Chem. Pharm. Bull. 27(11)2760—2766(1979)

UDC 547.594.3.04 : 547.466.26.04

Stereoselective Reactions. III.[1] A highly Efficient Method for the Asymmetric Synthesis of 2-Alkylcycloalkanones *via* Chiral Chelated Lithioenamines[2]

Shun-ichi Hashimoto and Kenji Koga

Faculty of Pharmaceutical Sciences, University of Tokyo[3]

(Received May 7, 1979)

A novel method was devised for the asymmetric synthesis of 2-alkylcycloalkanones (**10**) by metalation and alkylation of chiral cyclic imines (**8**), using an optically active α-amino acid *tert*-butyl ester (**7**) as a chiral source. The present method provides 2-alkylcycloalkanones (**10**) of unequivocally predictable absolute configuration in quite high enantiomeric purities, allowing easy recovery of the chiral reagent without any racemization for reuse.

The present method is also shown to be applicable for the creation of an asymmetric quaternary carbon atom, as exemplified in the synthesis of 2-methyl-2-phenylcycloalkanones (**13**).

The mechanism of the reaction is proposed.

Keywords——asymmetric synthesis; asymmetric alkylation; chelate; 2-alkylcycloalkanone; 2-methyl-2-phenylcycloalkanone; metalloenamine; bidentate ligand; reaction mechanism

Substitution reaction at the α-position to a carbonyl group has constituted the backbone of synthetic organic chemistry. Evaluating wide utility of this process as a most common and versatile way to form carbon-carbon bonds, we attempted to devise methods to carry out this process under highly asymmetrical regulation.

In previous papers[1,4] from our laboratory, we have reported highly efficient carbon-carbon bond-forming reactions which provide optically active β-substituted aldehydes *via* 1,4-addition reaction of Grignard reagents or diethyl malonate to chiral α,β-unsaturated aldimines prepared from α,β-unsaturated aldehydes and optically active α-amino acid esters. It was shown that high enantioselectivities in these reactions are due to the "fixation" of the reactive conformation by virtue of chelation of the metals with the unshared electron pairs on oxygen and nitrogen of the chiral moiety. As an extension of our studies on this type of asymmetric syntheses utilizing chelate formation, we describe here the results of asymmetric synthesis of 2-alkylcycloalkanones by means of a substitution reaction at α-position to the carbonyl group *via* metalation and alkylation of chiral cyclic imines prepared from cyclic ketones and optically active α-amino acid *tert*-butyl esters.

Many investigations have hitherto been reported on this type of asymmetric synthesis.[5]

1) Part II: S. Hashimoto, N. Komeshima, S. Yamada, and K. Koga, *Chem. Pharm. Bull.* (Tokyo), **27**, 2437 (1979).
2) Preliminary communication: S. Hashimoto and K. Koga, *Tetrahedron Lett.*, **1978**, 573.
3) Location: *7-3-1, Hongo, Bunkyo-ku, Tokyo 113, Japan.*
4) *a*) S. Hashimoto, S. Yamada, and K. Koga, *J. Am. Chem. Soc.*, **98**, 7450 (1976); *b*) S. Hashimoto, N. Komeshima, S. Yamada, and K. Koga, *Tetrahedron Lett.*, **1977**, 2907; *c*) S. Hashimoto, S. Yamada, and K. Koga, *Chem. Pharm. Bull.* (Tokyo), **27**, 771 (1979).
5) *cf. a*) J.D. Morrison and H.S. Mosher, "Asymmetric Organic Reactions," Prentice-Hall, Englewood Cliffs, N.J., 1971; *b*) J.W. Scott and D. Valentine, Jr., *Science*, **184**, 943 (1974); *c*) D. Valentine, Jr. and J.W. Scott. *Synthesis*, **1978**, 329; *d*) H.B. Kagan and J.C. Fiaud, in "Topics in Stereochemistry," Vol. 10, ed. by E.L. Eliel and N.L. Allinger, Wiley-Interscience, New York, N.Y., 1978, p. 175; *e*) A.I. Meyers, *Accounts of Chem. Res.*, **11**, 375 (1978).

They may be classified as the enamine method,[6] the metalloenamine method,[7] and the rigid metalloenamine method.[8] In the last method, the conformation of the transition state of the reaction is successfully fixed by chelation, giving products usually in high enantiomeric purities. The present asymmetric synthesis is a method belonging the last type, and can provide a variety of 2-alkylcycloalkanones of predictable configuration in quite high enantiomeric purities, offering operational simplicity as well as easy recovery of the chiral reagent without any racemization for reuse, and exhibiting general utility.

Results and Discussion

Design of the Reaction and Selection of the Reaction Conditions

To examine the possibility of obtaining 2-alkylcycloalkanones *via* chelated intermediates using bidentate ligands and appropriate metals, preliminary experiments on metalation and alkylation (methylation) of the imine (**1**), prepared from cyclohexanone and DL-*tert*-leucine *tert*-butyl ester, were performed under various conditions as shown in Chart 1. The results are summarized in Table I.

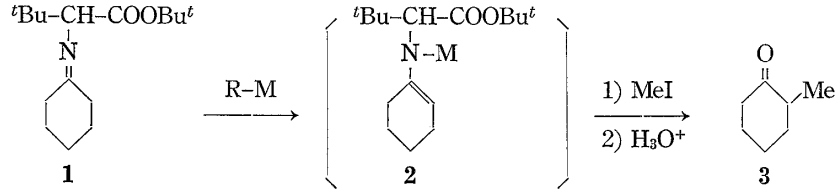


Chart 1

Table I. Metalation and Methylation of **1**[a]

R–M	Metalation step				Methylation step	
	Temp. (°C)	Time (min)	Color	Recovery of cyclohexanone (%)[b]	Temp. (°C)	Yield of **3** (%)[b]
LDA	−23	10	Tan	23[c]	−65—0	~0
LDA	−50	15	Pale yellow	42	−50	25
LDA	−78	15	Yellow	83	−78	75
LDA (inverse)	−78	15	Yellow	72	−78	67
EtMgBr	−23	20	Yellow	97	−23—0	~0
i-PrMgBr	−23	20	Tan	94	−23—0	~0
KH	0	20	Orange	87	−23—0	~0

a) The reaction was carried out with **1** (40 mg, 0.15 mmol), using the indicated base (1.05 eq.), methyl iodide (1.10 eq.), and durene (6 mg) in THF. The yields of product are based on VPC analyses (15% SE-30, 1 m, 95°), using durene as an internal standard.
b) After metalation for the indicated time, an aliquot of the reaction mixture was hydrolyzed with 10% aq. citric acid, and the ethereal extract was subjected to VPC analyses.
c) Trimethylpyruvic acid *tert*-butyl ester was also detected.

It was shown that 2-methylcyclohexanone (**3**), the target compound in this reaction, could be obtained using LDA in THF at low temperatures; the yields of **3** paralleled with

6) *a*) S. Yamada, K. Hiroi, and K. Achiwa, *Tetrahedron Lett.*, **1969**, 4233; *b*) S. Yamada and G. Otani, *ibid.*, **1969**, 4237.
7) *a*) D. Mea-Jacheet and A. Horeau, *Bull. Soc. Chim. Fr.*, **1968**, 4571; *b*) K. Kitamoto, K. Hiroi, S. Terashima, and S. Yamada, *Chem. Pharm. Bull.* (Tokyo), **22**, 459 (1974).
8) *a*) A.I. Meyers, D.R. Williams, and M. Druelinger, *J. Am. Chem. Soc.*, **98**, 3032 (1976); *b*) D. Enders and H. Eichenauer, *Angew. Chem. Int. Ed. Engl.*, **15**, 549 (1976); *c*) J.K. Whitesell and M.A. Whitesell, *J. Org. Chem.*, **42**, 377 (1977); *d*) D. Enders and H. Eichenauer, *Tetrahedron Lett.*, **1977**, 191; *e*) A.I. Meyers and D.R. Williams, *J. Org. Chem.*, **43**, 3246 (1978).

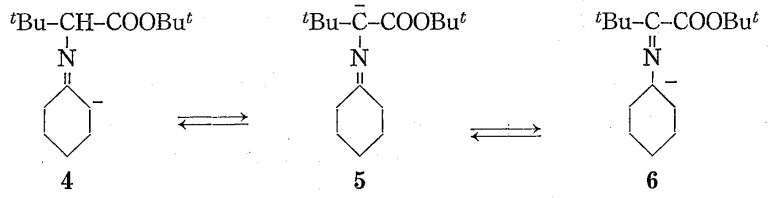


Chart 2

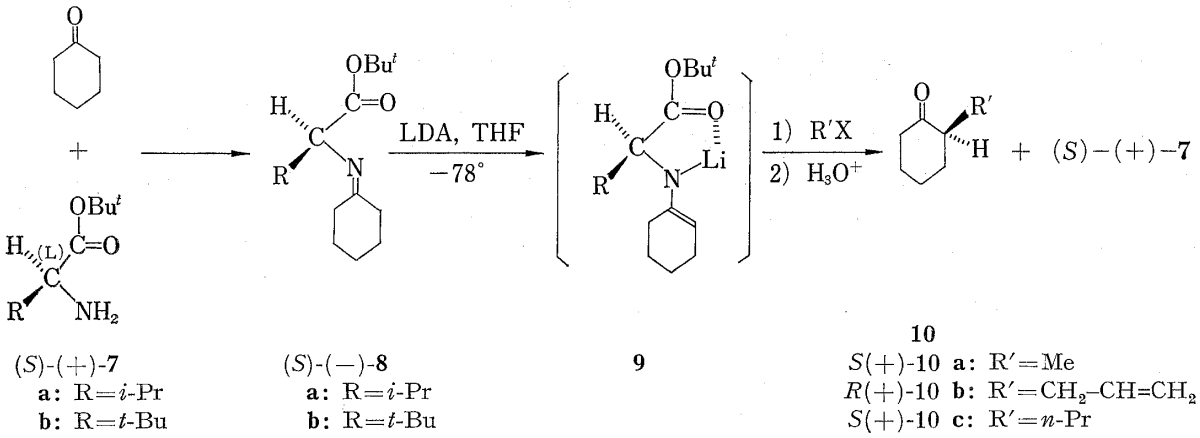


Chart 3

the yields of cyclohexanone recovered from the reaction mixture before methylation. On the other hand, the existence of trimethylpyruvic acid *tert*-butyl ester in the hydrolysate of the reaction mixture at −23° before methylation suggests the abstraction of a proton by LDA from the asymmetric carbon atom or (and) the undesired isomerization of **4** to **5** and **6**, as shown in Chart 2, because proton abstraction from a carbon atom which is activated by both ester carbonyl and imine functions is a well-known process.[9] Since such side processes, which cause racemization of the chiral moiety, might occur even under conditions where the yield of **3** was most satisfactory (Table I), optically active imines ((*S*)-(−)-**8a** and **b**) were prepared from cyclohexanone and (*S*)-valine *tert*-butyl ester ((*S*)-(+)-**7a**) and (*S*)-*tert*-leucine *tert*-butyl ester ((*S*)-(+)-**7b**), respectively, and were metalated with LDA and alkylated in THF at −78° as shown in Chart 3. In all the cases examined (runs 1, 3, 4, and 5 in Table II below), amino acid esters ((*S*)-(+)-**7a**, (*S*)-(+)-**7b**) were recovered in good yield without any racemization. Therefore, this reaction condition was concluded to be suitable for the present asymmetric synthesis.

Asymmetric Synthesis of 2-Alkylcyclohexanones

The results of asymmetric synthesis of 2-alkylcyclohexanones (**10**) are summarized in Table II, and are very promising from the following four points of view. First, the optical purities of **10** are reasonably high, even in cases where (*S*)-(+)-**7a** was used as a chiral source. Second, the absolute configuration of **10** is the same in all cases where (*S*)-amino acid esters ((*S*)-**7**) are used as chiral sources, as shown in Chart 3. This stereochemical result suggests the possibility of predicting the configurations of 2-alkylcycloalkanones obtained by the present method in advance of experiments with a high degree of confidence. Third, the optical purities of (*S*)-(+)-2-methylcyclohexanone ((*S*)-(+)-**10a**) prepared from (*S*)-(−)-**8b** with dimethyl sulfate (run 3) and methyl iodide (run 4) are almost the same. In view of the reported result that methyl iodide is too reactive to afford reasonable stereoselectivity com-

9) *a*) S. Yamada, T. Oguri, and T. Shioiri, *Chem. Commun.*, **1976**, 136; *b*) G. Stork, A.Y.W. Leong, and A. Touzin, *J. Org. Chem.*, **41**, 3491 (1976); *c*) P. Bey and J.P. Vevert, *Tetrahedron Lett.*, **1977**, 1455.

Table II. Asymmetric Synthesis of 2-Alkylcyclohexanones (**10**)

Run	**8** R	R′X	**10** Yield[c] (%)	**10** Optical purity[d,e] (Confign.)
1	*i*-Pr[a]	Me_2SO_4	59	84(S)[f]
2	*i*-Pr[a]	CH_2=CH–CH_2Br	71	73(R)[g]
3	*t*-Bu[b]	Me_2SO_4	65	98(S)[f]
4	*t*-Bu[b]	MeI	57	97(S)[f]
5	*t*-Bu[b]	CH_2=CH–CH_2Br	75	84(R)[g]
6	*t*-Bu[b]	*n*-PrI	70	97(S)[h]

a) Optically pure (*S*)-(+)-**7a** was used.
b) (*S*)-(+)-**7b** of 90.5% optical purity was used.
c) Isolation yield based on (*S*)-(−)-**8** after purification by short-path column chromatography followed by vacuum distillation.
d) Corrected for the optical purity of (*S*)-(+)-**7b** used.
e) Based on the highest rotational value in the literature.
f) Based on $[\alpha]_D$ 14° (MeOH) reported in ref. 13.
g) Based on $[\alpha]_D^{25}$ 15.8° (MeOH) reported in ref. 8*a*.
h) Based on $[\alpha]_D^{25}$ 28.2° (MeOH) reported in ref. 8*a*.

pared to methyl sulfate,[10] the present reaction probably proceeds through a highly rigid chelate intermediate. Fourth, the yields of **10** are good, and chiral reagents are also recovered in good yield without any racemization for reuse, so that the present method is applicable to practical asymmetric syntheses.

Asymmetric Synthesis of 2-Methyl-2-phenylcycloalkanones

The present method was further applied successfully to the creation of asymmetric quaternary carbon atoms from 2-phenylcycloalkanones (**11**) as shown in Chart 4. Thus, lithiation of chiral enamines ((*S*)-(+)-**12**) with LDA at −78°, followed by methylation at −78° to 0° in THF afforded, after hydrolysis, optically active 2-methyl-2-phenylcycloalkanones ((−)-**13**) whose absolute configuration was S on the basis of reported data.[11] It should be noted in Table 3 that the optical yields of (*S*)-(−)-**13** are again quite high, and that the configurational relationship between the chiral source ((*S*)-(+)-**7b**) and products ((*S*)-(−)-**13**) is similar to that in the asymmetric synthesis of **10** described above.

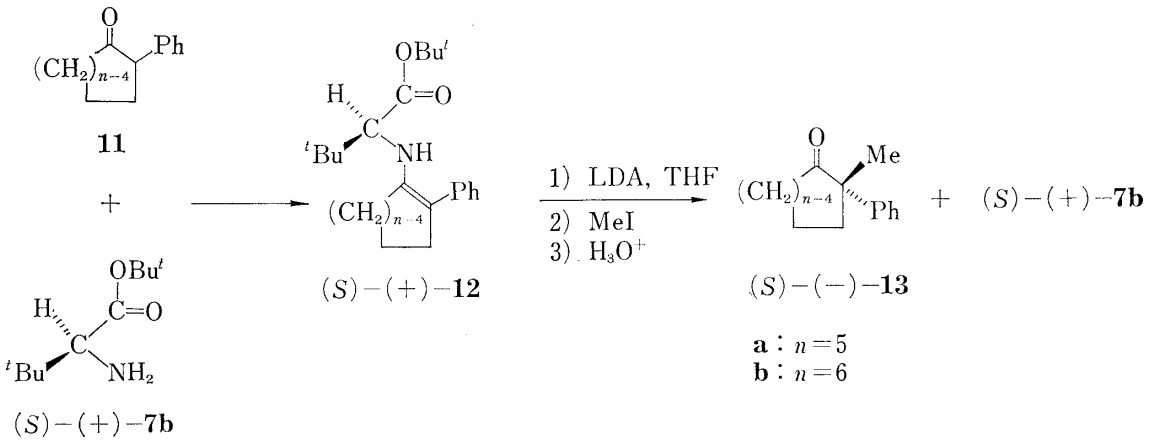


Chart 4

10) A.I. Meyers, G. Knaus, K. Kamata, and M.E. Ford, *J. Am. Chem. Soc.*, **98**, 567 (1976).
11) *a*) T.D. Hoffman and D.J. Cram, *J. Am. Chem. Soc.*, **91**, 1000 (1969); *b*) A.G. Brook, H.W. Kucera, and D.M. MacRae, *Can. J. Chem.*, **48**, 818 (1970).

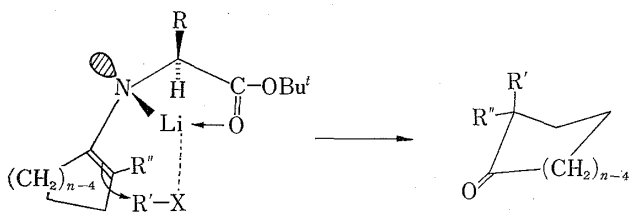
Table III. Asymmetric Synthesis of 2-Methyl-2-phenylcycloalkanones (**13**)

Run	**13**		
	n	Yield (%)[a]	Optical purity[b] (Confign.)
1	5	62	94 (*S*)[c]
2	6	40	96 (*S*)[d]

a) Isolation yield based on (*S*)-(+)-**12**.
b) Corrected for 85.1% optical purity of (*S*)-(+)-**7b** used.
c) Based on $[\alpha]_D^{25}$ +95.3° (EtOH) for optically pure (*R*)-**13a** reported in ref. 11a.
d) Determined in CCl_4 using the chiral shift reagent tris[3-(heptafluoropropylhydroxymethylene)-*d*-camphorato]europium (III). The absolute configuration is assigned in ref. 11*b*.

Stereochemical Mechanism

All the experimental results described above can be explained by the mechanism shown in Chart 5, which is synonymous with that proposed by Meyers *et al.* for reactions in a similar system.[8a] Thus, a five-membered cyclic complex formed by coordination of the lithium cation with the unshared electron pairs on the oxygen atom of the ester carbonyl is expected to be formed in the lithioenamine, in which the cycloalkenyl ring on the nitrogen atom and the bulky *R* group are considered to orient themselves exclusively in a trans conformation for steric reasons. In the alkylation step, the halogen of the alkyl halide is coordinated to the lithium cation, while the alkyl group (R′) is attacked by the π-electrons of the double bond from the backside of the halogen in the conformation where the orbitals of the double bond and the nitrogen-lithium bond are effectively overlapping, as shown in **14**. It should be noted that the coordination of the unshared electron pairs on both the oxygen atom of the ester carbonyl group and the halogen atom of alkyl halide to the lithium cation as well as the stereoelectronic effects, play a central role in controlling the reactive conformation in this highly oriented alkylation, while the bulkiness of the R group displaces the equilibrium between the *cis* and *trans* conformers markedly towards the latter by inversion at the nitrogen atom. It may be said that the present 1,4-asymmetric induction is, in fact, controlled by 1,2-asymmetric induction at the step of generation of a new chirality at the nitrogen atom.



14 **15**

Chart 5

Applications of the present asymmetric synthesis will be reported shortly.

Experimental[12]

N-(Cyclohexylidene)-(*S*)-valine *tert*-Butyl Ester ((*S*)-(−)-8a)——A solution of cyclohexanone (1.62 g, 16.5 mmol) and optically pure (*S*)-valine *tert*-butyl ester ((*S*)-(+)-**7a**)[4b] ($[\alpha]_D^{25}$ +25.6° (neat)) (2.60 g, 15.0 mmol) in benzene (80 ml) was heated under reflux using a Dean-Stark apparatus for 13 hr. The solvent

12) All boiling points are uncorrected. IR spectra were recorded with a JASCO DS-402G or a JASCO IRA-1 grating infrared spectrometer. NMR spectra were measured with a JNM PS-100 (100 MHz) or a Hitachi R-24 (60 MHz) spectrometer. Tetramethylsilane was used as an internal standard. Abbreviations are as follows: s, singlet; d, doublet; t, triplet; m, multiplet. Optical rotations were measured with a Yanaco OR-50 automatic polarimeter. MS were recorded with a JEOL JMS-01 SG-2 mass spectrometer.

was removed *in vacuo*, and the residue was distilled to give (*S*)-(−)-**8a** (3.39 g, 89%) as a colorless oil of bp 103—105° (2 mmHg). $[\alpha]_D^{20}$ −128.3° (*c*=1.52, benzene). IR ν_{max}^{film} cm^{-1}: 1735, 1665, 1150. NMR (CCl_4) δ: 0.86; 0.90 (6H, two d, *J*=6.5 Hz, $(C\underline{H}_3)_2CH$–), 1.45 (9H, s, –OC$(C\underline{H}_3)_3$), 1.53—2.51 (11H, m), 3.58 (1H, d, *J*=6.5 Hz, –C<u>H</u>–COO–). MS *m/e*: 254 [$(M+1)^+$], 258 (M^+).

N-(Cyclohexylidene)-(*S*)-*tert*-leucine *tert*-Butyl Ester ((*S*)-(−)-8b)——This sample was prepared in the same way as (*S*)-(−)-**8a** using (*S*)-(+)-**7b** of α_D^{20} +1.52° (*l*=0.03, neat) (corresponding to 90.5% optical purity[4b]) in 90% yield as a colorless oil of bp 104—105° (2 mmHg). $[\alpha]_D^{20}$ −84.2° (*c*=1.98, benzene). IR ν_{max}^{film} cm^{-1}: 1735, 1665. NMR (CCl_4) δ: 0.95 (9H, s, $(C\underline{H}_3)_3C$–), 1.42 (9H, s, –O–C$(C\underline{H}_3)_3$), 1.48—2.48 (10H, m), 3.52 (1H, s, –C<u>H</u>–COO–). MS *m/e*: 268 [$(M+1)^+$], 267 (M^+).

(*S*)-(+)-2-Methylcyclohexanone ((*S*)-(+)-10a)——a) Run 1 in Table II (General procedure): A solution of 1.46 M BuLi in hexane (7.74 ml, 11.3 mmol) was added to a solution of diisopropylamine (1.16 g, 11.5 mmol) in THF (20 ml) under argon at −78°, and the whole was stirred at the same temperature for 25 min. A solution of (*S*)-(−)-**8a** (2.79 g, 11 mmol) in THF (5 ml) was added, and the resulting yellow solution was stirred for 30 min. A solution of dimethyl sulfate (1.45 g, 11.5 mmol) in THF (10 ml) was next added dropwise, and the whole was stirred at −78° for 1 hr. After adding 10% aq. citric acid (13 ml), the resulting mixture was poured into ice-cold 10% aq. citric acid (60 ml). The whole was stirred vigorously for 20 min, and then extracted with ether (100 ml×2). The combined ethereal extracts were washed with aq. $NaHCO_3$ until the aq. layer reached pH 6, and were then washed with satd. aq. NaCl, and dried over $MgSO_4$. Removal of the solvent gave a yellow oil (1.37 g), which was purified by column chromatography (silica gel, ether–pentane (1: 6)) followed by vacuum distillation to give (*S*)-(+)-**10a** (728 mg, y. 59%) as a colorless oil of bp 104° (125 mmHg). $[\alpha]_D^{25}$ +11.7° (*c*=5.13, MeOH) (reported[13] $[\alpha]_D$ +14° (*c*=0.23, MeOH)). IR ν_{max}^{film} cm^{-1}: 1710. NMR (CCl_4) δ: 0.97 (3H, d, *J*=6 Hz, $C\underline{H}_3$–CH), 1.10—2.60 (9H, m).

From the above acidic aq. layer, (*S*)-(+)-**7a** (1.28 g, y. 67%) was recovered by the usual method as a colorless oil of $[\alpha]_D^{25}$ +25.4° (neat).

b) Run 3 in Table II: (*S*)-(+)-**10a** had $[\alpha]_D^{25}$ +12.4° (*c*=4.85, MeOH). (*S*)-(+)-**7b** (recovery y. 68%) had α_D^{20} +1.52° (*l*=0.03, neat).

c) Run 4 in Table II: (*S*)-(+)-**10a** had $[\alpha]_D^{25}$ +12.3° (*c*=5.01, MeOH). (*S*)-(+)-**7b** (recovery y. 67%) had α_D^{20} +1.523° (*l*=0.03, neat).

(*R*)-(+)-2-Allylcyclohexanone ((*R*)-(+)-10b)——a) Run 2 in Table II: (*R*)-(+)-**10b** was obtained as a colorless oil of bp 100° (50 mmHg). $[\alpha]_D^{25}$ +11.6° (*c*=3.14, MeOH). IR ν_{max}^{film} cm^{-1}: 1712, 1640. NMR ($CDCl_3$) δ: 1.10—2.70 (11H, m), 4.84—5.13 (2H, m, –CH=C<u>H</u>$_2$), 5.52—5.97 (1H, m, –C<u>H</u>=CH$_2$).

b) Run 5 in Table II: (*R*)-(+)-**10b** had $[\alpha]_D^{25}$ +12.0° (*c*=3.25, MeOH). (*S*)-(+)-**7b** (recovery y. 70%) had α_D^{20} +1.521° (*l*=0.03, neat).

(*S*)-(+)-2-Propylcyclohexanone ((*S*)-(+)-10c)——Run 6 in Table II: (*S*)-(+)-**10c** was obtained as a colorless oil of bp 108° (70 mmHg). $[\alpha]_D^{25}$ +24.7° (*c*=4.28, MeOH). IR ν_{max}^{film} cm^{-1}: 1710. NMR (CCl_4) δ: 0.90 (3H, t, *J*=6 Hz, $C\underline{H}_3CH_2$–), 1.00—2.48 (13H, m).

N-(2-Phenylcyclopenten-1-yl)-(*S*)-*tert*-leucine *tert*-Butyl Ester ((*S*)-(+)-12a)——A solution of 2-phenylcyclopentanone (**11a**)[14] (802 mg, 5.0 mmol), (*S*)-(+)-**7b** (α_D^{20} +1.43° (*l*=0.03, neat), corresponding to 85.1% optical purity[4b]) (937 mg, 5.0 mmol) and BF_3·OEt_2 (60 mg) in benzene (55 ml) was heated under reflux using a Dean-Stark apparatus for 14 hr. The solvent was removed *in vacuo*, and the residue was distilled to give (*S*)-(+)-**12a** (1.24 g, y. 75%) as a pale yellow viscous oil of bp 126—128° (0.2 mmHg). $[\alpha]_D^{20}$ +97.5° (*c*=0.71, benzene). IR ν_{max}^{film} cm^{-1}: 1725, 1635, 1595, 1145. NMR (CCl_4) δ: 0.97 (9H, s, $(C\underline{H}_3)_3C$–C), 1.38 (9H, s, $(C\underline{H}_3)_3C$–O), 1.68—2.89 (6H, m), 3.37 (1H, s after D_2O treatment, C<u>H</u>–COO), 4.56 (1H, broad d, *J*= 11 Hz, exchangeable with D_2O, N<u>H</u>), 6.98—7.36 (5H, m, $C_6\underline{H}_5$–). MS *m/e*: 329 (M^+).

N-(2-Phenylcyclohexen-1-yl)-(*S*)-*tert*-leucine *tert*-Butyl Ester ((*S*)-(+)-12b)——This sample was prepared from 2-phenylcyclohexanone (**11b**)[15] by the procedure used for (*S*)-(+)-**12a** as a colorless viscous oil of bp 128—130° (0.2 mmHg) in 79% yield. $[\alpha]_D^{20}$ +27.3° (*c*=1.18, benzene). IR ν_{max}^{film} cm^{-1}: 1725, 1650, 1595, 1145. NMR (CCl_4) δ: 0.83 (9H, s, $(C\underline{H}_3)_3C$–C), 1.39 (9H, s, $(C\underline{H}_3)_3C$–O), 1.52—2.48 (8H, m), 3.20 (1H, s after D_2O treatment, C<u>H</u>–COO), 3.88 (1H, broad d, *J*=11 Hz, exchangeable with D_2O, N<u>H</u>), 7.0—7.27 (5H, m, $C_6\underline{H}_5$). MS *m/e*: 343 (M^+).

(*S*)-(−)-2-Methyl-2-phenylcyclopentanone ((*S*)-(−)-13a)——A solution of (*S*)-(+)-**12a** (989 mg, 3.0 mmol) in THF (8 ml) was added dropwise to a solution of LDA (3.2 mmol) in THF (8 ml) under nitrogen at −78°, and the resulting orange solution was stirred at the same temperature for 30 min. A solution of methyl iodide (469 mg, 3.3 mmol) in THF (5 ml) was added, and the temperature of the reaction mixture was raised to 0° over a period of 2 hr. To this reaction mixture was added 2 N aq. HCl (15 ml) under ice-cooling, and the whole was stirred vigorously for 20 min. The whole was extracted with ether (50 ml×2), and the combined ethereal extracts were washed with aq. $NaHCO_3$, satd. aq. NaCl, and dried over $MgSO_4$. Removal of the solvent gave a reddish oil (510 mg), which was purified by column chromatography (silica

13) C. Beard, C. Djerassi, J. Sicher, F. Šipoš, and M. Tichý, *Tetrahedron*, **19**, 919 (1963).
14) K. Mislow and C.L. Hamermesh, *J. Am. Chem. Soc.*, 77, 1590 (1955).
15) A.S. Hussey and R.R. Herr, *J. Org. Chem.*, **24**, 843 (1959).

gel, ether–hexane (1: 6)) to give (*S*)-(−)-**13a** (324 mg, y. 62%) as a slightly yellow oil. $[\alpha]_D^{25}$ −76.3° (c= 2.26, EtOH). IR ν_{max}^{film} cm^{-1}: 1730, 1595. NMR (CCl_4) δ: 1.31 (3H, s, $C\underline{H}_3$–C), 1.58—2.75 (6H, m), 6.97—7.34 (5H, m, $C_6\underline{H}_5$–). MS m/e: 174 (M^+). This sample was shown to be 79—80% optically pure by NMR analysis in CCl_4 using tris[3-(heptafluoropropyl hydroxymethylene)-*d*-camphorato]europium (III). The IR and NMR spectra as well as TLC and VPC behavior of this sample were identical with those of racemic **13a** prepared by the reported method.[16]

(*S*)-(−)-2-Methyl-2-phenylcyclohexanone ((*S*)-(−)-13b)——This sample was obtained from (*S*)-(+)-**12b** as described above for the preparation of (*S*)-(−)-**13a**, $[\alpha]_D^{25}$ −133° (c=1.92, cyclohexane). IR ν_{max}^{film} cm^{-1}: 1710, 1600. NMR (CCl_4) δ: 1.22 (3H, s, $C\underline{H}_3$), 1.43—2.85 (8H, m), 6.91—7.42 (5H, m, $C_6\underline{H}_5$–). MS m/e: 188 (M^+). This sample was shown to be 81—82% optically pure by NMR analysis using the shift reagent described above. The IR and NMR spectra as well as TLC and VPC behavior of this sample were identical with those of racemic **13b** prepared by the reported method.[16]

16) M.S. Newman and M.D. Farbman, *J. Am. Chem. Soc.*, **66**, 1550 (1944).