plet at 3.3 ppm (indistinct) (*H*COC=C), and multiplet at 0.8–2.2 ppm (remaining protons).

Anal. Calcd for $C_9H_{14}O$: C, 78.21; H, 10.21. Found: C, 78.48; H, 10.20.

Reductive Cyclization of Methyl γ-(2-Ketocyclohexane)butyrate (20).—A 4.14-g (0.022 mole) sample of methyl γ-(2-ketocyclohexane)butyrate[35] was subjected to reductive cyclization with sodium naphthalenide in tetrahyrofuran according to the conditions described above. The crude product was distilled through a short-path apparatus to yield 0.71 g of a pale yellow liquid which was shown by vpc analysis to contain unreacted starting material and 11% of 6-hydroxybicyclo[4.4.0]decan-7-one. The hydroxy ketone was separated by means of preparative-scale vpc and obtained as a colorless oil, $\tilde{\nu}^{\text{liquid}}$ 3600 (hydroxyl) and 1720 cm^{-1} (cyclohexanone carbonyl).

Anal. Calcd for $C_{10}H_{16}O_2$: C, 71.39; H, 9.59. Found: C, 71.04; H, 9.98.

Reductive Cyclization of Methyl β-(2-Ketocyclopentane)-propionate (18).—A 3.78-g (0.022 mole) sample of methyl β-(2-ketocyclopentane)propionate[36] was subjected to reductive cyclization with sodium naphthalenide in tetrahydrofuran according to the conditions described above. The crude product was distilled through a short-path apparatus to give 0.31 g of a yellow liquid which was shown by vpc analysis to contain a small amount of unreacted starting material, 30% of 5-hydroxybicyclo[3.3.0]octan-6-one, and 70% of unidentified higher boiling materials. A small sample of the hydroxy ketone was separated by means of vpc and was obtained as a colorless oil, $\tilde{\nu}^{\text{liquid}}$ 3520 (hydroxyl) and 1740 cm^{-1} (cyclopentanone carbonyl).

Reductive Cyclization of Methyl β-(4,4-Dimethyl-2-ketocycloheptane)propionate (21).—Following the procedure described above, a sodium naphthalenide solution was prepared from 600 ml of tetrahydrofuran, 15.9 g (0.124 mole) of naphthalene, and 2.85 g (0.124 g-atom) of sodium. To this was added, over a period of 1 hr, 7.0 g (0.03 mole) of methyl β-(4,4-dimethyl-2-ketocycloheptane)propionate (21) in 30 ml of tetrahydrofuran. The reaction mixture was allowed to stand overnight and was then processed in the previously described fashion to yield, after chromatography over alumina, 1.60 g (27%) of 4,4-dimethyl-7-hydroxy-8-ketobicyclo[5.3.0]decane (22). Recrystallization from petroleum ether furnished colorless crystals: bp 99–101° (0.07 mm); mp 59.5–60.5°; $\tilde{\nu}^{\text{KBr}}$ 3400 (hydroxyl) and 1745 cm^{-1} (cyclopentanone carbonyl); and nmr (in CCl_4) one-proton multiplet at 3.66 ppm (hydroxyl), six-proton unsymmetrial triplet at 0.90, 0.96, and 1.0 ppm (methyl groups), and 13-proton multiplet from 1.2 to 2.6 ppm (remaining protons) (the multiplets of the hydroxyl and methyl resonances suggest that the compound is not a pure stereoisomer but probably a mixture of the two epimeric forms).

Anal. Calcd for $C_{12}H_{20}O_2$: C, 73.48; H, 10.25. Found: C, 73.70; H, 10.12.

Treatment of 22 with 2,4-dinitrophenylhydrazone under the usual acid-catalyzed conditions for hydrazone formation yielded the 2,4-dinitrophenylhydrazone of 4,4-dimethylbicyclo[5.3.0]dec-1-en-8-one, mp 196–197° after recrystallization from ethanol.

Anal. Calcd for $C_{18}H_{22}N_4O_4$: C, 60.32; H, 6.19. Found: C, 60.68; H, 6.33.

Registry No.—**1**, 10407-26-8; α-**2**, 10407-27-9; β-**2**, 10407-28-0; **3**, 769-32-4; **4**, 10407-30-4; **5**, 10407-31-5; **6**, 10407-32-6; **11**, 10407-33-7; **12**, 10421-80-4; **16**, 7106-07-2; **17**, 10407-35-9; **18**, 10407-36-0; **20**, 1205-19-2; **21**, 10407-38-2; **22**, 10407-39-3; 2,4-dinitrophenylhydrazone of 4,4-dimethylbicyclo[5.3.0]dec-1-en-8-one, 10407-40-6; *t*-butyl β-(2-ketocycloheptane)-propionate, 10407-41-7; 6-hydroxybicyclo[4.4.0]decan-7-one, 10407-42-8; 5-hydroxybicyclo[3.3.0]octan-6-one, 10407-43-9.

(35) R. Huisgen and D. Pawellek, *Ann.*, **641**, 71 (1961); A. Chaterjee, *Tetrahedron Letters*, 959 (1965).

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

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Sodium α-phenylglycinate was found to be hydrogenolyzed easily to ammonia and phenylacetic acid using palladium as the catalyst. By using this reaction, asymmetric syntheses of α-amino acids from their corresponding α-keto acids with optically active α-phenylglycine in aqueous alkaline solution were investigated. Optically active alanine, α-amino-*n*-butyric acid, glutamic acid, and aspartic acid were synthesized. Optical purities of these synthesized amino acids were in the 40–60% range.

Several asymmetric syntheses of α-amino acids have been reported. However, a few studies have been made on the nonenzymatic synthesis of optically active amino acids from their corresponding α-keto acids.[2-8] Octopine was first synthesized from L-arginine and pyruvic acid.[2] Later the synthesized octopine was found to be isooctopine.[3,9] A pyridoxal–copper(II) complex catalyzed reaction of α-ketoglutaric acid with L-alanine and L-phenylalanine was reported by Longenecker and Snell.[4] Hiskey and Northrop[5a] reported the formation of optically active α-amino acids (optical purity 12–80%) by hydrogenation and hydrogenolysis of the Schiff base of α-keto acids with (+)- and (−)-α-methylbenzylamine. They also reported the synthesis of alanylalanine[5b] from the Schiff base of pyruvyl-(*S*)-alanine with benzylamine by catalytic hydrogenation. Kanai and Mitsui[6] synthesized optically active phenylglycine using the Hiskey reaction. Harada and Matsumoto[7] studied various Hiskey-type reactions and proposed possible steric courses for the syntheses. They also reported the syntheses of optically active amino acids by catalytic hydrogenation of the oximes of the Schiff bases of *l*-menthyl esters of α-keto acids with benzylamine.[8]

In the previous communication of this investigation,[10] it was reported that several amino acids were

(1) Sterically Controlled Synthesis of Optically Active Organic Compounds. IV. For part III, see K. Harada, *Nature*, **212**, 1571 (1966). Contribution No. 077 of the Institute of Molecular Evolution, University of Miami.

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(3) R. M. Herbst and E. A. Swart, *J. Org. Chem.*, **11**, 366 (1946).

(4) J. B. Longenecker and E. E. Snell, *Proc. Natl. Acad. Sci. U. S.*, **42**, 221 (1956).

(5) (a) R. G. Hiskey and R. C. Northrop, *ibid.*, **83**, 4798 (1961); (b) *ibid.*, **85**, 1753 (1965).

(6) A. Kanai and S. Mitsui, *J. Chem. Soc. Japan, Pure Chem. Sec.*, **87**, 183 (1966).

(7) K. Harada and K. Matsumoti, *J. Org. Chem.*, **32**, 1794 (1967).

(8) K. Matsumoto and K. Harada, *J. Org. Chem.*, **31**, 1965 (1966).

(9) S. Akasi, *J. Biochem.* (Tokyo), **35**, 261, 281, 291 (1937).

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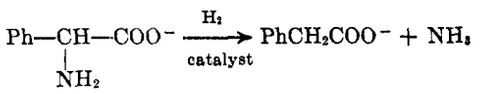
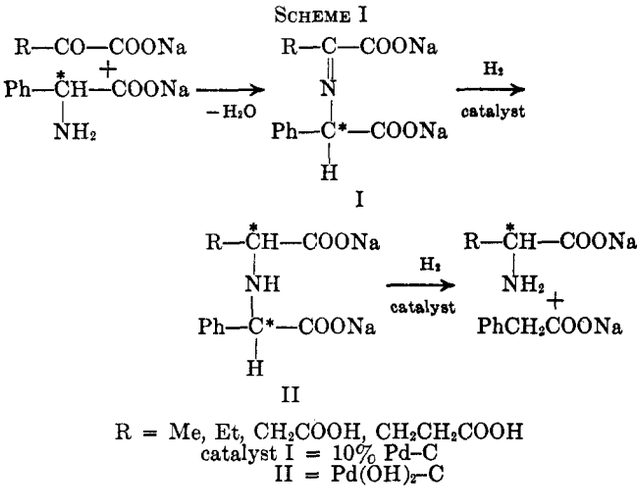
synthesized from their corresponding α-keto acids with optically active α-phenylglycine by the use of catalytic hydrogenation and hydrogenolysis procedures.

During the course of the hydrogenolysis study 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 and by other catalysts. As a first application of this finding, new sterically controlled syntheses of optically active α-amino acids from their



corresponding α-keto acids and optically active (*R*)- and (*S*)-phenylglycine in aqueous solution were investigated. The schematic route of this synthesis is shown in Scheme I. By this synthetic method, 40–

SCHEME I

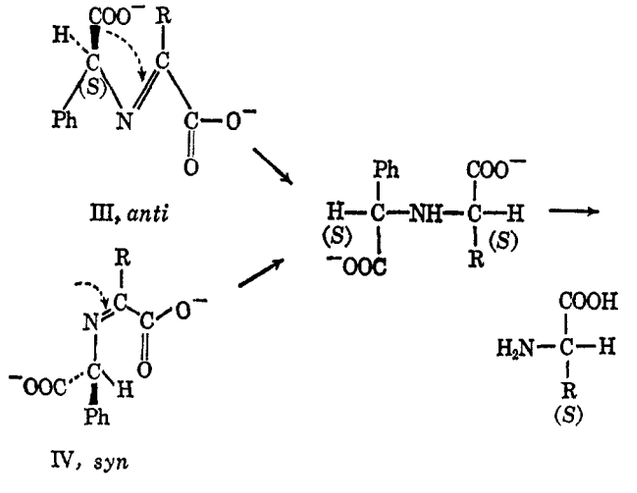


R = Me, Et, CH_2COOH, CH_2CH_2COOH
catalyst I = 10% Pd-C
II = $Pd(OH)_2$-C

60% optically active α-amino acids were usually obtained. Summarized results are listed in Table I.

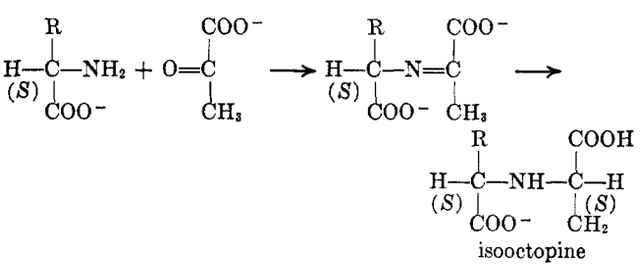
The structure of the Schiff base I in Scheme I might be in two forms, *anti* and *syn*. The two most likely structures of these might be structures III and IV in Scheme II. Structures III and IV each gave (*S*)-

SCHEME II



amino acid when (*S*)-phenylglycine was used as an asymmetric center. Observed results show that the optical purity of the resulting amino acids does not decrease considerably dependent on the increase of alkyl group of the α-keto acids. If structure III is a major conformation, steric hindrance between the alkyl group of the α-keto acid and the carboxylate group of phenylglycine would increase[7] with the increase of alkyl group of the α-keto acids. Therefore, the contribution of structure III would decrease while the contribution of structure IV increased. In a solvent which has a high dielectric constant, such as water including electrolytes, repulsion of the two charged carboxylate groups in structure IV might not be so great and might allow the molecule to take the *syn* structure in Scheme II. However, it is difficult to decide which structure of these two is preferred in the synthesis. In the reaction mixture, the Schiff base might exist as a mixture of structures III and IV. Both *anti* and *syn* structures could result in the (*S*)-phenylglycine-(*S*)-amino acid structure by hydrogenation. The resulting *S,S* structure was then hydrogenolyzed to (*S*)-amino acid and phenylacetic acid. The formation of isooctopine[2,3] (*S*)-arginine-(*S*)-alanine from (*S*)-arginine and pyruvic acid in the alkaline solution by catalytic hydrogenation could be explained in a way similar to that in this study (Scheme III).

SCHEME III



R = $(CH_2)_3NHC(NH_2)=NH$

It has been known that partially optically active amino acids are fractionated during the isolation and purification procedures.[8] When alanine was isolated from the crude reaction mixture (salts were already eliminated), considerable fractionation was observed. Isolated alanine showed 70–90% optical purity; however, the real optical purity of the product without fractionation should be about 50% by DNP-amino acid column chromatography. To avoid the fractionation of the synthesized partially optically active amino acid, the desalted crude mixture was applied to Dowex 50 resin and any contaminating organic acids and remaining salts were eliminated. Fractions containing the amino acid were collected and evaporated. The crude amino acid was purified by recrystallization without considerable fractionation. A part of the crude amino acid was treated with 1-fluoro-2,4-dinitrobenzene to yield DNP-amino acid. The resulting DNP-amino acid was isolated by column chromatography as in a previous study.[7,8] By the use of this DNP method, accurate optical purities of the synthesized amino acids were measured.

After the catalytic hydrogenation of the Schiff base (I), intermediate compound II (in Scheme I, R = CH_3) was isolated. From II, optically active alanine (optical purity 90%) was obtained by hydrogenolysis. The optical purity is higher than that obtained from the reaction product (40–60%). This suggests that

TABLE I

OPTICALLY ACTIVE AMINO ACIDS SYNTHESIZED BY HYDROGENOLYTIC ASYMMETRIC TRANSAMINATION

Amino acid prepared	Confign of Ph-Gly[a]	Ph-Gly:keto acid[b]	Catalyst[c]	Yield,[d] %	Confign of product	$[\alpha]^{25}D$ of amino acid, deg (c, 5 N HCl)[f] (optical purity, %)	$[\alpha]^{25}D$ of DNP-amino acid, deg (c, 1 N NaOH)[g] (optical purity, %)
1 (Ala)	R	1:1	I, II	35	R	−6.0 (1.53) (41)	−79.8 (0.655) (56)
2	R	1:2	I, II	35	R	−7.8 (1.46) (53)	−77.5 (0.670) (54)
3	R	1:3	I, II	37	R	−6.5 (1.62) (43)	−67.6 (0.667) (47)
4	S	1:1	I	35	S	+6.0 (2.08) (41)	+91.8 (0.545) (64)
5	R	1:1	II	28	R	−7.2 (1.37) (49)	−64.0 (0.448) (45)
6	R	1:1	II	23	R	−5.8 (1.17) (40)	−57.0 (0.534) (41)
7	R	1:2 (10 ml)	I, II	41	R	−4.5 (1.50) (31)	
8	R	1:2 (20 ml)	I, II	40	R	−7.5 (1.81) (51)	
9	R	1:2 (40 ml)	I, II	33	R	−7.8 (1.80) (53)	
10 (α-NH_2-But)	R	1:1	I, II	41	R	−8.0 (1.22) (39)	−41.3 (0.600) (42)
11	R	1:2	I, II	43	R	−6.0 (1.44) (32)	−29.4 (0.717) (30)
12	R	1:1	II	38	R	−4.9 (2.10) (24)	−30.4 (0.462) (31)
13	S	1:1	I	40	S	+7.3 (1.49) (36)	+43.0 (0.523) (44)
14 (Asp)	R	1:1	I	e	R	e	−43.3 (0.400) (47)
15	R	1:1	II	e	R	e	−45.4 (0.443) (45)
16	S	1:1	I	e	S	e	+53.2 (0.364) (58)
17 (Glu)	R	1:1	I	26	R	−11.2 (1.01) (35)	+39.0 (0.532) (48)[h]
18	R	1:1	II	25	R	−17.9 (1.18) (56)	+39.3 (0.489) (49)[h]

[a] (R)-Phenylglycine, $[\alpha]^{25}D$ −168.0° (c 1.11, 5 N HCl); (S)-phenylglycine, $[\alpha]^{25}D$ +164.2° (c 1.18, 5 N HCl). [b] α-Keto acids (0.01 mole) were used in each reaction. Hydrogenation reactions were carried out in 20 ml of aqueous solution. After mixing phenylglycine and α-keto acid, the solution was allowed to stand for 30 min at room temperature. [c] Catalyst I, 10% palladium on charcoal; catalyst II, palladium hydroxide on charcoal. I, II means that hydrogenation was carried out by the use of catalyst I, and catalyst II was used for hydrogenolysis. [d] Yields listed are shown after one recrystallization. [e] The products are a mixture of aspartic acid and alanine. [f] Optical rotations were measured after one recrystallization. Optical purity is defined as ($[\alpha]D$ obsd/$[\alpha]D$ lit.) × 100. (S)-alanine, $[\alpha]^{25}D$ +14.6° (5 N HCl); (S)-α-aminobutyric acid, $[\alpha]^{25}D$ + 20.6° (5 N HCl); (S)-glutamic acid, $[\alpha]^{25}D$ +31.8° (5 N HCl). J. P. Greenstein and M. Winitz, "Chemistry of the Amino Acids," Vol. 3, John Wiley and Sons, Inc., New York, N. Y., 1961: alanine, p 1819; α-aminobutyric acid, p 2401; glutamic acid, p 1929. [g] Optical purity is defined as ($[\alpha]D$ obsd/$[\alpha]D$ lit.) × 100. DNP-(S)-Ala, $[\alpha]D$ +143.9° (1 N NaOH); DNP-(S)-α-NH_2-but, $[\alpha]D$ +98.8° (1 N NaOH); DNP-(S)-Asp, $[\alpha]D$ +92.0° (1 N NaOH); DNP-(S)-Glu, $[\alpha]D$ −80.8° (AcOH). K. R. Rao and H. A. Sober, *J. Am. Chem. Soc.*, **76**, 1328 (1954). [h] Optical rotations were measured in glacial acetic acid.

the fractionation of diastereomers of structure II would take place during the isolation procedure. II was difficult to purify by recrystallization or by sublimation. However, carboxyl group equivalent molecular weight (116–118) shows the compound is relatively pure (calcd, 112). II was hydrogenolyzed in alkaline solution to convert it to alanine.

The reaction products from oxaloacetic acid were found to be a mixture of optically active aspartic acid and alanine. This problem will be described in detail in a separate article.

Crude products of alanine and glutamic acid prepared from pyruvic acid and α-ketoglutaric acid contain some unknown impurity which is less soluble in water than is alanine or glutamic acid. Alanine, α-amino-*n*-butyric acid, and glutamic acid could be purified by using this property of the impurity.

It is known that phenylglycine is one of the most racemizable amino acids; it is also known that, in general, amino acids racemize more easily when they combine with a carbonyl compound to form the Schiff base. Therefore, racemization of optically active phenylglycine during the synthesis was examined. After 2 hr of standing at room temperature, the Schiff base composed of (R)-phenylglycine and pyruvic acid was decomposed by addition of 6 N HCl. The isolated (R)-phenylglycine showed a specific rotation of $[\alpha]^{25}D$ −167°, whereas the starting (R)-phenylglycine had $[\alpha]^{25}D$ −168°. This suggests that the racemization of phenylglycine during the reaction in a short time could be little or none.

These reactions are interesting in connection with the biochemical transamination because these are essentially a kind of asymmetric transamination reaction between α-keto acid and phenylglycine performed by catalytic hydrogenation and hydrogenolysis.

Experimental Section[11]

Optically Active Phenylglycine.—(R)- and (S)-phenylglycine were prepared using the method described by Fischer.[12] (R)-Phenylglycine was also obtained from Kay-Fries Chemicals, Inc., New York, N. Y. Specific rotations of (R)- and (S)-phenylglycine were as follows: (R)-phenylglycine, $[\alpha]^{25}D$ −168.0° (c 1.11, 5 N HCl); (S)-phenylglycine, $[\alpha]^{25}D$ +164.2° (c 1.18, 5 N HCl).

Hydrogenolysis of Sodium Phenylglycinate.—(R)-Phenylglycine (1.51 g, 0.01 mole) was dissolved in a mixture of 15 ml of water and 5.3 ml of 2 N sodium hydroxide. After the phenylglycine was dissolved, 2.0 g of 10% palladium on charcoal (catalyst I) was added. Hydrogenolysis was carried out at room temperature for 24 hr (initial pressure, 40 psi). After hydrogenolysis was completed, the aqueous solution containing ammonia was acidified to pH 2 by addition of 6 N hydrochloric acid. Liberated phenylacetic acid was extracted with ether (four 25-ml portions). The ether solution was washed once with a small amount of water and dried with anhydrous sodium sulfate. By evaporation of ether, phenylacetic acid was crystallized: 1.20 g (88%), mp 76–76.5°.

(11) All temperature measurements were uncorrected. All optical rotation measurements were carried out by the use of the Rudolph Model 80 polarimeter with a PEC-101 photometer. All hydrogenation and hydrogenolysis were performed by the use of the Parr 3910 shaker-type hydrogenation apparatus. Elemental analyses were carried out by Micro-Tech Laboratories, Skokie, Ill.

(12) E. Fischer and O. Weichhold, *Ber.*, **41**, 1292 (1908).

Anal. Calcd for $C_8H_8O_2$: C, 70.57; H, 5.92. Found: C, 70.79; H, 5.84.

In a similar way, sodium (*R*)-phenylglycinate was hydrogenolyzed by the use of palladium hydroxide on charcoal (catalyst II). Phenylacetic acid, 1.21 g (89%), was obtained.

Synthesis of Optically Active α-Amino-*n*-butyric Acid.—α-Keto-*n*-butyric acid (1.02 g, 0.01 mole) and (*S*)-phenylglycine (1.51 g, 0.01 mole) were dissolved in 20 ml of 1 *N* sodium hydroxide. The mixture was shaken to dissolve the phenylglycine completely. If necessary, a few drops of 2 *N* sodium hydroxide was added. After 30 min, the yellow solution was mixed with 2.5 g of catalyst I and hydrogenated and hydrogenolyzed for 24 hr at room temperature (initial hydrogen pressure was 40 psi). After hydrogenolysis was completed, the catalyst was removed by filtration. The filtrate was evaporated to about 20 ml under reduced pressure, and 6 *N* hydrochloric acid was added to the solution to bring the pH to about 1. The precipitated phenylacetic acid was extracted with ether (four 25-ml portions). 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 evaporated to dryness, and the remaining crude α-amino-*n*-butyric acid hyrochloride was dissolved in 15 ml of water. The aqueous solution was applied to a Dowex 50X2 column (hydrogen form, 100–200 mesh, 2 × 15 cm). Nonamino 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, 0.65 g, was obtained. The crude amino acid, 0.55 g, was dissolved in 1.2 ml of water at room temperature; then undissolved material was filtered. By addition of 4.0 ml of alcohol, 267 mg of (*S*)-α-amino-*n*-butyric acid was precipitated: yield 40%, $[\alpha]^{25}D$ +7.3° (*c* 1.49, 5 *N* HCl). The α-amino-*n*-butyric acid is pure by paper chromatography. Infrared absorption spectra were found to be the same as that of optically active α-amino-*n*-butyric acid. The amino acid was recrystallized once more for elemental analysis.

Anal. Calcd for $C_4H_9NO_2$: C, 46.60; H, 8.80; N, 13.59. Found: C, 46.39; H, 8.74; N, 13.64.

Optically active alanine and glutamic acid were synthesized in the same way as above. However, to eliminate the contaminating impurity from the crude amino acid, the mixture was purified as follows. Crude alanine, 1.0 g, was dissolved in 2.0 ml of water at room temperature. The mixture was filtered to remove the water-insoluble material. To the filtrate, 4 ml of alcohol was added to precipitate alanine. Glutamic acid was purified in the same way.

Two kinds of catalyst, 10% palladium on charcoal (catalyst I) and palladium hydroxide on charcoal (catalyst II),[5a] were used in this study. However, the rate of hydrogenolysis by the use of catalyst II seems to be a little faster than that by the use of catalyst I. On the other hand, the optical purity of the resulting amino acid by the use of catalyst I seems to be a little higher than that by the use of catalyst II.

It was observed that the amount of solvent (H_2O) in the reaction affected the optical purity of the resulting amino acid. Optical purities of the product by the use of different amounts of water are as follows: 10 ml (optical purity 31%), 20 ml (51%), 40 ml (53%). In this study, therefore, 20 ml of water was used in all reactions because, in addition to the lesser optical purity, more solvent resulted in a lesser yield of amino acid: 10 ml (41%), 20 ml (40%), 40 ml (33%).

DNP-α-amino-*n*-butyric Acid.—Crude α-amino-*n*-butyric acid (100 mg) was treated with 1-fluoro-2,4-dinitrobenzene by the usual method.[13] DNP-α-amino-*n*-butyric acid was isolated by Celite column chromatography.[14] The Celite (50 g) was treated with 25 ml of pH 7.0 phosphate–citrate buffer (0.2 *M*). The charged DNP derivative was developed with a mixture of chloroform and ether (4:1). The DNP-α-amino-*n*-butyric acid band was cut off, dried, and dissolved in 1.5% sodium hydrogen carbonate. The solution was acidified, and the DNP-amino acid was extracted with ethyl acetate. The ethyl acetate solution was evaporated, and the optical rotation of the remaining DNP-α-amino-*n*-butyric acid was measured: $[\alpha]^{25}D$ +43.0° (*c* 0.523, 1 *N* NaOH); 44% optically active; mp 128–130°.

Isolation of Intermediate N-Alkylamino Acid.—Sodium pyruvate (3.30 g, 0.03 mole) and (*R*)-phenylglycine (4.53 g, 0.03 mole) were dissolved in a mixture of 2 *N* sodium hydroxide (15 ml) and water (45 ml). After standing 30 min at room temperature, 3.0 g of 10% palladium on charcoal was added to the solution. Then hydrogenation of the mixture was carried out until 0.03 mole of hydrogen was adsorbed (approximately 1 hr). The catalyst was removed by filtration and the filtrate was diluted with water to about 120 ml. The pH of the solution was adjusted to about 7.0, and 120 ml of alcohol was added to the solution. Unreacted phenylglycine (total 1.52 g, 33%) was precipitated. During the evaporation of the solution (fraction I) and after evaporation (fraction II), the intermediate N-alkylalanine was precipitated: fraction I, 0.47 g, mp 244–245° dec; fraction II, 2.00 g, mp 219–222° dec. Both fractions I and II are ninhydrin negative. These two fractions were difficult to purify by recrystallization or by sublimation. After washing with alcohol, these fractions showed similar specific rotations: fraction I, $[\alpha]^{25}D$ −138.2° (*c* 1.56, 5 *N* HCl); fraction II, $[\alpha]^{25}D$ −127.8° (*c* 1.87, 5 *N* HCl). Molecular weights were determined by titration in dimethylformamide by 0.02 *N* sodium methoxide, thymol blue being used as indicator: fraction I, 118 per COOH; fraction II, 116 per COOH; calcd 112. By recrystallization from water, intermediate II was purified in poor recovery and the nitrogen analysis agreed with theoretical value: mp 244° dec.

Anal. Calcd for $C_{11}H_{13}NO_4$: N, 5.28. Found: N, 5.27.

Fraction II (1.20 g) was dissolved in a mixture of 2 *N* sodium hydroxide (5.0 ml) and water (15 ml). The solution was hydrogenolyzed with 2.50 g of catalyst I for 24 hr. From the reaction mixture, 0.42 g of alanine was isolated as described earlier. The alanine was sublimed at 210° (2 mm): $[\alpha]^{25}D$ −13.1° (*c* 0.711, 5 *N* HCl); 90% optically pure. Infrared absorption spectra of the alanine agreed with that of pure (*S*)-alanine.

DNP-(*S*)-alanine was prepared and isolated in the same manner: $[\alpha]^{11}D$ −127° (*c* 0.572, 1 *N* NaOH); 88% optically pure. DNP-(*S*)-alanine obtained from fraction I showed $[\alpha]^{25}D$ −131° (*c* 0.510, 5 *N* HCl) and was 92% optically pure.

Registry No.—(*R*)-Phenylglycine, 10333-78-5; (*S*)-phenylglycine, 10353-28-3; phenylacetic acid, 103-82-2; (*S*)-α-amino-*n*-butyric acid, 10385-46-3; α-amino-*n*-butyric acid, 4470-69-3; II, 10353-29-4; DNP-(*S*)-alanine, 10333-81-0; (*R*)-alanine, 10353-30-7; (*S*)-alanine, 10333-82-1; (*R*)-α-amino-*n*-butyric acid, 10333-83-2; (*R*)-aspartic acid, 10333-84-3; (*S*)-aspartic acid, 10353-31-8; (*R*)-glutamic acid, 10333-85-4.

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