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OPTICAL RESOLUTION OF DL-ASPARTIC ACID IN THE PRESENCE OF OPTICALLY ACTIVE AMINO ACID AND COPPER (II) ION

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Optically active aspartic acid copper complex crystallized from an aqueous mixture of DL-aspartic acid, copper (II) ion and optically active amino acid. When L-amino acid was used, D-aspartic acid copper complex crystallized. A possible rationalization for the optical resolution of aspartic acid copper complex is suggested.

The last communication reported the optical resolution of DL-aspartic acid by adding a solution of DL-aspartic acid to solutions of copper complexes of D- or L-alanine, D- or L-glutamic acid, and L-proline.[1] A detailed study of this type of optical resolution of DL-aspartic acid has been carried out.[2] The optical resolution of DL-aspartic acid was explained by a stereoselective ligand exchange mechanism and subsequent preferential crystallization.[1] However, attempts to observe the possible stereoselective ligand exchange by the absorption spectrum and the mutarotation of the reaction mixture were unsuccessful. These observations together with the rapid ligand exchange in copper complexes suggest that the proposed stereoselective ligand exchange mechanism may not represent the mechanism of these reactions.

When copper carbonate was added to the aqueous mixtures of free DL-aspartic acid and optically active L-amino acid, D-aspartic acid copper complex crystallized. When an optically active D-amino acid was used, L-aspartic acid copper complex precipitated. The optically active amino acids used were L-glutamic acid, D-glutamic acid, L-alanine, and L-proline. Some of the results are summarized in Table I. The results are very similar to those obtained in the previous studies.[1,2] This could indicate that the mechanism of this resolution reaction and the previous studies are the same.

Fig. 1 shows the optical rotatory dispersion (ORD) curve of D-aspartic acid copper complex and ORD curves of several mixtures of L-proline copper complex with varying amounts of DL-aspartic acid. The ORD curve of L-proline copper complex shows a negative trough at 295 mμ. The trough decreased steadily depending on the increased addition of DL-aspartic acid to the aqueous solution of L-proline copper complex. When the concentration of DL-aspartic acid reached three times that of L-proline copper complex, the ORD curve of the mixture agreed exactly with that of L-proline. If the resolution reaction takes place in a

Table I

Optical Resolution of DL-Aspartic Acid in the Presence of Copper Ion and Optically Active Amino Acid

Chiral amino acid used (mole)	DL-Aspartic acid (mole)	Copper* (mole)	Optically active aspartic acid copper complex		Optically active aspartic acid	
			Crop	Weight, g	Confign.	Optical purity, %**
L-Glutamic acid (0.01)	0.02	0.01	1st	1.00	D	81
			2nd	0.62	L	90
D-Glutamic acid (0.01)	0.02	0.01	1st	0.95	L	76
			2nd	0.66	D	91
L-Alanine (0.01)	0.02	0.01	1st	1.85	D	55
			2nd	0.50	L	69
L-Proline (0.01)	0.02	0.01	1st	1.09	D	63
			2nd	1.16	L	41

*Cupric carbonate basic (copper content 53.0%) was used. Total volume of the aqueous solution is 225 ml.

**Specific rotation of pure L-aspartic acid: $[\alpha]_D^{24}$ +24.6° (c = 2, 6 N HCl). Optical purity is defined as: observed value/24.6° x 100.

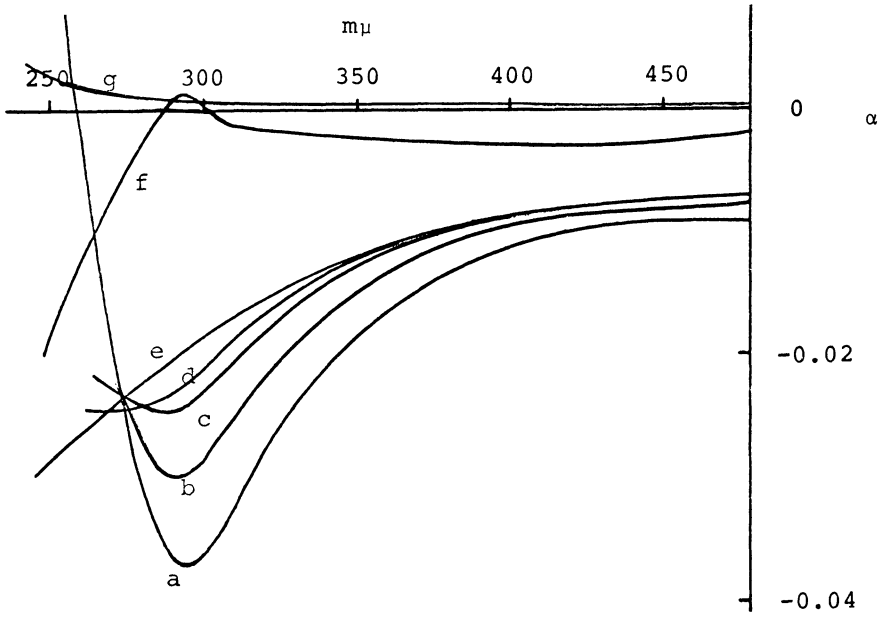

Fig. 1. ORD Curve of L-proline copper complex with varying amounts of DL-aspartic acid in aqueous solution. Stock solution A: 4×10^{-4} mole of L-proline and 2×10^{-4} mole of cupric acetate monohydrate in 25 ml of water. Stock solution B: 4×10^{-4} mole of DL-aspartic acid in 25 ml of water. (a) 0.5 ml A + 1.5 ml H_2O. (b) 0.5 ml A + 0.1 ml B + 1.4 ml H_2O. (c) 0.5 ml A + 0.25 ml B + 1.25 ml H_2O. (d) 0.5 ml A + 0.5 ml B + 1 ml H_2O. (e) 0.5 ml A + 0.75 ml B + 0.75 ml H_2O, and also 8×10^{-6} mole of L-proline and 8×10^{-6} mole of acetic acid in 2 ml of water. (f) D-aspartic acid (4×10^{-6} mole) and 4×10^{-6} mole of cupric acetate monohydrate in 2 ml of water. (g) L-aspartic acid (4×10^{-6} mole) in 2 ml of water. ORD Curves were measured by the use of a JASCO-ORD-CD-UV-5 Spectropolarimeter using 10 mm cell.

stereoselective ligand exchange mechanism, as proposed in the previous report, D-aspartic acid copper complex and L-aspartic acid would be formed in the reaction mixture. As is shown in Fig. 1, the contribution in ORD curve of D-aspartic acid copper complex is negative, and the contribution of L-aspartic acid is slightly positive in all region measured. Therefore, if the stereoselective ligand exchange reaction takes place, the ORD curve of the reaction mixture with excess DL-aspartic acid would be more negative than that of L-proline.

These experiments indicate that the optical resolution of DL-aspartic acid using copper (II) ion and optically active amino acid is not based on the stereoselective ligand exchange reaction. It might be explained that the optically active amino acid competitively inhibits the crystal growth of optically active aspartic acid copper complex that has the same configuration. In other words, when L-amino acid was in the reaction mixture, the crystal growth of L-aspartic acid copper complex could be inhibited, and D-aspartic acid copper complex is crystallized faster from the reaction mixture. When an aqueous solution of DL-aspartic acid, L-glutamic acid with copper ion was inoculated with pulverized D- or L-aspartic acid copper complex, D-aspartic acid copper complex precipitated quickly relative to L-aspartic acid copper complex. The amount of precipitated copper complex of the former was more than three times that of the latter. The preferential crystallization of aspartic copper complex[3] in the presence of L-glutamic acid also supports the importance of the crystallization step in the resolution reaction.

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