Novel Optical Resolution of Racemic α-Amino-acids *via* Formation of Mixed Ligand Copper(II) Complexes with Electrostatic Ligand–Ligand Interactions

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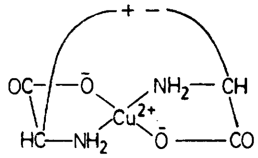
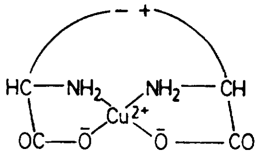
Summary Optical resolution of DL-aspartic acid and DL-glutamic acid has been achieved *via* the stereospecific formation of ternary copper(II) complexes composed of one of these amino-acids and a basic L-α-amino-acid interacting with each other electrostatically through oppositely charged side chains.

STEREOSELECTIVITY due to the steric requirements for co-ordination of a ligand around copper(II), often contained in a macromolecular ligand, has been reported to lead to the optical resolution of racemic α-amino-acids with a bulky side chain.[1] More recently, electrostatic ligand–ligand interactions between the charged groups in the side chains of co-ordinated α-amino-acids have been shown to give rise to geometrical isomerism in the ternary copper(II) complexes Cu(A)(B), where (A) refers to aspartic acid or glutamic acid and (B) to arginine, lysine, or ornithine.[2] Molecular models suggested a *trans* structure (**1**) for Cu(L-A)(L-B) and a *cis* structure (**2**) for Cu(D-A)(L-B), and this geometrical isomerism indicated the possibility of a novel approach to the optical resolution of racemic α-amino-acids with a charged side chain. We now report the resolution of DL-(A) into enantiomers *via* the formation of mixed ligand copper(II) complexes with L-(B).

For every pair of ligands (A) and (B), a ternary complex, Cu(A)(L-B), was isolated according to the following procedure. A neutralised solution (pH 7—9) containing $Cu(ClO_4)_2$, DL-(A), and L-(B) in the molar ratio of 1:2:1 was stirred for 1 h at room temperature and concentrated *in vacuo* to a small volume at <50 °C. Addition of ethanol to the residue gave blue crystals, which were recrystallised once from aqueous ethanol to give the pure product. After copper(II) had been removed by treating an aqueous solution of the complex with hydrogen sulphide, the incorporated amino-acid (A) was separated from L-(B) through a column packed with Dowex CCR-2 ion exchange resin by eluting


Cu(L-A)(L-B)

(1)


Cu(D-A)(L-B)

(2)

Table. Yields and optical purities of D-aspartic acid and D-glutamic acid resolved *via* formation of the ternary complexes, Cu(A)(B).

Ligand (A)	Ligand (B)	Cu(A)(B) isolated		(A) isolated	
		Yield[a] (%)	Optical purity[b] (%)	Yield[c] (%)	Optical purity[d] (%)
DL-Aspartic acid	L-arginine	17	93	12	89
	L-lysine	28	79	11	89
	L-ornithine	28	50	14	44
DL-Glutamic acid	L-arginine	61	42	53	33
	L-lysine	26	51	4	41
	L-ornithine	21	39	12	35

[a] Yield of the isolated complex based on the amount of copper(II) used. [b] The optical purity of (A) estimated by comparing the c.d. spectra of the isolated ternary copper(II) complexes in aqueous solution with those of the ternary systems containing known amounts of copper(II), L-(B), and (A) with different optical purities. [c] Yield of isolated (A) based on the half amount of DL-(A) used. [d] The specific rotations ($[\alpha]^{20}$) of pure L-aspartic acid and L-glutamic acid used were +25.7° and +31.3° (in 3 M HCl; c=1), respectively.

with water, and was recrystallised from aqueous ethanol when it was necessary to remove inorganic salts.

The specific rotations (in 3 M HCl; $c = 1$) of aspartic acid and glutamic acid, respectively, obtained from three systems each containing a different L-(B) established that the isolated ternary complexes had incorporated preferentially the D-enantiomers of the acidic amino-acids (Table). The same results were obtained from the c.d. curves of the isolated complexes in aqueous solution (pH 7·5—8). The difference between the optical purities of D-(A) evaluated from the isolated complex and from isolated (A) (Table) may be due to the inaccuracies pertaining to the c.d. calibration curves. The high D-(A) contents indicate that the isolated complexes are Cu(D-A)(L-B) (**2**), whose preferred crystallisation is probably attributed to the combined effects of the stability and solubility factors.

The present optical resolution of DL-(A) in turn implies that the resolution of DL-(B), which is in progress in our laboratory, is feasible.

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[1] I. I. Peslyakas, S. V. Rogozhin, and V. A. Davankov, *Izvest. Akad. Nauk S.S.S.R., Ser. khim.*, 1974, 174, and papers cited therein; K. Harada and T. Iwasaki, *Chem. Letters*, 1972, 1057, and papers cited therein; R. V. Snyder, R. J. Angelici, and R. B. Meck, *J. Amer. Chem. Soc.*, 1972, **94**, 2660.

[2] T. Sakurai O Yamauchi, and A. Nakahara, *Bull. Chem. Soc. Japan*, 1976, **49**, 169.