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Stereochemical Studies. XXV.[1] The Absolute Configuration and Optical Purity of (+)-4-Methyl-4-phenyl-2-cyclohexenone

GENJI OTANI[2a] and SHUN-ICHI YAMADA[2]

Faculty of Pharmaceutical Sciences, University of Tokyo[2]

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(+)-4-Methyl-4-phenyl-2-cyclohexenone ((+)-I), obtained by asymmetric synthesis, was chemically correlated to (*S*)-(+)-2-methyl-2-phenylbutanoic acid, whose absolute configuration is known. It was shown that (+)-4-methyl-4-phenyl-2-cyclohexenone ((+)-I) has (*R*) configuration. In determining the configuration, the optical ratation of optically pure (+)-4-methyl-4-phenyl-2-cyclohexenone ((+)-I) was estimated to be +130° in ethanol at D ray.

In a previous paper,[1] we reported the asymmetric synthesis of (+)-4-methyl-4-phenyl-2-cyclohexenone ((+)-I) with enamine alkylation. The present paper deals with determining the absolute configuration of (+)-I and estimating the optical rotation of the optically pure compound.

Determination of the configuration was carried out by chemical interconversion which did not affect the bonds to the asymmetric carbon; the so-called chemical correlation. As illustrated by the pathway given in the chart, the (+)-4-methyl-4-phenyl-2-cyclohexenone ((+)-I) obtained by asymmetric synthesis was correlated to optically active 4-cyano-4-phenylpentanoic acid (IV) obtained by optical resolution. Then optically active pentanoic acid IV was correlated to (*S*)-(+)-2-methyl-2-phenylbutanoic acid ((*S*)-(+)-XIII), whose absolute configuration is known.[3]

(+)-Cyclohexenones((+)-I), (a) $[\alpha]_D^{30}$ +27.6° (EtOH) and (b) $[\alpha]_D^{18}$ +46.0° (EtOH), obtained by asymmetric synthesis, were oxidized with $KMnO_4$ in acetone. They produced acidic compounds which without purification were heated with acetic anhydride. The resulting (−)-2-methyl-2-phenylglutaric anhydrides ((−)-III), (a) $[\alpha]_D^{23}$ −31.4° (THF) and (b) $[\alpha]_D^{24}$ −49.7° (THF), were isolated and purified by column chromatography and vacuum distillation.

Diastereomers of pentanoic acid IV, prepared by optical resolution, the *dextro* isomer ((+)-IV), $[\alpha]_D^{22}$ +20.0° (EtOH), and the *levo* isomer ((−)-IV), $[\alpha]_D^{13}$ −20.7° (EtOH), were hydrolyzed and gave the respective *dextro* isomer ((+)-V), $[\alpha]_D^{18}$ +21.4° (EtOH), and *levo* isomer ((−)-V), $[\alpha]_D^{18}$ −22.3° (EtOH), of 2-methyl-2-phenylglutaric acid (V). Both the glutaric acids, ((+)-V and (−)-V)), were heated with acetic anhydride and respectively produced the *levo* isomer ((−)-VI), $[\alpha]_D^{19}$ −144° (THF), and *dextro* isomer ((+)-VI), $[\alpha]_D^{18}$ +147° (THF), of 2-methyl-2-phenylglutaric anhydride (VI).

First, both (+)-cyclohexenones ((+)-I) and (+)-pentanoic acid ((+)-V) gave the same *levo*-rotatory glutaric anhydridee ((−)-III and (−)-VI). Second, by a comparison of the optical rotations of the optically pure glutaric anhydrides, ((+)-VI and (−)-VI), the optical purities of the glutaric anhydrides ((−)-III) derived from the cyclohexenones (+)-I obtained by asymmetric synthesis, were estimated. Since no operation which alters optical purity was used in the conversion of cyclohexenones ((+)-I) to glutaric anhydrides ((−)-III), the optical purities

1) Part XXIV: G. Otani and S. Yamada, *Chem. Pharm. Bull.* (Tokyo), **21**, 2112 (1973).
2) Location: *Hongo, Bunkyo-ku, Tokyo, 150, Japan*; *a*) Present Address: *Tokyo Research Laboratories, Kowa Company Ltd., Higashimurayama, Tokyo.*
3) *a*) D.J. Cram and J. Allinger, *J. Am. Chem. Soc.*, **76**, 4516 (1954); *b*) W.A. Bonner and T.W. Greenlee, *J. Am. Chem. Soc.*, **81**, 3336 (1959).

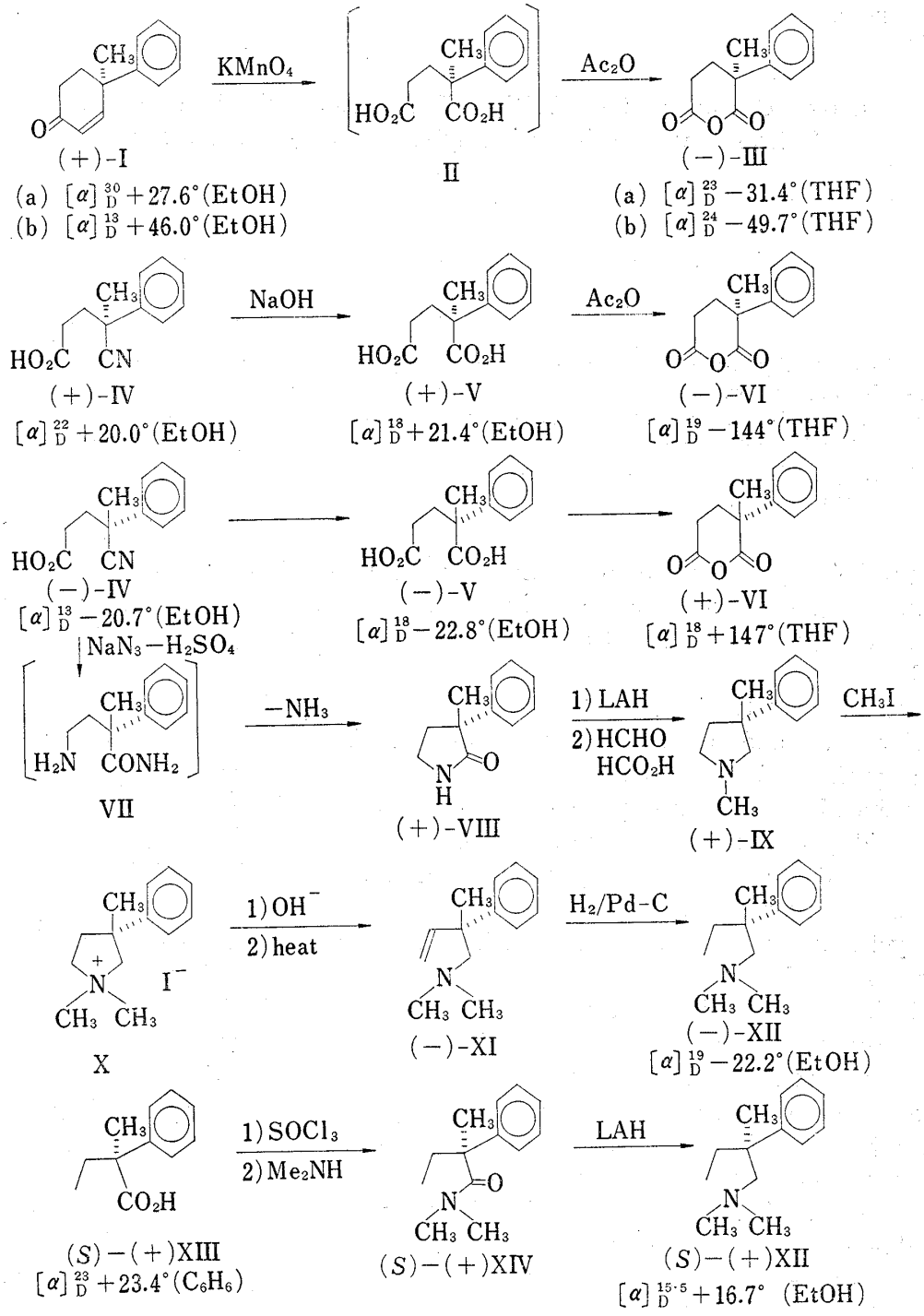

Chart 1

of the cyclohexenones used are the same as those of the glutaric anhydrides. From these results, the optical rotation of optically pure cyclohexenone ((+)-I) was estimated as $[\alpha]_D$ +130° (EtOH).

For the conversion to determine the configuration, *levo* pentanoic acid ((−)-IV) was used, because the *levo* isomer, rather than the *dextro* isomer, was easily obtained by optical resolution. The Schmidt reaction with pentanoic acid (−)-IV produced amino amide VII, accompanied by hydrolysis of the cyano group. During work-up, amino amide VII lost ammonia to give (+)-3-methyl-3-phenyl-2-pyrrolidone ((+)-VIII), $[\alpha]_D^{25}$ +100.5° (EtOH). Pyrrolidone (+)-VIII was reduced and methylated to give (+)-1,3-dimethyl-3-phenylpyrrolidine ((+)-IX). After quaternarization with methyl iodide, the quaternary amine X was submitted to

Hofmann degradation and gave (−)-N,N-dimethyl-2-phenyl-2-vinylpropylamine ((−)-XI), $[\alpha]_D^{19}$ −22.3° (MeOH). The olefin (−)-XI was reduced catalytically to produce (−)-N,N,2-trimethyl-2-phenylbutylamine ((−)-XII), $[\alpha]_D^{19}$ −22.2° (EtOH).

(*S*)-(+)-2-Methyl-2-phenylbutanoic acid ((*S*)-(+)-XIII), $[\alpha]_D^{23}$ +23.4° (C_6H_6), 78% optically pure,[2] whose absolute configuration is known,[3] was converted *via* its dimethyl amide (+)-XIV to (+)-N,N,2-trimethyl-2-phenylbutylamine ((+)-XII), $[\alpha]_D^{15.5}$ +16.7° (EtOH). This butylamine (+)-XII was identical with the butylamine (−)-XII derived from pentanoic acid (−)-IV except optical rotation.

Based on these results, the absolute configurations of the compounds on the pathway are illustrated in the chart in relation to the reference compound, (*S*)-(+)-2-methyl-2-phenylbutanoic acid ((*S*)-(+)-XIII). Hence, the absolute configuration of (+)-cyclohexenone (+)-I in question was determined as (*R*) configuration.

Prior to experiments with optically active compounds, racemic modifications were used to find out the favorable reaction conditions and to identify the optical active compounds by comparison with racemates. The experimental data on racemic compounds were described in detail in Experimental Part.

Experimental[4]

4-Cyano-4-phenylpentanoic Acid ((±)-IV)——Methyl 4-cyano-4-phenylbutyrate[5] (20.3 g, 0.10 mole) and sodium hydride (50% oil, 5.5 g, 0.11 mole) were added to anhydrous tetrahydrofuran (200 ml) and stirred for 1 hr at room temperature. Methyl iodide (22.8 g, 0.16 mole) was added dropwise to the cooled stirred mixture for 30 min and the reaction mixture was stirred for 4 hr below 10°. Methyl iodide (5.0 g) was then added and the mixture was allowed to stand overnight. Water (50 ml) was added to and the whole was stirred for 30 min then evaporated under reduced pressure. Saturated sodium carbonate solution (20 ml) was added to the residue and the oil liberated was extracted with ether. The extract was washed with water, then it was dried over sodium sulfate and evaporated. The residual oil (18 g) and a 5% sodium carbonate solution (140 ml) were dissolved in methanol (200 ml) after which the solution was heated under reflux for 2 hr. It was then evaporated under reduced pressure and the residue was dissolved in water (100 ml). An insoluble oil was eliminated by extraction with ether. The aqueous layer was acidified to pH 3 with dilute sulfuric acid, then it was extracted with ether. The extract was washed with water, dried over sodium sulfate and evaporated. The residue was recrystallized from ether–hexane and 4-cyano-4-phenylpentanoic acid to give white needles, mp 76—79° (lit.[6] mp 77—78°), 10.8 g (50%). IR ν_{max}^{KBr} cm^{-1}: 2220, 1710; $\nu_{max}^{CHCl_3}$ cm^{-1}: 2220, 1720. NMR ($CDCl_3$) τ: −0.53 (1H, singlet), 2.60 (5H, singlet), 7.6—7.9 (4H, multiplet), 8.28 (3H, singlet). *Anal.* Calcd. for $C_{12}H_{13}O_2N$: C, 70.91; H, 6.45; N, 6.89. Found: C, 71.02; H, 6.30; N, 6.99.

Resolution of 4-Cyano-4-phenylpentanoic Acid ((±)-IV)——Racemic 4-cyano-4-phenylpentanoic acid ((±)-IV) (10.3 g) and brucine (21.0 g) were dissolved in acetone (100 ml) by heating them, then water (20 ml) was added and the solution was allowed to stand. A white powder, mp 90—100° (foaming), $[\alpha]_D^{11}$ −20.8° (c=0.53, EtOH), precipitated and was filtered and dried. Twenty-six grams of powder was obtained. The powder was recrystallized two more times from acetone (100 ml) producing white small prisms, 6.8 g, mp 113—122°, $[\alpha]_D^{17}$ −31.0° (c=0.44, EtOH). Another recrystallization from acetone neither altered the melting point nor the optical rotation. *Anal. Calcd.* for $C_{25}H_{29}O_6N_3 \cdot \frac{1}{2}H_2O$: C, 67.30; H, 6.78; N, 6.73. Found: C, 67.30; H, 6.77; N, 7.09.

The brucine salt (6.8 g) was suspended in water and 10% hydrochloric acid was added to give pH 3. The acidified solution was extracted with ether, then the extract was washed with water, dried over sodium sulfate and evaporated. The residue was recrystallized from ether–hexane producing (−)-4-cyano-4-phenylpentanoic acid ((−)-IV), 2.1 g, as white prisms, mp 82—84°, $[\alpha]_D^{13}$ −20.7° (c=0.58, EtOH). Its IR spectrum

4) All melting and boiling points are uncorrected. Optical rotations were measured with Yanagimoto Model OR-10 polarimeter. Optical rotatory dispersion (ORD) curves were recorded on Nippon Bunko Model ORD/UV-5 spectropolarimeter. Infrared (IR) spectra were obtained with Nippon Bunko Models IR-S and DS-403G spectrophotometers. Nuclear magnetic resonance (NMR) spectra were recorded at 60 Mc on a Japan Electron Optics Model JNM C-60 NMR spectrometer. Gaschromatographic analyses were carried out in Shimadzu Model GC-1 and Perkin-Elmer Model 800 gaschromatographs with dual flame ionization detectors.

5) R. Bertocchio and J. Dreux, *Bull. Soc. Chim. France*, **1962**, 1809.

6) F. Salmon-Legagneur and C. Neveu, *Bull. Soc. Chim. France*, **1953**, 70.

in the solid state differed from that of the racemic compound, and in a chloroform solution IR spectra of the *levo* and racemic compounds were identical. ORD (c=0.45, MeOH) $[M]^{17}$ (mμ): −31° (700), −42° (589), −726° (230) (trough), −500° (200).

Mother liquors from the recrystallization of brucine salt were collected and evaporated, then the residue was recrystallized twice from acetone. Crystals, 6.3 g, mp 111—120°, $[\alpha]_D^{12}$ −30.6° (c=0.33, EtOH), were obtained from which free acid (2.0 g) was liberated. Recrystallization from ether–hexane gave crystals containing needles and prisms, mp 72—76°. Repeated recrystallization from acetone gave prisms, 1.10 g, mp 81—84°, $[\alpha]_D^{14}$ +20.7° (c=0.46, EtOH). The IR spectrum in the solid state was identical with that of the *levo* isomer. The ORD curve was antipodal to that of the *levo* isomer.

(±)-2-Methyl-2-phenylglutaric Anhydride ((±)-VI) from (±)-4-Cyano-4-phenylpentanoic Acid ((±)-IV)——A solution of (±)-4-cyano-4-phenylpentanoic acid ((±)-IV) (2.17 g) in 10% sodium hydroxide (30 ml) was heated under reflux for 2.5 hr. The cooled solution was acidified to pH 3 with dilute sulfuric acid after which it was extracted with ether. The extract was washed with water, dried over sodium sulfate and evaporated. The residue was recrystallized from ether–hexane to give (±)-2-methyl-2-phenylglutaric acid ((±)-V) (1.95 g, 82%), mp 126—128° (lit.[6] mp 130°), as a white powder. IR ν_{max}^{KBr} cm^{-1}: 1715. NMR ($CDCl_3$) τ: −1.20 (2H, singlet), 2.75 (5H, singlet), 7.70 (4H, singlet), 8.42 (3H, singlet).

A solution of (±)-2-methyl-2-phenylglutaric acid ((±)-V) (1.95 g) in acetic anhydride was heated under reflux for 1 hr, then it was evaporated. The residue was distilled under reduced pressure and the distillate which boiled at 157—160° (2 mmHg) crystallized instantly. Recrystallization from a mixture of ether and hexane produced (±)-2-methyl-2-phenylglutaric anhydride ((±)-VI) (1.41 g, 80%), mp 75—78° (lit.[6] mp 77—78°), as white needles. IR ν_{max}^{KBr} cm^{-1}: 1810, 1765; $\nu_{max}^{CHCl_3}$ cm^{-1}: 1810, 1770. NMR (CCl_4) τ: 2.70 (5H, multiplet), 7.2—7.8 (4H, multiplet), 8.36 (3H, singlet). *Anal.* Calcd. for $C_{12}H_{12}O_3$: C, 70.57; H, 5.92. Found: C, 70.30; H, 5.67.

(−)-2-Methyl-2-phenylglutaric Anhydride ((−)-VI) from (+)-4-Cyano-4-phenylpentanoic Acid ((+)-IV)——(+)-4-Cyano-4-phenylpentanoic acid ((+)-VI) (610 mg) was submitted to hydrolysis following the procedure for the (±) isomer described above. (+)-2-Methyl-2-phenylglutaric acid ((+)-V) (550 mg, 82%), mp 121—123°, $[\alpha]_D^{18}$ +21.4° (c=0.56, EtOH) was obtained as white prisms. Its IR spectrum in the solid state differed from that of the racemic compounds. In a chloroform solution the IR spectra of the *dextro* and racemic compounds were identical. ORD (c=0.56, EtOH) $[M]^{21.5}$ (mμ): +31.7° (700), +52° (589), +2000° (230).

(+)-2-Methyl-2-phenylglutaric acid ((+)-V) (550 mg) was treated with acetic anhydride following the procedure for the racemic isomer described above. Recrystallization from benzene–hexane gave (−)-2-methyl-2-phenylglutaric anhydride ((−)-VI) (343 mg, 56%), mp 112—114°, $[\alpha]_D^{19}$ −144° (c=0.54, THF) as white needles. Its IR spectrum in the solid state was identical with that of the racemic compound. ORD (c=0.54, THF) $[M]^{19}$ (mμ): −20.8° (700), −284° (589), −9200° (230).

(+)-2-Methyl-2-phenylglutaric Anhydride ((+)-VI) from (−)-4-Cyano-4-phenylpentanoic Acid ((−)-IV)——(−)-4-Cyano-4-phenylpentanoic acid ((−)-IV) (610 mg) was submitted to hydrolysis following the procedure described above to obtain (−)-2-methyl-2-phenylglutaric acid ((−)-V) (610 mg, 91%), mp 121—123°, $[\alpha]_D^{18}$ −22.3° (c=0.62, EtOH) as white prisms. Its IR spectrum in the solid state was identical with that of the dextro isomer and differed from that of the racemic compound. Its ORD curve was antipodal to that of the dextro isomer.

(−)-2-Methyl-2-phenylglutaric acid ((−)-V) (540 mg) was treated with acetic anhydride to give (+)-2-methyl-2-phenylglutaric anhydride ((+)-IV) (290 mg, 49%), mp 112—114°, $[\alpha]_D^{18}$ +147° (c=0.43, THF) as white needles. Its IR spectrum in the solid state was identical with that of the *levo* isomer. Its ORD curve was antipodal to that of the *levo* isomer.

Synthesis of (±)-2-Methyl-2-phenylglutaric Anhydride ((±)-VI) from (±)-4-Methyl-4-phenyl-2-cyclohexenone ((±)-I)——Potassium permanganate (1.58 g) was added portion-wise to a solution of (±)-4-methyl-4-phenyl-2-cyclohexenone ((±)-I) (744 mg) in acetone (50 ml) over 30 min with stirring. After the color of the potassium permanganate disappeared, the precipitate was filtered and washed with acetone, then with water (10 ml×3). Washings were collected and acidified with dilute sulfuric acid (pH 1) and extracted with ether. The extracts were washed with water, then dried over sodium sulfate and evaporated. The residual oil (690 mg) was dissolved in acetic anhydride (20 ml). This solution was heated under reflux for 1.5 hr then was evaporated under reduced pressure. The orange oil obtained was chromatographed on a silica gel column (40 g) with chloroform and the desired fraction was submitted to distillation. The distillate which boiled at 175—179° (4 mmHg) crystallized with a mp of 74—77°. Its IR spectrum in the solid state was identical with that of an authentic sample derived from (±)-4-cyano-4-phenylpentanoic acid ((±)-IV). Only one spot was detectable on thin-layer chromatography (TLC) (silica gel, chloroform).

Synthesis of (−)-2-Methyl-2-phenylglutaric Anhydride ((−)-III) from (+)-4-Methyl-4-phenyl-2-cyclohexenone ((+)-I) obtained by Asymmetric Synthesis[1]——(+)-4-Methyl-4-phenyl-2-cyclohexenone ((+)-I) (730 mg), $[\alpha]_D^{30}$ +27.6° (c=2.04, EtOH) was treated following the procedure for the (±) isomer described above and produced (−)-2-methyl-2-phenylglutaric anhydride ((−)-III) (170 mg), bp 155—160° (3 mmHg), mp 73—105°, $[\alpha]_D^{23}$ −31.4° (c=1.13, THF). Its IR and NMR spectra were identical with those of a sample derived from 4-cyano-4-phenylpentanoic acid. Only one spot was detectable on TLC (silica gel, chloroform).

Using (+)-4-methyl-4-phenyl-2-cyclohexenone ((+)-I), $[\alpha]_D^{13}$ +46.0° (c=1.12, EtOH), (−)-2-methyl-2-phenylglutaric anhydride ((−)-III), bp 155—158° (3 mn.Hg), mp 70—105°, $[\alpha]_D^{24}$ −49.7° (c=2.09, THF), was obtained.

(±)-3-Methyl-3-phenyl-2-pyrrolidone ((±)-VIII)——Sulfuric acid (28 ml) was added to a solution of (±)-4-cyano-4-phenylpentanoic acid ((±)-IV) (10.0 g, 0.0493 mol) in chloroform (100 ml), then sodium azide (4.0 g, 0.061 mol) was added portionwise with stirring over 30 min at 40°. After stirring it at 50° for 3 hr, the mixture was allowed to stand overnight. The mixture was then poured onto ice (200 g) and the organic layer was removed. Powdered sodium carbonate was added to the aqueous solution to make the solution alkaline, after which the solution was extracted continuously for 10 hr with chloroform. At that time the evolution of ammonia was observed. The extract was evaporated and distilled. The distillate, bp 165—167° (3 mmHg), crystallized and was recrystallized from ether–hexane producing (±)-3-methyl-3-phenyl-2-pyrrolidone ((±)-VIII) (5.4 g, 62.5%), mp 81—84° as white prisms. IR ν_{max}^{KBr} cm^{-1}: 3200, 3090, 1690; $\nu_{max}^{CHCl_3}$ cm^{-1}: 3460, 3230, 1695. NMR ($CDCl_3$) τ: 2.1 (1H, broad singlet), 2.70 (5H, singlet), 6.71 (2H, triplet), 7.3—8.1 (2H, multiplet), 8.46 (3H, singlet). *Anal.* Calcd. for $C_{11}H_{13}ON$: C, 75.40; H, 7.49; N, 7.99. Found: C, 75.38; H, 7.60; N, 7.93.

(+)-3-Methyl-3-phenyl-2-pyrrolidone ((+)-VIII)——The treatment of (−)-4-cyano-4-phenylpentanoic acid ((−)-IV) (4.1 g, 0.0202 mole) following the procedure for the (±) compound described above gave (+)-3-methyl-3-phenyl-2-pyrrolidone ((+)-VIII) (1.60 g, 45%), bp 167—170° (4 mmHg), mp 92—95° as white prisms, $[\alpha]_D^{25}$ +100.5° (c=1.19, EtOH). ORD (c=1.19, EtOH) $[M]^{29}$ (mμ): +125° (700), +177° (589), +3900° (240). Its IR spectrum in the solid state differed from that of the (±) compound and the spectrum in a chloroform solution was identical that of the (±) compound.

(±)-1,3-Dimethyl-3-phenylpyrrolidine ((±)-IX)——Lithium aluminium hydride (1.0 g, 0.026 mole) and (±)-3-methyl-3-phenyl-2-pyrrolidone ((±)-VIII) (3.0 g, 0.017 mole) were added to anhydrous toluene (60 ml), then the mixture was heated under reflux for 4 hr. After cooling, a small amount of methanol was added to decompose excess lithium aluminium hydride, then 10% aqueous sodium hydroxide solution (5 ml) was added dropwise with stirring. After filtering the precipitate was washed with ether. The filtrate and washings were collected and extracted with 10% hydrochloric acid twice. The aqueous layer was made alkaline (pH 10) with 10% aqueous sodium hydroxide solution, then it was extracted with ether. The extract was dried over potassium carbonate and evaporated, after which the residue was distilled under reduced pressure. (±)-3-Methyl-3-phenylpyrrolidine (1.9 g, 69.4%), bp 122—124° (14 mmHg), was obtained. NMR (CCl_4) τ: 2.81 (5H, singlet), 6.8—7.0 (4H, multiplet), 7.8—8.3 (3H, multiplet), 8.70 (3H, singlet).

Its picrate, mp 142—144°, as yellow plates, was prepared as usual and recrystallized from ethanol. *Anal.* Calcd. for $C_{17}H_{18}O_7N_4$: C, 52.30; H, 4.65; N, 14.35. Found: C, 52.16; H, 4.59; N, 14.49.

A mixture of (±)-3-methyl-3-phenylpyrrolidine (0.80 g, 5.0 mmoles), 99% formic acid (2.3 g, 50 mmoles), and formalin (4.1 ml, 50 mmoles) was heated under reflux for 4 hr. Water (10 ml) and 10% aqueous sodium hydroxide solution were added to the cooled mixture to make the solution alkaline (pH 10). It was then extracted with ether. The extract was dried over potassium carbonate and evaporated. The residue was distilled under reduced pressure producing (±)-1,3-dimethyl-3-phenylpyrrolidine ((±)-IX) (0.73 g, 83.4%), bp 82° (4 mmHg) as a colorless liquid. NMR (CCl_4) τ: 2.81 (5H, singlet), 7.1—8.2 (9H, multiplet), 8.60 (3H, singlet). Gas-liquid chromatography (GLC) (3%, Carbowax 20M, column length 1.8 m, column temp. 110°) retention time: 10 min 32 sec. *Anal.* Calcd. for $C_{12}H_{17}N$: C, 82.23; H, 9.78; N, 7.99. Found: C, 82.22; H, 9.81; N, 7.64.

Its picrate, mp 151—152°, as yellow needles, was recrystallized from ethanol. *Anal.* Calcd. for $C_{18}H_{20}O_7N_4$: C, 53.46; H, 4.99; N, 13.86. Found: C, 53.71; H, 5.17; N, 13.74.

(+)-1,3-Dimethyl-3-phenylpyrrolidine ((+)-IX)——Reduction of (+)-3-methyl-3-phenyl-2-pyrrolidone ((+)-VIII) (1.50 g, 8.6 mmoles) followed the procedure for the (±) compound described above and gave 3-methyl-3-phenylpyrrolidine (1.00 g, 72%). Its IR spectrum was identical with that of the (±) compound. Methylation of 3-methyl-3-phenylpyrrolidine (1.00 g) followed the procedure described above and gave (+)-1,3-dimethyl-3-phenylpyrrolidine ((+)-IX) (0.91 g, 84%), bp 112—113° (15 mmHg). $[\alpha]_D^{25}$ +23.6° (c=1.23, EtOH) as a colorless liquid. This was identical with the (±) compound in its IR and GLC. ORD (c=1.23, EtOH) $[M]^{28}$ (mμ): +31° (700), +44° (589), +390° (280).

(±)-N,N-Dimethyl-2-phenyl-2-vinylpropylamine ((±)-XI)——Methyl iodide (1.40 g, 10 mmoles) was added to a solution of (±)-1,3-dimethyl-3-phenylpyrrolidine ((±)-IX) (1.20 g, 6.86 mmoles) in methanol (10 ml) and the whole was allowed to stand for 3 hr. The disappearance of the starting material was ascertained by TLC and the solution was evaporated. The residual yellow oil was dissolved in water (5 ml) and added to a column containing Amberlite IRA-400 (OH^- type, 30 ml). The column was eluted with water and fractions having pH values of 9—11 were collected and evaporated. The residual yellow liquid was heated on an oil bath and decomposition with bubbling started at about 190°. Bubbling ceased after heating the oil at 190—195° for 5 min. A colorless liquid (0.9 g) was distilled at 100—130° under reduced pressure (with a water pump) and displayed 3 spots on TLC (alumina). It was chromatographed on alumina (100 g) and fractions which exhibited the top spot on TLC were collected and evaporated. The residue was distilled under reduced pressure and gave (±)-N,N-dimethyl-2-phenyl-vinylpropylamine ((±)-XI) (0.53 g, 39%), bp 109° (14 mmHg). Only one peak was detectable on GLC (3% Carbowax 20M, column length 1.8 m.

column temp. 110°), retention time: 7 min 20 sec. NMR (CCl_4) τ: 2.75 (5H, singlet), 3.80 (1H, quartet, J= 10.5 and 16.5 cps), 5.05 (2H, octet, J=2, 10.5, and 16.5 cps), 7.43 (2H, singlet), 7.96 (6H, singlet), 8.59 (3H, singlet).

Its picrate, mp 173—174° as yellow plates, was recrystallized from ethancl. *Anal.* Calcd. for $C_{19}H_{22}O_7N_4$: C, 54.54; H, 5.30; N, 13.39. Found: C, 54.71; H, 5.42; N, 13.20.

(−)-N,N-Dimethyl-2-phenyl-2-vinylpropylamine ((−)-XI)——Quaternarization of (+)-1,3-dimethyl-3-phenylpyrrolidine ((+)-IX) (800 mg, 4.6 mmoles), as described above, produced quaternary amine X, mp 164—166° as white prisms, $[\alpha]_D^{20}$ +4.0° (c=0.90, EtOH).

Degradation of quarternary amine X, as described above, gave (−)-N,N-dimethyl-2-phenyl-2-vinylpropylamine ((−)-XI) (150 mg), bp 110° (14 mmHg), $[\alpha]_D^{20}$ −22.3° (c=1.41, MeOH). It was identical with the (±) compound in its IR spectrum and GLC.

(±)-2,N,N-Trimethyl-1-phenylbutylamine ((±)-XII)——(A) Synthesis from (±)-2-Methyl-2-phenylbutanoic Acid Dimethylamide ((±)-XIV): Lithium aluminium hydride (0.38 g, 10 mmoles) was added to a solution of (±)-2-methyl-2-phenylbutanoic acid dimethylamide ((±)-XIV) (750 mg, 3.66 mmoles) in anhydrous toluene (15 ml) and the mixture was heated under reflux for 4 hr. Aqueous sodium hydroxide solution (10%, 1 ml) was carefully added dropwise with stirring to the cooled mixture. The precipitate was filtered and washed with benzene. The filtrate and washings were collected and extracted twice with 10% hydrochloric acid (10 ml and 5 ml). The extract was made alkaline (pH 10) with sodium hydroxide, then it was extracted with ether. The ether extract was dried over sodium carbonate and evaporated. The residual colorless oil (400 mg) displayed 2 spots on TLC (alumina) and was chromatographed on an alumina column (30 g). Fractions which exhibited the upper spot on TLC were collected and evaporated. Distillation of the residue gave (±)-2,N,N-trimethyl-2-phenylbutylamine ((±)-XII) (340 mg, 49%), bp 107° (14 mmHg). NMR (CCl_4) τ: 2.84 (5H, singlet), 7.62 (2H, singlet), 8.03 (6H, singlet), 8.1—8.6 (2H, multiplet), 8.71 (3H, singlet), 9.35 (3H, triplet). GLC (3% Carbowax 20M, column length 1.8 m, column temp. 110°C) retention time: 5 min 45 sec.

Its picrate, mp 166—169° as yellow needles, was recrystallized from ethanol. *Anal.* Calcd. for $C_{19}H_{24}O_7N_4$: C, 54.28; H, 5.75; N, 13.33. Found: C, 54.31; H, 5.89; N, 13.23.

(B) Synthesis from (±)-N,N-Dimethyl-2-phenyl-2-vinylpropylamine ((±)-XI): A palladium catalyst (5% on carbon, 50 mg) was added to a solution of (±)-N,N-dimethyl-2-phenyl-2-vinylpropylamine ((±)-XI) (200 mg, 1.06 mmoles) in methanol (10 ml) and the mixture was stirred under a hydrogen atmosphere. Within a few minutes 32 ml of hydrogen was absorbed (calculated amount, 26 ml) then absorption ceased. After further stirring for 30 min, the catalyst was filtered and the filtrate was evaporated. The residue was distilled under reduced pressure producing (±)-2,N,N-trimethyl-2-phenylbutylamine ((±)-XII) (0.12 g, 60%), bp 109° (15 mmHg). It was identical with a sample derived from the (±)-2-methyl-2-phenylbutanoic acid dimethylamide ((±)-XIV) described above in its IR spectrum and GLC.

(−)-2,N,N-Trimethyl-2-phenylbutylamine ((−)-XII)——The catalytic reduction of (−)-N,N-dimethyl-2-phenyl-2-vinylpropylamine ((−)-XI) (140 mg) followed the procedure described above and gave (−)-2,N,N-trimethyl-2-phenylbutylamine ((−)-XII) (70 mg, 50%), bp 109° (14 mmHg), $[\alpha]_D^{19}$ −22.2° (c=1.03, EtOH). ORD (c=1.03, EtOH) $[M]^{19}$ (mμ): −33.4° (700), −44.5° (589), −213° (290) (trough), +40° (270), (peak), −170° (266).

This was identical with the authentic samples described above in its IR spectrum and GLC.

(+)-2,N,N-Trimethyl-2-phenylbutylamine ((+)-XII)——The reduction of (+)-2-methyl-2-phenylbutanoic acid dimethylamide ((+)-XIV) (1.03 g, 5.0 mmol) was run as described above and gave (+)-2,N,N-trimethyl-2-phenylbutylamine ((+)-XII) (400 mg), bp 116—118° (20 mmHg), $[\alpha]_D^{15.5}$ +16.7° (c=1.50, EtOH). ORD (c=1.50, EtOH) $[M]^{14.5}$ (mμ): +25.5° (700), +37° (589), +185° (290) (peak), −25° (270) (trough), +115° (266). It was identical with the authentic samples described above in its IR spectrum and GLC.

(±)-2-Methyl-2-phenylbutanoic Acid Dimethylamide ((±)-XIV)——Thionyl chloride (2.0 ml) was added to a solution of (±)-2-methyl-2-phenylbutanoic acid ((±)-XIII)[3a] (1.00 g, 5.6 mmoles) in ether (10 ml) and the whole was allowed to stand overnight after which it was heated under reflux for 1 hr, then evaporated. The residue was dissolved in tetrahydrofuran (10 ml). A solution of dimethylamine in tetrahydrofuran was added to it and the whole was allowed to stand overnight. The solution was evaporated and water was added to the residue. Water-insoluble material was extracted with benzene. The extract was washed with aqueous sodium carbonate solution and water, then dried over sodium sulfate and evaporated. Distillation of the residue gave (±)-2-methyl-2-phenylbutanoic acid dimethylamide ((±)-XIV) (1.00 g, 87%), bp 117—118° (4 mmHg) as a colorless liquid. IR ν_{max}^{Cap} cm^{-1}: 1635. NMR (CCl_4) τ: 2.75 (5H, multiplet), 7.27 (6H, singlet), 7.96 (2H, quartet, J=7 cps), 8.50 (3H, singlet), 9.18 (3H, triplet, J=7 cps). GLC (3% Carbowax 20M, column length 1.8 m, column temp. 160°) retention time: 8 min 13 sec. *Anal.* Calcd. for $C_{13}H_{19}ON$: C, 76.05; H, 9.33; N, 6.82. Found: C, 75.70; H, 9.51; N, 6.84.

(+)-2-Methyl-2-phenylbutanoic Acid Dimethylamide ((+)-XIV)——Treatment of (+)-2-methyl-2-phenylbutanoic acid[3a] (1.30 g, 7.3 mmoles), $[\alpha]_D^{23}$ +23.4° (c=2.08, C_6H_6), 78% optically pure, following the procedure for the (±) compound described above, produced (+)-2-methyl-2-phenylbutanoic acid dimethylamide ((+)-XIV) (1.20 g), bp 117—118° (4 mmHg), $[\alpha]_D^{20}$ +3.62° (c=1.16, EtOH). This was identical with the (±) compound in its IR spectrum and GLC.