A Facile Chemoenzymatic Route to Optically Active 4,5-Disubstituted-2*E*-hexenoate Derivatives. I[1)]

Hiroyuki AKITA,*[,a] Isao UMEZAWA,[a] Michika TAKANO,[b] Chiiko OHYAMA,[b] Hiroko MATSUKURA,[b] and Takeshi OISHI[b,2)]

School of Pharmaceutical Science, Toho University,[a] 2–2–1, Miyama, Funabashi, Chiba 274, Japan and Riken Institute (The Institute of Physical and Chemical Research),[b] 2–1, Hirosawa, Wako-shi, Saitama 351–01, Japan.
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The reaction of (±) methyl 4,5-*trans*-epoxy-2*E*-hexenoate (2) with aromatic nucleophiles having an electron-donating group in the presence of $BF_3 \cdot Et_2O$ gave the 4,5-*anti*-5-hydroxy-4- or/and 2,5-*anti*-5-hydroxy-2-substituted products. The 5-acetates of the 4,5-*anti*-4-substitution products were subjected to enantioselective hydrolysis with lipase to provide the optically active 4,5-disubstituted 2-hexenoate derivatives.

Keywords methyl 4,5-*trans*-epoxy-2*E*-hexenoate; boron trifluoride etherate; enantioselective hydrolysis; epoxy ring opening; lipase; phenol; polymethoxybenzene

In connection with our work directed towards the synthesis of optically active 2,3-disubstituted butyrate derivatives **A**, which were obtained by the reaction of an optically active 2,3-*trans*-epoxy butyrate **1** and nucleophilic reagents in the presence of Lewis acid,[3a,b)] the reaction of (±)-4,5-*trans*-epoxy-2*E*-hexenoate (**B**), a vinylogous derivative of **1**, with various kinds of nucleophiles has aroused our interest. The reaction of (±)-**B** and alcohols in the presence of Lewis acid was reported to give selectively (±)-4,5-*anti* **C**,[4a,b)] while the reaction of (±)-**B** and acetoacetate in the presence of palladium catalyst[5)] or methyl-metal reagent[6a,b)] was reported to produce the (±)-4,5- or/and 2,5-disubstituted compounds (**C** or/and **D**).

Optically acitive 4,5-*anti*-disubstituted-2*E*-hexenoate derivatives **C** are expected to be chiral intermediates for the synthesis of biologically active compounds such as amino sugars or related compounds.[4b)] We now report the regioselective synthesis of (±)-4,5-*anti* **C** and enantioselective hydrolysis of the 5-acetate of (±)-4,5-*anti* **C** with lipase.

The Reaction of (±) Methyl 4,5-*trans*-Epoxy-2*E*-hexenoate (2) with Various Nucleophiles By applying the reported method,[6a)] the epoxide (±)-**2** was obtained by the epoxidation of methyl sorbate with *m*-chloroperbenzoic acid (MCPBA) in 85% yield.

i) The Reaction of (±)-**2** and Phenol Analogues: In a preliminary experiment, when the reaction of (±)-**2** (5 mmol) with *p*-methoxyphenol (5 mmol) in the presence of boron trifluoride etherate ($BF_3 \cdot Et_2O$, 5 mmol) in CH_2Cl_2 (10 ml) was carried out for 1 h at −78 °C, the (±)-4,5-*anti*-4-aryl ether (*O*-substituted compound) **3a** (14%) and the (±)-4,5-*anti*-4-aryl substitution products (*C*-substituted compounds **4a** (24%) and **5a** (4%)) were obtained along with the starting (±)-**2** (4%) and *p*-methoxyphenol (30%). To ensure complete consumption of the nucleophile (*p*-methoxyphenol), 2 molar eq of (±)-**2** and $BF_3 \cdot Et_2O$ with respect to *p*-methoxyphenol were employed under the same conditions as above, giving (±)-**3a** (25%), (±)-**4a** (48%) and (±)-**5a** (6%). In this case, chemical yields of the products were calculated based on the amount of *p*-methoxyphenol.

The structure of (±)-**3a** was determined as follows. Acetylation of (±)-**3a** provided an acetate (±)-**3b** whose nuclear magnetic resonance (NMR) spectrum showed the presence of an acetoxyl group at the C_5-position, because the signal due to C_5-H was a double quartet at 5.11 ppm with two coupling constants ($J_{5,Me}=6$ Hz, $J_{4,5}=4$ Hz). The 4,5-*anti*-configuration of (±)-**3a** (or (±)-**3b**) was deduced by comparison with the reported reaction result[4a,b)] using (±)-**B** and alcohol. Structure elucidations of (±)-**4a** and (±)-**5a** were carried out as follows. Acetylation of (±)-**4a** and (±)-**5a** gave the corresponding acetates (±)-**4b** and (±)-**5b**, respectively. The substitution pattern in the aromatic ring of (±)-**4b** and (±)-**5b** was determined by a nuclear Overhauser effect (NOE) experiment as shown in Chart 2. These determinations were supported by the fact that methylation (Me_2SO_4/K_2CO_3 in acetone) of (±)-**4a** or (±)-**5a** afforded the same (±)-4,5-*anti*-dimethoxy compound **6a**, whose structure determination is described below. Then the reaction of (±)-**2** with phenol analogues was examined, and the same results as in the previous case were obtained, as shown in Table I. The similarity of the NMR spectra of these products ((±)-**7a**—(±)-**14a**) to those

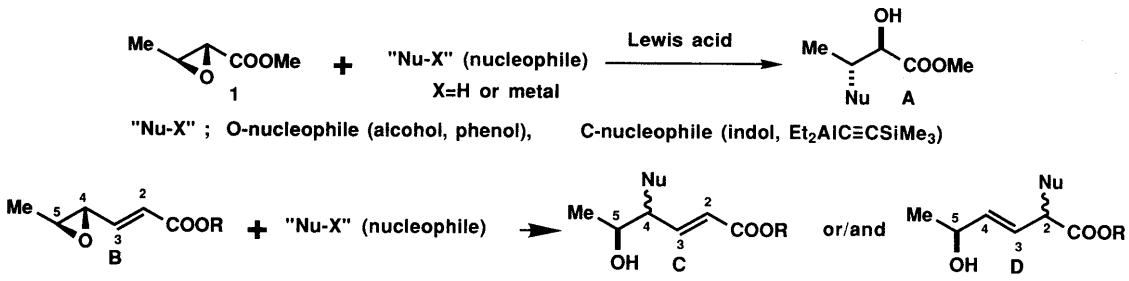


Chart 1

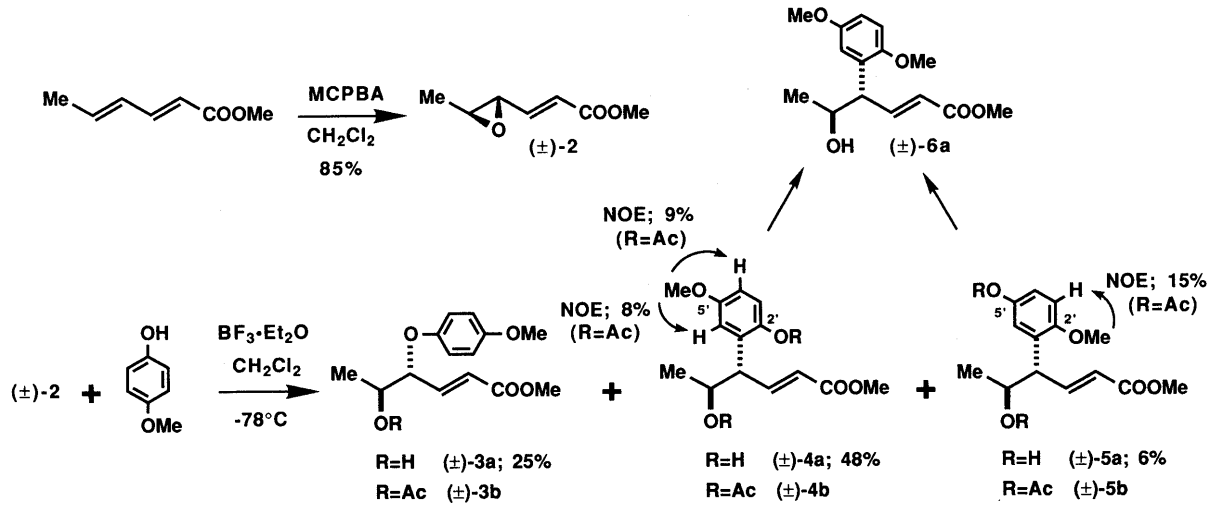
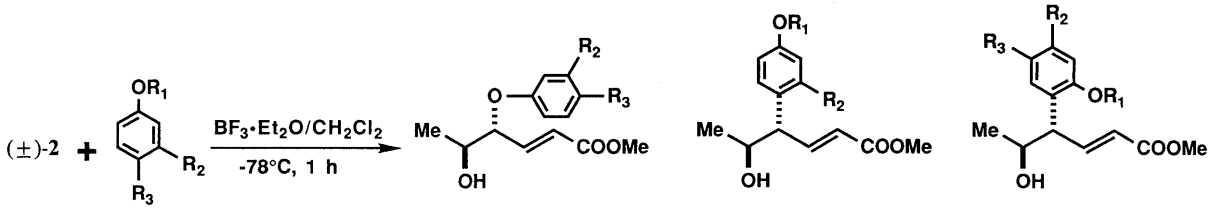
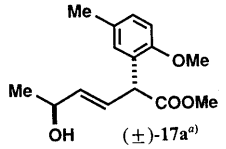


Chart 2

TABLE I



Entry	R_1	R_2	R_3			
1	H	H	H	(±)- **7a**[a] (8%)	(±)- **8a**[a] (31%)	(±)- **9a**[a] (12%)
2	H	H	Me	(±)-**10a**[a] (17%)	—	(±)-**11a**[a] (69%)
3	H	Me	H	(±)-**12a**[a] (9%)	(±)-**14a**[a] (26%)	(±)-**13a**[a] (48%)
4	Me	H	H	—	(±)-**15a**[a] (33%)	—
5[b]	Me	H	Me	—	—	(±)-**16a**[a] (15%)



a) Products **7a**—**17a** were converted to the corresponding acetates **7b**—**17b**. *b*) In entry 5, the (±)-2,5-disubstituted product **17a** (5%) was additionally obtained.

of (±)-**3a**, (±)-**4a** and (±)-**5a** suggested the structures shown in Table I. In the case of the reaction of (±)-**2** and *p*-chlorophenol, the starting materials were recovered.

For the purpose of obtaining selectively the *C*-substituted compound, the reaction of (±)-**2** and various kinds of polymethoxybenzene analogues was examined.

ii) The Reaction of (±)-**2** and Methoxybenzene Analogues: The reaction of (±)-**2** and anisole provided (±)-**15a** in 33% yield while the reaction of *p*-methoxytoluene yielded (±)-**16a** (15%) and its regio-isomer (±)-**17a** (5%, δ 4.57, 1H, d, $J_{2,3}=8$ Hz; C_2-H), as shown in Table I. Structure elucidation of (±)-**15a** and (±)-**16a** was the same as the case of i). The structure elucidation of (±)-**17a** will be dealt with in connection with that of the similar compound (±)-**18a** (see below, and Table II).

iii) The Reaction of (±)-**2** and Dimethoxybenzene Analogues: The reaction of (±)-**2** and 1,4-dimethoxybenzene provided the two *C*-substitution products ((±)-**6a** (27%) and (±)-**18a** (25%, δ 4.57, 1H, d, $J_{2,3}=8$ Hz; C_2-H)). Hydrogenation of (±)-**6a** and the subsequent lactonization produced the (±)-δ-lactone **19**. From a decoupling experiment with (±)-**19**, the coupling constant due to C_4-H and C_5-H was 10 Hz and this result indicates that (±)-**6a** possessed 4,5-*anti*-configuration.[7] Compound (±)-**18a** was also converted into the δ-lactone (±)-**20** in the same way as (±)-**6a**. From a decoupling experiment with (±)-**20**, the signal due to C_5-H appears as a double quartet at 4.60 ppm ($J_{5,Me}=6$ Hz, $J_{4,5}=11$ Hz, $J_{4,5}=2$ Hz) and the signal due to C_2-H as a double doublet at 3.54 ppm ($J_{2,3}=11$ Hz, $J_{2,3}=7$ Hz). These data indicate that the starting (±)-**18a** possessed 2,5-*anti*-configuration. The reaction of (±)-**2** and 1,2-dimethoxybenzene afforded (±)-4,5-*anti* **21a** (77%), while the reaction of (±)-**2** and 1,3-dimethoxybenzene provided (±)-4,5-*anti* **22a** (75%) together with (±)-2,5-*anti* **23a** (10%, δ 4.53, 1H, d, $J_{2,3}=8$ Hz; C_2-H) as given in Table II.

iv) The Reaction of (±)-**2** and Trimethoxybenzene Analogues: In order to increase the chemical yield of *C*-substitution product, the reaction of (±)-**2** and trimethoxybenzene analogues having greater nucleophilicity of the aromatic ring as compared with mono- or dimethoxybenzene analogues was examined. The results are

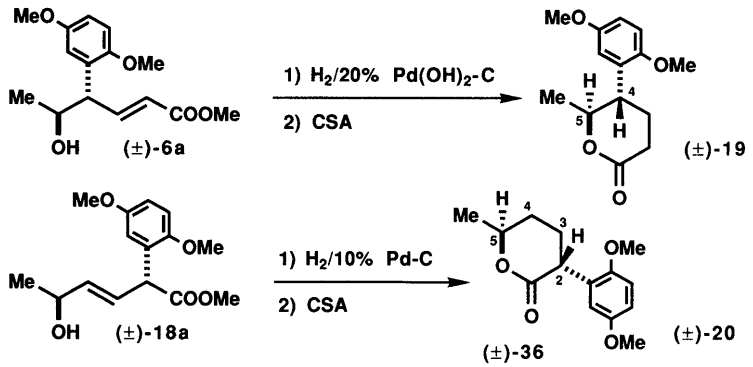
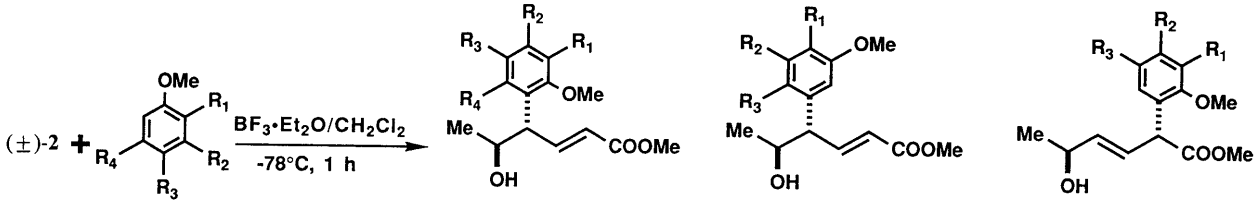
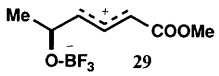


Chart 3

TABLE II



Entry	R_1	R_2	R_3	R_4			
1	H	H	OMe	H	(±)- **6a** (27%)	—	(±)-**18a** (25%)
2	OMe	H	H	H	—	(±)-**21a** (77%)	—
3	H	OMe	H	H	(±)-**22a** (75%)	—	(±)-**23a** (10%)
4	H	OMe	H	OMe	(±)-**24a** (91%)	—	—
5	H	OMe	OMe	H	(±)-**25a** (89%)	—	(±)-**26a** (7%)
6	OMe	OMe	H	H	(±)-**27a** (7%)	(±)-**28a** (7%)	—



29

Products **6a**, **18a**, **21a**—**28a** were converted to the corresponding acetates **6b**, **18b**, **21b**—**28b**.

summarized in Table II. The reaction of (±)-**2** and 1,3,5-trimethoxybenzene yielded exclusively (±)-4,5-*anti* **24a** (91%). When 1,2,4-trimethoxybenzene was employed, (±)-2,5-*anti* **26a** (7%, δ 4.59, 1H, d, $J_{2,3}=8$ Hz; C_2-H) and (±)-4,5 *anti* **25a** (89%) were obtained. In the case of the reaction of (±)-**2** and 1,2,3-trimethoxybenzene, two 4,5-*anti*-4-substitution products ((±)-**27a** (7%) and (±)-**28a** (7%)) were obtained. Substitution patterns of the benzene ring of (±)-**27a** (δ 6.65 and 6.84, each 1H, d, $J=9$ Hz; $C_{5'}$-H or/and $C_{6'}$-H) and (±)-**28a** (δ 6.41, 2H, s; $C_{2'}$-H and $C_{6'}$-H) were determined as shown in Table II.

The regioselectivity of the nucleophilic reagent toward (±)-**2** was found to be subtly affected by the reagents used. In the reaction of (±)-**2** with nucleophilies in the presence of $BF_3 \cdot Et_2O$, the possibility of forming the π-allyl complex **29** (see Table II) from (±)-**2** should be considered. If the complex formation takes place, then the nucleophilic attack from the less hindered side (*anti*-direction) should give the 4,5-*anti*-4-substituted compounds or the 2,5-*anti*-2-substitution products. In the reaction of (±)-**2** and various kinds of methyl-copper reagents, it was reported that the harder nucleophiles attack predominantly the C_4-position while the softer reagents react predominantly at the C_2-position.[6a] In the present case, it is difficult to explain the regioselectivity quantitatively on the basis of differences in softness among the nucleophiles used. From the present results, it seemed more reasonable to assume that the chemical yield of the *C*-substituted compound at the C_4-position of (±)-**2** increases with increasing nucleophilicity of the aromatic ring and carbon-carbon bond formation takes place between the C_4-position of (±)-**2** and the *ortho*- or *para*-position of the oxygen-substituted aromatic nucleophile.

Enantioselective Hydrolysis of (±)-4,5-*anti*-5-Acetoxy-4-substituted Esters with Lipase At first, in order to determine the absolute structure and optical purity of the enzymatic reaction products, optically active authentic samples ((4*S*,5*R*)-**3a** (44% ee), (4*R*,5*R*)-**21a** (44% ee), (4*R*,5*R*)-**22a** (44% ee), (4*R*,5*R*)-**6a** (43% ee), (4*R*,5*R*)-**24a** (44% ee)) were obtained by the reaction of the known (4*R*,5*R*)-**2** (44% ee)[8] and nucleophiles as described for the racemic compounds (Chart 4).

i) Enantioselective Hydrolysis of (±)-**3b** with Lipases: Compound (±)-**3b** was exposed to various kinds of lipases and the results of the enzymatic reaction are shown in Table III. The best result was obtained when the lipase Amano M-10 from *Mucol javanicus* was employed (entry 3). It was found that the stereochemistry of the products depended upon the enzymes used. The absolute structure and optical purity of the hydrolyzed products were confirmed by an analysis of the 400 MHz NMR spectra of their (+)-α-methoxy-α-trifluoromethylacetates ((+)-MTPA ester)[9] in comparison with the spectra of the authentic (4*S*,5*R*)-**3a**-(+)-MTPA (δ 3.73, 3H, s; COOMe) and a mixture of two

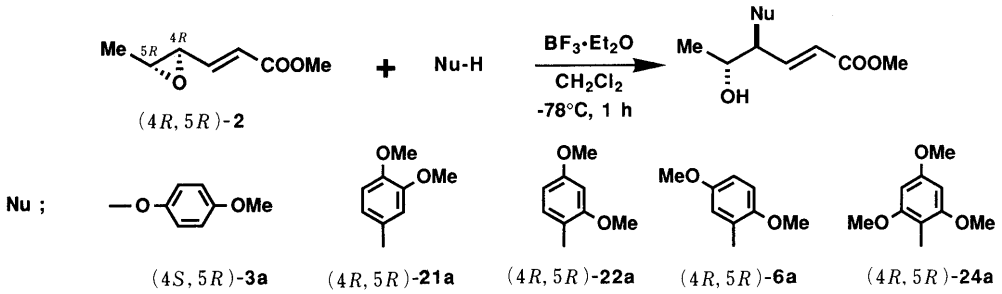
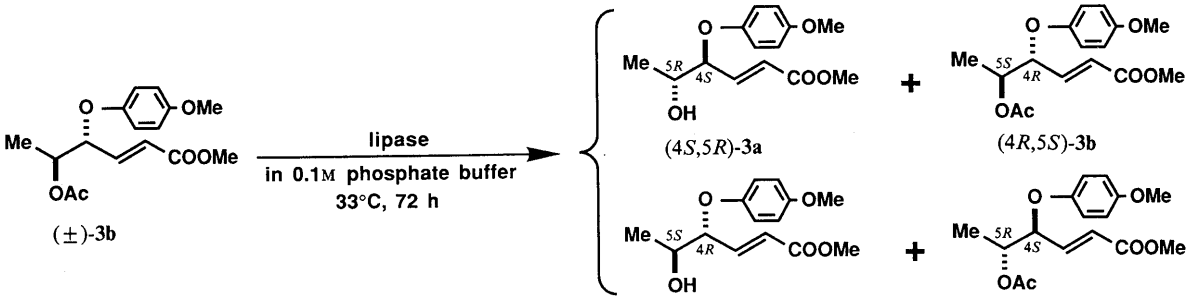


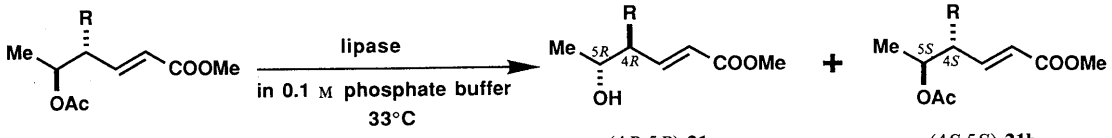
Chart 4

TABLE III



Entry	Substrate (mg)	Lipase	Product (yield, (%), optical purity (% ee))	
1	(93)	Amano A-6 (*Aspergillus niger*)	(4*S*,5*R*)-**3a** (43%, 68% ee)	(4*R*,5*S*)-**3b** (50%, 47% ee)
2	(92)	Amano A (*Aspergillus niger*)	(4*S*,5*R*)-**3a** (37%, 75% ee)	(4*R*,5*S*)-**3b** (53%, 34% ee)
3	(95)	Amano M-10 (*Mucol javanicus*)	(4*S*,5*R*)-**3a** (25%, 92% ee)	(4*R*,5*S*)-**3b** (59%, 28% ee)
4	(120)	Amano F-AP-15 (*Rhizopus javanicus*)	(4*S*,5*R*)-**3a** (43%, 61% ee)	(4*R*,5*S*)-**3b** (21%, 61% ee)
5	(95)	Amano D-10 (*Rhizopus delemar*)	(4*R*,5*S*)-**3a** (36%, 42% ee)	(4*S*,5*R*)-**3b** (53%, 48% ee)
6	(95)	OF-360 (*Candida cylindracea*)	(4*R*,5*S*)-**3a** (37%, 59% ee)	(4*S*,5*R*)-**3b** (8%, 60% ee)

TABLE IV



R=3′,4′-dimethoxyphenyl (±)-**21b**
R=2′,4′-dimethoxyphenyl (±)-**22b**
R=2′,5′-dimethoxyphenyl (±)-**6b**

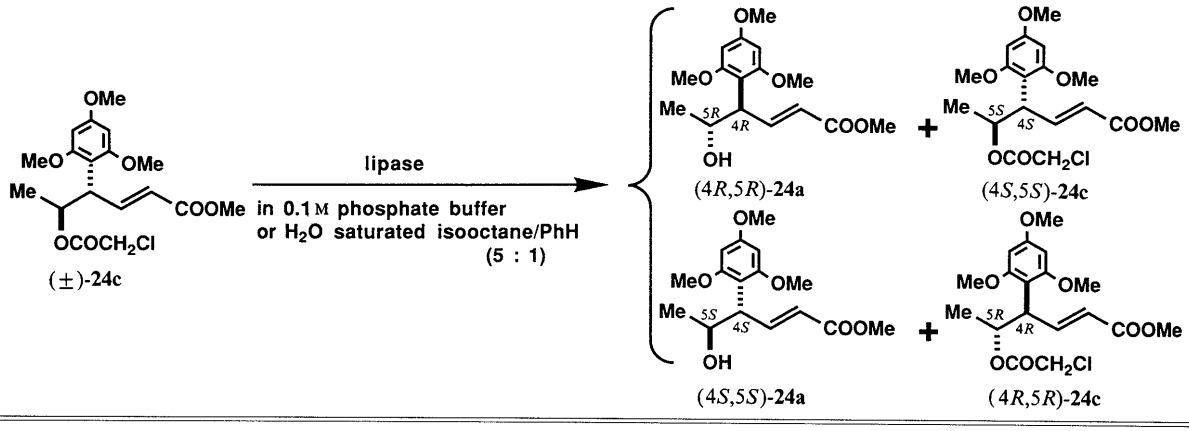
(4*R*,5*R*)-**22a**
(4*S*,5*S*)-**22b**
(4*R*,5*R*)-**6a**
(4*S*,5*S*)-**6b**

Entry	Substrate (mg)	Lipase	Time (h)	Product (yield (%), optical purity (% ee))	
1	(±)-**40**, (109)	MY-30 (*Candida cylindracea*)	72	(4*R*,5*R*)-**21a** (13.6%, >99% ee)	(4*S*,5*S*)-**21b** (82.6%, 16% ee)
2	(±)-**40**, (115)	OF-360 (*Candida cylindracea*)	72	(4*R*,5*R*)-**21a** (73.5%, 31% ee)	(4*S*,5*S*)-**21b** (24.1%, 85% ee)
3	(±)-**40**, (143)	Amano A-6 (*Aspergillus niger*)	72	(4*R*,5*R*)-**21a** (53.9%, 62% ee)	(4*S*,5*S*)-**21b** (30.8%, 99% ee)
4	(±)-**40**, (100)	PL 679 (*Alcaligenes* sp.)	72	(4*R*,5*R*)-**21a** (85.0%, 15% ee)	(4*S*,5*S*)-**21b** (13.0%, 83% ee)
5	(±)-**41**, (111)	PPL	72	(4*R*,5*R*)-**22a** (5.6%, 84% ee)	(4*S*,5*S*)-**22b** (87.2%, 8% ee)
6	(±)-**41**, (113)	Nagase P (*Pseudomonas* sp.)	72	(4*R*,5*R*)-**22a** (14.1%, 87% ee)	(4*S*,5*S*)-**22b** (83.5%, 12% ee)
7	(±)-**33**, (108)	Amano M-10 (*Mucol javanicus*)	166	(4*R*,5*R*)-**6a** (68%, 10% ee)	(4*S*,5*S*)-**6b** (21%, 26% ee)
8	(±)-**33**, (97)	W.G (*Wheat germ*)	166	(4*R*,5*R*)-**6a** (43%, 90% ee)	(4*S*,5*S*)-**6b** (52%, 67% ee)

(+)-MTPA esters ((4*S*,5*R*)-3a-(+)-MTPA and (4*R*,5*S*)-**3a**-MTPA (δ 3.72, 3H, s; COOMe) obtained by the reaction of (±)-**3a**- and (+)-MTPACl.[9] The absolute structure and optical purity of the unchanged acetates were also confirmed by the NMR analysis of their (+)-MTPA esters obtained by hydrolysis and subsequent (+)-MTPA esterification.

ii) Enantioselective Hydrolysis of (±)-**21b**, (±)-**22b** and (±)-**6b**: Three kinds of acetates were exposed to the enzymatic reaction using various kinds of lipases, and selected data are shown in Table IV. In every case, the hydrolyzed products had (4*R*,5*R*)-configuration and the unchanged acetates had (4*S*,5*S*)-configuration. In the determination of the stereochemistry and the optical purity of the enzymatic reaction products obtained from (±)-**21b** and (±)-**22b**, high-performance liquid chromatographic (HPLC) analysis with a chiral column (Chiracel OD (4.6 mm i.d. × 250 mm)) was employed. Details are given in the experimental section. The enzymatic reaction

TABLE V



Entry	Substrate (mg)	Lipase	Time (h)	Product (yield (%), optical purity (% ee))	
1	(511)	Amano A-6 (*Aspergillus niger*)	46	(4*R*,5*R*)-**24a** (30%, 85% ee)	(4*S*,5*S*)-**24c** (69%, 37% ee)
2	(129)	Amano A-6 (*Aspergillus niger*)/Celite	193	(4*R*,5*R*)-**24a** (15%, 94% ee)	(4*S*,5*S*)-**24c** (74%, 5% ee)
3	(100)	Amano M-10 (*Mucol javanicus*)/Celite	193	(4*R*,5*R*)-**24a** (13%, 96% ee)	(4*S*,5*S*)-**24c** (75%, 2% ee)
4	(110)	Amano A (*Aspergillus niger*)/Celite	193	(4*R*,5*R*)-**24a** (17%, 90% ee)	(4*S*,5*S*)-**24c** (75%, 10% ee)
5	(105)	OF-360 (*Candida cylindracea*)/Celite	193	(4*S*,5*S*)-**24a** (49%, 16% ee)	(4*R*,5*R*)-**24c** (43%, 35% ee)

products obtained from (±)-**6b** were identified in the same way as described above [authentic (4*R*,5*R*)-**6a**-(+)-MTPA (δ 3.70, 3H, s; COOMe), a mixture of two (+)-MTPA esters ((4*S*,5*S*)-**6a**-(+)-MTPA (δ 3.68, 3H, s; COOMe) and (4*R*,5*R*)-**6a**-(+)-MTPA)]. From Table IV, it is clear that the desired absolute configuration concerning the 4,5-*anti* stereochemistry can be obtained by the differential usage of lipases.

iii) Enantioselective Hydrolysis of (±)-**24b** and (±)-**24c**: In a preliminary experiment on the hydrolysis of (±)-**24b** with various kinds of lipases in phosphate buffer solution, hydrolysis rarely occurred. So, the substrate was changed to the chloroacetate (±)-**24c** which was obtained by the reaction of (±)-**24a** and chloroacetic anhydride. The enantioselective hydrolysis of (±)-**24c** with lipase or immobilized enzymes on Celite[10] was carried out in phosphate buffer solution or water-saturated organic media, respectively. Selected data are shown in Table V.

The absolute structure and the optical purity of the reaction products were confirmed by the 400 MHz NMR analysis of their (+)-MTPA esters obtained in the same way as described above [authentic (4*R*,5*R*)-**24a**-(+)-MTPA (δ 3.68, 3H, s; COOMe), a mixture of two (+)-MTPA esters ((4*R*,5*R*)-**24a**-(+)-MTPA and (4*S*,5*S*)-**24a**-(+)-MTPA (δ 3.65, 3H, s; COOMe)]. The stereochemistry of the products was found to depend upon the lipases used. The optical purity of (4*R*,5*R*)-**24a** was found to be high when immobilized enzyme was employed in water-saturated organic media (entries 2—4).

In conclusion, (±) methyl 4,5-*trans*-epoxy-2*E*-hexenoate (**2**) was reacted with aromatic nucleophiles having an electron-donating group in the presence of $BF_3 \cdot Et_2O$ to provide the 4,5-*anti*-5-hydroxy-4- or/and 2,5-*anti*-5-hydroxy-2-substituted products and the corresponding C_5-acetates of the 4,5-*anti*-4-substituted products were exposed to the lipases to give the optically active 4,5-disubstituted-2*E*-hexenoate derivatives. Application of these optically active compounds to the synthesis of optically active natural products is being undertaken.

Experimental

IR spectra (CCl_4) were measured on a JASCO A-3 spectrophotometer. NMR spectra were measured on a JEOL GX-400 instrument. Spectra were taken with 5—10% (w/v) solutions in $CDCl_3$ with Me_4Si as an internal reference. High-resolution mass spectra (HRMS) were obtained with a JEOL JMS-D 300 spectrometer. Optical rotations were measured on a Perkin-Elmer model 241 MC polarimeter. The HPLC system was composed of two SSC instruments (ultraviolet (UV) detector 3000B and flow system 3100). All the reactions were carried out in an atmosphere of argon. For column chromatography, silica gel (Wakogel C-200) was employed. All organic solvents were washed with saturated brine and dried over anhydrous magnesium sulfate ($MgSO_4$). All evaporations were performed under reduced pressure.

(±) Methyl (4,5)-*trans*-Epoxy-(2*E*)-hexenoate (2) A solution of methyl sorbate (25.2 g) and MCPBA (44 g) in CH_2Cl_2 (500 ml) was stirred for 24 h at room temperature. The reaction mixture was filtered and the filtrate was washed with aqueous saturated $NaHCO_3$. The organic layer was evaporated to give a residue, which was chromatographed on silica gel (500 g) to afford **2** as a colorless oil (24.2 g, 85% yield). IR: 1720 cm^{-1}. NMR δ: 1.39 (3H, d, $J_{Me,5}$ = 5 Hz, 5-Me), 2.97 (1H, dq, $J_{5,Me}$ = 5 Hz, $J_{4,5}$ = 2 Hz, 5-H), 3.19 (1H, dd, $J_{4,5}$ = 2 Hz, $J_{3,4}$ = 7 Hz, 4-H), 3.75 (3H, s, COOMe), 6.13 (1H, d, $J_{2,3}$ = 16 Hz, 2-H), 6.69 (1H, dd, $J_{2,3}$ = 16 Hz, $J_{3,4}$ = 7 Hz, 3-H).

General Procedure of the Reaction of (±)-2 and Various Kinds of Nucleophiles in the Presence of $BF_3 \cdot Et_2O$, and Acetylation of Each Product $BF_3 \cdot Et_2O$ (10 mmol) was added to a solution of (±)-**2** (10 mmol) and a nucleophile (5 mmol) in CH_2Cl_2 (10 ml) under dry ice/acetone cooling, and the whole was stirred for 1 h at the same temperature. The reaction mixture was diluted with H_2O and extracted with ether. The organic layer was washed with aqueous saturated $NaHCO_3$. Evaporation of the organic solvent gave an oily product, which was chromatographed on silica gel (50 g) to afford a homogeneous oil from the AcOEt–*n*-hexane (1 : 9—1 : 3, *v*/*v*) eluate. The chemical yield of each product was calculated based on the nucleophile used. All products were treated with excess Ac_2O and a catalytic amount of *p*-dimethylaminopyridine (DMAP) in pyridine at room temperature. The reaction mixture was diluted with H_2O and extracted with ether. The ether layer was washed with 10% aqueous HCl and aqueous saturated $NaHCO_3$. Evaporation of the organic solvent gave an oily product, which was chromatographed on silica gel to provide the corresponding acetate from the AcOEt–*n*-hexane (1 : 9—1 : 4, v/v) eluate.

(±) Methyl (4,5)-*anti*-5-Hydroxy-4-(*p*-methoxyphenoxy)-(2*E*)-hexenoate (3a) and Its Acetate (±)-3b (±)-**3a**: pale yellow oil. 25% yield. *Anal.* HRMS Calcd for $C_{14}H_{18}O_5$(M^+; *m*/*z*): 266.115. Found: 266.116. IR: 3560, 1720, 1650 cm^{-1}. NMR δ: 1.28 (3H, d, $J_{5,Me}$ = 6 Hz, 5-Me), 4.09 (1H, dq, $J_{5,Me}$ = 6 Hz, $J_{4,5}$ = 4 Hz, 5-H), 3.73 (3H, s, COOMe), 3.76 (3H, s, 4′-OMe), 4.62 (1H, dd, $J_{3,4}$ = 5 Hz, $J_{4,5}$ = 4 Hz, 4-H), 6.07 (1H, d, $J_{2,3}$ = 16 Hz, 2-H), 6.99 (1H, dd, $J_{2,3}$ = 16 Hz, $J_{3,4}$ = 5 Hz, 3-H). (±)-**3b**: pale yellow oil. 97%

yield. *Anal.* HRMS Calcd for $C_{16}H_{20}O_6$ (M^+; *m/z*): 308.125. Found: 308.123. IR: 1735, 1658 cm^{-1}. NMR δ: 1.33 (3H, d, $J_{5,Me}=6$ Hz, 5-Me), 2.04 (3H, s, 5-OAc), 3.74 (3H, s, COOMe), 3.76 (3H, s, 4'-OMe), 4.75 (1H, dd, $J_{3,4}=5$ Hz, $J_{4,5}=4$ Hz, 4-H), 5.11 (1H, dq, $J_{5,Me}=6$ Hz, $J_{4,5}=4$ Hz, 5-H), 6.11 (1H, d, $J_{2,3}=16$ Hz, 2-H), 6.95 (1H, dd, $J_{3,4}=5$ Hz, $J_{2,3}=16$ Hz, 3-H).

(±) Methyl (4,5)-*anti*-5-Hydroxy-4-(2'-hydroxy-5'-methoxyphenyl)-(2*E*)-hexenoate (4a) and Its Acetate (±)-4b (±)-**4a**: pale yellow oil. 48% yield. *Anal.* HRMS Calcd for $C_{14}H_{18}O_5$ (M^+; *m/z*): 266.155. Found: 266.117. IR: 3580, 3320, 1720. 1690(sh), 1640 cm^{-1}. NMR δ: 1.26 (3H, d, $J_{5,Me}=6$ Hz, 5-Me), 3.67—3.71 (1H, m, 4-H), 3.73 (3H, s, COOMe), 3.75 (3H, s, 5'-OMe), 4.35 (1H, br s, 5-H), 5.91 (1H, d, $J_{2,3}=16$ Hz, 2-H), 6.59 (1H, d, $J_{4',6'}=3$ Hz, 6'-H), 6.72 (1H, dd, $J_{4',6'}=3$ Hz, $J_{3',4'}=9$ Hz, 4'-H), 6.82 (1H, d, $J_{3',4'}=9$ Hz, 3'-H), 7.33 (1H, dd, $J_{2,3}=16$ Hz, $J_{3,4}=8$ Hz, 3-H). (±)-**4b**: pale yellow oil. 75% yield. *Anal.* HRMS Calcd for $C_{18}H_{22}O_7$ (M^+; *m/z*): 350.137. Found: 350.134. IR: 1760, 1730, 1645 cm^{-1}. NMR δ: 1.12 (3H, d, $J_{5,Me}=6$ Hz, 5-Me), 2.05 (3H, s, 5-OAc), 2.33 (3H, s, 2'-OAc), 3.66 (1H, dd, $J_{3,4}=8$ Hz, $J_{4,5}=6$ Hz, 4-H), 3.71 (3H, s, COOMe), 3.79 (3H, s, 5'-OMe), 5.26 (1H, dq, $J_{5,Me}=6$ Hz, $J_{4,5}=6$ Hz, 5-H), 5.80 (1H, d, $J_{2,3}=16$ Hz, 2-H), 6.76 (1H, d, $J_{4',6'}=3$ Hz, 6'-H), 6.82 (1H, dd, $J_{4',6'}=3$ Hz, $J_{3',4'}=9$ Hz, 4'-H), 7.01 (1H, d, $J_{3',4'}=9$ Hz, 3'-H), 7.07 (1H, dd, $J_{2,3}=16$ Hz, $J_{3,4}=8$ Hz, 3-H).

(±) Methyl (4,5)-*anti*-5-Hydroxy-4-(5'-hydroxy-2'-methoxyphenyl)-(2*E*)-hexenoate (5a) and Its Acetate (±)-5b (±)-**5a**: pale yellow oil. 6% yield. *Anal.* HRMS Calcd for $C_{14}H_{18}O_5$ (M^+; *m/z*): 266.115. Found: 266.120. IR: 3580, 3400, 1720, 1700 (sh), 1640 cm^{-1}. NMR δ: 1.13 (3H, d, $J_{5,Me}=6$ Hz, 5-Me), 3.71 (3H, s, COOMe), 3.73—3.75 (1H, m, 5-H), 3.76 (3H, s, 2'-OMe), 3.80 (1H, dd, $J_{3,4}=9$ Hz, $J_{4,5}=7$ Hz, 4-H), 5.92 (1H, d, $J_{2,3}=16$ Hz, 2-H), 6.70 (1H, dd, $J_{4',6'}=3$ Hz, $J_{3',4'}=9$ Hz, 4'-H), 6.73 (1H, d, $J_{4',6'}=3$ Hz, 6'-H), 6.75 (1H, d, $J_{3',4'}=9$ Hz, 3'-H), 7.33 (1H, dd, $J_{3,4}=9$ Hz, $J_{2,3}=16$ Hz, 3-H). (±)-**5b**: pale yellow oil, 63% yield. *Anal.* HRMS Calcd for $C_{18}H_{22}O_7$ (M^+; *m/z*): 380.137. Found: 380.139. IR: 1758, 1730, 1720, 1640 cm^{-1}. NMR δ: 1.14 (3H, d, $J_{5,Me}=6$ Hz, 5-Me), 2.01 (3H, s, 5-OAc), 2.27 (3H, s, 5'-OAc), 3.72 (3H, s, COOMe), 3.82 (3H, s, 2'-OMe), 3.96—4.00 (1H, m, 4-H), 5.29 (1H, dq, $J_{5,Me}=6$ Hz, $J_{4,5}=6$ Hz, 5-H), 5.87 (1H, d, $J_{2,3}=16$ Hz, 2-H), 6.85 (1H, d, $J_{3',4'}=9$ Hz, 3'-H), 6.87 (1H, d, $J_{4',6'}=3$ Hz, 6'-H), 6.96 (1H, dd, $J_{4',6'}=3$ Hz, $J_{3',4'}=9$ Hz, 4'-H), 7.17 (1H, dd, $J_{2,3}=16$ Hz, $J_{3,4}=9$ Hz, 3-H).

(±) Methyl (4,5)-*anti*-5-Hydroxy-4-phenoxy-(2*E*)-hexenoate (7a) and Its Acetate (±)-7b (±)-**7a**: pale yellow oil. 8% yield. *Anal.* HRMS Calcd for $C_{13}H_{16}O_4$ (M^+; *m/z*): 236.104. Found: 236.103. IR: 3560, 1720, 1640 cm^{-1}. NMR δ: 1.29 (3H, d, $J_{5,Me}=6$ Hz, 5-Me), 2.36 (1H, br s, 5-OH), 3.72 (3H, s, COOMe), 4.10 (1H, br s, 5-H), 4.74 (1H, dd, $J_{3,4}=5$ Hz, $J_{4,5}=4$ Hz, 4-H), 6.08 (1H, d, $J_{2,3}=16$ Hz, 2-H), 7.01 (1H, dd, $J_{3,4}=5$ Hz, $J_{2,3}=16$ Hz, 3-H). (±)-**7b**: pale yellow oil. 99% yield. *Anal.* HRMS Calcd for $C_{15}H_{18}O_5$ (M; *m/z*): 278.115. Found: 278.114. IR; 1725, 1650 cm^{-1}. NMR δ: 1.35 (3H, d, $J_{5,Me}=7$ Hz, 5-Me), 2.03 (3H, s, 5-OAc), 3.74 (3H, s, COOMe), 4.86—4.89 (1H, m, 4-H), 5.13 (1H, dq, $J_{5,Me}=7$ Hz, $J_{4,5}=4$ Hz, 5-H), 6.12 (1H, d, $J_{2,3}=16$ Hz, 2-H), 6.96 (1H, dd, $J_{3,4}=5$ Hz, $J_{2,3}=16$ Hz, 3-H).

(±) Methyl (4,5)-*anti*-5-Hydroxy-4-(4'-hydroxyphenyl)-(2*E*)-hexenoate (8a) and Its Acetate (±)-8b (±)-**8a**: pale yellow oil. 31% yield. *Anal.* HRMS Calcd for $C_{13}H_{16}O_4$ (M^+; *m/z*): 236.104. Found: 236.100. IR: 3630, 3550, 1700, 1640 cm^{-1}. NMR δ: 1.10, (3H, d, $J_{5,Me}=6$ Hz, 5-Me), 3.30 (1H, dd, $J_{3,4}=9$ Hz, $J_{4,5}=7$ Hz, 4-H), 3.72 (3H, s, COOMe), 4.03 (1H, dq, $J_{5,Me}=6$ Hz, $J_{4,5}=7$ Hz, 5-H), 5.90 (1H, d, $J_{2,3}=16$ Hz, 2-H), 6.79 (2H, d, $J_{2',3'}=J_{5',6'}=9$ Hz, 3'-H and 5'-H), 7.01 (2H, d, $J_{2',3'}=J_{5',6'}=9$ Hz, 2'-H and 6'-H), 7.26 (1H, dd, $J_{3,4}=9$ Hz, $J_{2,3}=16$ Hz, 3-H). (±)-**8b**: pale yellow oil. 70% yield. Anal. HRMS Calcd for $C_{17}H_{20}O_6$ (M^+ − AcOH; *m/z*): 260.104. Found: 260.105. EI-MS *m/z*: 260 (M^+ − AcOH), CI-MS *m/z*: 321 ($M^+ + 1$), 261 ($M^+ + 1 -$ AcOH). IR: 1760, 1730, 1720, 1640 cm^{-1}. NMR δ: 1.14 (3H, d, $J_{5,Me}=6$ Hz, 5-Me), 2.03 (3H, s, 5-OAc), 2.29 (3H, s, 4'-OAc), 3.54 (1H, t(dd), $J_{3,4}=J_{4,5}=8$ Hz, 4-H), 3.72 (3H, s, COOMe), 5.22 (1H, dq, $J_{5,Me}=6$ Hz, $J_{4,5}=8$ Hz, 5-H), 5.85 (1H, d, $J_{2,3}=16$ Hz, 2-H), 7.07 (2H, d, $J=9$ Hz, aromatic H), 7.12 (1H, dd, $J_{3,4}=8$ Hz, $J_{2,3}=16$ Hz, 3-H). 7.21 (2H, d, $J=9$ Hz, aromatic-H).

(±) Methyl (4,5)-*anti*-5-Hydroxy-4-(2'-hydroxyphenyl)-(2*E*)-hexenoate (9a) and Its Acetate (±)-9b (±)-**9a**: pale yellow oil. 12% yield. *Anal.* HRMS Calcd for $C_{13}H_{16}O_4$ (M^+; *m/z*): 236.104. Found: 236.101. IR: 3575, 3300, 1717, 1690 (sh), 1640 cm^{-1}. NMR δ: 1.28 (3H, d, $J_{5,Me}=6$ Hz, 5-Me), 2.72 (1H, br s, 5-OH), 3.67—3.70 (1H, m, 4-H), 3.73 (3H, s, COOMe), 4.37 (1H, dq, $J_{5,Me}=6$ Hz, $J_{4,5}=6$ Hz, 5-H), 5.90 (1H, d, $J_{2,3}=16$ Hz, 2-H), 7.37 (1H, dd, $J_{3,4}=8$ Hz, $J_{2,3}=16$ Hz, 3-H), 7.83 (1H, br s, 2'-OH). (±)-**9b**: pale yellow oil. 54% yield. *Anal.* HRMS Calcd for $C_{17}H_{20}O_6$ (M^+ − AcOH; *m/z*): 260.105. Found: 260.104. CI-MS *m/z*: 321 ($M^+ + 1$). IR: 1775, 1740, 1730, 1650 cm^{-1}. NMR δ: 1.11 (3H, d, $J_{5,Me}=6$ Hz, 5-Me), 2.05 (3H, s, 5-OAc), 2.35 (3H, s, 2'-OAc), 3.71 (3H, s, COOMe), 3.73 (1H, t, (dd), $J_{3,4}=J_{4,5}=8$ Hz, 4-H), 5.28 (1H, dq, $J_{5,Me}=6$ Hz, $J_{4,5}=8$ Hz, 5-H), 5.79 (1H, d, $J_{2,3}=16$ Hz, 2-H), 7.10 (1H, dd, $J_{3,4}=8$ Hz, $J_{2,3}=16$ Hz, 3-H).

(±) Methyl (4,5)-*anti*-5-Hydroxy-4-(4'-methylphenoxy)-(2*E*)-hexenoate (10a) and Its Acetate (±)-10b (±)-**10a**: pale yellow oil. 17% yield. *Anal.* HRMS Calcd for $C_{14}H_{18}O_4$(M^+; *m/z*): 250.120. Found: 250.117. IR: 3550, 1720, 1645 cm^{-1}. NMR δ: 1.28 (3H, d, $J_{5,Me}=6$ Hz, 5-Me), 2.21 (1H, d, $J_{5,OH}=6$ Hz, 5-OH), 2.28 (3H, s, 4'-Me), 3.72 (3H, s, COOMe), 4.09 (1H, dq, $J_{5,Me}=6$ Hz, $J_{4,5}=4$ Hz, 5-H), 4.69 (1H, dd, $J_{3,4}=5$ Hz, $J_{4,5}=4$ Hz, 4-H), 6.07 (1H, d, $J_{2,3}=16$ Hz, 2-H), 7.00 (1H, dd, $J_{3,4}=5$ Hz, $J_{2,3}=16$ Hz, 3-H). (±)-**10b**: pale yellow oil. 96% yield. *Anal.* HRMS Calcd for $C_{16}H_{20}O_5$ (M^+; *m/z*): 292.131. Found: 292.132. IR: 1740, 1660 cm^{-1}. NMR δ: 1.33 (3H, d, $J_{5,Me}=6$ Hz, 5-Me), 2.03 (3H, s, 5-OAc), 2.27 (3H, s, 4'-Me), 3.73 (3H, s, COOMe), 4.82 (1H, dd, $J_{3,4}=5$ Hz, $J_{4,5}=4$ Hz, 4-H), 5.11 (1H, dq, $J_{5,Me}=6$ Hz, $J_{4,5}=4$ Hz, 5-H), 6.11 (1H, d, $J_{2,3}=16$ Hz, 2-H), 6.95 (1H, dd, $J_{3,4}=5$ Hz, $J_{2,3}=16$ Hz, 3-H).

(±) Methyl (4,5)-*anti*-5-Hydroxy-4-(2'-hydroxy-5'-methylphenyl)-(2*E*)-hexenoate (11a) and Its Acetate (±)-11b (±)-**11a**: pale yellow oil. 69% yield. *Anal.* HRMS Calcd for $C_{14}H_{18}O_4$ (M^+; *m/z*): 250.120. Found: 250.120. IR: 3560, 3300, 1715, 1685 (sh), 1635 cm^{-1}. NMR δ: 1.25 (3H, d, $J_{5,Me}=6$ Hz, 5-Me), 2.24 (3H, s, 5'-Me), 3.19 (1H, br s, 5-OH), 3.61 (1H, dd, $J_{3,4}=8$ Hz, $J_{4,5}=4$ Hz, 4-H), 3.72 (3H, s, COOMe), 4.30—4.37 (1H, m, 5-H), 5.89 (1H, d, $J_{2,3}=16$ Hz, 2-H), 6.77 (1H, d, $J_{3',4'}=8$ Hz, 3'-H), 6.81 (1H, d, $J_{4',6'}=2$ Hz, 6'-H), 6.94 (1H, dd, $J_{3',4'}=8$ Hz, $J_{4',6'}=2$ Hz, 4'-H), 7.38 (1H, dd, $J_{3,4}=8$ Hz, $J_{2,3}=16$ Hz, 3-H). 7.87 (1H, br s, 2'-OH). (±)-**11b**: pale yellow oil. 80% yield. *Anal.* HRMS Calcd for $C_{18}H_{22}O_6$(M^+; *m/z*): 334.141. Found: 334.141. IR: 1770, 1740, 1660 cm^{-1}. NMR δ: 1.10 (3H, d, $J_{5,Me}=6$ Hz, 5-Me), 2.04 (3H, s, 5-OAc), 2.33 (6H, s, 5'-Me and 2'-OAc), 3.67 (1H, dd, $J_{3,4}=8$ Hz, $J_{4,5}=9$ Hz, 4-H), 3.70 (3H, s, COOMe), 5.27 (1H, dq, $J_{5,Me}=6$ Hz, $J_{4,5}=9$ Hz, 5-H), 5.79 (1H, d, $J_{2,3}=16$ Hz, 2-H), 6.96 (1H, d, $J_{3',4'}=8$ Hz, 3'-H), 7.05 (1H, d, $J_{4',6'}=2$ Hz, 6'-H), 7.08 (1H, dd, $J_{3',4'}=8$ Hz, $J_{4',6'}=2$ Hz, 4'-H), 7.08 (1H, dd, $J_{3,4}=8$ Hz, $J_{2,3}=16$ Hz, 3-H).

(±) Methyl (4,5)-*anti*-5-Hydroxy-4-(3'-methylphenoxy)-(2*E*)-hexenoate (12a) and Its Acetate (±)-12b (±)-**12a**: pale yellow oil. 9% yield. *Anal.* HRMS Calcd for $C_{14}H_{18}O_4$ (M^+; *m/z*): 250.121. Found: 250.123. IR: 3620, 1735, 1670 cm^{-1}. NMR δ: 1.29 (3H, d, $J_{5,Me}=6$ Hz, 5-Me), 2.13 (1H, br s, 5-OH), 2.31 (3H, s, 3'-Me), 3.73 (3H, s, COOMe), 4.09 (1H, dq, $J_{4,5}=4$ Hz, $J_{5,Me}=6$ Hz, 5-H), 4.74 (1H, $J_{3,4}=5$ Hz, $J_{4,5}=4$ Hz, 4-H), 6.08 (1H, $J_{2,3}=16$ Hz, 2-H), 7.01 (1H, dd, $J_{3,4}=5$ Hz, $J_{2,3}=16$ Hz, 3-H). (±)-**12b**: pale yellow oil. 96% yield. *Anal.* HRMS Calcd for $C_{16}H_{20}O_5$(M^+; *m/z*): 292.131. Found: 292.133. IR: 1740, 1660 cm^{-1}. NMR δ: 1.34 (3H, d, $J_{5,Me}=6$ Hz, 5-Me), 2.03 (3H, s, 5-OAc), 2.31 (3H, s, 3'-Me), 3.73 (3H, s, COOMe), 4.87 (1H, dd, $J_{3,4}=5$ Hz, $J_{4,5}=4$ Hz, 4-H), 5.11 (1H, dq, $J_{5,Me}=6$ Hz, $J_{4,5}=4$ Hz, 5-H), 6.11 (1H, d, $J_{2,3}=16$ Hz, 2-H),
6.96 (1H, dd, $J_{3,4}=5$ Hz, $J_{2,3}=16$ Hz, 2-H).

(±) Methyl (4,5)-*anti*-5-Hydroxy-4-(2'-hydroxy-4'-methylphenyl)-(2*E*)-hexenoate (13a) and Its Acetate (±)-13b (±)-**13a**: pale yellow oil. 48% yield. *Anal.* HRMS Calcd for $C_{14}H_{18}O_4$ (M^+; *m/z*): 250.120. Found: 250.121. IR: 3610, 1730, 1700 (sh), 1650 cm^{-1}. NMR δ: 1.24 (3H, d, $J_{5,Me}=6$ Hz, 5-Me), 2.26 (3H, s, 4'-Me), 3.62 (1H, dd, $J_{3,4}=8$ Hz, $J_{4,5}=4$ Hz, 4-H), 3.16 (1H, br s, 5-OH), 3.71 (3H, s, COOMe), 4.32 (1H, dq, $J_{5,Me}=6$ Hz, $J_{4,5}=4$ Hz, 5-H), 5.88 (1H, d, $J_{2,3}=16$ Hz, 2-H), 6.65—6.71 (2H, m, 3'-H and 5'-H), 6.88 (1H, d, $J_{5',6'}=8$ Hz, 6'-H), 7.37 (1H, dd, $J_{3,4}=8$ Hz, $J_{2,3}=16$ Hz, 3-H), 8.17 (1H, br s, 2'-OH). (±)-**13b**: pale yellow oil. 99% yield. CI-MS *m/z*: 335 ($M^+ + 1$), 275 ($M^+ + 1 -$ AcOH). IR: 1775, 1740, 1660 cm^{-1}. NMR δ: 1.10 (3H, d, $J_{5,Me}=6$ Hz, 5-Me), 2.04 (3H, s, 5-OAc), 2.329 (3H, s, 4'-Me), 2.332 (3H, s, 2'-OAc), 3.67 (1H, t(dd), $J_{3,4}=J_{4,5}=8$ Hz, 4-H), 3.70 (3H, s, COOMe), 5.26 (1H, dq, $J_{5,Me}=6$ Hz, $J_{4,5}=8$ Hz, 5-H), 5.78 (1H, d, $J_{2,3}=16$ Hz, 2-H), 6.89—7.05 (2H, m, 3'-H and 5'-H), 7.08 (1H, dd, $J_{3,4}=8$ Hz, $J_{2,3}=16$ Hz, 2-H), 7.13 (1H, d, $J_{5',6'}=8$ Hz, 6'-H).

(±) Methyl (4,5)-*anti*-5-Hydroxy-4-(4'-hydroxy-2'-methylphenyl)-(2*E*)-hexenoate (14a) and Its Acetate (±)-14b (±)-**14a**: pale yellow oil. 26% yield. CI-MS *m/z*: 251 ($M^+ + 1$). IR. 3630, 1730, 1650 cm^{-1}. NMR δ: 1.12 (3H, d, $J_{5,Me}=6$ Hz, 5-Me), 2.27 (3H, s, 2'-Me), 3.57 (1H, t(dd), $J_{3,4}=J_{4,5}=8$ Hz, 4-H), 3.72 (3H, s, COOMe), 4.08 (1H, dq, $J_{5,Me}=6$ Hz, $J_{4,5}=8$ Hz, 5-H), 5.86 (1H, d, $J_{2,3}=16$ Hz, 2-H), 6.64—6.68 (2H, m, 3'-H and 5'-H), 7.01 (1H, d, $J_{5',6'}=8$ Hz, 6'-H), 7.22 (1H, dd, $J_{3,4}=8$ Hz, $J_{2,3}=16$ Hz, 3-H). (±)-**14b**: pale yellow oil. 93% yield. CI-MS *m/z*: 335 ($M^+ + 1$), 275 ($M^+ + 1 -$ AcOH). IR: 1775, 1745, 1730, 1650 cm^{-1}. NMR δ: 1.13 (3H, d, $J_{5,Me}=6$ Hz, 5-Me), 2.05 (3H, s, 5-OAc), 2.28 (3H, s, 4'-OAc), 2.33 (3H, s, 2'-Me), 3.71 (3H, s, COOMe), 3.79 (1H, t(dd),

$J_{3,4}=J_{4,5}=9$ Hz, 4-H), 5.27 (1H, dq, $J_{5,Me}=6$ Hz, $J_{4,5}=9$ Hz, 5-H), 5.78 (1H, d, $J_{2,3}=16$ Hz, 2-H), 6.92—6.95 (2H, m, 3'-H and 5'-H), 7.06 (1H, dd, $J_{3,4}=8$ Hz, $J_{2,3}=16$ Hz, 3-H), 7.18 (1H, d, $J_{5',6'}=8$ Hz, 6'-H).

(±) Methyl (4,5)-*anti*-5-Hydroxy-4-(4'-methoxyphenyl)-(2*E*)-hexenoate (15a) and Its Acetate (±)-15b (±)-**15a**: pale yellow oil. 33% yield. *Anal.* HRMS Calcd for $C_{14}H_{18}O_4$ (M^+; *m/z*): 250.120. Found: 250.118. IR: 3560, 1715, 1640 cm^{-1}. NMR δ: 1.11 (3H, d, $J_{5,Me}=6$ Hz, 5-Me), 3.32 (1H, dd, $J_{3,4}=9$ Hz, $J_{4,5}=6$ Hz, 4-H), 3.72 (3H, s, COOMe), 3.79 (3H, s, 4'-OMe), 4.05 (1H, dq, $J_{5,Me}=6$ Hz, $J_{4,5}=6$ Hz, 5-H), 5.90 (1H, d, $J_{2,3}=16$ Hz, 2-H), 6.87, 7.11 (each 2H, d, $J=9$ Hz, aromatic H), 7.26 (1H, dd, $J_{3,4}=9$ Hz, $J_{2,3}=16$ Hz, 3-H). (±)-**15b**: pale yellow oil. 82% yield. *Anal.* HRMS Calcd for $C_{16}H_{20}O_5$ (M^+; *m/z*): 292.131. Found: 292.130. IR: 1740, 1725, 1650 cm^{-1}. NMR δ: 1.12 (3H, d, $J_{5,Me}=6$ Hz, 5-Me), 2.03 (3H, s, 5-OAc), 3.47 (1H, t (dd), $J_{3,4}=J_{4,5}=8$ Hz, 4-H), 3.71 (3H, s, COOMe), 3.79 (3H, s, 4'-OMe), 5.20 (1H, dq, $J_{5,Me}=6$ Hz, $J_{4,5}=8$ Hz, 5-H), 5.82 (1H, d, $J_{2,3}=16$ Hz, 2-H), 6.86, 7.10 (each 2H, d, $J=9$ Hz, aromatic H), 7.12 (1H, dd, $J_{3,4}=8$ Hz, $J_{2,3}=16$ Hz, 3-H).

(±) Methyl (4,5)-*anti*-5-Hydroxy-4-(2'-methoxy-5'-methylphenyl)-(2*E*)-hexenoate (16a) and Its Acetate (±)-16b (±)-**16a**: pale yellow oil. 15% yield, *Anal.* HRMS Calcd for $C_{15}H_{20}O_4$ (M^+; *m/z*): 264.136. Found: 264.132. IR: 3570, 1720, 1640 cm^{-1}. NMR δ: 1.10 (3H, d, $J_{5,Me}=6$ Hz, 5-Me), 2.17 (1H, br s, 5-OH), 2.27 (3H, s, 5'-Me), 3.71 (3H, s, COOMe), 3.74—3.79 (1H, m, 4-H), 3.79 (3H, s, 2'-OMe), 4.18 (1H, dq, $J_{5,Me}=6$ Hz, $J_{4,5}=6$ Hz, 5-H), 5.90 (1H, d, $J_{2,3}=16$ Hz, 2-H), 6.77 (1H, d, $J_{3',4'}=8$ Hz, 3'-H), 6.94 (1H, d, $J_{4',6'}=2$ Hz, 6'-H), 7.01 (1H, dd, $J_{3',4'}=8$ Hz, $J_{4',6'}=2$ Hz, 4'-H), 7.35 (1H, dd, $J_{3,4}=9$ Hz, $J_{2,3}=16$ Hz, 3-H). (±)-**16b**: pale yellow oil. 99% yield. *Anal.* HRMS Calcd for $C_{17}H_{22}O_5$ (M^+; *m/z*): 306.147. Found: 306.148. IR: 1740, 1725, 1650 cm^{-1}. NMR δ: 1.10 (3H, d, $J_{5,Me}=6$ Hz, 5-Me), 2.02 (3H, s, 5-OAc), 2.26 (3H, s, 5'-Me), 3.71 (3H, s, COOMe), 3.79 (3H, s, 2'-OMe), 3.94 (1H, t (dd), $J_{3,4}=J_{4,5}=9$ Hz, 4-H), 5.33 (1H, dq, $J_{5,Me}=6$ Hz, $J_{4,5}=9$ Hz, 5-H), 5.83 (1H, d, $J_{2,3}=16$ Hz, 2-H), 6.76 (1H, d, $J_{3',4'}=8$ Hz, 3'-H), 6.93 (1H, d, $J_{4',6'}=2$ Hz, 6'-H), 7.01 (1H, $J_{3',4'}=8$ Hz, $J_{4',6'}=2$ Hz, 4'-H), 7.18 (1H, dd, $J_{3,4}=9$ Hz, $J_{2,3}=16$ Hz, 3-H).

(±) Methyl (2,5)-*anti*-5-Hydroxy-2-(2'-methoxy-5'-methylphenyl)-(3*E*)-hexenoate (17a) and Its Acetate (±)-17b (±)-**17a**: pale yellow oil. 5% yield. *Anal.* HRMS Calcd for $C_{15}H_{20}O_4$ (M^+; *m/z*): 264.136. Found: 264.140. IR: 3600, 1725 cm^{-1}. NMR δ: 1.24 (3H, d, $J_{5,Me}=6$ Hz, 5-Me), 2.28 (3H, s, 5'-Me), 3.67 (3H, s, COOMe), 3.78 (3H, s, 2'-OMe), 4.28—4.35 (1H, m, 5-H), 4.57 (1H, d, $J_{2,3}=8$ Hz, 2-H), 5.61 (1H, dd, $J_{3,4}=16$ Hz, $J_{4,5}=6$ Hz, 4-H), 6.01 (1H, dd, $J_{2,3}=8$ Hz, $J_{3,4}=16$ Hz, 3-H), 6.77 (1H, d, $J_{3',4'}=9$ Hz, 3'-H), 7.00 (1H, d, $J_{4',6'}=2$ Hz, 6'-H), 7.04 (1H, dd, $J_{3',4'}=9$ Hz, $J_{4',6'}=2$ Hz, 4'-H). (±)-**17b**: pale yellow oil. 67% yield. *Anal.* HRMS Calcd for $C_{17}H_{22}O_5$ (M^+; *m/z*): 306.147. Found: 306.147. IR: 1735 cm^{-1}. NMR δ: 1.29 (3H, d, $J_{5,Me}=6$ Hz, 5-Me), 2.03 (3H, s, 5-OAc), 2.28 (3H, s, 5'-Me), 3.68 (3H, s, COOMe), 3.78 (3H, s, 2'-OMe), 4.57 (1H, d, $J_{2,3}=8$ Hz, 2-H), 5.37 (1H, dq, $J_{5,Me}=J_{4,5}=6$ Hz, 5-H), 5.54 (1H, dd, $J_{3,4}=16$ Hz, $J_{4,5}=6$ Hz, 4-H), 6.06 (1H, d, $J_{2,3}=8$ Hz, $J_{3,4}=16$ Hz, 3-H), 6.77 (1H, d, $J_{3',4'}=8$ Hz, 3'-H), 7.00 (1H, d, $J_{4',6'}=2$ Hz, 6'-H), 7.04 (1H, dd, $J_{3',4'}=8$ Hz, $J_{4',6'}=2$ Hz, 4'-H).

(±) Methyl (4,5)-*anti*-4-(2',5'-Dimethoxyphenyl)-5-hydroxy-(2*E*)-hexenoate (6a) and Its Acetate (±)-6b (±)-**6a**: pale yellow oil. 27% yield. *Anal.* HRMS Calcd for $C_{15}H_{20}O_5$ (M^+; *m/z*): 280.131. Found: 280.133. IR: 3580, 1720, 1640 cm^{-1}. NMR δ: 1.12 (3H, d, $J_{5,Me}=6$ Hz, 5-Me), 3.72 (3H, s, COOMe), 3.76, 3.78 (each 3H, s, 2'-OMe and 5'-OMe), 4.18 (1H, dq, $J_{5,Me}=6$ Hz, $J_{4,5}=6$ Hz, 5-H), 5.91 (1H, d, $J_{2,3}=16$ Hz, 2-H), 6.73—6.83 (3H, m, aromatic H), 7.32 (1H, dd, $J_{3,4}=9$ Hz, $J_{2,3}=16$ Hz, 3-H). (±)-**6b**: pale yellow oil. 68% yield. *Anal.* HRMS Calcd for $C_{17}H_{22}O_6$ (M^+; *m/z*): 322.142. Found: 322.140. IR: 1740, 1725, 1650 cm^{-1}. NMR δ: 1.12 (3H, d, $J_{5,Me}=6$ Hz, 5-Me), 2.03 (3H, s, 5-OAc), 3.76 (3H, s, COOMe), 3.77, 3.89 (each 3H, s, 2'-OMe and 5'-OMe), 3.92—3.97 (1H, m, 4-H), 5.32 (1H, dq, $J_{5,Me}=6$ Hz, $J_{4,5}=6$ Hz, 5-H), 5.84 (1H, d, $J_{2,3}=16$ Hz, 2-H), 6.71 (1H, d, $J_{4',6'}=3$ Hz, 6'-H), 6.75 (1H, dd, $J_{3',4'}=9$ Hz, $J_{4',6'}=3$ Hz, 4'-H), 6.80 (1H, d, $J_{3',4'}=9$ Hz, 3'-H), 7.18 (1H, dd, $J_{3,4}=8$ Hz, $J_{2,3}=16$ Hz, 3-H).

(±) Methyl (2,5)-*anti*-2-(2',5'-Dimethoxyphenyl)-5-hydroxy-(3*E*)-hexenoate (18a) and Its Acetate (±)-18b (±)-**18a**: pale yellow oil. 25% yield. *Anal.* Calcd for $C_{15}H_{20}O_5$ (M^+; *m/z*): 280.131. Found: 280.132. IR: 3590, 1730 cm^{-1}. NMR δ: 1.25 (3H, d, $J_{5,Me}=6$ Hz, 5-Me), 3.68 (3H, s, COOMe), 3.76, 3.77 (each 3H, s, 2'-OMe and 5'-OMe), 4.32 (1H, dq, $J_{5,Me}=6$ Hz, $J_{4,5}=6$ Hz, 5-H), 4.57 (1H, d, $J_{2,3}=8$ Hz, 2-H), 5.62 (1H, dd, $J_{4,5}=6$ Hz, $J_{3,4}=16$ Hz, 4-H), 6.00 (1H, dd, $J_{2,3}=8$ Hz, $J_{3,4}=16$ Hz, 3-H), 6.75—6.82 (3H, m, aromatic H). (±)-**18b**: pale yellow oil. 67% yield. *Anal.* HRMS Calcd for $C_{17}H_{22}O_6$ (M^+; *m/z*): 322.142. Found: 322.138. IR: 1720 cm^{-1}. NMR δ: 1.29 (3H, d, $J_{5,Me}=6$ Hz, 5-Me), 2.03 (3H, s, 5-OAc), 3.68 (3H, s, COOMe), 3.761, 3.764 (each 3H, s, 2'-OMe and 5'-OMe), 4.59 (1H, d, $J_{2,3}=8$ Hz, 2-H), 5.37 (1H, dq, $J_{5,Me}=6$ Hz, $J_{4,5}=6$Hz, 5-H). 5.56 (1H, dd, $J_{3,4}=16$ Hz, $J_{4,5}=6$ Hz, 4-H), 6.04 (1H, dd, $J_{2,3}=8$ Hz, $J_{3,4}=16$ Hz, 3-H), 6.77 (1H, dd, $J_{3',4'}=9$ Hz, $J_{4',6'}=3$ Hz, 4'-H), 6.80 (1H, d, $J_{4',6'}=3$ Hz, 6'-H), 6.81 (1H, d, $J_{3',4'}=9$ Hz, 3'-H).

(±) Methyl (4,5)-*anti*-4-(3',4'-Dimethoxyphenyl)-5-hydroxy-(2*E*)-hexenoate (21a) and Its Acetate (±)-21b (±)-**21a**: pale yellow oil. 77% yield. *Anal.* HRMS Calcd for $C_{15}H_{20}O_5$ (M^+; *m/z*): 280.131. Found: 280.132. IR: 3560, 1715, 1640 cm^{-1}. NMR δ: 1.13 (3H, d, $J_{5,Me}=6$ Hz, 5-Me), 3.30 (1H, dd, $J_{3,4}=8$ Hz, $J_{4,5}=6$ Hz, 4-H), 3.73 (3H, s, COOMe), 3.86, 3.88 (each 3H, s, 3'-OMe and 4'-OMe), 4.07 (1H, $J_{5,Me}=6$ Hz, $J_{4,5}=6$ Hz, 5-H), 5.92 (1H, d, $J_{2,3}=16$ Hz, 2-H), 6.71 (1H, d, $J_{2',6'}=2$ Hz, 2'-H), 6.75 (1H, dd, $J_{2',6'}=2$ Hz, $J_{5',6'}=8$ Hz, 6'-H), 6.84 (1H, d, $J_{5',6'}=8$ Hz, 5'-H), 7.27 (1H, dd, $J_{3,4}=8$ Hz, $J_{2,3}=16$ Hz, 3-H). (±)-**21b**: pale yellow oil. 97% yield. *Anal.* HRMS Calcd for $C_{17}H_{22}O_6$ (M^+; *m/z*): 322.142. Found: 322.141. IR: 1723 (sh), 1718, 1640 cm^{-1}. NMR δ: 1.13 (3H, d, $J_{5,Me}=6$ Hz, 5-Me), 2.04 (3H, s, 5-OAc), 3.45 (1H, t, $J_{3,4}=J_{4,5}=8$ Hz, 4-H), 3.72 (3H, s, COOMe), 3.86, 3.88 (each 3H, s, 3'-OMe and 4'-OMe), 5.21 (1H, dq, $J_{5,Me}=6$ Hz, $J_{4,5}=8$ Hz, 5-H), 5.84 (1H, d, $J_{2,3}=16$ Hz, 2-H), 6.68 (1H, d, $J_{2',6'}=2$ Hz, 2'-H), 6.75 (1H, dd, $J_{5',6'}=8$ Hz, $J_{2',6'}=2$ Hz, 6'-H), 6.83 (1H, d, $J_{5',6'}=8$ Hz, 5'-H), 7.12 (1H, dd, $J_{3,4}=8$ Hz, $J_{2,3}=16$ Hz, 3-H).

(±) Methyl (4,5)-anti-4-(2'-4'-Dimethoxyphenyl)-5-hydroxy-(2*E*)-hexenoate (22a) and Its Acetate (±)-22b (±)-**22a**: pale yellow oil. 75% yield. *Anal.* HRMS Calcd for $C_{15}H_{20}O_5$ (M^+; *m/z*): 280.131. Found: 280.130. IR: 3560, 1715, 1640 cm^{-1}. NMR δ: 1.10 (3H, d, $J_{5,Me}=6$ Hz, 5-Me), 1.89 (1H, d, $J_{5,OH}=4$ Hz, 5-OH), 3.70—3.71 (1H, m, 4-H), 3.71 (3H, s, COOMe), 3.78, 3.79 (each 3H, s, 2'-OMe and 4'-OMe), 4.16 (1H, dq, $J_{5,Me}=6$ Hz, $J_{4,5}=6$ Hz, 5-H), 5.89 (1H, d, $J_{2,3}=16$ Hz, 2-H), 6.45 (1H, dd, $J_{3',5'}=3$ Hz, $J_{5',6'}=9$ Hz, 5'-H), 6.46 (1H, d, $J_{3',5'}=3$ Hz, 3'-H), 7.04 (1H, d, $J_{5',6'}=9$ Hz, 6'-H), 7.32 (1H, dd, $J_{3,4}=9$ Hz, $J_{2,3}=16$ Hz, 3-H). (±)-**22b**: pale yellow oil. 89% yield. *Anal.* HRMS Calcd for $C_{17}H_{22}O_6$ (M^+; *m/z*): 322.142. Found: 322.142. IR: 1723 (sh), 1718, 1640 cm^{-1}. NMR δ: 1.10 (3H, d, $J_{5,Me}=6$ Hz, 5-Me), 2.01 (3H, s, 5-OAc), 3.70 (3H, s, COOMe), 3.79, 3.80 (each 3H, s, 2'-OMe and 4'-OMe), 3.88 (1H, t, $J_{3,4}=J_{4,5}=8$ Hz, 4-H), 5.30 (1H, dq, $J_{5,Me}=6$ Hz, $J_{4,5}=8$ Hz, 5-H), 5.81 (1H, d, $J_{2,3}=16$ Hz, 2-H), 6.42 —6.47 (2H, m, 3'-H and 5'-H), 7.03 (1H, d, $J_{5',6'}=9$ Hz, 6'-H), 7.17 (1H, dd, $J_{3,4}=8$ Hz, $J_{2,3}=16$ Hz, 3-H).

(±) Methyl (2,5)-*anti*-2-(2',4'-Dimethoxyphenyl)-5-hydroxy-(3*E*)-hexenoate (23a) and Its Acetate (±)-23b (±)-**23a**: pale yellow oil. 10% yield. *Anal.* HRMS $C_{15}H_{20}O_5$ (M^+; *m/z*): 280.131. Found: 280.133. IR: 3580, 1725 cm^{-1}. NMR δ: 1.25 (3H, d, $J_{5,Me}=6$ Hz, 5-Me), 3.67 (3H, s, COOMe), 3.79, 3.80 (each 3H, s, 2'-OMe and 4'-OMe), 4.32 (1H, dq, $J_{5,Me}=6$ Hz, $J_{4,5}=6$ Hz, 5-H), 4.53 (1H, d, $J_{2,3}=8$ Hz, 2-H), 5.59 (1H, dq, $J_{3,4}=16$ Hz, $J_{4,5}=6$ Hz, 4-H), 6.00 (1H, dd, $J_{2,3}=8$ Hz, $J_{3,4}=16$ Hz, 3-H), 6.45—6.48 (2H, m, 3'-H and 5'-H), 7.11 (1H, d, $J_{5',6'}=8$ Hz, 6'-H). (±)-**23b**: pale yellow oil. 84% yield. *Anal.* HRMS Calcd for $C_{17}H_{22}O_6$ (M^+; *m/z*): 322.142. Found: 322.146. IR: 1740 cm^{-1}. NMR δ: 1.28 (3H, d, $J_{5,Me}=6$ Hz, 5-Me), 2.03 (3H, s, 5-OAc), 3.67 (3H, s, COOMe), 3.78, 3.80 (each, 3H, s, 2'-OMe and 4'-OMe), 4.54 (1H, d, $J_{2,3}=8$ Hz, 2-H), 5.36 (1H, dq, $J_{5,Me}=J_{4,5}=6$ Hz, 5-H), 5.52 (1H, dd, $J_{4,5}=6$ Hz, $J_{3,4}=16$ Hz, 4-H), 6.04 (1H, dd, $J_{3,4}=16$ Hz, $J_{2,3}=8$ Hz, 3-H), 6.45 (1H, d, $J_{3',5'}=2$ Hz, 3'-H), 6.47 (1H, dd, $J_{3',5'}=2$ Hz, $J_{5',6'}=8$ Hz, 5'-H), 7.10 (1H, d, $J_{5',6'}=8$ Hz, 6'-H).

(±) Methyl (4,5)-*anti*-5-Hydroxy-4-(2',4',6'-trimethoxyphenyl)-(2*E*)-hexenoate (24a) and Its Acetate (±)-24b (±)-**24a**: pale yellow oil. 91% yield. *Anal.* HRMS Calcd for $C_{16}H_{22}O_6$ (M^+; *m/z*): 310.141. Found: 310.137. IR: 3580, 1720, 1640 cm^{-1}. NMR δ: 1.06 (3H, d, $J_{5,Me}=6$ Hz, 5-Me), 3.70 (3H, s, COOMe), 3.78 (6H, s, 2'-OMe and 6'-OMe), 3.80 (3H, s, 4'-OMe), 4.00 (1H, dd, $J_{3,4}=8$ Hz, $J_{4,5}=7$ Hz, 4-H), 4.37 (1H, dq, $J_{5,Me}=6$ Hz, $J_{4,5}=7$ Hz, 5-H), 5.83 (1H, d, $J_{2,3}=16$ Hz, 2-H), 6.12 (2H, s, 3'-H and 5'-H), 7.52 (1H, dd, $J_{2,3}=16$ Hz, $J_{3,4}=8$ Hz, 3-H). (±)-**24b**: pale yellow oil. 86% yield. *Anal.* HRMS Calcd for $C_{18}H_{24}O_7$ (M^+; *m/z*): 352.152. Found: 352.150. IR: 1730, 1650 cm^{-1}. NMR δ: 1.01 (3H, d, $J_{5,Me}=6$ Hz, 5-Me), 2.04 (3H, s, 5-OAc), 3.68 (3H, s, COOMe), 3.79 (6H, s, 2'-OMe and 6'-OMe), 3.80 (3H, s, 4'-OMe), 4.18 (1H, dd, $J_{3,4}=8$ Hz, $J_{4,5}=10$ Hz, 4-H), 5.57 (1H, dd, $J_{5,Me}=6$ Hz, $J_{4,5}=10$ Hz, 5-H), 5.74 (1H, d, $J_{2,3}=16$ Hz, 2-H), 6.11 (2H, s, 3'-H and 5'-H), 5.23 (1H, dd, $J_{2,3}=16$ Hz, $J_{3,4}=8$ Hz, 3-H).

(±) Methyl (4,5)-*anti*-5-Hydroxy-4-(2',4',5'-trimethoxyphenyl)-(2*E*)-hexenoate (25a) and Its Acetate (±)-25b (±)-**25a**: pale yellow oil. 89% yield. *Anal.* HRMS Calcd for $C_{16}H_{22}O_6$ (M^+; *m/z*): 310.141. Found: 310.145. IR: 3620, 1730, 1650 cm^{-1}. NMR δ: 1.12 (3H, d, $J_{5,Me}=6$ Hz, 5-Me), 3.72 (3H, s, COOMe), 3.80, 3.83, 3.88 (each 3H, s, 2'-OMe, 4'-OMe 5'-OMe), 4.16 (1H, dq, $J_{5,Me}=6$ Hz, 5-H), 5.90 (1H, d, $J_{2,3}=16$ Hz, 2-H), 6.53, 6.69 (each 1H, s, 3'-H or/and 6'-H), 7.31 (1H, dd, $J_{2,3}=16$ Hz,

$J_{3,4}=9$ Hz, 3-H). (±)-**25b**: pale yellow oil. 99% yield. *Anal.* HRMS Calcd for $C_{18}H_{24}O_7$ (M^+; *m/z*): 352.152. Found: 352.152. IR: 1740, 1730, 1650 cm^{-1}. NMR δ: 1.11 (3H, d, $J_{5,Me}=6$ Hz, 5-Me), 2.03 (3H, s, 5-OAc), 3.71 (3H, s, COOMe), 3.81, 3.82, 3.88 (each 3H, s, 2′-OMe, 4′-OMe and 5′-OMe), 5.28 (1H, dq, $J_{5,Me}=6$ Hz, $J_{4,5}=6$ Hz, 5-H), 5.83 (1H, d, $J_{2,3}=16$ Hz, 2-H), 6.52, 6.65 (each 1H, s, 3′-H or/and 6′-H), 7.16 (1H, dd, $J_{2,3}=16$ Hz, $J_{3,4}=9$ Hz, 3-H).

(±) Methyl (2,5)-*anti*-5-Hydroxy-2-(2′,4′,5′-trimethoxyphenyl)-(3*E*)-hexenoate (26a) and Its Acetate (±)-26b (±)-**26a**: pale yellow oil. 7% yield. *Anal.* HRMS Calcd for $C_{16}H_{22}O_6$ (M^+; *m/z*): 310.141. Found: 310.145. IR: 3620, 1740 cm^{-1}. NMR δ: 1.25 (3H, d, $J_{5,Me}=6$ Hz, 5-Me), 3.69 (3H, s, COOMe), 3.80, 3.83, 3.88 (each 3H, s, 2′-OMe, 4′-OMe and 5′-OMe), 4.32 (1H, dq, $J_{5,Me}=6$ Hz, $J_{4,5}=6$ Hz, 5-H), 4.59 (1H, d, $J_{2,3}=8$ Hz, 2-H), 5.60 (1H, dd, $J_{4,5}=6$ Hz, $J_{3,4}=16$ Hz, 4-H), 6.01 (1H, dd, $J_{2,3}=8$ Hz, $J_{3,4}=16$ Hz, 3-H), 6.53, 6.78 (each 1H, s, 3′-H or/and 6′-H). (±)-**26b**: pale yellow oil. 88% yield. *Anal.* HRMS Calcd for $C_{18}H_{24}O_7$ (M^+; *m/z*): 352.152. Found: 352.151. IR: 1740 cm^{-1}. NMR δ: 1.29 (3H, d, $J_{5,Me}=6$ Hz, 5-Me), 2.03 (3H, s, 5-OAc), 3.69 (3H, s, COOMe), 3.79, 3.83, 3.88 (each 3H, s, 2′-OMe, 4′-OMe, 5′-OMe), 4.59 (1H, d, $J_{2,3}=7$ Hz, 2-H), 5.37 (1H, dq, $J_{5,Me}=6$ Hz, $J_{4,5}=6$ Hz, 5-H), 5.53 (1H, dd, $J_{4,5}=6$ Hz, $J_{3,4}=16$ Hz, 4-H), 6.04 (1H, dd, $J_{3,4}=16$ Hz, $J_{2,3}=7$ Hz, 3-H), 6.53, 6.77 (each 1H, s, 3′-H or/and 6′-H).

(±) Methyl (4,5)-*anti*-5-Hydroxy-4-(2′,3′,4′-trimethoxyphenyl)-(2*E*)-hexenoate (27a) and Its Acetate (±)-27b (±)-**27a**: pale yellow oil. 7% yield. *Anal.* HRMS Calcd for $C_{16}H_{22}O_6$ (M^+; *m/z*): 310.141. Found: 310.139. IR: 3600, 1730, 1650 cm^{-1}. NMR δ: 1.12 (3H, d, $J_{5,Me}=6$ Hz, 5-Me), 3.71 (3H, s, COOMe), 3.84, 3.86, 3.88 (each 3H, s, 2′-OMe, 3′-OMe and 4′-OMe), 4.10 (1H, dq, $J_{5,Me}=6$ Hz, 5-H), 5.89 (1H, d, $J_{2,3}=16$ Hz, 2-H), 6.65, 6.84 (each 1H, d, $J_{5',6'}=9$ Hz, 5′-H or/and 6′-H), 7.30 (1H, dd, $J_{3,4}=9$ Hz, $J_{2,3}=16$ Hz, 3-H). (±)-**27b**: pale yellow oil. 99% yield. *Anal.* HRMS Calcd for $C_{18}H_{24}O_7$ (M^+; *m/z*): 352.152. Found: 352.155. IR: 1740, 1730, 1650 cm^{-1}. NMR δ: 1.12 (3H, d, $J_{5,Me}=6$ Hz, 5-Me), 2.04 (3H, s, 5-OAc), 3.71 (3H, s, COOMe), 3.84, 3.85, 3.88 (each 3H, s, 2′-OMe, 3′-OMe and 4′-OMe), 5.24 (1H, dq, $J_{5,Me}=6$ Hz, $J_{4,5}=8$ Hz, 5-H), 5.82 (1H, d, $J_{2,3}=16$ Hz, 2-H), 6.64, 6.83 (each 1H, d, $J_{5',6'}=9$ Hz, 5′-H or/and 6′-H), 7.14 (1H, dd, $J_{2,3}=16$ Hz, $J_{3,4}=8$ Hz, 3-H).

(±) Methyl (4,5)-*anti*-5-Hydroxy-4-(3′,4′,5′-trimethoxyphenyl)-(2*E*)-hexenoate (28a) and Its Acetate (±)-28b (±)-**28a**: pale yellow oil. 7% yield. *Anal.* HRMS Calcd for $C_{16}H_{22}O_6$ (M^+; *m/z*): 310.141. Found: 310.138. IR: 3600, 1730, 1650 cm^{-1}. NMR δ: 1.15 (3H, d, $J_{5,Me}=6$ Hz, 5-Me), 3.28 (1H, dd, $J_{3,4}=9$ Hz, $J_{4,5}=6$ Hz, 4-H), 3.74 (3H, s, COOMe), 3.83 (3H, s, 4′-OMe), 3.86 (6H, s, 3′-OMe and 5′-OMe), 4.07 (1H, dq. $J_{5,Me}=J_{4,5}=6$ Hz, 5-H), 5.94 (1H, d, $J_{2,3}=16$ Hz, 2-H), 6.41 (2H, s, 2′-H and 6′-H), 7.25 (1H, dd, $J_{2,3}=16$ Hz, $J_{3,4}=9$ Hz, 3-H). (±)-**28b**: pale yellow oil. 84% yield. *Anal.* HRMS Calcd for $C_{18}H_{24}O_7$ (M^+; *m/z*): 352.152. Found: 352.154. IR: 1740, 1730, 1650 cm^{-1}. NMR δ: 1.15 (3H, d, $J_{5,Me}=6$ Hz, 5-Me), 2.05 (3H, s, 5-OAc), 3.42 (1H, t(dd), $J_{3,4}=J_{4,5}=9$ Hz, 4-H), 3.73 (3H, s, COOMe), 3.83 (3H, s, 4′-OMe), 3.85 (6H, s, 3′-OMe and 5′-OMe). 5.22 (1H, dq, $J_{5,Me}=6$ Hz, $J_{4,5}=9$ Hz, 5-H), 5.85 (1H, d, $J_{2,3}=16$ Hz, 2-H), 6.39 (2H, s, 2′-H and 6′-H), 7.10 (1H, dd, $J_{2,3}=16$ Hz, $J_{3,4}=9$ Hz, 3-H).

Methylation of (±)-4a A mixture of (±)-**4a** (110 mg), Me_2SO_4 (2 ml) and K_2CO_3 (3 g) in acetone (20 ml) was refluxed for 1 h with stirring. The reaction mixture was filtered and the filtrate was evaporated. The residue was diluted with ether. The organic layer was washed with saturated brine and evaporated to give an oily product which was chromatographed on silica gel (40 g) to afford (±)-**6a** (77 mg, 67% yield). The spectral data of (±)-**6a** were identical with those the previously mentioned (±)-**6a**.

Methylation of (±)-5a A mixture of (±)-**5a** (126 mg), Me_2SO_4 (2 ml) and K_2CO_3 (3 g) in acetone (20 ml) was refluxed for 1 h with stirring. The reaction mixture was worked up by the same way as previously mentioned to provide (±)-**6a** (51 mg. 38% yield). The spectral data of (±)-**6a** were identical with those of authentic (±)-**6a**.

(±) (4,5)-*trans*-5-Methyl-4-(2′,5′-dimethoxyphenyl)-5-pentanolide (19) A solution of (±)-**6a** (270 mg) in a mixed solvent (EtOH 5 ml and AcOEt 5 ml) was subjected to hydrogenation in the presence of 20% $Pd(OH)_2$–C (40 mg). After hydrogen absorption ceased, the reaction mixture was filtered and the filtrate was evaporated. A solution of the crude product and camphor-sulfonic acid (CSA, 1 mg) in toluene (10 ml) was refluxed for 2 h with stirring. The reaction mixture was diluted with ether and the organic layer was washed with aqueous saturated $NaHCO_3$. Evaporation of the organic solvent gave an oily product, which was chromatograhed on silica gel (50 g) with 25% AcOEt in *n*-hexane to afford a colorless oil (±)-**19** (210 mg, 87% yield). (±)-**19**: *Anal.* HRMS Calcd for $C_{14}H_{18}O_4$ (M^+; *m/z*): 250.121. Found: 250.122. IR: 1740 cm^{-1}. NMR δ: 1.18 (3H, d, $J_{5,Me}=6$ Hz, 5-Me), 3.10 (1H, dt, $J_{4,5}=10$ Hz, 4-H), 3.77, 3.80 (each 3H, s, 2′-OMe and 5′-OMe), 4.69 (1H, dq, $J_{4,5}=10$ Hz, $J_{5,Me}=6$ Hz, 5-H), 6.70 (1H, d, $J_{4',6'}=3$ Hz, 6′-H), 6.77 (1H, dd, $J_{4',6'}=3$ Hz, $J_{3',4'}=9$ Hz, 4′-H), 6.84 (1H, d, $J_{3',4'}=9$ Hz, 3′-H).

(±) (2,5)-*trans*-5-Methyl-2-(2′,5′-dimethoxyphenyl)-5-pentanolide (20) A solution of (±)-**18a** (130 mg) in EtOH (10 ml) was subjected to hydrogenation in the presence of 10% Pd–C (50 mg). After hydrogen absorption ceased, the reaction mixture was filtered and the filtrate was evaporated. A solution of the crude product and CSA (2 mg) in toluene (10 ml) was refluxed for 30 min with stirring. The reaction mixture was worked up in the same way as described above to afford a colorless oil (±)-**20** (54 mg, 47% yield). (±)-**20**: *Anal.* HRMS Calcd for $C_{14}H_{18}O_4$ (M^+; *m/z*): 250.121. Found: 250.123. IR: 1740 cm^{-1}. NMR δ: 1.42 (3H, d, $J_{5,Me}=6$ Hz, 5-Me), 3.54 (1H, dd, $J_{2a,3a}=11$ Hz, $J_{2a,3e}=7$ Hz, 2-H), 4.60 (1H, dq, $J_{5,Me}=6$ Hz, $J_{5a,4a}=11$ Hz, $J_{5a,4e}=2$ Hz, 5-H), 3.75, 3.78 (each 3H, s, 2′-OMe and 5′-OMe), 6.75 (1H, dd, $J_{4',6'}=3$ Hz, $J_{3',4'}=8$ Hz, 4′-H), 6.78 (1H, d, $J_{4',6'}=3$ Hz, 6′-H), 6.83 (1H, d, $J_{3',4'}=8$ Hz, 3′-H), 1.60—2.12 (4H, m, 3-H_2 and 4-H_2).

(±) Methyl (4,5)-*anti*-5-Chloroacetoxy-4-(2′,4′,6′-trimethoxyphenyl)-(2*E*)-hexenoate (24c) A solution of (±)-**24a** (2.606 g) and chloroacetic anhydride (2.16 g) in pyridine (10 ml) was stirred for 3 h at 0 °C. The reaction mixture was diluted with water and extracted with AcOEt. The organic layer was washed with 10% aqueous HCl and aqueous saturated $NaHCO_3$. Evaporation of the organic solvent gave an oily product, which was chromatographed on silica gel (60 g) to afford (±)-**24c** as a pale yellow oil (3.15 g, 97% yield). (±)-**24c**: *Anal.* HRMS Calcd for $C_{18}H_{23}O_7Cl$ (M^+; *m/z*): 386.113. Found: 386.111. IR: 1755, 1720, 1645 cm^{-1}. NMR δ: 1.07 (3H, d, $J_{5,Me}=6$ Hz, 5-Me), 3.68 (3H, s, COOMe), 3.799 (6H, s, 2′-OMe and 6′-OMe), 3.803 (3H, s, 4′-OMe), 4.05 (2H, s, $OCOCH_2Cl$), 4.20—4.25 (1H, m, 4-H), 5.66 (1H, dq, $J_{5,Me}=6$ Hz, $J_{4,5}=6$ Hz, 5-H), 5.76 (1H, d, $J_{2,3}=16$ Hz, 2-H), 6.11 (2H, s, 3′-H and 5′-H), 7.21 (1H, dd, $J_{2,3}=16$ Hz, $J_{3,4}=8$ Hz, 3-H).

Synthesis of Authentic Samples of (4*S*,5*R*)-3a, (4*R*,5*R*)-21a, (4*R*,5*R*)-22a, (4*R*,5*R*)-6a and (4*R*,5*R*)-24a The authentic (4*R*,5*R*)-**2** (44% ee, $[\alpha]_D^{27}+4°$ ($c=1.5$, $CHCl_3$)[8]) was reacted with various nucleophiles to give the optically active authentic samples. (4*S*,5*R*)-**3a**; (20% yield, $[\alpha]_D^{25}+23.2°$ ($c=0.83$, $CHCl_3$), corresponds to 44% ee), (4*R*,5*R*)-**21a**; (81% yield, $[\alpha]_D^{22}-5.91°$ ($c=4.65$, $CHCl_3$), corresponds to 44% ee), (4*R*,5*R*)-**22a**; (76% yield, $[\alpha]_D^{24}+3.7°$ ($c=4.08$, $CHCl_3$), corresponds to 44% ee), (4*R*,5*R*)-**6a**; (27% yield, $[\alpha]_D^{23}-1.87°$ ($c=1.23$, $CHCl_3$), corresponds to 43% ee), (4*R*,5*R*)-**24a**; (97% yield, $[\alpha]_D^{26}+1.73°$ ($c=1.1$, $CHCl_3$), corresponds to 44% ee).

Preparation of the Authentic (+)-MTPA Esters (+)-MTPA esterification of the racemic alcohols ((±)-**3a**, (±)-**6a** and (±)-**24a**) and the optically active alcohols ((4*S*,5*R*)-**3a**, (4*R*,5*R*)-**6a** and (4*R*,5*R*)-**24a** was carried out by the reported procedure.[11] A mixture of (4*S*,5*R*)-**3a**-(+)-MTPA and (4*R*,5*S*)-**3a**-(+)-MTPA; NMR δ: 3.72, 3.73 (each 3H, s, COOMe), (4*S*,5*R*)-**3a**-(+)-MTPA; NMR δ: 3.73 (3H, s, COOMe). A mixture of (4*R*,5*R*)-**6a**-(+)-MTPA and (4*S*,5*S*)-**6a**-(+)-MTPA; NMR δ: 3.68, 3.70 (each 3H, s, COOMe), (4*R*,5*R*)-**6a**-(+)-MTPA; NMR δ: 3.70 (3H, s, COOMe). A mixture of (4*R*,5*R*)-**24a**-(+)-MTPA and (4*S*,5*S*)-**24a**-(+)-MTPA; NMR δ: 3.65, 3.68 (each 3H, s, COOMe), (4R,5R)-**24a**-(+)-MTPA; NMR δ: 3.68 (3H, s, COOMe).

HPLC Analysis of the Racemic Alcohols ((±)-21a and (±)-22a) and Acetates ((±)-21b and (±)-22b) by Using a Chiral Column A 1 : 1 mixture of two racemates ((±)-**21a** and (±)-**21b**) gave four well separated peaks ((±)-**21a**; 41.90 min and 45.79 min, (±)-**21b**, 13.42 min and 14.88 min) corresponding to each enantiomer under the following analytical conditions (eluent, *n*-hexane–EtOH–iso-PrOH (400 : 10 : 5); detection, UV at 280 nm; flow rate, 1 ml/min).

The assignment of these peaks was achieved by comparing them with those of the previously mentioned authentic samples ((4*R*,5*R*)-**21a** and (4*R*,5*R*)-**21b**[12]). Namely, the peak with shorter retention time ($t_R=$ 14.88 min) was found to correspond to that of the (4*R*,5*R*)-**21b** enantiomer and the peak with longer retention time ($t_R=45.79$ min) to that of the (4*R*,5*R*)-**21a** enantiomer. HPLC analysis of the 1 : 1 mixture of two racemates ((±)-**22a** and (±)-**22b**) was also carried out under the following analytical conditions (eluent, *n*-hexene–EtOH–iso-PrOH (400 : 15 : 15); detection, UV at 280 nm; flow rate, 1 ml/min).

t_R: (±)-**22b**, 7.14 min and 8.99 min; (4*R*,5*R*)-**22b**,[13] 7.14 min; (±)-**22a**, 14.02 min and 17.11 min; (4*R*,5*R*)-**22a**; 14.02 min.

General Procedure of Enantioselective Hydrolysis A mixture of substrate (*ca.* 100 mg) in 0.1 M phosphate buffer solution (pH 7.25, 20 ml) was shaken at 33 °C for 72—193 h. The reaction mixture was filtered with the aid of Celite and the filtrate was extracted with AcOEt.

Evaporation of the organic solvent gave an oily product which was subjected to silica gel (40 g) column chromatography. In case of the (+)-MTPA method, the resulting alcohol was converted to the corresponding (+)-MTPA ester and acetate was also converted to the corresponding (+)-MTPA ester after alkaline hydrolysis (K_2CO_3 in MeOH). NMR analysis of the resulting (+)-MTPA ester provided the data summarized in Tables III, IV, and V. In the case of the HPLC method, the resulting alcohol and acetate were directly analyzed and results are shown in Table IV. Chemical yields and $[\alpha]_D$ values of all reaction products were as follows: with lipase Amano M-10; ((4*S*,5*R*)-**3a**, 25% yield, 92% ee, $[\alpha]_D^{25}$ +48.3° (c=0.94, $CHCl_3$), ((4*R*,5*S*)-**3b**, 59% yield, 28% ee, $[\alpha]_D^{25}$ −20.14° (c=2.87, $CHCl_3$)), with lipase Amano A-6; ((4*R*,5*R*)-**21a**, 53.9% yield, 62% ee, $[\alpha]_D^{24}$ −8.23° (c=2.10, $CHCl_3$)), ((4*S*,5*S*)-**21b**, 30.8% yield, 99% ee, $[\alpha]_D^{24}$ +10.50° (c=1.77, $CHCl_3$)), with lipase "Nagase p; ((4*R*,5*R*)-**22a**, 14.1%, 87% ee, $[\alpha]_D^{24}$ +7.30° (c=1.15, $CHCl_3$)), (4*S*,5*S*)-**22b**, 83.5% yield, 12% ee, $[\alpha]_D^{24}$ −1.47° (c=4.09, $CHCl_3$), with lipase from wheat germ; ((4*R*,5*R*)-**6a**, 43% yield, 90% ee, $[\alpha]_D^{18}$ −3.55° (c=1.52, $CHCl_3$)), (4*S*,5*S*)-**6b**, 52% yield, 67% ee, $[\alpha]_D^{18}$ −4.88° (c=3.28, $CHCl_3$), with lipase Amano A-6; ((4*R*,5*R*)-**24a**, 30% yield, 85% ee, $[\alpha]_D^{27}$ +3.23° (c=1.3, $CHCl_3$)), ((4*S*,5*S*)-**24c**, 69% yield, 37% ee, $[\alpha]_D^{27}$ −0.6° (c=1.0, $CHCl_3$)).

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References and Notes

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