Asymmetric Hydrogenation of Olefins with Aprotic Oxygen Functionalities Catalyzed by BINAP–Ru(II) Complexes

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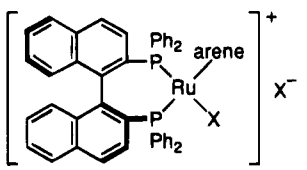
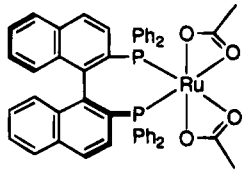
Cyclic α,β-unsaturated ketones, alkylidene lactones, and alkenyl ethers have been hydrogenated in high enantiomeric excesses by use of BINAP–Ru(II) complexes (BINAP = 2,2′-bis(diphenylphosphino)-1,1′-binaphthyl) as catalysts. 2-Alkylidenecyclopentanones were hydrogenated in the presence of [RuCl(BINAP)(benzene)]Cl, $Ru_2Cl_4(BINAP)_2(NEt_3)$, or $Ru(OCOCH_3)_2(BINAP)$ in up to 98% ee, while in the case of 2-benzylidene- and 2-(3-phenylpropylidene)cyclopentanones, enantiomeric excesses of the hydrogenation were below 50% under the same conditions. The sense of asymmetric induction as well as the enantioselectivity (95% ee) obtained in the hydrogenation of (*E*)-2-propylidene-γ-butyrolactone were the same as those of the (*Z*)-isomer. Lactones, 2- and 4-alkylidene-γ-butyrolactones, were converted to the corresponding saturated γ-butyrolactones in 95% ee. Hydrogenation of diketene with the catalytic system derived from {RuCl[(*S*)-BINAP](benzene)}Cl and triethylamine or complex $Ru_2Cl_4[(S)\text{-BINAP}]_2(NEt_3)$ established a new synthetic route to (*R*)-4-methyl-2-oxetanone, a promising monomer of biodegradable polymers, in up to 97% selectivity and 92% ee. Alkenyl ethers, 2-methylenetetrahydrofuran, and 2-methyl-3,4-dihydrofuran have also been hydrogenated to give 2-methyltetrahydrofuran in 91 and 87% ee, respectively.

Introduction

Optically active organic compounds are important for the synthesis of pharmaceuticals, harvest protecting chemicals, vitamins, fragrances, and so on.[1] They have also been attracting much attention as components of new materials such as color liquid crystals and biodegradable polymers.[2] Asymmetric hydrogenation is one of the most powerful tools for the synthesis of this class of compounds.[3] We have already reported several highly efficient BINAP–Ru(II) complex[4] catalysts for asymmetric hydrogenations of functionalized olefins such as α-(acylamino)acrylic acids,[5] enamides,[6] α,β-unsaturated carboxylic acids,[7] and allylic and homoallylic alcohols.[8] In contrast, highly enantioselective hydrogenation of olefins with aprotic oxygen functionalities like ketones, esters, and ethers has rarely been attained with conventional chiral catalysts,[3,9] though their hydrogenation products are important as synthetic intermediates. For the synthesis of such optically active compounds, enzyme-mediated reactions[10] and chemical synthesis from optically active starting materials[1,11] have so far been used. We here wish to report enantioselective hydrogenation of α,β-unsaturated carbonyl compounds, alkylidene lactones, and alkenyl ethers catalyzed by BINAP-Ru(II) complexes **1**–**4**.[12]



(*S*)-**1**: X = Cl, arene = benzene
(*S*)-**2**: X = I, arene = *p*-cymene



(*S*)-**3**

$Ru_2Cl_4[(S)\text{-BINAP}]_2(NEt_3)$

(*S*)-**4**

Results and Discussion

Asymmetric Hydrogenation of α,β-Unsaturated Carbonyl Compounds. First, we investigated suitable

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(1) Reviews: (a) Tomioka, K.; Koga, K. In *Asymmetric Synthesis*; Morrison, J. D., Ed.; Academic Press, Inc.: Orlando, 1983; Vol. 2, p 201. (b) Bergbreiter, D. E.; Newcomb, M. In *Asymmetric Synthesis*; Morrison, J. D., Ed.; Academic Press, Inc.: Orlando, 1983; Vol. 2, p 243. (c) Enders, D. In *Asymmetric Synthesis*; Morrison, J. D., Ed.; Academic Press, Inc.: Orlando, 1983; Vol. 3, p 275.

(2) (a) Goodby, J. W.; Nishiyama, I.; Slaney, A. J.; Booth, C. J.; Toyne, K. J. *Liq. Cryst.* **1993**, *14*, 37. (b) Lentz, R. P. *Adv. Polym. Sci.* **1993**, *107*, 1.

(3) (a) Koenig, K. E. In *Asymmetric Synthesis*; Morrison, J. D., Ed.; Academic Press, Inc.: Orlando, 1985; Vol. 5, Chapter 3, p 71. (b) Takaya, H.; Noyori, R. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon Press: Oxford, 1991; Vol. 8, Chapter 3.2, p 443. (c) Takaya, H.; Ohta, T.; Noyori, R. In *Catalytic Asymmetric Synthesis*; Ojima, I., Ed.; VCH Publishers: New York, 1993. (d) Noyori, R. *Asymmetric Catalysis in Organic Synthesis*; John Wiley & Sons, Inc.: New York, 1994; Chapter 2.

(4) (a) Noyori, R.; Takaya, H. *Acc. Chem. Res.* **1990**, *23*, 345. (b) Takaya, H.; Ohta, T.; Mashima, K.; Kitamura, M.; Noyori, R. In *Future Opportunities in Catalytic and Separation Technology*; Misono, M., Moro-oka, Y., Kimura, S., Eds.; Elsevier: Amsterdam, 1990; p 322. (c) Takaya, H.; Ohta, T.; Mashima, K.; Noyori, R. *Pure Appl. Chem.* **1990**, *62*, 1135. (d) Mashima, K.; Kusano, K.; Sato, N.; Matsumura, Y.; Nozaki, K.; Kumobayashi, H.; Sayo, N.; Hori, Y.; Ishizaki, T.; Akutagawa, S.; Takaya, H. *J. Org. Chem.* **1994**, *59*, 3064. Asymmetric hydrogenation of ketones: (e) Noyori, R.; Ohkuma, T.; Kitamura, M.; Takaya, H.; Sayo, N.; Kumobayashi, H.; Akutagawa, S. *J. Am. Chem. Soc.* **1987**, *109*, 5856. (f) Kitamura, M.; Ohkuma, T.; Inoue, S.; Sayo, N.; Kumobayashi, H.; Akutagawa, S.; Ohta, T.; Takaya, H.; Noyori, R. *J. Am. Chem. Soc.* **1988**, *110*, 629. For asymmetric hydrogenation by BINAP–Ru(II) complexes, see ref 15 and: (g) Kawano, H.; Ishii, Y.; Ikariya, T.; Saburi, M.; Yoshikawa, S.; Uchida, Y.; Kumobayashi, H. *Tetrahedron Lett.* **1987**, *28*, 1905. (h) Kawano, H.; Ishii, Y.; Saburi, M.; Uchida, Y. *J. Chem. Soc., Chem. Commun.* **1988**, 87. (i) Kawano, H.; Ikariya, T.; Ishii, Y.; Saburi, M.; Yoshikawa, S.; Uchida, Y.; Kumobayashi, H. *J. Chem. Soc., Perkin Trans. 1* **1989**, 1571. (j) Shao, L.; Miyata, S.; Muramatsu, H.; Kawano, H.; Ishii, Y.; Saburi, M.; Uchida, Y. *J. Chem. Soc., Perkin Trans. 1* **1990**, 1441. (k) Saburi, M.; Shao, L.; Sakurai, T.; Uchida, Y. *Tetrahedron Lett.* **1992**, *33*, 7877. (l) Shao, L.; Kawano, H.; Saburi, M.; Uchida, Y. *Tetrahedron* **1993**, *49*, 1997.

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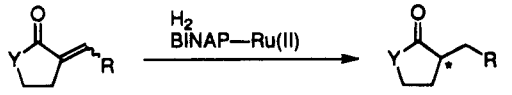
catalysts and reaction conditions for the hydrogenation of 2-methylene-γ-butyrolactone (**5a**) (eq 1 and Table 1).



(1)

5 **6**

a: Y = O R = H
b: Y = O R = C_2H_5
c: Y = CH_2 R = *n*-C_3H_7
d: Y = CH_2 R = *n*-C_4H_9
e: Y = CH_2 R = C_6H_5
f: Y = CH_2 R = $C_2H_4C_6H_5$

Hydrogenation was usually carried out at 50 °C under high H_2 pressure (100 atm) in order to achieve satisfactory conversions. Among several BINAP-Ru(II) complexes used as catalysts, the complexes bearing chloride ions showed the highest catalytic activities and enantioselectivities. Hydrogenation catalyzed by complex **2** having iodide ions proceeded in lower enantioselectivities than those with complexes **1**, **3**, and **4**. Moreover, complex **3** exhibited lower catalytic activity than other halogen-containing complexes. In this hydrogenation, CH_2Cl_2 and THF were the solvents of choice, although methanol was usually the best solvent in the hydrogenation reported previously.[4] Hydrogen pressure influenced reaction rate, but did not affect the enantiomeric excesses of the products.

In consideration of the above results, we have carried out asymmetric hydrogenation of various α,β-unsaturated carbonyl compounds catalyzed by BINAP–Ru(II) complexes in CH_2Cl_2 or THF. Results are shown in Tables 1 and 2. γ-Butyrolactones **5a** and **5b** and cyclopentanones **5c** and **5d** were hydrogenated in high enantiomeric excesses (>94% ee), which indicates that an alkyl substituent at the sp^2 carbon β to the carbonyl carbon does not produce an unfavorable effect on enantioselectivity.

Table 1. Asymmetric Hydrogenation of 5-Membered α,β-Unsaturated Carbonyl Compounds Catalyzed by BINAP–Ru(II) Complexes[a]

	substrate				product		
run		Y	R	cat.		% ee[b,c]	config[d]
1	**5a**	O	H	(*S*)-**1**	**6a**	95 (91)	*R*
2	**5a**	O	H	(*S*)-**2**	**6a**	84	*R*
3	**5a**	O	H	(*R*)-**3**	**6a**	92	*S*
4	**5a**	O	H	(*S*)-**4**	**6a**	93 (96)	*R*
5[e]	**5a**	O	H	(*R*)-**3**	**6a**	94	*S*
6[f]	**5a**	O	H	(*S*)-**3**	**6a**	82	*R*
7[g]	**5a**	O	H	(*S*)-**3**	**6a**	95	*R*
8	**5b** (7/3)[h]	O	C_2H_5	(*R*)-**4**	**6b**	92 (98)	*S*
9[i]	**5b** (0/1)[h]	O	C_2H_5	(*S*)-**4**	**6b**	95	*R*
10	**5b** (1/0)[h]	O	C_2H_5	(*R*)-**4**	**6b**	95	*S*
11	**5c** (1/0)[h]	CH_2	*n*-C_3H_7	(*R*)-**3**	**6c**	96	(+)
12	**5d** (1/0)[h]	CH_2	*n*-C_4H_9	(*R*)-**3**	**6d**	98	*S*[j]
13	**5e** (1/0)[h]	CH_2	C_6H_5	(*R*)-**4**	**6e**	9	(+)
14	**5f** (19/1)[h]	CH_2	$C_2H_4C_6H_5$	(*R*)-**3**	**6f**	50	(+)
15[k]	**8**			(*S*)-**4**	**9**	(83)	*R*
16	**10**			(*S*)-**4**	**6a**	(10)	*S*
17[l]	**11a**	O		(*R*)-**3**	**12a**	(5)	*S*
18	**11b**	CH_2		(*S*)-**3**	**12b**	(~0)	*m*

[a] A mixture of substrate, catalyst (0.2–0.5 mol% of substrate), and CH_2Cl_2 (10 mL) was stirred at 50 °C under 100 atm of hydrogen for 20–60 h, and conversions of substrates determined by GLC and/or ^1H NMR were 100% unless otherwise mentioned. [b] Enantiomeric excess was determined by HPLC. [c] Optical purity calculated based on the reported optical rotation values is given in parentheses. [d] Absolute configuration was determined by the sign of optical rotation value and/or HPLC analysis. The sign of optical rotation is given in parentheses, when the absolute configuration has not been determined. [e] Tetrahydrofuran was used as solvent. [f] Methanol was used as solvent. [g] The initial hydrogen pressure was 3 atm. The conversion was 96% by GC (SE-30, 125 °C). [h] Figures in parentheses are the ratios of *E*/*Z* of the substrates. [i] The conversion was 67% by ^1H NMR. [j] Absolute configuration was determined based on optical rotation of (*S*)-5-methyl-δ-valerolactone which was converted from **6d** by Baeyer–Villiger oxidation (see Experimental Section). [k] s/c = 1000. Tetrahydrofuran (10 mL) was used as solvent. [l] s/c = 1600. [m] Almost racemic.

Table 2. Asymmetric Hydrogenation of α,β-Unsaturated Carbonyl Compounds Catalyzed by BINAP–Ru(II) Complexes[a]

	substrate				product		
run		*n*	R	cat.		% ee[b,c]	config[d]
1	**13a**	1	C_2H_5	(*R*)-**3**	**14a**	(19)	*S*
2	**13b**	1	C_6H_5	(*R*)-**4**	**14b**	3	*R*
3[e]	**13c**	3	H	(*S*)-**4**	**14c**	(9)	*S*
4[e]	**13d**	6	H	(*S*)-**4**	**14d**	79[f]	(-)[g]
5[e]	**13e**	7	H	(*R*)-**1**	**14e**	(80)	*S*
6[e]	**15**			(*S*)-**4**	**16**	62	*R*
7[h]	**17**			(*S*)-**4**			
8[i]	**18**			(*S*)-**4**			

[a] A mixture of substrate, catalyst (1.0–2.0 mol % of substrate), and CH_2Cl_2 (10 mL) was stirred at 50 °C under H_2 (100 atm) for 20–60 h, and conversions of substrates determined by GLC were 100% unless otherwise mentioned. [b] Enantiomeric excess was determined by HPLC analysis. [c] Optical purity calculated based on the reported optical rotation values is given in parentheses. [d] Absolute configuration was determined based on the sign of optical rotation value. [e] Tetrahydrofuran (10 mL) was used as solvent. [f] Enantiomeric excess is determined by ^1H NMR using $Eu(hfc)_3$ as chiral shift reagent. [g] Since the absolute configuration has not been determined, the sign of optical rotation is given in parentheses. [h] No hydrogenation occurred at 30 °C. [i] The substrate was not converted at 50 °C.

(5) Lubell, W. D.; Kitamura, M.; Noyori, R. *Tetrahedron: Asymmetry* **1991**, *2*, 543.
(6) (a) Noyori, R.; Ohta, M.; Hsiao, Y.; Kitamura, M.; Ohta, T.; Takaya, H. *J. Am. Chem. Soc.* **1986**, *108*, 7117. (b) Kitamura, M.; Hsiao, Y.; Noyori, R.; Takaya, H. *Tetrahedron Lett.* **1987**, *28*, 4829. (c) Kitamura, M.; Hsiao, Y.; Ohta, M.; Tsukamoto, M.; Ohta, T.; Takaya, H.; Noyori, R. *J. Org. Chem.* **1994**, *59*, 297.
(7) (a) Ohta, T.; Takaya, H.; Kitamura, M.; Nagai, K.; Noyori, R. *J. Org. Chem.* **1987**, *52*, 3174. (b) Ohta, T.; Takaya, T.; Noyori, R. *Tetrahedron Lett.* **1990**, *31*, 7189. (c) Zhang, X.; Uemura, T.; Sayo, N.; Kumobayashi, H.; Takaya, H. *SYNLETT* **1994**, 501.
(8) Takaya, H.; Ohta, T.; Sayo, N.; Kumobayashi, H.; Akutagawa, S.; Inoue, S.-I.; Kasahara, I.; Noyori, R. *J. Am. Chem. Soc.* **1987**, *109*, 1596, 4129.
(9) (a) Burk, M. J. *J. Am. Chem. Soc.* **1991**, *113*, 8518. (b) Koenig, K. E.; Bachman, G. L.; Vineyard, B. D.; *J. Org. Chem.* **1980**, *45*, 2362. (c) Merrill, R. E. *CHEMTECH* **1981**, 118. (d) Hayashi, T.; Kanehira, K.; Kumada, M. *Tetrahedron Lett.* **1981**, *22*, 4417.
(10) Matsumoto, K.; Tsutsumi, S.; Ihori, T.; Ohta, H. *J. Am. Chem. Soc.* **1990**, *112*, 9614.
(11) (a) Meyers, A. I.; Williams, D. R.; Erickson, G. W.; White, S.; Druelinger, M. *J. Am. Chem. Soc.* **1981**, *103*, 3081. (b) Mori, K.; Senda, S. *Tetrahedron* **1985**, *41*, 541.
(12) A part of this work has been reported in: (a) Ohta, T.; Miyake, T.; Seido, N.; Kumobayashi, H.; Akutagawa, S.; Takaya, H. *Tetrahedron Lett.* **1992**, *33*, 635. (b) Ohta, T.; Miyake, T.; Takaya, H. *J. Chem. Soc., Chem. Commun.* **1992**, 1725.
(13) Mashima, K.; Kusano, K.; Ohta, T.; Noyori, R.; Takaya, H. *J. Chem. Soc., Chem. Commun.* **1989**, 1208.
(14) Ohta, T.; Takaya, H.; Noyori, R. *Inorg. Chem.* **1988**, *27*, 566.
(15) Ikariya, T.; Ishii, Y.; Kawano, H.; Arai, T.; Saburi, M.; Yoshikawa, S.; Akutagawa, S. *J. Chem. Soc., Chem. Commun.* **1985**, 922.
(16) Helmchen, G.; Nill, G.; Flockerzi, D.; Schühle, W.; Youssef, M. S. K. *Angew. Chem., Int. Ed. Engl.* **1979**, *18*, 63.
(17) Meyers, A. I.; Yamamoto, Y.; Michelich, E. D.; Bell, R. A. *J. Org. Chem.* **1980**, *45*, 2792.
(18) Berner, E.; Leonardsen, R.; Grøntoft, A. T.; Dahl, K. *Liebigs Ann. Chem.* **1939**, *538*, 1.
(19) Leuenberger, H. G. W.; Boguth, W.; Barner, R.; Schmid, M.; Zell, R. *Helv. Chim. Acta* **1979**, *62*, 455.
(20) Eisenbraun, E. J.; McElvain, S. M. *J. Am. Chem. Soc.* **1955**, *77*, 3383.
(21) Hafner, T.; Reissig, H.-U. *Liebigs Ann. Chem.* **1989**, 937.
(22) Huisgen, R.; Rüchardt, C. *Liebigs Ann. Chem.* **1956**, *601*, 21.
(23) Keinan, E.; Seth, K. K.; Lamed, R. *J. Am. Chem. Soc.* **1986**, *108*, 3474.

Scheme 1

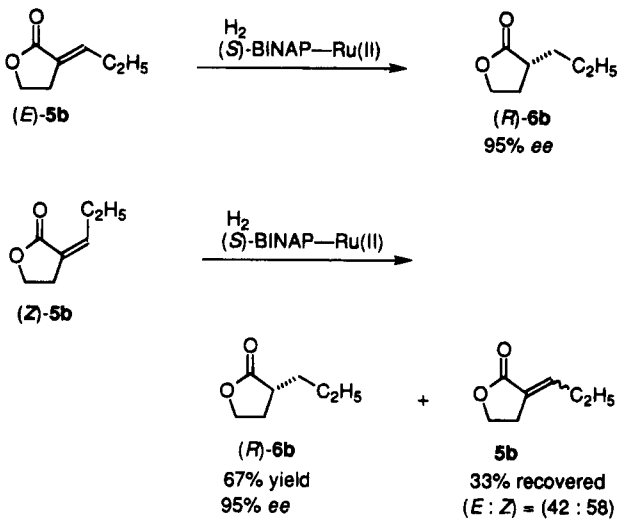


Table 3. ^{1}H NMR Analysis of 6b and Products 6b-d_2 Obtained by Deuteration of (*E*)- and (*Z*)-5b

	ppm		
	1.3–1.5 $H_a + H_b$	1.8–1.9 H_c	2.5–2.6 H_d
6b	3.0 H	1.0 H	1.0 H
6b-d_2 obtained from (*E*)-**5b**	3.0 H	~0 H	~0 H
6b-d_2 obtained from (*Z*)-**5b**	2.4 H	0.6 H	~0 H

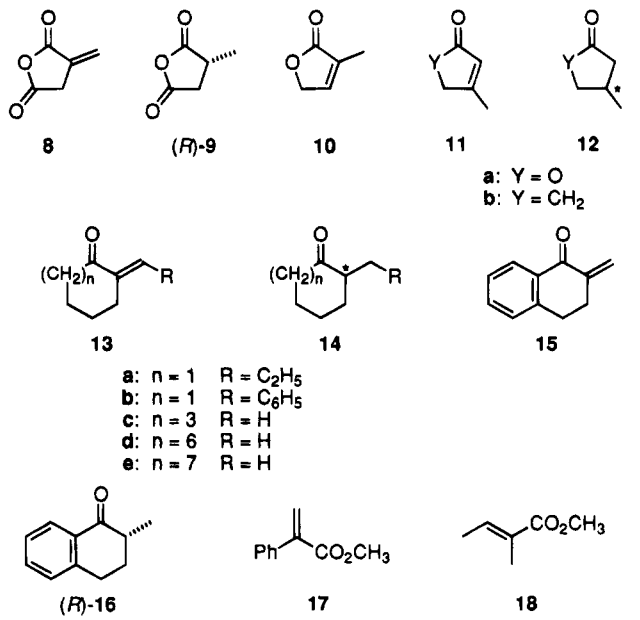
Products (*R*)- and (*S*)-**6d** are useful perfumes with a jasmine-like odor. Absolute configuration of **6d** was determined based on the sign of the optical rotation value of 5-pentyl-δ-valerolactone (**7**) derived from **6d** by Baeyer–Villiger oxidation (eq 2).

(2)

When a 7:3 mixture of (*E*)- and (*Z*)-2-propylidene-γ-butyrolactone [(*E*)-**5b** and (*Z*)-**5b**] was used as starting material, hydrogenation catalyzed by (*R*)-**4** gave (*S*)-**6b** in 92% ee (Table 1, run 8). The reaction of stereochemically pure (*E*)-**5b** or (*Z*)-**5b** also proceeded smoothly, and the same sense of asymmetric induction was obtained in almost the same enantiomeric excesses (Table 1, runs 9 and 10) (Scheme 1). The above results show that the proportion of (*E*)- and (*Z*)-isomers does not affect the enantioselectivity. However, the possibility that hydrogenation proceeds through a $Z \rightarrow E$ isomerization can not be ruled out, since the rate of the reaction of *Z* isomer was slower than that of *E* isomer (*Z* isomer: 67% conversion at 50 °C for 60 h, *E* isomer: >99% conversion at 50 °C for 40 h) and the recovered substrates at 67% conversion was a 42:58 mixture of *E* and *Z* isomers, which suggests that at least a part of the product arises via $Z \rightarrow E$ isomerization. In fact, ^{1}H NMR analysis of the deuteration product **6b**-d_2 of (*E*)-**5b** showed that the deuterium incorporation was limited to Hc and Hd positions, while in the products from (*Z*)-**5b** deuterium was distributed over Hb, Hc, and Hd in a 0.4:0.6:1.0 ratio (Table 3). Since deuteration can be considered to occur completely in cis fashion,[7b] we can estimate that in deuteration of (*Z*)-**5b**, 60% of the product arose from direct reduction of (*Z*)-**5b** and 40% of that was given via $Z \rightarrow E$ isomerization followed by deuteration. These facts suggest that the BINAP–Ru(II) complex differentiates the enantiofaces of the sp^2 carbon α to the carbonyl function but almost ignores the difference in the geometry at the β-sp^2 carbon of **5b**.[8]

For cyclopentanone derivatives, introduction of a phenyl or β-phenethyl substituent on the olefin moiety caused a dramatic decrease in enantioselectivities as shown for **5e** and **5f**. Itaconic anhydride (**8**), the compound structurally related to **5a**, was also hydrogenated smoothly to give the product arisen from the same sense of asymmetric induction with that of **5a** in high ee. 5-Membered substrates **10** and **11** with endocyclic double bonds were hydrogenated in low enantioselectivities.

In most cases, enantioselectivities observed for 6- and 8-membered α,β-unsaturated carbonyl compounds were lower than those obtained for 5-membered analogues. 2-Alkylidene- and 2-benzylidenecyclohexanone (**13a** and **13b**) and 2-methylenecyclooctanone (**13c**) were hydrogenated in low enantioselectivities, while 2-methylene-1-tetralone (**15**) was converted to **16** in moderate enantioselectivity (62% ee) (Table 2). Interestingly, high optical yields (ca. 80%) have been again attained for hydrogenation of higher homologs, 2-methylenecycloundecanone (**13d**) and 2-methylenecyclododecanone (**13e**), to give 2-methylcycloundecanone (**14d**) and 2-methylcyclododecanone (**14e**), respectively. Unfortunately, acyclic substrates, such as methyl atropate (**17**) and methyl tiglate (**18**), were not hydrogenated under the standard conditions (Table 2).

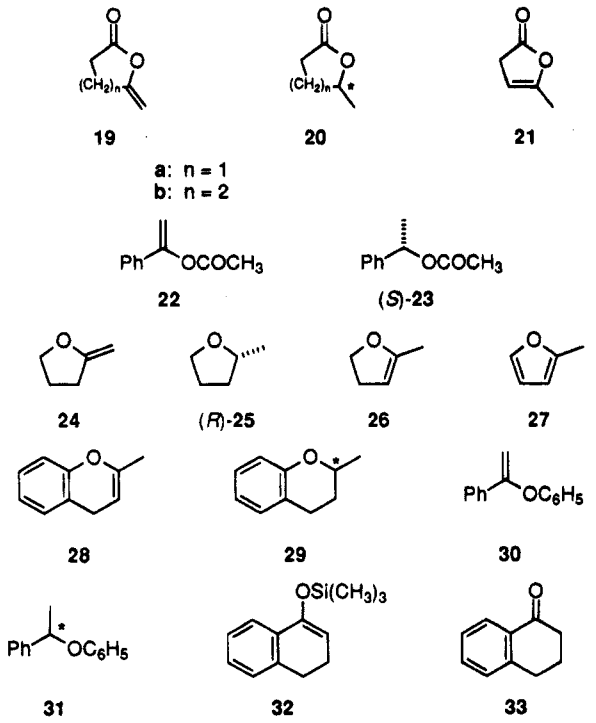


Asymmetric Hydrogenation of Alkenyl Esters and Alkenyl Ethers. Hydrogenation of 4-methylene-γ-butyrolactone (**19a**) catalyzed by (*R*)-**3** afforded (*R*)-**20a** in 94% ee. The endo isomer **21** was also smoothly hydrogenated, but in low enantioselectivity (Table 4).

In order to clarify the role of carbonyl function of **19a**, 2-methylenetetrahydrofuran (**24**) was subjected to reduction catalyzed by (*S*)-**3** to give (*R*)-2-methyltetrahydrofuran [(*R*)-**25**] in 91% ee. This shows that the carbonyl

moiety of **19a** does not have an important role in the present hydrogenation. Interestingly, endo type substrate, 2-methyl-3,4-dihydrofuran (**26**), was also hydrogenated by (*R*)-**4** in 87% ee to give (*S*)-**25**. 2-Methylfuran (**27**) was also hydrogenated in the presence of (*R*)-**4** to give 2-methyltetrahydrofuran [(*S*)-**25**], but only in 50% ee.

Acyclic alkenyl ester **22** and alkenyl ether **30** were also hydrogenated smoothly in comparison with acyclic α,β-unsaturated carboxylic esters (no reaction under standard conditions, *vide supra*) to give the corresponding saturated ester and ether in 70–73% ee's. In the case of 6-membered substrates **19b** and **28**, hydrogenation products **20b** and **29** were obtained in 62% optical yield and 64% ee, respectively. Substrate **32** was converted to 1-tetralone under this catalytic condition.



Asymmetric Hydrogenation of Diketene.[12b] An efficient synthesis of (*R*)- and (*S*)-4-methyl-2-oxetanone (**35**) has been realized by the asymmetric hydrogenation of commercially available diketene (**34**) by use of the BINAP–Ru(II) catalysts. Compound (*R*)-**35** is a promising starting monomer[24,25] of biodegradable polymers such as poly-(*R*)-3-hydroxybutyrate[26] and BIOPOL, commercially available biodegradable plastics developed by ICI Co., Ltd.[27]

Representative results are listed in Table 5. Higher reaction temperature does not cause any substantial loss of enantioselectivity over the range 50–70 °C. Use of aprotic solvents is important for high product selectivities. Precatalyst derived from {RuCl[(*S*)- or (*R*)-BINAP](benzene)}Cl and 0.5–0.9 equiv of NEt_3 gave the best results in both selectivity and enantiomeric excess. In

Table 4. Asymmetric Hydrogenation of Alkenyl Esters and Alkenyl Ethers Catalyzed by BINAP–Ru(II) Complexes[a]

				product		
run	substrate	cat.	solvent		% ee[b]	config[c]
1	**19a**	(*R*)-**3**	CH_2Cl_2	**20a**	94 (90)	*S*
2	**19b**	(*S*)-**4**	CH_2Cl_2	**20b**	(62)	*R*
3	**21**	(*S*)-**3**	CH_2Cl_2	**20a**	(20)	*S*
4	**22**	(*R*)-**4**	CH_2Cl_2	**23**	40	*S*
5	**22**	(*R*)-**4**	THF	**23**	64	*S*
6[d]	**22**	(*R*)-**4**	dioxane[e]	**23**	73	*S*
7	**22**	(*S*)-**4**	MeOH	**23**	20	*S*
8[f]	**24**	(*S*)-**3**	CH_2Cl_2	**25**	91	*R*
9[g]	**26**	(*R*)-**4**	CH_2Cl_2	**25**	87	*S*
10[h]	**27**	(*R*)-**4**	CH_2Cl_2	**25**	50	*S*
11	**28**	(*R*)-**1**	THF	**29**	64	(-)
12	**30**	(*S*)-**4**	CH_2Cl_2	**31**	70	*i*
13	**32**	(*R*)-**4**	CH_2Cl_2	**33**[j]		

[a] A mixture of substrate, catalyst (0.2–1.0 mol %), and solvent (10 mL) was stirred at 50 °C under 100 atm of hydrogen for 20–60 h, and conversions of substrates determined by GLC or ^1H NMR were 100% unless otherwise mentioned. [b] Enantiomeric excesses were determined by GC or by ^1H NMR spectroscopy with chiral shift reagent Eu(hfc)$_3$. Optical purity calculated based on the reported optical rotation values is given in parentheses. [c] Absolute configuration was determined based on the sign of optical rotation value. The sign of optical rotation is given in parentheses, when the absolute configuration has not been determined. [d] The conversion was 80% by ^1H NMR spectroscopy. [e] A mixture of dioxane (10 mL) and $C_2H_4Cl_2$ (0.1 mL) was used as solvent. [f] The conversion was 98% by ^1H NMR spectroscopy. [g] Reaction was carried out at 40 °C. [h] Reaction was carried out at 70 °C. [i] Since conversion was 25%, isolation of the pure product was difficult. [j] The product was 1-tetralone.

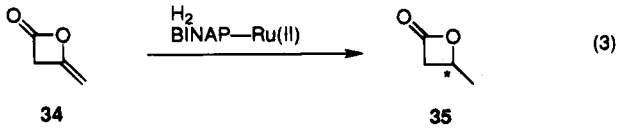
Table 5. Asymmetric Hydrogenation of Diketene (34) Catalyzed by BINAP–Ru(II) Complexes[a]

			4-methyl-2-oxetanone		
run	cat.[b]	solvent	select.[c] (%)	% ee[d]	config[e]
1	(*R*)-**4**	CH_2Cl_2	95	90	*S*
2[f]	(*R*)-**4**	CH_2Cl_2	90	90	*S*
3	(*R*)-**4**	THF	95	90	*S*
4	(*R*)-**4**	dioxane	98	86	*S*
5	(*R*)-**4**	CH_3OH	40[g]		
6	(*S*)-**3**	CH_2Cl_2	76	70	*R*
7	(*R*)-**36**	CH_2Cl_2	70	70	*S*
8	(*R*)-**1**	CH_2Cl_2	69	70	*S*
9	(*R*)-**37**	CH_2Cl_2	17		
10	(*R*)-**1**–0.5 NEt_3[h]	THF	97	90	*S*
11	(*R*)-**1**–0.9 NEt_3[h]	THF	97	92	*S*
12	(*S*)-**1**–0.9 NEt_3[h]	THF	97	92	*R*
13	(*R*)-**36**–2 NEt_3[i]	CH_2Cl_2	38[j]	89	*S*
14	(*R*)-**36**–10 NEt_3[i]	CH_2Cl_2	0[k]		*S*

[a] A mixture of diketene (0.84–2.08 g), catalyst (0.1–0.2 mol %), and solvent (10 mL) was stirred at 50 °C under initial hydrogen pressure of 100 atm for 20–60 h. Conversion was 100% unless otherwise noted. [b] (*R*)-**36**; an empirical formula $RuCl_2$[(*R*)-BINAP],[4e] (*R*)-**37**; {$RhCl_2$[(*R*)-BINAP]}$_2$.[28] [c] Determined by ^1H NMR. The other product is butyric acid. [d] Determined by ^1H NMR analysis of the (*R*)-MTPA ester of methyl 3-hydroxybutyrate derived from methanolysis of **35**. [e] Determined by optical rotation. [f] At 70 °C. [g] The major product is a mixture of methyl 3-hydroxybutyrate and methyl 3-oxobutyrate. [h] {RuCl[(*R*)-BINAP](benzene)}Cl was treated with triethylamine (0.5–0.9 equiv to Ru(II)), and then the mixture was added to the substrate. [i] An excess amount of triethylamine relative to Ru(II) was added to the substrate and then the mixture was added to $RuCl_2$[(*R*)-BINAP]. [j] Conversion was 80%. The other products were butyric acid (2%) and polymeric materials (60%). [k] Only polymeric materials were formed.

(24) Shelton, J. R.; Lando, J. B.; Agostini, D. E. *J. Polym. Sci., B: Polym. Lett.* **1971**, *9*, 173.
(25) Tanahashi, N.; Doi, Y. *Macromolecules* **1991**, *24*, 5732.
(26) Delafield, F. P.; Doudoroff, M.; Palleroni, N. J.; Lusty, C. J.; Contopoulos, R. *J. Bacteriol.* **1965**, *90*, 1455.
(27) Holmes, P. A. *Phys. Technol.* **1985**, *16*, 32.
(28) Inoue, S.-I.; Osada, M.; Koyano, K.; Takaya, H.; Noyori, R. *Chem. Lett.* **1985**, 1007.

the absence of triethylamine, competitive hydrogenolysis occurred to give butyric acid in 30% yield. The use of excess amine (more than 2 equiv), however, caused polymerization of the substrate **34** (eq 3). The addition



34 **35** (3)

of excess *p*-toluenesulfonic acid to the catalytic system containing amine-treated complex did not increase the amount of butyric acid. These observations suggest that the role of added amine is to suppress the catalytic activity of the ruthenium species which causes hydrogenolysis of the β-lactone ring. The catalytically active species, however, is not clear at present, since the complexes derived from {RuCl[(*S*)-BINAP](benzene)}Cl and 0.9 equiv of NEt_3 are a mixture of many species as proved by ^{31}P NMR spectroscopy. When a neutral BINAP–Rh(I) complex derived from $[RhCl(cod)]_2$ and 2.05 equiv of (*R*)-BINAP was used as catalyst, the major product was butyric acid in addition to desired product (*R*)-**35** in 17% yield.

Optically active (*R*)-4-methyl-2-oxetanone has so far been prepared by optical resolution of 3-bromobutyric acid with (*R*)-1-naphthylethylamine followed by cyclization.[29] The present catalytic asymmetric synthesis seems to be more convenient and to give the product with optical purity high enough for biodegradable polymers.

Recently, usefulness of (*R*)-**35** as monomer for the preparation of biodegradable polymers has been demonstrated by the Takasago group.[30] Poly-[(*R*)-3-hydroxybutyrate] was prepared from (*R*)-**35** catalyzed by distannoxane. This polymerization gives the corresponding polymers with sufficiently high molecular weight (M_n > 100 000) without racemization.[30b] Also, copolymerization of (*R*)-**35** and ε-caprolactone proceeded smoothly by the same catalyst.[30a]

Origin of Enantioselectivity. The stereoselectivity of the present asymmetric hydrogenation depends highly on relative positions of C=C bonds and oxygen functionalities. For the hydrogenation of unsaturated compounds catalyzed by BINAP–Ru(II) complexes, high enantioselectivities have usually been attained only with substrates that have another functional group at a neighboring position.[4] Such reactions are considered to proceed by chelation control. In the present reaction, chelation of the substrates to the Ru(II) species also seems to be important for high enantioselectivities (Figure 1).

Substrates having exocyclic C=C bonds can be considered to form chelate complexes **38**–**41** in which the olefinic part and the oxygen functionality coordinate to Ru simultaneously. Although ethereal oxygen has not been demonstrated as a good chelating substituent for asymmetric hydrogenation of olefins,[31] it has been shown to act as a coordinating group in the hydrogenation catalyzed by Rh and Ir complexes.[32]

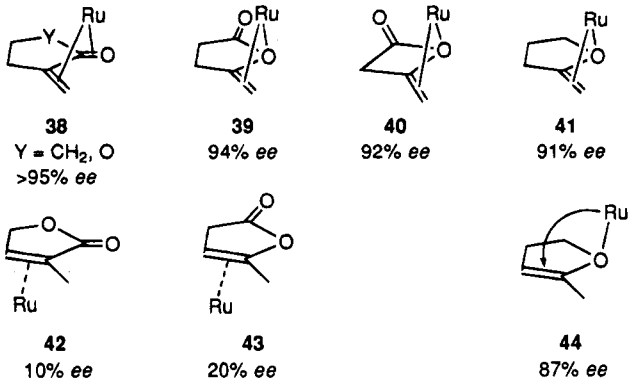
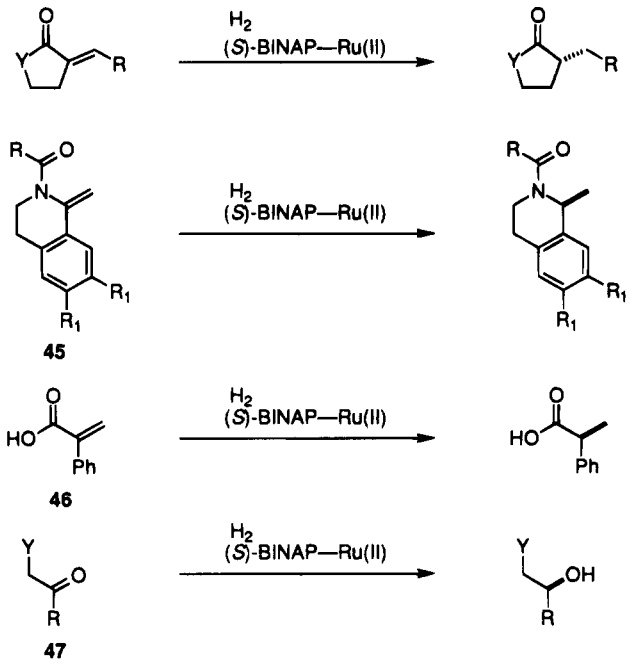


Figure 1. Coordination modes of the substrates to the catalytic center at enantioface-differentiation step.

Scheme 2



In contrast, endocyclic olefins, such as α,β-unsaturated lactone **10** and alkenyl lactone **21**, are thought not to form a chelate complex from the standpoint of steric constraints. Thus, hydrogenation via complexes **42** and **43** in which only C=C bonds coordinate to ruthenium might result in low enantioselectivities. Although formation of a chelate complex also seems to be difficult for **26**, higher basicity of ethereal oxygen of **26** than that of compound **21** might allow transient oxygen–ruthenium interaction prior to coordination of C=C bond, and this might contribute to high enantioselectivities.

In the present asymmetric catalysis, 5-membered substrates **5a**–**d**, **19a**, **24**, and diketene (**34**) which have exocyclic double bonds were hydrogenated in very high enantiomeric excesses. When (*S*)-BINAP–Ru(II) complexes were used as catalysts, products with (*R*)-configuration were obtained. As shown in Scheme 2, this stereochemistry is opposite to that observed in the hydrogenation of acyclic olefins such as *N*-acyl-1-methylene-1,2,3,4-tetrahydroisoquinolines (**45**) and atropic acid (**46**), and α- or β-functionalized ketones **47** catalyzed by (*S*)-BINAP–Ru(II) complexes. In the present catalysis, the rigid cisoid and planar arrangement of C=C and oxygen functionalities favors the formation of chelate

(29) (a) Sato, T.; Itoh, T.; Hattori, C.; Fujisawa, T. *Chem. Lett.* **1983**, 1391. (b) Sato, T.; Kawara, T.; Nishizawa, A.; Fujisawa, T. *Tetrahedron Lett.* **1980**, *21*, 3377.

(30) (a) Hori, Y.; Takahashi, Y.; Yamaguchi, A.; Nishihata, T. *Macromolecules* **1993**, *26*, 4388. (b) Hori, Y.; Suzuki, M.; Yamaguchi, A.; Nishihata, T. *Macromolecules* **1993**, *26*, 5533.

(31) In the case of hydrogenation of ketones, see: Cesarotti, E.; Mauri, A.; Pallavicini, M.; Villa, L. *Tetrahedron Lett.* **1991**, *32*, 4381.

(32) (a) Brown, J. M. *Angew. Chem., Int. Ed. Engl.* **1987**, *26*, 190. (b) Crabtree, R. H.; Davis, M. W. *J. Org. Chem.* **1986**, *51*, 2655.

complexes **38**–**41**. On the other hand, formation of such types of complexes involving side-one coordination of carbonyl moieties might be unfavorable for acyclic substrates **45** and **47**, due to the conformational flexibility. These facts might be related to the difference in stereochemistry of hydrogenation between these two classes of substrates.

Another characteristic feature of the present asymmetric hydrogenation is a remarkable solvent effect. In this catalysis, methanol is always not a good solvent, which is in contrast with the fact that methanol is essential for high catalytic activities and enantioselectivities in the asymmetric hydrogenation of *N*-acyl-1-methylene-1,2,3,4-tetrahydroisoquinolines, acrylic acids, allylic and homoallylic alcohols, and α- or β-functionalized ketones. Lower diastereo- and enantioselectivities[4d,33] in methanol have also been observed for the hydrogenation of methyl 2-[(acylamino)methyl]-3-oxobutyrate and olefins without heteroatom functionalities such as 1-methylenetetraline.[34]

The nature of anions in complexes **1**–**3** sometimes affects catalytic activities and enantioselectivities. Upon reaction of hydrogen, these complexes are considered to give catalytically active RuX(H)(BINAP) (X = halogen, carboxylate).[7b] The steric and electronic characters of the counter ion X remaining on Ru should be reflected on the catalytic properties of BINAP–Ru(II) species. Moreover, the liberated acids might also exert some influence on catalytic activities and enantioselectivities. Thus, the choice of the most appropriate catalyst precursors is requisite for achieving high efficiencies.

Conclusion

The substrates for the asymmetric hydrogenation catalyzed by BINAP–Ru(II) complexes have been expanded to various cyclic α,β-unsaturated carbonyl compounds, alkenyl esters, and alkenyl ethers. Five-membered cyclic ketones, lactones, and ethers having exocyclic C=C bonds are hydrogenated in very high enantioselectivities. In the case of alkenyl esters and ethers, ethereal oxygen takes an important role for the enantioface differentiation. The asymmetric hydrogenation has been successfully applied to the synthesis of (*R*)-4-methyl-2-oxetanone, a promising monomer for biodegradable polymers.

Experimental Section

General Remarks. All manipulations of oxygen- and moisture-sensitive materials were conducted under purified argon atmosphere (BASF-Catalyst R3-11) by use of standard Schlenk techniques.

Apparatus. ^{1}H NMR spectra were taken on a JEOL EX-270 (270 MHz) spectrometer using tetramethylsilane as an internal standard. Optical rotations were measured on a JASCO DIP-360 polarimeter. Analyses of gas chromatography were performed on a Hitachi 263-30 and a Shimadzu GC-15APF. Liquid chromatographic (HPLC) analyses were conducted on a TOSOH CCPM equipped with CO-8000 injection unit and UV-8000 detector. Low resolution mass spectra (LRMS) were recorded on a Shimadzu GC-MS QP-1000 mass spectrometer.

Chemicals. All solvents were dried by standard methods and distilled under argon. Commercial reagents **5a**, **8**, **10**, **11a**, **11b**, **18**, **19a**, **21**, **26**, **27**, and **34** were purchased from Wako Pure Chemical Industries, Ltd., Nacalai tesque, Tokyo Kaseikogyo Co., Ltd., or Aldrich Chemical Co., Inc., and used without further purification. 2-Pentylidenecyclopentanone (**5d**),[35] 2-benzylidenecyclopentanone (**5e**),[36] 2-benzylidenecyclohexanone (**13b**),[36] 2-methylenecyclooctanone (**13c**),[37] 2-methylenecyclododecanone (**13e**),[37] 2-methylene-1-tetralone (**15**),[37] 5-methylene-δ-varelolactone (**19b**),[38] 1-acetoxy-1-phenylethene (**22**),[9b] 2-methylenetetrahydrofuran (**24**),[39] 2-methyl-3,4-dihydrochmarine (**28**),[40] 1-phenoxy-1-phenylethene (**30**),[41] [RuCl(BINAP)(benzene)]Cl (**1**),[13] [RuI(BINAP)(*p*-cymene)]I (**2**),[13] [Ru(OAc)$_2$(BINAP)] (**3**),[14] Ru$_2$Cl$_4$(BINAP)$_2$(NEt$_3$) (**4**),[15] RuCl$_2$(BINAP),[4e] and [RhCl(BINAP)]$_2$ (**37**)[28] were made by literature methods. 2-Propylidene-γ-butyrolactone (**5b**),[42] 2-butylidenecyclopentanone (**5c**),[35] 2-(3-phenylpropylidene)cyclopentanone (**5f**),[42] 2-propylidenecyclohexanone (**13a**),[43] 2-methylenecycloundecanone (**13d**),[37] and 1-(trimethylsiloxy)-3,4-dihydronaphthalene (**32**)[44] were prepared by slightly modified methods based on the literature procedures. Methyl atropate (**17**) was prepared by the reaction of atropic acid[45] with diazomethane.

Asymmetric Hydrogenation of 2-Methylene-γ-butyrolactone (5a) Catalyzed by [RuCl((*S*)-BINAP)(benzene)]Cl [(*S*)-1]. This is a typical procedure for the asymmetric hydrogenation. The substrate **5a** (95 mg, 1.0 mmol) in dichloromethane (10.0 mL) was degassed by freeze–thaw techniques. To this was added complex (*S*)-**1** (17.4 mg, 1.9 × 10^{-2} mmol), and the solution was stirred in an autoclave at 50 °C under hydrogen atmosphere (100 kg/cm^2). The conversion was measured by GLC (SE-30, 125 °C), which showed that the reaction finished in 45 h. The product (*R*)-**6a** (90 mg, 0.90 mmol, 93% yield) was obtained by a Kugelrohr distillation. Enantiomeric excess (95% ee) of (*R*)-**6a** was determined by HPLC (Chiralcel OD, hexane:2-propanol = 99:1 (0.5 mL/min), UV (230 nm), t_R = 40.0 min and t_S = 45.5 min). Absolute configuration (*R*) and optical purity of **6a** (91% o.p. based on the value (lit.[16] (*R*)-**6a** $[\alpha]^{23}_D$ +23.1° (*c* 9.7, EtOH)) were determined from the optical rotation value $[\alpha]^{18}_D$ +21.1° (*c* 1.9, EtOH).

Determination of Absolute Configuration and Optical Purity and/or Enantiomeric Excess. (*S*)-2-Propylidene-γ-butyrolactone [(*S*)-6b] (from 5b (*E*/*Z* = 7/3)): $[\alpha]^{20}_D$ +10.8° (*c* 2.0, EtOH) (lit.[17] 73% of (*R*)-**6b** $[\alpha]_D$ −8.05° (*c* 5.7, EtOH)); 92% ee by HPLC (Chiralcel OD, hexane:2-propanol = 497:3 (1 mL/min), UV (230 nm), t_R = 23.8 min, t_S = 25.3 min).

2-Butylcyclopentanone [(+)-6c]: 96% ee by HPLC (Wakosil 5 sil (4.6 mm × 30 mm) and Chiralcel OJ (4.6 mm x 250 mm), hexane:2-propanol = 199:1 (0.5 mL/min), UV (220 nm), *t* = 15.0 and 16.4 min). Product from the reaction by (*S*)-**4** at 70 °C showed 89% ee by HPLC and $[\alpha]^{24}_D$ −29.5° (*c* 2.7, MeOH).

(*S*)-2-Pentylcyclopentanone [(*S*)-6d]: 89% isolated yield, $[\alpha]^{25}_D$ +55.8° (*c* 1.9, MeOH), 98% ee by HPLC (Chiralcel OJ, hexane:2-propanol = 249:1 (0.5 mL/min), UV (220 nm), t_R = 16.3 min, t_S = 18.2 min). Absolute configuration was determined by the sign of optical rotation value of 5-pentyl-δ-valerolactone (*S*)-**7** derived from the hydrogenated product (+)-**6d** by Baeyer–Villiger oxidation (see below).

2-Benzylcyclopentanone [(+)-6e]: 85% isolated yield, $[\alpha]^{25}_D$ +15.4° (*c* 2.1, MeOH), 9% ee by HPLC (Chiralcel OJ,

(33) Mashima, K.; Matsumura, Y.; Kusano, K.; Kumobayashi, H.; Sayo, N.; Hori, Y.; Ishizaki, T.; Akutagawa, S.; Takaya, H. *J. Chem. Soc., Chem. Commun.* **1991**, 609.

(34) Ohta, T.; Ikegami, H.; Takaya, H. To be published.

(35) Edger, O. B.; Johnson, D. H. *J. Chem. Soc.* **1958**, 3925.

(36) Emerson, W. S.; Birum, G. H.; Longley Jr., R. I. *J. Am. Chem. Soc.* **1953**, *75*, 1312.

(37) (a) Gras, J.-L. *Tetrahedron lett.* **1978**, *24*, 2111. (b) Gras, J.-L. *Org. Synth.* **1981**, *60*, 88.

(38) Lambert, C.; Utimoto, K.; Nozaki, H. *Tetrahedron Lett.* **1984**, *25*, 5323.

(39) Ireland, R. E.; Häbich, D. *Chem. Ber.* **1981**, *114*, 1418.

(40) Baker, W.; Walker, J. *J. Chem. Soc.* **1935**, 646.

(41) (a) Pine, S. H.; Pettit, R. J.; Geib, G. D.; Cruz, S. G.; Gallego, C. H.; Tijerina, T.; Pine, R. D. *J. Org. Chem.* **1985**, *50*, 1212. (b) Pine, S. H.; Kim, G.; Lee, V. *Org. Synth.* **1990**, *69*, 72.

(42) Ksander, G. M.; McMurry, J. E.; Johnson, M. *J. Org. Chem.* **1977**, *42*, 1180.

(43) Tamura, M.; Katumata, H.; Urakawa, K.; Ohtani, Y. *Chem. Abstr.* **1986**, *104*, p19370h; Ger. Offen. DE 3,435,003.

(44) Hoffman, R. V.; Carr, C. S.; Jankowski, B. C. *J. Org. Chem.* **1985**, *50*, 5148.

(45) Raper, H. S. *J. Chem. Soc.* **1923**, 2557.

hexane:2-propanol = 199:1, (1.0 mL/min), UV (254 nm), t = 19.7 and 22.3 min).

2-(3-Phenylpropyl)cyclopentanone [(+)-6f]: 91% isolated yield, $[\alpha]^{20}_D$ +65.1° (*c* 4.6, MeOH), 50% ee by HPLC (Chiralcel OD, hexane:2-propanol = 49:1 (1.0 mL/min) UV (254 nm), t = 12.2 and 13.7 min).

(*R*)-Methylsuccinic anhydride [(*R*)-9]: 75% isolated yield, $[\alpha]^{21}_D$ +25.7° (*c* 1.7, EtOH) (lit.[18] (*R*)-**9** $[\alpha]^{20}_D$ +32.1° (*c* 4.024, EtOH)).

(*S*)-3-Methyl-γ-butyrolactone [(*S*)-12a]: $[\alpha]^{25}_D$ −1.3° (*c* 1.9 MeOH) (lit.[19] (*S*)-**12a** $[\alpha]^{20}_D$ −24.7° (*c* 4, MeOH)).

(+)-3-Methylcyclopentanone [(+)-12b]: $[\alpha]^{25}_D$ +1.5° (*c* 0.6, MeOH) (lit.[20] (*R*)-**12b** $[\alpha]_D$ +154.8° (*c* 0.73, $CHCl_3$)).

(*S*)-2-Propylcyclohexanone [(*S*)-14a]: $[\alpha]^{23}_D$ +5.4° (*c* 4.0, MeOH) (lit.[11a] 99% ee of (*S*)-**14a**; $[\alpha]_D$ +27.9° (*c* 4, MeOH)).

(*R*)-2-Benzylcyclohexanone [(*R*)-14b]: 88% isolated yield, $[\alpha]^{20}_D$ +0.7° (*c* 2.0, MeOH) (lit.[11a] 88% ee of (*R*)-**14b** $[\alpha]_D$ +41.4° (*c* 5, MeOH)), 3.0% ee by HPLC (Chiralcel OJ, hexane:2-propanol = 199:1 (1 mL/min), UV (254 nm), t_R = 18.1 min, t_S = 20.7 min).

(*S*)-2-Methylcyclooctanone [(*S*)-14c]: 86% isolated yield, 9% o.p. by $[\alpha]^{20}_D$ +3.7° (*c* 7, $CHCl_3$) (lit.[11a] 20% ee of (*S*)-**14c** $[\alpha]_D$ +8.07° (*c* 7, $CHCl_3$)).

(−)-2-Methylcycloundecanone [(−)-14d]: 93% isolated yield, $[\alpha]^{22}_D$ −19.8° (*c* 4, $CHCl_3$), 79% ee by ^1H NMR with chiral shift reagent Eu(hfc)$_3$.

(*S*)-2-Methylcyclododecanone [(*S*)-14e]: 88% isolated yield, 80% o.p. by $[\alpha]^{18}_D$ −11.7° (*c* 4.2, $CHCl_3$) (lit.[10] 95% ee of (*R*)-**14e** $[\alpha]^{23}_D$ +13.9° (*c* 1.09, $CHCl_3$)).

(*R*)-2-Methyl-1-tetralone [(*R*)-16]: 77% isolated yield, $[\alpha]^{19}_D$ +37.9° (*c* 2.3, dioxane) (lit.[11a] 79% ee of (*S*)-**16** $[\alpha]^{19}_D$ −40.5° (*c* 3, dioxane)), 62% ee by HPLC (Chiralcel OD, hexane:2-propanol = 199:1 (1 mL/min), UV (254 nm), t_R = 8.2 min, t_S = 9.3 min).

(*R*)-4-Methyl-γ-butyrolactone [(*R*)-20a]: 77% isolated yield, $[\alpha]^{23}_D$ +31.5° (*c* 0.7, $CHCl_3$) (lit.[21] (*S*)-**20a** $[\alpha]^{20}_D$ −31.6° (*c* 0.95, $CHCl_3$)), 94% ee by GLC (Cp Cyclodex-B-236M, 80 °C, He (1.8 kg/cm^2), t_R = 34.0 min, t_S = 33.4 min).

(*R*)-5-Methyl-δ-valerolactone [(*R*)-20b]: 62% optical purity, $[\alpha]^{20}_D$ +22.9° (*c* 3.0, EtOH) (lit.[11b] (*R*)-**20b** $[\alpha]_D$ +37.2° (*c* 1.83, EtOH)).

(*S*)-1-Phenylethyl acetate [(*S*)-23]: 80% conversion, $[\alpha]^{20}_D$ −28° (*c* 3.0, CH_2Cl_2) (lit.[22] (*S*)-**23** $[\alpha]^{21}_D$ −124.5° (*c* 2.1, benzene), 40% ee by GLC (Cyclodex B-PH, 80 °C, He (1.0 kg/cm^2), t_R = 11.6 min, t_S = 11.1 min).

(*R*)-2-Methyltetrahydrofuran [(*R*)-25]: $[\alpha]^{27}_D$ −15.3° (*c* 0.7, $CDCl_3$ and a small amount of CH_2Cl_2) (lit.[23] 98% *ee* of (*S*)-**25** $[\alpha]_D$ +19.36° (*c* 28.5, $CHCl_3$)), 91% ee by ^1H NMR with chiral shift reagent Eu(hfc)$_3$.

2-Methylchroman [(−)-29]: $[\alpha]^{18}_D$ −94.3° (*c* 5.2, $CHCl_3$), 64% ee by HPLC (Chiralcel OD, hexane:2-propanol = 224:1 (1.0 mL/min), UV (254 nm), t = 5.7 and 6.4 min).

Phenyl 1-phenylethyl ether (31): 25% conversion, 70% ee by GLC (cyclodex B-PH, 130 °C, He (1.0 kg/cm^2), t = 36.1 and 36.7 min).

Baeyer–Villiger Oxidation of (+)-2-Pentylcyclopentanone [(+)-6d]. This was performed by the modified method of literature procedure.[10] To a solution of (+)-**6d** (92 mg, 0.60 mmol) in CH_2Cl_2 (5.0 mL) was added *m*-CPBA (70%) (294 mg, 1.23 mmol) with stirring at 0 °C, and the mixture was stirred overnight at room temperature. The reaction was quenched with water, and the products were extracted with CH_2Cl_2, washed twice with saturated aqueous $Na_2S_2O_3$ solution and once with brine, and dried over anhydrous Na_2SO_4. After evaporation, the residue was purified with flash column chromatography (hexane/AcOEt = 7/1) to give 5-pentyl-δ-valerolactone [(*S*)-7] (71 mg, 0.42 mmol, 70% yield). Absolute configuration of (*S*)-(+)-**6d** was determined from the sign of optical rotation value of the lactone ($[\alpha]^{23}_D$ −33.0° (*c* 2.1, $CHCl_3$) (lit.[46] (*R*)-5-pentyl-δ-valerolactone [(*R*)-7] $[\alpha]^{23}_D$ +50.8° (*c* 0.32, $CHCl_3$))).

(46) Nishida, F.; Mori, Y.; Isobe, S.; Furuse, T.; Suzuki, M.; Meerootisom, V.; Flegel, T. W.; Thebtaranonth, Y. *Tetrahedron Lett.* **1988**, *29*, 5287.

Deuteration of (*E*)-5b. A mixture of (*E*)-**5b** (126 mg, 1.0 mmol), (*S*)-**4** (17 mg, 10 μmol), and THF (5 mL) was stirred at 75 °C for 60 h under D_2 (20 atm). Conversion of the product was 100% by ^1H NMR, and concentration followed by bulb-to-bulb distillation gave the product (*R*)-**6b**-d_2 in 95% isolated yield (123 mg): ^1H NMR ($CDCl_3$) δ 0.96 (m, 3H, C*H*$_3$), 1.3–1.5 (m, 3H, CH*H*CH$_2$CH$_3$), 1.9–2.0 (m, 1H, OCH$_2$C*H*H), 2.3–2.5 (m, 1H, OCH$_2$CH*H*), 4.1–4.3 (m, 1H, OC*H*H), 4.3–4.4 (m, 1H, OCH*H*). Enantiomeric excess (94% ee) was determined by HPLC (Chiralcel OD, hexane:2-propanol = 199:1 (1 mL/min), 230 nm, t = 23 and 25 min).

Deuteration of (*Z*)-5b. A mixture of (*Z*)-**5b** (40 mg, 0.32 mmol), (*R*)-**1** (6 mg, 6.9 μmol), and THF (2 mL) was stirred at 75 °C for 240 h under D_2 (14 atm). After removal of the solvent and bulb-to-bulb distillation gave a mixture of (*Z*)-**5b**, (*E*)-**5b**, and **6b**-d_2 in 47:16:37 ratio. Product **6b**-d_2 was isolated by column chromatagraphy (silica gel) in 20% yield (9 mg, 95% purity): ^1H NMR δ 0.96 (m, 3H, C*H*$_3$), 1.3–1.5 (m, 2.4H, CH*H*CH$_2$CH$_3$), 1.8–1.9 (m, 0.6H, C*H*HCH$_2$CH$_3$), 1.9–2.0 (m, 1H, OCH$_2$C*H*H), 2.3–2.5 (m, 1H, OCH$_2$CH*H*), 4.1–4.3 (m, 1H, OC*H*H), 4.3–4.4 (m, 1H, OCH*H*).

Asymmetric Hydrogenation of Diketene (34). A degassed solution of NEt_3 (3.65 mg, 3.61 × 10^{-2} mmol) and [RuCl((*S*)-binap)(benzene)]Cl [(*S*)-**1**] (35.0 mg, 4.01 × 10^{-2} mmol) in THF (5.5 mL) was stirred at room temperature for 2 h, and then the volume of the mixture was reduced to about half of its initial volume in vacuo. To this was added a solution of diketene **34** (2.08 g, 24.7 mmol) in THF (10.0 mL) which had been degassed by three freeze–thaw cycles. This mixture was transferred to a 50-mL stainless steel autoclave equipped with a quartz vessel and heated at 50 °C under 100 kg/cm^2 of hydrogen for 44 h. Crude products (2.01 g) were obtained by evaporation of the solvent. ^1H NMR of this material showed that the mixture was composed of 4-methyl-2-oxetanone (97%) (**35**) and butanoic acid (3%). No starting material was detected. Purified sample by column chromatography (silica gel, hexane–ether, 1.82 g, 85% yield) has $[\alpha]^{22}_D$ +25.9° (*c* 4.6, $CHCl_3$) (lit.[29] 95% ee of (*S*)-**35** $[\alpha]^{22}_D$ −28.8° (*c* 4.3, $CHCl_3$)). Methanolysis of the product (500 mg, 5.8 mmol) by NaOH (20 mg, 0.5 mmol) and methanol (10 mL) for 5 h at room temperature gave methyl 3-hydroxybutyrate (evaporation of the solvent and bulb-to-bulb distillation, 450 mg, 66% yield). This alcohol (50 mg, 0.42 mmol) was converted to MTPA ester by the reaction with (*R*)-MTPACl (127 mg, 0.50 mmol) in pyridine (2.0 mL) in the presence of 4-(dimethylamino)pyridine (61 mg, 0.50 mmol) for 48 h at room temperature. The mixture was diluted with ethyl acetate (5 mL) and benzene (5 mL) and washed with 2 N HCl, water, $NaHCO_3$ aq, and brine. Drying of the organic layer over Na_2SO_4, concentration, and then bulb-to-bulb distillation gave pure MTPA ester of methyl 3-hydroxybutyrate (130 mg, 93% yield). Diastereomeric excess of this MTPA ester was 91.8% by ^1H NMR analysis. Irradiation at 5.5 ppm made peaks at 1.25 and 1.35 ppm, which are methine signals of two diastereomers, singlet and sharp separation: ^1H NMR of ester (equimolar amount of diastereomeric mixture) ($CDCl_3$, 270 MHz) δ 1.25 (d, 3H, J = 6.2 Hz), 1.35 (d, 3H, J = 6.2 Hz), 2.4–2.8 (m, 4H), 3.4 (s, 6H), 3.5 (s, 3H), 3.6 (s, 3H), 5.5 (m, 2H), 7.2–7.6 (m, 10H).

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