Thermodynamic Parameters for the Complexation of Some 3d Divalent Transition Metal Ions with L-Proline, L-Thiaproline and *trans*-4-Hydroxy-L-proline in an Aqueous Solution

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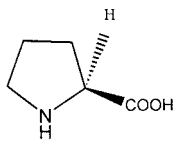
Received May 21, 2001

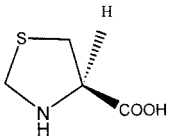
Keywords : Thermodynamic parameters, Transition metals, L-Proline, Complexation.

Transition metal complexes with optically pure amino acids have been used as a chiral mobile phase in a chiral ligand exchange chromatograph (CLEC) to resolve α-amino acids.[1] The most frequently used transition metal ion is Cu^{2+}. The Co^{2+}, Ni^{2+}, Zn^{2+} and Cd^{2+} ions also have been adopted in the CLEC system. The evaluation of the thermodynamic parameters for the complexation of amino acids with various transition metal ions may be useful because the separability of the optically active amino acids in CLEC is closely related to the stability of the complexes.[2] Previously we[3] reported that the lanthanide(III) metal complexes with the optically active L-proline are stable in an aqueous solution, and introduced the lanthanide(III) metal ions in CLEC. We found that the capacity factor of CLEC increases due to the high nuclear charge and the high coordination numbers of lanthanide(III) metal ions.[4]

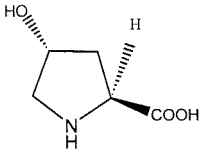
In this study, we selected L-proline, L-thiaproline and *trans*-4-hydroxy-L-proline as optically active amino acids and determined the thermodynamic parameters for the complexation of these selected ligands with some 3d divalent transition metal ions in an aqueous solution.



L-proline



L-thiaproline



trans-4-hydroxy-L-proline

We also focused our attention on understanding the role of the 4-sulfur donor atom and the 4-hydroxy group in the ligands in the complexation process.

Experimental Section

Metal (Co^{2+}, Ni^{2+}, Cu^{2+}, Cd^{2+}) solutions were prepared by dissolving the anhydrous metal chloride, and the concentration of the metal ions was determined by EDTA titration in a buffer solution. Zinc powder (99.998%) was used to prepare the zinc solution. Stock solutions of the ligands were prepared by dissolving the solid ligands in CO_2– free water, and the concentration was determined by using a standard NaOH solution. All of the working solutions were adjusted to result in a total ionic strength of 0.10 M by using $NaClO_4$.

The stability constants were determined by pH titration method at 25.0 ± 0.1 °C in a jacked titration vessel by using a Fisher 520 digital pH meter in conjunction with a Fisher standard combination electrode. The initial pH of metal and ligand solutions was adjusted to approximately the value of the p*K*a of the ligand. The calorimetric titrations were performed by using a Tronac model 450 solution calorimeter. The calorimeter was tested by measuring the amount of heat of protonation of THAM (trishydroxymethylaminomethane). The procedure for the calorimetric titration has been described earlier.[5] In a typical run, 50.0 of a metal solution (~10^{-2} M) was titrated with incremental additions of 2.0 mL of the ligand solution (~10^{-1} M). To form 1 : 1 complex, the concentration of the total ligand was controlled to be less than that of the total metal concentration. The heat of dilution was measured by adding the ligand solution into the 0.10 M $NaClO_4$ solution.

Results and Discussion

Previously we reported the acid constants and the thermodynamic parameters for the protonation of L-proline,[3] L-thiaproline,[6] and *trans*-4-hydroxy-L-proline[7] in an aqueous solution. The stability constants for the complexation reactions were determined by titrating the metal solutions with the ligand buffer solutions. The average number of the ligands bound per cation, bar $\bar{n}$, was calculated from the pH titration data. Table 1 shows a typical set of pH titration data of the Cu(II)-L-proline complex. The enthalpy titration data for the complexation of copper(II) with L-proline are summerized in Table 2.

A linear least square analysis of the equation $(\bar{n}/1-\bar{n}) = \beta_1[L]$ (where [L] is the free ligand concentration) resulted in the value of β_1. The concentration of the ligand used in this experiment did not allow the formation of 1 : 2 complex, ML_2. Figure 1 shows a good linear relationship between $(\bar{n}/1-\bar{n})$ and [L] for the Cu(II)-L-proline complex. The calculated stability constants (1 : 1) are summarized in Table 3.

The stability constants increase in the series $Co^{2+} \sim Cu^{2+}$, and then decrese with Zn^{2+} or Cd^{2+}, as it is expected from the

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Table 1. pH titration data for complexation of Cu^{2+}-L-proline at 25.0 °C and at 0.10 M ionic strength

Volume of titrant (mL)	pH	$[L] \times 10^{-4}$(M)	$\bar{n}$
1.0	2.917	0.077	0.021
1.5	2.908	0.174	0.030
2.0	2.899	0.165	0.042
2.5	2.890	0.189	0.053
3.0	2.881	0183	0.065
3.5	2.873	0.212	0.077
4.0	2.865	0.228	0.089
4.5	2.858	0.273	0.101
5.0	2.851	0.307	0.113
5.5	2.844	0.328	0.126
6.0	2.837	0.338	0.139
6.5	2.831	0.381	0.152
7.0	2.825	0.414	0.165
7.5	2.825	0.483	0.178
8.0	2.815	0.542	0.191
8.5	2.810	0.592	0.204
9.0	2.805	0.635	0.218
9.5	2.801	0.714	0.231
10.0	2.797	0.786	0.245

initial volume = 50.00 mL, initial pH = 2.937. $[Cu^{2+}] = 8.554 \times 10^{-3}$ M, $[HL] = 4.194 \times 10^{-3}$M. $[L^{-}]_T = 9.276 \times 10^{-3}$ M.

Table 2. Enthalpy titration data for complexation of Cu^{2+}-L-proline at 25.0 °C and at 0.10 M ionic strength

Volume of titrant (mL)	Q_{Total} (mJ)	$Q_{corrected}$ (mJ)	$[L]_T \times 10^3$ (M)
0	1774	1761	3.934
1.1	1951	1937	4.319
1.2	2128	2113	4.702
1.3	2306	2289	5.084
1.4	2483	2465	5.465
1.5	2660	2641	5.844
1.6	2838	2817	6.221

Williams-Irving effect.[8] The stability constants for the metal ions increase as L-thiaproline < L-proline < *trans*-4-hydroxy-L-proline, and these results parallel the increased basicity of the ligands. Kapinos *et al*.[9] have examined the relationship between complex stability and the ligand basicity, and they found that the complex stability (log β_1) in divalent metal ions increased as the ligand basicity (p*K*a) increased in imidazole-type ligands. This was taken as an indication that the interaction between the ligand and the metal ion is an inner-sphere type.

The observed stability constants of divalent metal ions on complexation are different from those of the lanthanide(III) metal complexes, where the stability constant of Eu^{3+}-L-thiaproline ($\log\beta_1 = 3.34$)[6] is larger than that of Eu^{3+}-L-proline ($\log\beta_1 = 2.32$)[3] or Eu^{3+}-*trans*-4-hydroxy-L-proline ($\log\beta_1 = 2.73$).[7] This enhanced stability of L-thiaproline-lanthanide(III) metal ion complexes was interpreted to be the result of an interaction between the lone pair electrons of the 4-sulfur atom in L-proline and the large lanthanide metal

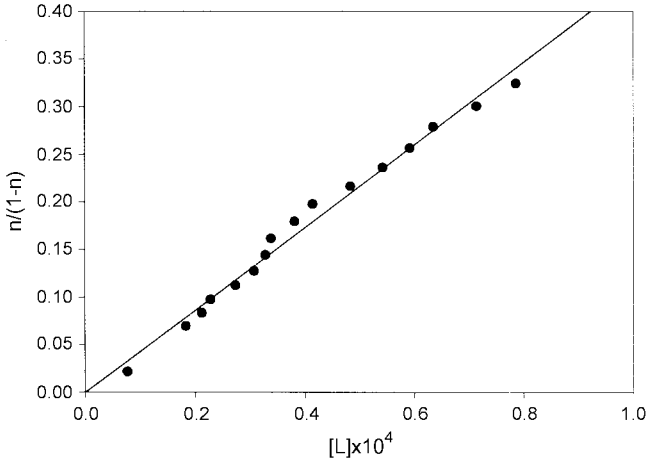

Figure 1. Plot of $\bar{n}/(1-\bar{n})$ *vs* [L] for Cu^{2+}-L-proline.

ions.[6] In this study, we observed that L-thiaproline complexes with divalent 3d transition metal ions are less stable than the corresponding L-proline complexes. This result suggests that the 4-sulfur atom does not bond with the metal ions. This may be due either to the relatively small size or to the divalent charge of the 3d transition metal ions compared to the lanthanide(III) metal ions.

All of the amounts of the heat measured were corrected for the dilution and the deprotonation of the ligand (see Table 2). The thermodynamic parameters for some transition metal ions with L-proline, L-thiaproline, and *trans*-4-hydroxy-L-proline are given in Table 3. The positive changes of enthalpy and entropy during the complexation clearly indicate that the driving force for the complexation is an entropy effect resulting from extra dehydration during complexation, and that the inner-sphere complexes are formed in the aqueous solution.[10] In inner-sphere complexes, the hydration

Table 3. Themodynamic parameters for the formation of L-proline, L-thiaproline and *trans*-4-hydroxy-L-proline complexes at 25.0 °C and at 0.10M ionic strength

Metal	$\log\beta_1$	$-\Delta G_1$ (kJM^{-1})	ΔH_1 (kJM^{-1})	ΔS_1 (JK^{-1}M^{-1})
		L-proline		
Co	3.49 ± 0.06	19.94 ± 0.17	7.75 ± 0.02	92.8 ± 2.7
Ni	3.62 ± 0.10	20.67 ± 0.30	7.89 ± 0.03	95.8 ± 4.8
Cu	3.51 ± 0.05	20.03 ± 0.13	8.96 ± 0.03	97.2 ± 2.3
Zn	3.30 ± 0.05	18.85 ± 0.21	8.44 ± 0.03	90.8 ± 0.4
Cd	3.52 ± 0.35	20.07 ± 0.17	8.63 ± 0.17	96.2 ± 6.8
		L-thiaproline		
Co	3.40 ± 0.04	19.41 ± 0.24	2.03 ± 0.11	71.9 ± 1.9
Ni	3.46 ± 0.05	19.75 ± 0.31	2.04 ± 0.21	73.1 ± 2.8
Cu	3.64 ± 0.02	20.78 ± 0.15	3.06 ± 0.23	80.0 ± 2.2
Zn	3.50 ± 0.04	19.98 ± 0.23	2.92 ± 0.05	76.8 ± 1.9
Cd	3.53 ± 0.06	20.15 ± 0.32	2.71 ± 0.04	76.7 ± 2.5
		trans-4-hydroxy-L-proline		
Co	3.69 ± 0.08	21.16 ± 0.18	2.04 ± 0.04	77.5 ± 2.7
Ni	3.87 ± 0.11	22.09 ± 0.31	2.07 ± 0.02	81.0 ± 4.7
Cu	3.99 ± 0.07	22.77 ± 0.15	2.12 ± 0.02	83.4 ± 2.2
Zn	3.67 ± 0.08	20.95 ± 0.23	2.10 ± 0.03	77.3 ± 2.3
Cd	3.59 ± 0.25	20.49 ± 0.26	2.14 ± 0.06	75.9 ± 4.6

Table 4. Thermodynamic parameters of Ni(II) complexes

Ligand	log β_1	-ΔG (kJM^{-1})	ΔH (kJM^{-1})	ΔS ($JK^{-1}M^{-1}$)	Ref.
L-proline	3.62	20.66	+7.89	+95.8	[3]
L-thioproline	3.46	19.74	+2.04	+73.1	[6]
4-hydroxy-L-proline	3.87	22.16	+2.07	+81.3	[7]
pyrrole-2-carboxylate	1.40	8.31	+0.42	+29.3	[10]
glycine	5.78	32.54	-18.83	+46.0	[10]
L-alanine	5.40	31.27	-15.06	+54.4	[10]

structure is disrupted to a great extent, which results in a net endothermic enthalpy term during the reaction. The elimination of water molecules from the inner hydration zone results in a net positive entropy effect.

The thermodynamic parameters for some Ni^{2+} complexes are collected in Table 4. It can be seen from Table 4 that the glycine and L-alanine complexes are stabilized by the exothermic enthalpy effect as well as the entropy effect, whereas L-proline and its analogous complexes are stabilized by the positive entropy term as mentioned above. The endothermic enthalpy changes in L-proline and its analogous complexes can be explained by the presence of the rigid heterocyclopentanyl ring in L-proline, which causes the steric hindrance to form chelate complexes. When edta (ethylenediaminetetraacetate) and dcta (*trans*-1,2-diaminocyclohexane-N,N-tetraacetate) react with the Ni^{2+} metal ion, the ΔH value for the formation of the dcta complex (ΔH = -22.47 $kJmol^{-1}$ at μ = 0.1 M) is more positive than that of the edta complex (ΔH = -30.88 $kJmol^{-1}$ at μ = 1.5 M).[12] It has been suggested that the steric hindrance caused by the rigid cyclohexyl ring in dcta is responsible for this endothermic effect. Moreover, the entropy changes of reaction of the dcta complexes are greater than those of the corresponding edta complexes. In this study, we found that the entropy changes for L-proline and its analogous complexes are greater than those of glycine and L-alanine complexes. These results can be explained by the supposition that the L-proline molecule before the complexation process is probably arranged in a favorable position to react with the metal ions. Thus, less conformational freedom is lost when the L-proline is bounded to the metal ions. Similar effects of ligand rigidity on thermodynamic parameters in lanthanide(III) complexes have also been reported.[13]

The entropy changes for the different metal ions decrease as L-proline > *trans*-4-hydroxy-L-proline > L-thiaproline, as shown in Table 3. The maximum entropy change in L-proline due to the extra dehydration during the complexation indicates that the 4-sulfur atom and the 4-hydroxy group are definately not involved in the complex formation.

Thus, it may be concluded that the nitrogen atom in a proline ring and the carboxylic group are involved in the formation of chelates by 3d transition metal ions with L-proline and its derivatives. The complexes are stabilized by an excess entropy effect, and the endothermic enthalpy changes are caused by the steric hindrance of the rigid heterocyclopentanyl ring in L-proline.

Acknowlegment. This work was supported by the Basic Science Research Program Ministry of Education Korea (BSRI-98-3410).

References

1. Souter, R. W. *Chromatographic Separation of Stereoisomers*, 3rd Ed.; CRC Press: 1987.
2. Galaverna, G.; Corradini, R.; Dossena, A.; Chiavaro, E.; Marchelli, R.; Dallavalle, F.; Folesani, F. *J. Chromatogr. A* **1998**, *829*, 101.
3. Choi, Y. I.; Kim, Y. I.; Choi, S. N.; Hyun, M. H. *J. Korean Chem. Soc.* **1993**, *37*, 105.
4. Hyun, M. H.; Ryoo, J. J.; Choi, S. N.; Kim, Y. I.; Jyung, K. K. *Bull. Korean Chem. Soc.* **1994**, *15*, 86.
5. Yun, S. S.; Kim, I. H.; Kim, Y. I. *Thermochimica Acta* **1990**, *162*, 341.
6. Kim, J. A.; Kim, Y. I. *Bull. Korean Chem. Soc.* **1996**, *17*, 398.
7. Cho, J. J.; Kim, Y. I.; Choi, S. N. *J. Korean Chem. Soc.* **1995**, *39*, 466.
8. Sigel, H.; McCormick, D. B. *Acc. Chem. Res*. **1970**, *3*, 201.
9. Kapinos, L. E.; Song, B.; Sigel, H. *Inorg. Chim. Acta* **1998**. *280*, 50.
10. Huskens, J.; Bekkum, J.; Peter, J. A.; Choppin, G. R. *Inorg. Chim. Acta* **1996**, *245*, 51.
11. Sillen, L. G.; Martell, A. E. *Stability Constants of Metal-Ion Complexes*, Suppl. I, Special Publication No. 25; The Chemical Society: London, 1971.
12. Aschroft, S. J.; Mortimer, C. T. *Thermochemistry of Transition Metal Complexes*; Academic Press: New York, 1970 and references therein.
13. Feil-Jenkins, J. F.; Nash, K. L.; Rogers, R. D. *Inorg. Chim. Acta* **1995**, *236*, 67.