Found : C, 57.39; H, 4.92; N, 6.34. Rf 0.45.*3 The IR spectrum of this sample was superimposable with that of D-(V) derived from the chemical resolution of DL-(IV).

The ethanolic mother liquor after removal of the insoluble L-(V) was evaporated *in vacuo* to dryness. The residue was dissolved in H_2O (20 cc.) and combined with the aqueous washings obtained in the isolation of L-(V). This aqueous solution was treated with 10% HCl to bring its pH to 1~2. After standing in a refrigerator overnight, the crystatls that separated was filtered, washed with H_2O, and dried, giving 2.32 g. (94%) of D-(IV), m.p. 155~158°. It was recrystallized from H_2O (ca. 50 cc.) (charcoal) to give D-(IV) as colorless needles, m.p. 158~159°, $[\alpha]_D^{23}$ −52.4° (c=3.584, EtOH, l=1). Yield. 1.74 g. (69.3%). *Anal.* Calcd. for $C_{12}H_{13}O_5N$: C, 57.37; H, 5.22°; N, 5.58. Found : C, 57.10; H, 4.84; N, 5.64. This sample was found to be identical by admixture and IR comparison with D-(IV) obtained by the chemical resolution of DL-(IV).

The absolute configurations of these sampes, L-(V) and D-(IV), were confirmed by converting them into 3-(3,4-dihydroxyphenyl)-L-, and -D-alanine. The data will be described in the following paper.[9]

When the above asymmetric hydrolysis was carried out with 0.4 g. or 0.2 g. of Takadiastase during an incubation period 90 hr. or 135 hr. instead of 0.3 g. of the former and 110 hr. of the latter, the result was as good as when with 0.3 g. of Takadiastase during an incubation period of 110 hr.

The authors are grateful to Dr. S. Tsurufuji of this Faculty for advices on the photometric ninydrin method. Thanks are also due to the members of the Central Analysis Room of this Faculty for elemental analyses and spectral data.

Summary

The preparation of 3-(3,4-methylenedioxyphenyl)-D-, and -L-alanine (D- and L-(V)) was carried out by the chemical or biological resolution of N-acetyl-3-(3,4-methylenedioxyphenyl)-DL-alanine (DL-(IV)). The N-acetyl-DL-amino acid prepared from 3,4-methylenedioxybenzyl chloride (II) and diethyl acetamidomalonate (I), via the diester (III), was resolved into two forms, D- and L-(IV), by means of fractional recrystallization of their cinchonine salts from ethanol, followed by the liberation of cinchonine base. Asymmetric hydrolysis of DL-(IV) was also smoothly effected by Takadiastase to give the L-amino acid (L-(V)) and N-acetyl-D-amino acid (D-(IV)). The latter as well as the one derived from the chemical resolution was converted by boiling it with 10% hydrochloric acid into the D-amino acid (D-(V)) in good yield.

(Received May 5, 1961)

UDC 547.466.02

110. Shun-ichi Yamada, Takayuki Shioiri, and Tozo Fujii : Studies on Optically Active Amino Acids. II.*1 Partially Asymmetric Synthesis of 3-(3,4-Methylenedioxyphenyl)alanine.

(*Faculty of Pharmaceutical Sciences, University of Tokyo**2)

In the preceding paper*1 the authors described the preparation of optically active 3-(3,4-methylenedioxyphenyl) alanine (V) by two resolution methods; chemical resolution and enzymatic asymmetric hydrolysis. Now we wish to report that the optically active amino acids (V) can also be prepared conveniently by the partially asymmetric synthesis, which seems to be one of the most important problems in amino acids syntheses.

*1 Part I : This Bulletin, **10**, 680 (1962).

*2 Hongo, Tokyo (山田俊一, 塩入孝之, 藤井澄三).

Many attempts[1] have been made to obtain optically active amino acids by hydrogenating the intermediates asymmetrically at some stage. Pedrazzoli[1h] prepared *p*-substituted D- and L-phenylalanines by partially asymmetric hydrogenation of *l*-menthyl *α*-benzamido-4-substitutedcinnamate followed by acid hydrolysis. We applied his procedure to the preparation of (V) as shown in Chart 1.

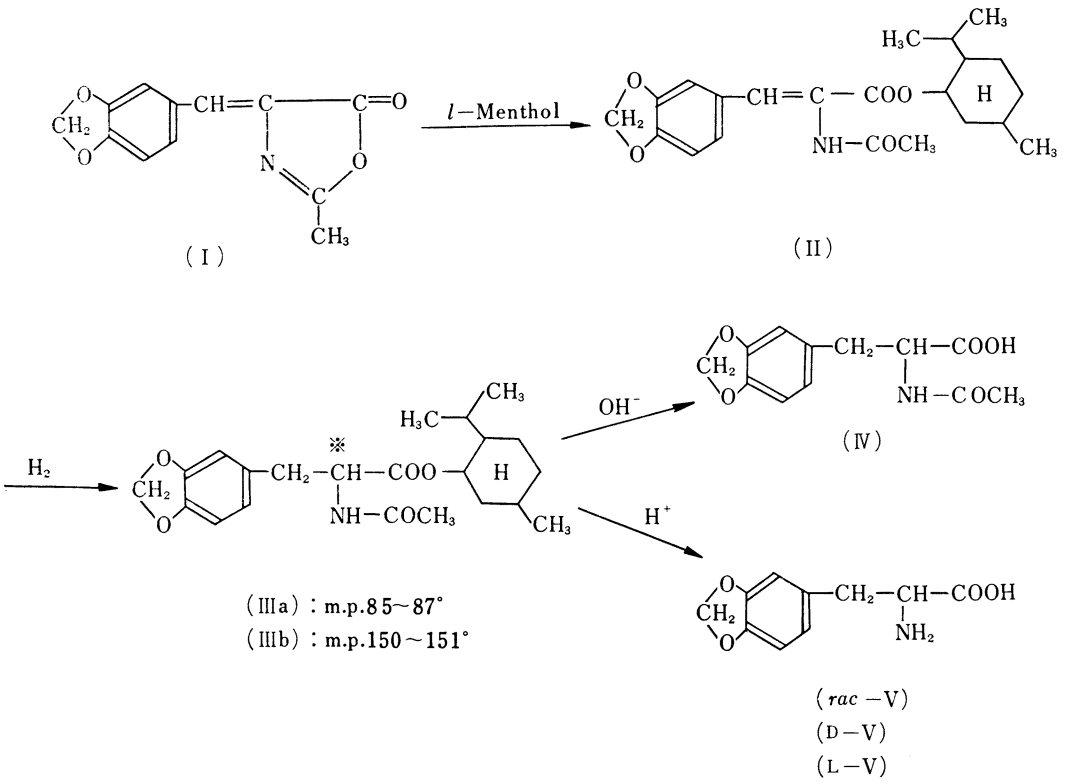

Chart 1.

The oxazolone (I), when treated with sodium *l*-mentholate in benzene, gave the unsaturated ester (II) as colorless needles, m.p. 115°, $[\alpha]_D^{28}$ −29.1° (c=2.85, ethanol), which easily became gelatinous in ethanol, benzene, hexane etc.

The ester (II) was hydrogenated catalytically by two variations : i) 10% palladium-carbon in ethanol, ii) 10% palladium-carbon in benzene (Table I). It is very interesting that an excess isomer of (III) was (IIIb), which was proved to N-acetyl-3-(3,4-methylenedioxyphenyl)-L-alanine *l*-menthyl ester as shown below, and in this hydrogenation the use of a polar solvent gave a better result than that of a nonpolar solvent. The influence of hydrogenation temperatures, however, cannot be ignored, for anomalous

1) *a*) S. Akabori : Kagaku, **25**, 54 (1955). *b*) S. Mitsui : Yuki Gosei Kagaku, **17**, 640 (1959). *c*) M. Bergmann, L. Zervas, V. du Vigneaud : Ber., **62**, 1905 (1929). *d*) M. Bergmann, J. E. Tietzman: J. Biol. Chem., **155**, 538 (1944). *e*) S. Akabori, T. Ikenaka, K. Matsumoto : Nippon Kagaku Zasshi, **73**, 112 (1952). *f*) G. Maeda : *Ibid.*, **77**, 1011 (1956). *g*) S. Akabori, S. Sakurai : *Ibid.*, **78**, 1629 (1957). *h*) A. Pedrazzoli : Chimia (Switz), **10**, 260 (1956); *Idem* : Helv. Chim. Acta, **40**, 80 (1957). *i*) F. Knoop, C. Martius : Z. physiol. Chem., Hoppe-Seyler's, **258**, 238 (1939). *j*) R. M. Herbst, E. A. Swart : J. Org. Chem., **11**, 368 (1946). *k*) M. Nakazaki : Nippon Kagaku Zasshi, **75**, 831 (1954). *l*) S. Akabori, Y. Izumi, Y. Fujii, S. Sakurai : *Ibid.*, **77**, 1374 (1956). *m*) S. Akabori, Y. Izumi, Y. Fujii : *Ibid.*, **78**, 886 (1957). *n*) T. Isoda, A. Ichikawa, T. Shimamoto : Kagaku Kenkyûsho Hôkoku, **34**, 134; 143 (1958).

addition (*trans*) of hydrogen[2] is rather enhanced at higher temperatures and the rate of asymmetric hydrogenation, *P*%, decreases.

Generally, it is considered that the influence of the asymmetry either in the molecule or in its surroundings is an essential factor for asymmetric hydrogenation,[1,3] but the above results suggest that the rate of asymmetric hydrogenation is greatly influenced by the reaction conditions.

TABLE I. Asymmetric Hydrogenation of (II)

Catalyst	Solvent	Hydrogenation temp.	Hydrogenation time	Total yield	M.p. of [a] mixture	$[\alpha]_D$ of [b] mixture	Rate of [c] asymmetric hydrogenation, *P*%	Excess isomer
10% Pd-C	EtOH	ca. 26°	5 hr.	95.4%	107~137°	−26.4°	12.0%	(IIIb)
10% Pd-C	Benzene	ca. 50°	5 hr.	90.0%	85~125°	−29.3°	0.8%	(IIIb)

a) Purity of mixture was confirmed by intensity of absorption at 326 mμ in UV spectrum, which was attributable to (II). (II) mixed with (III) was less than 1% in each case, which was negligible in $[\alpha]_D$ measurements.

b) $[\alpha]_D$ was measured in benzene solution in which the difference of $[\alpha]_D$ between (IIIa) and (IIIb) was the largest.

c) $P=\left\{\frac{2(\gamma-\beta)}{\alpha-\beta}-1\right\}\times 100$. α=rotation of excess isomer, β=rotation of less isomer, γ=rotation of mixture. All of them are values of rotation in benzene solution.

The diastereoisomeric mixture, which was obtained by the hydrogenation of (II) with 10% palladium-carbon in ethanol, was separated into (IIIa) and (IIIb) by repeated fractional crystallization as shown in the Experimental section. Purified (IIIa) and (IIIb) show m.p. 85~87° and 150~151°, $[\alpha]_D^{12}$ −55.2° (c=1.50, benzene) and $[\alpha]_D^{13}$ −3.8° (c=1.52, benzene), respectively. Optical rotatory dispersion curves of these compounds in methanol are illustrated in Fig. 1 in comparison with *l*-menthyl acetate.

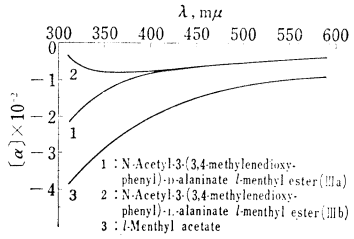

Fig. 1. Rotatory Dispersion Curves (MeOH) of *l*-Menthyl Esters

The conversion of (IIIb) to N-acetyl amino acid (IV) in alkaline medium proceeded in good yield, but unfortunately partial racemization occurred even at room temperature. (IV) thus obtained gave $[\alpha]_D^{26}$ +11.9° (c=2.32, ethanol), which corresponded to about 78% racemization. The inductive effect of the acetamido group[4] seems to facilitate racemization when saponification occurs.

Direct acid hydrolysis of (III) by hydrochloric acid in acetic acid or dioxane gave (V) in very poor yield or an unknown reddish brown resin.

In order to obtain the desired amino acid (V), it was found advantageous to carry out transesterification and hydrolysis without isolation of any intermediates. The diastereoisomeric mixture of (IIIa) and (IIIb) (m.p. 107~137°) was transesterified in methanol saturated with hydrogen chloride at room temperature, and then refluxed with 10%

2) R. P. L. Linstead, W. E. Doering, S. B. Davis, P. Levine, R. R. Whestone: J. Am. Chem. Soc., **64**, 1958 (1942).
3) V. Prelog, H. Schener: Helv. Chim. Acta, **42**, 2227 (1959).
4) S. Akabori, S. Mizushima: "Chemistry of Proteins," Vol. 1, 442 (1954), Kyoritsu-Shuppan Co. Ltd. (Tokyo).

hydrochloric acid for 2 hours. The free amino acid (*rac*-V) thus obtained in 62% yield formed colorless crystals, m.p. 250~251° (decomp.) and had no specific rotation. Transesterification of (IIIa) was carried out in 10 w/w% methanolic hydrogen chloride at reflux temperature for 15 hours, followed by a similar hydrolysis. From the melting point and the specific rotation ($[\alpha]_D^8$ +12.0° (c=1.66, *N* HCl)) the product was confirmed to be 3-(3,4-methylenedioxyphenyl)-D-alanine (D-V).*1 By a similar process, L-isomer (L-V) was obtained from (IIIb), and had $[\alpha]_D^{19}$ −14.0° (c=1.63, *N* HCl). The yields of (D-Va) nd (L-V) based on (IIIa) and (IIIb) were 48.0% and 57.6%, respectively. The structures of (*rac*-V), (D-V) and (L-V) were confirmed by comparisons of optical rotations, melting points, infrared spectra and paper chromatographic behaviors with those of the corresponding amino acids obtained in the preceding paper.*1 (IIIa), (IIIb), (D-V), and (L-V) were converted to optically active 3-(3,4-dihydroxyphenyl)alanines, which will be reported in the following paper,*3 and thus the absolute configurations of these substances were established unambiguously.

On hydrolysis of (IIIa) and (IIIb), followed by steam distillation, *l*-menthol was recovered in good yield, and since its specific rotation and melting point indicate that it is optically pure, it can be used again without any further purification, in this preparative method.

Experimental*4

***l*-Menthyl α-Acetamido-3,4-methylenedioxycinnamate (II)**——A mixture of *l*-menthol*5 (4.10 g., 0.026 mole) and Na powder (0.69 g., 0.030 atom) in anhyd. benzene (20 cc.) was kept standing overnight at room temperature (ca. 10°) and then refluxed for 2 hr. After filtering off the excess Na, anhyd. benzene (130 cc.) was added. To this yellow clear solution the fine powdered oxazolone*1 (I) (4.60 g., 0.020 mole) was added in portions under stirring at room temperature, and the resultant blood-red color solution was stirred for 4 hr. and kept standing overnight. After filtration (when (I) was not pure, a red powder was obtained), the solution was mixed with AcOH (1.6 cc.), heated to boil on a water bath, cooled, diluted with benzene (200 cc.), and then washed with H_2O (200 cc.). The benzene layer was dried and passed through a column of Al_2O_3 (40 g.) and evaporated *in vacuo*. The residue, which was at first gelatious, solidified on standing in EtOH, m.p. 90~103°, 6.30 g. (81.3%). Repeated recrystallization from 60% EtOH afforded colorless needles, m.p. 115°, $[\alpha]_D^{28}$ −29.1° (c=2.85, EtOH). *Anal.* Calcd. for $C_{22}H_{29}O_5N$: C, 68.19; H, 7.54; N, 3.62. Found: C, 68.17; H, 7.19; N, 3.65. IR ν_{max}^{Nujol} cm^{-1}: 3350 (NH), 1711 (COOR), 1657 (CONH), 1041, 931 (-O·CH_2·O-), 812 (C=C). UV $\lambda_{max}^{95\%\ EtOH}$ mμ (log ε): 233 (4.07), 294 (4.08), 326 (4.24). $\lambda_{min}^{95\%\ EtOH}$ mμ (log ε): 263 (3.65), 303 (4.05).

N-Acetyl-3-(3,4-methylenedioxyphenyl)-D-alanine *l*-Menthyl Ester (IIIa) and -L-alanine L-Menthyl Ester (IIIb): Asymmetric Hydrogenation of (II)——i) 10% Pd-C in EtOH: (II) (23.3 g., 0.06 mole) in EtOH (300 cc.) was hydrogenated catalytically in the presence of 10% Pd-C catalyst[5] (3.0 g.) for 5 hr. at room temperature (ca. 26°). The catalyst was filtered off and washed with EtOH (300 cc.) and the combined filtrates were evaporated *in vacuo*, giving a semi-crystalline residue which, after trituration with Et_2O, crystallized, m.p. 107~137°, 22.3 g. (95.3%). *Anal.* Calcd. for $C_{22}H_{31}O_5N$: C, 67.84; H, 8.02; N, 3.60. Found: C, 67.65; H, 7.97; N, 4.13. $[\alpha]_D^{14}$ −26.4° (c=3.00, benzene), $[\alpha]_D^{23}$ −31.3 (c=2.24, EtOH).

The mixture (20 g.) was extracted three times with hot hexane (100 cc., 50 cc., 50 cc.), and once with Et_2O (100 cc.). The hexane extract was evaporated *in vacuo*, giving a white solid (7.56 g.). Fractional crystallization of this with Et_2O-hexane gave (IIIa) of m.p. 70~83° (7.26 g.) and (IIIb) of m.p. 146~148° (0.23 g.). From the Et_2O extract, (IIIa) of m.p. 76~83° (2.87 g.) and (IIIb) of m.p. 147.5~149° (0.23 g.) were obtained by similar fractional crystallization. The residue from extraction with hexane

*3 Part III: This Bulletin, **10**, 693 (1962).

*4 All m.p.s are uncorrected. Instrumental measurements and paper chromatography were carried out as described in the following paper.*3 Optical rotatory dispersion curves were measured with the Rudolph photoelectric spectropolarimeter model 200 S~80 Q. All of the starting materials in each reaction were optically pure.

*5 *l*-Menthol used was a sample of J.P. VI., m.p. 43~44°, $[\alpha]_D^{17}$ −50.6° (c=8.91, EtOH).

*6 Most of this was identified with α-acetamido-3,4-methylenedioxycinnamic acid*1 by admixture and infrared spectrum.

5) Org. Syntheses, Coll. Vol. III, 687.

and Et_2O melted at 147.5～150°(9.18 g.), $[\alpha]_D^{25}$ −31.5° (c=1.38, EtOH). Each amount of (IIIa) and (IIIb) was 10.13 g. (43.3%) and 9.64 g. (41.2%), respectively.

(IIIa) was recrystallized several times from Et_2O-hexane, giving colorless fluffy needles, m.p. 85～87°, $[\alpha]_D^{12}$ −40.6° (c=1.43, dioxane), $[\alpha]_D^{12}$ −55.2° (c=1.50, benzene, $[\alpha]_D^{12}$ −34.2° (c=2.19, EtOH), $[\alpha]_D^{9}$ −38.2° (c=1.52, MeOH). RD in MeOH (c=0.638, Hg): $[\alpha]_{589}^{17}$ −35°, $[\alpha]_{546}$ −41°, $[\alpha]_{436}$ −71°, $[\alpha]_{404}$ −87°, $[\alpha]_{366}$ −114°, $[\alpha]_{334}$ −159°, $[\alpha]_{313}$ −218°. *Anal.* Calcd. for $C_{22}H_{31}O_5N$: C, 67.84; H, 8.02; N, 3.60. Found: C, 67.41; H, 7.92; N, 3.22. IR ν_{max}^{KBr} cm^{-1}: 3400, 3350 (NH), 1722 (COOR), 1654 (CONH), 1038, 928 (-O·CH_2·O-). $\nu_{max}^{CHCl_3}$ cm^{-1}: 3425 (NH), 1730 (COOR), 1678 (CONH), 1040, 934 (-O·CH_2·O-). UV $\lambda_{max}^{95\%\ EtOH}$ mμ (log ε): 236 (3.63), 287 (3.59). $\lambda_{min}^{95\%\ EtOH}$ mμ (log ε): 223 (3.50), 256 (2.55).

Recrystallization of (IIIb) from EtOH afforded colorless small needles, m.p. 150～151°, $[\alpha]_D^{33}$ −18.4° (c=1.63, dioxane), $[\alpha]_D^{13}$ −3.8° (c=1.52, benzene), $[\alpha]_D^{29}$ −33.2° (c=2.67, EtOH), $[\alpha]_D^{9}$ −24.7° (c=1.50, MeOH). RD in MeOH (c=0.733, Hg): $[\alpha]_{589}^{18}$ −34°, $[\alpha]_{546}$ −41°, $[\alpha]_{436}$ −64°, $[\alpha]_{404}$ −72°, $[\alpha]_{366}$ −80°, $[\alpha]_{334}$ −75°, $[\alpha]_{313}$ −41°. *Anal.* Calcd. for $C_{22}H_{31}O_5N$: C, 67.84; H, 8.02; N, 3.60. Found: C, 68.24; H, 8.00; N, 3.42. IR ν_{max}^{KBr} cm^{-1}: 3360 (NH), 1728 (COOR), 1650 (CONH), 1038, 928 (-O·CH_2·O-). $\nu_{max}^{HCl_3}$ cm^{-1}: 3430 (NH), 1730 (COOR), 1678 (CONH), 1041, 936 (-O·CH_2·O-). UV $\lambda_{max}^{95\%\ EtOH}$ mμ (log ε): 236 (3.63), 287 (3.59). $\lambda_{min}^{95\%\ EtOH}$ mμ (log ε): 223 (3.50), 256, (2.55). Infrared spectra of (IIIa) and (IIIb) in $CHCl_3$ solution are very similar, but not identical. Ultraviolet spectra of them, however, are superimposable.

ii) 10% Pd-C in benzene: As in i), (II) (2.32 g., 0.006 mole) in anhyd. benzene (30 cc.) was hydrogenated over 10% Pd-C (0.40 g.) for 5 hr. at ca. 50°. In this case no hydrogen was absorbed at room temperature. The crude product (2.10 g. or 90.0%) showed m.p. 85～125°, $[\alpha]_D^{14}$ −29.3° (c=1.53, benzene). Further purification was not carried out.

***l*-Menthyl Acetate**——*l*-Menthyl acetate was prepared from *l*-menthol and Ac_2O by the usual method. $b.p._5$ 99～100°. RD in MeOH (c=0.690, Hg): $[\alpha]_{589}^{18}$ −89°, $[\alpha]_{546}$ −101°, $[\alpha]_{436}$ −167°, $[\alpha]_{404}$ −200°, $[\alpha]_{366}$ −256°, $[\alpha]_{334}$ −323°, $[\alpha]_{313}$ −384°.

N-Acetyl-3-(3,4-methylenedioxyphenyl)alanine (IV)——(IIIb) (1.17 g., 0.003 mole) was dissolved in EtOH (10 cc.), and to this 50 w/w% aq. KOH (0.30 g., 0.0026 mole) was added. A mixture was warmed at 50～53°(bath temp.) for 30 min. and evaporated *in vacuo* at the same temperature for 40 min. The white oily residue was dissolved in H_2O (3 cc.), extracted with Et_2O (2 cc.) and acidified with conc. HCl. The white precipitate was filtered and washed with H_2O, showing m.p. 177.5～178°, $[\alpha]_D^{26}$ +11.9° (c=2.32, EtOH).*7 Yield 0.60 g. (80%). Recrystallization from H_2O afforded colorless needles, m.p. 176～177.5°, $[\alpha]_D^{24}$ +2.0° (c=2.60, EtOH), which showed no depression on mixed m.p. test with N-acetyl-3-(3,4-methylenedioxyphenyl)-DL-alanine.*1

A similar result was obtained when (IIIb) was treated at 30° for 1.5 hr. or at room temperature (ca. 18°) for 18 hr.

3-(3,4-Methylenedioxyphenyl)-DL-alanine (*rac*-V)——Into a suspension of diastereoisomeric mixture (3.90 g., 0.01 mole) of (IIIa) and (IIIb) (m.p. 107～137°, $[\alpha]_D^{14}$ −26.4°) in MeOH (50 cc.), dry HCl gas was introduced under ice-cooling until saturated. After being kept standing at room temperature (ca. 15°) for 90 hr., the mixture was evaporated *in vacuo*. The residue was refluxed with 10% HCl (16 cc.) for 2 hr. at 130～140°(bath temp.). The mixture was diluted with H_2O (20 cc.), washed with $CHCl_3$ (16 cc.), and evaporated to a white solid, m.p. 241°(decomp.); 2.0 g. (81.3%). It was dissolved in hot EtOH (60 cc.), treated with aniline (2 cc.) and the solution allowed to cool in a refrigerator. A white precipitate was collected, washed with EtOH and dried. It weighed 1.3 g. (62%); m.p. 236～238°, $[\alpha]_D^{23}$ ±0° (c=2.09, *N* HCl). Recrystallization from H_2O came as colorless minute leafletts, m.p. 250～251° (decomp.). *Anal.* Calcd. for $C_{10}H_{11}O_4N$: C, 57.41; H, 5.30; N, 6.70. Found: C, 56.99; H, 5.40; N, 6.54.

HCl salt: colorless needles (from H_2O), m.p. 246～248°(decomp.). *Anal.* Calcd. for $C_{10}H_{11}O_4N$·HCl: Cl, 14.42. Found: Cl, 14.31.

3-(3,4-Methylenedioxyphenyl)-L-alanine (L-V)——(IIIb) (2.34 g., 0.006 mole) in 10 w/w% MeOH-HCl (30 cc.) was refluxed for 15 hr. at 85～90°(bath temp.). After evaporation of the solvent at 25～30° (bath temp.) *in vacuo*, 10% HCl (8 cc.) was added to the residue. The mixture was refluxed for 2 hr. at 130～140°(bath temp.) and steamdistilled until 100 cc. of a distillate came over. H_2O (20 cc.) was added to the residue, which was extracted three times with $CHCl_3$ (20 cc.) while hot. The aqueous layer was evaporated *in vacuo*, giving white crystals, m.p. 229～231°(decomp.); 1.0 g. (68.0%). These crystals were dissolved in EtOH (70 cc.) under reflux treated with aniline (1 cc.), cooled and allowed to stand in a refrigerator overnight. The resultant white precipitate was collected and washed with EtOH, m.p. 237～239°(decomp.); 0.6 g. Another crop (0.12 g.) was obtained from the filtrate. Yield 0.72 g. (57.6%). Purification from H_2O using charcoal afforded colorless needles, m.p. 236.5～237°(decomp.), $[\alpha]_D^{19}$ −14.0° (c=1.63, *N*HCl). *Anal.* Calcd. for $C_{10}H_{11}O_4N$: C, 57.41; H, 5.30; N, 6.70. Found: C, 57.03; H, 5.39; N, 6.58.

*7 Optically pure (L-IV) shows $[\alpha]_D^{13}$ +53.4° (c=2.262, EtOH).*1

HCl salt : colorless needles (from H_2O), m.p. 250～250.5°(decomp.). *Anal.* Calcd. for $C_{10}H_{11}O_4N \cdot HCl$: Cl, 14.42. Found : Cl, 14.16.

On the other hand, a distillate from the steam distillation was extracted with Et_2O (3×20 cc.) and $CHCl_3$ (3×20 cc.), the combined organic layers were dried and evaporated *in vacuo* below 30° (bath temp.), giving a white solid, m.p. 42～42.5°, $[\alpha]_D^{19}$ −49.3°(c=3.06, EtOH), 0.60 g. (63.8%), which was identical with *l*-menthol on mixed m.p. test and infrared spectrum comparison.

3-(3,4-Methylenedioxyphenyl)-D-alanine (D-V)——In the same way as that of (L-V), 1.0 g. (68.0%) of the HCl salt was obtained. Adjustment with 10% NH_4OH to pH 5.8, gave 0.45 g. of (D-V) and from the filtrate an additional amount of 0.15 g. was obtained. Yield, 0.60 g. (48.0%). The crude (D-V) was purified from H_2O to colorless needles, m.p. 239～240°(decomp.), $[\alpha]_D^8$ +12.0°(c=1.66, *N* HCl). *Anal.* Calcd. for $C_{10}H_{11}O_4N$: C, 57.41; H, 5.30; N, 6.70. Found : C, 57.42; H, 5.13; N, 6.52.

HCl salt : colorless needles (from H_2O), m.p. 250～250.5°(decomp.). *Anal.* Calcd. for $C_{10}H_{11}O_4N \cdot HCl$: Cl, 14.42. Found : Cl, 14.49. *l*-Menthol was recovered in 56.4% yield (0.53 g.) as white crystals of m.p. 39～42°, $[\alpha]_D^{15}$ −48.0° (c=4.62, EtOH).

The authors express their gratitudes to Dr. M. Suzuki of Tokyo Research Laboratory, Tanabe Seiyaku Co., Ltd. for his kind advices and measurements of optical rotatory dispersion curves.

They are grateful to the members of the Central Analysis Room of this Faculty for microanalytical, infrared and ultraviolet spectral data.

Summary

Asymmetric hydrogenation of *l*-menthyl α-acetamido-3,4-methylenedioxycinnamate was carried out by two methods : i) 10% palladium-carbon in ethanol, ii) 10% palladium-carbon in benzene. Hydrogenation products were separated by fractional crystallization, and were converted to optically active 3-(3,4-methylenedioxyphenyl)alanines by transesterification followed by acid hydrolysis.

(Received May 8, 1961)

UDC 547.466.02

111. Shun-ichi Yamada, Tozo Fujii, and Takayuki Shioiri : Studies on Optically Active Amino Acids. III.*1 Preparation of 3-(3,4-Dihydroxyphenyl)-DL-, -D-, and -L-alanine.

(*Faculty of Pharmaceutical Sciences, University of Tokyo**2)

In 1913 Torquati[1] isolated from the velvet bean (*Vicia faba*) 3-(3,4-dihydroxyphenyl)-L-alanine (L-Dopa), whose identification and absolute configuration were later established by Guggenheim,[2] and other investigators.[3] It is now known that Dopa plays an important part in mammalian metabolism of tyrosine[4] and also in the hypothetical biogenesis of some alkaloids.[5]

*1 Part II : This Bulletin, **10**, 688 (1962).

*2 Hongo, Tokyo (山田俊一, 藤井澄三, 塩入孝之).

1) T. Torquati : Arch. farm. sper., **15**, 213, 308 (1913). (C. A., **7**, 2774 (1913)).

2) M. Guggenheim : Z. physiol. Chem., **88**, 276 (1913).

3) *a*) E. Waser, M. Lewandowski : Helv. Chim. Acta, **4**, 657 (1921). *b*) S. Goldschmidt, G. Freyss : Ber., **66**, 784 (1933). *c*) P. A. Levene, S. Mardashew : J. Biol. Chem., **117**, 179 (1937). *d*) E. Waser, E. Brauchli : Helv. Chim. Acta, **7**, 740 (1924). *e*) R. S. Coffey, M. Green, G. W. Kenner : J. Chem. Soc., **1959**, 4100. *f*) O. Lutz, B. Jirgensons : Ber., **64**, 1221 (1931). *g*) R. R. Sealock : J. Biol. Chem., **166**, 1 (1946).

4) C. E. Dalgliesh : "Advances in Protein Chemistry," Vol. 10, 65 (1955). Academic Press, Inc., New York.

5) *a*) *Idem* : *Ibid.*, Vol. 10, 117 (1955). *b*) R. Robinson : "The Structural Relations of Natural Products," (1955). Clarendon Press, Oxford.