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A Solubility Phase Diagram Study on Optical Resolution of Bis(ethylenediamine)oxalatocobalt(III) (1+) by L-α-Amino Dicarboxylate(1−)

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Synopsis. The binary and ternary solubility phase diagrams for the system of Δ- and Λ-[Co(ox)(en)$_2$]X (X=L-glutamate (L-Hglu$^-$) and L-aspartate (L-Hasp$^-$)) were determined in water. It was found that the former anion L-Hglu$^-$ behaves as an excellent resolving agent for [Co(ox)(en)$_2$]$^+$ but the latter anion L-Hasp$^-$ forms a pseudoracemate *rac*-[Co(ox)(en)$_2$](L-Hasp).

An application of L-amino acid cation as a resolving agent for metal complexes has been reported.[1] In this note, L-α-amino acid anion, L-glutamate (L-Hglu$^-$) and L-aspartate (L-Hasp$^-$), are examined as a resolving agent for the resolution of [Co(ox)(en)$_2$]$^+$, the former anion leading to the successful optical resolution. The binary and ternary solubility phase diagrams of these systems are presented here.

Experimental

Δ- *and* Λ-*[Co(ox)(en)$_2$](L-Hglu)·5.5H$_2$O*: To a solution of *rac*-[Co(ox)(en)$_2$]CH$_3$CO$_2$[2] (100 g, 0.307 mol) dissolved in 300 cm^3 of water was added a solution of Na(L-Hglu)·H$_2$O (57.4 g, 0.307 mol) in 200 cm^3 of water. The mixed solution was evaporated to *ca.* 450 cm^3 and cooled in an ice bath. The less soluble Λ-diastereomer deposited was filtered, washed with methanol and acetone and then air-dried at room temperature. Further concentration of the filtrate gave the second crop (the final filtrate was reserved for Δ-diastereomer). The total yield was 72 g. The diastereomer was recrystallized from hot water. Found: C, 25.97; H, 6.78; N, 13.64%. Calcd for Λ-[Co(ox)(en)$_2$](L-Hglu)·5.5H$_2$O=C$_{11}$H$_{35}$N$_5$O$_{13.5}$Co: C, 25.79; H, 6.89; N, 13.67%. $\Delta\varepsilon_{523}$=+2.88 and ε_{497}=119.6 mol^{-1} dm^3 cm^{-1}.

An excess of conc. HCl was added to the above filtrate to give Δ-[Co(ox)(en)$_2$]Cl·3H$_2$O. The chloride salt was converted into the L-Hglu salt using a column of QAE-Sephadex A-25 (L-Hglu$^-$ form). Found: C, 25.94; H, 6.73; N, 13.63%. Calcd for Δ-[Co(ox)(en)$_2$](L-Hglu)·5.5H$_2$O=C$_{11}$H$_{35}$N$_5$O$_{13.5}$Co: C, 25.79; H, 6.89; N, 13.67%. $\Delta\varepsilon_{523}$=−2.91 and ε_{497}=120.3 mol^{-1} dm^3 cm^{-1}.

rac-, Δ-, *and* Λ-*[Co(ox)(en)$_2$](L-Hasp)·nH$_2$O*: The same process as described above except for the use of Na(L-Hasp)·H$_2$O instead of Na(L-Hglu)·H$_2$O gave the pseudoracemate *rac*-[Co(ox)(en)$_2$](L-Hasp). Found: C, 29.96; H, 5.57; N, 17.52%. Calcd for *rac*-[Co(ox)(en)$_2$](L-Hasp)=C$_{10}$H$_{22}$N$_5$O$_8$Co: C, 30.08; H, 5.55; N, 17.54%. ε_{497}=119.4 mol^{-1} dm^3 cm^{-1}.

The active diastereomers Δ-and Λ-[Co(ox)(en)$_2$](L-Hasp) were prepared from the corresponding active complexes Δ-[Co(ox)(en)$_2$]Cl·3H$_2$O and Λ-[Co(ox)(en)$_2$](L-Hglu)·5.5H$_2$O, respectively, using a column of QAE-Sephadex A-25 (L-Hasp$^-$ form). Found for Δ-diastereomer: C, 26.66; H, 6.22; N, 15.56%. Found for Λ-diastereomer: C, 26.69; H, 6.20; N, 15.55%. Calcd for [Co(ox)(en)$_2$](L-Hasp)·3H$_2$O=C$_{10}$H$_{28}$N$_5$O$_{11}$Co: C, 26.50; H, 6.23; N, 15.45%. $\Delta\varepsilon_{523}$=−2.86 and ε_{497}=119.3 mol^{-1} dm^3 cm^{-1} for Δ-diastereomer, and $\Delta\varepsilon_{523}$=+2.85 and ε_{497}=118.7 mol^{-1} dm^3 cm^{-1} for Λ- one.

Measurement. Solubility in water was determined according to the previously reported method.[3] The solid phases were identified by elemental analysis, absorption,

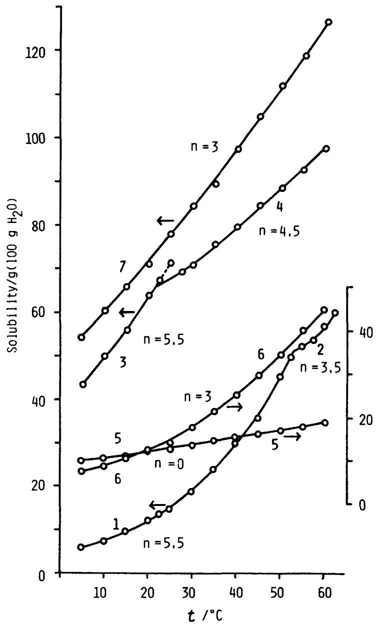

Fig. 1. Binary solubility curves of [Co(ox)(en)$_2$]X·nH$_2$O; X=L-Hglu: Λ form (**1**, **2**) and Δ form (**3**, **4**), and X=L-Hasp: racemic form (**5**), Λ form (**6**), and Δ form (**7**).

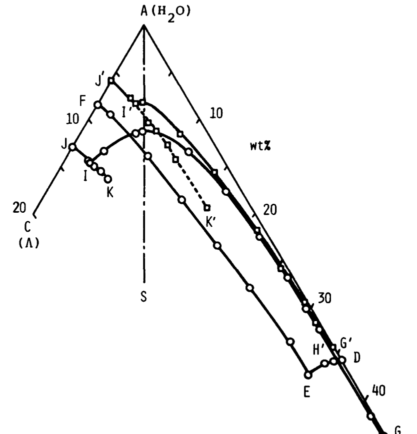

Fig. 2. Solubility isotherm of the ternary system, (A) H$_2$O—(B) Δ-[Co(ox)(en)$_2$]X—(C) Λ-[Co(ox)(en)$_2$]X; DEF: X=L-Hglu at 15 °C (○), GHIJ: X=L-Hasp at 25 °C (○), and G′H′I′J′: X=L-Hasp at 2 °C (□). See Table 2 for the solid phase compositions.

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TABLE 1. SOLUBILITY OF THE COMPLEX SALTS (grams of anhydrous salt in 100 g of water)

t/°C	No. of complex salt$^{a)}$ 1	2	3	4	5	6	7
5	5.90		43.3		9.87	7.26	54.5
10	7.40		49.9		10.2	8.47	60.6
15	9.49		56.0		10.9	10.4	66.0
20	12.1		63.8		11.9	12.4	71.0
22.5	13.5		67.5				
25	14.9		71.3		12.5	14.9	78.2
27.5				69.4			
30	18.9			71.0	13.5	17.6	84.6
35	24.1			75.6	14.6	21.4	89.7
40	30.0			79.6	15.4	25.2	97.9
45	36.0			84.7	16.1	29.5	105
50	45.5			88.7	17.0	34.4	112
52.5	50.0						
55		52.6		93.0	18.0	40.0	119
57.5		54.0					
60		57.1		97.8	18.8	44.8	127
62.5		60.4					

a) **1**: Λ-[Co(ox)(en)$_2$](L-Hglu)·5.5H$_2$O, **2**: Λ-[Co(ox)(en)$_2$](L-Hglu)·3.5H$_2$O, **3**: Δ-[Co(ox)(en)$_2$](L-Hglu)·5.5H$_2$O, **4**: Δ-[Co(ox)(en)$_2$](L-Hglu)·4.5H$_2$O, **5**: *rac*-[Co(ox)(en)$_2$](L-Hasp), **6**: Λ-[Co(ox)(en)$_2$](L-Hasp)·3H$_2$O, and **7**: Δ-[Co(ox)(en)$_2$](L-Hasp)·3H$_2$O.

and circular dichroism (CD) spectra. Optical densities were measured with a Hitachi 330 spectrophotometer and CD with a JASCO MOE-1 spectropolarimeter.

Results and Discussion

The solubility data for the binary and ternary systems are given in Tables 1 and 2, respectively.

System containing L*-Hglu*$^-$. The binary solubility curves are shown in Fig. 1. The solubility of Δ-diastereomer is very higher than that of Λ-one at 5—60 °C. The Δ-diastereomer showed an inflection at *ca.* 21.5 °C, where solid phase changes from 5.5-hydrate to 4.5-hydrate. A similar inflection appeared at *ca.* 53.5 °C for Λ-diastereomer, corresponding to the transition from 5.5-hydrate to 3.5-hydrate. The ternary isotherm at 15 °C showed one invariant point E near the Δ-diastereomer side (Fig. 2). Therefore, when an aqueous solution of pseudoracemic mixture is concentrated at 15 °C, the less soluble Λ-diastereomer will be obtained as solid deposit. The maximum yield of optical resolution calculated from the liquid phase composition at point E is 89%,[4] which ranks with those of the most excellent resolving agents such as Δ(or Λ)-[Co(edta)]$^-$(93%) and hydrogen tartrate (*R*,*R*)-C$_4$H$_5$O$_6$$^-$ (79%).[3]

System containing L*-Hasp*$^-$. The binary solubility curves are shown in Fig. 1. The solubility of Δ-diastereomer is the highest among three complexes. The curve of pseudoracemate intersects that of Λ-diastereomer at *ca.* 19 °C, the solubility of the latter being less than that of the former below this temperature. The ternary isotherm at 25 °C (Fig. 2) showed two invariant points H and I in agreement with the preparative formation of pseudoracemate Δ-[Co(ox)(en)$_2$]·Λ-[Co(ox)(en)$_2$](L-Hasp)$_2$=*rac*-[Co(ox)(en)$_2$](L-Hasp). The fundamental feature of the ternary isotherm was unaltered at 2 °C in equilibrium conditions. However, certain metastable states, which were at least maintained for several hours, were observed at this temperature. Especially, it is noteworthy that the curve I'K' intersects the racemic line AS, which means that the pseudoracemic mixture is optically resolvable in metastable state at 2 °C.

TABLE 2. SOLUBILITY IN THE TERNARY SYSTEMS (H$_2$O—Δ-[Co(ox)(en)$_2$]X—Λ-[Co(ox)(en)$_2$]X)

X	a)	Liquid phase composition (wt%) Δ-salt	Λ-salt	Solid phase$^{b)}$
L-Hglu	D	35.5	0	**3**
15 °C		34.9	0.73	**3**
		34.2	1.58	**3**
	E	33.5	3.71	**1+3**
		29.9	3.76	**1**
		23.4	4.54	**1**
		18.3	5.10	**1**
		12.7	5.85	**1**
		7.27	6.73	**1**
		1.64	7.94	**1**
	F	0	8.55	**1**
L-Hasp	G	43.6	0	**7**
25 °C	H	43.5	0.22	**5+7**
		41.2	0.19	**5**
		32.0	0.31	**5**
		29.6	0.47	**5**
		26.3	0.43	**5**
		21.6	0.77	**5**
		16.2	1.28	**5**
		10.7	2.70	**5**
		5.37	5.78	**5**
		4.97	6.54	**5**
		3.03	10.4	**5**
	I	2.42	12.2	**5+6**
		2.10	12.2	**6**
	J	0	12.9	**6**
L-Hasp		3.05	12.0	**6**
25 °C$^{c)}$		3.93	11.6	**6**
	K	4.93	11.4	**6**
L-Hasp	G'	34.2	0	**7**
2 °C	H'	34.4	0.08	**5+7**
		31.2	0.31	**7**
		29.2	0.20	**7**
		25.3	0.55	**7**
		21.1	0.72	**7**
		14.2	1.39	**7**
		8.97	2.64	**7**
		3.93	4.27	**7**
		3.28	4.91	**7**
	I'	3.31	5.03	**5+6**
		2.61	5.16	**6**
	J'	0	5.88	**6**
L-Hasp		33.6	1.34	**7**
2 °C$^{c)}$		5.48	4.86	**6**
		6.71	4.56	**6**
		8.39	4.34	**6**
		9.98	4.27	**6**
	K'	15.4	3.96	**6**

a) The capital letters D, E,···K, K' are identical to those in Fig. 2. b) Nos. of solid phase denote the complex salts in Table 1. c) Metastable phase.

References

1) R. D. Gillard, P. R. Mitchell, and C. F. Weick, *J. Chem. Soc., Dalton Trans.*, **1974**, 1635.

2) This complex was prepared by N. Koine (private communication): the reaction solution of *rac*-[Co(ox)(en)$_2$]-CH$_3$CO$_2$ prepared by the procedure of Dwyer *et al.* (*J. Am. Chem. Soc.*, **83**, 1285 (1961)) was concentrated without any addition of H$_2$SO$_4$ and HCl to give the crystals of the desired salt.

3) Y. Shimura and K. Tsutsui, *Bull. Chem. Soc. Jpn.*, **50**, 145 (1977).

4) The general equation of resolution yield in ternary system has been given by A. Fuyuhiro (D. Thesis, Univ. of Osaka (1982), p. 95). If the angle between AE and AS in Fig. 2 is θ, the resolution yield is represented as follows: $\text{yield}(\%)=\{\sin\theta/(\cos\theta/2\sqrt{3}+\sin\theta/2)\}\times 100$.