CH_2), 4.96-5.05 (m, C=CH_2, 2 H), 2.57-2.63 (m, C=CCH_2), 2.19-2.25 (m, C=CCH_2); IR (film) 3083, 2929, 2859, 1644, 1618, 1444, 1408, 1327, 1168, 1117, 1067, 1014, 913, 844, 724 cm^{-1}; MS (EI, 70 eV) *m/e* (relative percent) 228 (M, 100), 213 (73), 173 (32), 167 (44), 159 (61), 131 (73), 117 (48). Integration of the small apparent singlets at δ 5.15 and 5.32 (due to the terminal methylene group of d_0 and d_1 diene) relative to the two hydrogen signal at 4.96-5.05 for the terminal vinyl group showed that the deuterium content was 1.94.

Preparation of Bis(hexanenitrile)palladium Dichloride. Palladium dichloride (5.0 g, 28 mmol) was added to freshly distilled hexanenitrile (30 mL), and the resulting mixture was stirred overnight under an argon atmosphere. The resulting orange mixture was filtered through glass wool, and the filtrate was treated with pentane (200 mL). The resulting yellow precipitate was filtered with use of a Schlenk apparatus and washed with pentane (2 × 100 mL). The orange-yellow crystals were dried under vacuum (2 mm, 2 h) to give 8.9 g (85%) of the bis(hexanenitrile) complex.

Kinetic Studies. Rearrangements were carried out at ambient temperature in the probe of a Bruker WM-250 spectrometer. The probe temperature was 25 ± 2 °C ($HOCH_2CH_2OH$). NMR tubes were charged with the starting diene in $CDCl_3$ (ca. 0.4 mL) then 3-40 μL of $[PdCl_2(C_5H_{11}CN)_2]$ solution (0.09 M in $CDCl_3$ with 1% TMS) was added to give a final diene concentration of 0.10 M. The ratio of the vinylic hydrogen at δ 5.7-5.9 to the terminal methylene hydrogens which appeared at δ 5.1-5.3 was determined by integration. Rate constants were obtained by least-squares analysis of $\ln [A_e - A_o]/[A_t - A_e] = -kt$, where A_e was assumed to be $^1/_2A_o$. Duplicate runs were conducted at three concentrations of $PdCl_2$. Pseudo-first-order plots were linear over one half-life and were considered acceptable if the correlation coefficient was ≥0.988. A typical example of the NMR traces, raw data, and first-order plots is provided as supplementary material as is a listing of the pseudo-first-order rate constants measured at all the $PdCl_2$ concentrations investigated.

Acknowledgment. The financial support of the National Science Foundation (Grant No. CHE-8618451) is gratefully acknowledged.

Registry No. 2a, 125996-98-7; **2b**, 125996-99-8; **2c**, 3240-29-7; **2d**, 26954-31-4; **2e**, 125997-00-4; **2f**, 125997-01-5; **2g**, 53342-47-5; **2h**, 35204-91-2; **3a**, 125997-02-6; **3b**, 125997-03-7; **3c**, 125997-04-8; **3d**, 125997-05-9; **3e**, 125997-06-0; **3f**, 125997-07-1; **3g**, 125997-08-2; **3h**, 125997-09-3; $MeOC_6H_4$-*m*-CHO, 591-31-1; $F_3CC_6H_4$-*m*-CHO, 454-89-7; PhCHO, 100-52-7; MeC_6H_4-*p*-CHO, 104-87-0; BrC_6H_4-*m*-CHO, 3132-99-8; FC_6H_4-*m*-CHO, 456-48-4; $F_3CC_6H_4$-*p*-CHO, 455-19-6; ClC_6H_4-*p*-CHO, 104-88-1; $H_2C{=}CH(CH_2)_2MgBr$, 7103-09-5; $H_2C{=}CH(CH_2)_2CHOHC_6H_4$-*m*-OMe, 125997-10-6; $H_2C{=}CH(CH_2)_2CHOHC_6H_4$-*m*-$CF_3$, 125997-11-7; $H_2C{=}CH(CH_2)_2CHOHPh$, 54525-86-9; $H_2C{=}CH(CH_2)_2CHOHC_6H_4$-*p*-Me, 125997-12-8; $H_2C{=}CH(CH_2)_2CHOHC_6H_4$-*m*-Br, 125997-13-9; $H_2C{=}CH(CH_2)_2CHOHC_6H_4$-*m*-F, 125997-14-0; $H_2C{=}CH(CH_2)_2CHOHC_6H_4$-*p*-$CF_3$, 125997-15-1; $H_2C{=}CH(CH_2)_2CHOHC_6H_4$-*p*-Cl, 102058-50-4; $MeOC_6H_4$-*p*-$CH{=}CH_2$, 637-69-4; $H_2C{=}C(p\text{-}MeOC_6H_4)Me$, 1712-69-2; $D_2C{=}C(p\text{-}F_3CC_6H_4)Me$, 125997-16-2; $PdCl_2$, 7647-10-1; $PdCl_2(C_5H_{11}CN)_2$, 87370-16-9; $H_3C(CH_2)_4CN$, 628-73-9.

Supplementary Material Available: ^1H NMR traces, raw data, and pseudo-first-order kinetic plot for the rearrangement of diene **3e** and a complete summary of second-order rate constants for $PdCl_2$-catalyzed rearrangements of dienes **3a-h** (7 pages). Ordering information is given on any current masthead page.

Catalytic Asymmetric Glyoxylate-Ene Reaction: A Practical Access to α-Hydroxy Esters in High Enantiomeric Purities

Koichi Mikami,* Masahiro Terada, and Takeshi Nakai*

Contribution from the Department of Chemical Technology, Tokyo Institute of Technology, Meguro-ku, Tokyo 152, Japan. *Received October 16, 1989*

Abstract: An efficient asymmetric catalysis is developed for the glyoxylate-ene reaction to afford the α-hydroxy esters of biological and synthetic importance. The key to the success is the use of the chiral titanium complex prepared in situ from $(i\text{-}PrO)_2TiX_2$ (X = Cl or Br) and the (*R*)- or (*S*)-binaphthol in the presence of molecular sieves (MS 4A). The presence of the molecular sieves (zeolite) is clarified to facilitate the alkoxy-ligand exchange reaction. Thus, the use of MS is shown to be essential for the in situ preparation step of the chiral catalyst and not for the ene reaction step. The present catalytic process is applicable to various 1,1-disubstituted olefins by the judicious choice of the dichloro or dibromo catalyst.

The development of asymmetric catalysis, for C-C bond-forming reactions in particular, is the most challenging and formidable endeavor in organic synthesis.[1] Recently impressive progress has been made on catalytic asymmetric aldol[2] and Diels-Alder reactions.[3] However, the catalytic asymmetric ene reaction with prochiral glyoxylate, which is potentially useful for the asymmetric synthesis of α-hydroxy esters of biological and synthetic importance,[4] has never been developed,[5,6] while Yamamoto has recently reported the first example of a catalytic ene reaction with halogenated aldehydes by using the modified binaphthol-derived aluminum reagent.[7a] In this paper we wish to describe a full account of the asymmetric glyoxylate-ene reaction[8] catalyzed by the chiral titanium complex of type (*R*)-**1a**[9] prepared in situ from $(i\text{-}PrO)_2TiX_2$[10] and the optically pure binaphthol

(1) For reviews: (a) Morrison, J. D. *Asymmetric Synthesis*; Academic Press: New York, 1984; Vol. 3B. (b) Bosnich, B. *Asymmetric Catalysis*; Martinus Nijhoff Publishers: Dordrecht, 1986. (c) Kagan, H. B. In *Comprehensive Organometallic Chemistry*; Wilkinson, G., Ed.; Pergamon: New York, 1982; Vol. 8.

(2) Iio, Y.; Sawamura, M.; Hayashi, T. *J. Am. Chem. Soc.* **1986**, *108*, 6405.

(3) (a) Narasaka, K.; Iwasawa, N.; Inoue, M.; Yamada, T.; Nakashima, M.; Sugimori, J. *J. Am. Chem. Soc.* **1989**, *111*, 5340 and references cited therein. (b) Maruoka, K.; Itoh, T.; Shirasaka, T.; Yamamoto, H. *Ibid.* **1988**, *110*, 310. (c) Corey, E. J.; Imwinkelried, R.; Pikul, S.; Xiang, Y. B. *J. Am. Chem. Soc.* **1989**, *111*, 5493.

(4) For reviews on α-hydroxy acids and their derivatives see: Omura, S. *J. Synth. Org. Chem. Jpn.* **1986**, *44*, 127. Hanessian, S. *Total Synthesis of Natural Products: The Chiron Approach*; Pergamon: New York, 1983; Chapter 2. Mori, K. in *The Total Synthesis of Natural Products*; Apsimon, J., Ed.; Wiley Interscience: New York, 1981; Chapter 1. Seebach, D.; Hungerbuhler, E. In *Modern Synthetic Methods*; Scheffold, R., Ed.; Otto Salle Verlag: Frankfurt am Mein, Germany, 1980.

(5) Reviews on ene reactions: (a) Snider, B. B. *Acc. Chem. Res.* **1980**, *13*, 426. (b) Hoffmann, H. M. R. *Angew. Chem., Int. Ed. Engl.* **1969**, *8*, 556. (c) Oppolzer, W.; Snieckus, V. *Angew. Chem., Int. Ed. Engl.* **1978**, *17*, 476. (d) Taber, D. F. *Intramolecular Diels-Alder and Alder Ene Reactions*; Springer-Verlag: Berlin, 1984.

(6) Reported so far is the only substrate-based asymmetric version using a chiral glyoxylate and a stoichiometric amount of a Lewis acid: Whitesell, J. K. *Acc. Chem. Res.* **1985**, *18*, 280 and references cited therein.

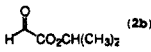
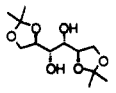
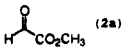
(7) The most recent catalytic asymmetric ene reactions were reported. (a) Intermolecular reaction: Maruoka, K.; Hoshino, Y.; Shirasaka, S.; Yamamoto, H. *Tetrahedron Lett.* **1988**, *29*, 3967. (b) Intramolecular reaction: Narasaka, K.; Hayashi, Y.; Shimada, S. *Chem. Lett.* **1988**, 1609.

(8) For our preliminary communication of this work, see: Mikami, K.; Terada, M.; Nakai, T. *J. Am. Chem. Soc.* **1989**, *111*, 1940; *Chem. Express* **1989**, *4*, 589.

(9) A similar type of chiral Ti complex has previously been prepared via the reaction of $TiCl_4$ with the dilithium salt of (*R*)-BINOL and used as a catalyst for the aldol and Diels-Alder reactions to provide low optical yields (8-16% ee): Reetz, M. T.; Kyung, S.-H.; Bolm, C.; Zierke, T. *Chem. Ind.* **1986**, 824.

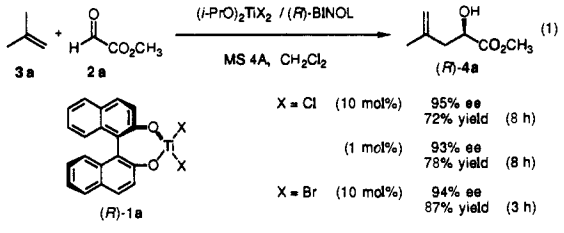
0002-7863/90/1512-3949$02.50/0

Table I. Asymmetric Glyoxylate–Ene Reactions Catalyzed by Various Titanium Complexes[a]

entry	chiral diol (5)	olefin (3)	glyoxylate (2)	%yield	% ee[b]
1	 (5b)[c]	 (3b)	 (2b)	60	4
2	 (5c)[d]	3b	2b	57	6
3	 (5d)	3b	2b	72	34
4	 (5e)	3b	2b	40	15
5	 (5f)	3b	2b	45	10
6	 (5g)[e]	3b	2b	70	44
7	 (5a)	3b	2b	82	86
8	5a	 (3a)	2b	78	65
9	5a	3a	 (2a)	72	95

[a] All reactions were run in the same manner as described for the reaction of **2a** and **3a** catalyzed by (*R*)-**1a**. [b] Determined by LIS–NMR analysis of the α-methoxy derivative. See ref 12. [c] Prepared from (*S*)-isopropyl lactate and PhMgBr (2.5 equiv); $[\alpha]_D$ −99.9° (*c* 1.6, $CHCl_3$). [d] Prepared from (*S*)-methyl mandelate and PhMgBr (2.5 equiv); $[\alpha]_D$ −220.8° (*c* 2.1, $CHCl_3$). [e] Seebach, D.; Beck, A. K.; Schiess, M.; Widler, L.; Wonnacott, A. *Pure Appl. Chem.* **1983**, *55*, 1807. Reference 3a.

(BINOL) in the presence of molecular sieves as exemplified in eq 1.

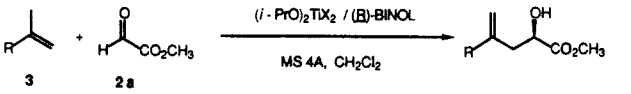


Catalytic Asymmetric Glyoxylate–Ene Reactions

A typical experimental procedure for the catalytic asymmetric glyoxylate–ene reactions is exemplified by the reaction of methyl glyoxylate **2a** with isobutylene **3a** catalyzed by the chiral titanium complex of type (*R*)-**1a** (eq 1). To a mixture of activated powder molecular sieves (MS 4A)[11] (500 mg) and (*R*)-BINOL[11] (0.10 mmol) in dichloromethane (5 mL) was added a 0.30 M toluene solution (0.33 mL, 0.10 mmol) of $(i\text{-PrO})_2TiCl_2$ at room temperature under argon atmosphere. The mixture was stirred for 1 h and cooled to −70 °C. To the mixture was added successively isobutylene **3a** (ca. 2 mmol) and methyl glyoxylate **2a** (1.0 mmol). The mixture was then warmed to −30 °C and stirred for 8 h. The resultant mixture was poured into saturated $NaHCO_3$ (10 mL). Usual workup followed by column chromatography furnished the ene product **4a** in 72% yield. The enantiomeric purity was determined to be 95% ee by HPLC analysis by using chiral column (SUMICHIRAL OA-2500I) and/or lanthanide induced shift (LIS) NMR measurement with (+)-Eu(DPPM)$_3$ after conversion to the α-methoxy ester.[12] The configuration of **4a** was assigned to be *R* through conversion to the known (*R*)-(+)-leucic acid.[11] Even a similar use of 1.0 mol % of the catalyst in the presence of MS 4A (50 mg) was found to provide equally satisfactory results (78% yield and 93% ee).

(10) Prepared from $TiCl_4$ and $(i\text{-PrO})_4Ti$ according to the literature method: Dijkgraff, C.; Rousseau, J. P. G. *Spectrochim. Acta A* **1968**, *2*, 1213.
(11) Available from Aldrich Chemical Company, Inc. and Wako Pure Chemical Industries Ltd.

Table II. The Specific Role of Molecular Sieves[a]



		R = CH_3		R = Ph	
entry	MS 4A (mg)	% yield	% ee	% yield	% ee
1[b]	500	72	95	100	97
2[c]	none	79	7	81	10
3[d]	500 → none	76	95	96	97
4[e]	none			95	93

[a] All reactions were run using 1.0 mmol of methyl glyoxylate and 0.1 mmol of $(i\text{-PrO})_2TiCl_2$ and BINOL. [b] Carried out via the in situ preparation of the chiral catalyst as described in the text. [c] Carried out in the absence of MS 4A. [d] The ene reaction was carried out in the absence of MS 4A after filtering off the molecular sieves used for preparing the chiral catalyst. [e] The chiral catalyst was prepared from $TiCl_4$ and BINOL dilithium salt in the absence of MS 4A.

Various Chiral Dialkoxytitanium Complexes as an Asymmetric Catalyst

The discovery of the BINOL-derived chiral catalyst was made after extensive screening of various chiral catalysts (**1**) derived from optically active diols. Table I shows the representative results, which reveal significant trends in terms of the structure–enantioselectivity relationship for the chiral diols **5**. (1) The catalyst derived from the diol **5d** endowed with C_2 symmetry exhibits a relatively high enantioselectivity compared to those derived from **5b** and **5c**. These results clearly indicate the effectiveness of such C_2 symmetry for attaining a high level of enantiocontrol in the ene reaction (entry 1, 2, vs 3). (2) The catalyst derived from the diol **5g**, which has previously been reported to provide a high level of catalytic enantiocontrol in the Diels–Alder and intramolecular ene reactions,[7b] shows only a moderate level of enantioselectivity in the intermolecular ene reaction (entry 6). (3) More significantly, the use of BINOL (**5a**) as the ligand was found to afford the remarkably enhanced levels of enantiocontrol (entry 7, 8, and 9). The high levels of enantiocontrol and rate acceleration observed with the BINOL-derived titanium catalyst are apparently due to the strong influence of the inherent C_2 symmetry and the higher acidity of BINOL compared to that of aliphatic diols. Of special interest is that the use of methyl glyoxylate **2a** instead of isopropyl glyoxylate **2b** provides a remarkably enhanced enantiocontrol (entry 8 vs 9).

The Specific Role of Molecular Sieves

The most striking feature in the present asymmetric process is the role of molecular sieves in obtaining the high enantioselectivity (Table II). In the absence of MS 4A (entry 2), the catalytic ene reaction, which although does proceed smoothly, affords quite low optical yield. Sharpless has already reported a similar importance of molecular sieves in the catalytic asymmetric epoxidation.[13] In his case, however, the catalytic epoxidations proceed slowly and generally stop after 50–60% conversion in the absence of MS 4A. In the present catalytic ene reaction, in contrast, no significant difference in rate and chemical yield between the presence and the absence of MS 4A was ob-

(12) Mikami, K.; Kasuga, T.; Fujimoto, K.; Nakai, T. *Tetrahedron Lett.* **1986**, *27*, 4185.
(13) Several catalytic asymmetric reactions have been carried out successfully by the use of MS 4A: Hanson, R. M.; Sharpless, K. B. *J. Org. Chem.* **1986**, *51*, 1922. Gao, Y.; Hanson, R. M.; Klunder, J. M.; Ko, S. Y.; Masamune, H.; Sharpless, K. B. *J. Am. Chem. Soc.* **1987**, *109*, 5765. Also see refs 3a and 7a.

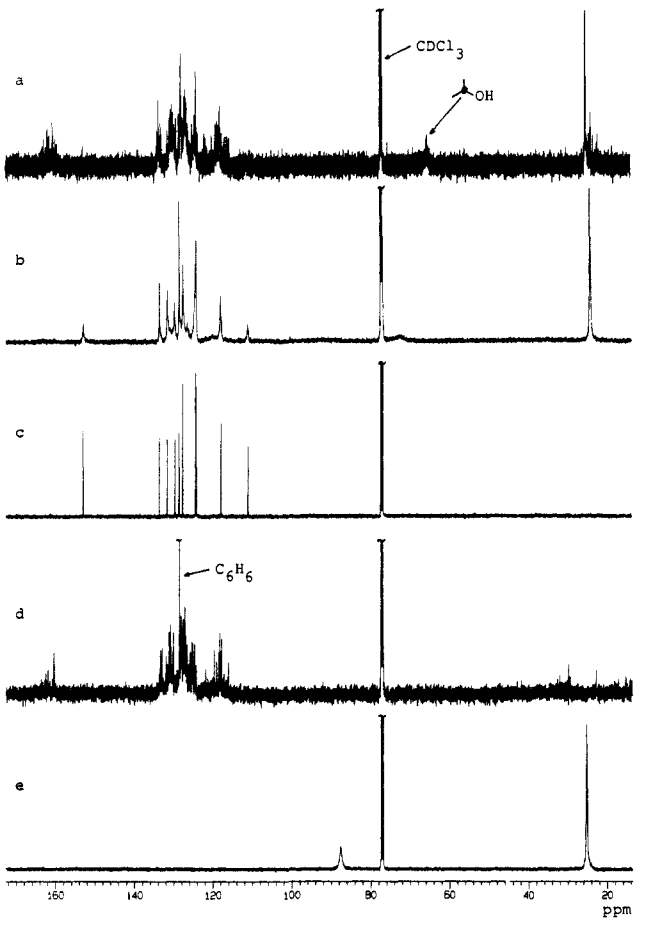


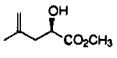
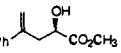
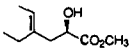
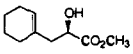
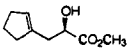
Figure 1. ^{13}C NMR spectrum of chiral titanium complex (*R*)-**1a** (X = Cl): (a) treated with molecular sieves 4A (method A); (b) untreated with molecular sieves 4A (method B); (c) BINOL only; (d) prepared from $TiCl_4$ and BINOL dilithium salt; (e) $(i\text{-PrO})_2TiCl_2$.

served. On the basis of ^{13}C NMR analyses in the absence of MS, no change was observed on the hydroxy-carbon signal (s, 153 ppm) of BINOL just by mixing it with $(i\text{-PrO})_2TiCl_2$ (Figure 1) (parts b and c).[14] In fact, we have found that $(i\text{-PrO})_2TiCl_2$ itself can act as a catalyst for the glyoxylate-ene reaction. However, the addition of MS 4A to a solution of BINOL and $(i\text{-PrO})_2TiCl_2$ was observed to lead to the downfield shift of the hydroxy-carbon signal (m, 160–163 ppm), suggesting the formation of the BINOL-derived chiral catalyst (Figure 1a). Significantly enough, the use of this chiral catalyst solution prepared by filtering off the MS 4A was found to provide the same level of high enantioselectivity in the absence of MS 4A (entry 3). Furthermore, the use of the complex **1a**,[15] prepared independently from $TiCl_4$ and BINOL dilithium salt,[9] was found to provide an equally high level of optical yield in the absence of MS 4A (entry 4). Thus these results clearly show that MS 4A is essential for the formation of the chiral catalyst not for the catalytic ene reaction. In other words, MS 4A significantly facilitates the alkoxy-ligand exchange reaction in the in situ preparation step of the chiral catalyst.

Dibromo vs Dichloro Catalysts

Particularly noteworthy is the significant difference in asymmetric catalysis between the dichloro and dibromo catalysts. In certain glyoxylate-ene reactions involving a methyl hydrogen (eq 1), the dichloro catalyst is superior to the dibromo catalyst in enantioselectivity, though lower in reactivity. In a reaction involving a methylene hydrogen (eq 2), the dibromo catalyst is superior in both reactivity and enantioselectivity; the dibromo catalyst provides a higher % ee, while both catalysts provide equally high levels (ca. 90%) of E selectivity. In cases where the regiochemical problem arises (eq 3 and 4), both catalysts show a similar level of regioselectivity. In the competitive case of methyl vs methylene (eq 3), moderate levels of preference for a methylene hydrogen shift are observed. The observed preference for a methylene hydrogen shift is in contrast to the preference for a methyl hydrogen shift observed with achiral catalysts such as $(i\text{-PrO})_2TiCl_2$ and $TiCl_4$. It is rather surprising that the sterically bulky chiral titanium complex (**1a**) abstracts more preferentially a methylene hydrogen rather than a methyl hydrogen.[16] In the competition of methyl vs methine hydrogen (eq 4), relatively high levels of preference for a methyl hydrogen shift are observed with both catalysts.

Table III. Catalytic Asymmetric Ene Reactions with Different Olefins[a]

entry	olefin	$(i\text{-PrO})_2TiX_2$ (X)	catalyst mol%	time h	product	%yield	%ee[b]
A		Cl	10	8		72	95 *R*
						68	95 *S*[c]
B		Cl	1.0	8		97	97 (*R*)
		Br	1.0	3		98	95 (*R*)
C		Br	5	3		73[d]	98[e] (*R*)
D		Cl	10	8		82	97 (*R*)
		Br	5	3		89	98 (*R*)
E		Cl	10	8		87	48 (*R*)
		Br	5	3		92	89 (*R*)

[a] All reactions were run by the representative procedure described in the text. [b] Determined by LIS-NMR analysis of the α-methoxy derivative as described in ref 12. The configuration in parentheses could be assigned by the similarity in shift pattern seen in the LIS-NMR spectra using (+)-Eu(DPPM)$_3$ as a chiral shift reagent. [c] (*S*)-BINOL was used instead of the (*R*)-counterpart. [d] The combined yield of the *E* and *Z* isomer. [e] Refers to the optical purity of the major *E* product.

The Scope and Limitation of the Asymmetric Process for α-Hydroxy Esters

The present catalytic method is applicable to a variety of 1,1-disubstituted olefins to provide the ene products in extremely high enantiomeric purities by the judicious choice of the dichloro or dibromo chiral catalyst (Table III). Generally speaking, the dibromide is superior to the dichloride in both the reactivity and enantioselectivity for the glyoxylate-ene reactions involving a methylene hydrogen shift in particular (entry C, D, and E). On the other hand, the dichloride is lower in reactivity but superior in enantioselectivity for certain glyoxylate-ene reactions involving a methyl hydrogen shift (entry A and B). Since both (*R*)- and (*S*)-BINOL are commercially available in optically pure form, the present asymmetric process allows the synthesis of both enantiomers of α-hydroxy esters and their derivatives. Unfortunately, however, the present asymmetric process is not applicable to mono- and 1,2-disubstituted olefins. In these cases no ene product was obtained.

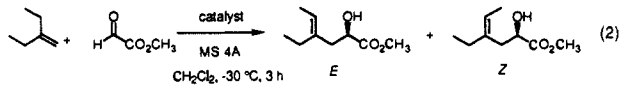
Thus, we have developed an efficient asymmetric catalysis for the glyoxylate-ene reaction which provides a practical access to α-hydroxy esters of high enantiomeric purities, a class of biological and synthetic importance. Further works on the applications of the catalytic asymmetric processes and the characterization of

(14) Recently, Narasaka reported the formation of the tartrate-derived chiral titanium complex **1g** just by mixing the diol **5g** with $(i\text{-PrO})_2TiCl_2$ even in the absence of MS 4A, though incomplete (the complex **1g**:the diol **5g** = 87:13). Addition of MS increased the complex formation: Iwasawa, N.; Hayashi, Y.; Sakurai, H.; Narasaka, K. *Chem. Lett.* **1989**, 1581.

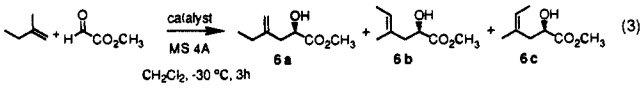
(15) Its ^{13}C NMR spectrum (Figure 1d) is essentially identical with those of the Ti complex prepared in situ in the presence of MS 4A (Figure 1a).

(16) The steric accessibility of the hydrogen abstracted is reported to be important in determining the regiochemistry of the ene reactions (ref 5a).

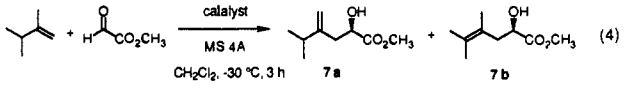
(17) Bear, E. Fischer, J. *J. Am. Chem. Soc.* **1939**, *61*, 761.



(i-PrO)$_2$TiBr$_2$ / (R)-BINOL (5 mol%)	91 (98% ee)	9 (>90% ee)	(73%)
(i-PrO)$_2$TiCl$_2$ / (R)-BINOL (10 mol%)	89 (94% ee)	11 (>90% ee)	(68%)
(i-PrO)$_2$TiCl$_2$ (10 mol%)	67	33	(65%)
TiCl$_4$ (10 mol%)	64	36	(75%)



(i-PrO)$_2$TiBr$_2$ / (R)-BINOL (5 mol%)	39 (91% ee)	57 (>98% ee)	4 (>90% ee)	(93%)
(i-PrO)$_2$TiCl$_2$ / (R)-BINOL (10 mol%)	42	54	4	(68%)
(i-PrO)$_2$TiCl$_2$ (10 mol%)	60	35	5	(62%)
TiCl$_4$ (10 mol%)	59	27	14	(88%)



(i-PrO)$_2$TiBr$_2$ / (R)-BINOL (5 mol%)	83 (92% ee)	17 (>98% ee)	(91%)
(i-PrO)$_2$TiCl$_2$ / (R)-BINOL (10 mol%)	87	13	(73%)

the chiral catalyst actually involved therein are in progress.

Experimental Section

Materials. Molecular sieves 4A (activated powder) was purchased from Aldrich Chemical Co. (*R*)- and (*S*)-1,1'-bi-2-naphthol (**5a**) were purchased from Wako Pure Chemical Industries Ltd. (1*S*,2*S*)-1,2-Diphenyl-1,2-ethanediol (**5d**) was purchased from Kanto Chemical Co. (2*S*,4*S*)-2,4-Pentanediol (**5f**) was presented by Takasago Research Institute Inc. (+)-Eu(DPPM)$_3$ (30 w/v% CCl_2FCClF_2 solution) was purchased from Daiichi Kagaku Yakuhin Co.

General. Melting points are uncorrected. ^{1}H and ^{13}C NMR spectra were measured on a Varian EM390 or GEMINI 200 or a JEOL GSX-500 spectrometer. IR spectra were measured on a JASCO FT/IR-5000 spectrometer. Optical rotations were measured on a JASCO DIP-140. Mass spectra were obtained with a JEOL JMS-300. Gas chromatographic analysis was conducted on a Shimazu GC-8A instrument. Liquid chromatographic analysis was conducted on a JASCO TRI ROTAR SR or a Shimazu LC-6A instrument. All experiments were carried out under an argon atmosphere. Dichloromethane and toluene were freshly distilled from CaH_2 and sodium benzophenone ketyl, respectively.

Preparation of Chiral Diols. (2*S*)-1,1-Diphenyl-1,2-propanediol (5b). To a THF solution of PhMgBr (75 mmol) was added a THF solution of (*S*)-isopropyl lactate (30 mmol, 3.69 g) at 0 °C. After having been stirred for 10 h, the reaction mixture was poured into saturated NH_4Cl solution. The combined mixture was extracted with ethyl acetate, and the organic layer was washed with brine and dried over $MgSO_4$. The solvent was removed under reduced pressure and the residue was purified by column chromatography. The separated product was recrystallized from hexane/ether to afford **5b** in 65% yield (3.98 g): ^{1}H NMR (90 MHz, $CDCl_3$) δ 1.08 (d, J = 7.0 Hz, 3 H), 1.93 (br s, 1 H), 3.07 (s, 1 H), 4.82 (q, J = 7.0 Hz, 1 H), 7.1–7.8 (m, 10 H) ppm; IR (KBr) 3500, 1450, 1270, 880, 700 cm^{-1}; $[\alpha]_D^{25}$ −99.9° (c 1.6, $CHCl_3$); mp 91.5–92.0 °C.

(2*S*)-1,1,2-Triphenyl-1,2-ethanediol (5c). **5c** was prepared in a similar procedure described for the preparation of **5b** except for the use of (*S*)-methyl mandelate (30 mmol, 4.99 g) instead of isopropyl lactate. The product was recrystallized from hexane/ether to afford **5c** in 72% yield (5.31 g): ^{1}H NMR (90 MHz, $CDCl_3$) δ 2.45 (d, J = 3.0 Hz, 1 H), 3.15 (s, 1 H), 5.27 (d, J = 3.0 Hz, 1 H), 7.1–7.9 (m, 15 H) ppm; IR (KBr) 3500, 1450, 1270, 1100, 880, 700 cm^{-1}; $[\alpha]_D^{25}$ −220.8° (c 1.3, $CHCl_3$); mp 123.5–124.5 °C.

(2*R*,3*R*,4*R*,5*R*)-1,2,5,6-Di-*O*-isopropylidene-D-mannitol (5e). **5e** was prepared according to the literature procedure.[17]

(2*R*,3*R*)-2,3-*O*-(1-Phenylethylidene)-1,1,4,4-tetraphenyl-1,2,3,4-butanetetraol (5g). **5g** was prepared according to the literature procedure:[3a] ^{1}H NMR (90 MHz, $CDCl_3$) δ 1.30 (s, 3 H), 2.90 (br, 2 H), 5.04 (d, J = 6.0 Hz, 1 H), 5.08 (d, J = 6.0 Hz, 1 H), 6.8–7.7 (m, 25 H) ppm; IR (KBr) 3330, 1590, 1490, 1440, 750, 700 cm^{-1}; $[\alpha]_D^{20}$ +82.9° (c 1.2, $CHCl_3$) (lit.[3a] $[\alpha]_D^{23}$ +83° (c 1.3, $CHCl_3$)).

Preparation of Diisopropoxytitanium(IV) Dichloride.[10] To a solution of titanium(IV) isopropoxide (2.98 mL, 10 mmol) in hexane (10 mL) was added titanium(IV) chloride (1.10 mL, 10 mmol) slowly at room temperature. On addition of titanium(IV) chloride, heat was evolved. After stirring for 10 min, the solution was allowed to stand for 6 h at room temperature, and the precipitate was then collected. The precipitate was washed with hexane (5 mL × 2) and recrystallized from hexane (3 mL). The crystalline was dried under reduced pressure and then dissolved in toluene to give a 0.3 M toluene solution.

Prepartion of Diisopropoxytitanium(IV) Dibromide. Diisopropoxytitanium(IV) dibromide was prepared in a similar manner described for the preparation of the diisopropoxytitanium(IV) dichloride. Lumps of titanium(IV) bromide (3.67 g, 10 mmol) were dissolved in hexane (5 mL) at room temperature. To the resultant solution was added titanium(IV) isopropoxide (2.98 mL, 10 mmol) slowly. Heat was evolved on addition of titanium(IV) isopropoxide. The reaction mixture was stirred for 10 min and allowed to stand for 6 h at room temperature. After recrystallization from hexane the crystalline was dissolved in toluene to give a 0.2 M toluene solution.

General Procedure of the Catalytic Ene Reaction: Preparation of Methyl 2-Hydroxy-4-methyl-4-pentenoate (4a). Method A, Via the in Situ Preparation of the Catalyst. To a suspension of activated powder molecular sieves 4A (500 mg) in CH_2Cl_2 (5 mL) was added a 0.3 M toluene solution of diisopropoxytitanium dichloride (0.33 mL, 0.10 mmol) and (*R*)-(+)- or (*S*)-(−)-binaphthol (**5a**) (28.6 mg, 0.10 mmol) at room temperature under an argon atmosphere. After stirring for 1 h at room temperature, the mixture was cooled to −70 °C. To the mixture was bubbled an excess of isobutylene (**3a**) (ca. 2 equiv), and freshly distilled methyl glyoxylate (**2a**) (88 mg, 1.0 mmol) was added. The mixture was then warmed to −30 °C and stirred for 8 h. The solution was poured into saturated $NaHCO_3$ (10 mL). Molecular sieves 4A was filtered off through a pad of Celite, and the filtrate was extracted with ethyl acetate. The combined organic layer was washed with brine. The extract was then dried over $MgSO_4$ and evaporated under reduced pressure. Separation by silica gel chromatography (hexane/ethyl acetate = 20:1) gave methyl 2-hydroxy-4-methyl-4-pentenoate (**4a**), which was assigned by ^{1}H NMR and IR analyses.

Method B. In the Absence of Molecular Sieves 4A. The ene reaction was carried out as described in method A except for the absence of molecular sieves 4A. To a solution of BINOL (28.6 mg, 0.10 mmol) in dichloromethane (5 mL) was added 0.3 M diisopropoxytitanium dichloride toluene solution (0.33 mL, 0.1 mmol) at room temperature.

Method C. In the Absence of Molecular Sieves 4A after Filtering off the Molecular Sieves Used for Preparing the Chiral Titanium Catalyst. The ene reaction was performed as described in method A except for the use of the chiral titanium catalyst solution after filtering off the molecular sieves. To a suspension of molecular sieves 4A (500 mg) in CH_2Cl_2 (2 mL) was added a 0.3 M toluene solution of diisopropoxytitanium dichloride (0.33 mL, 0.10 mmol) and (*R*)-binaphthol (28.6 mg, 0.10 mmol) at room temperature. After stirring for 1 h at room temperature, the suspension was centrifuged, and the molecular sieves was sedimented. The supernatant solution was filtered through a pad of Celite. The filtrate was diluted with CH_2Cl_2 (3 mL) in the absence of molecular sieves and used as a catalyst solution.

Method D. Via the Preparation of the Catalyst from $TiCl_4$ and Binaphthol Dilithium Salt in the Absence of Molecular Sieves 4A. The ene reaction was performed as described in method A except for the absence of molecular sieves 4A and the use of the chiral titanium catalyst prepared from $TiCl_4$ and binaphthol dilithium salt according to the literature procedure.[9]

(*R*)-(+)- and (*S*)-(−)-Methyl 2-Hydroxy-4-methyl-4-pentenoate (4a). ^{1}H NMR (90 MHz, $CDCl_3$) δ 1.80 (s, 3 H), 2.35 (dd, J = 8.0, 14.0 Hz, 1 H), 2.58 (dd, J = 5.0, 14.0 Hz, 1 H), 2.70 (br, 1 H), 3.78 (s, 3 H), 4.35 (dd, J = 8.0, 5.0 Hz, 1 H), 5.82 (m, 1 H), 5.88 (m, 1 H) ppm; IR (neat) 3490, 2950, 1740, 1440, 1100, 905 cm^{-1}; $[\alpha]_D^{20}$ +7.26° (c 2.46, $CHCl_3$) 95% ee (*R*), $[\alpha]_D^{20}$ −7.20° (c 2.23, $CHCl_3$) 95% ee (*S*); HRMS for $C_7H_{12}O_3$ calcd 144.0786, found 144.0781; HPLC (SUMICHIRAL OA-2500I, eluent, hexane/1,2-dichloroethane/ethanol = 180:19:1, flow rate 1.0 mL/min), t_R of (*R*)-(+)-**4a** 10.7 min and (*S*)-(−)-**4a** 11.6 min.

(+)-Isopropyl 3-(1'-Cyclohexenyl)-2-hydroxypropionate. ^{1}H NMR (90 MHz, $CDCl_3$) δ 1.27 (d, J = 6.6 Hz, 6 H), 1.60 (m, 4 H), 1.88 (m, 4 H), 2.28 (dd, J = 7.5, 14.0 Hz, 1 H), 2.47 (dd, J = 5.5, 14.0 Hz, 1 H), 2.50 (br, 1 H), 4.32 (dd, J = 5.5, 7.5 Hz, 1 H), 5.18 (heptet, J = 6.6 Hz, 1 H), 5.60 (m, 1 H) ppm; IR (neat) 3440, 2950, 1740, 1200, 1120 cm^{-1}; $[\alpha]_D^{22}$ +13.25° (c 2.12, $CHCl_3$), 86% ee; HRMS for $C_{12}H_{20}O_3$ calcd 212.1413, found 212.1419.

(−)-Methyl 2-Hydroxy-4-phenyl-4-pentenoate. ^{1}H NMR (90 MHz, $CDCl_3$) δ 2.76 (br s, 1 H), 2.88 (dd, J = 8.1, 13.5 Hz, 1 H), 3.13 (dd, J = 4.5, 13.5 Hz, 1 H), 3.68 (s, 3 H), 4.33 (m, 1 H), 5.28 (br s, 1 H), 5.48 (br s, 1 H), 7.4 (m, 5 H) ppm; ^{13}C NMR (50 MHz, $CDCl_3$) δ 40.4, 52.2, 69.2, 116.5, 126.6, 127.9, 128.6, 140.4, 143.7, 175.1 ppm; IR (neat) 3450, 2940, 1730, 1440, 1030, 910, 780, 710 cm^{-1}; $[\alpha]_D^{23}$ −30.55° (c 4.83, $CHCl_3$) 97% ee; HRMS for $C_{12}H_{14}O_3$ calcd 206.0943, found 206.0936; HPLC (SUMICHIRAL OA-2500I, eluent, hexane/1,2-dichloroethane/ethanol = 200:40:1, flow rate 0.5 mL/min), t_R of (−)-isomer 16.8 min and (+)-isomer 18.3 min.

(+)-Methyl 3-(1′-Cyclohexenyl)-2-hydroxypropionate. ^{1}H NMR (90 MHz, $CDCl_3$) δ 1.60 (m, 4 H), 1.98 (m, 4 H), 2.27 (dd, J = 7.5, 13.5 Hz, 1 H), 2.40 (br, 1 H), 2.48 (dd, J = 5.5, 13.5 Hz, 1 H), 3.77 (s, 3 H), 4.30 (dd, J = 7.5, 5.5 Hz, 1 H), 5.60 (m, 1 H) ppm; ^{13}C NMR (50 MHz, $CDCl_3$) δ 22.1, 22.8, 25.3, 28.4, 43.2, 52.4, 69.4, 125.8, 133.2, 175.7 ppm; IR (neat) 3490, 2950, 1740, 1440, 1100, 760, 740, 700 cm^{-1}; $[\alpha]_D^{19}$ +12.27° (c 3.35, $CHCl_3$) 98% ee; HRMS for $C_{10}H_{16}O_3$ calcd 184.1100, found 184.1107; HPLC (SUMICHIRAL OA-2500I, eluent, hexane/1,2-dichloroethane/ethanol = 400:40:1, flow rate 0.5 mL/min), t_R of (+)-isomer 32.0 min and (−)-isomer 33.5 min.

(+)-Methyl 3-(1′-Cyclopentenyl)-2-hydroxypropionate. ^{1}H NMR (90 MHz, $CDCl_3$) δ 1.90 (m, 2 H), 2.30 (m, 4 H), 2.58 (m, 2 H), 2.73 (br s, 1 H), 3.85 (s, 3 H), 4.40 (m, 1 H), 5.62 (m, 1 H) ppm; IR (neat) 3460, 2980, 1730, 1040 cm^{-1}; $[\alpha]_D^{23}$ +7.55° (c 4.20, $CHCl_3$) 89% ee; HRMS for $C_9H_{14}O_3$ calcd 170.0943 found 170.0932.

The Reaction of 2-Ethyl-1-butene and Methyl Glyoxylate (2a). (*E*)/(*Z*)-Methyl 4-Ethyl-2-hydroxy-4-hexenoate. The E/Z ratio of the ene products was determined by HPLC analysis. The E/Z stereochemistry was assigned on the basis of ^{13}C NMR analysis: HPLC (Zorbax SIL, eluent, hexane/ethyl acetate = 10:1, flow rate 1.0 mL/min), t_R of E isomer 16.9 min and Z isomer (minor) 15.3 min; ^{1}H NMR (90 MHz, $CDCl_3$) δ 0.98 (t, J = 6.6 Hz, 3 H), 1.00 (t, J = 6.6 Hz, 3 H) (minor), 1.63 (d, J = 7.3 Hz, 3 H), 2.09 (q, J = 7.8 Hz, 2 H) (minor), 2.11 (q, J = 7.8 Hz, 2 H), 2.53 (m, 2 H), 2.60 (br, 1 H), 3.85 (s, 3 H), 4.35 (m, 1 H), 5.41 (q, J = 7.3 Hz, 1 H), 5.55 (q, J = 7.3 Hz, 1 H) (minor) ppm; ^{13}C NMR (50 MHz, $CDCl_3$) δ 12.3, 12.7 (minor), 13.2, 13.4 (minor), 22.8, 29.8 (minor), 35.1 (minor), 41.7, 52.2, 69.9, 70.0 (minor), 121.3 (minor), 122.4, 136.9 (minor), 137.1, 175.4, 175.5 (minor) ppm; IR (neat) 3500, 2970, 1730, 1440, 1210, 1110, 1030, 980, 830 cm^{-1}; HRMS for $C_9H_{16}O_3$ calcd 172.1100, found 172.1120.

The Reaction of 2-Methyl-1-butene and Methyl Glyoxylate (2a). Methyl 4-Ethyl-2-hydroxy-4-pentenoate (6a) and (*E*)/(*Z*)-Methyl 2-Hydroxy-4-methyl-4-hexenoate (6b,c). The stereoisomer ratio was determined by HPLC analysis. The E/Z stereochemistry was assigned on the basis of ^{13}C NMR analysis. HPLC (Zorbax SIL, eluent, hexane/ethyl acetate = 10:1, flow rate 1.0 mL/min), t_R of **6a** (regioisomer) 17.3 min, **6b** (E isomer) 18.8 min, and **6c** (Z isomer) 16.8 min; ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.07 (t, J = 6.6 Hz, 3 H) (**6a**), 1.63 (d, J = 7.8 Hz, 3 H) (**6b**), 1.68 (s, 3 H) (**6b**), 2.14 (q, J = 6.6 Hz, 2 H) (**6a**), 2.43 (dd, J = 6.6, 15.0 Hz, 1 H) (**6b**), 2.45 (dd, J = 8.1, 15.0 Hz, 1 H) (**6a**), 2.63 (dd, J = 5.6, 15.0 Hz, 1 H) (**6b**), 2.65 (dd, J = 5.1, 15.0 Hz, 1 H) (**6a**), 3.03 (m, 1 H) (**6b**), 3.08 (br s, 1 H) (**6a**), 3.87 (s, 3 H) (**6b**), 3.88 (s, 3 H) (**6a**), 4.45 (m, 1 H), (**6a**), 5.00 (m, 2 H) (**6a**), 5.50 (q, J = 7.8 Hz, 1 H) (**6b**), 5.68 (q, J = 7.8 Hz, 1 H) (**6c**) ppm; ^{13}C NMR (50 MHz, $CDCl_3$) δ 12.2 (**6a**), 13.6 (**6b**), 15.8 (**6b**), 28.8 (**6a**), 38.7 (**6c**), 41.4 (**6a**), 44.9 (**6b**), 52.5 (**6b**), 52.6 (**6a**), 53.0 (**6c**), 69.1 (**6c**), 69.7 (**6a,b**), 112.0 (**6a**), 123.5 (**6b**), 123.7 (**6c**), 128.7 (**6c**), 131.3 (**6b**), 146.9 (**6a**), 175.8 (**6a**), 175.9 (**6b**), 176.2 (**6c**) ppm; IR (neat) 3450, 2950, 1730, 1430, 1100, 890 cm^{-1}; HRMS for $C_8H_{14}O_3$ calcd 158.0943, found 158.0934.

The Reaction of 2,3-Dimethyl-1-butene and Methyl Glyoxylate (2a). Methyl 4-Isopropyl-2-hydroxy-4-pentenoate (7a) and Methyl 2-Hydroxy-4,5-dimethyl-4-hexenoate (7b). The regioisomer ratio was determined by GC analysis; GC (ULBON HR-20M, 50 m, carrier N_2 0.86 mL/min, column temperature 110 °C), t_R of **7a** 30.4 min and **7b** (minor) 39.1 min; ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.05 (d, J = 6.6 Hz, 3 H), 1.06 (d, J = 6.6 Hz, 3 H), 1.68 (s, 9 H) (minor), 2.30 (m, 1 H), 2.52 (m, 2 H) (minor), 2.53 (m, 2 H), 2.90 (br, 1 H), 3.78 (s, 3 H) (minor), 3.83 (s, 3 H), 4.40 (m, 1 H), 4.45 (m, 1 H) (minor), 4.97 (m, 1 H), 5.03 (m, 1 H), ppm; ^{13}C NMR (50 MHz, $CDCl_3$) δ 18.8 (minor), 20.6 (minor), 20.9 (minor), 21.7, 21.8, 33.6, 39.7 (minor), 39.9, 52.5, 69.9, 70.2 (minor), 110.4, 123.0 (minor), 129.2 (minor), 151.4, 175.7, 176.1 (minor) ppm; IR (neat) 3430, 2940, 2850, 1730, 1430, 1210, 1100, 890 cm^{-1}; HRMS for $C_9H_{16}O_3$ calcd 172.1100, found 172.1077.

Determination of the Absolute Configuration of the Ene Products. A solution of (+)-methyl 2-hydroxy-4-methylpentanoate (100 mg, 93% ee) in ethyl acetate (5 mL) was stirred for 1 day at room temperature in the presence of PtO_2 (5 mg) under a H_2 atmosphere. The solution was then filtered through a pad of Celite. The filtrate was evaporated under reduced pressure to give methyl 2-hydroxy-4-methyl-4-pentenoate (95% yield). The solution of the product (50 mg) in THF (5 mL) containing

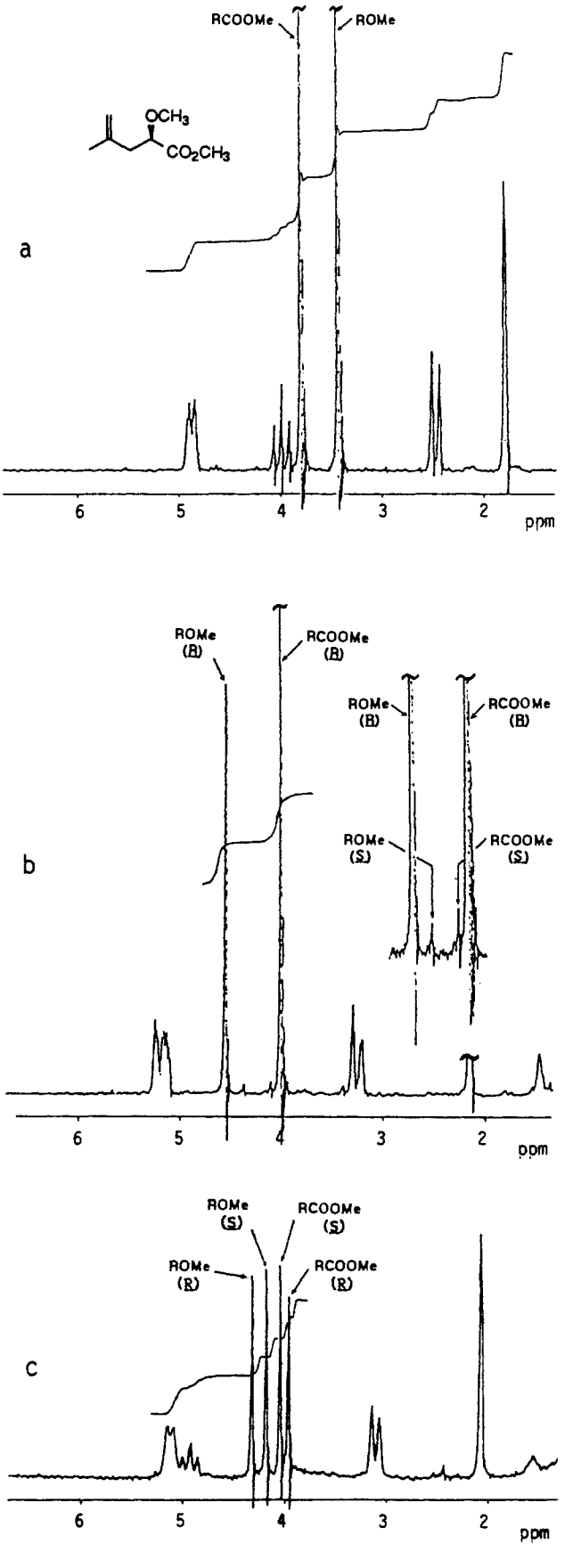


Figure 2. LIS-NMR analyzed spectrum of methyl ether derivative of **4a**: (a) in the absence of (+)-Eu(DPPM)$_3$; (b) methyl ether derivative of (+)-**4a** (25 mg) in the presence of (+)-Eu(DPPM)$_3$ (28 μL); (c) methyl ether derivative of (±)-**4a** (28 mg) in the presence of (+)-Eu(DPPM)$_3$ (35 μL).

10% aqueous solution of LiOH (1 mL) was stirred for 3 h at room temperature. The resultant solution was acidified with 1 N HCl (2 mL) and saturated with NaCl. The mixture was extracted with ethyl acetate. The organic layer was washed with brine. The extract was dried over $MgSO_4$ and evaporated under reduced pressure. The silica gel chromatography gave the known (*R*)-(+)-2-hydroxy-4-methylpentanoic acid (leucic acid) in 98% yield: ^{1}H NMR (90 MHz, $CDCl_3$) δ 0.96 (d, J = 6.2 Hz, 6 H), 1.60 (m, 2 H), 1.88 (m, 1 H), 4.33 (t, J = 6.6 Hz, 1 H), 6.33 (br, 2 H) ppm; IR (neat) 3400, 2960, 1725, 1140, 1090 cm^{-1}; $[\alpha]_D^{22}$ +25.6° (*c* 0.87, 1 N NaOH), cf. (*S*)-(−)-leucic acid (Aldrich Chemical Company, Inc.) $[\alpha]_D^{20}$ −26.3° (*c* 1, 1 N NaOH).

Determination of the Optical Yield of the Ene Products. HPLC Analysis. The optical yield of the ene products (α-hydroxy esters) was analyzed by HPLC by using chiral column (SUMICHIRAL OA-2500I; eluent, hexane/1,2--dichloroethane/ethanol mixture, flow rate 0.5–1.0 mL/min, detection, 254 or 212 nm light). The t_R of (*R*)-isomers was shorter than that of (*S*)-isomers.

LIS-NMR Analysis.[12] (1) Preparation of 2-Methoxy Esters. To a mixture of methyl iodide (0.3 mL) and the ene product (0.5 mmol) in ether was added Ag_2O (0.23 g). The reaction mixture was stirred for 1 day at room temperature. The suspension was filtered through a pad of Celite. The filtrate was evaporated under reduced pressure. Chromatographic purification gave the corrseponding 2-methoxy esters in 95–100% yield. **(2) ^{1}H NMR Shift Analysis Using (+)-Eu(DPPM)$_3$ as a Chiral NMR Shift Reagent.** To a solution of methyl 2-methoxy-4-methyl-4-pentenoate (25 mg) in $CDCl_3$ (0.4 mL) was added a 30 w/v% CCl_2FCClF_2 solution of (+)-Eu(DPPM)$_3$ (30 μL). The chemical shifts of the methoxy groups of (*R*)-methoxy esters were lower than those of the (*S*)-isomers.

Methyl 2-Methoxy-4-methyl-4-pentenoate. ^{1}H NMR (90 MHz, $CDCl_3$) δ 1.74 (s, 3 H), 2.43 (d, J = 6.5 Hz, 2 H), 3.38 (s, 3 H), 3.73 (s, 3 H), 3.90 (t, J = 6.5, 1 H), 4.74 (m, 2 H), 4.82 (m, 1 H) ppm. On addition of (+)-Eu(DPPM)$_3$ (28 μL) to the solution of methyl ether in $CDCl_3$ (25 mg, in 0.4 mL), the singlet of methyl ether at δ 3.38 was changed into the two singlets at δ 4.60 ((*R*)-isomer) and 4.40 ((*S*)-isomer) (relative intensity = 97.5:2.5); the ^{1}H NMR ratio was almost identical with the HPLC ratio (97.8:2.2) (Figure 2).

Isopropyl 3-(1′-Cyclohexenyl)-2-methoxypropionate. ^{1}H NMR (90 MHz, $CDCl_3$) δ 1.25 (d, J = 6.0 Hz, 3 H), 1.27 (d, J = 6.0 Hz, 3 H), 1.60 (m, 4 H), 2.03 (m, 4 H), 2.40 (d, J = 7.2 Hz, 2 H), 3.37 (s, 3 H), 3.90 (t, J = 7.2 Hz, 1 H), 5.18 (heptet, J = 6.0 Hz, 1 H), 5.58 (m, 1 H) ppm. On addition of (+)-Eu(DPPM)$_3$ (31 μL) to the solution of methyl ether in $CDCl_3$ (27 mg, in 0.4 mL), the singlet of methyl ether at δ 3.37 was changed into the two singlets at δ 4.53 ((*R*)-isomer) and 4.37 ((*S*)-isomer) (relative intensity = 93:7).

Methyl 2-Methoxy-4-phenyl-4-pentenoate. ^{1}H NMR (90 MHz, $CDCl_3$) δ 2.98 (m, 2 H), 3.35 (s, 3 H), 3.72 (s, 3 H), 3.90 (dd, J = 6.0, 7.5 Hz, 1 H), 5.26 (d, J = 2.5 Hz, 1 H), 5.45 (d, J = 2.5 Hz, 1 H), 7.45 (m, 5 H) ppm. On addition of (+)-Eu(DPPM)$_3$ (28 μL) to the solution of methyl ether in $CDCl_3$ (20 mg, in 0.4 mL), the singlet of methyl ether at δ 3.35 was changed into the two singlets at δ 4.42 ((*R*)-isomer) and 4.23 ((*S*)-isomer) (relative intensity = 98.5:1.5); the ^{1}H NMR ratio was almost identical with the HPLC ratio (98.2:1.8).

Methyl 3-(1′-Cyclohexenyl)-2-methoxypropionate. ^{1}H NMR (90 MHz, $CDCl_3$) δ 1.60 (m, 4 H), 1.98 (m, 4 H), 2.38 (d, J = 6.9 Hz, 2 H), 3.40 (s, 3 H), 3.77 (s, 3 H), 3.93 (t, J = 6.9 Hz, 1 H), 5.57 (m, 1 H), ppm. On addition of (+)-Eu(DPPM)$_3$ (35 μL) to the solution of methyl ether in $CDCl_3$ (33 mg, in 0.4 mL), the singlet of methyl ether at δ 3.40 was changed into the two singlets at δ 4.50 ((*R*)-isomer) and 4.30 ((*S*)-isomer) (relative intensity = 99:1); the ^{1}H NMR ratio was identical with the HPLC ratio (99.2:0.8).

Methyl 3-(1′-Cyclopentenyl)-2-methoxypropionate. ^{1}H NMR (90 MHz, $CDCl_3$) δ 1.90 (m, 2 H), 2.33 (m, 4 H), 2.56 (d, J = 6.4 Hz, 2 H), 3.43 (s, 3 H), 3.80 (s, 3 H), 3.98 (t, J = 6.4 Hz, 1 H), 5.55 (m, 1 H) ppm. On addition of (+)-Eu(DPPM)$_3$ (32 μL) to the solution of methyl ether in $CDCl_3$ (23 mg, in 0.4 mL), the singlet of methyl ether at δ 3.43 was changed into the two singlets at δ 4.45 ((*R*)-isomer) and 4.30 ((*S*)-isomer) (relative intensity = 94.5:5.5).

(*E*)- and (*Z*)-Methyl 4-Ethyl-2-methoxy-4-hexenoate. ^{1}H NMR (90 MHz, $CDCl_3$) δ 0.97 (t, J = 7.8 Hz, 3 H), 0.98 (t, J = 7.8 Hz, 3 H) (minor), 1.60 (d, J = 6.6 Hz, 3 H), 1.67 (d, J = 6.6 Hz, 3 H) (minor), 2.07 (m, 2 H) (minor), 2.12 (q, J = 7.8 Hz, 2 H), 2.43 (m, 2 H), 2.51 (m, 2 H) (minor), 3.40 (s, 3 H), 3.75 (s, 3 H) (minor), 3.79 (s, 3 H), 3.90 (t, J = 6.0 Hz, 1 H) (minor), 3.92 (t, J = 6.0 Hz, 1 H), 5.35 (q, J = 6.6 Hz, 1 H), 5.45 (q, J = 6.6 Hz, 1 H) (minor) ppm. On addition of (+)-Eu(DPPM)$_3$ (45 μL) to the solution of methyl ether in $CDCl_3$ (30 mg, in 0.4 mL), the singlet of methyl ether at δ 3.40 was changed into the four singlets at δ 5.18 ((*E*,*R*)-isomer), 5.03 ((*Z*,*R*)-isomer), 4.88 ((*E*,*S*)-isomer), and 4.80 ((*Z*,*S*)-isomer) (relative intensity of *E* isomer = 99:1 and *Z* isomer = >95:<5).

Methyl Ether Derivative of 6. Methyl 4-Ethyl-2-methoxy-4-pentenoate (8a) and (*E*)/(*Z*)-Methyl 2-Methoxy-4-methyl-4-hexenoate (8b,c). ^{1}H NMR (90 MHz, $CDCl_3$) δ 1.03 (t, J = 6.6 Hz, 3 H) (**8a**), 1.58 (d, J = 7.8 Hz, 3 H) (**8b**), 1.65 (m, 3 H) (**8b**), 2.10 (q, J = 6.8 Hz, 2 H) (**8a**), 2.42 (d, J = 6.6 Hz, 2 H) (**8b**), 2.48 (d, J = 6.6 Hz, 2 H) (**8a**), 3.40 (s, 3 H) (**8a,b,c**), 3.77 (s, 3 H), (**8b**), 3.80 (s, 3 H) (**8a**), 3.94 (t, J = 6.6 Hz, 1 H) (**8b**), 3.96 (t, J = 6.6 Hz, 1 H) (**8a**), 4.82 (m, 1 H) (**8a**), 4.90 (m, 1 H) (**8a**), 5.37 (m, 1 H) (**8b**) ppm. On additon of (+)-Eu(DPPM)$_3$ (60 μL) to the solution of methyl ether in $CDCl_3$ (28 mg, in 0.4 mL), the singlet of methyl ether at δ 3.40 was changed into the six singlets at δ 4.95 ((*R*)-**8b**), 4.71 ((*R*)-**8c**), 4.68 ((*S*)-**8b**), 4.60 ((*R*)-**8a**), 4.48 ((*S*)-**8c**), and 4.40 ((*S*-**8a**) (relative intensity of **8a** = 95.5:4.5, **8b** = 99:1, and **8c** = >95:<5).

Methyl Ether Derivative of 7. Methyl 4-Isopropyl-2-methoxy-4-pentenoate (9a) and Methyl 4,5-Dimethyl-2-methoxy-4-hexenoate (9b). ^{1}H NMR (90 MHz, $CDCl_3$) δ 1.05 (d, J = 6.6 Hz, 6 H), (**9a**), 1.69 (s, 9 H) (**9b**), 2.31 (m, 1 H) (**9a**), 2.50 (d, J = 6.6 Hz, 2 H) (**9a,b**), 3.42 (s, 3 H) (**9b**), 3.43 (s, 3 H), (**9a**), 3.81 (s, 3 H) (**9a**), 3.82 (s, 3 H) (**9b**), 3.98 (t, J = 6.7 Hz, 1 H) (**9b**), 4.00 (t, J = 6.6 Hz, 1 H) (**9a**), 4.88 (br s, 1 H) (**9a**), 4.95 (br s, 1 H) (**9b**) ppm. On addition of (+)-Eu(DPPM)$_3$ (35 μL) to the solution of methyl ether in $CDCl_3$ (22 mg, in 0.4 mL), the two singlets of methyl ether at δ 3.42 (**9b**) and 3.43 (**9a**) was changed into the two singlets respectively at δ 4.67 ((*R*)-**9b**), 4.45 ((*S*)-**9b**), 4.23 ((*R*)-**9a**), and 4.10 ((*S*)-**9a**) (rel intensity of **9a** = 96:4 and **9b** = >99:<1).

General Procedure for NMR Study. All FID collections at the appropriate timing were stored on a floppy diskette. Samples for NMR experiments were prepared as follows.

Method A. BINOL (0.2 mmol, 57.2 mg) was placed in a dry test tube and dissolved in $CDCl_3$ (1.0 mL) in the presence of molecular sieves 4A (1.0 g) under an argon atmosphere. To the solution of BINOL was added a 1.0 M $CDCl_3$ solution of diisopropoxytitanium dichloride (0.2 mL). After stirring for 1 h at room temperature, the resultant suspension was centrifuged, and then the molecular sieves was sedimented. The supernatant solution was displaced in a 5-mm NMR tube under an argon atmosphere.

Method B. BINOL (0.1 mmol, 28.6 mg) was placed in a dry 20-mL flask and dissolved in $CDCl_3$ (0.5 mL) under an argon atmosphere. To the solution of BINOL was added a 1.0 M $CDCl_3$ solution of diisopropoxytitanium dichloride (0.1 mL). After stirring for 1 h at room temperature, the resultant solution was displaced in a 5-mm NMR tube under an argon atmosphere.

Acknowledgment. We thank Prof. I. Shimizu, Waseda University, for high-resolution mass spectrometry measurements. Thanks are also due to Dr. T. Kusaba and Dr. K. Kamoshita of Sumitomo Chemical Co., Ltd. for their valuable contribution in the HPLC analysis. This work was aided by *Synth. Org. Chem., Jpn.* Award (Asahi-Kasei Award).