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Amino Acids and Peptides. XIX.*[1] Synthetic Study of optically Active Carene Skeleton from α-Amino Acid. Total Synthesis of (+)-2-Carene

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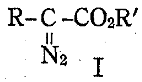
For a total synthesis of the optically active carene congeners from optically active α-amino acids, several attempts were made on intramolecular cyclization of 2-cyclohexenyl esters of α-substituted α-diazoacetic acid (III) which were derived from the corresponding amino acid esters. One of the optically active diastereoisomers (X) which was obtained by separation of 2-cyclohexenyl L-alaninate was diazotized with isoamylnitrite and then cyclized using Cu powder as a catalyst to afford the optically active lactone (XIX). XIX was then converted into the key intermediate (XXI) having the bicyclo[4,1,0]heptane ring system, from which (+)-2-carene was synthesized.

In a series of our investigation on reactivities and utilizations[3] of the α-substituted α-diazo esters (I) which are easily available from the corresponding α-amino acid esters,[4] we have studied on carbene-olefin addition reactions of I. Although the reactions of diazoacetic



$$\underset{\underset{N_2}{\|}}{R-C}-CO_2R'$$

I

esters with various unsaturated compounds to form three-membered rings have extensively been examined under thermal, catalytic and photochemical conditions,[5] the cyclopropanation reactions of I have scarcely been reported because I have the methyl, methylene or methine group adjacent to the diazocarbon and 1,2-hydrogen shift may therefore be preferable to give a mixture of isomeric olefins when I are submitted to a carbene reaction. Actually, in our experiments, intermolecular addition reactions between benzyl 2-diazopropionate (I, $R=CH_3$, $R'=C_6H_5CH_2$) and 2-cyclohexenone or 2-cyclohexenol were practically unsuccessful, and the main product isolated was benzyl 2-(2-cyclohexenyloxy)-propionate in the latter case (40% yield).

On the other hand, the intramolecular addition reactions gave the desired three-membered ring products. When (±)-2-cyclohexenyl 2-diazopropionate (IIIa) was heated in benzene or dioxane in the presence of copper powder (2 eq) as a catalyst, (±)-9-methyl-7-oxatricyclo-[4,3,0,$0^{2,9}$]nonan-8-one (IVa) was obtained as a major product. (±)-2-Cyclohexenyl 2-diazo-4-methylpentanoate (IIIb) and (±)-2-cyclohexenyl 2-diazo-3-phenylpropionate (IIIc) were also treated in the similar reaction conditions to afford (±)-9-isobutyl-(IVb) and (±)-9-benzyl-7-oxatricyclo[4,3,0,$0^{2,9}$]nonan-8-one (IVc) respectively, though the corresponding isomeric

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* Dedicated to the memory of Prof. Eiji Ochiai.

[1] This work was presented at the 18th Symposium on the Chemistry of Natural Products, Kyoto, Oct. 1974. Part XVIII: M. Konda, T. Shioiri, and S. Yamada, *Chem. Pharm. Bull.* (Tokyo), **23**, 1063 (1975).

[2] Location: *a) 7-3-1, Hongo, Bunkyo-ku, Tokyo, 113, Japan; b) 2-2-50, Kawagishi, Toda-shi, Saitama, 335, Japan.*

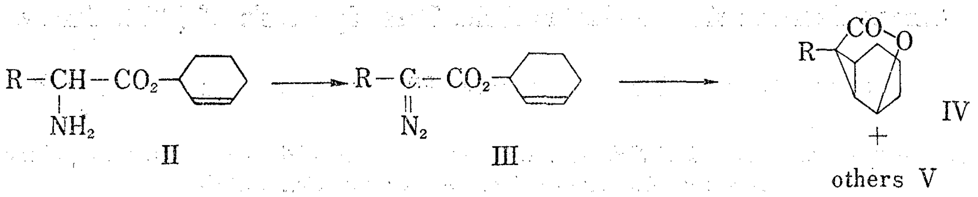
[3] N. Takamura, T. Mizoguchi, and S. Yamada, *Tetrahedron Letters*, **1973**, 4267; *idem, Chem. Pharm. Bull.* (Tokyo), **23**, 299 (1975).

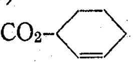
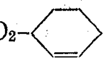
[4] N. Takamura, T. Mizoguchi, K. Koga, and S. Yamada, *Tetrahedron Letters*, **1971**, 4495; *idem, Tetrahedron*, **31**, 227 (1975).

[5] V. Dave and E.W. Warnhoff, "Organic Reactions," Vol. 18, ed. by W.G. Dauben, John Wiley and Sons, Inc., New York, 1970, p. 217.

olefins (Vb and Vc) were mainly produced in these cases. The yields are given in Table I together with reaction conditions employed in each case. IVa could also be obtained from IIIa in fair yield (20%) using anhydrous cupric sulfate as a catalyst in cyclohexane at room temperature. UV irradiation on IIIa was unsatisfactory for this internal cyclization which only afforded 2-cyclohexenyl acrylate in 35% yield.

Table I



	R	reflux time (hr)	Products (yield,[a)] %) IV	V
a	CH_3	6	(32)	two dimers[b)] (20)
b	$(CH_3)_2CHCH_2$	11	(8.6)	$(CH_3)_2CHCH=CHCO_2$-  (72)
c	$C_6H_5CH_2$	5	(9.3)	$C_6H_5CH=CHCO_2$-  (69)

a) Yields basd on II.
b) Structural assignments are not performed.

A variety of approaches have recently been reported for syntheses of isoprene homologues of 2-carene, such as sesquicarene and sirenin.[6)] However, all of them were reported to give only the racemic products. Thus, application of this intramolecular cyclization is quite attractive for the synthesis of the natural bicyclo[4,1,0]heptane derivatives, as it may provide a new means to introduce the optical activity at the very beginning of the synthesis when an optically active amino acid is used as the starting material. As an example, we now wish to report a total synthesis of (+)-2-carene, a monoterpene isolated by Simonsen[7)] from *Andropogen iwarancusa.*

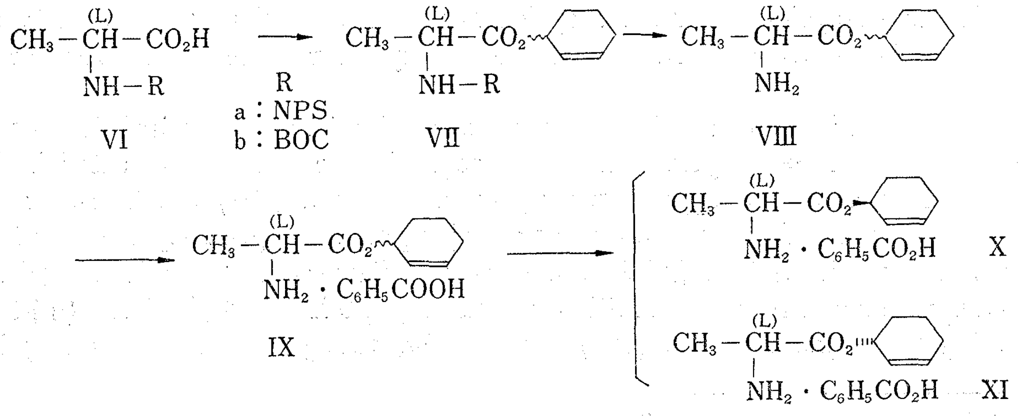


Chart 1

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6) *a)* E.J. Corey and K. Achiwa, *Tetrahedron Letters*, **1969**, 1837; *b)* E.J. Corey and K. Achiwa, *Tetrahedron Letters*, **1969**, 3257; *c)* R.M. Coates and R.M. Freidinger, *Chem. Comm.*, **1969**, 871; *idem, Tetrahedron*, **26**, 3487 (1970); *d)* E.J. Corey and K. Achiwa and J.A. Katzenellbogen, *J. Am. Chem. Soc.*, **91**, 4318 (1969); *e)* P.A. Grieco, *J. Am. Chem. Soc.*, **91**, 5660 (1969); *f)* J.J. Plattner, U.T. Bhalerao, and H. Rapoport, *J. Am. Chem. Soc.*, **91**, 4933 (1969); **92**, 3429 (1970); *g)* E.J. Corey and K. Achiwa, *Tetrahedron Letters*, **1970**, 2245; *h)* K. Mori and M. Matsui, *Tetrahedron Letters*, **1969**, 4435; *idem, Tetrahedron*, **26**, 2801 (1970).

7) J.L. Simonsen, *J. Chem. Soc.*, **121**, 2292 (1922).

Condensation of NPS[8)]-L-alanine (VIa) with recemic 3-bromo-cyclohexene in dimethyl formamide (DMF) in the presence of triethylamine afforded a diastereomeric mixture of NPS-L-alanine 2-cyclohexenyl ester (VIIa) in a good yield (85%). Prior to this reaction, attempts were made on esterification of N-protected-L-alanine (VI) with 2-cyclohexenol using DCCD[8)] or CDI[8)] as a coupling reagent, but the yields of N-protected-L-alanine 2-cyclohexenyl ester (VII) were less satisfactory (DCCD; R=NPS (VIIa), 14% yield. R=BOC[8)] (VIIb), 47% yield. CDI; VIIa, 44% yield).

Removal of the protecting groups from VII with 2.5 N HCl in ethyl acetate caused a concomitant cleavage of the ester bond and consequently afforded a diastereomeric mixture of L-alanine 2-cyclohexenyl ester (VIII) only in a poor yield (21% yield from VIIb). The method of Kessler and Iselin,[9)] in which thiourea was employed for mild cleavage of the NPS group was very successful (73% yield) in this case.

As the optically active center of the L-alanine moiety is lost in the next diazotization step, each isomer of diastereomeric VIII was separated as shown in Chart 1 to transfer the optical activity to the asymmetric carbon of 2-cyclohexenyl group. Benzoic acid salt (IX) of VIII was recrystallized from ethyl acetate to obtain constant optical rotation giving a less soluble diastereoisomer (X) as colorless prisms (mp 100°, $[\alpha]_D^{20}$ −114° ($CHCl_3$)).

The absolute configuration of the 2-cyclohexenyl moiety of X was confirmed as follows. Reductive cleavage of the free base of X with lithium aluminum hydride in ether yielded (−)-2-cyclohexenol (XII, $[\alpha]_D^{20}$ −112° ($CHCl_3$)), whose absolute configuration has already been established as (*S*),[10)] and is also suitable for the synthesis of natural (+)-2-carene as shown in Chart 2.

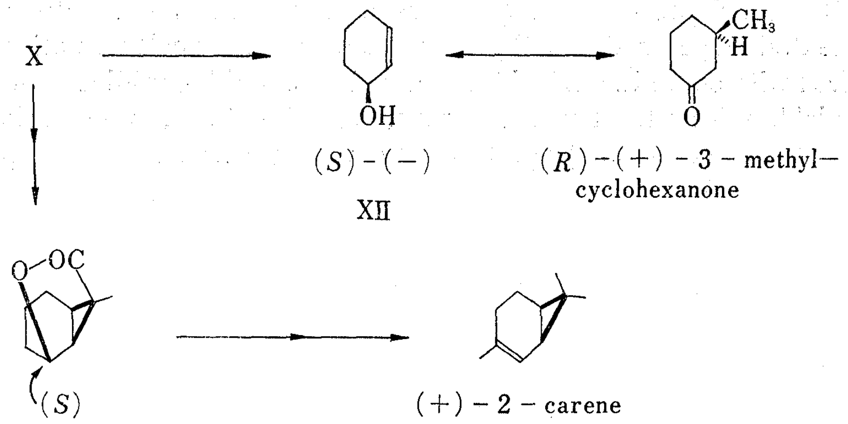

Chart 2

Several methods were studied for conversion of the lactone carbonyl group of the racemic IVa into methyl group to yield dimethyl alcohol (XVII), the optically active form of which is the key intermediate for (+)-2-carene (Chart 3). Reduction of IVa with lithium aluminum hydride gave, in 91% yield, the corresponding diol (XIII) as colorless prisms. Selective acylation or tosylation of the primary alcohol group of XIII, however, was unsuccessful. Alternatively, (±)-2,2-ethylenedioxy-7-hydroxy-methyl-7-methylbicyclo[4,1,0]heptane (XIV), prepared from IVa as outlined in Chart 3, was treated with pyridine-sulfur trioxide, tosyl chloride or mesyl chloride, but such an activation of the hydroxy group was again found to be unsuccessful. Investigation was then made on another route (Chart 4). Reduction of the lactone (IVa) with diisobutylaluminum hydride in toluene at −78° to corresponding lactol

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[8)] Abbreviation NPS: *ortho*-nitrophenylthio, BOC: *t*-butyloxycarbonyl, DCCD: dicyclohexylcarbodiimide, CDI: carbodiimidazole.

[9)] W. Kessler and B. Iselin, *Helv. Chim. Acta*, **49**, 1330 (1966).

[10)] R.K. Hill and J.W. Morgan, *J. Org. Chem.*, **33**, 927 (1968).

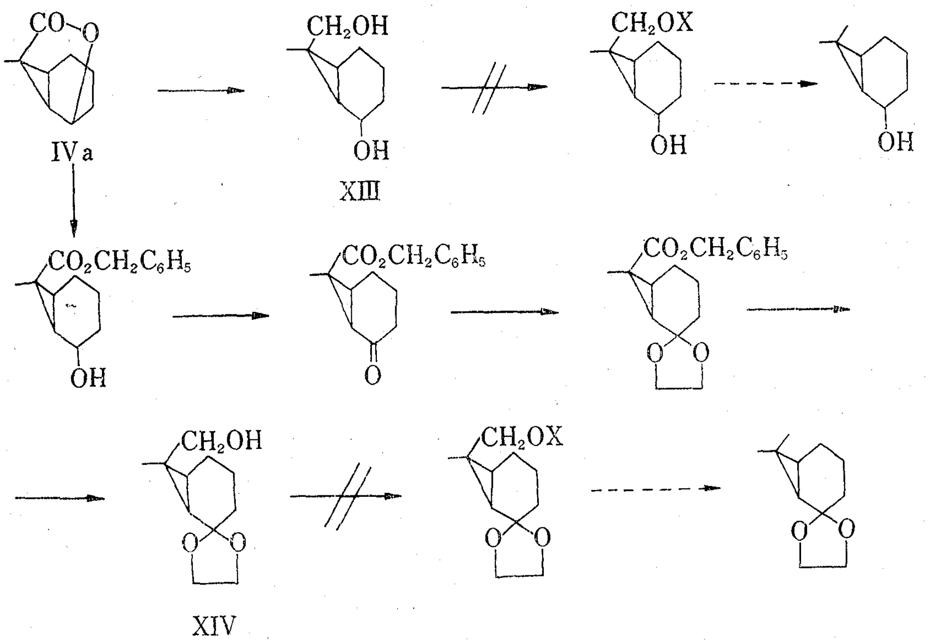

Chart 3

(XV), followed by treatment with tosylhydrazine in ethanol in the presence of acetic acid, gave (±)-tosylhydrazone derivative (XVI) in an overall yield of 81%. Reductive cleavage of the imino bond of XVI was performed according to the method reported by Caglioti and Grasselli;[11] XVI was reduced with a large excess of lithium aluminum hydride in tetrahydrofuran to give the desired geminal dimethyl compound (XVII) as colorless prisms (21% yield). Oxidation of XVII with chromium trioxide in methylene chloride-pyridine afforded oily ketone (XVIII, 91% yield, 2,4-dinitrophenylhydrazone, mp 156—157°), whose infrared (IR) and nuclear magnetic resonance (NMR) spectral data were identical to those reported by Mori and Matsui.[12]

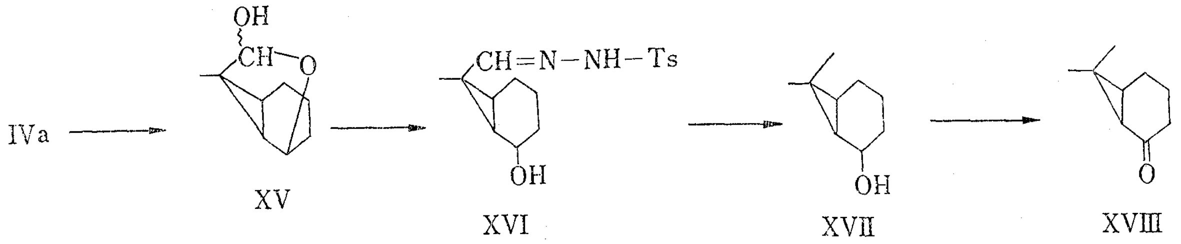

Chart 4

A new synthetic approach to the bicyclo[4,1,0]heptane ring system was thus achieved, which allowed us to study further on the first synthesis of optically active 2-carene from the optically active amino acid.

X (mp 97.5—99°, $[\alpha]_D^{20}$ −104° (c=1.32, $CHCl_3$)) was diazotized and submitted to intramolecular cyclization to afford optically active lactone (XIX) as a colorless oil (41% yield from X, $[\alpha]_D^{20}$ −19.7° ($CHCl_3$)). Reduction of XIX with diisobutylaluminum hydride and subsequent treatment with tosylhydrazine gave the tosylhydrazone (XX). Optically active XX thus obtained was more soluble in ethyl acetate than the corresponding racemic compound (XVI) and separation of each compound was found to be quite easy. This fact allowed us to use impure X, contaminated by its diastereoisomer XI, as the starting material. Reduction of XX with a large excess of lithium aluminum hydride gave the optically active key inter-

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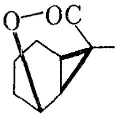
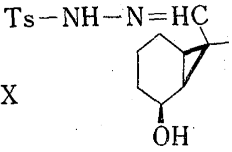
[11] L. Caglioti and P. Grasselli, *Chem. and Ind.*, **1964**, 153.
[12] K. Mori and M. Matsui, *Tetrahedron*, **25**, 5013 (1969).

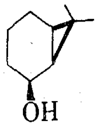
mediate (XXI) as colorless prisms (14.5% yield from XIX, $[\alpha]_D^{20}$ $-56.8°$ (MeOH)), which was oxidized with chromium trioxide to the corresponding ketone (XXII, 90% yield, $[\alpha]_D^{20}$ $-262°$ ($CHCl_3$)). The optical rotatory dispersion spectrum of XXII shows a negative Cotton effect with a trough at 308 nm, which is opposite in sign to the reversed Octant rule. This result is comparable with the Djerassi's observation that (+)-carone does not fit the rule.[13]



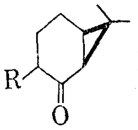
XIX



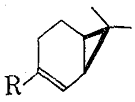
XX



XXI



XXII : R=H
XXIII: R=CO_2CH_3



XXIV : R=CO_2CH_3
XXV : R=CH_2OH
(+)-2-carene: R=CH_3

Methoxycarbonylation of XXII with sodium hydride and an excess of methyl carbonate in benzene under gentle reflux afforded the β-keto ester (XXIII) as a colorless oil (93% yield, $[\alpha]_D^{20}$ $-128°$ (MeOH)). Reduction of XXIII with sodium borohydride in ethanol at $-10°$—$-20°$ for 4 hr gave the corresponding β-hydroxy ester derivative (62% yield), which was esterified with benzoyl chloride in pyridine (94% yield) and subsequently treated with potassium t-butoxide in benzene at room temperature to give the α,β-unsaturated ester (XXIV, 98% yield, $[\alpha]_D^{20}$ $-118°$ (MeOH)). Reduction of oily XXIV using lithium aluminum hydride in ether at $-20°$—$-30°$ for 30 min afforded XXV as a colorless oil (90% yield, $[\alpha]_D^{22}$ $+67.8°$ (benzene); 3,5-dinitrobenzoate mp 86—87°), whose physical data were identical to those reported by Gollnick and Schade.[14] The final step to (+)-2-carene was performed according to the method of Corey and Achiwa.[15] Thus, XXV was treated carefully with sulfur trioxide-pyridine complex in tetrahydrofuran at 0° and the resulting mixture was directly reduced with an excess of lithium aluminum hydride to yield, after purification by preparative gas-liquid chromatography (GLC), (+)-2-carene as a colorless oil (69% yield, $[\alpha]_D^{20}$ $+84.4°$ (EtOH)).[16] The IR and NMRdata of this product were satisfactorily identical to those of the authentic sample which was prepared from (+)-3-carene by the method of Ohloff, *et al.*[17]

Experimental[18]

2-Cyclohexenol——To a stirred suspension of $LiAlH_4$ (10.1 g, 0.267 moles) in ether (750 ml) was added at $-20°$—$-25°$ a solution of 2-cyclohexenone (43.2 g, 0.45 moles) in ether (150 ml) during a period of 12 min. The reaction mixture was then stirred for 12 min at the same temperature, the excess hydride was destroyed

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[13] C. Djerassi, W. Klyne, T. Norin, G. Ohloff, and E. Klein, *Tetrahedron*, **21**, 163 (1965).

[14] K. Gollnick and G. Schade, *Tetrahedron Letters*, **1966**, 2335.

[15] E.J. Corey and K. Achiwa, *J. Org. Chem.*, 34, 3667 (1969). This reaction depends considerably on the property of SO_3-pridine complex employed, varying a yield of the product.

[16] W. Cocker, P.V.R. Shannon, and P.A. Staniland, *J. Chem. Soc.* (*C*), **1967**, 485; $[\alpha]_D^{20}$ $+83°$ ($c=0.18$, EtOH).

[17] G. Ohloff, K.H. Schulte-Elte, and W. Giersch, *Helv. Chim. Acta*, **48**, 1665 (1965).

[18] All the melting and boiling points were uncorrected. Infrared (IR) spectra were taken with Hitachi 215 spectrophotometer and JASCO DS-402G spectrophotometer. Nuclear magnetic resonance (NMR) spectra were recorded at 60 Mc on JEOL-NMR spectrometer, Model JNM-MH-60 II and Hitachi NMR spectrometer, Model R-24, (Abbreviation; s: singlet, d: doublet, t: triplet, q: quartet, m: multiplet). Mass spectra were determined on a Hitachi Mass spectrometer, Model RMS-4. Optical rotations were measured on a Yanaco OR-50 Automatic Polarimeter. Optical rotatory dispersion (ORD) spectrum was recorded on a JASCO ORD, Model UV-5. Analytical and preparative GLC were carried out on Shimadzu Model GC-4B (1.5 meter, 25% Polyethylene Glycol on Celite) and Perkin Elemer F-21 (4.5 meter, 20% Polyethylene Glycol on Celite) gaschromatograph, respectively.

with acetone (60 ml) and the complex formed was decomposed with water (60 ml). The mixture was poured into 5% HCl (800 ml) and then extracted with ether. The ether extract was washed with satd. NaCl and dried over K_2CO_3. Filtration and evaporation gave an oily residue which was distilled at 76.5—78°/25 mmHg to afford a colorless oil (34 g, 77%). IR $\nu_{\max}^{\text{liq.}}$ cm^{-1}: 3320, 3020, 1650, 1050. NMR ($CDCl_3$) τ: 8.90—7.70 (6H, m), 7.29 (1H, s), 5.83 (1H, m), 4.20 (2H, s).

Benzyl 2-(2-Cyclohexenyloxy)propionate——A mixture of benzyl 2-diazopropionate (0.95 g, 5 mmoles)4) and Cu powder (0. 63 g, 10 mmoles) in 2-cyclohexenol (2 ml) was stirred for 48 hr at room temperature and filtered. The filtrate and washings (benzene) were evaporated *in vacuo* to afford an oil which was purified on column chromatography (silica gel, eluent: hexane 4–AcOEt 1) to give a colorless oil (0.52 g, 40%). *Anal.* Calcd. for $C_{16}H_{20}O_3$: C, 73.82; H, 7.74. Found: C, 74.09; H, 7.80. IR $\nu_{\max}^{\text{liq.}}$ cm^{-1}: 1748. NMR ($CDCl_3$) τ: 8.85—7.85 (6H, m),8.60 (3H, d, 7 Hz), 6.10 (1H, m), 5.85 (1H, q, 7 Hz), 4.85 (2H, s), 4.24 (2H, broad s), 2.68 (5H, s). Mass Spectrum *m/e*: 260 (M^+), 169, 164, 97, 91, 81 (base).

NPS-L-alanine 2-Cyclohexenyl Ester (VIIa)——i) DCCD Method: A mixture of NPS-L-alanine (VIa, 8.0 g, 33 mmoles),19) 2-cyclohexenol (6.50 g, 66 mmoles) and DCCD (7.50 g, 36.3 mmoles) in tetrahydrofuran (THF) (100 ml) was stirred for 64 hr at room temperature. Filtration and evaporation gave a yellow residue which was taken up in AcOEt and successively washed with 5% H_2SO_4, H_2O, 10% K_2CO_3 and H_2O, and then dried over Na_2SO_4. After evaporation of the solvent the residue was chromatographed over silica gel (eluent: benzene 10–AcOEt 1) to afford VIIa as a yellow oil (1.52 g, 14%). *Anal.* Calcd. for $C_{15}H_{18}O_4N_2S$: C, 55.89; H, 5.63; N, 8.69. Found: C, 55.51; H, 5.55; N, 8.69. IR $\nu_{\max}^{\text{liq.}}$ cm^{-1}: 3330, 3095, 3075, 3035, 1730. NMR ($CDCl_3$) τ: 8.70—7.65 (6H, m), 8.55 (3H, d, 7 Hz), 6.80—6.05 (2H, m), 4.85—3.80 (3H, m), 2.95—1.50 (4H, m).

ii) CDI Method: A solution of VIa (4.84 g, 20 mmoles) and CDI (3.56 g, 22 mmoles)20) in THF (40 ml) was stirred for 3 min and to the mixture was added 2-cyclohexenol (2.16 g, 22 mmoles) in THF (10 ml) and NaH (1.1 mmoles). The whole was stirred for 1 hr at room temperature and for 4 hr at 50—55°, and concentrated *in vacuo* to remove THF. The residue was dissolved in benzene and washed with H_2O, 0.5M citric acid, H_2O, satd. $NaHCO_3$ and H_2O. The dried solution was evaporated to dryness to leave a yellow oil (2.83 g, 44%), whose IR and NMR spectra were identical with those of an authentic sample.

iii) From 3-Bromocyclohexene: A mixture of VIa (177 g, 0.73 mole), triethylamine (74 g, 0.73 mole) and 3-bromocyclohexene (117.4 g, 0.73 mole)21) in dimethylformamide (DMF) (700 ml) was kept standing overnight and then concentrated *in vacuo* to remove DMF. The brown residue was treated with AcOEt–H_2O and the aqueous phase separated was extracted with AcOEt. The combined AcOEt solutions were successively washed with 5% H_2SO_4, H_2O, 10% K_2CO_3, and H_2O, and then dried over Na_2SO_4. Filtration and evaporation gave a yellow oil (198.1 g, 85%). This product had superimposable IR and NMR spectra, in addition to an identical *Rf* with an authentic VIIa.

BOC-L-alanine 2-Cyclohexenyl Ester (VIIb)——A mixture of BOC-L-alanine (VIb, 6.25 g, 33 mmoles),22) 2-cyclohexenol (6.50 g, 66 mmoles) and DCCD (7.50 g, 36.3 mmoles) in THF (100 ml) was stirred for 64 hr at room temperature and treated in a manner similar to that for VIIa (i). Purification on column chromatography (silica gel, eluent: benzene 10–AcOEt 1) afforded a colorless oil (4.19 g, 47%). *Anal.* Calcd. for $C_{14}H_{23}O_4N$: C, 62.43; H, 8.61; N, 5.20. Found: C, 62.45; H, 8.36; N, 5.06. IR $\nu_{\max}^{\text{liq.}}$ cm^{-1}: 3360, 3030, 1715, 1657 (shoulder). NMR ($CDCl_3$) τ: 8.95—7.70 (9H, m), 8.59 (9H, s), 5.74 (1H, m), 5.20—3.80 (4H, m).

NPS-L-leucine 2-Cyclohexenyl Ester——A mixture of NPS-L-leucine (5.69 g, 20 mmoles),19) tirethylamine (2.23 g, 22 mmoles) and 3-bromocyclohexene (3.55 g, 22 mmoles) in DMF (30 ml) was allowed to stand for 22 hr at room temperature. Working-up of the reaction mixture in a similar manner described above for VIIa (iii) gave a yellow oil (5.22 g, 72%). IR $\nu_{\max}^{\text{liq.}}$ cm^{-1}: 3320, 1732. NMR ($CDCl_3$) τ: 9.06 (6H, d, 6 Hz), 8.60—7.60 (9H, m), 7.00—6.24 (2H, m), 4.89—3.84 (3H, m), 3.00—1.65 (4H, m).

NPS-L-phenylalanine 2-Cyclohexenyl Ester——A reddish yellow mixture of NPS-L-phenylalanine (6.20 g, 19.4 mmoles),19) triethylamine (2.16 g, 21.34 mmoles) and 3-bromocyclohexene (3.44 g, 21.34 mmoles) in DMF (30 ml) was kept standing for 22 hr at room temperature and treated in a similar manner to that described above to yield a reddish yellow viscous oil (5.72 g, 74%). IR $\nu_{\max}^{\text{lip.}}$ cm^{-1}: 3330, 1734. NMR ($CDCl_3$) τ: 8.70—7.55 (6H, m), 7.35—6.05 (4H, m), 4.95—3.85 (3H, m), 3.15—1.78 (4H, m), 2.80 (5H, s).

L-Alanine 2-Cyclohexenyl Ester (IIa = VIII)——i) From VIIa: To a methanolic solution of VIIa (199.3 g, 0.619 moles in 1000 ml) was added thiourea (94.5 g, 1.238 moles) and AcOH (200 ml), and the reaction mixture was allowed to stand for 30 min at room temperature. Pale yellow precipitate was removed by filtration and the filtrate was concentrated *in vacuo* to evaporate methanol. The residue was treated with AcOEt–H_2O and the AcOEt phase separated was extracted with 2N AcOH. The aqueous AcOH layers were combined, washed with AcOEt, basified with powder K_2CO_3 and then extracted with AcOEt. The AcOEt extracts were washed with satd. NaCl, dried and evaporated to dryness to give a pale yellow oil (76.1 g, 73%). IR

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19) L. Zervas, D. Borovas, and E. Gazis, *J. Am. Chem. Soc.*, **85**, 3660 (1963).

20) R. Paul and G.W. Anderson, *J. Am. Chem. Soc.*, **82**, 4596 (1960).

21) L.F. Hatch and G. Bachmann, *Chem. Ber.*, **97**, 132 (1964).

22) R. Schwyzer, P. Sieber, and H. Kappeler, *Helv. Chim. Acta*, **42**, 2622 (1959).

$\nu_{\max}^{\text{liq.}}$ cm^{-1}: 3375, 3310, 3030, 1730. NMR ($CDCl_3$) τ: 8.90—7.60 (8H, m), 8.69 (3H, d, 7 Hz), 6.49 (1H, q, 7 Hz), 4.90—3.70 (3H, m).

ii) From VIIb: A solution of VIIb (1.0 g) in AcOEt (5 ml) was treated with 2.5N dry HCl in AcOEt (10 ml) for 5 min at room temperature and then evaporated *in vacuo* to remove HCl and AcOEt. The residue was taken up in H_2O (15 ml) and washed with AcOEt. The aqueous solution was basified with powdered K_2CO_3 and worked up in a similar manner to that described above to give a yellow oil (0.13 g, 21%). IR and NMR spectra of the product were superimposable with those of an authentic sample.

L-Leucine 2-Cyclohexenyl Ester (IIb)——A mixture of NPS-L-leucine 2-cyclohexenyl ester (4.55 g, 12.5 mmoles), thiourea (1.90 g, 25 mmoles) and AcOH (6 ml) in MeOH (50 ml) was kept standing for 20 min at room temperature and treated in a similar manner to that for IIa to give IIb as a yellow oil (1.87 g, 71%). IR $\nu_{\max}^{\text{liq.}}$ cm^{-1}: 3375, 3315, 3030, 1730. NMR ($CDCl_3$) τ: 9.06 (6H, d, 6 Hz), 8.80—7.60 (11H, m), 6.60 (m, 1H), 4.95—3.85 (3H, m).

L-Phenylalanine 2-Cyclohexenyl Ester (IIc)——A mixture of NPS-L-phenylalanine 2-cyclohexenyl ester (5.0 g, 12.5 mmoles), thiourea (1.90 g, 25 mmoles) and AcOH (6 ml) in MeOH (50 ml) was allowed to stand for 20 min at room temperature and worked up as usual to afford a yellow oil (2.06 g, 67%). IR $\tau_{\max}^{\text{liq.}}$ cm^{-1}: 3375, 3320, 3090, 3065, 3035, 1730. NMR ($CDCl_3$) τ: 8.80—7.70 (8H, m), 7.40—6.70 (2H, m), 6.27 (1H, m), 4.95—3.75 (3H, m), 2.72 (5H, s).

(±)-9-Methyl-7-oxatricyclo[4,3,0,0^{2,9}]nonan-8-one(IVa)——A mixture of IIa (1.30 g, 7.7 mmoles), isoamylnitrite (1.08 g, 9.2 mmoles) and AcOH (0.14 g, 2.3 mmoles) in $CHCl_3$ (40 ml) was refluxed for 20 min. Working-up of the yellow solution in a manner similar to that reported[4] gave crude 2-cyclohexenyl 2-diazopropionate (IIIa) as a golden yellow oil (1.24 g).[23]

A mixture of the oil (1.24 g) and Cu powder (0.88 g, 13.5 matoms) in benzene (70 ml, or dioxane) was refluxed for 6 hr. Filtration and evaporation left an oil (1.07 g), which was chromatographed on silica gel (eluent: benzene) to afford IVa as a colorless oil (0.37 g, 32% from IIa, *Rf*: 0.2) and a mixture of two dimers, formed by dimerization of the carbene intermediate, as a colorless oil (0.23 g, 20% from IIa, *Rf*: 0.3—0.4). The latter was separated into two isomers by preparative TLC (eluent: benzene, Va_1=*Rf*: 0.3, Va_2=*Rf*: 0.4). IVa; *Anal.* Calcd. for $C_9H_{12}O_2$: C, 71.02; H, 7.95. Found: C, 71.38; H, 7.97. IR $\nu_{\max}^{\text{liq.}}$ cm^{-1}: 1762. NMR ($CDCl_3$) τ: 9.10—7.60 (8H, m), 8.66 (3H, s), 5.26 (1H, m). Mass Spectrum *m/e*: 152 (M^+), 96 (base). Va_1; IR $\nu_{\max}^{\text{liq.}}$ cm^{-1}: 3035, 1725, 1655. NMR ($CDCl_3$) τ: 8.90—7.75 (18H, m), 5.00—3.85 (6H, m). Mass Spectrum *m/e*: 304 (M^+), 81 (base). Va_2; IR $\nu_{\max}^{\text{liq.}}$ cm^{-1}: 3040, 1720, 1650. NMR ($CDCl_3$) τ: 9.00—7.50 (18H, m), 5.05—3.85 (6H, m). Mass Spectrum *m/e*: 304 (M^+), 127 (base).

(±)-9-Isobutyl-7-oxatricyclo[4,3,0,0^{2,9}]nonan-8-one (IVb)——A mixture of IIb (1.65 g, 7.8 mmoles), isoamylnitrite (1.10 g, 9.36 mmoles) and AcOH (0.14 g, 2.34 mmoles) in $CHCl_3$ (40 ml) was refluxed for 20 min and treated as usual to afford crude 2-cyclohexenyl 2-diazo-4-methylpentanoate (IIIb, 1.65 g), which was submitted to cyclization reaction in benzene (75 ml) in the presence of Cu powder (0.95 g, 14.9 mmoles) under reflux for 11 hr to give an oil (1.44 g). This was purified on column chromatography (silica gel, eluent: benzene) to yield IVb as a colorless oil (0.13 g, 8.6% from IIb, *Rf*: 0.2) and *trans*-(Vb_1, 0.63 g, 42% from IIb, *Rf*: 0.7) and *cis*-2-cyclohexenyl 4-methyl-2-pentenoate (Vb_2, 0.46 g, 30% from IIb, *Rf*: 0.8). IVb; *Anal.* Calcd. for $C_{12}H_{18}O_2$: C, 74.19; H, 9.34. Found: C, 74.00; H, 9.20. IR $\nu_{\max}^{\text{liq.}}$ cm^{-1}: 1755. NMR ($CDCl_3$) τ: 9.07 (6H, d, 6 Hz), 9.20—7.60 (11H, m), 5.10 (1H, m). Mass Spectrum *m/e*: 194 (M^+), 151, 138, 79 (base). Vb_1; IR $\nu_{\max}^{\text{lip.}}$ cm^{-1}: 3030, 1710, 1655, 1650. NMR ($CDCl_3$) τ: 8.92 (6H, d, 7 Hz), 8.75—7.75 (6H, m), 7.56 (1H, m), 4.90—3.80 (3H, m), 4.20 (1H, dd, 16 Hz, 1.5 Hz), 3.00 (1H, dd, 16 Hz, 7 Hz). Mass Spectrum *m/e*: 194 (M^+), 97 (base). Vb_2; IR $\nu_{\max}^{\text{liq.}}$ cm^{-1}: 3030, 1715, 1640. NMR ($CDCl_3$) τ: 8.98 (6H, d, 7 Hz), 8.70—7.70 (6H, m), 6.40 (1H, m), 4.90—3.80 (3H, m), 4.35 (1H, d, 12 Hz), 3.95 (1H, dd, 9 Hz, 12 Hz). Mass Spectrum *m/e*: 194 (M^+), 97 (base).

(±)-9-Benzyl-7-oxatricyclo[4,3,0.0^{2,9}]nonan-8-one (IVc)——A mixture of IIc (1.74 g, 7.1 mmoles), isoamylnitrite (1.0 g, 8.5 mmoles) and AcOH (0.13 g, 2.13 mmoles) in $CHCl_3$ (40 ml) was refluxed for 20 min and worked up as usual to give crude 2-cyclohexenyl 2-diazo-3-phenylpropionate (IIIc, 1.70 g) as a yellow oil. A mixture of the diazoester (1.70 g) and Cu powder (0.85 g, 13.3 mmoles) in benzene (70 ml) was heated under reflux for 5 hr to give an oil (1.53 g), which was purified on column chromatography (silica gel, eluent: benzene 100–AcOEt 1) to give a colorless oil (IVc, 0.15 g, 9.3% from IIc, *Rf*: 0.2) and a mixture of *trans*- and *cis*-2-cyclohexenyl cinnamate as a colorless oil (Vc, 1.11 g, 69% from IIc, *Rf*: 0.6).[24] IVc; *Anal.* Calcd. for $C_{15}H_{16}O_2$: C, 78.92; H, 7.06. Found: C, 79.20, H, 7.12. IR $\nu_{\max}^{\text{liq.}}$ cm^{-1}: 1755. NMR ($CDCl_3$) τ: 8.85—7.70 (8H, m), 7.21 (1H, d, 15 Hz), 6.64 (1H, d, 15 Hz), 5.20 (1H, m), 2.69 (5H, s). Mass Spectrum *m/e*: 228 (M^+), 183 (base).

Photochemical Decomposition of IIIa to 2-Cyclohexenyl Acrylate——A yellow solution of IIIa (120 mg) in dioxane (10 ml) was irradiated with a 30 W low pressure Hg lamp for 2 hr under flowing argon gas. The resultant colorless solution was evaporated to dryness *in vacuo* to give an oil, which was purified on preparative

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[23] This crude IIIa was purified on column chromatography using Al_2O_3 to give an analytical sample. *Anal.* Calcd. for $C_9H_{12}O_2N_2$: C, 59.98; H, 6.71; N, 15.55. Found: C, 59.30; H, 6.73; H, 15.32. IR $\nu_{\max}^{\text{liq.}}$ cm^{-1}: 3030, 2070, 1690. NMR ($CDCl_3$) τ: 8.65—7.70 (6H, m), 8.05 (3H, s), 4.95—3.85 (3H, m).

[24] The NMR of the mixture showed that the *trans/cis* ratio was 3/1.

TLC (silica gel, eluent: benzene) to afford 2-cyclohexenyl acrylate as a colorless oil (35 mg, 35%). IR $\nu_{\text{max}}^{\text{liq.}}$ cm^{-1}: 3030, 1725, 1640, 1620. NMR (CDCl$_3$) τ: 8.60—7.70 (6H, m), 4.90—3.30 (6H, m). Mass Spectrum *m/e*: 152 (M$^+$), 97, 79, 55 (base).

Separation of the Benzoic Acid Salt (IX) of Diastereomeric L-Alanine 2-Cyclohexenyl Ester (VIII)——An ethereal solution (200 ml) of benzoic acid (55 g, 0.45 moles) was added to a solution of L-alanine 2-cyclohexenyl ester (IIa=VIII, 76.1 g, 0.45 moles) in ether (200 ml) and the precipitate was collected by suction (IX, 108.6 g, mp 87—89°). The precipitate (420 g) thus obtained was recrystallized once from isopropyl ether and then three times from AcOEt affording colorless prisms (80 g, mp 97.5—99°, $[\alpha]_{\text{D}}^{20}$ $-104°$ (c=1.32, CHCl$_3$)) which was used for the total synthesis of (+)-2-carene as a starting material. A portion of this product was further recrystallized twice from AcOEt to obtain constant optical rotation giving less soluble diastereomer (X) as colorless prisms (mp 100°, $[\alpha]_{\text{D}}^{20}$ $-114°$ (c=1.05, CHCl$_3$)). *Anal.* Calcd. for $C_{16}H_{21}O_4N$: C, 65.95; H, 7.27; N, 4.81. Found: C, 65.77; H, 7.31; N, 5.01. IR $\nu_{\text{max}}^{\text{Nujol}}$ cm^{-1}: 2900—2000, 1745, 1650 (shoulder), 1625, 1590, 1510. NMR (CDCl$_3$) τ: 8.80—7.80 (6H, m), 8.55 (3H, d, 7 Hz), 6.10 (1H, m), 5.00—3.90 (3H, m), 3.00—2.30 (6H, m), 2.15—1.85 (2H, m).

(*S*)-(−)-2-Cyclohexenol——X (200 mg, 0.69 mmole, $[\alpha]_{\text{D}}^{20}$ $-114°$ (CHCl$_3$)) was dissolved in satd. NaHCO$_3$ and extracted with ether. The organic layer was washed with satd. NaHCO$_3$ and satd. NaCl, dried over MgSO$_4$ and evaporated to dryness to leave an oil (90 mg). The oil (90 mg) in ether (10 ml) was reduced with LiAlH$_4$ (53 mg, 1.38 mmoles), for 20 min at room temperature and excess hydride was decomposed with H$_2$O. After filtration to remove precipitated solid the filtrate was washed with 2% HCl and satd. NaCl and dried over MgSO$_4$. Filtration and evaporation gave an oil, which was submitted to a short path distillation to give a colorless oil (30 mg, $[\alpha]_{\text{D}}^{20}$ $-112.0°$ (c=0.60, CHCl$_3$)). IR $\nu_{\text{max}}^{\text{liq.}}$ cm^{-1}: 3330, 3020, 1650, 1050. NMR (CDCl$_3$) τ: 8.70—7.70 (6H, m), 7.21 (1H, s), 5.84 (1H, broad s), 4.24 (2H, s). Mass spectrum *m/e*: 98 (M$^+$), 97,83, 70 (base). These IR and NMR data were identical with those of (±)-2-cyclohexenol.

(±)-7-Hydroxymethyl-7-methylbicyclo[4,1,0]heptan-2-ol (XIII)——To a mixture of LiAlH$_4$ (76 mg, 2 mmoles) in ether (15 ml) was added a solution of IVa (0.15 g, 1 mmoles) in ether (5 ml) and the whole was refluxed for 50 min. The excess hydride was decomposed with AcOEt and the complex formed was hydrolized as usual. Filtration and evaporation gave colorless prisms (0.14 g, 91%, mp 66—67°). IR $\nu_{\text{max}}^{\text{Nujol}}$ cm^{-1}: 3240, 1055, 1035, 1005. NMR (CDCl$_3$) τ: 9.30—7.70 (8H, m), 8.84 (3H, s), 6.27 (2H, s), 6.50—5.40 (3H, m). Mass Spectrum *m/e*: 138, 109 (base).

(±)-Benzyl 2,2-Ethylenedioxy-7-methylbicyclo[4,1,0]heptane-7-carboxylate——A mixture of IVa (1.52 g, 10 mmoles) and 1N NaOH (10 ml, 10 mmoles) in EtOH (15 ml) was kept at 60° for 30 min and evaporated to dryness *in vacuo* to give a pale brown residue which was triturated with absolute ether and thoroughly dried. A solution of the sodium salt and benzyl bromide (1.88 g, 11 mmoles) in DMF (6 ml) was allowed to stand for 50 min at room temperature. After evaporation of the solvent, the residue was taken up in AcOEt, washed with H$_2$O, dried over Na$_2$SO$_4$ and evaporated to dryness to give (±)-benzyl 2-hydroxy-7-methylbicyclo[4,1,0]heptane-7-carboxylate as an oil (2.66 g). IR $\nu_{\text{max}}^{\text{liq.}}$ cm^{-1}: 3500, 1712.

The oil (2.66 g) was directly oxidized with CrO$_3$ (12 g) in methylene chloride (80 ml) and pyridine (15 ml) at room temperature for 40 min. The reaction mixture was filtered and the filtrate and washings were evaporated to give a brown residue, which was taken up in benzene and filtered to remove insoluble material. Evaporation of benzene afforded (±)-benzyl 2-oxo-7-methylbicyclo[4,1,0]heptane-7-carboxylate as a pale yellowoil (2.19 g). IR $\nu_{\text{max}}^{\text{liq.}}$ cm^{-1}: 1730, 1700, 750, 700. NMR (CDCl$_3$) τ: 8.90—7.60 (8H, m), 8.60 (3H, s), 4.88 (2H, s), 2.64 (5H, s). Mass Spectrum *m/e*: 258 (M$^+$), 230, 167, 91 (base).

A mixture of the oil (2.19 g) thus obtained and ethylene glycol (7 ml) in benzene (100 ml) was refluxed for 4.5 hr in the presence of *p*-toluenesulfonic acid (500 mg) using Cope's apparatus. The resultant mixture was washed with satd. NaHCO$_3$ and H$_2$O, dried, and evaporated to dryness to give an oily residue, which was purified on preparative TLC (silica gel, eluent: cyclohexane 4–AcOEt 1) to afford (±)-benzyl 2,2-ethylenedioxy-7-methylbicyclo[4,1,0]heptane-7-carboxylate as a colorless oil (1.72 g, 57% from IVa). IR $\nu_{\text{max}}^{\text{liq.}}$ cm^{-1}: 1725. NMR (CDCl$_3$) τ: 9.00—7.80 (8H, m), 8.67 (3H, s), 6.05 (4H, s), 4.84 (2H, s), 2.60 (5H, s). Mass Spectrum *m/e*: 302 (M$^+$), 211 (base), 167.

(±)-2,2-Ethylenedioxy-7-hydroxymethyl-7-methylbicyclo[4,1,0]heptane (XIV)——A solution of (±)-benzyl 2,2-ethylenedioxy-7-methylbicyclo[4,1,0]heptane-7-carboxylate (1.39 g, 4.6 mmoles) in ether (90 ml) was treated with LiAlH$_4$ (0.35 g, 9.2 mmoles) for 30 min at room temperature. H$_2$O was carefully added to decompose the excess hydride, and the organic layer was separated by filtration. After evaporation of the solvent, the residual oil was purified on preparative TLC using Al$_2$O$_3$ (eluent: cyclohexane 12–AcOEt 1) to yield a colorless oil (0.60 g, 66%). IR $\nu_{\text{max}}^{\text{liq.}}$ cm^{-1}: 3500. NMR (CDCl$_3$) τ: 9.30—7.90 (8H, m), 8.86 (3H, s), 7.25 (1H, m), 6.31 (2H, m), 6.04 (4H, s). Mass Spectrum *m/e*: 198 (M$^+$), 196, 181, 180, 167, 155, 141, 139, 99 (base).

(±)-7-Methyl-7-tosylhydrazonomethylbicyclo[4,1,0]heptan-2-ol (XVI)——A solution of IVa (1.52 g, 10 mmoles) in toluene (40 ml) was cooled to $-78°$. To this was added a solution of (isobutyl)$_2$AlH in hexane (11.4 ml of 25% (w/v) solution, 20 mmoles) and the reaction mixture was stirred for 40 min at the same temperature. The excess hydride was carefully destroyed with MeOH (4 ml) and the complex formed was decomposed with H$_2$O (5 ml). AcOEt (60 ml) was added to the mixture and the whole was stirred for additional

30 min. Fitration and evaporation left (±)-9-methyl-7-oxatricyclo[4,3,0,$0^{2,9}$]nonan-8-ol as a pale yellow oil (XV, 1.54 g). IR $\nu_{\max}^{\text{liq.}}$ cm^{-1}: 3400. NMR (CCl_4) τ: 9.30—7.70 (8H, m), 8.82 (3H, s), 5.40 (1H, m), 5.20 (1H, s), 5.00 (1H, s).

A mixture of XV (1.54 g, 10 mmoles), $TsNHNH_2$ (2.23 g, 12 mmoles) and AcOH (0.60 g, 10 mmoles) in EtOH (40 ml) was kept standing overnight to afford colorless prisms (2.10 g, mp 146—147°). After concentration of the mother liquor, another crop was obtained (0.50 g, mp 144—145°, total yield 81% from IVa). Recrystallization from EtOH afforded an analytical sample, mp 148°, as colorless prisms. *Anal.* Calcd. for $C_{16}H_{22}O_3N_2S$: C, 59.61; H, 6.88; N, 8.69. Found: C, 59.37; H, 6.89; N, 8.88. IR $\nu_{\max}^{\text{KBr}}$ cm^{-1}: 3400 (broad), 3230, 1600, 1495, 1461, 1452, 1333, 1162. NMR (d_6-DMSO) τ: 8.98 (3H, s), 7.66 (3H, s), 5.95 (1H, m), 2.72 (2H, d, 9 Hz), 2.58 (1H, s), 2.33 (2H, d, 9 Hz).

(±)-7,7-Dimethylbicyclo[4,1,0]heptan-2-ol (XVII)——To a clear solution of XVI (805 mg, 2.5 mmoles) in THF (45 ml) was added $LiAlH_4$ (950 mg, 25 mmoles) and the reaction mixture was stirred for 72 hr at room temperature, and then diluted with ether (80 ml). The excess hydride was destroyed with AcOEt (3 ml) and the complex was hydroliyzed (H_2O, 4 ml). The organic layer separated by filtration was washed with satd. NaCl, dried over $MgSO_4$ and evaporated to leave an oil (400 mg), which was chromatographed on silica gel column (eluent: hexane 5–AcOEt 1) to yield XVII as colorless crystals (75 mg, 21%, mp 50—52°). Recrystallization from hexane afforded colorless crystals, mp 53—54°.25) *Anal.* Calcd. for $C_9H_{16}O$: C, 77.09; H, 11.50. Found: C, 76.60; H, 11.71. IR $\nu_{\max}^{\text{KBr}}$ cm^{-1}: 3330, 1036. NMR (CCl_4) τ: 9.30—7.50 (8H, m), 8.94 (3H, s), 8.84 (3H, s), 7.73 (1H, s), 5.90 (1H, m).

(±)-7,7-Dimethylbicyclo[4,1,0]heptan-2-one (XVIII)——To a solution of XVII (190 mg, 1.35 mmoles) in methylene chloride (20 ml) and pyridine (2 ml) was added CrO_3 (2.70 g, 27 mmoles) during a period of 1 hr and the mixture was then allowed to stand for 30 min at room temperature. Filtration and evaporation gave an oil which was passed through the silica gel column (2 g, eluent: cyclohexane 3–AcOEt 1) to afford a colorless oil (0.17 g, 91%). IR $\nu_{\max}^{\text{liq.}}$ cm^{-1}: 1690, 1455, 1425, 1380, 1344, 1327, 1243, 1216, 1180, 1118, 1075, 1044, 982, 959, 935, 892, 758. NMR (CCl_4) τ: 8.86 (3H, s), 8.84 (3H, s), 8.90—7.60 (8H, m). 2,4-Dinitrophenylhydrazone: orange colored prisms, mp 156—157° (lit.,12) mp 150—151°). *Anal.* Calcd. for $C_{15}H_{18}O_4N_4$: C, 56.59; H, 5.70; N, 17.60. Found: C, 56.64; H, 5.82; N, 17.62. IR $\nu_{\max}^{\text{Nujol}}$ cm^{-1}: 3300, 1624, 1589, 1535, 1506, 1424, 1380, 1343, 1308, 1273, 1255, 1213, 1136, 1074, 920, 834, 765, 743, 723. NMR ($CDCl_3$) τ: 9.01 (3H, s), 8.60 (3H, s). The IR and NMR spectra of XVIII and its 2,4-dinitrophenylhydrazone derivative were superimposable to those reported by Mori and Matsui.12)

(1*S*,2*R*,6*S*,9*R*)-(−)-9-Methyl-7-oxatricyclo[4,3,0,$0^{2,9}$]nonan-8-one (XIX)——A solution of X (29.1 g, 100 mmoles, mp 97.5—99°, $[\alpha]_D^{20}$ −104° (c=1.32, $CHCl_3$)) and isoamylnitrite (14.1 g, 120 mmoles) in $CHCl_3$ (600 ml) was refluxed for 20 min and worked up as usual to give crude (*S*)-2-cyclohexenyl 2-diazopropionate as a yellow oil (18.0 g).

A mixture of this yellow oil (18.0 g, 100 mmoles) and Cu powder (12.7 g, 200 mmoles) in benzene (1000 ml) was refluxed for 14 hr and filtered to remove Cu powder. Evaporation of the filtrate left an oily residue which was chromatographed on silica gel column (eluent: benzene 20–AcOEt 1) to afford XIX as a pale yellow oil (6.20 g, 41% from X). A part of the oil was distilled to give an analytical sample. $[\alpha]_D^{20}$ −19.7° (c=1.57, $CHCl_3$). *Anal.* Calcd. for $C_9H_{12}O_2$: C, 71.02; H, 7.95. Found: C, 71.33; H, 8.00. IR $\nu_{\max}^{\text{liq.}}$ cm^{-1}: 1760. NMR ($CDCl_3$) τ: 8.90—7.65 (8H, m), 8.64 (3H, s), 5.15 (1H, m). Mass Spectrum *m/e*: 152M^+, 96 (base).

A mixture of two dimers was also obtained as a pale yellow oil (29% from X).

(1*S*,2*S*,6*R*)-(−)-7,7-Dimethylbicyclo[4,1,0]heptan-2-ol (XXI)——A solution of XIX (3.04 g, 20 mmoles) in toluene (80 ml) was cooled to −78°. To this was added a solution of $(isobutyl)_2AlH$ in hexane (20 ml of 25% (w/v) solution, 35.2 mmoles) and the reaction mixture was treated similary to the case of racemic form (XV) to give the corresponding optically active lactol as a pale yellow oil (3.08 g).

A mixture of the oil, $TsNHNH_2$ (4.46 g, 24 mmoles) and AcOH (1.20 g, 20 mmoles) in EtOH (80 ml) was allowed to stand overnight at room temperature and evaporated to dryness to leave an oil, which was dissolved in AcOEt (40 ml)-hexane (40 ml) and cooled in an ice-bath to give colorless prisms (0.96 g, mp 136—137°). Infrared and NMR data of this product were identical with those of XVI. After evaporation of the mother liquor of XVI, crude XX was obtained as a glassy solid (6.42 g). IR $\nu_{\max}^{\text{KBr}}$ cm^{-1}: 3440, 3200, 1598. NMR (d_6-DMSO) τ: 8.97 (3H, s), 7.65 (3H, s), 5.95 (1H, m), 2.69 (2H, d, 9 Hz), 2.54 (1H, s), 2.29 (2H, d, 9 Hz).

A mixture of XX (6.42 g) and $LiAlH_4$ (10 g) in THF (220 ml) was stirred for 6.5 hr at 60—65° and for 15 hr at room temperature and worked up in a similar manner to that described for XVII to give colorless crystals (0.41 g, 14.5% from XIX). Recrystallization from hexane afforded colorless long prisms, mp 84—88°, $[\alpha]_D^{20}$ −56.8° (c=0.37, MeOH)).25) IR $\nu_{\max}^{\text{KBr}}$ cm^{-1}: 3350, 1035. NMR (CCl_4) τ: 9.30—7.50 (8H, m), 8.98 (3H, s), 8.87 (3H, s), 7.10 (1H, s), 5.90 (1H, m). Mass Spectrum *m/e*: 140 (M^+), 125, 122, 107, 97 (base).

(1*S*,6*R*)-(−)-7,7-Dimethylbicyclo[4,1,0]heptan-2-one (XXII)——To a solution of XXI (400 mg, 2.86 mmoles) in methylene chloride (30 ml) and pyridine (4 ml) was added CrO_3 (5.72 g, 57.2 mmoles) during a period of 45 min. The mixture was then kept standing for 15 min and treated in a manner similar to that of XVIII

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25) This compound was very volatile.

to give a pale yellow oil (356 mg, 90%). A portion of the product was purified on preparative TLC to afford a colorless oil. $[\alpha]^{20}_{D}$ $-262°$ ($c=1.02$, $CHCl_3$). ORD (MeOH) $[\alpha]^{26}$ (nm): $-234°$ (589), $-327°$ (500), $-455°$ (450), $-665°$ (400), $-1165°$ (350), $-3160°$ (308, trough), $+735°$ (271, peak), $-1165°$ (250). IR $\nu^{\text{liq.}}_{\text{max}}$ cm^{-1}: 1690. NMR (CCl_4) τ: 8.84 (3H, s), 8.83 (3H, s), 8.90—7.60 (8H, m). The IR and NMR data were identical with those of the racemic compound (XVIII).

(1*S*,6*R*)-(−)-Methyl 7,7-Dimethyl-2-oxobicyclo[4,1,0]heptane-3-carboxylate (XXIII)——To a mixture of NaH (1.52 g of 64% dispersions, 40.6 mmoles, washed with three portions of dry ether under nitrogen) in dimethyl carbonate (9 ml) was added a solution of XXI (560 mg, 4.06 mmoles) in benzene (6 ml) at 60° over a period of 3 min, and heated under gentle reflux for 30 min. After cooling the reaction mixture in an ice bath, AcOH (4 ml) in ether (50 ml) was added, and the mixture was then diluted with H_2O (20 ml) and extracted with ether. The combined organic extracts were washed with satd.$NaHCO_3$ and satd.NaCl, and dried over $MgSO_4$. Removal of the solvent left XXIII as a pale yellow oil (738 mg, 93%) which was used as such for the reduction described below. A pure sample of the β-keto ester was obtained by preparative TLC (silica gel, eluent: hexane 10-AcOEt 1). $[\alpha]^{20}_{D}$ $-128°$ ($c=1.10$, MeOH). IR $\nu^{\text{liq.}}_{\text{max}}$ cm^{-1}: 1750, 1689, 1645, 1615. NMR (CCl_4) τ: 9.00—7.40 (6H, m), 8.95 (3H, s), 8.81 (3H, s), 6.33 (3H, s), -2.20 (1H, s). Mass Spectrum *m/e*: 196 (M^+), 181, 164, 153, 136, 121 (base).

(1*S*,6*R*)-Methyl 2-Hydroxy-7,7-dimethylbicyclo[4,1,0]heptane-3-carboxylate——A solution of XXIII (910 mg, 4.64 mmoles) in EtOH (10 ml) was cooled to $-78°$. To this was added a solution of $NaBH_4$ (527 mg, 13.92 mmoles) in EtOH (15 ml) and the reaction mixture was stirred for 4 hr at -10—$-20°$, diluted with satd. NaCl (20 ml) and extracted with ether. The ethereal extract was washed with satd.NaCl, dried, and evaporated. The remaining residue was chromatographed over silica gel (eluent: hexane 3–AcOEt 1) to give, with recovery of the starting keto ester (XXIII, 223 mg), the corresponding β-hydroxy ester (430 mg, 62% based upon recovered keto ester) as a colorless oil. IR $\nu^{\text{liq.}}_{\text{max}}$ cm^{-1}: 3460, 3000, 2950, 2865, 1742. NMR (CCl_4) τ: 9.20—7.60 (7H, m), 8.93 (3H, s), 8.84 (3H, s), 7.21 (1H, s), 6.35 (3H, s), 5.67 (1H, m).

(1*S*,6*R*)-Methyl 2-Benzoyloxy-7,7-dimethylbicyclo[4,1,0]heptane-3-carboxylate——To the β-hydroxy ester (160 mg, 0.81 mmoles) mentioned above, dissolved in pyridine (3 ml), was added benzoyl chloride (227 mg, 1.62 mmoles), and the mixture was stirred for 1.5 hr at room temperature. H_2O (0.5 ml) was added to the mixture, and the whole was stirred for additional 1 hr and then extracted with ether. The ethereal extract was washed with satd.$NaHCO_3$, H_2O, 5% HCl and H_2O, and dried over $MgSO_4$. Removal of the ether left the desired diester as colorless prisms (230 mg, 94%, mp 58—60°). IR $\nu^{\text{KBr}}_{\text{max}}$ cm^{-1}: 1740, 1702, 1604, 1585. NMR (CCl_4) τ: 9.20—7.35 (7H, m), 9.02 (3H, s), 8.84 (3H, s), 6.45 (3H, s), 4.30 (1H, dd, 7 Hz, 10 Hz), 2.69 (3H, m), 2.10 (2H, m).

(1*S*,6*R*)-(−)-Methyl 7,7-Dimethylbicyclo[4,1,0]hept-2-ene-3-carboxylate(XXIV)——The foregoing diester (600 mg, 1.99 mmoless) was dissolved in benzene (10 ml) and treated with *t*-BuOK (446 mg, 3.98 mmoles) under a nitrogen atmosphere. After being stirred for 30 min at room temperature, the reaction mixture was cooled in an ice bath and acidified with an ethereal solution (30 ml) of AcOH (1 ml). The organic extract was washed with satd.$NaHCO_3$ and satd.NaCl and dried over $MgSO_4$. Evaporation of the solvent left a yellow oil (350 mg, 98%), which was used for the next reaction. A pure sample was prepared by column chromatography (silica gel, eluent: benzene 1–hexane 1) as a colorless oil. $[\alpha]^{20}_{D}$ $-118°$ ($c=0.40$, MeOH). IR $\nu^{\text{liq.}}_{\text{max}}$ cm^{-1}: 1716, 1637. NMR (CCl_4) τ: 9.10—7.30 (6H, m), 9.08 (3H, s), 8.85 (3H, s), 6.36 (3H, s), 2.89 (1H, s). Mass Spectrum *m/e*: 180 (M^+), 165, 137, 121, 105 (base).

(1*S*,6*R*)-(+)-3-Hydroxymethyl-7,7-dimethylbicyclo[4,1,0]hept-2-ene (XXV)——The α,β-unsaturated ester (XXIV, 350 mg, 1.94 mmoles) was dissolved in ether (25 ml) and cooled to $-30°$. To this was added $LiAlH_4$ (221 mg, 5.82 mmoles) and the mixture was stirred at $-20°$—$-30°$ for 30 min, treated with H_2O (1 ml), and filtered. The ethereal solution was dried over $MgSO_4$, and evaporated to give a pale yellow oil. Futher purification over silica gel (eluent: benzene 5–AcOEt 1) afforded XXV as a colorless oil (265 mg, 90%). $[\alpha]^{22}_{D}$ $+67.8°$ ($c=0.47$, benzene) (lit.,14) $[\alpha]^{20}_{D}$ $+66.5°$ ($c=2.2$, benzene)). IR $\nu^{\text{liq.}}_{\text{max}}$ cm^{-1}: 3330, 3000, 2930, 2865, 1664. NMR (CCl_4) τ: 9.20—7.70 (6H, m), 9.12 (3H, s), 8.92 (3H, s), 6.46 (1H, s), 6.15 (2H, s), 4.25 (1H, broad s). Mass Spectrum *m/e*: 152 (M^+), 137, 134, 121, 119, 109, 93, 91, 81, 79 (base), 77. 3,5-Dinitrobenzoate: silightly yellow crystals, mp 86—87° (lit.,14) mp 85—87°). *Anal.* Calcd. for $C_{17}H_{18}O_6N_2$: 58.95; H, 5.24; N, 8.09. Found: C, 59.10; H, 5.33; N, 8.08. IR $\nu^{\text{Nujol}}_{\text{max}}$ cm^{-1}: 1730, 1625. Mass Spectrum *m/e*: 346 (M^+), 303, 212, 195, 134, 119, 105, 92, 91 (base), 79.

(+)-2-Carene——To a solution of XXV (130 mg, 0.855 mmoles) in THF (3 ml) was added at 0° pyridine-sulfur trioxide complex15) (272 mg, 1.71 mmoles), and the suspension was stirred at 0—5° for 3 hr. A solution of $LiAlH_4$ (195 mg, 5.13 mmoles) in THF (2 ml) was then added and the whole was stirred at 0—5° for 30 min and at room temperature for 3 hr. After treatment with H_2O (1 ml) and subsequent addition of *n*-pentane (20 ml), the mixture was filtered to remove the precipitated mass, which was then washed with *n*-pentane. The filtrate and washings were successively washed with H_2O, 1% HCl, H_2O, satd.$NaHCO_3$ and HO_2, and then dried over $MgSO_4$.26) Careful evaporation of the solvent left a yellow oil, which was purified on pre-

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26) The analitical GLC18) using *cis*-decaline as an internal standard showed that the content of (+)-2-carene in this *n*-pentane solution was 80.6 mg (69% from XXV).

parative GLC[18] to give (+)-2-carene as a colorless oil (35 mg). $[\alpha]_D^{20}$ +84.4° (c=0.52, EtOH) (lit.,[16] $[\alpha]_D^{20}$ +83° (c=0.18, EtOH)). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3000, 2920, 2880, 2860, 2730, 1664, 1452, 1440, 1376, 860, 830. NMR (CCl_4) τ: 9.30—7.60 (6H, m), 9.15 (3H, s), 8.94 (3H, s), 8.35 (3H, s), 4.50 (1H, s). Mass Spectrum m/e: 136 (M^+), 121, 93 (base), 91. The IR and NMR spectra were identical to those of the authentic sample which was prepared from (+)-3-carene according to the method of Ohloff, *et al.*[17]

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