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Stereochemical Studies. XXIV.[1] Asymmetric Synthesis of optically Active (+)-4-Methyl-4-phenyl-2-cyclohexenone with Enamine Alkylation using Proline Derivatives[2]

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Alkylation of enamines prepared from 2-phenylpropanal and L-proline derivatives, with methyl vinyl ketone, was successful and gave, after hydrolysis and cyclization, optically active (+)-4-methyl-4-phenyl-2-cyclohexanone ((+)-IV). The effects of L-proline derivatives, solvents, and reaction temperature on the alkylation were discussed. Under selected conditions the optical yield reached about 50%. Asymmetric induction was clearly thermodynamically controlled.

As there have been few known methods[4] for effectively resolving racemic carbonyl compounds, it has been difficult to obtain optically active carbonyl compounds, which are important materials in synthetic organic chemistry. Consequently, the asymmetric synthesis of optically active carbonyl compound has been studied in our laboratory.[5]

Among the many methods for the alkylation of carbonyl compounds, enamine alkylation has been vigorously investigated since G. Stork and his co-workers[6] showed that this alkylation is widely available for organic synthesis. In the alkylation, pyrrolidine is generally used as the amine.[6c] Asymmetric induction is expected in enamine alkylation when using L-proline derivatives, that is, pyrrolidines with an asymmetric center. Based on this, asymmetric induction producing optically active 2-substituted cyclohexanones with the alkylation of enamines prepared from cyclohexanone and L-proline esters, has been reported from our laboratory.[5] Because of easy racemization, optically active 2-substituted cyclohexanones are rarely available intermediates in synthetic organic chemistry.

To solve the problem of racemization, it is necessary to make the asymmetric center a quaternary carbon. Since it is known[6] that enamine alkylation of 2-substituted cyclohexanones produces mainly 2,6-disubstituted derivatives, rather than 2,2-disubstituted ones, this has been a difficult problem to solve with cyclohexanones. However, it is also known[6] that disubstituted acetaldehyde can be alkylated to produce trisubstituted acetaldehyde. Consequently, we supposed that enamines prepared from a disubstituted acetaldehyde and a L-proline derivative, could be alkylated to give an optically active aldehyde with asymmetric center composed of quaternary carbon that is not subject to racemization.

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2) A preliminary report has been published as a communication: S. Yamada and G. Otani, *Tetrahedron Letters*, **1969**, 4237.

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4) W.R. Adams, O.L. Chapman, J.B. Sieja, and W.J. Welstead, Jr., *J. Am. Chem. Soc.*, **88**, 162 (1966), and cited therein. P.H. Boyle, *Quart. Rev.* (London), **25**, 323 (1971).

5) S. Yamada, K. Hiroi, and K. Achiwa, *Tetrahedron Letters*, **1969**, 4233; K. Hiroi, K. Achiwa, and S. Yamada, *Chem. Pharm. Bull.* (Tokyo), **20**, 246 (1972); K. Hiroi and S. Yamada, *ibid.*, **21**, 47 (1973).

6) *a*) G. Stork, R. Terrell, and J. Szumuszkovicz, *J. Am. Chem. Soc.*, **76**, 2029 (1954); *b*) G. Stork and H. Landesman, *ibid.*, **78**, 5128 (1956); *c*) G. Stork, A. Brizzolara, H. Landesman, J. Szumuszkovicz, and R. Terrell, *ibid.*, **85**, 207 (1963).

First, we studied asymmetric induction using 2-phenylpropanal as the model compound for disubstituted acetaldehyde. To determine the reaction conditions for the alkylation and isolation of products, the enamine prepared from 2-phenylpropanal and pyrrolidine in benzene by azeotropic distillation of water with benzene was used. Alkylation of the enamine with electrophilic olefins, *e.g.* methyl vinyl ketone, acrylonitrile, and methyl acrylate, was tried. Alkylation clearly did not occur with any olefin in benzene or dioxane but it did occur with methyl vinyl ketone in the presence of alcohols such as methanol and ethanol.

Keto-aldehyde (III) was obtained by hydrolysis after alkylation, and was easily dehydrated to cyclize to 4-methyl-4-phenyl-2-cyclohexenone (IV). Therefore, it was found to be preferable to isolate cyclohexenone (IV) rather than keto-aldehyde (III).

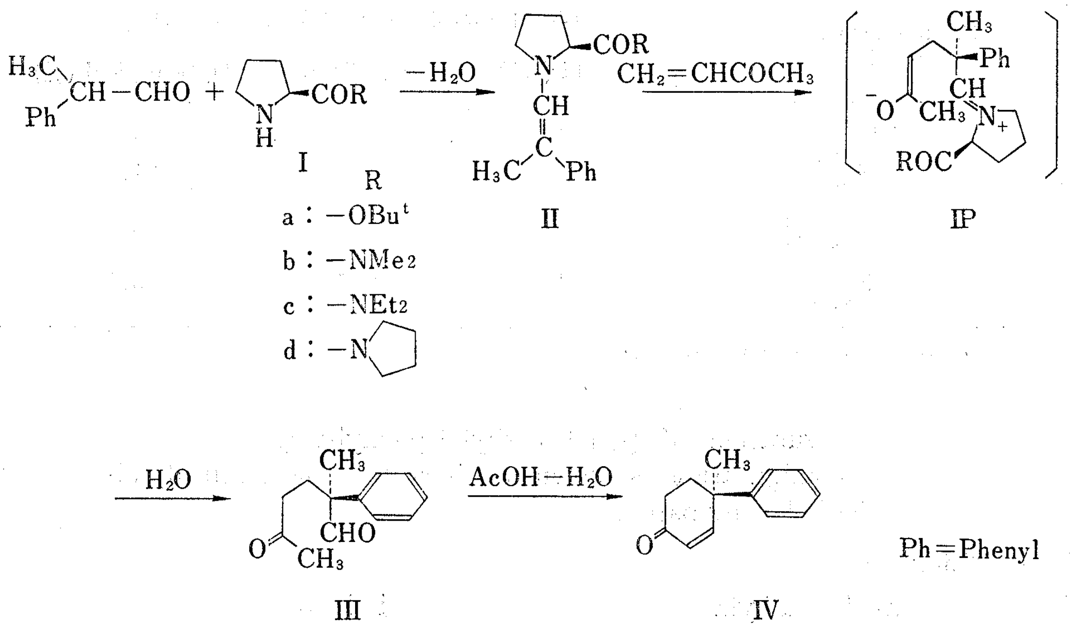

Chart. 1

Enamines (IIa—d) were prepared from 2-phenylpropanal and the equivalent L-proline derivatives (Ia—d) in benzene by azeotropic distillation described above or with molecular sieves. The crude enamines, obtained after evaporation of the solvent did not racemize but the enamines almost completely racemized under distillation. Besides, enamines (II) were gradually hydrolyzed with atmospheric moisture. Therefore, the crude enamines obtained were not purified for use in alkylation.

Accordingly, the general procedure for asymmetric synthesis was established as follows. The crude enamine was alkylated with methyl vinyl ketone in a suitable solvent, then this alkylated enamine was hydrolyzed by adding aqueous acetic acid and the neutral portion was extracted. The extract was then heated with pyrrolidine and aqueous acetic acid for cyclization. After purification by column chromatography on silica gel and distillation, 4-methyl-4-phenyl-2-cyclohexenone (IV) was isolated and its optical rotation was measured.

(a) Effect of L-Proline Derivatives (Ia—d)

With cyclohexanone enamines, we reported[5] that the optical yield became higher as the ester group of L-proline esters became bulkier. This shows that the steric effect of the ester group controls the stereoselectivity of asymmetric alkylation. Consequently, if the branching position of the ester group can be brought closer to the asymmetric center, the steric effect should become more effective. However, this is impossible with L-proline esters, so we used the N,N-disubstituted amides of L-proline, *e.g.* dimethylamide (Ib), diethylamide (Ic), and pyrrolidide (Id).

The results of asymmetric alkylation of the L-proline derivatives; *t*-butyl ester (IIa), dimethylamide (IIb), diethylamide (IIc), and pyrrolidide (IId) with methyl vinyl ketone, are shown in Table I. Alkylation of enamines with methyl vinyl ketone was carried out at 0° in methanol for 4 hr. In all cases, *dextro*-rotatory 4-methyl-4-phenyl-2-cyclohexenone (IV) was obtained. As expected, optical yields[7] were extremely high compared to the optical yield with L-proline *t*-butyl ester. In addition, among the three L-proline amides, the optical yield with L-proline pyrrolidide (Id) was the highest. Thus, in the following, L-proline pyrrolidide (Id) was used exclusively.

TABLE I.[a] Asymmetric Synthesis of IV with L-Proline Derivatives (I) at 0° in CH_3OH, 4 hr

L-Proline derivatives (I)	R	4-Methyl-4-phenyl-2-cyclohexenone (IV)		
		Yield (%)[b]	$[\alpha]_D$ (EtOH)	Optical yield (%)
a	OBu^t	43	+ 7.6°	6.0
b	$N\begin{matrix}\diagup CH_3\\ \diagdown CH_3\end{matrix}$	42	+40.3°	31.0
c	$N\begin{matrix}\diagup C_2H_5\\ \diagdown C_2H_5\end{matrix}$	53	+34.9°	26.8
d		48	+47.4°	36.5

a) Values of at least three runs were averaged.
b) Yield based on I used.

The absolute configuration of (+)-4-methyl-4-phenyl-2-cyclohexenone ((+)-IV) was determined to be (*R*) configuration as shown in Chart 1. The detail of this determination will be discussed in the following paper.

(b) Effect of Solvents

The solvents used in alkylation significantly effected the optical yields. Enamine (IId) was alkylated with methyl vinyl ketone only in the presence of alcohols, as was pyrrolidine enamine. The results of alkylation in various solvents at 0° for 24 hr are listed in Table II.

TABLE II. Solvent Effects on the Alkylation of Enamine (IId)

Solvent	4-Methyl-4-phenyl-2-cyclohexenone (IV)	
	$[\alpha]_D$ (EtOH)	Optical yield (%)
MeOH–THF (10:3)	+47.2°	36.3
EtOH–THF (10:3)	+35.7°	27.5
t-BuOH–THF (10:3)	+28.0°	21.5
MeOH–DMSO (1:9)	+18.7°	14.4
MeOH–$CHCl_3$ (1:9)	+53.0°	40.8
MeOH–CCl_4 (1:9)	+61.6°	47.3
MeOH–C_6H_6 (1:9)	+63.8°	49.1

Among the alcohols, *e.g.* methanol, ethanol, and *t*-butanol, methanol gave the highest optical yield. Tetrahydrofuran was added to *t*-butanol to inhibit freezing at 0°. To compare *t*-butanol with methanol and ethanol the same ratio of tetrahydrofuran was added to both. By comparing with Table I, it turned out that tetrahydrofuran added to methanol,

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7) These were calculated on the basis of the deduced value of optically pure 4-methyl-4-phenyl-2-cyclohexenone, $[\alpha]_D$+130° (EtOH). The optical purity of 4-methyl-4-phenyl-2-cyclohexenone will be discussed in detail in another paper.

to this extent, did not affect optical yields. However, when methanol was diluted to 1:9 with non-hydroxylic solvents, the polarity[8] of the non-hydroxylic solvents seems to affect the optical yields. Methanol diluted with a more polar solvent, *e.g.* dimethylsulfoxide, gave a lower optical yield, and methanol diluted with a less polar solvent, *e.g.* CCl_4 or C_6H_6, gave a higher optical yield.

(c) Effect of Reaction Temperature on Alkylation

Enamine (IId) in methanol was alkylated with methyl vinyl ketone at the temperature described in Table III. In this alkylation, (later discussed in detail) the optical yield increased with time and reached a constant value which was dependent on the reaction temperature. Thus, the reaction time at the each temperature in Table III was sufficient for the reaction to reach the constant value. Results reveal that the optical yield of alkylation depends on the reaction temperature. The higher is the reaction temperature, the lower is the optical clear. But when the reaction temperature was below 0°, the effect of temperature was not yield.

TABLE III.[a] Effect of the Reaction Temperature on the Alkylation of Enamine (IId)

Reaction temperature (°C)	Reaction time (hr)	4-Methyl-4-phenyl-2-cyclohexenone (IV)		
		Yield (%)[b]	$[\alpha]_D$ (EtOH)	Optical yield (%)
−75	18	0	—	—
−20	27	35	+46.1°	35.5
−10	24	41	+41.7°	32.1
0	4	40	+47.4°	36.5
20	3	49	+41.2°	31.5
40	2	41	+33.6°	25.9
64	1	47	+26.1°	20.1

a) Values of at least three runs were averaged.
b) Yield based on I used.

(d) Evidence of Thermodynamically Controlled[9] Asymmetric Synthesis

The alkylation of enamine (IId) in methanol at 0° was initiated by adding methyl vinyl ketone and the time-courses for its yield and optical yield were followed (Fig. 1).

The yield reached a constant value during the first hour, whereas the optical yield at that time was low and increasing. The optical yield ceased increasing after another two hours and remained constant. The increase in optical yield with time at the initial stage of alkylation is not necessarily in conflict with a kinetically controlled[9] mechanism, but the further increase in the optical yield after the yield had become constant, strongly suggests a thermodynamically controlled mechanism. This was confirmed by the following experiments.

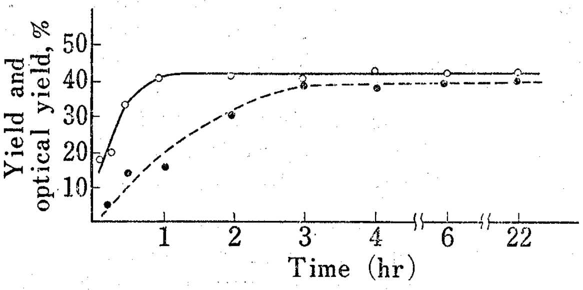

Fig. 1. Time-Course for the Yield (—○—) and Optical Yield (---●---) from the Alkylation of Enamine IId at 0° in CH_3OH

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[8] Reported dipole moment (D); C_6H_6 0, CCl_4 0, $CHCl_3$ 1.15, MeOH 1.664, EtOH 1.68, *t*-BuOH 1.66, DMSO 3.95.

[9] E.L. Eliel, "Stereochemistry of Carbon Compounds," McGraw-Hill, New York, 1962, p. 200.

In methanol at 0° enamine (IId) was alkylated with methyl vinyl ketone for 4 hr. The reaction mixture was divided into two portions. One was immediately treated as usual to obtain cyclohexenone (IV) and the other was similarly treated after being heated for 2 hr to refluxing. The former gave cyclohexenone (IV), and exhibited $[\alpha]_D$ +51.0° (EtOH), optical yield 39.2%. The latter gave cyclohexenone (IV), $[\alpha]_D$ +37.6° (EtOH), optical yield 28.9%. In addition, from each reaction mixture in the alkylation, L-proline pyrrolidide (Id) was recovered as a benzyloxycarbonyl derivative. Id recovered from the former, exhibited $[\alpha]_D$ −13.8° (MeOH), and Id recovered from the latter, exhibited $[\alpha]_D$ −13.2° (MeOH). Therefore, in each reaction, for practical purposes L-proline pyrrolidide (Id) did not racemize.

These results reveal the presence of an inversion process in the configuration of the initial product (Ip) at the induced asymmetric center during this reaction. Since the asymmetric center induced by alkylation is a quaternary carbon which does not racemize, it is reasonable to suppose that the inversion process passes through the reverse reaction[10] of alkylation.

This is the first work ever reported on the efficient asymmetric synthesis using alkylation of aldehyde enamines and we could find out that optical yield of this kind of asymmetric synthesis reached at about 50% by selecting reaction conditions. An extension of this work to the synthesis of optically active (+)-mesembrine will be reported in detail in a subsequent paper.

Experimental[11]

(±)-4-Methyl-4-phenyl-2-cyclohexenone (IV)——A solution of 2-phenylpropanal[12] (0.01 mole) and pyrrolidine (0.01 mole) in benzene (50 ml) was heated to reflux for 15 min. The H_2O produced was removed using a Dean-Stark column. The benzene was evaporated under reduced pressure and the residue was submitted to distillation, bp 114—116° (4 mmHg), giving a pale yellow oil of enamine (1.4 g, 75%). IR ν_{max}^{Cap} cm^{-1}: 1635, 1595. UV λ_{max}^{EtOH} mμ (ε): 237 (5780), 305 (6500). NMR (CCl_4) τ: 2.9 (5H, multiplet), 3.74 and 4.02 (combined to 1H, quartet, respectively, $J=1$ cps), 6.6—7.3 (4H, multiplet), 7.9—8.5 (7H, multiplet).

Methyl vinyl ketone (0.01 mole, the fraction boiling at 81—82° in a commercial material from Tokyo Kasei Co.) was added to the solution of enamine (1.4 g) in MeOH (13 ml) and the reaction mixture was allowed to stand for 4 hr at room temperature. Aq. AcOH (33%, 1 ml) was added and the solution was heated under reflux for 2 hr. The solution was evaporated under reduced pressure and the residue was dissolved in benzene and washed successively with H_2O, 10% HCl and H_2O after which it was dried over Na_2SO_4. The solvent was evaporated under reduced pressure.

Thus, the crude 4-methyl-4-phenyl-2-cyclohexenone (IV), containing mainly 2-phenylpropanal, was chromatographed on silica gel (40 g) with $CHCl_3$ and the desired fraction was submitted to distillation, bp 120—122° (3 mmHg). Purity was assayed by gas chromatography (3% Carbowax 20M, column temperature 125°). IR ν_{max}^{Cap}: 1685 cm^{-1}. UV λ_{max}^{EtOH} mμ (ε): 198 (20400), 305 (590). NMR (CCl_4) τ: 2.75 (5H, singlet), 3.19 (1H, doublet, $J=11$ cps), 4.01 (1H, doublet, $J=11$ cps), 7.87 (4H, singlet), 8.48 (3H, singlet). *Anal.* Calcd. for $C_{13}H_{14}O$: C, 83.83; H, 7.58. Found: C, 84.05; H, 7.58.

Its semicarbazone, mp 193—195°, as white prisms, was prepared by the usual method and was recrystallized from EtOH. *Anal.* Calcd. for $C_{14}H_{17}ON_3$: C, 69.11; H, 7.04; N, 17.27. Found: C, 69.23; H, 7.11; N, 17.08.

Its 2,4-dinitrophenylhydrazone, mp 157—159° (decomp.), as an orange powder, was prepared by the usual method and purified by washing it with EtOH. *Anal.* Calcd. for $C_{19}H_{18}O_4N_4$: C, 62.28; H, 4.95; N, 15.27. Found: C, 62.07; H, 4.95; N, 15.57.

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[10] The initial product of enamine alkylation was studied in detail by I. Fleming and his co-workers, and its thermal instability was revealed. I. Fleming and J. Harley-Mason, *J. Chem. Soc.*, **1964**, **2165**; I. Fleming and M.H. Karger, *ibid.*, **1967** (*C*), 226.

[11] All melting and boiling points are uncorrected. Optical rotations were measured with a Yanagimoto Model OR-10 polarimeter and optical rotatory dispersion (ORD) curves were recorded on a 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. Gas chromatographic analyses were carried out by a Shimazu Model GC-1 and a Perkin-Elmer Model 800 gas chromatograph with dual flame ionization detectors.

[12] C.F.H. Allen and J. van Allan, "Organic Syntheses," Coll. Vol. III, ed. by E.C. Horning, John Wiley and Sons, Inc., New York, 1955, p. 733.

General Procedure of Asymmetric Synthesis of 4-Methyl-4-phenyl-2-cyclohexenone (IV)——A solution of 2-phenylpropanal (0.01 mole) and a L-proline derivative (0.01 mole) in benzene (50 ml) was heated under reflux for 15 min. The H_2O produced was removed with a Dean-Stark column. The benzene was evaporated under reduced pressure and the residue was dissolved in a solvent to make a solution of 10% concentration. The solution of enamine was maintained at the prescribed temperature with a thermostat. Methyl vinyl ketone (0.012 mole) was added to the solution of enamine and the reaction mixture was allowed to stand for the prescribed time.

Hydrolysis and cyclization were accomplished by either the procedure described above for (±)-IV or one immediately following. To recover L-proline derivatives the latter is preferable.

The reaction mixture was poured into 10% HCl (20 ml) and the neutral portion was extracted with $CHCl_3$. The extract was washed with H_2O and evaporated under reduced pressure. The residue was dissolved in MeOH (15 ml) containing 33% AcOH (1 ml) and pyrrolidine (0.5 ml), then was heated under reflux for 2 hr. The mixture was evaporated under reduced pressure and the residue was dissolved in benzene and washed successively with H_2O, 10% HCl and H_2O, after which it was dried over Na_2SO_4. The solvent was evaporated under reduced pressure.

The crude 4-methyl-4-phenyl-2-cyclohexenone (IV) obtained was purified according to the procedure described above.

An example of optical rotatory dispersion: ORD ($c=1.212$, MeOH) $[M]^{31}$ (mμ): +70° (700), +101° (589), +961° (362) (peak), +885° (350) (shoulder), +283° (320) (trough), +2660° (280). CD ($c=1.212$, MeOH) $[\theta]^{31}$ (mμ): +760 (330) (positive maximum).

***t*-Butyl L-Prolinate (Ia)**——This was prepared according to the procedure described by Anderson and Callahan.[13] bp 55° (3 mmHg), $[\alpha]_D^{13}$ −54.4° ($c=0.75$, EtOH).

L-Proline Dimethylamide (Ib)——A solution of N-carbobenzoxy-L-proline[14] (35 g, 0.143 mole) and triethylamine (14.3 g, 0.143 mole) in THF was cooled with ice. Ethyl chlorocarbonate (15.5 g, 0.143 mole) was added to this solution at 5—10° for 15 min with stirring and the pasty reaction mixture was stirred for additional 30 min under cooling. A solution of dimethylamine (9 g, 0.2 mole) in THF was then added to the stirred mixture dropwise for 15 min at a temperature kept below 10°. After stirring the whole for 1 hr under cooling, it was filtered and the crystals were washed with AcOEt. The filtrate and washings were combined and evaporated under reduced pressure. The residue was dissolved in AcOEt and washed with H_2O and an aq. $NaHCO_3$ solution. The organic layer was dried over Na_2SO_4 and evaporated. N-Carbobenzoxy-L-proline dimethylamide (17 g, 44%) was obtained as a yellow oil. IR ν_{max}^{Cap} cm^{-1}: 1700, 1650.

The washing containing aq. $NaHCO_3$ was acidified with dil. HCl and extracted with AcOEt. The extract was washed with H_2O and dried over Na_2SO_4, then it was evaporated. N-Carbobenzoxy-L-proline (19.2 g, 55%) was recovered.

N-Carbobenzoxy-L-proline dimethylamide (17 g) was dissolved in EtOH (100 ml). Pd-C (5%, 1.0 g) was added. The mixture was vigorously stirred under a slow stream of hydrogen and the progress of the reaction was followed by thin-layer chromatography (TLC) analysis of the mixture. After the completion of the reaction was confirmed (3—4 hr), the mixture was filtered and the filtrate was evaporated. Distillation of the residue gave L-proline dimethylamide (Ib), bp 98—100° (3 mmHg), as a colorless liquid, 5.4 g (61%). $[\alpha]_D^{10}$ −103° ($c=1.65$, EtOH). IR ν_{max}^{Cap} cm^{-1}: 3400, 1640. NMR (CCl_4) τ: 6.27 (1H, multiplet) 7.00, 7.10, 7.12 (8H) 7.8—8.8 (4H, multiplet).

Its picrate was recrystallized from MeOH. mp 154—156°, as yellow needles. *Anal.* Calcd. for $C_{13}H_{17}O_8N_5$: C, 42.05; H, 4.62; N, 18.86. Found: C, 42.09; H, 4.79; N, 19.05.

L-Proline Diethylamide (Ic)——N-Carbobenzoxy-L-proline diethylamide was prepared following the procedure for dimethylamide (Ib) described above, except that diethylamine was used. Using 21.0 g (0.086 mole) of N-carbobenzoxy-L-proline, 14.3 g (55%) of N-carbobenzoxy-L-proline diethylamide as an yellow oil was obtained. IR ν_{max}^{Cap} cm^{-1}: 1705, 1650.

Hydrogenation of N-carbobenzoxy-L-proline diethylamide (14.3 g) was carried out using the procedure described above for dimethylamide (Ib), and gave L-proline diethylamide (Ic) (4.6 g, 57.5%), bp 107—108° (5 mmHg), as a colorless liquid, $[\alpha]_D^{29}$ −96.4° ($c=2.49$, EtOH). IR ν_{max}^{Cap} cm^{-1}: 3350, 1650. NMR (CCl_4) τ: 6.34 (1H, multiplet), 6.70 (4H, triplet), 7.05 (2H, multiplet), 7.55 (1H, singlet), 8.2—8.5 (4H, multiplet), 8.85 (6H, quartet).

Its picrate, mp 140—142°, as yellow needles, was recrystallized from EtOH. *Anal.* Calcd. for $C_{15}H_{21}O_8N_5$: C, 45.11; H, 5.30; N, 17.54. Found: C, 45.15; H, 5.38; N, 17.43.

L-Proline Pyrrolidide (Id)——N-Carbobenzoxy-L-proline pyrrolidine was prepared following the procedure for dimethylamide (Ib) described above, except that pyrrolidine was used. Using 49.0 g (0.20 mole) of N-carbobenzoxy-L-proline, 33.0 g (55%) of N-carbobenzoxy-L-proline pyrrolidine, mp 130—133°, as white prisms, was obtained and recrystallized from acetone. The melting point of this sample was not altered by repeated recrystallizations from acetone $[\alpha]_D^{22}$ −14.1° ($c=1.61$, MeOH). IR ν_{max}^{KBr} cm^{-1}: 1700, 1630. NMR

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13) G.W. Anderson and F.M. Callahan, *J. Am. Chem. Soc.*, **82**, 3359 (1960).
14) A. Berger, J. Kurtz, and E. Katchalsky, *J. Am. Chem. Soc.*, **76**, 5552 (1954).

(CCl_4) τ: 2.67 (5H, doublet), 4.90 (2H, multiplet), 5.5 (1H, multiplet), 6.0—7.0 (6H, multiplet), 7.5—8.5 (8H, multiplet). *Anal.* Calcd. for $C_{17}H_{22}O_3N_2$: C, 67.52; H, 7.33; N, 9.27. Found: C, 67.35; H, 7.45; N, 9.50.

Hydrogenation of N-carbobenzoxy-L-proline pyrrolidide (12.4 g) was carried out using the procedure described above and gave L-proline pyrrolidide (5.7 g, 83%), bp 134—136° (4 mmHg), as a colorless liquid. $[\alpha]_D^{26}$ $-112.5°$ (c=0.91, EtOH). IR ν_{max}^{cap} cm^{-1}: 3500, 1640. NMR (CCl_4) τ: 6.2—7.0 (7H, multiplet), 7.20 (1H, singlet), 7.8—8.6 (8H, multiplet).

Its picrate, mp 196—198°, as yellow needles, was recrystallized from EtOH. *Anal.* Calcd. for $C_{18}H_{19}O_8N_5$: C, 45.34; H, 4.82; N, 17.63. Found: C, 45.11; H, 4.88; N, 17.82.