Chem. Pharm. Bull.
31(3) 837—851 (1983)

Asymmetric Reduction of Various Types of Ketones with Lithium Aluminum Hydride partially decomposed with (−)-*N*-Methylephedrine and *N*-Ethylaniline[1]

Norihiko Tanno and Shiro Terashima*

Faculty of Pharmaceutical Sciences, University of Tokyo, 7-3-1, Hongo, Bunkyo-ku, Tokyo 113, Japan

(Received July 9, 1982)

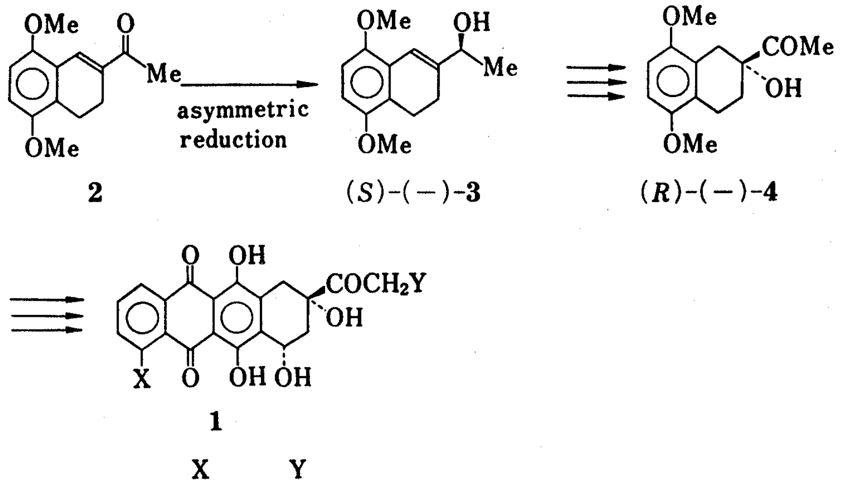
The asymmetric reduction of open chain enones to the corresponding optically active allylic alcohols was achieved in higher chemical (92—100%) and optical (78—98% e.e.) yields than those for cyclic enones (58—88% chemical and 34—58% optical yields). The observed high optical yields for optically active allylic alcohols can be explained on the assumption that, unlike cyclic enones in which the double bonds are fixed in *s-trans* conformation, open chain enones can be reduced in their *s-cis* conformations. An optically active propargylic alcohol was similarly produced from an ynone in 88% chemical and 76% optical yields by means of the present asymmetric reduction.

When the same asymmetric reduction was applied to simple aromatic and aliphatic ketones by using 1.8 eq of the chiral reducing agent, the corresponding optically active alcohols were obtained in 88—100% chemical and 51—90% optical yields (for aromatic ketones) and in 78—98% chemical and 0—67% optical yields (for aliphatic ketones).

On the basis of the results obtained in this and the preceding paper, a possible structure of the exploited chiral reducing agent is proposed and the transition states for the asymmetric reduction are discussed.

Keywords——asymmetric reduction; modified lithium aluminum hydride; open chain enone; open chain ynone; cyclic enone; optically active allylic alcohol; aromatic ketone; aliphatic ketone; optically active secondary alcohol; *s-cis* conformation; structure of chiral metal hydride; transition state of asymmetric reduction

In the preceding paper,[2] we reported the successful asymmetric synthesis of optically active anthracyclinones (**1**), the aglycones of anthracycline antibiotics, which are currently attracting much attention because of their promising anticancer activities. Thus, the novel chiral hydride originally prepared by partially decomposing lithium aluminum hydride (LAH) with (1*R*, 2*S*)-(−)-*N*-methylephedrine ((−)-*N*-methylephedrine) (1.0 equivalent (eq)) and



2 (*S*)-(−)-**3** (*R*)-(−)-**4**

1

	X	Y
a :	OMe	OH
b :	OMe	H
c :	H	OH
d :	H	H

N-ethylaniline (2.0 eq), was found to reduce the α,β-unsaturated ketone (**2**), giving the allylic alcohol ((*S*)-(−)-**3**) in high chemical (100%) and optical (92% e.e.) yields under the optimized conditions. Further synthetic operations gave the optically pure key intermediate ((*R*)-(−)-**4**) for anthracyclinone synthesis, from which optically pure (+)-4-demethoxyadriamycinone ((+)-**1c**) and (+)-4-demethoxydaunomycinone ((+)-**1d**), important anthracyclinones from the viewpoint of developing improved anticancer agents, were actually synthesized.[2]

It is noteworthy that, from various points of view, such as high chemical and optical yields, operational simplicity (no chromatographic separation), use of readily available (−)-*N*-methylephedrine as a chiral source, and efficient recovery of the chiral source and the additive for reuse (simple extractive isolation and distillation), the asymmetric reduction of **2** to (*S*)-(−)-**3** appears to fulfill the criteria proposed for practical asymmetric synthesis.[3,4]

Since asymmetric reduction of achiral ketones has been of increasing interest in recent years, and high optical yields have been realized using LAH partially decomposed with various chiral sources as reducing agents,[5-9] further examination of the novel chiral hydride developed by us was carried out by employing various structural types of achiral ketones as reduction substrates. These studies led us to explore the general applicability of the present reducing and we propose a possible structure for the chiral hydride and discuss the transition agent, states for the asymmetric reduction.

A. Asymmetric Reduction of Various α,β-Unsaturated Ketones by the Present Chiral Reducing Agent

The previous studies have shown that the present chiral reducing agent is quite effective in the asymmetric reduction of **2**,[2] and thus the applicability of the chiral hydride to the asymmetric reduction of α,β-unsaturated ketones (enones) was further studied by selecting benzalacetone (**5**), having a more general structure than **2**, as a reduction substrate. As shown in Table I, when LAH partially decomposed with (*S*)-(+)-2-(anilinomethyl)pyrrolidine[8] or with

Table I. Asymmetric Reduction of Benzalacetone (**5**) with Various Types of Chiral Reducing Agents[a]

5 (*S*)-(−)-**6**

Run	Chiral reducing agent (molar ratio to **5**) LAH: chiral source[b]: additive[c]	Reaction conditions Temp. (°C)	Time (h)	(*S*)-(−)-4-Phenyl-3(*E*)-buten-2-ol ((*S*)-(−)-**6**) Chemical yield(%)[d]	$[\alpha]^{D}_{20}$(°) (*c*, $CHCl_3$)	Optical yield(% e.e.)[e]
1	3.3:3.8 (A)[f]	−78	3	75	−7.9(3.83)	32(36)[g]
2	3.3:3.3 (E):6.6 (D)[h]	−20	3	7[i]	—[j]	—[j]
3	3.3:3.4 (E):6.8 (T)[k]	−78	3	98	−24.2(5.00)	98

a) All chiral reducing agents were prepared by partially decomposing LAH according to the reported methods.[2,7,8] Ether was used as a reaction solvent in all experiments.

b) A, (*S*)-(+)-2-(Anilinomethyl)pyrrolidine; E, (−)-*N*-methylephedrine.

c) D, 3,5-Dimethylphenol; T, *N*-ethylaniline.

d) Based on **5** after purification by preparative TLC (CH_2Cl_2).

e) Optically pure (*R*)-(+)-**6** gives $[\alpha]^{rt}_{D}+24.7°$ ($c=5.000$, $CHCl_3$). See ref. 10.

f) See ref. 8.

g) The value in parenthesis was corrected for the optical purity of (*S*)-(+)-2-(anilinomethyl)pyrrolidine (90% e.e.). See the experimental sections

h) See ref. 7.

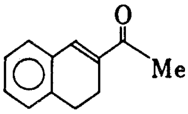
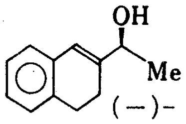
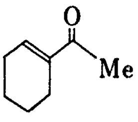
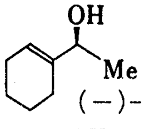
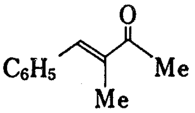
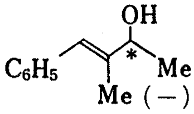
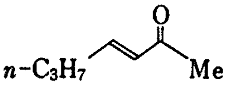
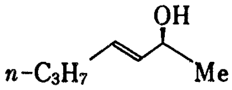
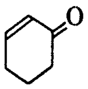
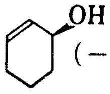
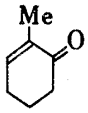
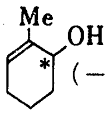
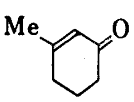
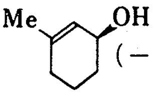
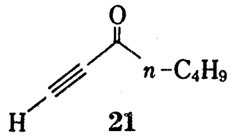
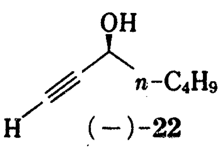
i) Recovery of the starting material (**5**) was 84%,

j) The optical rotation was not measured due to the low chemical yield.

k) See ref. 2.

a combination of (—)-*N*-methylephedrine and 3,5-dimethylphenol[7] was used to reduce **5**, 4-phenyl-3(*E*)-buten-2-ol (**6**) was obtained in 75 or 7% yield (Table I, runs 1, 2). Measurement of the optical rotation of **6** obtained with the former reagent showed that the asymmetric reduction afforded a 36% optical yield of (*S*)-(—)-**6** (corrected for the optical purity of the chiral source).[10] On the other hand, the use of our novel chiral hydride was found to give (*S*)-(—)-**6**

TABLE II. Asymmetric Reduction of Various α,β-Unsaturated Ketones by Lithium Aluminum Hydride partially decomposed with (—)-*N*-Methylephedrine and *N*-Ethylaniline[a]

Run	α,β-Unsaturated ketone	Optically active allylic or propargylic alcohol			
		Structure	Chemical yield(%)[b]	Optical yield(% e.e.)	Absolute configuration
1	 **7**	 (−)- **8**	100	>90[c]	(*S*)[d]
2	 **9**	 (−)-**10**	92	78[e]	(*S*)[e]
3	 **11**	 (−)-**12**	100	>90[c]	—[f]
4	 **13**	 (−)-**14**	92	88[e]	(*S*)[e]
5	 **15**	 (−)-**16**	58	45[g]	(*S*)[g]
6	 **17**	 (−)-**18**	51	58[c]	—[f]
7	 **19**	 (−)-**20**	88	34[g]	(*S*)[g]
8	 **21**	 (−)-**22**	88	76[g]	(*S*)[g]

[a] All reactions were carried out using LAH (3.3 eq) partially decomposed with (—)-*N*-methylephedrine (3.4 eq) and *N*-ethylaniline (6.8 eq) in ether at —78°C for 3 h.

[b] Based on the α,β-unsaturated ketone after purification by column chromatography or preparative TLC (except for run 2) (see the experimental section).

[c] Determined by measuring the ^{1}H-NMR spectrum in the presence of tris[3-(heptafluoropropylhydroxymethylene)-*d*-camphorato]europium (III) (Eu(hfc)$_3$).

[d] Tentatively assigned by considering the result for the asymmetric reduction of **2**.[3]

[e] The optical yield and absolute configuration were determined by converting the reduction product to the corresponding saturated alcohol by catalytic hydrogenation (see the experimental section).

[f] The absolute configuration of this sample could not be determined owing to the lack of a reference compound.

[g] The optical yield and absolute configuration of this sample were determined by directly comparing the observed optical rotation with that reported (see the experimental section).

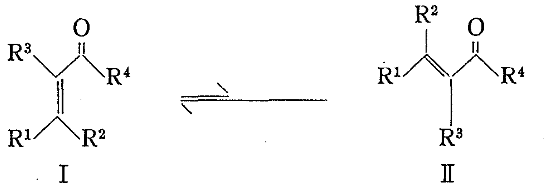
in 98% chemical and 98% optical yields (Table I, run 3).[10] These results clearly show that the chiral reagent originally developed by us is superior to various other reported chiral hydrides.[12]

Next, the asymmetric reductions of various structural types of enones were examined, as summarized in Table II.

Among the reduction substrates, the enones (**7**, **11**, and **13**) were synthesized from the corresponding acids by treatment with an excess of methyllithium in ether[13] in a manner similar to that used for the preparation of **2**.[2] The cyclohexenone derivatives (**17** and **19**) were prepared according to the reported methods.[14,15] As to the other enones (**9** and **15**), commercial samples were distilled, then directly subjected to the asymmetric reduction. The α,β-acetylenic ketone (ynone) (**21**) was obtained by oxidation of the commercially available propargylic alcohol with Jones reagent.[16]

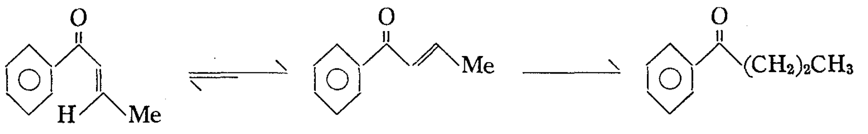
The results shown in Table II indicate that the open chain enones (**7**, **9**, **11**, and **13**) can be effectively reduced by the chiral hydride in high chemical and optical yields similarly to **2** and **5**. On the other hand, the asymmetric reductions of the cyclic enones (**15**, **17**, and **19**) proceed less stereoselectively than those of the open chain enones. The ynone (**21**) gave an optical yield slightly lower than the reported values.[7c,9c]

It seems reasonable to expect that an open chain enone can exist in an equilibrium of *s-trans-* and *s-cis*-conformers (I and II) in which the former (I) should predominate due to increased delocalization of the resonance system when steric hindrance is not excessive. The results summarized in Tables I and II can be rationalized by assuming that the open chain enones (**5**, **7**, **9**, **11**, and **13**) which can adopt *s-cis*-conformations due to C–CO bond rotation are successfully reduced in high chemical and optical yields and that the cyclic enones (**15**, **17**, and **19**) in which the enone systems are fixed in *s-trans*-conformations give poor chemical and optical yields in the asymmetric reductions. Accordingly, when open chain enones such as **2**, **5**, **7**, **9**, **11**, and **13** are subjected to asymmetric reduction by the use of our chiral hydride, highly stereoselective reduction should take place after conformational change from I to II in the transition state due to a possible electronic interaction between the enone system and the π-electrons involved in the modified chiral hydride. This explanation might also be compatible with the higher optical yield of (*S*)-(−)-**14** than of (*S*)-(−)-**20**, since electronic and steric effects of the parent enone (**13**) clearly differ from those of the cyclic enone (**19**) in the *s-cis*-conformation.



I II

When 1-phenyl-2(*E*)-buten-1-one (**23**), a structural isomer of **5** which may be preferentially present in the *s-cis*-conformation (**23**II) due to steric interaction between the phenyl group and the C_2-hydrogen, was subjected to the asymmetric reduction, *n*-butyrophenone (**24**) was produced as a sole reduction product in 86% yield. This shows that a subtle change in the balance of electronic and steric effects between two substituents of the ketonic group might affect the mode of interaction of the enone system with the chiral hydride.



I **23** II **24**

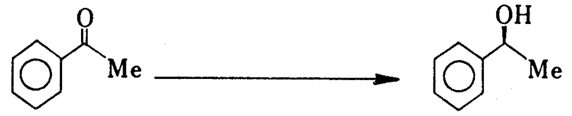
Structural similarity between the ynone (**21**) and the *s-cis*-conformers (II) of open chain enones might explain the fairly high optical yield of the propargylic alcohol ((*S*)-(−)-**22**).

From the above studies, it appeared evident that the exploited chiral hydride could efficiently reduce open chain enones which could adopt *s-cis*-conformations due to C–CO bond rotation.

B. Asymmetric Reduction of Various Aromatic and Aliphatic Ketones

Excellent chemical and optical yields observed for open chain enones, whose electrophilicity at the carbonyl carbon is clearly lowered more than that of aromatic and aliphatic ketones, might reflect the enhanced nucleophilicity of the hydride in the exploited chiral hydride. Therefore, it was expected that the amount of reducing agent could be decreased in the asymmetric reduction of more reactive aromatic and aliphatic ketones. To check this, the minimum amount of the chiral hydride required for effecting the asymmetric reduction of these ketones was investigated by employing acetophenone (**25**) as a reaction substrate. The results in Table III indicate that the use of 1.8 eq of the hydride with respect to **25** efficiently affords (*S*)-(−)-1-phenylethanol ((*S*)-(−)-**26**) in 94% chemical and 84% optical yields (Table III, run 3). The observed optical yield compares well with those of the best reported results for asymmetric reduction of **25**.[7–9] Since asymmetric reduction of **25** is usually attempted using 2.4[7] or 3.3 eq[8,9] of the chiral reducing agent, the reducing ability of our chiral hydride is clearly superior to that of the other reported hydrides.[5–9] When the reaction temperature was lowered to −100°C, the optical yield of (*S*)-(−)-**26** was further improved to 88% e.e. (Table III, run 5). As detailed in the experimental section, the chiral source and additive could be simply recovered by extractive isolation followed by fractional distillation, as in the case of the asymmetric reduction of **2**.[2]

Table III. Asymmetric Reduction of Acetophenone (**25**) by Lithium Aluminum Hydride partially decomposed with (−)-*N*-Methylephedrine and *N*-Ethylaniline[a]



25 (*S*)-(−)-**26**

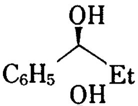
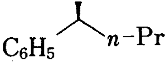
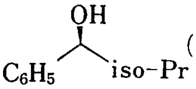
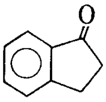
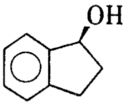
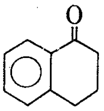
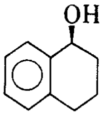
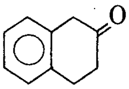
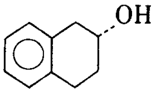
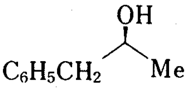
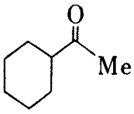
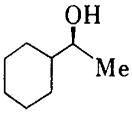
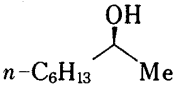
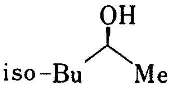
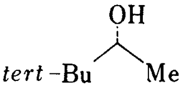
Run	Chiral reducing agent (molar ratio to **25**) LAH : E[b] : T[c]	Reaction temp. (°C)	(*S*)-(−)-1-Phenylethanol ((*S*)-(−)-**26**) Chemical yield(%)[d]	$[\alpha]_D^{20}$(°) (*c*, cyclopentane)[e]	Optical yield(% e.e.)[f]
1	3.3 : 3.4 : 6.8	−78	90	−35·4(6.80)	82
2	2.4 : 2.47 : 4.95	−78	90	−36.2(6.21)	84
3	1.8 : 1.86 : 3.72	−78	94	−36.2(5.53)	84
4	1.2 : 1.24 : 2.48	−78	71	−34.5(4.00)	80
5	1.8 : 1.86 : 3.72	−100	86	−37.9(5.98)	88

a) All reactions were performed in ether for 3 h. (*S*)-(−)-Phenylethanol((*S*)-(−)-**26**) was obtained as a sole reaction product.
b) (−)-*N*-Methylephedrine used as a chiral source.
c) *N*-Ethylaniline used as an additive.
d) Based on **25** after purification by preparative TLC (CH_2Cl_2).
e) Measurement of the optical rotation was carried out using a sample further purified by bulb-to-bulb distillation.
f) Based on $[\alpha]_D^{21}$ −43.1° (*c*=7.19, cyclopentane). See ref. *5a,b* and experimental section.

The asymmetric reduction of various aromatic and aliphatic ketones was studied under the established conditions, as summarized in Table IV. Among the reduction substrates, cyclohexyl methyl ketone (**41**) was prepared from cyclohexanecarboxylic acid in the same manner as described for the open chain enones (**7**, **11**, and **13**).[13] As to other ketones, commercial samples were distilled, then directly used for the asymmetric reduction.

It was found that the optically active secondary alcohols ((*S*)-(−)-**28**, (*S*)-(−)-**30**, (*S*)-(−)-

TABLE IV. Asymmetric Reduction of Various Aromatic and Aliphatic Ketones by Lithium Aluminum Hydride partially decomposed with (−)-*N*-Methylephedrine and *N*-Ethylaniline[a]

Run	Aromatic or aliphatic ketone		Optically active secondary alcohols[b]				
			Structure		Chemical yield (%)[c]	Optical yield (% e.e.)[d,e]	Absolute configuration[e]
1	C_6H_5COEt	**27**		(−)-**28**	96	90	(*S*)
2	C_6H_5CO*n*-Pr	**29**		(−)-**30**	100	80	(*S*)
3	C_6H_5CO iso-Pr	**31**		(−)-**32**	95	78	(*S*)
4		**33**		(+)-**34**	88	71	(*S*)
5		**35**		(+)-**36**	96	51	(*S*)
6		**37**		(+)-**38**	98	67	(*R*)
7	$C_6H_5CH_2COMe$	**39**		(+)-**40**	90	41	(*S*)
8[f]		**41**		(+)-**42**	90	35	(*S*)
9	*n*-$C_6H_{13}COMe$	**43**		(±)-**44**	94	0	—
10	iso-BuCOMe	**45**		(+)-**46**	94	36	(*S*)
11	*tert*-BuCOMe	**47**		(−)-**48**	78	15	(*R*)

[a] All reactions were carried out using LAH (1.8 eq) partially decomposed with (−)-*N*-methylephedrine (1.8 eq) and *N*-ethylaniline (3.72 eq) in ether at −78°C for 3 h (except for run 8) (see the experimental section).

[b] The optical rotation and spectral (IR and ^1H-NMR) properties of optically active secondary alcohol were given in the experimental section.

[c] Based on the starting ketone after purification by preparative TLC (except for runs 10 and 11) (see the experimetal section).

[d] The optical rotation was measured on a sample further purified by bulb-to-bulb distillation.

[e] The optical yield and absolute configuration of optically active secondary alcohol were determined based on the reported sign and value for optical rotation (see the experimental section and references cited therein).

[f] 3.9 eq of the reducing agent was required for completing the asymmetric reduction of **41**.

32, (*S*)-(+)-**34**, and (*S*)-(+)-**36**) could be produced from the aromatic ketones (**27**, **29**, **31**, **33**, and **35**) in high chemical and optical yields similar to those achieved by the use of other reported reagents[7–9] (Table IV, runs 1—5).

While the steric course of asymmetric reduction of β-tetralone (**37**) might be rationalized by assuming that the steric bulkiness of the $ArCH_2CH_2$ group is larger than that of the $ArCH_2$ group, the optical yield of (*R*)-(+)-**38**, which is much too high to be explained by steric factors, suggests the possible intervention of an effective electronic interaction between the aromatic ring of **37** and the modified chiral hydride (Table IV, run 6).

The results obtained by using aliphatic ketones other than **37** as reduction substrates were also found to be comparable with or superior to those reported[5-9] (Table IV, runs 7—10). The inverted steric course observed in the asymmetric reduction of *tert*-butyl methyl ketone (**47**) might be explained by the possible CH-π interaction[17] between the *tert*-butyl group and the chiral hydride (Table IV, run 11).

Thus, it is established that aromatic ketones can be effectively reduced by the exploited chiral hydride similarly to open chain enones.

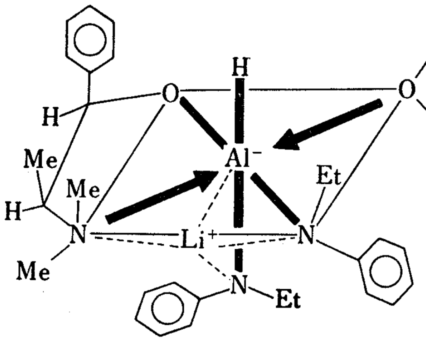
C. Structure of the Exploited Reducing Agent and Transition State for the Asymmetric Reduction

Based on the experimental results accumulated in this and the preceding paper,[2] structure elucidation of the chiral hydride was attempted.

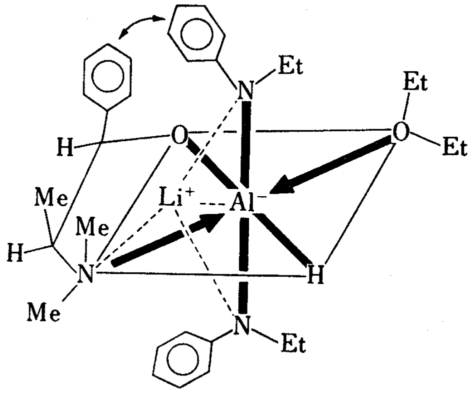
The chiral hydride prepared by decomposing LAH successively with 1.0 eq of (—)-*N*-methylephedrine and 2.0 eq of *N*-ethylaniline should have the composition $LiAlH(NEtPh)_2(OCHPhCHMeNMe_2)$. Since aluminum may produce a regular-octahedral six-coordinated complex, as can be seen in $[AlF_6]^{-3}$ and $[Al(H_2O)_6]^{3+}$,[18] the lone pair of the dimethylamino group present in the *N*-methylephedrine residue should coordinate with the central aluminum atom. Occupation of the remaining vacant coordination site by the lone pair of ether may give the monomeric complex, because it is well known that a solvent molecule having a lone pair strongly coordinates with trivalent aluminum.[19] The lithium cation produced from LAH might be located as a contact ion pair with the negatively charged aluminum in the vicinity of the nitrogen atoms of (—)-*N*-methylephedrine and *N*-ethylaniline, and be able to interact with these nitrogen atoms. The presence of the lithium cation in or near the formed aluminum complex is considered to be essential for achieving the asymmetric reduction in high optical yield, since the attempted reduction of **2** in the presence of tetramethylethylenediamine (TMEDA), which might remove the lithium cation from the aluminum complex,[8b,19,20] was found to give (*S*)-(—)-**3** in 44% chemical and 54% optical yields. The results obtained for the asymmetric reduction of **2** in various reaction solvents could be partly explained by similar considerations (see Table IVB in the preceding paper).[2]

Thus, we would like to propose the complex (III) shown in Fig. 1 as a probable structure for the chiral reducing agent. Another possible structure for the chiral aluminum hydride (IV), in which two molecules of *N*-ethylaniline coordinate across the central aluminum atom, should be more unstable than III due to the steric interaction between the (—)-*N*-methylephedrine residue and the phenyl (or the ethyl) group of *N*-ethylaniline (see arrow in IV).

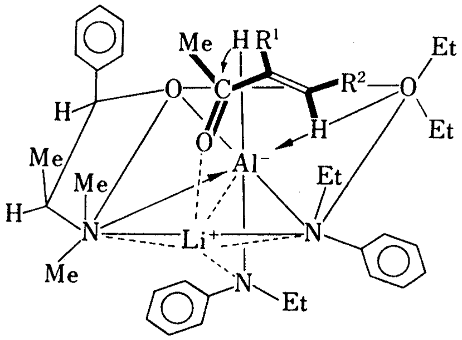
In the asymmetric reduction of open chain enones and aromatic ketones, the steric interaction of the substituents of the ketonic function with the phenyl and methyl groups of (—)-*N*-methylephedrine, and the electronic interaction of the lithium cation with the oxygen atom of the ketonic group will control the direction in which a reduction substrate approaches the chiral reducing agent, giving the transition state (V) in Fig. 1. Further possible electronic interactions of the aluminum and/or the phenyl group of *N*-ethylaniline with the π-electrons involved in a reduction substrate might assist preferential formation of a highly ordered transition state such as V. This explanation is consistent with the highly enantioselective formation of optically active alcohols, regularly having (*S*)-configurations, from open chain enones and aromatic ketones. Smaller steric differences between the substituents of the ketonic group and/or lack of the electronic interaction through π-electrons might be the reason why cyclic enones and aliphatic ketones afford lower optical yields than open chain enones and aromatic



III



IV



R^1=H or alkyl; R^2=aryl or alkyl

V

ketones. A transition state similar to V might be also compatible with the result in the asymmetric reduction of the ynone (**21**).

Recently, Cram introduced the new term "chiral reaction efficiency" given by the following equation to evaluate the effectiveness of asymmetric synthesis.[21] According to this equation, the chiral reaction efficiencies obtained in the asymmetric reductions of some representative

chiral reaction efficiency (%)=optical yield × chemical yield/100

ketones (**2**, **5**, **25**, and **27**) with the present chiral hydride could be calculated as 92, 96, 79, and 86%, respectively. The best value (96%) achieved in the asymmetric reduction of **5** is very much higher than those hitherto recorded for the asymmetric reduction of ketones with various types of modified LAH.[5-9,22] This value also shows that the same order of efficiency as those of enzymic reactions[23] has been achieved for the first time by our chiral reducing agent in the asymmetric reduction of ketones.

On the basis of numerous novel aspects, including high chemical and optical yields, the asymmetric reduction of ketones with the present chiral hydride seems promising for the asymmetric synthesis not only of optically active anthracyclinones[2] but also of various optically active natural products.

Experimental[24]

2-Acetyl-3,4-dihydronaphthalene (7)——Prepared from 3,4-dihydro-2-naphthoic acid[25] in 93% yield in the reported manner.[2,13] Colorless oil, bp 210°C (5 mmHg). Infrared (IR) spectra, IR $\nu_{\max}^{\text{film}}$ cm^{-1}: 1680 (ketone). ^{1}H- Nuclear magnetic resonance (^{1}H-NMR) spectra, ^{1}H-NMR (in $CDCl_3$): 2.42 (3H, s, $COC\underline{H}_3$), 2.50—3.05 (4H, m, $C\underline{H}_2C\underline{H}_2$), 7.21 (4H, s, aromatic protons), 7.38 (1H, br s, $C\underline{H}$–).

3-Methyly-4-phenyl-3(*E*)-buten-2-one (11)——Prepared in 54% yield from *trans*-α-methylcinnamic acid[26] in a manner similar to that described for 7.[2,13] Colorless oil, bp 124—125°C (11 mmHg) (lit.,[27] bp 127—130°C (12 mmHg)). IR $\nu_{\max}^{\text{film}}$ cm^{-1}: 1680 (ketone). ^{1}H-NMR (in $CDCl_3$): 2.05 (3H, d, $J=2$ Hz, $=CC\underline{H}_3$), 2.45 (3H, s, $COC\underline{H}_3$), 7.39 (5H, s, aromatic protons), 7.53 (1H, br s, $C\underline{H}=$).

3(*E*)-Hepten-2-one (13)——Prepared in 30% yield from commercially available 2(*E*)-hexenoic acid in a manner similar to that described for 7.[2,13] Colorless oil, bp 72—73°C (47 mmHg) (lit.,[28] bp 51—52°C (11 mmHg)). IR $\nu_{\max}^{\text{film}}$ cm^{-1}: 1680 (ketone). ^{1}H-NMR (in $CDCl_3$): 0.91 (3H, br t, $J=6$ Hz, $C\underline{H}_3(CH_2)_2$), 1.15—1.85 (2H, m, $CH_3C\underline{H}_2CH_2$), 2.00—2.40 (2H, m, $CH_3CH_2C\underline{H}_2$), 2.22 (3H, s, $COC\underline{H}_3$), 6.05 (1H, br d, $J=17$ Hz, $=C\underline{H}CO$), 6.58—7.05 (1H, m, $CH_2C\underline{H}=$).

2-Methyl-2-cyclohexen-1-one(17)——Preparation of this sample was carried out according to the reported method.[14] Colorless oil, bp 86—88°C (35 mmHg) (lit.,[14] bp 83—85.5°C (35 mmHg)).

3-Methyl-2-cyclohexen-1-one (19)——This was prepared according to the reported method.[15] Colorless oil, bp 86—90°C (18 mmHg) (lit.,[15] bp 88—90°C (18 mmHg)).

1-Heptyn-3-one (21)——Oxidation of commercially available 1-heptyn-3-ol with Jones reagent[16a] according to the reported procedure[16b] gave **21** in 82% yield. Colorless oil, bp 45°C (18 mmHg). IR $\nu_{\max}^{\text{film}}$ cm^{-1}: 2100 (C≡C), 1680 (ketone). ^{1}H-NMR (in $CDCl_3$): 0.92 (3H, br t, $J=6$ Hz, $C\underline{H}_3CH_2$), 1.10—1.95 (4H, m, $CH_3(C\underline{H}_2)_2CH_2$), 2.45—2.75 (2H, m, $C\underline{H}_2C{\equiv}C$), 3.32 (1H, s, $C{\equiv}C\underline{H}$).

Cyclohexyl Methyl Ketone (41)——Prepared from commercially available cyclohexanecarboxylic acid in 30% yield in the same manner as described for 7.[2,13] Colorless oil, bp 55—57°C (8 mmHg) (lit.,[29] bp 64—67°C (11 mmHg)). IR $\nu_{\max}^{\text{film}}$ cm^{-1}: 1710 (ketone). ^{1}H-NMR (in $CDCl_3$): 1.0—2.10 (11H, m, $C_6\underline{H}_{11}CO$), 2.12 (3H, s, $COC\underline{H}_3$).

(*S*)-(−)-4-Phenyl-3(*E*)-buten-2-ol ((*S*)-(−)-6)——a) Table I, Run 3: An ethereal solution (20 ml) of (−)-*N*-methylephedrine (mp 86.5—87.5°C, $[\alpha]_{\text{D}}^{20}$ −29.5° ($c=4.88$, EtOH))[2] (1.83 g, 10.2 mmol) was added to a stirred suspension of LAH (376 mg, 9.9 mmol) in Et_2O (10 ml) under an argon atmosphere, and the mixture was heated at reflux for 1 h with stirring. A solution of *N*-ethylaniline (2.47 g, 20.4 mmol) in Et_2O (10 ml) was added to the reaction mixture, and the mixture was further heated at reflux for 1 h with stirring giving a solution of the reducing agent.[2]

An ethereal solution (5 ml) of **5** (439 mg, 3.0 mmol) was gradually added to the solution of the reducing agent cooled at −78°C, and the mixture was stirred at the same temperature for 3 h. After the reaction had been quenched by the addition of 1 N HCl (42 ml) at −78°C, the cooling bath was removed. The upper ethereal layer was separated, and the lower aqueous phase was extracted with Et_2O (10 ml × 1). The organic layers were combined, and washed successively with 1% HCl (20 ml × 2), 5% $NaHCO_3$ (20 ml × 1), and satd. NaCl (20 ml × 3). Filtration and concentration *in vacuo*, followed by purification by preparative thin layer chromatography (TLC) (CH_2Cl_2), gave (*S*)-(−)-**6** as a colorless oil (435 mg, 98%). This sample was subjected to bulb-to-bulb distillation to give pure (*S*)-(−)-**6** as a colorless oil (399 mg, 90%), bp 160°C (5 mmHg), $[\alpha]_{\text{D}}^{20}$ −24.2° ($c=5.16$, $CHCl_3$),[30] 98% e.e.[10] IR $\nu_{\max}^{\text{film}}$ cm^{-1}: 3400 (OH). ^{1}H-NMR (in $CDCl_3$): 1.37 (3H, d, $J=6$ Hz, $CH(OH)C\underline{H}_3$), 2.28 (1H, br s, $O\underline{H}$), 4.25—4.67 (1H, m, $C\underline{H}(OH)$), 6.24 (1H, dd, $J=16$ and 5 Hz, $=C\underline{H}CH(OH)$), 6.57 (1H, d, $J=16$ Hz, $C_6H_5C\underline{H}=$), 7.32 (5H, s, $C_6\underline{H}_5$). MS: *m/e*: 148 (M^+), 133 (M^+-CH_3), 115 ($M^+-CH_3-H_2O$), 91, 77.

b) Table I, Run 1: An ethereal solution (7 ml) of (*S*)-(+)-2-(anilinomethyl)pyrrolidine ($[\alpha]_{\text{D}}^{24}$ +17.8° ($c=2.32$, EtOH), 90% e.e.)[2,8] (673 mg, 3.82 mmol) was added to a suspension of LAH (125 mg, 3.29 mmol) in Et_2O (10 ml), and the mixture was heated at reflux for 1 h with stirring, to give a solution of the reducing agent.

An ethereal solution (4 ml) of **5** (146 mg, 1.0 mmol) was gradually added to a stirred solution of the reducing agent cooled at −78°C, and the whole was stirred at the same temperature for 3 h. The reaction was quenched by the addition of 10% HCl (10 ml) at −78°C, and the cooling bath was removed. The upper ethereal layer was separated, and the lower aqueous phase was extracted with EtOAc (10 ml × 2). The combined organic extracts were washed successively with 10% HCl (10 ml × 2), H_2O (10 ml × 1), 5% $NaHCO_3$ (10 ml × 1), H_2O (10 ml × 1), and satd. NaCl (10 ml × 3). Filtration and concentration *in vacuo*, followed by purification by preparative TLC (CH_2Cl_2), gave (*S*)-(−)-**6** as a colorless oil (111 mg, 75%). Measurement of the optical rotation was performed on a sample further purified by bulb-to-bulb distillation, bp 160°C (5 mmHg), $[\alpha]_{\text{D}}^{20}$ −7.9° ($c=3.83$, $CHCl_3$), 32% e.e. (36% e.e. corrected for the optical purity of (*S*)-(+)-2-(anilinomethyl)pyrrolidine).[8] IR and ^{1}H-NMR spectra of this sample were identical with those recorded in a).

c) Table I, Run 2: An ethereal solution (7 ml) of (−)-*N*-methylephedrine (mp 86.5—87.5°C, $[\alpha]_{\text{D}}^{20}$ −29.5° ($c=4.88$, MeOH))[2] (592 mg, 3.3 mmol) was added to a suspension of LAH (125 mg, 3.3 mmol) in Et_2O (5 ml), and the whole was stirred at room temperature for 1 h. A solution of 3,5-dimethylphenol (806 mg, 6.6 mmol) in Et_2O (7 ml) was further added to the reaction mixture, and the whole was stirred at room temperature for 1 h to afford a solution of the reducing agent.[7]

An ethereal solution (4 ml) of **5** (146 mg, 1.0 mmol) was gradually added to the stirred solution of the reducing agent cooled at −20°C, and the mixture was stirred at the same temperature for 3 h. After the reaction had been quenched by the addition of 1 N HCl (7 ml) at −20°C, the cooling bath was removed, and the lower aqueous phase was extracted with Et_2O (10 ml × 2). The combined organic extracts were washed successively with 1% HCl (10 ml × 2), H_2O (10 ml × 1), 10% NaOH (10 ml × 3), H_2O (20 ml × 2), and satd. NaCl (20 ml × 3). Filtration and concentration *in vacuo* gave an oily residue (202 mg), which was separated by preparative TLC (CH_2Cl_2) to afford **6** as an oil (10 mg, 7%) and the starting enone (**5**) as an oil (122 mg, 84%). Measurement of the optical rotation was not carried out on **6** because of its low yield. The reduction product (**6**) and the recovered enone (**5**) were identified from the spectral (IR and ^{1}H-NMR) data.

(*S*)-(−)-2-1′-Hydroxyethyl-3,4-dihydronaphthalene ((*S*)-(−)-8)——The same treatments of **7** (240 mg, 1.5 mmol) as described for **5** (Table I, run 3) gave (*S*)-(−)-**8** as a colorless oil (278 mg, quantitative yield) after purification by preparative TLC (CH_2Cl_2). The optical rotation was measured on a sample further purified by bulb-to-bulb distillation (253 mg, 97%), bp 230°C (7 mmHg), $[\alpha]_D^{19}$ −33.5° (c=5.04, $CHCl_3$). IR ν_{max}^{film} cm^{-1}: 3360 (OH). ^{1}H-NMR (in $CDCl_3$): 1.28 (3H, d, J=6 Hz, $CH(OH)C\underline{H}_3$), 2.00 (1H, s, $O\underline{H}$), 2.10—2.40 (2H, m, $CH_2C\underline{H}_2C$=), 2.65—2.95 (2H, m, $C\underline{H}_2CH_2C$=), 4.38 (1H, q, J=6 Hz, $C\underline{H}(OH)$), 6.42 (1H, br s, $C\underline{H}$=), 7.05 (4H, s, aromatic protons). MS: *m/e*: 174 (M^+), 159 (M^+-CH_3). The optical yield was determined as >90% e.e. since the ^{1}H-NMR spectrum of this sample measured in the presence of $Eu(hfc)_3$((*S*)-(−)-**8**: $Eu(hfc)_3$ 1: 1 in $CDCl_3$) exhibited the vinyl proton as two singlets at 8.75 and 8.60 ppm in an integration ratio of more than 95: 5. The authentic racemic alcohol ((±)-**8**) required for determining the optical yield was prepared by reducing **7** with $NaBH_4$ in EtOH. Spectral (IR and ^{1}H-NMR) properties of (±)-**8** were superimposable on those recorded for (*S*)(−)-**8**. The absolute configuration of (*S*)-(−)-**8** was tentatively assigned by considering the result of the asymmetric reduction of **2**.[2)]

(*S*)-(−)-1-1′-Hydroxyethyl-1-cyclohexene ((*S*)-(−)-10)——Treatments of **9** (373 mg, 3.0 mmol) in the manner described for **5** (Table I, run 3) gave pure (*S*)-(−)-**10** as a colorless oil (347 mg, 92%) after extractive isolation. The oily product was further subjected to bulb-to-bulb distillation to give pure (*S*)-(−)-**10** as a colorless oil (329 mg, 87%), bp 130°C (7 mmHg), $[\alpha]_D^{20}$ −9.8° (c=4.25, $CHCl_3$). IR ν_{max}^{film} cm^{-1}: 3360 (OH). ^{1}H-NMR (in $CDCl_3$): 1.21 (3H, d, J=6 Hz, $CH(OH)C\underline{H}_3$), 1.40—2.10 (9H, m, $(C\underline{H}_2)_4C$= and $O\underline{H}$), 4.11 (1H, q, J=6 Hz, $C\underline{H}(OH)$), 5.62 (1H, br s, $C\underline{H}$=). The optical yield and absolute configuration of this sample were determined by converting the product to (*S*)-(+)-1-cyclohexylethanol ((*S*)-(+)-**42**) by catalytic hydrogenation. Thus, a solution of (−)-**10** (300 mg, 2.38 mmol) in EtOH (5 ml) was added to a suspension of PtO_2 (10 mg) in EtOH (3 ml) pretreated with a hydrogen atmosphere, and the mixture was stirred at room temperature for 5 h under a hydrogen atmosphere. The catalyst was filtered off and washed with EtOH. The combined filtrate and washings were concentrated *in vacuo* to afford the crude product as an oil (264 mg, 86%). This was purified successively by column chromatography (CH_2Cl_2) and bulb-to-bulb distillation, giving pure (*S*)-(+)-**42** as an oil (183 mg, 60%), bp 130°C (8 mmHg), α_D^{20} +0.408° (l=0.1, neat). IR ν_{max}^{film} cm^{-1}: 3380 (OH). ^{1}H-NMR (in $CDCl_3$): 1.12 (3H, d, J=6 Hz, $CH(OH)C\underline{H}_3$), 1.10—1.90 (12H, m, $(C\underline{H}_2)_5C\underline{H}CH(O\underline{H})$), 3.50 (1H, br t, J=6 Hz $C\underline{H}(OH)$). Since optically pure (*S*)-(+)-**42** had been reported to give $[\alpha]_D^{20}$ +5.68° (neat), d_4^{20} 0.9254,[31,32)] the optical yield and absolute configuration of (−)-**10** were determined as 78% e.e. and (*S*)-series, respectively.

(+)-3-Methyl-4-phenyl-3(*E*)-buten-2-ol ((+)-12)——The enone (**11**) (240 mg, 1.5 mmol) was treated in the same manner as described for **5** (Table I, run 3), to give (+)-**12** as a colorless oil (252 mg, quantitative yield) after purification by preparative TLC (CH_2Cl_2). The optical rotation was measured on a sample further purified by bulb-to-bulb distillation. Colorless oil (231 mg, 95%), bp 180°C (8 mmHg), $[\alpha]_D^{19}$ +11.1° (c=4.40, $CHCl_3$). IR ν_{max}^{film} cm^{-1}: 3360 (OH). ^{1}H-NMR (in $CDCl_3$): 1.32 (3H, d, J=6 Hz, $CH(OH)C\underline{H}_3$), 1.80 (1H, s, $O\underline{H}$), 1.83 (3H, br s, $=CC\underline{H}_3$), 4.33 (1H, q, J=6 Hz, $C\underline{H}(OH)$), 6.50 (1H, br s, $C_6H_5C\underline{H}$=), 7.25 (5H, s, $C_6\underline{H}_5$). MS: *m/e*: 162 (M^+), 147 (M^+-CH_3). The optical yield of (+)-**12** was determined as >90% e.e. since the ^{1}H-NMR spectrum of this sample measured in the presence of $Eu(hfc)_3$((+)-**12**: $Eu(hfc)_3$ 1: 0.5 in $CDCl_3$) showed the methyl group as a set of doublets at 3.48 and 3.60 ppm in an integration ratio of more than 95: 5. The authentic racemic alcohol ((±)-**12**) required to determine the optical yield was prepared by reducing **11** with $NaBH_4$ in EtOH. Spectral (IR and ^{1}H-NMR) properties of (±)-**12** were superimposable on those recorded for (+)-**12**. The absolute configuration of (+)-**12** could not be determined due to the lack of reference data.

(*S*)-(−)-3(*E*)-Hepten-2-ol ((*S*)-(−)-14)——The same treatments of **13** (337 mg, 3.0 mmol) as described for **5** (Table I, run 3) gave (−)-**14** as a colorless oil (314 mg, 92%) after purification by column chromatography (CH_2Cl_2). The optical rotation was measured on a sample further purified by bulb-to-bulb distillation. Colorless oil (182 mg, 53%), bp 110°C (30 mmHg), $[\alpha]_D^{20}$ −8.2° (c=3.58, $CHCl_3$). IR ν_{max}^{film} cm^{-1}: 3380 (OH). ^{1}H-NMR (in $CDCl_3$): 0.90 (3H, t, J=6 Hz, $C\underline{H}_3(CH_2)_2$), 1.15 (3H, d, J=6 Hz, $CH(OH)C\underline{H}_3$), 1.20—2.20 (5H, m, $CH_3(C\underline{H}_2)_2$ and $O\underline{H}$), 4.27 (1H, br t, J=6 Hz, $C\underline{H}(OH)$), 5.50—5.70 (2H, m, $C\underline{H}$=$C\underline{H}$). The optical yield and absolute configuration were determined by converting (−)-**14** to (*S*)-(+)-heptan-2-ol by catalytic hydrogenation. Thus, an ethanolic solution (5 ml) of (−)-**14** (160 mg, 1.4 mmol) was added to a suspension of PtO_2 (30 mg) in EtOH (5 ml) pretreated in a hydrogen atmosphere, and the mixture was stirred at room temperature for 2 h under a hydrogen atmosphere. Filtration and concentration *in vacuo* gave the crude product as an oil (138 mg, 85%). This was purified successively by column chromatography (CH_2Cl_2) and bulb-to-bulb distillation to give pure (*S*)-(+)-heptan-2-ol as a colorless oil (77 mg, 47%), bp 140°C (80 mmHg), $[\alpha]_D^{20}$ +6.9° (c=7.50, EtOH). IR ν_{max}^{film} cm^{-1}: 3380 (OH). ^{1}H-NMR (in $CDCl_3$): 0.90 (3H, br t, J=6 Hz,

$C\underline{H}_3(CH_2)_4$), 1.20 (3H, d, $J=6$ Hz, $CH(OH)C\underline{H}_3$), 1.25—1.50 (8H, m, $CH_3(C\underline{H}_2)_4$), 1.85 (1H, br s, $O\underline{H}$), 3.75 (1H, br q, $J=6$ Hz, $C\underline{H}(OH)$)). Since optically pure (*S*)(+)-heptan-2-ol had been reported to give $[\alpha]^{20}_{D}$ +7.8° ($c=12.0$, EtOH),[34,35] the optical yield and absolute configuration of (−)-**12** were determined as 88% e.e. and (*S*)-series, respectively.

(*S*)-(−)-2-Cyclohexen-1-ol ((*S*)-(−)-**16**)——Treatments of **15** (288 mg, 3.0 mmol) in the same manner as described for **5** (Table I, run 3) gave (*S*)-(−)-**16** as a colorless oil (172 mg, 58%) after purification by column chromatography (CH_2Cl_2). The optical rotation was measured on a sample purified by bulb-to-bulb distillation. Colorless oil (139 mg, 47%), bp 100°C (23 mmHg), $[\alpha]^{20}_{577}$ −52.5° ($c=2.14$, CH_2Cl_2). IR ν^{film}_{max} cm^{-1}: 3360 (OH). ^1H-NMR (in $CDCl_3$): 1.50—2.35 (7H, m, $CH(O\underline{H})$ and $(C\underline{H}_2)_3$), 4.15 (1H, m, $C\underline{H}(OH)$), 5.75 (2H, s, $C\underline{H}=C\underline{H}$). MS: *m/e* 98 ($M^+$), 83 ($M^+-CH_3$), 70 ($M^+-C_2H_4$). Since (*S*)(−)-**16**, 100% e.e., had been reported to give $[\alpha]^{20}_{D}$ −112.0° ($c=0.60$, $CHCl_3$),[36] and another lot of (−)-**16** produced by the same asymmetric reduction gave $[\alpha]^{20}_{577}$ −35.4° ($c=4.5$, CH_2Cl_2) and $[\alpha]^{20}_{D}$ −33.9° ($c=0.80$, $CHCl_3$), the optical yield and absolute configuration of (−)-**16** obtained by this asymmetric reduction were determined as 45% e.e. and (*S*)-series. In the preliminary communication,[1b] the optical yield of this sample was calculated as 32% e.e. based on the reported result that (*R*)-(+)-**16** showing $[\alpha]^{rt}_{578}$ +21° (CH_2Cl_2) was 13% e.e.[37]

(−)-2-Methyl-2-cyclohexen-1-ol ((−)-**18**)——The enone (**17**) (331 mg, 3.0 mmol) was treated in the same manner as described for **5** (Table I, run 3) to give (−)-**18** as an oil (173 mg, 51%) after purification by column chromatography (CH_2Cl_2). The optical rotation was measured on a sample further purified by bulb-to-bulb distillation (142 mg, 42%), bp 110°C (25 mmHg), $[\alpha]^{20}_{D}$ −70.2° ($c=1.41$, $CHCl_3$). IR ν^{film}_{max} cm^{-1}: 3340 (OH). ^1H-NMR (in $CDCl_3$): 1.40—2.15 (10H, m, $C\underline{H}_3C=CH(C\underline{H}_2)_3CH(O\underline{H})$), 4.00 (1H, br s, $C\underline{H}(OH)$), 5.55 (1H, br s, $C\underline{H}=$). MS: *m/e*: 112 (M^+), 97 (M^+-CH_3), 83 ($M^+-C_2H_5$). The optical yield was determined as 58% e.e. since the ^1H-NMR spectrum of (−)-**18** measured in the presence of $Eu(hfc)_3$((−)-**18**: $Eu(hfc)_3$ 1: 0.75 in $CDCl_3$) showed the methyl group signal as a set of doublets at 4.10 and 3.97 ppm in an integration ratio of 79: 21. The authentic racemic alcohol ((±)-**18**) required for determining the optical yield of (−)-**18** was prepared by reducing **17** with $NaBH_4$ in EtOH. Spectral (IR and ^1H-NMR) properties of (±)-**18** were superimposable on those recorded for (−)-**18**. The absolute configuration of (−)-**18** could not be determined due to the lack of a reference compound.

(*S*)-(−)-3-Methyl-2-cyclohexen-1-ol ((*S*)-(−)-**20**)——The same treatments of **19** (165 mg, 1.5 mmol) as described for **5** (Table I, run 3) gave (−)-**20** as an oil (148 mg, 88%) after purification by preparative TLC (CH_2Cl_2). The optical rotation was measured on a sample further purified by bulb-to-bulb distillation (128 mg, 76%), bp 150°C (25 mmHg), $[\alpha]^{20}_{D}$ −32.9° ($c=4.08$, $CHCl_3$). IR ν^{film}_{max} cm^{-1}: 3360 (OH). ^1H-NMR (in $CDCl_3$): 1.40—2.00 (9H, m, $(C\underline{H}_2)_3C(C\underline{H}_3)=$), 2.08 (1H, s, $O\underline{H}$), 4.14 (1H, br s, $C\underline{H}(OH)$), 5.45 (1H, br s, $C\underline{H}=$). MS: *m/e*: 112 (M^+), 97 (M^+-CH_3), 84 ($M^+-C_2H_4$). Since optically pure (*S*)-(−)-**20** had been reported to give $[\alpha]^{20}_{D}$ −96.3±0.3° ($c=0.458$, $CHCl_3$),[38] the optical yield and absolute configuration of (−)-**20** were determined as 34% e.e. and (*S*)-series, respectively. In the preliminary communication,[1b] the optical yield of (−)-**20** was calculated as 24% e.e. based on the ^1H-NMR spectrum in the presence of $Eu(hfc)_3$.

(*S*)-(−)-1-Heptyn-3-ol ((*S*)-(−)-**22**)——Treatments of **21** (165 mg, 15 mmol) in the same manner as described for **5** (Table I, run 3) afforded (*S*)(−)-**22** as an oil (148 mg, 88%) after purification by column chromatography (CH_2Cl_2). The optical rotation was measured on a sample further purified by bulb-to-bulb distillation (104 mg, 62%), bp 130°C (20 mmHg), $[\alpha]^{25}_{D}$ −15.6° ($c=3.16$, dioxane). IR ν^{film}_{max} cm^{-1}: 3320 (OH). ^1H-NMR (in $CDCl_3$): 0.94 (3H, t, $J=6$ Hz, $C\underline{H}_3$), 1.10—1.95 (6H, m, $(C\underline{H}_2)_3$), 2.44 (1H, s, $C\equiv C\underline{H}$), 2.47 (1H, s, $O\underline{H}$), 4.37 (1H, br t, $J=5$ Hz, $C\underline{H}(OH)$). Since optically pure (*R*)-(+)-**22** has been reported to give $[\alpha]^{25}_{D}$ +20.5° ($c=3$, dioxane),[7c] the optical yield and absolute configuration of (−)-**22** were determined as 76% e.e. and (*S*)-series.

Asymmetric Reduction of 1-Phenyl-2(*E*)-buten-1-one (**23**)——The same treatments of commercially available **23** (439 mg, 3.0 mmol) as described for **5** (Table I, run 3) gave **24** as an oil (383 mg, 86%) after purification by preparative TLC (CH_2Cl_2). This sample was identified by comparing the spectral (IR and ^1H-NMR) data with those reported.[39]

(*S*)-(−)-1-Phenylethanol ((*S*)-(−)-**26**)——a) Table III, Run 3: An ethereal solution (5 ml) of (−)-*N*-methylephedrine (mp 86.5—87.5°C, $[\alpha]^{20}_{D}$ −29.5° ($c=4.88$, MeOH))[2] (499 mg, 2.78 mmol) was added to a stirred suspension of LAH (103 mg, 2.70 mmol) in Et_2O (5 ml) under an argon atmosphere, and the mixture was heated at reflux for 1 h with stirring. An ethereal solution (5 ml) of *N*-ethylaniline (674 mg, 5.56 mmol) was added to the reaction mixture, and the whole was further heated at reflux for 1 h with stirring, to give a solution of the reducing agent.

A solution of **25** (180 mg, 1.5 mmol) in Et_2O (5 ml) was added to a cooled (−78°C), stirred solution of the reducing agent prepared above, and the mixture was stirred at −78°C for 3 h. After the reaction had been quenched by the addition of 1 N HCl (12 ml) at −78°C, the cooling bath was removed. The upper ethereal layer was separated, and the lower aqueous phase was extracted with Et_2O (10 ml × 1). The combined organic layers were washed successively with 10% HCl (10 ml × 1) and satd. NaCl (10 ml × 3). Filtration and concentration *in vacuo* gave an oily residue, which was subjected to preparative TLC (CH_2Cl_2) to give (*R*)-(−)-**26** as a colorless oil (171 mg, 94%). Measurement of the optical rotation was carried out on a sample further purified by bulb-to-bulb distillation (161 mg, 89%), bp 160°C (17 mmHg), $[\alpha]^{20}_{D}$ −36.2° ($c=5.53$, cyclopentane), 84% e.e. (lit.,[5a,b] $[\alpha]^{21}_{D}$ +43.1° ($c=7.19$, cyclopentane) for optically pure (*R*)-(+)-**26**).[40] IR

ν_{max}^{film} cm^{-1}: 3380 (OH). ^{1}H-NMR (in CDCl$_3$): 1.49 (3H, d, J=6 Hz, $C\underline{H}_3$), 1.90 (1H, s, $O\underline{H}$), 4.88 (1H, q, J=6 Hz, $C\underline{H}$(OH)), 7.34 (5H, s, C_6H_5).

Other asymmetric reductions summarized in Tables III and IV were all performed by the same procedure as that described above.

b) Asymmetric Reduction of **25** with Recovery of the Chiral Source and Additive: The asymmetric reduction of **25** (360 mg, 3.0 mmol) with the chiral hydride prepared from LAH (206 mg, 5.4 mmol), (−)-*N*-methylephedrine (mp 86.5—87.5°C, $[\alpha]_D^{20}$ −29.5° (c=4.88, MeOH)) (1.00 g, 5.56 mmol), and *N*-ethylaniline (1.35 g, 11.1 mmol) in the same manner as described in a), gave crude (*S*)(−)-**26** as an oil (330 mg, 90%) after concentration of the ethereal extracts *in vacuo*. This sample was directly purified by bulb-to-bulb distillation to give pure (*S*)-(−)-**26** as a colorless oil (317 mg, 87%), bp 160°C (17 mmHg), $[\alpha]_D^{20}$ −36.4° (c=7.45, cyclopentane), 84% e.e. (see a)). Spectral (IR and ^{1}H-NMR) properties of this sample were identical with those shown in a).

The aqueous acidic layers obtained by the extractive isolation were combined, made alkaline (pH≒11), then extracted with EtOAc (50 ml × 3). The combined organic extracts were washed with satd. NaCl (50 ml × 3). Filtration and concentration *in vacuo* gave a mixture of (−)-*N*-methylephedrine and *N*-ethylaniline as a mixture of crystals and an oil (2.41 g, quantitative recovery), which was subjected to bulb-to-bulb distillation to give (−)-*N*-methylephedrine (817 mg, 82% recovery), bp 170°C (5 mmHg), mp 87.5—89.5°C, $[\alpha]_D^{20}$ −29.0° (c=6.50, MeOH), 98% e.e.,[2] and *N*-ethylaniline (1.32 g, 98% recovery), bp 130°C (10 mmHg). Recovered (−)-*N*-methylephedrine and *N*-ethylaniline were shown to be identical with authentic samples by spectral (IR and ^{1}H-NMR) comparisons.

(*S*)-(−)-1-Phenylpropan-1-ol ((***S***)-(**−**)-**28**)——Table IV, Run 1: The same treatments of **27** (201 mg, 1.5 mmol) as described for **25** (Table III, run 3) gave (*S*)-(−)-**28** as an oil (196 mg, 96%) after purification by preparative TLC (CH_2Cl_2). Measurement of the optical rotation was carried out on a sample further purified by bulb-to-bulb distillation (179 mg, 88%), bp 175°C (21 mmHg), $[\alpha]_D^{27}$ −41.0° (c=5.58, CHCl$_3$), 90% e.e. (lit.,[41] $[\alpha]_D$ −45.45° (c=5.15, CHCl$_3$) for optically pure (*S*)-(−)-**28**).[42] IR ν_{max}^{film} cm^{-1}: 3380 (OH). ^{1}H-NMR (in CDCl$_3$): 0.88 (3H, t, J=7 Hz, $C\underline{H}_3$), 1.70 (2H, m, $C\underline{H}_2$), 2.00 (1H, br s, $O\underline{H}$), 4.58 (1H, t, J=7 Hz, $C\underline{H}$(OH)), 7.41 (5H, s, $C_6\underline{H}_5$).

(*S*)-(−)-1-Phenylbutan-1-ol ((***S***)-(**−**)-**30**)[4]——Table IV, Run 2: The ketone (**29**) (222 mg, 1.5 mmol) was treated in the same manner as described for **25** (Table III, run 3) to give (*S*)-(−)-**30** as colorless needles (227 mg, 100%) after purification by preparative TLC (CH_2Cl_2). Measurement of the optical rotation was performed on a sample further purified by bulb-to-bulb distillation (210 mg, 93%), $[\alpha]_D^{22}$ −36.6° (c=5.04, C_6H_6), 80% e.e. (lit.,[44] $[\alpha]_D^{27}$ −45.93° (c=6.1, C_6H_6) for optically pure (*S*)-(−)-**30**).[45] This sample gradually solidified when kept standing at room temperature, mp 38—44°C. IR ν_{max}^{film} cm^{-1}: 3220 (OH). ^{1}H-NMR (in CDCl$_3$): 0.98 (3H, d, J=6 Hz, $C\underline{H}_3$), 1.10—1.85 (4H, m, $(C\underline{H}_2)_2$), 2.01 (1H, br s, $O\underline{H}$), 4.65 (1H, t, J=6 Hz, $C\underline{H}$(OH)), 7.30 (5H, s, $C_6\underline{H}_5$).

(*S*)-(−)-2-Methyl-1-phenylpropan-1-ol ((***S***)-(**−**)-**32**)——Table IV, Run 3: Treatments of **31** (222 mg, 1.5 mmol) in the same manner as described for **25** (Table III, run 3) gave (*S*)-(−)-**32** as an oil (214 mg, 95%) after purification by preparative TLC (CH_2Cl_2). Measurement of the optical rotation was carried out on a sample further purified by bulb-to-bulb distillation (207 mg, 92%), bp 165°C (15 mmHg), $[\alpha]_D^{20}$ −37.0° (c=6.95, Et$_2$O), 78% e.e. (lit.,[46] $[\alpha]_D^{20}$ −47.7° (c=6.8, Et$_2$O) for optically pure (*S*)-(−)-**32**).[47] IR ν_{max}^{film} cm^{-1}: 3400 (OH). ^{1}H-NMR (in CDCl$_3$): 0.82, 1.05 (6H, two d, J=each 7 Hz, $CH(C\underline{H}_3)_2$), 1.71—2.18 (2H, m, $O\underline{H}$ and $C\underline{H}(CH_3)_2$), 4.38 (1H, d, J=7 Hz, $C\underline{H}$(OH)), 7.32 (5H, s, $C_6\underline{H}_5$).

(*S*)-(+)-Indan-1-ol ((***S***)-(**+**)-**34**)——Table IV, Run 4: The same treatments of **33** (198 mg, 1.5 mmol) as described for **25** (Table III, run 3) gave (*S*)-(+)-**34** as colorless needles (177 mg, 88%) after purification by preparative TLC (CH_2Cl_2). Measurement of the optical rotation was carried out on a sample further purified by bulb-to-bulb distillation (165 mg, 82%), bp 210°C (5 mmHg), $[\alpha]_D^{20}$ +24.4° (c=2.01, CHCl$_3$), 71% e.e. (lit.,[48] $[\alpha]_D^{20}$ +34.4° (c=1.97, CHCl$_3$) for optically pure (*S*)-(+)-**34**).[49] This sample gradually solidified when kept standing at room temperature, mp 55—68°C. IR ν_{max}^{film} cm^{-1}: 3300 (OH). ^{1}H-NMR (in CDCl$_3$): 1.77 (1H, s, $O\underline{H}$), 1.90—3.10 (4H, m, $(C\underline{H}_2)_2$), 5.22 (1H, t, J=6 Hz, $C\underline{H}$(OH)), 7.15—7.50 (4H, m, aromatic protons).

(*S*)-(+)-1,2,3,4-Tetrahydro-1-naphthol ((***S***)-(**+**)-**36**)——Table IV, Run 5: Treatments of **35** (219 mg, 1.5 mmol) in the same manner as described for **25** (Table III, run 3) gave (*S*)-(+)-**36** as a colorless oil (213 mg, 96%) after purification by preparative TLC (CH_2Cl_2). The optical rotation was measured on a sample further purified by bulb-to-bulb distillation (207 mg, 93%), bp 180°C (15 mmHg), $[\alpha]_D^{17}$ +16.8° (c=4.61, CHCl$_3$), 51% e.e. (lit.,[50] $[\alpha]_D^{17}$ +32.65° (c=2.5, CHCl$_3$) for optically pure (*S*)(+)-**36**).[49] IR ν_{max}^{film} cm^{-1}: 3360 (OH). ^{1}H-NMR (in CDCl$_3$): 1.50—2.10 (4H, m, $CH_2C\underline{H}_2C\underline{H}_2CH(OH)$), 2.50—2.75 (3H, m, $C\underline{H}_2CH_2CH_2CH(O\underline{H})$), 4.60 (1H, m, $C\underline{H}$(OH)), 6.95—7.45 (4H, m, aromatic protons).

(*R*)-(+)-1,2,3,4-Tetrahydro-2-naphthol ((***R***)-(**+**)-**38**)——Table IV, Run 6: The ketone (**37**) (219 mg, 1.5 mmol) was treated in the same manner as described for **25** (Table III, run 3) to give (*R*)(+)-**38** as a colorless oil (217 mg, 98%) after purification by preparative TLC (CH_2Cl_2). The optical rotation was measured on a sample further purified by bulb-to-bulb distillation (190 mg, 85%), bp 180°C (4 mmHg), $[\alpha]_D^{19}$ +18.8° (c=6.31, CHCl$_3$), 67% e.e. (lit.,[51] $[\alpha]_D$ +28.20° (c=7.70, CHCl$_3$) for optically pure (*R*)-(+)-**38**).[49] IR ν_{max}^{film} cm^{-1}: 3360 (OH). ^{1}H-NMR (in CDCl$_3$): 1.80—2.15 (2H, m, $CH_2C\underline{H}_2CH(OH)$), 2.10 (1H, s, $O\underline{H}$), 2.75—3.05 (4H, m, $C\underline{H}_2CH_2CH(OH)C\underline{H}_2$), 3.95—4.35 (1H, m, $C\underline{H}$(OH)), 7.08 (4H, s, aromatic protons).

(*S*)-(+)-1-Phenylpropan-2-ol ((*S*)-(+)-**40**)——Table IV, Run 7: The same treatments of **39** (201 mg, 1.5 mmol) as described for **25** (Table III, run 3) gave (*S*)-(+)-**40** as a colorless oil (183 mg, 90%) after purification by preparative TLC (CH_2Cl_2). The optical rotation was measured on a sample further purified by bulb-to-bulb distillation (176 mg, 86%), bp 170°C (15 mmHg), $[\alpha]_D^{20}$ +17.0° (c=5.76, C_6H_6), 41% e.e. (lit.,41) $[\alpha]_D^{20}$ +41.82° (c=5.26, C_6H_6) for optically pure (*S*)(+)-**40**).52) IR ν_{max}^{film} cm^{-1}: 3380 (OH). ^{1}H-NMR (in $CDCl_3$): 1.22 (3H, d, J=7 Hz, $C\underline{H}_3$), 1.67 (1H, s, $O\underline{H}$), 2.71 (2H, d, J=7 Hz, $C\underline{H}_2CH(OH)$), 4.00 (1H, m, $C\underline{H}(OH)$), 7.24 (5H, s, $C_6\underline{H}_5$).

(*S*)-(+)-1-Cyclohexylethanol ((*S*)-(+)-**42**)——Table IV, Run 8: Treatments of **41** (319 mg, 2.53 mmol) in the same manner as described for **25** (Table III, run 3) gave (*S*)-(+)-**42** as an oil (292 mg, 90%) after purification by preparative TLC (CH_2Cl_2). In this case, 3.9 eq of the reducing agent was necessary for the complete reduction of **41**. Measurement of the optical rotation was carried out on a sample further purified by bulb-to-bulb distillation (262 mg, 81%), bp 130°C (8 mmHg), α_D^{20} +0.182 (l=0.1, neat), 35% e.e. (lit.,31) $[\alpha]_D^{20}$ +5.68° (neat), d_4^{20} 0.9254, for optically pure (*S*)(+)-42).32) IR and ^{1}H-NMR spectra of (*S*)-(+)-**42** were identical with those of the sample obtained from (*S*)(−)-**10**.

(±)-Octan-2-ol ((±)-**44**)——Table IV, Run 9: The ketone (**43**) (385 mg, 3.0 mmol) was treated in the same manner as described for **25** (Table III, run 3), giving pure (±)-**44** (368 mg, 94%) as an oil after purification by preparative TLC (CH_2Cl_2). The optical rotation was measured on a sample further purified by bulb-to-bulb distillation (339 mg, 87%), bp 120°C (14 mmHg), $[\alpha]_D^{25}$ +0.018° (c=0.1, neat) (lit.,53) $[\alpha]_D^{25}$ −9.57° (neat), d_4^{20} 0.820, for optically pure (*R*)-(−)-**44**).54) IR ν_{max}^{film} cm^{-1}: 3360 (OH). ^{1}H-NMR (in $CDCl_3$): 0.87 (3H, t, J=6 Hz, $C\underline{H}_3(CH_2)_5$), 1.15 (3H, d, J=6 Hz, $CH(OH)C\underline{H}_3$), 1.10—1.60 (10H, m, $CH_3(C\underline{H}_2)_5$), 2.30 (1H, br s, $O\underline{H}$), 3.60—3.95 (1H, m, $C\underline{H}(OH)$).

(*S*)-(+)-4-Methylpentan-2-ol ((S)-(+)-**46**)——Table IV, Run 10: The same treatments of **45** (600 mg, 6.0 mmol) as described for **25** (Table IV, run 3) gave pure (*S*)-(+)-**46** as a homogenous colorless oil (575 mg, 94%) after extractive isolation with ether followed by concentration *in vacuo*. The optical rotation was measured on a sample further purified by bulb-to-bulb distillation (544 mg, 89%), bp 150°C (760 mmHg), α_D^{21} +0.608° (l=0.1, neat), 36% e.e. (lit.,55) $\alpha_D^{19.5}$ +34.22° (l=2, neat), $d_4^{19.5}$ 0.8075, for optically pure (*S*)-(+)-**46**).56) IR ν_{max}^{film} cm^{-1}: 3360 (OH). ^{1}H-NMR (in $CDCl_3$): 0.92 (6H, d, J=6 Hz, $CH(C\underline{H}_3)_2$), 1.18 (3H, d, J=6 Hz, $CH(OH)C\underline{H}_3$), 1.10—1.45 (3H, m, $C\underline{H}C\underline{H}_2CH(OH)$), 1.65 (1H, br s, $O\underline{H}$), 3.87 (1H, m, $C\underline{H}(OH)$).

(*R*)-(−)-3,3-Dimethylbutan-2-ol ((*R*)-(−)-**48**)——Table IV, Run 11: The ketone (**47**) (1.10 g, 11 mmol) was treated in the same manner as described for **25** (Table III, run 3), to give (*R*) (−)-**48** as a homogenous colorless oil (880 mg, 78%) after extractive isolation with ether followed by concentration *in vacuo*. Measurement of the optical rotation was carried out on a sample further purified by bulb-to-bulb distillation (800 mg, 71%), bp 140°C (760 mmHg), α_D^{20} −0.095° (l=0.1, neat), 15% e.e. (lit.,41) $[\alpha]_D^{20}$ +7.71° (neat) and d_4^{20} 0.8199 for optically pure (*S*)-(+)-**48**).57) IR ν_{max}^{film} cm^{-1}: 3400 (OH). ^{1}H-NMR (in $CDCl_3$): 0.88 (9H, s, $C(C\underline{H}_3)_3$), 1.10 (3H, d, J=6 Hz, $CH(OH)C\underline{H}_3$), 1.95 (1H, br s, $O\underline{H}$), 3.46 (1H, q, J=6 Hz, $C\underline{H}(OH)$).

Acknowledgement The authors are grateful to Prof. Kenji Koga, Faculty of Pharmaceutical Sciences, University of Tokyo, for his encouragement and advice throughout this work.

References and Notes

1) Part of this work has been the subject of two preliminary communications: *a*) S. Terashima, N. Tanno, and K. Koga, *Chem. Lett.*, **1980**, 981; *b*) *Idem*, *J. Chem. Soc.*, *Chem. Commun.*, **1980**, 1026.
2) N. Tanno and S. Terashima, *Chem. Pharm. Bull.*, 31, 821. (1983)
3) E.L. Eliel, *Tetrahedron*, **30**, 1503 (1974).
4) *a*) J.D. Morrison and H.S. Mosher, "Asymmetric Organic Reactions," Prentice-Hall, Englewood Cliffs, New Jersey, 1971; *b*) D. Valentine, Jr. and J.W. Scott, *Synthesis*, **1978**, 329; *c*) H.B. Kagan and J.C. Fiaud, "Topics in Stereochemistry," ed. by E.L. Eliel and N.L. Allinger, John Wiley & Sons, New York, Vol. 10, 1978, pp. 175—285; *d*) J.W. ApSimon and R.P. Seguin, *Tetrahedron*, **35**, 2797 (1979).
5) *a*) S. Yamaguchi, H.S. Mosher, and A. Pohland, *J. Am. Chem. Soc.*, **94**, 9254 (1972); *b*) S. Yamaguchi and H.S. Mosher, *J. Org. Chem.*, **38**, 1870 (1973); *c*) R.S. Brinkmeyer and V.M. Kapoor, *J. Am. Chem. Soc.*, **99**, 8339 (1977).
6) D. Seebach and H. Daum, *Chem. Ber.*, **107**, 1748 (1974).
7) *a*) I. Jacquet and J.P. Vigneron, *Tetrahedron Lett.*, **1974**, 2065; *b*) J.P. Vigneron and I. Jacquet, *Tetrahedron*, **32**, 939 (1976); *c*) J.P. Vigneron and V. Bloy, *Tetrahedron Lett.*, **1979**, 2683.
8) *a*) T. Mukaiyama, M. Asami, J. Hanna, and S. Kobayashi, *Chem. Lett.*, **1977**, 783; *b*) M. Asami, H. Ohno, S. Kobayashi, and T. Mukaiyama, *Bull. Chem. Soc. Jpn.*, **51**, 1869 (1978); *c*) M. Asami and T. Mukaiyama, *Heterocycles*, **12**, 499 (1979).
9) *a*) R. Noyori, I. Tomino, and Y. Tanimoto, *J. Am. Chem. Soc.*, **101**, 3129 (1979); *b*) R. Noyori, I. Tomino, and M. Nishizawa, *ibid.*, **101**, 5843 (1979); *c*) M. Nishizawa, M. Yamada, and R. Noyori, *Tetrahedron Lett.*, **22**, 247 (1981).
10) The (−)-isomer has (*S*)-configuration (see ref. 11, p. 228 (e)). The optical yield was calculated by

assuming that (*R*)-(+)-**6** giving $[\alpha]_D$ +24.7° (c=5.000, $CHCl_3$) was optically pure (see J. Kenyon, S.M. Partridge, and H. Phillips, *J. Chem. Soc.*, **1936**, 85).

11) J. Jacquet, C. Gros, and S. Bourcier, "Absolute Configurations of 6000 Selected Compounds with One Asymmetric Carbon Atom," in "Stereochemistry, Fundamentals and Methods," Vol. 4, ed. by H.B. Kagan, Georg Thieme Publishers, Stuttgart, 1977.

12) Asymmetric reduction of **5** with the chiral hydride produced by decomposing LAH with optically active 2,2′-dihydroxy-1,1′-binaphthyl and ethanol[9] was not attempted since the chiral source should be prepared by optical resolution of the racemic binaphthyl derivative.

13) M.J. Jorgenson, "Organic Synthesis," Vol. 18, ed. by W.G. Dauben, John Wiley & Sons, New York, 1970, pp. 1—97.

14) E.W. Warnhoff, D.G. Martin, and W.S. Johnson, "Organic Syntheses," Coll. Vol. IV, p. 162.

15) M.W. Cronyn and G.H. Riesser, *J. Am. Chem. Soc.*, **75**, 1664 (1953).

16) *a*) L.F. Fieser and M. Fieser, "Reagents for Organic Synthesis," Vol. 1, Wiley-Interscience, 1967, p. 142; *b*) A. Nobuhara, *Agric. Biol. Chem.*, 33, 1264 (1969).

17) M. Nishio, *Kagaku no Ryoiki*, **33**, 422 (1979).

18) H. Yamadera, "Gendai Kagaku," Vol. 7, ed. by M. Oki and Y. Saito, Iwanami Shoten, Tokyo, 1980, p. 50.

19) J.R. Boone and E.C. Ashby, "Topics in Stereochemistry," Vol. 11, ed. by E.L. Eliel and N.L. Allinger, John Wiley & Sons, New York, 1979, pp. 54—67.

20) *a*) T. Sone, S. Terashima, and S. Yamada, *Chem. Pharm. Bull.*, **24**, 1293 (1976) and ref. 12 cited therein; *b*) K. Tomioka, *Farumashia*, **18**, 827 (1982).

21) J.M. Wilson and D.J. Cram, *J. Am. Chem. Soc.*, **104**, 881 (1982).

22) The following chiral reaction efficiencies can be calculated based on the reported chemical and optical yields: reaction substrate (calculated chiral reaction efficiency): acetophenone (**25**) (75,[5a,b] 75,[7a,b] 82.7,[8c] and 58%[9a]); propiophenone (**27**) (77,[7a,b] 86,[8c] and 61%[9c]); *n*-butyrophenone (**29**) (80[7a,b] and 78%[9a]); 1-iodo- or 1-bromo-1(*E*)-octen-3-one (92%).[9b]

23) C.J. Sih and J.P. Rosazza, "Application of Biological Systems in Organic Chemistry," Part 1, ed. by J.B. Jones, C.J. Sih, and D. Perlman, John Wiley & Sons, New York, 1976, pp. 69—106.

24) All melting points were determined with a Büchi 510 melting point apparatus and are uncorrected. All boiling points are uncorrected. A Büchi GKR-50 apparatus was used for bulb-to-bulb distillation. IR spectral measurements were performed with a JASCO DS-402G infrared spectrometer and a JASCO IRA-1 grating infrared spectrometer. ^{1}H-NMR spectra were measured with a JEOL JNM-PS-100 spectrometer (100 MHz) and a Hitachi R-24 high resolution spectrometer (60 MHz). All signals are expressed as ppm downfield from tetramethylsilane used as an internal standard (δ value). The following abbreviations are used: singlet (s), doublet (d), triplet (t), quartet (q), multiplet (m), broad (br). Measurements of optical rotations were carried out using a Yanaco OR-50 automatic polarimeter and a JASCO DIR-181 digital polarimeter. Mass spectra were taken with a JMS-01 SG-2 mass spectrometer. All reactions were performed using anhyd. solvents, and the combined organic extracts obtained in each experiment were dried over anhyd. Na_2SO_4 or anhyd. $MgSO_4$, then filtered and concentrated *in vacuo* with a rotary evaporator. Column chromatography and preparative thin layer chromatography (TLC) were all carried out using silica gel as an adsorbent. The following abbreviations are used for solvents: benzene (C_6H_6); chloroform ($CHCl_3$); dichloromethane (CH_2Cl_2); ethanol (EtOH); ether (Et_2O); ethyl acetate (EtOAc); hexane (C_6H_{14}); methanol (MeOH); tetrahydrofuran (THF).

25) S-s. Jew, S. Terashima, and K. Koga, *Chem. Pharm. Bull.*, **27**, 2351 (1979).

26) *a*) J.R. Johnson, "Organic Reactions," Vol. 1, ed. by R. Adams, John Wiley & Sons, New York, 1942, p. 251; *b*) S-s. Jew, S. Terashima, and K. Koga, *Tetrahedron*, **35**, 2337 (1979).

27) C. Harries and G.H. Müller, *Chem. Ber.*, **35**, 966 (1902).

28) V. Theus, W. Surber, L. Colombi, and H. Schinz, *Helv. Chim. Acta*, **38**, 239 (1955).

29) V. Theus and H. Schinz, *Helv. Chim. Acta*, **39**, 1290 (1956).

30) The optical rotation was erroneously reported as $[\alpha]^{20}_D$ −24.5° (c=5.16, $CHCl_3$) in the preliminary communication.[1b]

31) A. Domleo and J. Kenyon, *J. Chem. Soc.*, **128**, 1841 (1926).

32) See ref. 11, p. 224(*i*) and ref. 33. Vol. 1, p. 26.

33) K. Klyne and J. Buckingham, "Atlas of Stereochemistry," Vol. 1, Chapman and Hall, London, 1974, and Vol. 2, 1978.

34) J.C. Craig and S.K. Roy, *Tetrahedron*, **21**, 1847 (1965).

35) See ref. 11, p. 220(i) and ref. 33, Vol. 1, p. 26.

36) S. Yamada, N. Takamura, and T. Mizoguchi, *Chem. Pharm. Bull.*, **23**, 2539 (1975).

37) H. Wynberg and B. Marsman, *J. Org. Chem.*, **45**, 158 (1980).

38) K. Mori, S. Tamada, M. Uchida, N. Mizumachi, Y. Tachibana, and M. Matsui, *Tetrahedron*, **34**, 1901 (1978).

39) *a*) C.J. Pouchert, "The Aldrich Library of Infrared Spectra," Aldrich Chemical Company, Inc., Milwaukee, Wisconsin, 1975, p. 747; *b*) C.J. Pouchert and J.R. Campbell, "The Aldrich Library of

NMR Spectra," Vol. 6, Aldrich Chemical Company, Inc., Milwaukee, Wisconsin, 1974, p. 6.
40) See ref. 11, p. 229(b) and ref. 33, Vol. 1, p. 26.
41) R.H. Rickard and J. Kenyon, *J. Chem. Soc.*, **105**, 1115 (1914).
42) See ref. 11, p. 229(d) and ref. 33, Vol. 2, p. 21.
43) This compound was erroneously expressed as PhCO*n*-Bu in the preliminary communication.[1a]
44) K. Mislow and C.H. Hamermesh, *J. Am. Chem. Soc.*, **77**, 1590 (1955).
45) See ref. 11, p. 229(f) and ref. 33, Vol. 2, p. 21.
46) R. MacLeod, F.J. Welch, and H.S. Mosher, *J. Am. Chem. Soc.*, **82**, 876 (1960).
47) See ref. 11, p. 229(i) and ref. 33, Vol. 2, p. 21.
48) W. Hückel and F. Mössner, *Liebigs Ann. Chem.*, **637**, 57 (1960).
49) See ref. 33, Vol. 1, p. 29.
50) A.G. Davies and A.M. White, *J. Chem. Soc.*, **1952**, 3300.
51) R.H. Rikard and W.O. Littlebury, *J. Chem. Soc.*, **89**, 1254 (1906).
52) See ref. 11, p. 227(d) and ref. 33, Vol. 1, p. 25.
53) S.J. Cristol, B. Franzus, and A. Shadan, *J. Am. Chem. Soc.*, **77**, 2512 (1955).
54) See ref. 11, p. 220(m) and ref. 33, Vol. 1. p. 16.
55) J. Kenyon and H.E. Strauss, *J. Chem. Soc.*, **1949**, 2153.
56) See ref. 11, p. 222(k) and ref. 33, Vol. 1, p. 62.
57) See ref. 11, p. 225 (m) and ref. 33, Vol. 1, p. 16.