of the positive divalent Cu(Ⅱ) (11-3, a)[9].

The structures of metal complexes in Cu(Ⅱ)/$\mathbf{L}_1$ system are similar to those of Cu(Ⅱ)/$\mathbf{L}_2$, apart from the different chain length of the two amino nitrogen atoms, that is, n-propyl and ethyl in $\mathbf{L}_2$ and $\mathbf{L}_1$ respectively. In the Cu(Ⅱ)/$\mathbf{L}_3$ system, two amino nitrogen atoms coordinate to Cu(Ⅱ) to form a stable five-member ring while the third amino nitrogen atom is protonated in species 111. Although $\mathbf{L}_3$ has three secondary amino nitrogens, it can not form stable complex 112 due to the electrostatic repulsion effect. Since the five nitrogen atoms of $\mathbf{L}_3$ form four five-member rings in species 11-1 and 11-2. In species 11-3 the hydroxyl or the alkoxide participated in coordination. The other coordination conditions are analogous to those of the corresponding species in Cu(Ⅱ)/$\mathbf{L}_{1,2}$ systems.

From the stability constants comparison listed in Table 2, the order Cu$\mathbf{L}_2$>Cu$\mathbf{L}_3$>Cu$\mathbf{L}_1$ can be found. It is noted that the order of stability constants are consistent with that of protonation constants. This indicates that the basicity of the ligands play a main role in the stability of the complexes. On the other hand, the 5,6,5-member ring in Cu(Ⅱ)/$\mathbf{L}_2$ is much more stable than the 5,5,5 ring in Cu(Ⅱ)/$\mathbf{L}_1$ system because of the lower tensile force of the former and, as a consequence, the stability of Cu(Ⅱ)/$\mathbf{L}_2$ system is stronger than that of Cu(Ⅱ)/$\mathbf{L}_1$. However, the stability constants for $\mathbf{L}_3$ with Cu(Ⅱ) is lower than those of Cu(Ⅱ)/$\mathbf{L}_2$, which is attributed to the fact that the nitrogen chain of $\mathbf{L}_3$ has to be distorted to some extent when it coordinates to Cu(Ⅱ), and thus causing a torsion effect and thus the lower stability.

According to equilibrium (**3**) and formula (**2**), the standard molar enthalpy change $\Delta H_m^{\ominus}$ and standard molar entropy change $\Delta S_m^{\ominus}$ of the formation of the metal complexes were obtained. Since both $\Delta H_m^{\ominus}$ and $\Delta S_m^{\ominus}$ are negative values, it is indicated the formation reaction is controlled by $\Delta H_m^{\ominus}$. Furthermore, the pK_a values 8~9, according to the process of 11-2 → 11-3, indicate that these binary complexes are potential good nucleophilic reagents at neutral or slight basic solution. For instance, they can be used as model of hydrolytic enzyme, such as phosphoratase[10].

2.3 Ternary Systems

The stability constants of Cu^{2+} with ligand **L** and α-amino-acid (AA) were measured in aqueous solution at 25 ℃. The mole ratio of Cu(Ⅱ):**L**:AA is 1:1:1. The α-amino-acids are *L*-proline (Pro), *L*-isoleucine (Ile), *L*-valine (Val), glycine (Gly), *L*-serine (Ser), respectively. The stability constants according to equilibrium (**4**) are listed in Table 3. The species distribution curves for Cu(Ⅱ)/$\mathbf{L}_2$/Pro are shown in Fig.2. Compared with Fig.1, significant interactions take place when AA is introduced to the 1:1 Cu(Ⅱ):**L** system. The protonation constants and stability constants of different amino-acids are listed in Table 4 (Ref 11).

$$Cu + \mathbf{L} + AA + mH = Cu\mathbf{L}(AA)H_m$$

$$\beta = [Cu\mathbf{L}(AA)H_m]/[Cu][\mathbf{L}][AA][H]^m \qquad (4)$$

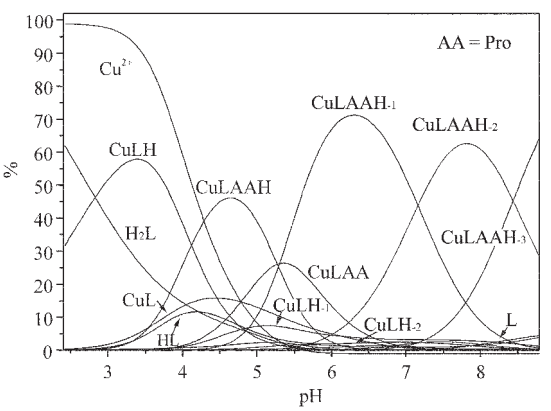


Fig.2 Distribution curves for species present in Cu(Ⅱ)/**L**/Pro system

The calculation of the potentiometric titration data of the Cu(Ⅱ)/**L**/AA systems reveals the presence of five species containing Cu(Ⅱ), **L** and AA in the measurable pH range 2.6~8.8, i.e. Cu$\mathbf{L}$AAH$_m$ (m = 1~−3). As seen from Fig.2, the complex Cu$\mathbf{L}$(Pro)H begins to form at pH 2.6 and reaches the maximum concentration at pH ca. 4.6. With the increase of pH, species Cu$\mathbf{L}$(Pro), Cu$\mathbf{L}$(Pro)H$_{-1}$, Cu$\mathbf{L}$(Pro)H$_{-2}$ and Cu$\mathbf{L}$(Pro)H$_{-3}$ forms at pH 3.7, 4.1, 5.4 and 6.9 and reaches the peak at pH ca. 5.3, 6.2, 7.8 and > 9 respectively. At pH < 4, the ligand $\mathbf{L}_2$ is mainly in the di-protonated form (H_2L) and Cu$\mathbf{L}$H, while Cu(Ⅱ) is in the combina-

Table 3　Stability Constants of Complexes Present in the Cu(Ⅱ):L:α-amino-acid (1:1:1)Solution at I = 0.1 mol·dm^{-3} KNO_3, 25±0.1 ℃

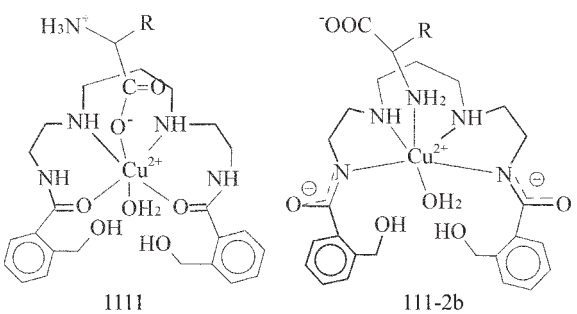
Cu-**L**$_1$	Pro	Ile	Val	Gly	Ser
$\lg\beta_{1111}$	23.14±0.05	22.50±0.06	22.64±0.07	22.37±0.04	21.51±0.08
$\lg\beta_{1110}$	18.28±0.06	17.60±0.08	17.64±0.05	17.56±0.03	16.55±0.07
$\lg\beta_{111\text{-}1}$	12.89±0.08	12.25±0.09	12.31±0.07	12.18±0.07	11.12±0.10
$\lg\beta_{111\text{-}2}$	6.03±0.11	5.33±0.04	5.38±0.06	5.17±0.08	4.04±0.12
$\lg\beta_{111\text{-}3}$	−2.13±0.10	−2.88±0.07	−2.91±0.10	−2.88±0.08	−3.85±0.09
Cu-**L**$_2$					
$\lg\beta_{1111}$	26.25±0.02	25.40±0.07	25.57±0.02	25.52±0.05	24.39±0.03
$\lg\beta_{1110}$	21.37±0.07	20.49±0.05	20.30±0.02	20.38±0.07	19.02±0.02
$\lg\beta_{111\text{-}1}$	16.42±0.06	15.52±0.04	15.39±0.01	15.49±0.05	14.07±0.04
$\lg\beta_{111\text{-}2}$	9.59±0.09	8.71±0.11	8.61±0.05	8.68±0.10	6.87±0.02
$\lg\beta_{111\text{-}3}$	2.35±0.03	1.33±0.05	1.42±0.03	1.45±0.08	−0.20±0.05
Cu-**L**$_3$					
$\lg\beta_{1111}$	25.05±0.05	23.36±0.06	23.13±0.02	23.20±0.04	20.23±0.05
$\lg\beta_{1110}$	19.80±0.04	18.57±0.11	18.43±0.07	18.51±0.05	15.06±0.03
$\lg\beta_{111\text{-}1}$	15.16±0.04	13.82±0.10	13.71±0.04	11.75±0.06	10.46±0.08
$\lg\beta_{111\text{-}2}$	9.43±0.02	7.98±0.08	7.92±0.09	7.92±0.03	5.38±0.02
$\lg\beta_{111\text{-}3}$	2.43±0.05	0.52±0.07	0.073±0.05	−0.57±0.04	−2.25±0.06

Table 4　Protonation Constants of Different Amino Acids and Stability Constants of Their Cu(Ⅱ) Complexes

	Pro	Ile	Val	Gly	Ser
$\lg\beta_1^H$	10.39	9.60	9.57	9.56	9.05
$\lg\beta_2^H$	12.16	11.90	11.91	11.92	11.34
$\lg\beta_{CuL}$	8.80	8.16	8.15	8.16	7.95

tion of complexes Cu**L**H and Cu**L**. It is observed that the ternary complexes have larger amount at neutral or slightly basic solution than that in slightly acidic solution, which is probably due to the stronger coordination ability of the second ligand, amino acid, at higher pH values.

An important characteristic of the Cu(Ⅱ)-**L**-AA system is the complexation sites AA. Generally, both the two functional sites, carboxyl oxygen atom and amino nitrogen atom, can bind metal ions when AA meet metal ion alone in aqueous solution. But in the ternary system, the chain of α-amino acid is not long enough to form chelate ring at the axis position, therefore, AA can only use one functional group to incorporate to Cu(Ⅱ) ion. Due to pK_{a1} = 9~11, pK_{a2} = 1.5~3 for the deprotonation of the amino group and carboxyl group of AA respectively, the carboxyl group and amino nitrogen atom coordinated to Cu(Ⅱ) in the acidic and neutral solution respectively. As shown in Fig.2, in both complex CuLAAH and CuL, it may be the carboxyl groups to interact with Cu(Ⅱ) at pH < 6, whereas, at pH > 6, the coordination site of AA could be the amino group. The possible structures of complexes Cu**L**AAH and Cu**L**AAH$_{-2}$ are shown as below.



1111　　111-2b

Linear free energy relationship[12] widely exists in chemical systems, that is, linearship exists between the stable constants of the complexes and the protonation constants of the analogous ligands. In our system, the entropy changes associated with the coordination reactions are approximately the same due to the similar coordination configures of Cu(Ⅱ) with AA. When

plot $lg\beta_{111n}$ (n = 1 ~ −3) of Cu(Ⅱ)/**L**$_2$/AA versus pK_{a1} of AA, as shown in Fig.3, the following linearships as follow are obtained.

$$lg\beta_{1111} = 12.865 + 1.305lg\beta_{0011} \quad \gamma = 0.991$$
$$lg\beta_{1110} = 4.684 + 1.630lg\beta_{0011} \quad \gamma = 0.993$$
$$lg\beta_{111\text{-}1} = -1.240 + 1.727lg\beta_{0011} \quad \gamma = 0.997$$
$$lg\beta_{111\text{-}2} = -9.697 + 1.888lg\beta_{0011} \quad \gamma = 0.994$$
$$lg\beta_{111\text{-}3} = -15.903 + 1.782lg\beta_{0011} \quad \gamma = 0.990$$

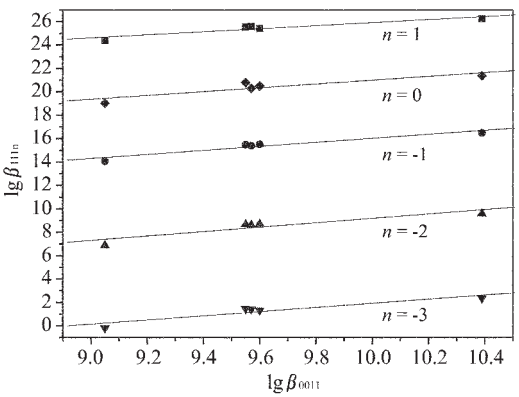


Fig.3 Relationship of $lg\beta_{111n}$ vs $lg\beta_{0011}$

LFER is also found between the stability constants of the ternary species and the stability constants of α-amino acids with the Cu(Ⅱ) ions, $lg\beta_{1010}$ of complex Cu**L**. This is due to the same complexation conformations of the Cu(Ⅱ) ion with the amino acids in the ternary systems, which leads to the same effect to the change of entropy.

$$lg\beta_{1111} = -20.108 + 6.252lg\beta_{1010} \quad \gamma = 0.994$$
$$lg\beta_{1110} = -23.921 + 6.091lg\beta_{1010} \quad \gamma = 0.994$$
$$lg\beta_{111\text{-}1} = -29.308 + 6.048lg\beta_{1010} \quad \gamma = 0.996$$
$$lg\beta_{111\text{-}2} = -34.499 + 6.106lg\beta_{1010} \quad \gamma = 0.992$$
$$lg\beta_{111\text{-}3} = -41.647 + 6.101lg\beta_{1010} \quad \gamma = 0.992$$

The other ternary systems of Cu(Ⅱ) also exist LFER between the $lg\beta_{111n}$ and the $lg\beta_{0011}$ or $lg\beta_{1010}$, and the linearship was not given.

3 Conclusion

In this paper, we have three novel ligands consisting of diamido and polyamino groups were synthesized. The potentiometric studies indicate that both the process of protonation and the formation of Cu(Ⅱ) metal complexes are controlled by $\Delta H_m^{\ominus}$. The metal complexes can recognize different amino acids in water solution, and linear free energy relationship exists between the stability constants of the ternary complexes and the first protonation constants of the amino acid or the stability constants of Cu-amino acid (CuAA).

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