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OPTICAL RESOLUTION OF DL-AMINO ACIDS WITH ALIPHATIC SIDE CHAIN BY USING L-PHENYLALANINE

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An aqueous solution containing L-phenylalanine (L-Phe) and DL-valine, DL-leucine or DL-isoleucine in the molar ratio of 1:2 gave adduct composed of equimolar amounts of L-Phe and the amino acids abounding in D-isomer as crystals. From the adducts, the recovered free aliphatic amino acids had about 100% optical purity.

A number of studies have been reported on the optical resolution of DL-amino acids by preferential crystallization and diastereomeric procedures.[1-8] Since most of the optical resolutions have been achieved on their derivatives, such as N-acyl compound and ester, it is tedious to recover the optically active amino acids from the resolved derivatives. It was attempted to resolve more easily DL-valine (DL-Val), DL-leucine (DL-Leu) and DL-isoleucine (DL-Ile) by formation of adduct with L-phenylalanine (L-Phe). Aqueous solutions containing L-Phe and these DL-amino acids gave adducts composed of L-Phe and the amino acids abounding in D-isomer as crystals.

L-Phe (0.005 mol) and 0.010 mol of DL-Val (1.172 g), DL-Leu (1.312 g) or DL-Ile (1.312 g) were dissolved in 15 cm^3 of 1 mol dm^{-3} aqueous sodium hydroxide. Only to the alkali solution containing L-Phe and DL-Leu was added 30 cm^3 of water. These solutions were kept at 0, 25 and 50 °C, and the pH was adjusted to 5-6 with 1 mol dm^{-3} hydrochloric acid. Crystals deposited from the solution containing L-Phe and DL-Leu after stirring for several minutes, while from the solutions containing L-Phe and DL-Val or DL-Ile it was crystallized by adding an appropriate amount of ethanol. These reaction mixtures were stirred for 5-120 min at the respective temperature, and the crystals were collected by filtration. It was found by the integrated data in the ^1H NMR spectra in deuterium oxide that the crystals were adduct composed of equimolar amounts of L-Phe and the aliphatic amino acids. The crystals were dissolved in small amount of water and the resulting solutions were shaken with active carbon for 5 h to remove L-Phe by adsorption.[9] After filtration, the free aliphatic amino acids were obtained by evaporating the filtrates to dryness under reduced pressure at the temperature below 40 °C. It was confirmed by ^1H NMR spectra that the amino acids were free from L-Phe. The specific rotations of the obtained amino acids were measured in 5 mol dm^{-3} hydrochloric acid at 589 nm without recrystallization. The resolved amino acids had an abundance of the D-isomer and the optical purities were calculated on the basis of the specific rotations of the corresponding L-amino acids.[10] The conditions and results of the optical resolutions were summarized in Table 1.

The optical resolution of DL-α-alanine (DL-Ala) was also attempted in a similar manner as above. However, at 0 °C, L-Phe crystallized out of a solution containing L-Phe and DL-Ala. The crystals which were crystallized at 25 °C by adding 300 cm^3 of ethanol were composed of Ala and L-Phe in the molar ratio of 1:2.7, and the recovered free Ala was racemate. On the other hand, in the optical resolution of DL-Val, DL-Leu and DL-Ile, the D-amino acids having about 100% optical purity were obtained. These results indicated that it was possible to resolve these DL-aliphatic amino acids, except DL-Ala, by this method.

TABLE 1. CONDITIONS AND RESULTS OF OPTICAL RESOLUTIONS

DL-Amino acids[a]	Conditions			D-Amino acids		
	Temperature °C	Stirring time min	Added amount of ethanol cm^3	Yield g(%[b])	Specific rotation[c] °	Optical purity %
DL-Val	0	5	10	0.154(26.3)	-28.8	100
	0	30	50	0.367(62.6)	-21.6	75.1
	25	30	50	0.207(35.3)	-28.8	100
	50	120	150	0.139(23.7)	-28.8	100
DL-Leu	0	5	0	0.157(23.9)	-16.0	100
	0	30	0	0.324(49.4)	-9.6	60.2
	25	30	0	0.240(36.6)	-6.0	37.3
	50	120	0	0.142(21.6)	-4.8	30.1
DL-Ile	0	30	10	0.324(49.4)	-29.6	73.2
	25	5	30	0.125(19.1)	-39.2	96.8
	25	10	30	0.160(24.4)	-35.8	88.4
	25	30	30	0.222(33.8)	-35.7	88.1
	50	30	250	0.115(17.5)	-24.3	60.1

a) 0.010 mol. b) Yield(%)=[Yield(g)×100]/(1/2)[Reaction amount of DL-amino acid(g)]. c) $[\alpha]_{589}^{20}$(c 1.0, 5 mol dm^{-3} hydrochloric acid).

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