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Syntheses of Optically Active α-Amino Acids from α-Keto Acids by Hydrogenolytic Asymmetric Transamination[1,2]

by

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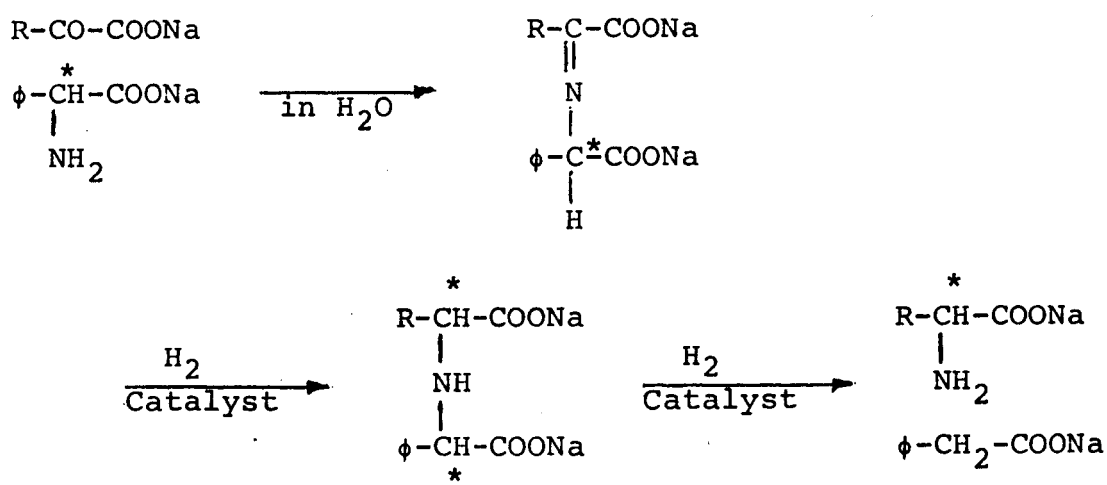
Several asymmetric syntheses of α-amino acids have been reported[3-19]. However, a few studies have been made on the nonenzymatic synthesis of optically active amino acids from their corresponding α-keto acids[3,6,15,17,18].

During the course of the study of hydrogenolysis in this laboratory, it was found that sodium phenylglycinate in aqueous solution was hydrogenolyzed easily to ammonia and phenylacetic acid by the use of palladium on charcoal, palladium hydroxide on charcoal[15], or by other catalysts. By the use of this finding, new asymmetric syntheses of various α-amino acids from their corresponding α-keto acids and optically active D and L-phenylglycine in aqueous solution were investigated. The schematic route of this synthesis is shown below.



By this synthetic method, 40-60% optically active α-amino acids were usually obtained. Some of the results are listed in Table I.

TABLE I

OPTICALLY ACTIVE AMINO ACIDS PREPARED BY

HYDROGENOLYTIC ASYMMETRIC TRANSAMINATION

	Config'n of Ph-glycine	Catalyst	Yield[a] %	Config'n of product	$[\alpha]_D^{25}$ of amino acid, 5 N HCl[b] (optical purity %)	$[\alpha]_D^{25}$ of DNP amino acid 1 N NaOH (optical purity %)
ala	L	Pd-C	36	L	+6.0 (41)	+91.8 (64)
α-NH_2bu	L	Pd-C	40	L	+7.3 (36)	+43.0 (44)
glu	D	Pd-$(OH)_2$-C	25	D	-17.9 (56)	+39.3[c] (49)

[a] Sodium salts of phenylglycine (0.01 mole) and α-keto acid (0.01 mole) were kept at room temperature for 30 minutes with 20 ml of water. After this, hydrogenation and hydrogenolysis were carried out. The yield shown is after one recrystallization.

[b] The specific rotations were measured after one recrystallization.

[c] The specific rotation was measured in glacial acetic acid.

A typical synthesis is as follows: α-ketobutyric acid, 1.02 g (0.01 mole), and L-phenylglycine, 1.51 g (0.01 mole) ($[\alpha]_D^{25}$ = -168°, 5 N HCl), were dissolved in a mixture of 10.0 ml of 2 N sodium hydroxide and 10 ml of water. After standing for 30 minutes at room temperature, the solution was then hydrogenated and hydrogenolyzed with 2.50 g of 10% palladium on charcoal (initial pressure 40 lbs.). After 24 hours of reaction, the catalyst was removed by filtration. The catalyst was washed with water repeatedly. The filtrate was concentrated to about 25 ml and 6 N hydrochloric acid was added to bring the pH to about 1. The precipitated phenylacetic acid was extracted with ether. The aqueous solution was evaporated to dryness. The amino acid hydrochloride was extracted with absolute alcohol and the undissolved sodium chloride was removed by filtration. The alcoholic solution was applied to a Dowex 50 x 2 column (hydrogen form, 100-200 mesh, 2 cm x 13 cm). α-Hydroxybutyric acid and other non-amino acid acidic materials were eluted with water, then α-amino-n-butyric acid was eluted with 1 N aqueous ammonia. Fractions containing the amino acid were combined and evaporated to dryness. Crude α-amino-n-butyric acid, 0.71 g, was obtained. Crude α-amino-n-butyric acid, 0.61 g, was recrystallized by dissolving in water and precipitating with alcohol, 0.36 g, $[\alpha]_D^{25}$ = +7.3°, optical purity 36%. A part of the crude α-amino-n-butyric acid was converted to its DNP-derivative by treatment with 2,4-dinitrofluorobenzene[18,19]. The DNP-α-amino-n-butyric acid was isolated

by celite column chromatography, $[\alpha]_D^{25} = +43.0°$ (1 N NaOH). The difference of optical purity of DNP- and free α-amino-n-butyric acid could be explained by fractionation during the isolation of free amino acid.

By the use of these results, synthesis of isooctopine[3,22] [L-(arginine)-L-(alanine)] from L-arginine and pyruvic acid in the alkaline solution by catalytic hydrogenation can be understood. This type of asymmetric synthesis is under further investigation.

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