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Stereochemical Studies. XLI.[1] Asymmetric Synthesis of optically Active 4a-Methyl-4,4a,9,10-tetrahydro-2(3H)-phenanthrone Derivatives, Key Intermediates for Total Syntheses of optically Active Diterpenes and Steroids[2]

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Exploitation of the synthetic route to optically active (*R*) (−)-4a-methyl-4,4a,9,10-tetrahydro-2(3H)-phenanthrone ((*R*) (−)-**6a**) and its 7-methoxy derivative ((*R*) (−)-**6b**) from optically active (*R*)-2-cyclohexenones ((*R*) (+)-**1**) or (*S*) (+)-δ-ketoaldehydes ((*S*) (+)-**2**) were attempted.

(*R*) (+)-**1** and (*S*) (+)-**2** could be obtained by the asymmetric synthesis *via* the enamines prepared from L-proline-derived pyrrolidines ((*S*)-**5**) and *dl*-2-arylpropionaldehydes (*dl*-**4**). Base-catalysed cyclization of (*S*) (+)-**2**, followed by ketalization and Jones oxidation, gave (*S*) (−)-cyclohexanone ((*S*) (−)-**7**). The same compounds could be also prepared from (*R*) (+)-**1** by successive epoxidation, ketalization, reduction, and Jones oxidation. Addition of N,N-dimethyl lithioacetamide 1,4-diazabicyclo[2,2,2]octane complex to (*S*) (−)-**7**, followed by reduction with Vitride and cyclization with polyphosphoric acid, afforded (*R*) (−)-**6a**, 85% optically pure, and (*R*) (−)-**6b**, $[\alpha]_D^{20}$ −223° (ethanol).

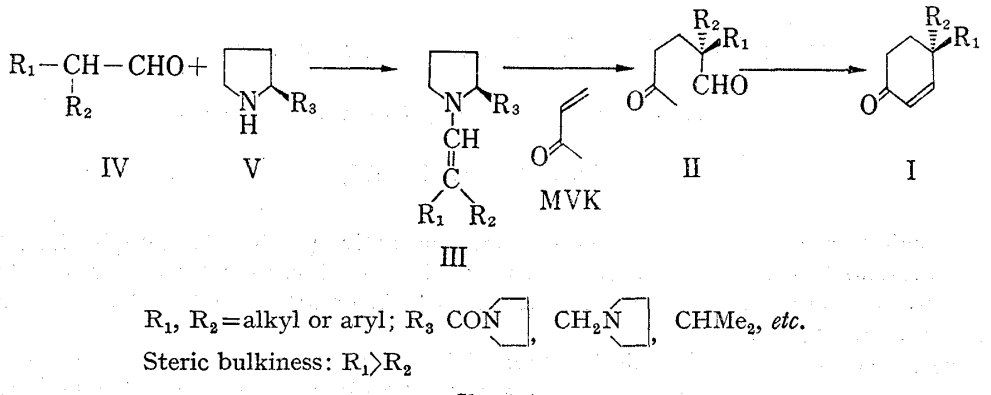
Detailed studies on reaction products and conditions, and preliminary experiments with racemic compounds were also carried out.

In order to synthesize optically active natural products from achiral starting materials by chemical means, it is necessary to utilize chemical resolution method or asymmetric synthesis in the early stage of the synthetic scheme. Considering effectiveness for producing optically active compounds, asymmetric synthesis is clearly superior to chemical resolution method. Asymmetric synthesis can produce optically pure compound in 100% yield theoretically, and can reduce one synthetic step when compared with resolution method.

Although there have been reported many studies on asymmetric syntheses of optically active compounds,[4] researches which aim to prepare optically active natural products, other than amino acids, by asymmetric syntheses, are quite scarce.[5]

1) Part XL: K. Aketa, S. Terashima, and S. Yamada, *Chem. Pharm. Bull.* (Tokyo), **24**, 621 (1976).
2) A part of this work has been presented at the 94th Annual Meeting of the Pharmaceutical Society of Japan, Sendai, April, 1974, and at the Symposium of the Society of Synthetic Organic Chemistry Japan, Tokyo, November, 1974.
3) Location: *Hongo, Bunkyo-ku, Tokyo, 113, Japan.*
4) J.D. Morrison and H.S. Mosher, "Asymmetric Organic Reactions," Prentice-Hall, Inc., Engelwood Cliffs, New Jersey, 1971.
5) Some recent reports which deal with asymmetric syntheses of natural products; *a*) Prostaglandin, J.J. Partridge, N.K. Chadha, and M.R. Uskoković, *J. Am. Chem. Soc.*, **95**, 7171 (1973); *b*) Loganin, *idem*, *ibid.*, **95**, 532 (1973); *c*) Steroids, R. Bucourt, L. Nédélec, J-C. Gasc, and J. Weill-Raynal, *Bull. Soc. Chim. France*, **1967**, 561; U. Eder, G. Sauer, and R. Wiechert, *Angew. Chem. Internat. Edit.*, **10**, 496 (1971); G. Saucy, R. Borer, and A. Fürst, *Helv. Chim. Acta*, **54**, 2034 (1971) and its accompanying papers. Z.G. Hajos and D.R. Parrish, *J. Org. Chem.*, **39**, 1615 (1974); K. Nagasawa, K. Hiroi, and S. Yamada, *Yakugaku-Zasshi*, **95**, 46 (1975) and its preceding paper; *d*) Mesembrine, G. Otani, and S. Yamada, *Chem. Pharm. Bull.* (Tokyo), **21**, 2130 (1973); *e*) Laudanosine and Reticuline, K. Konda, T. Shioiri, and S. Yamada, *ibid.*, **23**, 1025, 1065 (1975); *f*) *trans*-α-Damascone, M. Shibasaki, S. Terashima, and S. Yamada, *ibid.*, **23**, 279 (1975); *g*) *cis*-Tetrahydroactinidiolide, T. Kato, S. Kumazawa, and Y. Kitahara, *Synthesis*, **1972**, 537; S. Kumazawa, T. Kato, and Y. Kitahara, *Chemistry Letters*, **1973**, 633.

As shown in Chart 1, it was reported[6] that optically active 2-cyclohexenones (I) could be prepared *via* optically active δ-ketoaldehydes (II) by the asymmetric Michael addition of the enamines (III), obtained from racemic 2-substituted aldehydes (IV) and optically active pyrrolidines (V), to methyl vinyl ketone (MVK). Although isolation of II was not attempted on that occasion, it is found that treatment of the alkylated enamines with dilute acid can afford II in an excellent yield.



R_1, R_2=alkyl or aryl; R_3 CON⟨ ⟩, CH_2N⟨ ⟩, $CHMe_2$, *etc.*
Steric bulkiness: $R_1 > R_2$

Chart 1

Few reports which concern with synthetic approaches to optically active diterpenes[7] and steroids[5c] by asymmetric syntheses, have been published from these laboratories. Apart from these attempts, a new total asymmetric synthesis of optically active diterpenes and steroids by an application of the asymmetric synthesis of I and II, is studied.

This report describes a successful exploitation of the synthetic scheme from optically active (*R*)-2-cyclohexenones((*R*)-**1a** and (*R*)-**1b**)[8] or (*S*)-δ-ketoaldehydes ((*S*)-**2a** and (*S*)-**2b**) to optically active (*R*)-4a-methyl-4,4a,9,10-tetrahydro-2(3H)-phenanthrone ((*R*)-**6a**) and its 7-methoxy derivative ((*R*)-**6b**).[9] These optically active starting materials ((*R*)-**1** and (*S*)-**2**) can be easily obtained by the asymmetric synthesis which utilizes *dl*-2-phenylpropionaldehyde (*dl*-**4a**) and *dl*-2-(*p*-methoxyphenyl)propionaldehyde (*dl*-**4b**) as IV and optically active L-proline-derived pyrrolidines ((*S*)-**5**) as chiral additives.

The reason why (*R*)-**6** were selected as materials which should be synthesized, is that racemic phenanthrone derivatives (*dl*-**6**) have been frequently employed as starting materials for total syntheses of diterpenes and steroids in their racemic modifications.[9] Since (*S*)-**1** and (*R*)-**2** (antipodes of (*R*)-**1** and (*S*)-**2**) can be readily prepared when optically active D-proline-derived pyrrolidines ((*R*)-**5**) are used as chiral additives, and moreover, since (*R*) (*S*) conversion scheme has been established for (*R*)-**1a**,[10] accomplishment of the chemical scheme from

6) *a*) G. Otani and S. Yamada, *Chem. Pharm. Bull.* (Tokyo), **21**, 2112, 2119, 2125 (1973); b) T. Sone, K. Hiroi, and S. Yamada, *ibid.*, **21**, 2331 (1973).
7) K. Hiroi and S. Yamada, *Chem. Pharm. Bull.* (Tokyo), **23**, 1103 (1975).
8) Throughout this work, (*R*) (*S*) expression is used to designate the absolute configuration of the chiral center produced by asymmetric synthesis except for (*R*)- and (*S*)-**5**.
9) Typical diterpenes and steroids prepared from *dl*-**6**: *a*) Podocarpic acid from *dl*-**6a**, E. Wenkert and B.G. Jackson, *J. Am. Chem. Soc.*, **80**, 217 (1958); *idem*, *ibid*, **81**, 5601 (1959); E. Wenkert and A. Tahara, *ibid.*, **82**, 3229 (1960); *b*) Nimbiol from *dl*-**6a**, R.H. Bible, Jr., *Tetrahedron Letters*, **1960**, 20; *c*) Totarol from *dl*-**6b**, J.A. Barltrop and N.A. Rogers, *J. Chem. Soc.*, **1958**, 2566; *d*) Phyllocladene from *dl*-**6b**, R. F. Church, R.E. Ireland, and J.A. Marshall, *J. Org. Chem.*, **31**, 2526 (1966); R.B. Turner, K.H. Gänshirt, P.E. Shaw, and J.D. Tauber, *J. Am. Chem. Soc.*, **88**, 1776 (1966); *e*) (−)-Kaurene and atisirene from *dl*-**6b**, R.A. Bell, R.E. Ireland, and R.A. Partyka, *J. Org. Chem.*, **31**, 2530 (1966); *f*) Hibaene (Stachene) from *dl*-**6b**, R.A. Bell, R.E. Ireland, and L.N. Mander, *ibid.*, **31**, 2536 (1966); *g*) Steviol from *dl*-**6b**, K. Mori and M. Matsui, *Tetrahedron*, **24**, 3095 (1968); K. Mori, Y. Nakahara, and M. Matsui, *ibid.*, **28**, 3217 (1968); *h*) 5α-Pregnan-3β-ol-20-one from *dl*-**6b**, W. Nagata, T. Terasawa, and T. Aoki, *Tetrahedron Letters*, **1963**, 865.
10) T. Sone, S. Terashima, and S. Yamada, *Synthesis*, **1974**, 725.

(*R*)-**1** or (*S*)-**2** to (*R*)-**6** means that optically active phenanthrones which belong to either (*R*) or (*S*) series ((*R*)- or (*S*)-**6**), have become accessible by asymmetric synthesis as summarized in Chart 2.

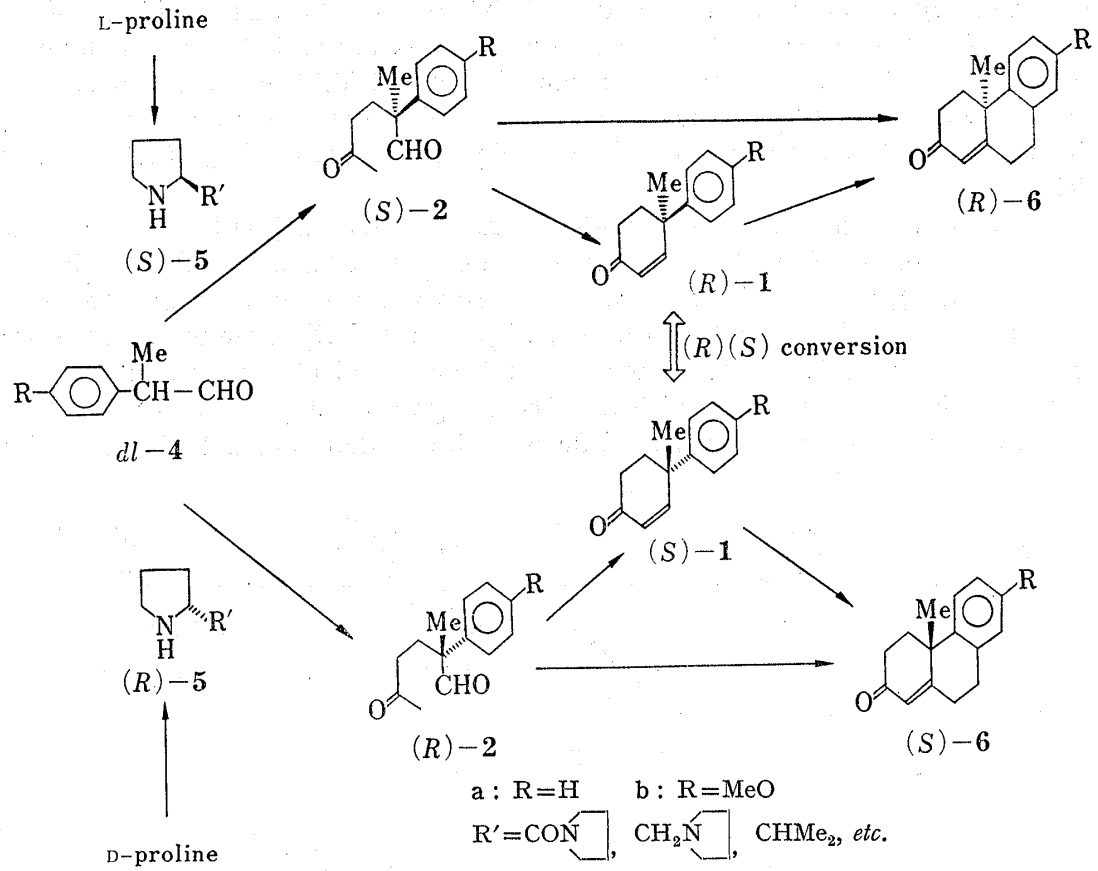


Chart 2

Naturally occurring diterpenes can be classified into two groups due to absolute configuration of the methyl group at A—B ring junction. Few diterpenes such as (—)-kaurene, atisirene, and stachene contain α-methyl groups whose absolute configurations are the same as those of C_{4a}-methyl groups of (*R*)-**6**, and the other large number of diterpenes and steroids have β-methyl groups whose absolute configurations are identical with those of C_{4a}-methyl groups of (*S*)-**6**. According to their absolute configurations at A—B ring junction, total synthetic schemes to these natural diterpenes and steroids can be planned from (*R*)- or (*S*)-**6** as a starting material.

Some preliminary experiments which were undertaken to optimize reaction conditions, were performed with racemic modifications, and were described in detail in experimental part.

Result and Discussion

After several unsuccessful attempts were carried out,[11] (*S*)-2-aryl-5,5-ethylenedioxy-2-methylcyclohexanones ((*S*)-**7a** and (*S*)-**7b**) were chosen as key intermediates for the chemical

11) As a method for converting (*R*)-**1a** into (*R*)-**6a**, introduction of a two carbon unit into the C_3-position of (*R*)-**1a** was first examined by 1,4-addition reaction. Reagents which were used for the 1,4-addition reaction are as follows: *a*) diethyl malonate, ethyl cyanoacetate, and malonodinitrile in the combination with several kinds of bases (sodium ethoxide, potassium *t*-butoxide, sodium hydride, sodium amide, and Triton B); *b*) vinylmagnesium bromide, allylmagnesium bromide, and allyl lithium in the presence of Cu(I) (cuprous iodide, cuprous acetate, and cuprous iodide-tributylphosphine complex). However, all these attempts were found to be useless for affording the desired 1,4-adducts due to the steric hindrance caused by the C_4-position of (*R*)-**1a**.

scheme from (*R*)-**1** or (*S*)-**2** to (*R*)-**6**, and the synthetic route to (*S*)-**7** was sought as described below.

The asymmetric Michael addition of the enamine, prepared from *dl*-**4a**[6a] and (*S*)(+)-2(1-pyrrolidinomethyl)pyrrolidine ((*S*)(+)-**5**, R′=$CH_2NC_4H_8$), to MVK in a mixture of benzene and methanol (9:1), followed by the work-up with a mixture of 10% aqueous hydrochloric acid and ice, gave (+)-**2a**, $[\alpha]_D^{20}$+12.8° (ethanol), in 80% yield.[12] The optical purity and the absolute configuration of (+)-**2a** thus prepared, were definitely determined to be 44% and (*S*)-series by the ready conversion of (+)-**2a** to oily (*R*)(+)-**1a**,[6,13] $[\alpha]_D^{20}$+57.1° (ethanol), in 96% yield.

The same asymmetric synthesis with *dl*-**4b**[14] gave (+)-**2b**, $[\alpha]_D^{20}$+13.0° (ethanol), in 75% yield. Treatment of (+)-**2b** under a similar condition to that for (*S*)(+)-**2a** afforded (+)-**1b**, $[\alpha]_D^{20}$+69.5° (ethanol), in 95% yield. Although (+)-**1b** was clearly determined to have (*R*)-configuration by comparing its optical rotatory dispersion (ORD) curve with that of (*R*)(+)-**1a**[6a] as shown in Figure 1, its optical purity could not be calculated since the pure optical rotation of (+)-**1b** had not been established. According to the preparation of (*R*)(+)-**1b** from (+)-**2b**, the absolute configuration of (+)-**2b** was clearly determined to be (*S*)-series.

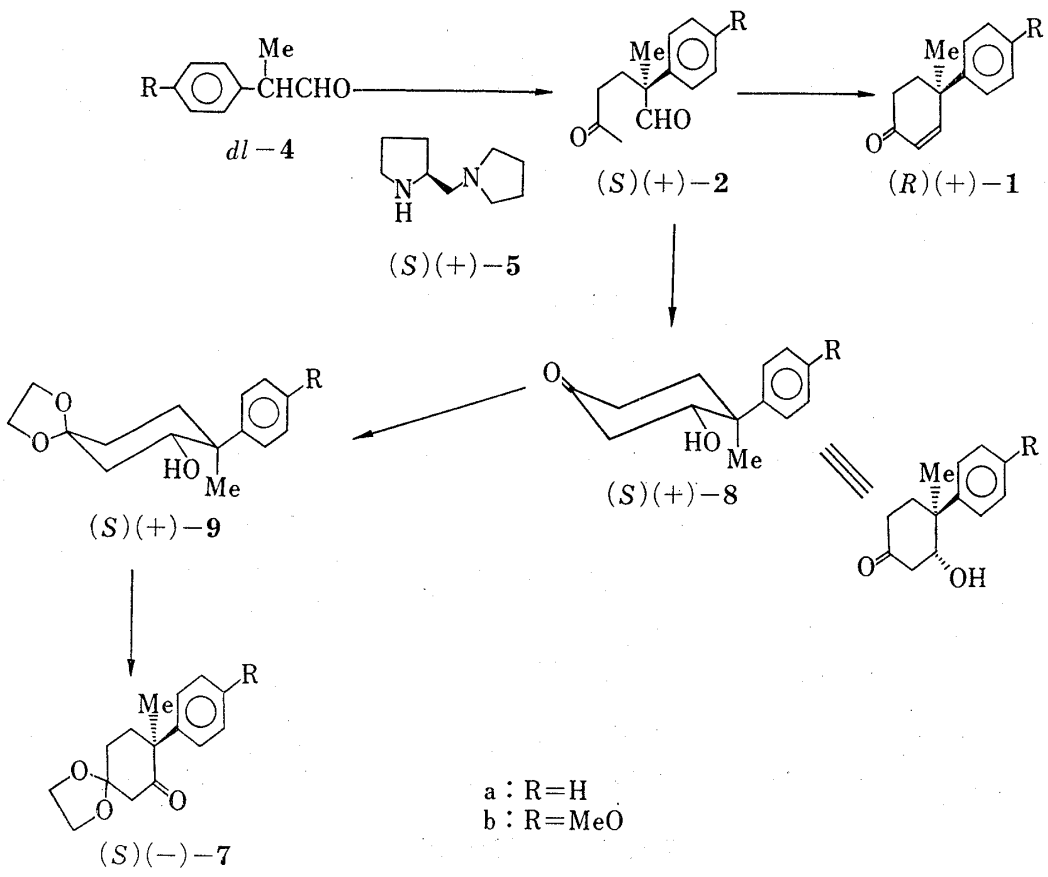
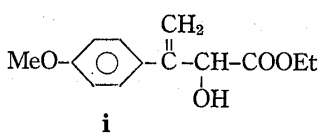


Chart 3

12) As mentioned above, this is the first case in which (*S*)-**2** could be isolated prior to the conversion to (*R*)-**1**.
13) In ref. 6*a*, it has been established that optically pure (*R*) (+)-**1a** shows $[\alpha]_D^{20}$ +130° (ethanol).
14) This aldehyde was prepared from *p*-methoxyacetophenone in a similar fashion to that for *dl*-**4a**. Darzen reaction of *p*-methoxyacetophenone with ethyl chloroacetate in the presence of sodium ethoxide afforded ethyl 2-hydroxy-3-(*p*-methoxyphenyl)-3-butenoate (**i**) instead of the expected glycidic acid ester. Saponification of **i**, followed by decarboxylation with acid, gave *dl*-**4b**. For preparation details, see experimental.



i

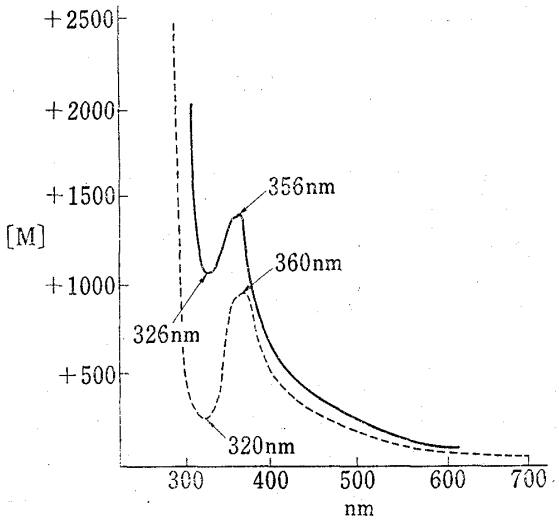


Fig. 1. ORD Curves of (*R*) (+)-4-Methyl-4-phenyl-2-cyclohexenone ((*R*)(+)-**1a**) and (+)-4-Methyl-4-(*p*-methoxyphenyl)-2-cyclohexenone ((+)-**1b**)

----------: (*R*)(+)−**1a**
————: (+)−**1b**
measured in methanol

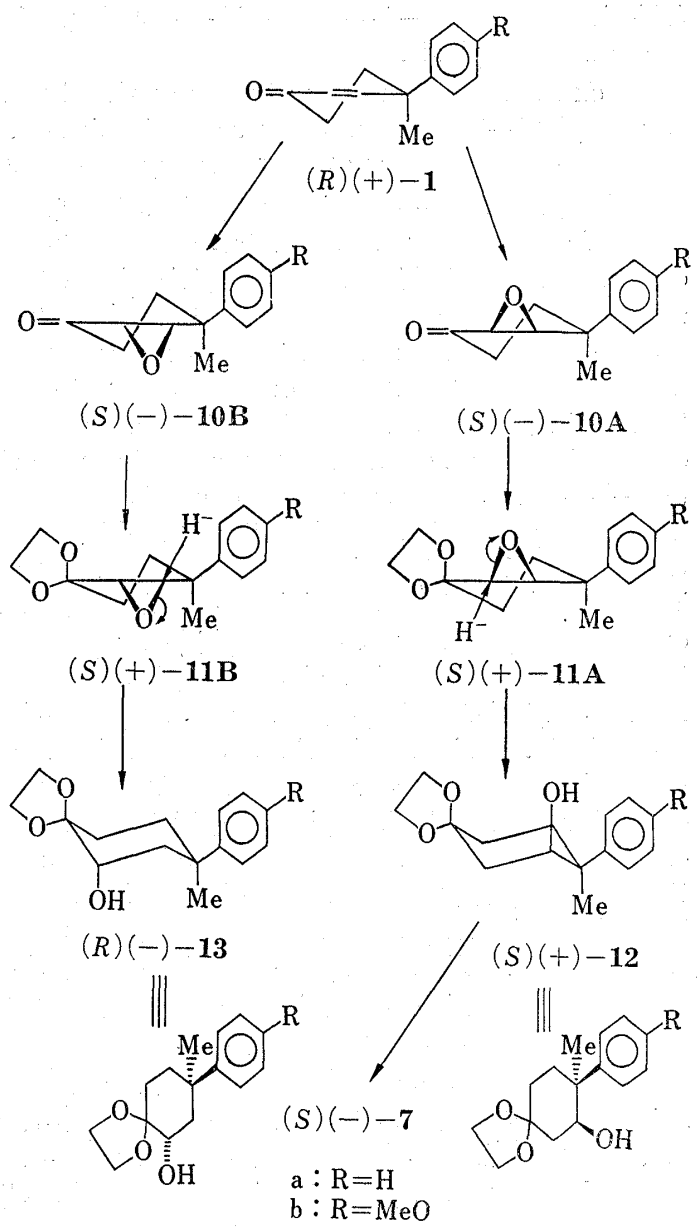


Chart 4

Ring closures of (*S*)(+)-**2a** and (*S*)-(+)-**2b**, which were effected with a dilute potassium hydroxide solution (0.06 eq.) in tetrahydrofuran (THF), afforded (*S*)(+)-hydroxyketones ((*S*)-(+)-**8a** and (*S*)(+)-**8b**),[15] $[\alpha]_D^{20}$+3.5° (ethanol) and $[\alpha]_D^{20}$+2.5° (ethanol), in 93% and 90% yields, respectively. The structures of (*S*)(+)-**8** are tentatively assigned as depicted in Chart 3, by considering higher conformational energy of aryl group than that of methyl group,[16] and by assuming that the ring closure might be a process under thermodynamic control.[17] However, detailed studies on the structures were not carried out because the chiral centers created here could be removed at the later stage. Ketalization of (*S*)(+)-**8a** with ethylene glycol in the presence of *p*-toluenesulfonic acid (0.01 eq.) in benzene for 2 hr, afforded (*S*)(+)-ketal ((*S*)(+)-**9a**), $[\alpha]_D^{20}$+3.1° (ethanol), in 90% yield and (*R*)-**1a**[18] in 4.4% yield. Treatment of (*S*)(+)-**8b** in a similar manner to the case for (*S*)(+)-**8a**, yielded (*S*)(+)-ketal ((*S*)(+)-**9b**), $[\alpha]_D^{20}$+2.4° (ethanol), in 87% yield and (*R*)-**1b**[18] in 9.3% yield. Oxidations of (*S*)(+)-**9a** and (*S*)(+)-**9b** with Jones reagent in acetone, gave oily

15) In the preliminary experiments using racemic compounds, *dl*-**8a**, which might be contaminated by the epimeric alcohol (*dl*-**12a**), could be prepared from *dl*-**1a** by the epoxidation with alkaline hydrogen peroxide (87% yield) (see later description), followed by openning of the epoxide ring with chromous acetate (38% yield) or aluminium amalgam (51% yield) (T. Sone, S. Terashima, and S. Yamada, unpublished results).

16) J.A. Hirsch, "Table of Conformational Energies-1967," in "Topics in Stereochemistry," Vol. 1, ed. by N.L. Allinger and E.L. Eliel, Interscience Publishers, Inc., New York, 1967, p. 199.

17) H.O. House, "Modern Synthetic Reactions," W.A. Benjamin, Inc., Melono Park, California, 1972, p. 629.

18) The optical rotation of this sample was not measured.

(*S*)(−)-ketones ((*S*)(−)-**7a** and (*S*)(−)-**7b**), $[\alpha]_D^{20}$−59.8° (ethanol) and $[\alpha]_D^{20}$−72.7° (ethanol), in 87% and 86% yields.

Next, development of another synthetic scheme to (*S*)(−)-**7a** and (*S*)(−)-**7b** from (*R*)(+)-**1a** and (*R*)(+)-**1b** was studied as shown in Chart 4.[19]

Epoxidation of (*R*)(+)-**1a**, $[\alpha]_D^{20}$+57.1° (ethanol), prepared above, with alkaline hydrogen peroxide gave (*S*)(−)-epoxide ((*S*)(−)-**10a**), $[\alpha]_D^{20}$−6.9° (ethanol), in 78% yield. The nuclear magnetic resonance (NMR) spectrum clearly showed that this epoxide was a mixture of two diastereoisomers ((*S*)(−)-**10aA** and (*S*)(−)-**10aB**) since the methyl group of the C_4-position appeared as two singlets at 1.45 and 1.54 ppm (relative intensity 3.5: 1). As it is expected that the methyl group of (*R*)(+)-**1a** occupies quasi-axial conformation due to its lower conformational energy than that of the phenyl group,[16] and that attack of the peroxide to the double bond of (*R*)(+)-**1a** occurrs preferentially from the less hindered side which is opposite to the quasi-axial methyl group, the major epoxide can be assigned as (*S*)(−)-**10aA** and the minor as (*S*)(−)-**10aB**. Since separation of the diastereomeric epoxides was unsuccessful, the mixture was directly submitted to ketalization with ethylene glycol and a catalytic amount of *p*-toluenesulfonic acid, giving (*S*)(+)-epoxyketal ((*S*)(+)-**11a**) as a mixture of two diastereoisomers ((*S*)(+)-**11aA** and (*S*)(+)-**11aB**), $[\alpha]_D^{20}$+12.8° (ethanol), in 93% yield. Reduction of the diastereomeric mixture of (*S*)(+)-**11a** with lithium aluminium hydride (LAH) in dioxane, followed by the separation with silica gel column, gave two kinds of the ketal alcohols ((*S*)(+)-**12a** and (*R*)(−)-**13a**[20]), $[\alpha]_D^{20}$+5.8° (ethanol) and $[\alpha]_D^{20}$−13.5° (ethanol), in 52% and 16% yields, respectively. It is conceivable that since reductive cleavage of the epoxide such as (*S*)(+)-**11a** with LAH usually occurrs from axial direction and liberates an axial alcohol,[21] (*S*)(+)-**11aA** derived from (*S*)(−)-**10aA**, gives (*S*)(+)-**12a** having an axial alcoholic function, and (*R*)(−)-**13a** can be prepared from (*S*)(+)-**11aB** derived from (*S*)(−)-**10aB**. Close identity of the formation ratio of (*S*)(+)-**12a** and (*R*)(−)-**13a** with the relative amount of (*S*)(−)-**10aA** and (*S*)(−)-**10aB** determined by the NMR spectrum, might further support the above-cited mechanistic consideration. That the optical rotation of (*S*)(+)-**12a**, $[\alpha]_D^{20}$+5.8° (ethanol), is clearly different from that of (*S*)(+)-**9a**, $[\alpha]_D^{20}$+3.5° (ethanol), is probably construed as the result of configurational difference of the hydroxy group.

Similar sequential treatments of (*R*)(+)-**1b**, $[\alpha]_D^{20}$+69.5° (ethanol), to the case for (*R*)(+)-**1a**, gave (*S*)(+)-**12b**, $[\alpha]_D^{20}$+13.8° (ethanol), and (*R*)(−)-**13b**, $[\alpha]_D^{20}$−19.4° (ethanol), by way of (*S*)(−)-**10b**, $[\alpha]_D^{20}$−11.1° (ethanol) and (*S*)(+)-**11b**, $[\alpha]_D^{20}$+18.0° (ethanol).[22]

Oxidations of (*S*)(+)-**12a**, $[\alpha]_D^{20}$+5.7° (ethanol), and (*S*)(+)-**12b**, $[\alpha]_D^{20}$+13.8° (ethanol), with Jones reagent under the same condition as that for (*S*)(+)-**9**, afforded (*S*)(−)-**7a** and (*S*)(−)-**7b**, $[\alpha]_D^{20}$−54.9° (ethanol) and $[\alpha]_D^{20}$−73.4° (ethanol), in 86% and 85% yields. These (*S*)(−)-ketones were respectively identified with the samples prepared from (*S*)(+)-**2** by spectral and chromatographic comparisons.

Since the key intermediates ((*S*)(−)-**7**) had become accessible from (*R*)(+)-**1** and (*S*)(+)-**2** as mentioned above, introduction of a two carbon unit into (*S*)(−)-**7** and subsequent cyclization to the aromatic ring were studied for completing a synthetic route to (*R*)-**6**.

After several kinds of organometallic reagents were attempted, it was found that N,N-dimethyl lithioacetamide[23] could exclusively afford the desired addition product ((*S*)-**14a**)

19) This synthetic scheme would be of value when the preparation of (*S*)-**6** is attempted by the asymmetric synthesis using (*S*)-**5** as chiral additives, followed by the (*R*) (*S*) conversion scheme.
20) This compound can be converted to (*R*) (+)-**1a** by Chugaev reaction, followed by acidic cleavage of the ketal group. See ref. 10.
21) *a*) C. Djerassi, "Steroid Reactions," Holden Day, San Fransisco, 1963, p. 615; *b*) S. A. Julia, P.A. Plattner, and H. Heusser, *Helv. Chim. Acta.*, **35**, 665 (1952).
22) Similar structural and mechanistic arguments to those presented on the reaction products derived from (*R*) (+)-**1a**, are possible for the preparation of (*S*) (+)-**12b** and (*R*) (−)-**13b**.
23) D.N. Crouse and D. Seebach, *Chem. Ber.*, **101**, 3113 (1968).

in the presence of 1,4-diazabicyclo[2,2,2]octane (DABCO).[24]

Treatment of (*S*)(−)-**7a** with a complex of N,N-dimethyl lithioacetamide (2.0 eq.) and DABCO (2.0 eq.) in THF at −25——30° for 3 hr, followed by the purification with silica gel column, afforded two sorts of the oily addition products ((*S*)(+)-**14aA** and (*S*)(+)-**14aB**), $[\alpha]_D^{20}$+27.9° (ethanol) and $[\alpha]_D^{20}$+15.1° (ethanol), in 74% and 10% yields, respectively, and (*S*)(−)-enol ether[24] ((*S*)(−)-**15a**), $[\alpha]_D^{20}$−153.2° (ethanol), in 7.1% yield. The structures of

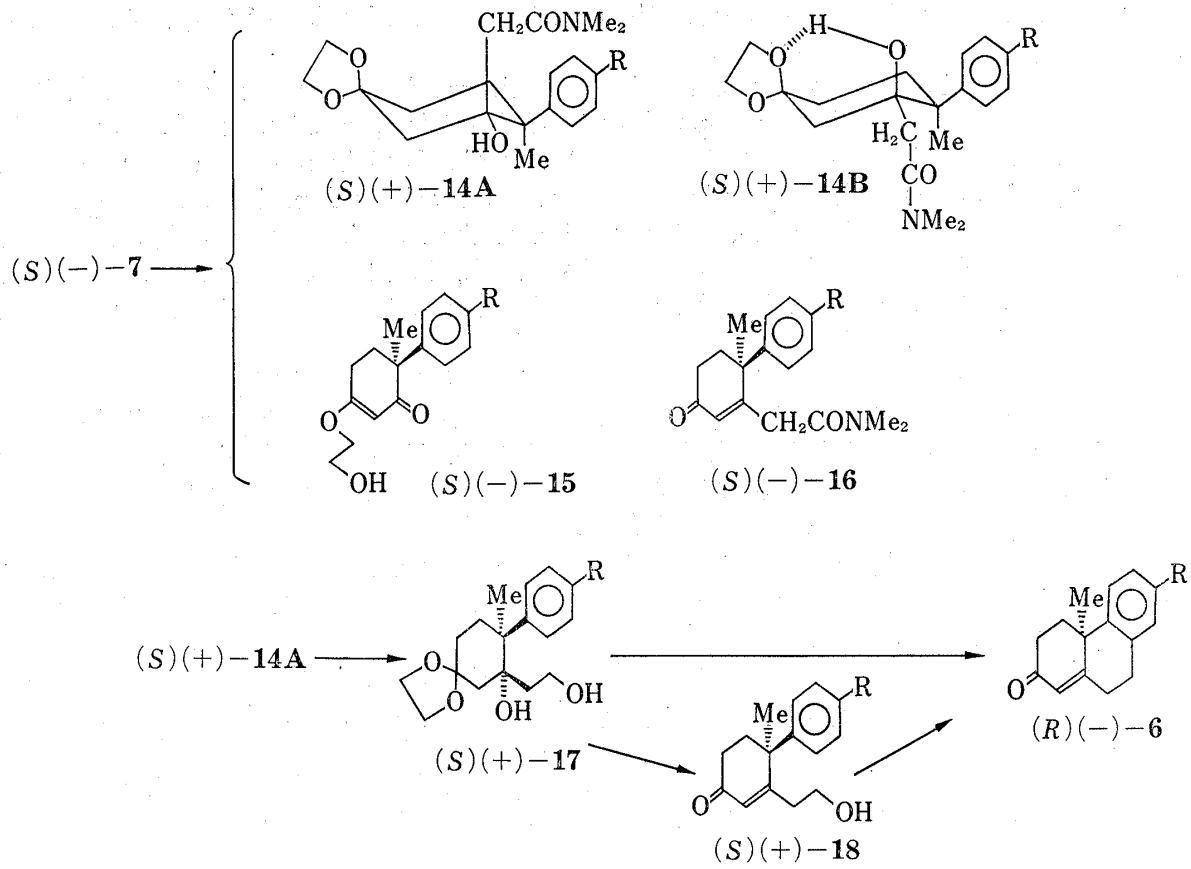


Chart 5

Table I. Spectral (IR and NMR) Properties of (*S*)(+)-Acetamides ((*S*)(+)-**14A** and (*S*)(+)-**14B**)

Spectra	Assignments	Compounds (*S*)(+)-**14aA**	(*S*)(+)-**14bA**	(*S*)(+)-**14aB**	(*S*)(+)-**14bB**
IR($CHCl_3$) cm^{-1}	ν_{O-H}	3490	3585	3330	3320
	$\nu_{C=O}$	1623	1623	1614	1610
NMR ($CDCl_3$) ppm	>C-Me	1.47	1.39	1.43	1.40
	NMe_2	2.38, 2.75	2.60, 2.99	2.84, 2.89	2.75, 2.82
	OH	4.30	4.35	6.20	6.15

24) Full accounts on the studies with several kinds of organometallic reagents and tertiary amines, and on the structural elucidation of the enol ether, will be a subject of the accompanying paper (T. Sone, S. Terashima, and S. Yamada, *Chem. Pharm. Bull.* (Tokyo), **24**, 1293 (1976).

(*S*)(+)-**14aA** and (*S*)(+)-**14aB** could be rigorously assigned as shown in Chart 5 by comparing their spectral data summarized in Table I, and by considering the direction of attack of the lithium reagent to the sterically hindered carbonyl group. IR and NMR spectra of the minor adduct ((*S*)(+)-**14aB**) clearly discloses the presence of the hydrogen-bonded hydroxy group. This spectral feature is in good agreement with the assigned structure. Since the methyl group of (*S*)(−)-**7a** occupies axial conformation due to its lower conformational energy than that of phenyl group,[16] and attack of the lithium reagent might occur from the sterically less-hindered side in a similar fashion to the case for the epoxidation of (*R*)(+)-**1**, the major adduct can be assigned as (*S*)(+)-**14aA**.

When the preliminary experiments with racemic modifications were attempted, it was found that the racemic amide corresponding to (*S*)(+)-**14aA**, could be easily recrystallized from ether. The major adducts ((*S*)(+)-**14aA**) was dissolved in a small amount of ether, and the racemic amide which crystallized out, was collected by filtration and recrystallized from a mixture of ether and hexane. Evaporation of the combined mother liquors from the recrystallizations *in vacuo* afforded oily (*S*)(+)-**14aA**, $[\alpha]_D^{20}$+57.3° (ethanol). According to this procedure, the optical purity of (*S*)(+)-**14aA** could be improved twice as much as that of the sample directly obtained from the reaction mixture.

The same treatment of (*S*)(+)-**7b** as that of (*S*)(+)-**7a**, gave (*S*)(+)-**14bA**, $[\alpha]_D^{20}$+25.3° (ethanol), (*S*)(+)-**14bB**, $[\alpha]_D^{20}$+16.4° (ethanol), (*S*)-enol ether ((*S*)-**15b**[18]), and (*S*)(−)-enone ((*S*)(−)-**16b**),[25] $[\alpha]_D^{20}$−13.3° (ethanol), in 54%, 7.8%, 5.1% and 13% yields. The optical purity of the major adduct ((*S*)(+)-**14bA**) was similarly increased, and (*S*)(+)-**14bA** showing $[\alpha]_D^{20}$+62.3° (ethanol), could be finally obtained.

Reduction of (*S*)(+)-**14aA**, $[\alpha]_D^{20}$+57.3° (ethanol), with sodium aluminium bis (2-methoxyethoxy)hydride (Vitride) in a mixture of ether and benzene at −20°, followed by the aqueous work-up, gave the oily crude aldehyde.[26]

The aldehyde was further reduced with Vitride without purification affording (*S*)(+)-diol ((*S*)(+)-**17a**), $[\alpha]_D^{20}$+48.7° (ethanol), in 72% yield from (*S*)(+)-**14aA**. Similar treatment of (*S*)(+)-**14bA**, $[\alpha]_D^{20}$+62.3° (ethanol), gave (*S*)(+)-**17b**, $[\alpha]_D^{20}$+51.4° (ethanol), in 65% yield.

Removal of the ketal group from (*S*)(+)-**17a**, $[\alpha]_D^{20}$+34.3° (ethanol)[27] with dil. hydrochloric acid gave (*S*)(+)-enone ((*S*)(+)-**18a**), $[\alpha]_D^{20}$+104.4° (ethanol) in 85% yield, with simultaneous dehydration of β-hydroxycyclohexanone system.

Heating a mixture of (*S*)(+)-**18a**, $[\alpha]_D^{20}$+104.4° (ethanol), and polyphosphoric acid (PPA) for 1 hr, afforded the desired (*R*)(−)-phenanthrone ((*R*)(−)-**6a**),[28] $[\alpha]_D^{27}$−217° (95% ethanol), 65% optically pure,[29] in 42% yield. Aiming to improve the chemical yield of (*R*)(−)-**6a** from (*S*)(+)-**17a**,[30] (*S*)(+)-**17a**, $[\alpha]_D^{20}$+48.7° (ethanol), was directly submitted for the cyclization

25) The structure of this compound was determined by its spectral data (see experimental). Formation of the similar compound ((*S*)-**16a**) was not observed for the reaction with (*S*) (−)-**7a**. Although addition of the organolithium reagent to (*S*)-**15**, followed by acid-catalyzed 1,3-rearrangement during work-up, might account for the formation of (*S*) (−)-**16b**, detailed studies on the formation mechanism were not carried out.

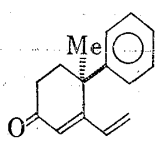
26) Reduction of (*S*) (+)-**14aA** to the aldehyde was examined by using reducing reagents other than Vitride in ether or THF. LAH and lithium aluminium bis(ethoxy)hydride were found to be less effective for selectively affording the aldehyde, and formation of a fairly large amount of the amine derivative was always observed. 9-Borabicyclo[3,3,1]nonane (9-BBN) did not reduce the amide group of (*S*) (+)-**14aA**.

27) Prepared independently from (*S*) (+)-**14aA**. Lower optical purity of this sample are simply due to insufficient removal of the racemic amide from (*S*) (+)-**14aA**.

28) W.R. Adams, O.L. Chapman, J.B. Sieja, and W.L. Welstead, Jr., *J. Am. Chem. Soc.*, **88**, 162 (1966).

29) (*R*) (−)-**6a** showing $[\alpha]_D^{27}$ −332° (95% ethanol), which was prepared by the resolution of *dl*-**6a** (see ref. 28), was assumed to be optically pure.

30) Fairly lower yield of the cyclization of (*S*) (+)-**18a** was considered due to dehydration of homoallylic alcohol of (*S*) (+)-**18a** which could give the dienone (**ii**). For suppressing the undesired dehydration, direct cyclization of (*S*) (+)-**17a** was attempted.



condition employed for (*S*)(+)-**18a**, to give (*R*)(−)-**6a**,[28] $[\alpha]_D^{27}$ −282° (95% ethanol), 85% optically pure,[29] in 64% yield, by simultaneous cyclization, removal of the protecting group, and dehydration. When (*S*)(+)-**17b**, $[\alpha]_D^{20}$ +51.4° (ethanol), was similarly treated with PPA, (*R*)(−)-phenanthrone ((*R*)(−)-**6b**),[31] $[\alpha]_D^{20}$ −223° (ethanol), could be obtained in 14% yield, in spite of the fact that the cyclization should occur at the *meta*-position to the methoxy group.

Since the chemical scheme from (*R*)-**1** or (*S*)-**2** to (*R*)-**6** has been completed as mentioned above, it is evident that naturally occurring diterpenes and steroids which have been synthesized from *dl*-**6a** or *dl*-**6b** in racemic modifications, have now become accessible by asymmetric synthesis if the scheme shown in Chart 2 is taken into consideration.[32] In order to visualize this conclusion, synthesis of optically active podocarpic acid, one of the most popular diterpene resin acids, was attempted by utilizing the reaction scheme developed here, and by using optically active D-proline-derived (*R*)(−)-2(1-pyrrolidinomethyl)pyrrolidine ((*R*)(−)-**5**, R′= $CH_2NC_4H_8$) as a chiral additive. This is a subject of the accompanying paper.[33]

Experimental[34]

(*S*) (+)-2-Methyl-2-phenyl-1,5-hexanedione ((*S*) (+)-2a)——A solution of *dl*-**4a**[6a] (5.36 g, 0.040 mole) and (*S*) (+)-5(R′-$CH_2NC_4H_8$)[6b] (6.16, 0.040 mole) in benzene (150 ml) was refluxed for 45 min, using a Dean-Stark apparatus to remove the water produced. Evaporation *in vacuo* afforded the crude enamine as a yellow oil. IR ν_{max}^{film} cm^{-1}: 1630 (C=C–N). To a solution of the crude enamine in a mixture of benzene and methanol (9: 1) (100 ml), was added MVK (3.08 g, 0.044 mole) with stirring in an ice-bath. The whole mixture was stirred at 5° for 48 hr, then was poured into a mixture of 10% HCl (20 ml) and ice (*ca.* 50 g). The upper organic layer was separated, and the lower aqueous phase was extracted with benzene. The combined benzene extracts were washed with 10% HCl and satd. NaCl, and finally dried over anhyd. $MgSO_4$. Filtration and evaporation *in vacuo* gave crude (*S*) (+)-**2a**, which was submitted to distillation to give pure (*S*) (+)-**2a** as a pale yellow oil (6.45 g, 80%), bp 111—114° (1 mmHg), $[\alpha]_D^{20}$ +12.8° (*c*=0.972, EtOH). IR ν_{max}^{film} cm^{-1}: 1740 and 1730 (CO and CHO). NMR (in CCl_4): 1.33 (3H, s, $C\underline{H}_3$), 1.95 (3H, s, $COC\underline{H}_3$), 2.14 (4H, s, $2\times C\underline{H}_2$), 7.20 (5H, s, $C_6\underline{H}_5$), 9.35 (1H, s, $C\underline{H}O$).

(*R*) (+)-4-Methyl-4-phenyl-2-cyclohexenone ((*R*) (+)-1a)——A mixture of (*S*) (+)-**2a** ($[\alpha]_D^{20}$ +12.8° (*c*= 0.972, EtOH)) (3.06 g, 0.015 mole), pyrrolidine (1 ml), and 33% acetic acid (2 ml) in methanol (30 ml) was heated at reflux for 2 hr,[6a] then evaporated *in vacuo* to afford an oily residue. The residue was dissolved in benzene (30 ml), and the benzene solution was successively washed with satd. NaCl. 10% HCl, and satd. NaCl, then dried over anhyd. Na_2SO_4. Filtration and evaporation *in vacuo*, followed by fractional distillation, gave pure (*R*) (+)-**1a** as a pale yellow oil (2.7 g, 96%), bp 123—124° (3 mmHg), $[\alpha]_D^{20}$ +57.1° (*c*=1.220, EtOH). IR and NMR spectra of this oil were completely identical with those of the authentic sample.[6a] The degree of the asymmetric induction for the preparation of (*S*) (+)-**2a** could be calculated as 44% since optically pure (*R*) (+)-**1a** was reported to show $[\alpha]_D^{20}$ +130° (EtOH).[6a]

***dl*-2-(*p*-Methoxyphenyl)propionaldehyde (*dl*-4b)**[14]——a) Ethyl 2-hydroxy-3-(*p*-methoxyphenyl)-3-butenoate (**i**): A mixture of *p*-methoxyacetophenone (60 g, 0.40 mole) and ethyl chloroacetate (98 g, 0.80 mole) in benzene (100 ml) was gradually added to an ethanolic solution of sodium ethoxide prepared from sodium (18.4 g, 0.80 g atom) and ethanol (300 ml), over a period of 1 hr with vigorous stirring and cooling in an ice bath. After the addition was over, the stirring was further continued at the same temperature for 1 hr, and at room temperature for 3 hr. The whole mixture was poured onto ice (*ca.* 500 g) containing acetic acid (60 ml), and extracted with benzene. The combined organic extracts were washed with satd. NaCl, then dried

31) The optical purity of this compound could not be determined because of the lack of its pure optical rotation.
32) See the introduction of this paper.
33) T. Sone, S. Terashima, and S. Yamada, *Chem. Pharm. Bull.* (Tokyo), **24**, 1288 (1976).
34) All melting and boiling points are uncorrected. IR spectra were recorded with spectrometers, JASCO Infrared Spectrometer Model DS-402G and JASCO IRA-1 Grating Infrared Spectrometer. NMR spectra were measured with spectrometers, JNM-PS 100 Spectrometer (100Mc) and Hitachi R-24 High Resolution NMR Spectrometer (60 Mc). All signals are expressed by the ppm downfield from tetramethylsilane used as an internal standard (δ value). Following abbreviations are used: singlet (s), doublet (d), triplet (t), quartet (q), multiplet (m), broad (br). Measurements of optical rotations were carried out using YANACO OR-50 Automatic Polarimeter, and ORD curves were recorded with a spectrometer, Model ORD/UV-5, Japan Spectroscopic Co. Ltd. Mass spectra measurements were performed with a spectrometer, JEOL JMS SG-2 Mass Spectrometer.

over anhyd. Na_2SO_4. Filtration and evaporation *in vacuo*, gave an oily residue, which was distilled *in vacuo* to afford pure **i** as a yellow oil (46 g, 49%), bp 140—145° (1.5 mmHg). IR ν_{max}^{film} cm^{-1}: 3480 (OH), 1700 (COOEt), 1680, 905 (>C=CH_2). NMR (in CCl_4): 1.05 (3H, t, J=7 Hz, CH_2CH_3), 3.55 (1H, s, OH), 3.90 (3H, s, OCH_3), 4.04 (2H, q, J=7 Hz, CH_2CH_3), 4.85 (1H, s, CH), 5.26 (2H, s, >C=CH_2), 6.61—7.31 (4H, m, C_6H_4).

b) *dl*-2-Hydroxy-3-(*p*-methoxyphenyl)-3-butenoic Acid: A mixture of **i** (11.8 g, 0.050 mole) and 4N NaOH (13 ml, 0.052 mole) was vigorously stirred at room temperature for 1 hr. After washed with benzene, the aqueous solution was acidified to pH 3 by the addition of 10% HCl in an ice bath. Formed precipitate was collected by filtration, washed with water, and finally dried over P_2O_5. It weighed 10.0 g (96%). Recrystallization from ethyl acetate–hexane gave the pure acid as colorless needles, mp 113—114°. IR ν_{max}^{KBr} cm^{-1}: 3500 (OH), 1745 (COOH), 1687, 905 (>C=CH_2). NMR (in DMSO-d_6): 3.70 (3H, s, OCH_3), 4.90 (1H, s, CH), 5.30 (2H, d, J=6 Hz, >C=CH_2), 6.7—7.5 (4H, m, C_6H_4). *Anal.* Calcd. for $C_{11}H_{12}O_4$: C, 63.45; H, 5.81. Found: C, 63.09; H, 6.12.

c) *dl*-**4b**: A suspension of the acid (10.4 g, 0.050 mole) prepared above, in 1N HCl (60 ml) was heated at 80° for 2 hr with stirring. After cooling, the mixture was extracted with benzene, and the combined benzene extracts were washed with satd. $NaHCO_3$ and satd. NaCl, then dried over anhyd. Na_2SO_4. Filtration and evaporation *in vacuo*, followed by fractional distillation, gave pure *dl*-**4b** as a colorless oil (5.28 g, 65%), bp 97—98° (4 mmHg). IR ν_{max}^{film} cm^{-1}: 1730 (CHO). NMR (in CCl_4): 1.42 (3H, d, J=7 Hz, CH_3), 3.55 (1H, doubled q, J=7 and 2 Hz, CH), 3.82 (3H, s, OCH_3), 6.7—7.2 (4H, m, C_6H_4), 9.49 (1H, d, J=2 Hz, CHO). *Anal.* Calcd. for $C_{10}H_{12}O_2$: C, 73.14; H, 7.37. Found: C, 72.96; H, 7.39.

(*S*) (+)-2-Methyl-2-(*p*-methoxyphenyl)-1,5-hexanedione ((*S*) (+)-**2b**)——Similar treatment of the enamine prepared from *dl*-**4b** (8.20 g, 0.050 mole) and (*S*) (+)-5 (R'=$CH_2NC_4H_8$)[6b] (3.85 g, 0.055 mole) to the case for (*S*) (+)-**2a**, gave pure (*S*) (+)-**2b** as a colorless oil (8.74 g, 75%), bp 111—115° (1 mmHg), $[\alpha]_D^{20}$ +13.0° (c=2.012, EtOH). IR ν_{max}^{film} cm^{-1}: 1720 (CO and CHO). NMR (in CCl_4): 1.32 (3H, s, CH_3), 2.00 (3H, s, $COCH_3$), 2.22 (4H, s, 2×CH_2), 3.74 (3H, s, OCH_3), 6.7—7.2 (4H, m, C_6H_4), 9.35 (1H, s, CHO).

(*R*) (+)-4-Methyl-4-(*p*-methoxyphenyl)-2-cyclohexenone ((*R*) (+)-**1b**)——Treatment of (*S*) (+)-**2b** ($[\alpha]_D^{20}$ +13.0° (c=2.012, EtOH)) (7.02 g, 0.030 mole) in a similar manner to the case for (*R*) (+)-**1a**, afforded pure (*R*) (+)-**1b** as a pale yellow oil (6.2 g, 95%), bp 146—149° (2 mmHg), $[\alpha]_D^{20}$ +69.5° (c=1.134, EtOH). IR ν_{max}^{film} cm^{-1}: 1675 (CO). NMR (in CCl_4): 1.42 (3H, s, CH_3), 2.12 (4H, s, 2×CH_2), 3.70 (3H, s, OCH_3), 5.90 (1H, d, J=11 Hz, COCH=CH), 6.6—7.3 (5H, m, C_6H_4 and COCH=CH). ORD (c=0.103, MeOH) [M][26] (nm): +151° (589), +1409° (356) (peak), +1359° (346) (shoulder), +1056° (326) (trough), +2428° (300). *Anal.* Calcd. for $C_{14}H_{16}O_2$: C, 77.75; H, 7.46. Found: C, 77.12; H, 7.49.

(*S*) (+)-3α-Hydroxy-4-methyl-4-phenylcyclohexanone ((*S*) (+)-**8a**)——A 0.3N KOH solution (1 ml, 0.30 mmole) was added to a solution of (*S*) (+)-**2a** ($[\alpha]_D^{20}$ +12.8° (c=0.972, EtOH)) (1.02 g, 5.0 mmole) in THF (10 ml) with stirring in an ice bath. The whole mixture was stirred at 5° overnight, then diluted with ether, and washed with satd. NaCl. After drying over anhyd. $MgSO_4$, filtration and evaporation *in vacuo* gave a pale yellow oil, which was submitted to column chromatography (silica gel, solvent ether: hexane 1: 1) to afford pure (*S*) (+)-**8a** as a pale yellow oil (948 mg, 93%), $[\alpha]_D^{20}$ +3.5° (c=2.082, EtOH). IR ν_{max}^{film} cm^{-1}: 3340 (OH), 1710 (CO). NMR (in CCl_4): 1.31 (3H, s, CH_3), 1.7—2.8 (6H, m, 3×CH_2), 3.25 (1H, s, OH), 4.45 (1H, m, CH), 7.0—7.6 (5H, m, C_6H_5). Mass: *m/e* 204 (M^+).

(*S*) (+)-3α-Hydroxy-4-methyl-4-(*p*-methoxyphenyl)cyclohexanone ((*S*) (+)-**8b**)——The same treatment of (*S*) (+)-**2b** ($[\alpha]_D^{20}$ +13.0° (c=2.012, EtOH)) (2.34 g, 0.010 mole) as that of (*S*) (+)-**2a** gave pure (*S*) (+)-**8b** as a colorless powder (2.11 g, 90%), mp 107—110°, $[\alpha]_D^{20}$ +2.5° (c=2.164, EtOH). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3340 (OH), 1700 (CO). NMR (in $CDCl_3$): 1.40 (3H, s, CH_3), 2.0—2.7 (6H, m, 3×CH_2), 2.20 (1H, s, OH), 3.89 (3H, s, OCH_3), 4.38 (1H, t, J=6 Hz, CH), 6.8—7.5 (4H, m, C_6H_4). *Anal.* Calcd. for $C_{14}H_{18}O_3$: C, 71.77; H, 7.74. Found: C, 71.58; H, 7.92.

(*S*) (+)-3-Hydroxy-4-methyl-4-phenylcyclohexanone Ethylene Ketal ((*S*) (+)-**9a**)——A mixture of (*S*) (+)-**8a** ($[\alpha]_D^{20}$ +3.5° (c=2.082, EtOH)) (746 mg, 3.7 mmole), ethylene glycol (1 ml, *ca.* 18 mmole) and *p*-toluenesulfonic acid monohydrate (7 mg, catalytic amount) in benzene (20 ml) was heated at reflux for 2 hr, using a Dean-stark apparatus to remove the water produced. After cooled, the solution was washed with water and dried over anhyd. $MgSO_4$. Filtration and evaporation *in vacuo* gave an oily residue, which was purified by column chromatography (silica gel, solvent ether: hexane 1: 1) to afford pure (*S*) (+)-**9a** as a pale yellow oil (816 mg, 90%), $[\alpha]_D^{20}$ +3.1° (c=1.824, EtOH). IR ν_{max}^{film} cm^{-1}: 3420 (OH). NMR (in $CDCl_3$): 1.23 (3H, s, CH), 1.5—2.8 (6H, m, 3×CH_2), 3.85 (4H, s, OCH_2CH_2O), 3.55 (1H, t, J=6 Hz, CH), 3.40 (1H, s, OH), 7.30 (5H, s, C_6H_5).

A small amount of (*R*)-**1a**[18] (30 mg, 4.4%) was also separated by the column chromatography attempted above, and was identified with the authentic (*R*) (+)-**1a** by spectral (IR) and chromatographic (TLC) comparisons.

(*S*) (+)-3α-Hydroxy-4-methyl-4-(*p*-methoxyphenyl)cyclohexanone Ethylene Ketal ((*S*) (+)-**9b**)——Similar treatment of (*S*) (+)-**8b** ($[\alpha]_D^{20}$ +2.5° (c=2.164, EtOH)) (4.76 g, 0.020 mole) to that of (*S*) (+)-**8a**, gave pure (*S*) (+)-**9b** as a pale yellow oil (4.87 g, 87%), $[\alpha]_D^{20}$ +2.4° (c=2.012, EtOH). IR ν_{max}^{film} cm^{-1}: 3440 (OH). NMR (in $CDCl_3$): 1.26 (3H, s, CH_3), 1.5—2.9 (6H, m, 3×CH_2), 3.40 (1H, s, OH), 3.72 (3H, s, OCH_3), 3.84 (4H, s, OCH_2CH_2O), 3.64 (1H, t, J=6 Hz, CH), 6.7—7.4 (4H, m, C_6H_4). Mass: *m/e* 278 (M^+).

A small amount of (*R*)-**1b**[18] (0.40 g, 9.3%) was similarly separated by the column chromatography and was identified with the authentic sample by spectral (IR) and chromatographic (TLC) comparisons.

***dl*-2,3-Epoxy-4-methyl-4-phenylcyclohexanone(*dl*-10a)**——A 4N NaOH solution (1 ml, 4.0 mmole) and 30% hydrogen peroxide (12 g, 0.11 mole) were added to a solution of *dl*-**1a**[6a] (9.3 g, 0.050 mole) in methanol (100 ml) with stirring at 0°. The mixture was kept standing in a freezer (−20°) for 70 hr, then was poured onto ice and extracted with ether. The combined ethereal extracts were washed with satd. NaCl, and dried over anhyd. $MgSO_4$. Filtration and evaporation *in vacuo* gave a pale yellow oil, which was submitted to fractional distillation to afford oily *dl*-**10a** as a diastereomeric mixture (8.65 g, 87%), bp 118—122° (1 mmHg). IR ν_{max}^{film} cm^{-1}: 1720 (CO). NMR (in CCl_4): 1.45, 1.54 (3H, doubled s, $C\underline{H}_3$), 2.0—2.5 (4H, m, $2\times C\underline{H}_2$), 3.19 (1H, d, J=5 Hz, $COC\underline{H}(O)-C\underline{H}$), 3.47, 3.49 (1H, doubled d, J=5 Hz, $COC\underline{H}(O)-CH$), 7.0—7.5 (5H, m, $C_6\underline{H}_5$). *Anal.* Calcd for $C_{13}H_{14}O_2$: C, 77.20; H, 6.98. Found: C, 77.26; H, 6.92.

(*S*) (−)-2,3-Epoxy-4-methyl-4-phenylcyclohexanone ((*S*) (−)-10a)——The same treatment of (*R*) (+)-**1a** ($[\alpha]_D^{20}$ +57.1° (*c*=1.220, EtOH)) (9.3 g, 0.050 mole) as that of *dl*-**1a** gave oily pure (*S*) (−)-**10a** as a diastereomeric mixture (7.92 g, 78%), bp 122—126° (2 mmHg), $[\alpha]_D^{20}$ −6.9° (*c*=1.542, EtOH). IR and NMR spectra of this oil were superimposable on those of *dl*-**10a** measured in the same states.

(*S*) (−)-2,3-Epoxy-4-methyl-4-(*p*-methoxyphenyl)cyclohexanone ((*S*) (−)-10b)——Treatment of (*R*) (+)-**1b** ($[\alpha]_D^{20}$ +69.5° (*c*=1.134, EtOH)) (4.7 g, 0.020 mole) in a similar manner to the case for (*R*) (+)-**1a** gave oily pure (*S*) (−)-**10b** as a diastereomeric mixture (4.7 g, 94%), bp 148° (0.05 mmHg), $[\alpha]_D^{20}$ −11.1° (*c*=1.184, EtOH). IR ν_{max}^{film} cm^{-1}: 1720 (CO). NMR (in CCl_4): 1.39, 1.50 (3H, doubled s, $C\underline{H}_3$), 1.6—2.4 (4H, m, $2\times C\underline{H}_2$), 3.1—3.5 (2H, m, $COC\underline{H}(O)-C\underline{H}$), 3.70 (3H, s, $OC\underline{H}_3$), 6.6—7.3 (4H, m, $C_6\underline{H}_4$). *Anal.* Calcd. for $C_{14}H_{16}O_3$: C, 72.39; H, 6.94. Found: C, 72.29; H, 6.99.

***dl*-2,3-Epoxy-4-methyl-4-phenylcyclohexanone Ethylene Ketal (*dl*-11a)**——A mixture of *dl*-**10a** (0.81 g, 4.0 mmole), ethylene glycol (1 ml, *ca.* 18 mmole), and *p*-toluenesulfonic acid monohydrate (10 mg, catalytic amount) in benzene (30 ml) was refluxed for 4 hr, using a Dean-Stark apparatus to remove the water produced. After cooled, the solution was washed with satd. NaCl, and dried over anhyd. Na_2SO_4. Filtration and evaporation *in vacuo* gave oily pure *dl*-**11a** as a diastereomeric mixture (9.6 g, 96%). NMR (in CCl_4): 1.35, 1.43 (3H, doubled s, $C\underline{H}_3$), 1.3—1.9 (4H, m, $2\times C\underline{H}_2$), 2.9—3.1 (2H, m, $C\underline{H}(O)-C\underline{H}$), 3.95 (4H, s, $OC\underline{H}_2C\underline{H}_2O$), 7.0—7.5 (5H, m, $C_6\underline{H}_5$). Mass: *m/e* 246 (M^+). TLC analysis of this oil showed a singlet spot whose *Rf* value was *ca.* 0.5 (silica gel, solvent ether: hexane 1: 2).

(*S*) (+)-2,3-Epoxy-4-methyl-4-phenylcyclohexanone Ethylene Ketal ((*S*) (+)-11a)——The same treatment of (*S*) (−)-**10a** ($[\alpha]_D^{20}$ −6.9° (*c*=1.542, EtOH)) (10.0 g, 0.050 mole) as that of *dl*-**10a** afforded oily pure (*S*) (−)-**10a** as a diastereomeric mixture (11.2 g, 93%), $[\alpha]_D^{20}$ +12.8° (*c*=2.102, EtOH). Spectral (IR and NMR) and chromatographic (TLC) behavior of this oil were identical with those of *dl*-**11a** recorded in the same states.

(*S*) (+)-2,3-Epoxy-4-methyl-4-(*p*-methoxyphenyl)cyclohexanone Ethylene Ketal ((*S*) (+)-11b)——Treatment of (*S*) (−)-**10b** ($[\alpha]_D^{20}$ −11.1° (*c*=1.184, EtOH)) (4.64 g, 0.020 mole) in a similar manner to the case for *dl*-**10a**, followed by purification with column chromatography (silica gel, solvent ether: hexane 1: 1), gave oily pure (*S*) (+)-**11b** as a mixture of diastereoisomers (3.0 g, 54%), $[\alpha]_D^{20}$ +18.0° (*c*=1.766, EtOH). NMR (in CCl_4): 1.30, 1.31 (3H, doubled s, $C\underline{H}_3$), 1.5—1.85 (4H, m, $2\times C\underline{H}_2$), 3.00—3.25 (2H, m, $C\underline{H}(O)-C\underline{H}$), 3.62, 3.63 (3H, doubled s, $OC\underline{H}_3$), 3.85 (4H, s, $OC\underline{H}_2C\underline{H}_2O$), 6.64—7.33 (4H, m, $C_6\underline{H}_4$). Mass: *m/e* 276 (M^+), 261.

***dl*-3β-Hydroxy-4-methyl-4-phenylcyclohexanone Ethylene Ketal (*dl*-12a) and *dl*-2α-Hydroxy-4-methyl-4-phenylcyclohexanone Ethylene Ketal (*dl*-13a)**——A solution of *dl*-**11a** (2.0 g, 8.1 mmole) in dioxane (10 ml) was gradually added to a suspension of LAH (0.3 g, 8.0 mmole) in dioxane (15 ml) at 0°. After the whole mixture was heated at reflux for 5 hr with stirring, the formed metal complex was decomposed by the successive addition of water (0.3 ml), 15% NaOH (0.3 ml), and water (0.3 ml) under ice-cooling. The white solid precipitated, was filtered and washed with ether. The combined filtrates and washings were evaporated *in vacuo* to give an oily residue, which was purified by column chromatography (silica gel, solvent ether: hexane 1: 2) to afford pure *dl*-**12a** as a colorless oil (1.05 g, 52%). IR ν_{max}^{film} cm^{-1}: 3470 (OH). NMR (in $CDCl_3$): 1.23 (3H, s, $C\underline{H}_3$), 1.4—2.1 (6H, m, $3\times C\underline{H}_2$), 2.39 (1H, s, $O\underline{H}$), 3.82 (4H, s, $OC\underline{H}_2C\underline{H}_2O$), 4.00 (1H, t, J=6 Hz, $C\underline{H}$), 7.0—7.4 (5H, m, $C_6\underline{H}_5$). These spectral properties are clearly different from those of (*S*) (+)-**9a** measured in the same states.

Further elution of the column with the same solvent system afforded *dl*-**13a** as a colorless solid (0.35 g, 17%). Recrystallization from isopropyl ether gave pure *dl*-**13a** as colorless prisms, mp 107—108°. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3395 (OH). NMR (in $CDCl_3$): 1.18 (3H, s, $C\underline{H}_3$), 1.3—1.8 (4H, m, $2\times C\underline{H}_2$), 2.0—2.5 (2H, m, $C\underline{H}_2$), 1.98 (1H, s, $O\underline{H}$), 4.0 (4H, m, $OC\underline{H}_2C\underline{H}_2O$), 3.42 (1H, m, $C\underline{H}$), 7.0—7.4 (5H, m, $C_6\underline{H}_5$). *Anal.* Calcd. for $C_{15}H_{20}O_3$: C, 72.55; H, 8.12. Found: C, 72.19; H, 8.35. TLC analyses of these two kinds of alcohols respectively showed single spots whose *Rf* value were *ca.* 0.4 (*dl*-**12a**) and *ca.* 0.35 (*dl*-**13a**) (silica gel, solvent ether: hexane 2: 1).

(*S*) (+)-3β-Hydroxy-4-methyl-4-phenylcyclohexanone Ethylene Ketal ((*S*) (+)-12a) and (*R*) (−)-2α-Hydroxy-4-methyl-4-phenylcyclohexanone Ethylene Ketal ((*R*) (−)-13a)——The same treatment of (*S*) (+)-**11a**

($[\alpha]_D^{20}$ +12.8° (c=2.102, EtOH)) (19.6 g, 0.080 mole) as that of *dl*-**11a** gave pure (*S*) (+)-**12a** as an oil (10.3 g, 52%), $[\alpha]_D^{20}$ +5.8° (c=2.034, EtOH), and pure (*R*) (−)-**13a** as an oil (3.2 g, 16%), $[\alpha]_D^{20}$ −13.5° (c=1.234, EtOH). Spectral (IR and NMR) and chromatographic (TLC) behavior of these alcohols were respectively identical with those of the corresponding racemic compounds measured in the same states.

(*S*) (+)-3β-Hydroxy-4-methyl-4-(*p*-methoxyphenyl)cyclohexanone Ethylene Ketal ((*S*) (+)-12b) and (*R*) (−)-2α-Hydroxy-4-methyl-4-(*p*-methoxyphenyl)cyclohexanone Ethylene Ketal ((*R*) (−)-13b)——Treatment of (*S*) (+)-**11b** ($[\alpha]_D^{20}$ +18.0° (c=1.766, EtOH)) (5.52 g, 0.020 mole) in a similar fashion to the case for *dl*-**11a** afforded pure (*S*) (+)-**12b** as a colorless oil (3.05 g, 55%), $[\alpha]_D^{20}$ +13.8° (c=1.120, EtOH), and pure (*R*) (−)-**13b** as a colorless oil (0.95 g, 17%), $[\alpha]_D^{20}$ −19.4° (c=0.948, EtOH). Spectral data of these compounds are as followes. (*S*) (+)-**12b**: IR ν_{max}^{film} cm^{-1}: 3400 (OH). NMR (in $CDCl_3$): 1.27 (3H, s, C$\underline{H}_3$), 2.35 (1H, s, O$\underline{H}$), 1.5—2.4 (6H, m, 3×C$\underline{H}_2$), 3.69 (3H, s, OC$\underline{H}_3$), 3.84 (4H, s, OC$\underline{H}_2$C$\underline{H}_2$O), 4.05 (1H, t, J=6 Hz, C$\underline{H}$), 6.7—7.5 (4H, m, $C_6\underline{H}_4$). Mass: *m/e* 278 (M^+), 263. These spectral properties are clearly different from those of (*S*) (+)-**9b** measured in the same states. (*S*) (−)-**13b**: IR ν_{max}^{film} cm^{-1}: 3400 (OH). NMR (in $CDCl_3$): 1.21 (3H, s, C$\underline{H}_3$), 1.5—1.8 (4H, m, 2×C$\underline{H}_2$), 2.2—2.5 (2H, m, C$\underline{H}_2$), 2.07 (1H, s, O$\underline{H}$), 3.72 (3H, s, OC$\underline{H}_3$), 3.46 (1H, doubled d, J=7 and 1.5 Hz, C$\underline{H}$), 4.02 (4H, s, OC$\underline{H}_2$C$\underline{H}_2$O), 6.7—7.5 (4H, m, $C_6\underline{H}_4$). Mass: *m/e* 278 (M^+), 263.

***dl*-5,5-Ethylenedioxy-2-methyl-2-phenylcyclohexanone (*dl*-7a)**——*dl*-**7a** from *dl*-12a: 2.5M Jones reagent (8.8 ml, 0.022 mole) was added to a solution of *dl*-**12a** (4.96 g, 0.020 mole) in acetone (80 ml) under cooling in a CCl_4–dry ice bath, and the whole mixture was vigorously stirred at −20° for 1 hr. After isopropanol (3 ml) was added to the reaction mixture to quench the reaction, the whole was stirred until the red color of the mixture changed to green. Cold water was added to the reaction mixture, and the whole mixture was extracted with ether. The combined ethereal extracts were washed with water, then dried over anhyd. $MgSO_4$. Filtration and evaporation *in vacuo* gave a pale yellow oil, which was purified by column chromatography (silica gel, solvent ether: hexane 1: 3) to give pure *dl*-**7a** as a pale yellow oil (4.35 g, 88%). IR ν_{max}^{film} cm^{-1}: 1715 (CO). NMR (in CCl_4): 1.22 (3H, s, C$\underline{H}_3$), 1.62—2.45 (6H, m, 3×C$\underline{H}_2$), 3.82 (4H, s, OC$\underline{H}_2$C$\underline{H}_2$O), 7.0—7.3 (5H, m, $C_6\underline{H}_5$). Mass: *m/e* 246 (M^+), 204, 186.

(*S*)(−)-5,5-Ethylenedioxy-2-methyl-2-phenylcyclohexanone ((*S*) (−)-7a)——(*S*) (−)-**7a** from (*S*) (+)-**9a**: Similar treatment of (*S*) (+)-**9a** ($[\alpha]_D^{20}$ +3.1° (c=1.824, EtOH)) (2.48 g, 0.010 mole) to the case for *dl*-**12a** gave pure (*S*) (−)-**7a** as a pale yellow oil (2.15 g, 87%), $[\alpha]_D^{20}$ −59.8° (c=0.894, EtOH). Spectral (IR and NMR) and chromatographic (TLC) behavior of this oil were identical with those of *dl*-**7a** recorded in the same states.

(*S*) (−)-**7a** from (*S*) (+)-**12a**: The same treatment of (*S*) (+)-**12a** ($[\alpha]_D^{20}$ +5.7° (c=2.998, EtOH)) (10.0 g, 0.040 mole) as that of *dl*-**12a** afforded pure (*S*) (−)-**7a** as an oil (8.55 g, 86%), $[\alpha]_D^{20}$ −54.9° (c=1.824, EtOH). This sample was identified with that prepared from (*S*) (+)-**9a** by spectral (IR and NMR) and chromatographic (TLC) comparisons.

(*S*)(−)-5,5-Ethylenedioxy-2-methyl-2-(*p*-methoxyphenyl)cyclohexanone ((*S*) (−)-7b)——(*S*) (−)-**7b** from (*S*) (+)-**9b**: Similar treatment of (*S*) (+)-9b ($[\alpha]_D^{20}$ +2.4° (c=2.012, EtOH)) (2.00 g, 7.2 mmole) to the case for *dl*-**12a** gave pure (*S*) (−)-**7b** as a pale yellow oil (1.71 g, 86%), $[\alpha]_D^{20}$ −72.7° (c=1.326, EtOH), after purification by column chromatography (silica gel, solvent ether: hexane 1: 2). IR ν_{max}^{film} cm^{-1}: 1720 (CO). NMR (in CCl_4): 1.25 (3H, s, C$\underline{H}_3$), 1.75—2.70 (6H, m, 3×C$\underline{H}_2$), 3.72 (3H, s, OC$\underline{H}_3$), 3.84 (4H, s, OC$\underline{H}_2$C$\underline{H}_2$O), 6.7—7.2 (4H, m, $C_6\underline{H}_4$). Mass: *m/e* 276 (M^+), 248, 233, 204, 186.

(*S*) (−)-**7b** from (*S*) (+)-**12b**: The same treatment of (*S*) (+)-**12b** ($[\alpha]_D^{20}$ +13.8° (c=1.592, EtOH)) (2.78 g, 0.010 mole) as that of *dl*-**12a** afforded pure (*S*) (−)-**7b** as an oil (2.35 g, 85%), $[\alpha]_D^{20}$ −73.4° (c=1.446, EtOH). This sample was identified with that prepared from (*S*) (+)-**9b**, by spectral (IR and NMR) and chromatographic (TLC) comparisons.

(*S*) (+)-N,N-Dimethyl-2-(5,5-ethylenedioxy-1-hydroxy-2-methyl-2-phenylcyclohexyl)acetamide ((*S*) (+)-14aA and (*S*) (+)-14aB) and (*S*)(−)-3-(2-Hydroxyethoxy)-6-methyl-6-phenyl-2-cyclohexenone ((*S*) (−)-15a)——

a) Preparation of N,N-Dimethyl Lithioacetamide-DABCO Complex: A solution of N,N-dimethyl acetamide (3.48 g, 0.040 mole) in THF (40 ml) was added to a solution of lithium diisopropylamide (0.040 mole) in THF (40 ml) prepared from 1.5M butyllithium solution (hexane) (0.040 mole) and diisopropylamine (0.040 mole), with stirring at −70° under nitrogen atmosphere. After the mixture was stirred at −70° for 1 hr, DABCO (4.48 g, 0.040 mole) in THF (40 ml) was added to the cooled solution. The whole solution was further stirred at −70° under nitrogen atmosphere for 1.5 hr, and was directly used for the next reaction.

b) (*S*) (+)-**14aA**, (*S*) (+)-**14aB**, and (*S*) (−)-**15a** from (*S*) (−)-**7a**: A solution of N,N-dimethyl lithioacetamide-DABCO complex (0.040 mole) prepared above, was added to a solution of (*S*) (−)-**7a** ($[\alpha]_D^{20}$ −59.8° (c=0.894, EtOH)) (4.92 g, 0.020 mole) in THF (100 ml) with stirring at −25° under nitrogen atmosphere. After the stirring at the same temperature was continued for 3 hr, satd. NH_4Cl (20 ml) was added to the reaction mixture, and the organic phase was separated. The aqueous phase was extracted with ether, and the combined organic layers were washed with satd. NH_4Cl and satd. NaCl, then dried over anhyd. $MgSO_4$. Filtration and evaporation *in vacuo* gave a yellow oily residue which was purified by column chromatography (silica gel, solvent ether) to afford (*S*) (+)-**14aA** (4.9 g, 74%), (*S*) (+)-**14aB** (0.68 g, 10%) as pale yellow oils, and (*S*) (−)-**15a** (0.35 g, 7.1%) as a yellow oil.

(*S*) (+)-**14aA**: $[\alpha]_D^{20}$ +27.9° (c=0.924, EtOH). This oily amide (4.9 g) was dissolved in a small amount of ether, and the ethereal solution was kept standing in a freezer (−20°). A precipitate was collected by filtration and recrystallized from a mixture of ether and hexane to give pure *dl*-**14aA** as colorless prisms (2.51

g), mp 149—150°, $[\alpha]_D^{20}$ 0° (*c*=*ca.* 3, EtOH). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3490 (OH), 1623 (CON). NMR (in $CDCl_3$): 1.47 (3H, s, CH_3), 1.5—2.9 (8H, m, $4\times CH_2$), 2.38, 2.75 (6H, doubled s, $N(CH_3)_2$), 4.30 (1H, s, OH), 3.96 (4H, s, OCH_2CH_2O), 7.1—7.7 (5H, m, C_6H_5). Mass: *m/e* 333 (M^+), 215, 204, 171. *Anal.* Calcd. for $C_{19}H_{27}O_4N$: C, 68.44; H, 8.16; N, 4.20. Found: C, 68.38; H, 8.25; N, 4.22. The combined mother liquors from the recrystallizations attempted above, were evaporated *in vacuo* to afford optically active (*S*) (+)-**14aA** as a pale yellow oil (2.37 g), $[\alpha]_D^{20}$ +57.3° (*c*=0.894, EtOH). Spectral (IR, NMR, and Mass) and chromatographic (TLC) behavior of this oil were completely identical with those of *dl*-**14aA** recorded in the same states.

(*S*) (+)-**14aB**: $[\alpha]_D^{20}$ +15.1° (*c*=3.378, EtOH). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3330 (OH), 1614 (CON). NMR (in $CDCl_3$): 1.43 (3H, s, CH_3), 1.5—2.6 (8H, m, $4\times CH_2$), 2.84, 2.89 (6H, doubled s, $N(CH_3)_2$), 3.86 (4H, s, OCH_2CH_2O), 6.20 (1H, br s, OH), 7.1—7.7 (5H, m, C_6H_5). Mass: *m/e* 333 (M^+), 215, 204, 171, 129, 118, 99.

(*S*) (−)-**15a**: $[\alpha]_D^{20}$ −153.2° (*c*=0.724, EtOH). UV $\lambda_{max}^{95\%\ EtOH}$ nm (log ε): 253 (4.17). IR ν_{max}^{film} cm^{-1}: 3300 (OH), 1600 (1,3-diketone enol ether). NMR (in CCl_4): 1.34 (3H, s, CH_3), 1.7—2.5 (4H, m, $2\times CH_2$), 3.14 (1H, s, OH), 3.80 (4H, s, OCH_2CH_2O), 5.37 (1H, s, =CH–), 7.16 (5H, s, C_6H_5). Mass: *m/e* 246 (M^+), 218, 204. These spectral data were identical with those of the racemic compound measured in the same states.[24]

(*S*) (+)-N,N-Dimethyl-2-[5,5-ethylenedioxy-1-hydroxy-2-methyl-2-(*p*-methoxyphenyl)cyclohexyl]acetamide ((*S*) (+)-14bA and (*S*) (+)-14bB), (*S*)-3-(2-Hydroxyethoxy)-6-methyl-6-(*p*-methoxyphenyl)-2-cyclohexenone ((*S*)-15b), and (*S*) (−)-N,N-Dimethyl-2-[6-methyl-6-(*p*-methoxyphenyl)-3-oxocyclohexenyl]acetamide ((*S*) (−)-16b)——Similar treatment of (*S*) (−)-**7b** ($[\alpha]_D^{20}$ −72.7° (*c*=1.326, EtOH)) (1.10 g, 4.0 mmole) with N,N-dimethyl lithioacetamide-DABCO complex (8.0 mmole) prepared above, to that of (*S*) (−)-**7a** afforded the crude reaction product as a yellow oil after evaporation of the organic extracts. The crude product was separated by column chromatography (silica gel, solvent ether: ethyl acetate 5: 1), to give four kinds of oily products: (*S*) (+)-**14bA** (778 mg, 54%), (*S*) (+)-**14bB** (113 mg, 7.8%), (*S*)-**15b** (56 mg, 5.1%), and (*S*) (−)-**16b** (155 mg, 13%).

(*S*) (+)-**14bA**: $[\alpha]_D^{20}$ +25.3° (*c*=3.646, EtOH). The optical activity of (*S*) (+)-**14bA** (778 mg) thus obtained, was increased by the same procedure as that for (*S*) (+)-**14aA**. *dl*-**14bA** (354 mg) was obtained as colorless prisms, and evaporation of the combined mother liquors from the recrystallization afforded (*S*) (+)-**14bA** (269 mg) as a colorless oil. *dl*-**14bA**: mp 147—148°, $[\alpha]_D^{20}$ 0° (*c*=*ca.* 3, EtOH). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3585 (OH), 1623 (CON). NMR (in $CDCl_3$): 1.39 (3H, s, CH_3), 1.7—2.6 (8H, m, $4\times CH_2$), 2.60, 2.99 (6H, doubled s, $N(CH_3)_2$), 3.72 (3H, s, OCH_3), 3.93 (4H, s, OCH_2CH_2O), 4.35 (1H, s, OH), 6.6—7.6 (4H, m, C_6H_4). Mass: *m/e* 363 (M^+), 215, 148, 133. *Anal.* Calcd. for $C_{20}H_{29}O_5N$: C, 66.09; H, 8.04; N, 3.85. Found: C, 65.88; H, 8.02; N, 3.70. (*S*) (+)-**14bA**: $[\alpha]_D^{20}$ +62.3° (*c*=1.368, EtOH). Spectral (IR, NMR, and Mass) and chromatographic (TLC) properties of this oil were completely identical with those of the racemic compound recorded in the same states.

(*S*) (+)-**14bB**: $[\alpha]_D^{20}$ +16.4° (*c*=2.296, EtOH). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3320 (OH), 1610 (CON). NMR (in $CDCl_3$): 1.40 (3H, s, CH_3), 1.5—2.5 (8H, m, $4\times CH_2$), 2.75, 2.82 (6H, doubled s, $N(CH_3)_2$), 3.70 (3H, s, OCH_3), 3.82 (4H, s, OCH_2CH_2O), 6.15 (1H, s, OH), 6.6—7.6 (4H, m, C_6H_4). Mass: *m/e* 363 (M^+), 276, 234, 215.

(*S*)-**15b**:[18] IR ν_{max}^{film} cm^{-1}: 3400 (OH), 1610 (1,3-diketone enol ether). NMR (in CCl_4): 1.37 (3H, s, CH_3), 1.9—2.6 (4H, m, $2\times CH_2$), 3.73 (3H, s, OCH_3), 3.83 (4H, s, OCH_2CH_2O), 5.38 (1H, s, =CH–), 6.7—7.2 (4H, m, C_6H_4). Mass: *m/e* 276 (M^+), 248, 204, 186, 148.

(*S*) (−)-**16b**: $[\alpha]_D^{20}$ −13.3° (*c*=0.662, EtOH). IR ν_{max}^{film} cm^{-1}: 1670 (shoulder, C–CH=CO), 1645 (CON). NMR (in CCl_4): 1.33 (3H, s, CH_3), 2.1—2.7 (4H, m, $2\times CH_2$), 2.81, 2.85 (6H, doubled s, $N(CH_3)_2$), 3.14 (2H, s, CH_2CON), 3.75 (3H, s, OCH_3), 5.90 (1H, s, COCH=), 6.7—7.3 (4H, m, C_6H_4).

***dl*-3-Hydroxy-3-(2-hydroxyethyl)-4-methyl-4-phenylcyclohexanone Ethylene Ketal (*dl*-17a)**——A benzene solution of Vitride[35] (70% or 3.6M solution) (0.25 ml, 0.90 mmole) was diluted with ether (0.25 ml), then was added to a suspension of *dl*-**14aA**[36] (270 mg, 0.81 mmole) in ether (1.6 ml) at −20°. The whole mixture was stirred at the same temperature for 2 hr, and then diluted with ether (10 ml) and satd. NH_4Cl (0.3 ml). The formed precipitate was removed by filtration through a pad of celite. The filtrate was washed with satd. NH_4Cl and satd. NaCl, then dried over anhyd. $MgSO_4$. Filtration and evaporation *in vacuo* gave the oily crude aldehyde, which was further reduced with Vitride according to the same procedure as that cited above, affording crude *dl*-**17a** as a colorless oil after evaporation of the ethereal filtrate. This was purified by column chromatography (silica gel, solvent ether: hexane 2: 1) to give pure *dl*-**17a** as a colorless oil (171 mg, 73%). IR ν_{max}^{film} cm^{-1}: 3430 (OH). NMR (in $CDCl_3$): 1.35 (3H, s, CH_3), 1.5—3.0 (8H, m, $4\times CH_2$), 3.3—3.8 (2H, m, CH_2OH), 3.10 (1H, br s, OH), 4.40 (1H, s, OH), 3.94 (4H, s, OCH_2CH_2O), 7.1—7.7 (5H, m, C_6H_5). Mass: *m/e* 292 (M^+), 230, 204.

(*S*)(+)-3-Hydroxy-3-(2-hydroxyethyl)-4-methyl-4-phenylcyclohexanone Ethylene Ketal ((*S*) (+)-17a)——The same treatment of (*S*) (+)-**14aA** ($[\alpha]_D^{20}$ +57.3° (*c*=0.894, EtOH)) (333 mg, 1.0 mmole) as that of *dl*-**14aA** gave pure (*S*) (+)-**17a** as a pale yellow oil (210 mg, 72%), $[\alpha]_D^{20}$ +48.7° (*c*=1.902, EtOH). Spectral (IR and

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36) This was also prepared from *dl*-**7a** according to the same experimental procedure as that described for (*S*) (−)-**7a**.

NMR) and chromatographic (TLC) behavior of this oil were identical with those of the racemic compound recorded in the same states.

(*S*)(+)-3-Hydroxy-3-(2-hydroxyethyl)-4-methyl-4-(*p*-methoxyphenyl)cyclohexanone Ethylene Ketal ((*S*)(+)-17b)——Similar treatment of (*S*) (+)-**14bA** ($[\alpha]_D^{20}$ +62.3° (c=1.368, EtOH)) (363 mg, 1.0 mmole) as the case for *dl*-**14aA**, afforded crude (*S*) (+)-**17b**, which was purified by column chromatography (silica gel, solvent ether: ethyl acetate 5: 1) to give pure (*S*) (+)-**17b** as a pale yellow oil (210 mg, 65%), $[\alpha]_D^{20}$ +51.4° (c=0.846, EtOH). IR ν_{max}^{film} cm^{-1}: 3440 (OH). NMR (in $CDCl_3$): 1.36 (3H, s, C$\underline{H}_3$), 1.40—3.0 (8H, m, 4×C$\underline{H}_2$), 3.4—3.7 (2H, m, C$\underline{H}_2$OH), 3.31 (1H, s, O$\underline{H}$), 4.35 (1H, s, O$\underline{H}$), 3.70 (3H, s, OC$\underline{H}_3$), 3.90 (4H, s, OC$\underline{H}_2$C$\underline{H}_2$O), 6.7—7.5 (4H, m, $C_6\underline{H}_4$). Mass: *m/e* 322 (M^+), 307.

***dl*-3-(2-Hydroxyethyl)-4-methyl-4-phenyl-2-cyclohexenone (*dl*-18a)**——A solution of *dl*-**17a** (292 mg, 1.0 mmole) in a mixture of ethanol (5 ml) and 10% HCl (2 ml) was heated at reflux for 20 min. The whole solution was concentrated *in vacuo*, giving a residue which was diluted with benzene. The benzene solution was washed with satd. $NaHCO_3$ and satd. NaCl, then dried over anhyd. $MgSO_4$. Filtration and evaporation *in vacuo* gave an orange oil, which was purified by column chromatography (silica gel, solvent ether) to afford pure *dl*-18a as a pale yellow oil (200 mg, 87%). IR ν_{max}^{film} cm^{-1}: 3400 (OH), 1680 (C–CH–CO). NMR (in $CDCl_3$): 1.50 (3H, s, C$\underline{H}_3$), 1.85—2.3 (6H, m, 3×C$\underline{H}_2$), 3.62 (2H, t, J=6 Hz, C$\underline{H}_2$OH), 3.60 (1H, s, O$\underline{H}$), 6.06 (1H, s, =C$\underline{H}$–), 7.20 (5H, s, $C_6\underline{H}_5$).

(*S*) (+)-3-(2-Hydroxyethyl)-4-methyl-4-phenyl-2-cyclohexenone ((*S*) (+)-18a)——The same treatment of (*S*) (+)-**17a** ($[\alpha]_D^{20}$ +34.3° (c=1.252, EtOH))[27] (292 mg, 1.0 mmole) as that of *dl*-**17a** gave pure (*S*) (+)-**18a** as a pale yellow oil (196 mg, 85%), $[\alpha]_D^{20}$ +104.4° (c=0.900, EtOH). Spectral (IR and NMR) and chromatographic (TLC) behavior of this oil were identical with those of the racemic compound recorded in the same states.

***dl*-4a-Methyl-4,4a,9,10-tetrahydro-2(3H)-phenanthrone (*dl*-6a)**——a) Authentic *dl*-**6a**: This compound was prepared from 1-methyl-β-tetralone[37] by the reaction with MVK in a mixture of aqueous KOH and methanol, according to the reported method.[38] *dl*-**6a** thus obtained, showed mp 88—90° (recrystallized from petr. ether) (lit.,[39a] mp 87—88°; lit.,[39b] mp 89—90°). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1675 (C=CH–CO). NMR (in CCl_4): 1.52 (3H, s, C$\underline{H}_3$), 2.05—3.07 (8H, m, 8×C$\underline{H}_2$), 5.72 (1H, s, =C$\underline{H}$–), 6.82—7.30 (4H, m, $C_6\underline{H}_4$). Mass: *m/e* 212 (M^+), 197, 184, 170, 169.

b) *dl*-**6a** from *dl*-**18a**: PPA prepared from phosphorous pentoxide (3 g) and 85% phosphoric acid (2 ml),[40] was added to a solution of *dl*-**18a** (161 mg, 0.70 mmole) in benzene (2 ml) at 80° with vigorous stirring. The whole mixture was stirred at the same temperature for 1 hr, then was diluted with ice-water. The aqueous solution was extracted with benzene, and the combined benzene extracts were washed with satd. $NaHCO_3$ and satd. NaCl. After drying over anhyd. $MgSO_4$, filtration and evaporation *in vacuo*, followed by purification with column chromatography (silica gel, solvent ether: hexane 1: 3), gave pure *dl*-**6a** as a crystalline solid (70 mg, 47%). Recrystallization from petr. ether gave completely pure *dl*-**6a** as colorless prisms, mp 88.5—89°. This sample was identified with the authentic sample by spectral (IR and NMR) and chromatographic (TLC) comparisons.

(*R*) (−)-4a-Methyl-4,4a,9,10-tetrahydro-2(3H)-phenanthrone ((*R*) (−)-6a)——a) (*R*) (−)-**6a** from (*R*) (+)-**18a**: The same treatment of (*S*) (+)-**18a** ($[\alpha]_D^{20}$ +104.4° (c=0.900, EtOH)) (136 mg, 0.60 mmole) as that of *dl*-**18a** gave pure (*R*) (−)-**6a** as a colorless oil (53 mg, 42%), $[\alpha]_D^{27}$ −217° (c=0.790, 95% EtOH). The optical purity of this oil could be calculated as 65% since optically pure (*R*) (−)-**6a** was reported to show $[\alpha]_D^{27}$ −332° (c=1, 95% EtOH).[29] This sample showed the identical spectral (IR and NMR) and chromatographic (TLC) behavior with those of *dl*-**6a**.

b) (*R*) (−)-**6a** from (*S*) (+)-**17a**: Treatment of (*S*) (+)-**17a** ($[\alpha]_D^{20}$ +48.7° (c=1.902, EtOH)) (220 mg, 0.75 mmole) in a similar manner to the case for *dl*-**18a**, gave pure (*R*) (−)-**6a** as a colorless oil (103 mg, 64%), $[\alpha]_D^{27}$ −282° (c=0.906, 95% EtOH). The optical purity of this sample could be similarly calculated as 85%.[29] Spectral (IR and NMR) and chromatographic (TLC) properties of this compound were completely identical with those of *dl*-**6a** recorded in the same states.

(*R*) (−)-7-Methoxy-4a-methyl-4,4a,9,10-tetrahydro-2(3H)-phenanthrone ((*R*) (−)-6b)——(*R*) (−)-**6b** from (*S*) (+)-**17b**: Treatment of (*S*) (+)-**17b** ($[\alpha]_D^{20}$ +51.4° (c=0.846, EtOH)) (177 mg, 0.55 mmole) in a similar fashion to the case for *dl*-**18a**, followed by purification with column chromatography (silica gel, solvent ether: hexane 1: 4), gave pure (*R*) (−)-**6b** as a pale yellow oil (18.5 mg, 14%), $[\alpha]_D^{20}$ −223° (c=0.370, EtOH).[31]

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IR ν_{max}^{film} cm^{-1}: 1665 (C=CH–CO). NMR (in CCl_4): 1.48 (3H, s, C<u>H</u>$_3$), 1.9—3.2 (8H, m, 4×C<u>H</u>$_2$), 3.70 (3H, s, OC<u>H</u>$_3$), 5.74 (1H, s, =C<u>H</u>–), 6.4—7.1 (3H, m, C_6<u>H</u>$_3$). Mass: *m/e* 242 (M^+), 227, 199, 171.

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