Total Synthesis of (±)-, (−)-, and (+)-Oudemansin X[1)]

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Three kinds of oudemansin X, (−)-1, (+)-1 and (±)-1, were totally synthesized. The key point in the present chiral synthesis was the enantioselective acetylation of the racemic alcohols, (±)-5 and (±)-8, using lipase in an organic solvent. The synthetic (−)-1 was found to exhibit strong antifungal activity against several molds and yeasts.

Key words oudemansin X; total synthesis; chiral synthesis; enantioselective acetylation; lipase; antifungal activity

(−)-Oudemansin X (**1**) was isolated from mycelial culture of *Oudemansiella radicata* by Steglich and his co-workers and exhibits strong antifungal activities.[2)] The total synthesis of (−)-**1** has already been achieved from an optically active cyclitol, L-quebrachitol.[3)] In the previously reported chiral syntheses of (−)-oudemansin A[4)] and (−)-oudemansin B,[5)] which are similar to (−)-**1**, synthetic chiral intermediates were obtained by the microbiological asymmetric reduction of α-methyl-β-keto ester or α-chloroacetoacetate.[6)] We describe here the synthesis of both enantiomers of **1**, as well as (±)-**1**, and the antifungal activities of these products against several microorganisms.

Total Synthesis of (±)-Oudemansin X (1) Reformatsky reaction of *p*-methoxycinnamaldehyde and methyl α-bromopropanoate gave the (±)-*syn*-α-methyl-β-hydroxy ester **2** (50% yield) and the (±)-*anti*-α-methyl-β-hydroxy ester **3** (42% yield). Oxidation of (±)-**3** with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) provided the (±)-β-keto ester **4** (92% yield), which was reduced with $Zn(BH_4)_2$ to give (±)-*syn*-**2** (14% yield) along with a small amount of (±)-*anti*-**3** (2% yield).[7)] As $Zn(BH_4)_2$ reduction of α-methyl-β-keto ester was reported to give predominantly the *syn*-α-methyl-β-hydroxy ester,[8)] the relative structure of the present (±)-**2** was assigned as *syn* and this was confirmed as described later in the text. Reduction of (±)-**2** with $LiBH_4$ provided the (±)-*syn* diol **5** in 96% yield. Monosilylation ((±)-**6**; 96% yield) of

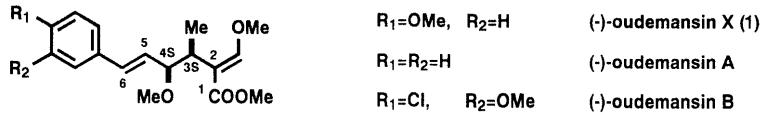

Chart 1

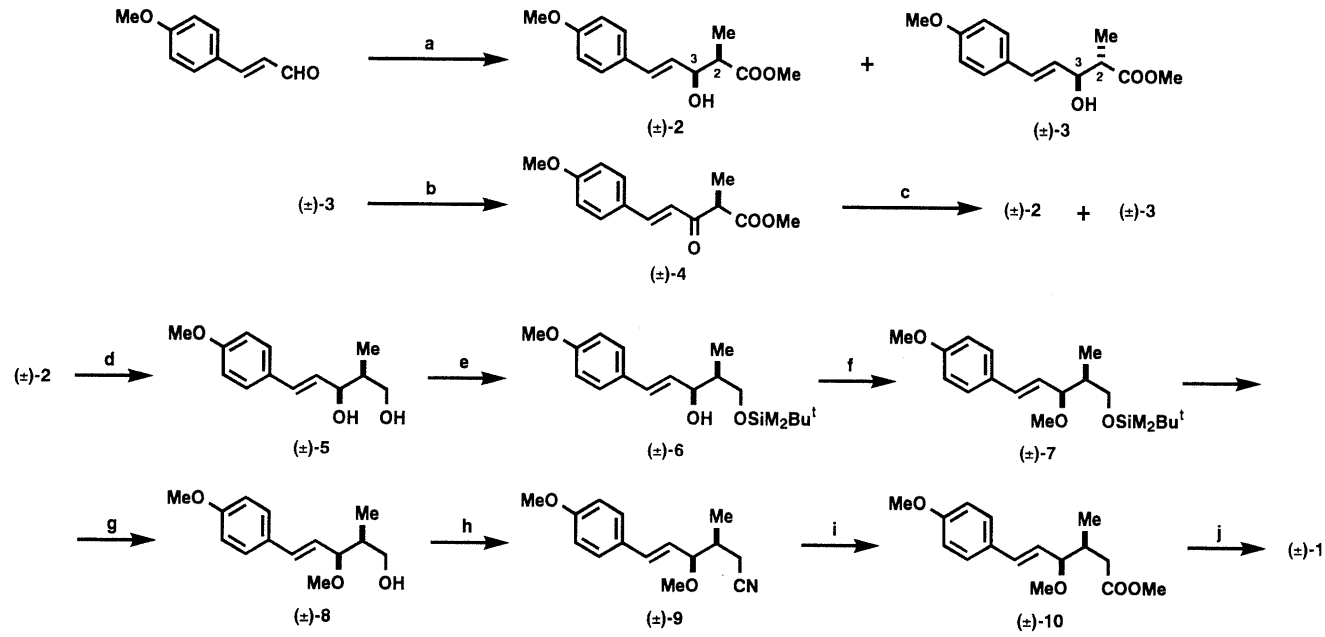

Chart 2

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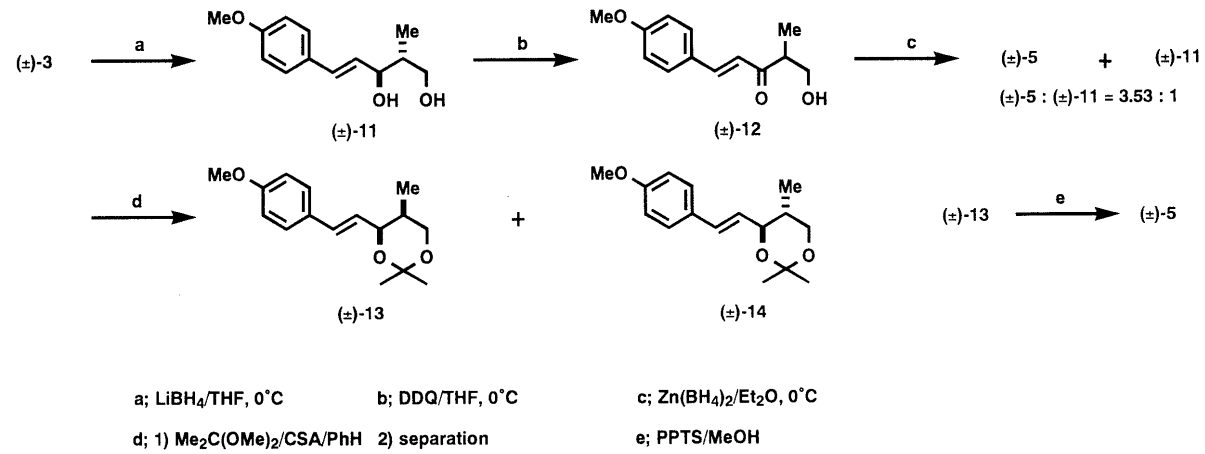


Chart 3

(±)-**5** followed by methylation ((±)-**7**; 95% yield) gave the (±)-3-methoxy silyl ether **7**, which was treated with tetrabutylammonium fluoride (TBAF) to give the (±)-3-methoxy alcohol **8** in 99% yield. Bromination of (±)-**8** followed by treatment with NaCN gave the (±)-4-methoxy nitrile **9** in 91% overall yield, and its spectral data (400 MHz nuclear magnetic resonance (NMR)) were identical with those reported for (3*S*,4*R*)-**9**.[3] Conversion of (±)-**9** into the methyl ester (±)-**10** was achieved by the standard procedure (three steps) in 87% overall yield. Formylation of (±)-**10** with lithium diisopropylamide (LDA) and methyl formate in tetrahydrofuran (THF) at −78 °C to 0 °C, followed by successive treatment with 10% aqueous NaOH, concentrated HCl, and CH_2N_2–MeOH produced (±)-oudemansin X (**1**) (25% overall yield) after purification by high-performance liquid chromatography (HPLC). The spectral data (400 MHz NMR) of the synthetic (±)-**1** were identical with those of synthetic natural (−)-oudemansin X (**1**).[2,3]

The (±)-**3** was successfully converted into the (±)-*syn* diol **5**. Reduction of (±)-**3** with $LiBH_4$ gave the (±)-*anti* diol **11** (96% yield), which was oxidized with DDQ to provide the (±)-*β*-keto alcohol **12** in 85% yield. Diastereoselective reduction of (±)-**12** using three kinds of reducing reagents was carried out and the results are shown in Table 1. The chemical yield was extremely high in every case and diastereoselectivity was found to be improved to 3.53 : 1 when $Zn(BH_4)_2$ was employed in Et_2O at 0 °C. In order to separate the diasteroisomers, a mixture of diols ((±)-**5** : (±)-**11** = 3.53 : 1) was treated with 2,2-dimethoxypropane in the presence of 10-camphorsulfonic acid (CSA) to give a mixture of acetonides, (±)-**13** and (±)-**14**, which were separated into (±)-*syn*-**13** (60% yield) and (±)-*anti*-**14** (17% yield). Removal of the acetal function of (±)-**13** thus obtained using pyridinium *p*-toluenesulfonate (PPTS) in MeOH afforded the (±)-*syn* diol **5** in 84% yield.

Preparation of Chiral Intermediates, (2*S*,3*S*)-*syn*-Diol 5 and (2*S*,3*S*)-*syn*-Alcohol 8 by Means of an Enzymatic Procedure The key point of the present chiral synthesis is the preparation of the optically active intermediates, *i.e.*, the (2*S*,3*S*)-*syn* diol **5** and the (2*S*,3*S*)-*syn* alcohol **8**. This was successfully achieved by carrying out an enantioselective monoacetylation of (±)-**5** and/or the (±)-alcohol **8** using lipase in organic solvent. In order to determine the optical purity of the enzymatic reaction products, two racemic monoacetates ((±)-**15** and (±)-**16**) were obtained by the acetylation of (±)-**5** and (±)-**8**, respectively. With the aid of HPLC analysis using a chiral column (Chiralcel OD, 4.6 × 250 mm), the two racemates ((±)-**5** and (±)-**15**) each gave two well separated peaks, and a 1:1 mixture of two racemates ((±)-**8** and (±)-**16**) afforded four well separated peaks. Details are given in the experimental section.

Table 1

Reducing reagent	Conditions	Yield (%)	Ratio (5 : 11)
Red-Al/toluene	0 °C, 10 min	99	1.75 : 1
DIBAL-H/CH_2Cl_2	−78 °C, 1 h	99	2 : 1
$Zn(BH_4)_2$/toluene–Et_2O (3 : 1)	0 °C, 1 h	99	3 : 1
$Zn(BH_4)_2$/Et_2O	0 °C, 1 h	99	3.53 : 1

i) Enantioselective Acetylation of (±)-**8** with Lipase: The alcohol (±)-**8** was subjected to enzymatic acetylation using various kinds of lipases and isopropenyl acetate as an acylating reagent, and selected data are shown in Table 2. In every case, the acetylated products had (2*R*,3*R*)-configuration and the unchanged alcohols had (2*S*,3*S*)-configuration. Determination of absolute structure of the acetate (2*R*,3*R*)-**16** will be described below. When the lipase "Nagase P" from *Pseudomonas* sp. was employed (entry 1), the acetate (2*R*,3*R*)-**16** ($[\alpha]_D$ −1.47°) was obtained with 74% ee.

ii) Enantioselective Monoacetylation of (±)-**5** with Lipase: The diol (±)-**5** was subjected to enzymatic monoacetylation using various kinds of lipases and isopropenyl acetate, and selected data are shown in Table 3. In every case, the monoacetylated products had (2*R*,3*R*)-configuration and the unchanged diols had (2*S*,3*S*)-configuration. When the lipase "Amano P" from *Pseudomonas* sp. was employed (entry 7), the unchanged diol (2*S*,3*S*)-**5** was obtained with 92% ee. Immobilized lipase "Amano P" was prepared by illumination of a mixture of a photo-crosslinkable resin prepolymer ENTP-4000,[9] a photo-sensitizer, benzoin ethyl ether, and the crude lipase "Amano P".[10] When (±)-**5** was subjected

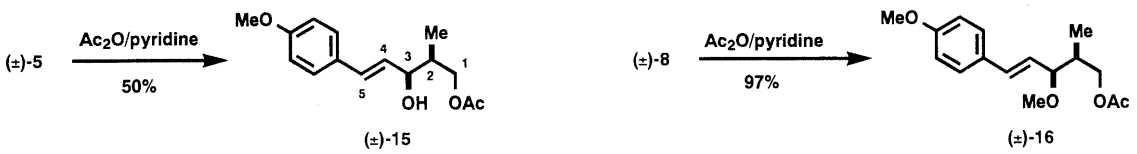
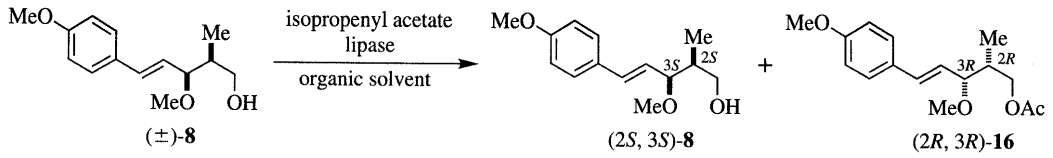


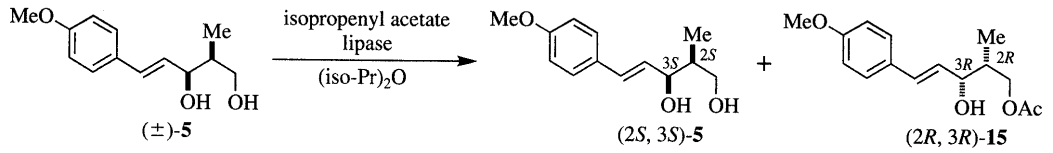
Chart 4

Table 2.



Entry	Substrate (mg)	Lipase	Solvent	Time (h)	Product (2S,3S)-8 %	(% ee)	(2R,3R)-16 %	(% ee)
1	208	Nagase P (*Pseudomonas* sp.)	Isooctane/(iso-Pr)$_2$O (40 ml/4 ml)	40	65	(15)	14	(74)
2	8.6	Nagase P (*Pseudomonas* sp.)	Isooctane (3 ml)	40	76	(15)	22	(53)
3	8.4	Amano M-10 (*Mucol javanicus*)	Isooctane (3 ml)	40	78	(15)	21	(53)
4	8.9	Amano P (*Pseudomonas* sp.)	Isooctane (3 ml)	16	31	(17)	47	(11)
5	8.9	AL (*Achromobactor* sp.)	Isooctane (3 ml)	16	28	(34)	69	(14)

Table 3.



Entry	Substrate (mg)	Lipase	Time (h)	Product (2S,3S)-5 %	(% ee)	(2R,3R)-15 %	(% ee)
1	100	Nagase P (*Pseudomonas* sp.)	72	57	(14)	35	(44)
2	100	B-4 (*Rhizopus japonicus*)	72	50	(29)	43	(49)
3	100	My-30 (*Candida cylindracea*)	8	39	(34)	27	(25)
4	100	PL-266 (*Alcaligenes* sp.)	8	30	(88)	42	(5)
5	100	AL (*Achromobactor* sp.)	8	54	(24)	41	(37)
6	100	Amano AY-30 (*Candida rugosa*)	9	57	(5)	14	(37)
7	100	Amano P (*Pseudomonas* sp.)	6	31	(92)	68	(43)
8	100	Immobilized lipase (Amano P)	16	27	(97)	66	(42)
9	100	Immobilized lipase (Amano P)	2	70	(23)	23	(94)
10	200	Immobilized lipase (Amano P)	3	74	(27)	23	(93)
11[a)]	300	Immobilized lipase (Amano P)	24	49	(88)	44	(41)

a) Optically active (2*S*,3*S*)-**5** (27% ee) was employed.

to enantioselective monoacetylation using the immobilized lipase for a long time (16 h, entry 8), (2*S*,3*S*)-**5** was obtained in 27% yield with 97% ee, while a short (2—3 h, entries 9 and 10) incubation gave of (2*R*,3*R*)-**15** in 23% yield with 93—94% ee. The recovered (2*S*,3*S*)-**5** having 27% enantiomeric excess was again subjected to the enzymatic reaction using the recovered immobilized lipase (entry 11) for 24 h to give (2*S*,3*S*)-**5** (49% yield, 88% ee) and (2*R*,3*R*)-**15** (44% yield, 41% ee). The key feature of the present kinetic resolution using immobilized lipase is that the desired stereostructure of the products was controlled by the selection of reaction time, and the immobilized biocatalyst could be repeatedly used. A single recrystallization of (2*S*,3*S*)-**5** (88% ee) gave optically pure (2*S*,3*S*)-**5** ($[\alpha]_D$ +17.6°; corresponding to 99% ee).

In order to confirm the absolute structure of the present (+)-**5**, (+)-**5** was successfully converted to the reported compound (3*S*,4*R*)-**9**[3,11] by using a procedure similar to that employed for the conversion of (±)-**5** into (±)-**9**. The spectral data ($[\alpha]_D$ −35.4° (c = 1.00, $CHCl_3$) and 400 MHz NMR) of the present 4-methoxy nitrile **9** were identical with those ($[\alpha]_D$ −35.5° (c = 0.30, $CHCl_3$)) of the reported (3*S*,4*R*)-**9**. Thus, the absolute structure of (+)-**5** was determined to be 2*S*, 3*S* and that of the monoacetate **15** was confirmed to be 2*R*, 3*R*. Next, the absolute structure of the unidentified (−)-3-methoxy acetate **16** was

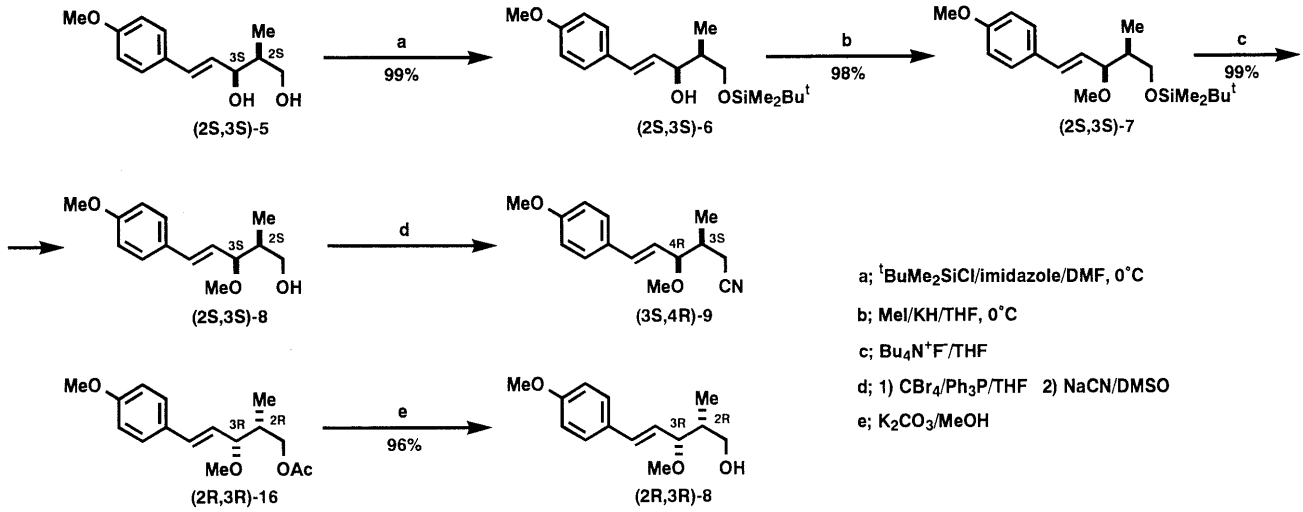


Chart 5

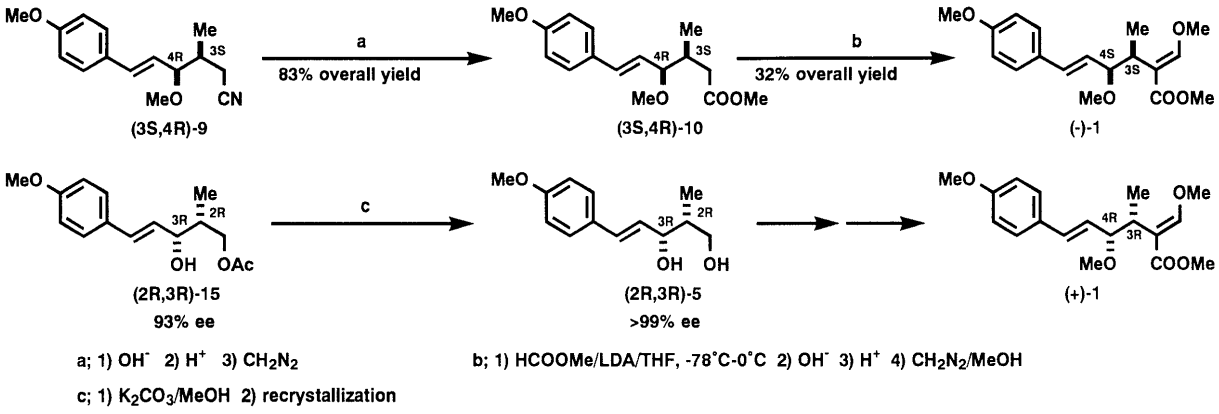


Chart 6

determined. Alkaline hydrolysis of (−)-**16** with K_2CO_3 in MeOH gave the (−)-3-methoxy alcohol **8** ($[\alpha]_D$ −30.2°; corresponding to 73% ee) whose sign of $[\alpha]_D$ was found to be opposite to that ($[\alpha]_D$ +43.2°; corresponding to 99% ee) of (2*S*,3*S*)-**8**. Thus, the absolute structure of (−)-**16** was determined to be 2*R*, 3*R* and that of the unchanged alcohol **8** was confirmed to be 2*S*, 3*S*.

Total Synthesis of (−)-Oudemansin X (1) and (+)-Oudemansin X (1) The optically pure (3*S*,4*R*)-**9** was converted to (−)-oudemansin X (**1**) ($[\alpha]_D$ −20° (*c*=1.0, EtOH)) in the same manner as described for the conversion of (±)-**9** into (±)-**1**. The spectral data (400 MHz NMR and $[\alpha]_D$) of the present synthetic (−)-**1** were identical with those ($[\alpha]_D$ −20° (*c*=0.16, EtOH)) of synthetic natural (−)-oudemansin X (**1**). On the other hand, the (2*R*,3*R*)-monoacetate **15** (93% ee) was hydrolyzed to give the (2*R*,3*R*)-diol **5**, which was recrystallized to afford optically pure (2*R*,3*R*)-**5**. Thus obtained (2*R*,3*R*)-**5** was converted to (+)-oudemansin X (**1**) ($[\alpha]_D$ +20.2° (*c*=0.75, EtOH)) in the same way as described for the conversion of (±)-**5** into (±)-**1**. The spectral data (400 MHz NMR) of the present synthetic (+)-**1** were identical with those of synthetic natural (−)-oudemansin X (**1**), except for the sign of $[\alpha]_D$.

Biological Activities of (−)-, (+)- and (±)-Oudemansin X (1) The biological activities of (−)-oudemansin X (**1**) were reported to resemble closely those of the other strobilurins and oudemansins.[12] The synthetic (−)-, (+)- and (±)-oudemansins X (**1**) do not exhibit antibacterial activities against *Arthrobacter* sp., *Acinetobacter calcoaceticus*, *Aeromonas hydrophila*, *Bacillus licheniformis*, *Bacillus subtilis*, *Brevibacterium ammoniagenes*, *Corynebacterium equi*, *Corynebacterium* sp., *Citrobacter diversus*, *Enterobacter cloacae*, *Escherichia coli*, *Erwinia carotovora*, *Pseudomonas aeruginosa*, *Pseudomonas diminuta*, *Microbacterium arborescens*, *Staphylococcus aureus*, *Staphylococcus aureus* (MRSA), *Streptomyces griseofuscus*, *Streptomyces albus*, and *Streptomyces coelicolor*. As shown in Table 4, (−)-**1**, (+)-**1** and (±)-**1** exhibit antifungal activities in the agar diffusion assay. Generally, the activity of the (−)-form (natural product) is stronger than that of the (±)-form, and the (+)-form is almost inactive.

Experimental

All melting points were measured on a Yanaco MP-S3 micro melting point apparatus and are uncorrected. IR spectra were measured on a Hitachi 260-30 infrared spectrometer or Shimadzu FT IR-8100 instrument. NMR spectra were measured on a JEOL EX 4000 instrument. Spectra were taken for 5—10% (w/v) solutions in $CDCl_3$ with Me_4Si as an internal reference (s; singlet, d; doublet, t; triplet, q; quartet, m; multiplet, br; broad). High-resolution mass spectra (HRMS) were obtained with a JEOL JMS-D 300 or JEOL JMS-DX 303 spectrometer. Optical rotations were measured on a JASCO DIP-370 digital polarimeter. The HPLC system was composed of two SSC instruments (ultraviolet (UV) detector 3000B and flow system 3100). All organic

Table 4. Antifungal Activity of Oudemansin X in the Agar Diffusion Assay

Microorganism		Diameter of inhibition zone (mm) μg/disc		
		0.1	1	10
Aspergillus awamori	(−)-**1**	+i	38i	45i
	(+)-**1**	—	—	—
	(±)-**1**	—	27i	39i
Aspergillus niger	(−)-**1**	33i	46i	55i
	(+)-**1**	—	—	—
	(±)-**1**	27i	40i	47i
Corticium rolfsii	(−)-**1**	14i	17i	30
	(+)-**1**	—	—	—
	(±)-**1**	13i	16i	17
Eupenicillium baarnense	(−)-**1**	+i	22i	30i
	(+)-**1**	—	—	—
	(±)-**1**	—	16i	24i
Mucor javanicus	(−)-**1**	+i	18i	24i
	(+)-**1**	—	—	11i
	(±)-**1**	+i	16i	24i
Paecilomyces merquandii	(−)-**1**	+i	24i	31i
	(+)-**1**	—	—	—
	(±)-**1**	—	19i	25i
Candida albicans	(−)-**1**	—	22i	32i
	(+)-**1**	—	—	—
	(±)-**1**	—	17i	28i
Candida tropicalis	(−)-**1**	—	17i	28i
	(+)-**1**	—	—	—
	(±)-**1**	—	12i	23i
Cryptococcus laurentii	(−)-**1**	—	11i	17i
	(+)-**1**	—	—	—
	(±)-**1**	—	10i	16i
Rhodotorula rubra	(−)-**1**	+i	25i	35i
	(+)-**1**	—	—	—
	(±)-**1**	—	12i	12
Saccharomyces uvarum	(−)-**1**	20i	41i	50i
	(+)-**1**	—	—	15i
	(±)-**1**	13i	36i	45i

—; no inhibition zone. i; inhibition incomplete.

solvent extracts were washed with saturated brine and dried over anhydrous magnesium sulfate ($MgSO_4$). All evaporations were performed under reduced pressure. For column chromatography, silica gel (Kieselgel 60) was employed.

(±)-Methyl (2,3-*syn*)-3-Hydroxy-5-(4-methoxyphenyl)-2-methyl-(4*E*)-pentenoate (2) and (±)-Methyl (2,3-*anti*)-3-Hydroxy-5-(4-methoxyphenyl)-2-methyl-(4*E*)-pentenoate (3) A mixture of *p*-methoxycinnamaldehyde (25.17 g), methyl α-bromopropanoate (29 g) and activated Zn dust (prepared from Zn 14 g) in dry benzene (200 ml) was refluxed for 1 h with stirring. The reaction mixture was diluted with H_2O and 10% aqueous HCl, and extracted with ether. The organic layer was washed with saturated aqueous $NaHCO_3$. Evaporation of the organic solvent provided a crude oily product, which was chromatographed on silica gel (400 g) to afford (±)-**2** from the *n*-hexane–ethyl acetate (9 : 1) eluate and (±)-**3** from the *n*-hexane–ethyl acetate (5 : 1) eluate. Both fractions were individually crystallized from *n*-hexane–ether to provide (±)-**2** (19.37 g, 50% yield) and (±)-**3** (16.36 g, 42% yield), each as colorless crystals. (±)-**2**: mp 80—82 °C. *Anal.* Calcd for $C_{14}H_{18}O_4$: C, 67.18, H, 7.25. Found: C, 66.99, H, 7.31. MS *m/z*: 250 (M^+). IR (Nujol): 3530, 1700, 1600 cm^{-1}. NMR δ: 1.23 (3H, d, *J*=6.8 Hz, 2-Me), 2.69—2.76 (2H, m, 3-OH and 2-H), 3.71 (3H, s, COOMe), 3.80 (3H, s, 4′-OMe), 4.54 (1H, br s, 3-H), 6.05 (1H, dd, *J*=15.6, 6.4 Hz, 4-H), 6.58 (1H, d, *J*=15.6 Hz, 5-H), 6.85 (2H, d, *J*=8.8 Hz, aromatic-H), 7.31 (2H, d, *J*=8.8 Hz, aromatic-H). (±)-**3**: mp 43—43.5 °C. *Anal.* HRMS Calcd for $C_{14}H_{18}O_4$ (M^+; *m/z*): 250.120. Found: 250.114. IR (Nujol): 3530, 1740, 1620 cm^{-1}. NMR δ: 1.20 (3H, d, *J*=7.3 Hz, 2-Me), 2.62—2.74 (2H, m, 3-OH and 2-H), 3.72 (3H, s, COOMe), 3.80 (3H, s, 4′-OMe), 4.32—4.38 (1H, m, 3-H), 6.03 (1H, dd, *J*=15.8, 7.2 Hz, 4-H), 6.57 (1H, d, *J*=15.8 Hz, 5-H), 6.85 (2H, d, *J*=8.8 Hz, aromatic-H), 7.32 (2H, d, *J*=8.8 Hz, aromatic-H).

Conversion of (±)-*anti* 3 into (±)-*syn* 2 A mixture of (±)-**3** (1.06 g) and DDQ (0.97 g) in ether (20 ml) was stirred for 30 min at room temperature. The reaction mixture was diluted with *n*-hexane and filtered. The filtrate was evaporated to give a residue, which was chromatographed on silica gel (50 g) to afford (±)-**4** as a pale yellow oil (0.97 g, 92% yield) from the *n*-hexane–ethyl acetate (9 : 1) eluate. A solution (20 ml) of $Zn(BH_4)_2$ in dry ether [prepared from a 0.9 M solution of $ZnCl_2$ in ether (80 ml) and $NaBH_4$ (4 g) in ether (300 ml)] was added to a solution of (±)-**4** (0.64 g) in dry ether (10 ml) under an argon atmosphere at 0 °C for 30 min. After the addition of 10% aqueous HCl, the whole was extracted with ether. The ether extract was washed with saturated aqueous $NaHCO_3$. Removal of the solvent gave a residue, which was chromatographed on silica gel (40 g) to provide (±)-**2** (90 mg, 14% yield) from the *n*-hexane–ethyl acetate (9 : 1) eluate and (±)-**3** (15 mg, 2% yield) from the *n*-hexane–ethyl acetate (5 : 1) eluate.

(±)-(2,3-*syn*)-5-(4-Methoxyphenyl)-2-methyl-(4*E*)-penten-1,3-diol (5) $LiBH_4$ (0.5 g) was added to a solution of (±)-**2** (2.06 g) in THF (30 ml) at 0 °C and the reaction mixture was stirred for 30 min at room temperature. The reaction mixture was diluted with H_2O and extracted with ether. Evaporation of the organic solvent gave crystals, which were recrystallized from *n*-hexane–ether to provide (±)-**5** as colorless prism (1.77 g, 96% yield). (±)-**5**: mp 72—74 °C. *Anal.* Calcd for $C_{13}H_{18}O_3 \cdot 1/2H_2O$: C, 67.51, H, 8.28. Found: C, 67.23, H, 8.24. MS *m/z*: 222 (M^+). IR (Nujol): 3200, 1600, 1500 cm^{-1}. NMR δ: 0.92 (3H, d, *J*=7.3 Hz, 2-Me), 1.84 (1H, s, OH), 1.99—2.09 (1H, m, 2-H), 2.76 (1H, d, *J*=3.9 Hz, OH), 3.65—3.77 (2H, m, 1-H_2), 3.80 (3H, s, 4′-OMe), 4.42—4.47 (1H, m, 3-H), 6.15 (1H, dd, *J*=15.6, 6.6 Hz, 4-H), 6.56 (1H, d, *J*=15.6 Hz, 5-H), 6.85 (2H, d, *J*=8.8 Hz, aromatic-H), 7.32 (2H, d, *J*=8.8 Hz, aromatic-H).

(±)-(2,3-*syn*)-1-*tert*-Butyldimethylsiloxy-3-hydroxy-5-(4-methoxyphenyl)-2-methyl-(4*E*)-pentene (6) *tert*-Butyldimethylsilylchloride (TBDMSCl; 2.33 g) in dimethylformamide (DMF, 10 ml) was added to a solution of (±)-**5** (3.26 g) and imidazole (1.10 g) in DMF (20 ml) over 20 min under ice-H_2O cooling with stirring. The reaction mixture was stirred for 2 h at the same temperature and diluted with benzene. The organic layer was washed with H_2O and saturated brine, and dried over $MgSO_4$. Evaporation of the organic solvent gave an oily product, which was chromatographed on silica gel (150 g) to afford (±)-**6** as a homogeneous oil (4.27 g, 86% yield) from the *n*-hexane–ethyl acetate (10 : 1) eluate. (±)-**6**: *Anal.* HRMS Calcd for $C_{19}H_{32}O_3Si$ (M^+; *m/z*): 336.212. Found: 336.207. IR (KBr): 3528, 1606, 1510 cm^{-1}. NMR δ: 0.08 (6H, s, $SiMe_2$), 0.92 (3H, d, *J*=6.8 Hz, 2-Me), 0.92 (9H, s, $SiBu^t$), 1.95—2.05 (1H, m, 2-H), 3.68 (1H, dd, *J*=9.8, 6.9 Hz, 1-H), 3.74 (1H, dd, *J*=9.8, 4.3 Hz, 1-H), 3.81 (3H, s, 4′-OMe), 4.43 (1H, br s, 3-H), 6.11 (1H, dd, *J*=15.9, 5.9 Hz, 4-H), 6.57 (1H, d, *J*=15.9 Hz, 5-H), 6.85 (2H, d, *J*=8.7 Hz, aromatic-H), 7.32 (2H, d, *J*=8.7 Hz, aromatic-H).

(±)-(2,3-*syn*)-1-*tert*-Butyldimethylsiloxy-3-methoxy-5-(4-methoxyphenyl)-2-methyl-(4*E*)-pentene (7) A suspension of KH (35% in mineral oil, 4.27 g) in THF (5 ml) was added to a solution of (±)-**6** (4.17 g) in THF (20 ml) under an argon atmosphere at 0 °C, and then a solution of MeI (7.93 g) in THF (5 ml) was added. The whole was stirred for 3 h at room temperature and diluted with ether. The organic layer was washed with H_2O and saturated brine, and dried over $MgSO_4$. Removal of the organic solvent gave an oily product, which was chromatographed on silica gel (150 g) to afford (±)-**7** as a homogeneous oil (4.20 g, 97% yield) from the *n*-hexane–ethyl acetate (20 : 1) eluate. (±)-**7**: *Anal.* HRMS Calcd for $C_{20}H_{34}O_3Si$ (M^+; *m/z*): 350.228. Found: 350.229. IR (KBr): 1606, 1510 cm^{-1}. NMR δ: 0.03 (3H, s, SiMe), 0.04 (3H, s, SiMe), 0.90 (9H, s, $SiBu^t$), 0.96 (3H, d, *J*=6.8 Hz, 2-Me), 1.75—1.85 (1H, m, 2-H), 3.29 (3H, s, 3-OMe), 3.48 (1H, dd, *J*=9.7, 5.8 Hz, 1-H), 3.62 (1H, dd, *J*=9.7, 6.2 Hz, 1-H), 3.74 (1H, dd, *J*=7.9, 5.4 Hz, 3-H), 3.81 (3H, s, 4′-OMe), 5.96 (1H, dd, *J*=15.9, 7.9 Hz, 4-H), 6.46 (1H, d, *J*=15.9 Hz, 5-H), 6.86 (2H, d, *J*=8.7 Hz, aromatic-H), 7.33 (2H, d, *J*=8.7 Hz, aromatic-H).

(±)-(2,3-*syn*)-3-Methoxy-5-(4-methoxyphenyl)-2-methyl-(4*E*)-penten-1-ol (8) Tetrabutylammonium fluoride (TBAF, 5.54 g) was added to a solution of (±)-**7** (4.10 g) in THF (40 ml) with stirring at room temperature and the reaction mixture was stirred for 4 h at the same temperature, then diluted with ether. The organic layer was washed with H_2O and saturated brine, and dried over $MgSO_4$. Evaporation of the organic solvent gave an oily product, which was chromatographed on silica gel (150 g) to provide (±)-**8** as a colorless semicrystalline compound (2.74 g, 99% yield) from the *n*-hexane–ethyl acetate (2 : 1) eluate. (±)-**8**:

mp 28—30 °C. *Anal.* HRMS Calcd for $C_{14}H_{20}O_3$ (M^+; *m/z*): 236.141. Found: 236.142. IR (KBr): 3380, 1606, 1510 cm^{-1}. NMR (DMSO-d_6) δ: 0.89 (3H, d, J=6.9 Hz, 2-Me), 1.60—1.73 (1H, m, 2-H), 3.20 (3H, s, 3-OMe), 3.24 (1H, ddd, J=10.7, 6.6, 5.3 Hz, 1-H), 3.46 (1H, ddd, J=10.7, 5.6, 5.3 Hz, 1-H), 3.69 (1H, dd, J=7.9, 4.9 Hz, 3-H), 3.75 (3H, s, 4'-OMe), 6.00 (1H, dd, J=16, 7.9 Hz, 4-H), 6.47 (1H, d, J=16 Hz, 5-H), 6.90 (2H, d, J=8.7 Hz, aromatic-H), 7.40 (2H, d, J=8.7 Hz, aromatic-H).

(±)-(3,4-*syn*)-4-Methoxy-6-(4-methoxyphenyl)-3-methyl-(5*E*)-hexenenitrile (9) Triphenylphosphine (Ph_3P, 981 mg) was added to a solution of carbon tetrabromide (CBr_4, 1.24 g) in THF (5 ml) under an argon atmosphere at 0 °C with stirring for 10 min, and then (±)-**8** (441 mg) was added. The reaction mixture was stirred for 10 min at 0 °C and for 40 min at room temperature, then dimethylsulfoxide (DMSO, 20 ml) and NaCN (1 g) were added at room temperature with stirring and the resulting mixture was stirred for 1 h at 60 °C. It was diluted with benzene and the organic layer was washed with H_2O and saturated brine, and dried over $MgSO_4$. Evaporation of the organic solvent gave an oily product, which was chromatographed on silica gel (100 g) to afford (±)-**9** as a pale yellow oil (417 mg, 91% yield) from the *n*-hexane–ethyl acetate (9:1) eluate. (±)-**9**: *Anal.* HRMS Calcd for $C_{15}H_{19}NO_2$ (M^+; *m/z*): 245.142. Found: 245.141. IR (KBr): 2245, 1607, 1512 cm^{-1}. NMR δ: 1.13 (3H, d, J=6.8 Hz, 3-Me), 2.06—2.15 (1H, m, 3-H), 2.28 (1H, dd, J=16.7, 7.6 Hz, 2-H), 2.51 (1H, dd, J=16.7, 5.8 Hz, 2-H), 3.31 (3H, s, 4-OMe), 3.66 (1H, dd, J=8, 5.5 Hz, 4-H), 3.81 (3H, s, 4'-OMe), 5.86 (1H, dd, J=16, 8 Hz, 5-H), 6.55 (1H, d, J=16 Hz, 6-H), 6.87 (2H, d, J=8.7 Hz, aromatic-H), 7.34 (2H, d, J=8.7 Hz, aromatic-H).

(±)-Methyl (3,4-*syn*)-4-Methoxy-6-(4-methoxyphenyl)-3-methyl-(5*E*)-hexenoate (10) A mixture of (±)-**9** (417 mg), NaOH (4 g), H_2O (4 ml), and ethanol (10 ml) was refluxed with stirring for 3 h. The reaction mixture was diluted with H_2O, acidified with aqueous 2 N HCl and extracted with CH_2Cl_2. The CH_2Cl_2 layer was evaporated to provide the crude acid (408 mg, 91% yield). A part of the crude acid (364 mg) in ether (20 ml) was treated with an excess of CH_2N_2–ether solution to afford the corresponding methyl ester, which was chromatographed on silica gel (80 g) to afford (±)-**10** as a colorless oil (369 mg, 96% yield) from the *n*-hexane–ethyl acetate (5:1) eluate. (±)-**10**: *Anal.* HRMS Calcd for $C_{16}H_{22}O_4$ (M^+; *m/z*): 278.151. Found: 278.148. IR (KBr): 1734, 1607 cm^{-1}. NMR δ: 1.00 (3H, d, J=6.8 Hz, 3-Me), 2.14 (1H, dd, J=15.1, 8.4 Hz, 2-H), 2.24—2.30 (1H, m, 3-H), 2.53 (1H, dd, J=15.1, 5.4 Hz, 2-H), 3.29 (3H, s, 4-OMe), 3.55 (1H, dd, J=8, 5.5 Hz, 4-H), 3.63 (3H, s, COOMe), 3.81 (3H, s, 4'-OMe), 5.90 (1H, dd, J=16, 8 Hz, 5-H), 6.48 (1H, d, J=16 Hz, 6-H), 6.86 (2H, d, J=8.7 Hz, aromatic-H), 7.33 (2H, d, J=8.7 Hz, aromatic-H).

(±)-Oudemansin X (1) *n*-Butyllithium (1.6 M in hexane, 1.6 ml) was added to a stirred solution of diisopropylamine (0.356 ml) in THF (3 ml) at −78 °C under an argon atmosphere and the mixture was stirred for 30 min at the same temperature. A solution of (±)-**10** (353 mg) in THF (5 ml) was added to the resulting LDA–THF solution at −78 °C. The reaction mixture was stirred for 30 min, then methyl formate (0.313 ml) was added and the whole was stirred for 10 min at −78 °C and then for 1 h at 0 °C. It was diluted with H_2O (2 ml) and 10% aqueous NaOH and extracted with ether (20 ml). The ether layer was washed with H_2O and saturated brine, and dried over $MgSO_4$. Evaporation of the ether gave the recovered starting material, (±)-**10** (52 mg). The alkaline layer was acidified with concentrated HCl and extracted with ether. The ether layer was washed with saturated brine, dried over $MgSO_4$ and evaporated to give an oily product (354 mg). A solution of the oily compound in MeOH (50 ml) was treated with an excess of CH_2N_2–ether solution and the mixture was stirred for 30 min. Removal of the solvent gave an oily product, which was chromatographed on silica gel (100 g) to afford the recovered (±)-**10** (49 mg) and crude (±)-**1** as a colorless oil in that order from the *n*-hexane–ethyl acetate (1000:75) eluate. The crude (±)-**1** was subjected to preparative HPLC (column, Spherisorb ODS-2 (30 × 250 mm): eluent, CH_3CN:MeOH=7:3; detection, UV at 254 nm; flow rate, 5 ml/min) to provide a homogeneous oil (±)-**1** (101 mg, 25% overall yield from (±)-**10**). (±)-**1**: *Anal.* HRMS Calcd for $C_{18}H_{24}O_5$ (M^+; *m/z*): 320.162. Found: 320.161. IR (KBr): 1698, 1632, 1607 cm^{-1}. NMR (CD_3OD) δ: 1.23 (3H, d, J=6.7 Hz, 3-Me), 2.94 (1H, dq, J=9.7, 6.9 Hz, 3-H), 3.28 (3H, s, OMe), 3.61 (3H, s, COOMe), 3.77 (3H, s, OMe), 3.80 (3H, s, OMe), 3.92 (1H, dd, J=9.7, 8.7 Hz, 4-H), 5.70 (1H, dd, J=15.9, 8.7 Hz, 5-H), 6.35 (1H, d, J=15.9 Hz, 6-H), 6.84 (2H, d, J=8.8 Hz, aromatic-H), 7.24 (2H, d, J=8.8 Hz, aromatic-H), 7.28 (1H, s, C=CH(OMe)).

(±)-(2,3-*anti*)-5-(4-Methoxyphenyl)-2-methyl-(4*E*)-pentene-1,3-diol (11) $LiBH_4$ (0.735 g) was added to a solution of (±)-**3** (3.37 g) in THF (30 ml) at 0 °C and the reaction mixture was stirred for 15 min at room temperature, then worked up in the same way as in the case of the $LiBH_4$ reduction of (±)-**2** to provide (±)-**11** as colorless crystals (2.865 g, 96% yield). (±)-**11**: mp 51—52 °C. MS *m/z*: 222 (M^+). IR (KBr): 3330 cm^{-1}. NMR δ: 0.89 (3H, d, J=7 Hz, 2-Me), 1.86—1.94 (1H, m, 2-H), 2.50 (1H, br s, OH), 2.67 (1H, br s, OH), 3.69 (1H, dd, J=11, 7.5 Hz, 1-H), 3.78 (1H, dd, J=11, 3.7 Hz, 1-H), 3.81 (3H, s, 4'-OMe), 4.18 (1H, t, J=7.5 Hz, 3-H), 6.10 (1H, dd, J=15.8, 7.5 Hz, 4-H), 6.54 (1H, d, J=15.8 Hz, 5-H), 6.86 (2H, d, J=8.8 Hz, aromatic-H), 7.32 (2H, d, J=8.8 Hz, aromatic-H).

(±)-5-(4-Methoxyphenyl)-2-methyl-3-oxo-(4*E*)-penten-1-ol (12) A mixture of (±)-**11** (2.86 g) and DDQ (3.22 g) in THF (30 ml) was stirred for 15 min at room temperature, then diluted with *n*-hexane and filtered. The filtrate was chromatographed on silica gel (100 g) to afford (±)-**12** as a pale yellow oil (2.41 g, 85% yield) from the *n*-hexane–ethyl acetate (2:1) eluate. (±)-**12**: MS *m/z*: 220 (M^+). IR (KBr): 3420, 1684, 1649 cm^{-1}. NMR δ: 1.21 (3H, d, J=7.2 Hz, 2-Me), 2.40 (1H, br s, 1-OH), 3.03—3.12 (1H, m, 2-H), 3.74 (1H, dd, J=11.1, 4.4 Hz, 1-H), 3.83 (1H, dd, J=11.1, 7.1 Hz, 1-H), 3.84 (3H, s, 4'-OMe), 6.70 (1H, d, J=16 Hz, 4-H), 6.91 (2H, d, J=8.8 Hz, aromatic-H), 7.51 (2H, d, J=8.8 Hz, aromatic-H), 7.60 (1H, d, J=16 Hz, 5-H).

Reduction of (±)-12 1) Red-Al (3.4 M in toluene, 0.104 ml) was added to a solution of (±)-**12** (71 mg) in toluene (2 ml) under an argon atmosphere at 0 °C, and the reaction mixture was stirred for 10 min. After the addition of saturated aqueous NH_4Cl, the whole was extracted with ether. The ether extract was washed with saturated aqueous $NaHCO_3$ and saturated brine and then dried over $MgSO_4$. Removal of the solvent gave 71 mg of a homogeneous oil. The *syn*/*anti* ratio was found to be 1.75:1 by NMR analysis. 2) DIBAL (1.5 M in toluene, 0.5 ml) was added to a solution of (±)-**12** (47 mg) in CH_2Cl_2 (5 ml) under an argon atmosphere at −78 °C, and the reaction mixture was stirred for 60 min. The reaction mixture was worked up in the same way as in the case of 1) to give 47 mg of a homogeneous oil. The *syn*/*anti* ratio was found to be 2:1 by NMR analysis. 3) A solution (1 ml) of $Zn(BH_4)_2$ in dry ether was added to a solution of (±)-**12** (20 mg) in toluene (3 ml) under an argon atmosphere at 0 °C, and the reaction mixture was stirred for 60 min. The reaction mixture was worked up in the same way as in the case of 1) to give 20 mg of a homogeneous oil. The *syn*/*anti* ratio was found to be 3:1 by NMR analysis. 4) A solution (12 ml) of $Zn(BH_4)_2$ in dry ether was added to a solution of (±)-**12** (0.653 g) in ether (10 ml) under an argon atmosphere at 0 °C, and the reaction mixture was stirred for 60 min, then worked up in the same way as in the case of 1) to give 660 mg of a homogeneous oil. The *syn*/*anti* ratio was found to be 3.53:1 by NMR analysis.

(±)-(2,3-*syn*)-1,3-(Isopropylidenedioxy)-5-(4-methoxyphenyl)-2-methyl-(4*E*)-pentene (13) and (±) (2,3-*anti*)-1,3-(Isopropylidenedioxy)-5-(4-methoxyphenyl)-2-methyl-(4*E*)-pentene (14) A solution of the 1,3-diol mixture ((±)-**5**:(±)-**11**=3.53:1, 660 mg), 2,2-dimethoxypropane (2 g) and CSA (0.5 mg) in benzene (25 ml) was stirred for 30 min under an argon atmosphere. The reaction mixture was diluted with benzene and was washed with saturated aqueous $NaHCO_3$. The organic layer was evaporated to give an oily product, which was chromatographed on silica gel (80 g) to provide (±)-*syn*-**13** (465 mg, 60% yield) and (±)-*anti*-**14** (131 mg, 17% yield), each as a homogeneous oil, in that order from the *n*-hexane–ether (20:1) eluate. (±)-**13**: mp 55—56 °C. MS *m/z*: 262 (M^+). IR (KBr): 1605, 1510 cm^{-1}. NMR δ: 1.13 (3H, d, J=6.9 Hz, 2-Me), 1.47, 1.51 (each 3H, s, MeCMe), 1.56—1.64 (1H, m, 2-H), 3.64 (1H, dd, J=11.5, 1.6 Hz, 1-H), 3.80 (3H, s, 4'-OMe), 4.19 (1H, dd, J=11.5, 2.8 Hz, 1-H), 4.67 (1H, dd, J=6, 2.6 Hz, 3-H), 6.03 (1H, dd, J=16, 6 Hz, 4-H), 6.53 (1H, d, J=16 Hz, 5-H), 6.84 (2H, d, J=8.8 Hz, aromatic-H), 7.32 (2H, d, J=8.8 Hz, aromatic-H). (±)-**14**: mp 52.5—53.5 °C. MS *m/z*: 262 (M^+). IR (KBr): 1607, 1512 cm^{-1}. NMR δ: 0.76 (3H, d, J=6.7 Hz, 2-Me), 1.45, 1.52 (each 3H, s, MeCMe), 1.73—1.85 (1H, m, 2-H), 3.60 (1H, t, J=11.5 Hz, 1-H), 3.78 (1H, dd, J=11.5, 5.2 Hz, 1-H), 3.80 (3H, s, 4'-OMe), 4.05 (1H, dd, J=10.1, 7.6 Hz, 3-H), 5.98 (1H, dd, J=15.8, 7.6 Hz, 4-H), 6.55 (1H, d, J=15.8 Hz, 5-H), 6.84 (2H, d, J=8.7 Hz, aromatic-H), 7.32 (2H, d, J=8.7 Hz, aromatic-H).

Conversion of (±)-*syn*-13 to (±)-*syn*-5 A solution of (±)-**13** (104 mg) and PPTS (5 mg) in MeOH (10 ml) was stirred for 40 min at room temperature, then diluted with ether and washed with saturated aqueous $NaHCO_3$. The organic layer was evaporated to give an oily compound, which was chromatographed on silica gel (50 g) to provide (±)-**5** (73 mg,

84% yield) from the *n*-hexane–ethyl acetate (1 : 1) eluate.

(±)-(2,3-*syn*)-1-Acetoxy-3-hydroxy-5-(4-methoxyphenyl)-2-methyl-(4*E*)-pentene (15) A solution of (±)-**5** (256 mg), Ac_2O (115 mg) and pyridine (102 mg) in CH_2Cl_2 was stirred for 4 h at room temperature. The reaction mixture was diluted with H_2O and extracted with ether. The organic layer was evaporated to give an oily product, which was chromatographed on silica gel (10 g) to afford (±)-**15** as a homogeneous oil (154 mg, 50% yield) from the *n*-hexane–ethyl acetate (5 : 1) eluate. (±)-**15**: *Anal.* HRMS Calcd for $C_{15}H_{20}O_4$ (M^+; *m/z*): 264.136. Found: 264.133. IR (Nujol): 1710, 1600 cm^{-1}. NMR (CD_3OD) δ: 1.00 (3H, d, J=7.3 Hz, 2-Me), 2.02 (3H, s, 1-OAc), 3.78 (3H, s, 4′-OMe), 3.96 (1H, dd, J=10.7, 6.4 Hz, 1-H), 4.14 (1H, dd, J=10.7, 6.4 Hz, 1-H), 4.18—4.22 (1H, m, 3-H), 6.10 (1H, dd, J=16.1, 6.8 Hz, 4-H), 6.52 (1H, d, J=16.1 Hz, 5-H), 6.86 (2H, d, J=8.8 Hz, aromatic-H), 7.33 (2H, d, J=8.8 Hz, aromatic-H).

(±)-(2,3-*syn*)-1-Acetoxy-3-methoxy-5-(4-methoxyphenyl)-2-methyl-(4*E*)-pentene (16) A solution of (±)-**8** (17 mg), Ac_2O (16 mg) and pyridine (1 ml) was stirred for 3 h at room temperature. The reaction mixture was diluted with H_2O and extracted with ether. The organic layer was evaporated to give an oily product, which was chromatographed on silica gel (5 g) to afford (±)-**16** as a homogeneous oil (16 mg, 96% yield) from the *n*-hexane–ethyl acetate (9 : 1) eluate. (±)-**16**: *Anal.* HRMS Calcd for $C_{16}H_{22}O_4$ (M^+; *m/z*): 278.151. Found: 278.149. IR (neat): 1725, 1600 cm^{-1}. NMR δ: 0.93 (3H, d, J=6.8 Hz, 2-Me), 1.97 (3H, s, 1-OAc), 3.22 (3H, s, 3-OMe), 3.57 (1H, dd, J=8.0, 5.4 Hz, 3-H), 3.74 (3H, s, 4′-OMe), 3.88 (1H, dd, J=10.7, 6.8 Hz, 1-H), 4.09 (1H, dd, J=10.7, 5.9 Hz, 1-H), 5.86 (1H, dd, J=16.1, 8.0 Hz, 4-H), 6.41 (1H, d, J=16.1 Hz, 5-H), 6.79 (2H, d, J=8.8 Hz, aromatic-H), 7.26 (2H, d, J=8.8 Hz, aromatic-H).

HPLC Analysis of the Racemic Alcohols ((±)-5 and (±)-8) and Acetates ((±)-15 and (±)-16) by Using a Chiral Column Two racemates ((±)-**5** and (±)-**15**) each gave two well separated peaks ((±)-**5**; 12.4 and 16.6 min, (±)-**15**; 11.2 and 16.5 min) corresponding to each enantiomer under the following analytical conditions (eluent, *n*-hexane–EtOH (9 : 1); detection, UV at 254 nm; flow rate, 1.0 ml/min). On the other hand, a 1 : 1 mixture of two racemates ((±)-**8** and (±)-**16**) provided four well separated peaks ((±)-**16**; 10.7 and 12.6 min, (±)-**8**; 56.2 and 67.9 min) corresponding to each enantiomer under the following analytical conditions (eluent, *n*-hexane–EtOH (500 : 2); detection, UV at 254 nm; flow rate, 1.0 ml/min).

Immobilization of Lipase with Photo Crosslinkable Prepolymer (ENTP 4000) One gram of ENTP 4000 was mixed with 10 mg of a photosensitizer, benzoin ethyl ether. The mixture was melted completely at 60 °C. The powdered lipase (100 mg) "Amano P" was added to the molten mixture under continnous mixing. The prepolymer–lipase mixture was layered on a framed sheet of transparent polyester film (thickness, *ca.* 0.5 mm). The layer was covered with transparent thin film and then illuminated with chemical lamps (wavelength range, 300—400 nm) for 3 min. The gel film thus formed was cut into small pieces (0.5 × 5 × 5 mm) and used for biochemical reactions.

General Procedure of Enantioselective Acetylation of Primary Alcohols 1) Using 10 mg of Substrate (±)-**8**: A mixture of (±)-**8** (*ca.* 10 mg) and lipase (10 mg) in the presence of isopropenyl acetate (*ca.* 30 mg) in isooctane (3 ml) was incubated at 33 °C for a suitable time. When spots of the starting material and product on TLC showed an approximately 1 : 1 ratio, the reaction was quenched. The reaction mixture was dried over $MgSO_4$ and evaporated to provide a crude product, which was analyzed by HPLC. The results are shown in Table 2.

2) Using 208 mg of Substrate (±)-**8**: A mixture of (±)-**8** (*ca.* 100 mg), lipase "Nagase P" (100 mg) and isopropenyl acetate (2 ml) in a mixed solvent (isooctane (20 ml)–(iso-Pr)$_2$O (2 ml)) was incubated at 33 °C for 40 h. This reaction was carried out twice (total amount of (±)-**8** was 208 mg). The reaction mixture was filtered and the filter was washed with ether. The combined filtrate and washings were evaporated to give a crude product, which was chromatographed on silica gel (10 g) to afford (2*R*,3*R*)-**16** (33 mg, 14% yield) from the *n*-hexane–ethyl acetate (9 : 1) eluate and (2*S*,3*S*)-**8** (135 mg, 65% recovery) from the *n*-hexane–ethyl acetate (1 : 1) eluate. Enantiomeric excess (ee) values of the alcohol **8** and acetate **16** were analyzed by HPLC and the results are shown in Table 2. (2*S*,3*S*)-**8**; t_R=56.2 min, $[\alpha]_D^{28}$ +6.7° (c=1.09, $CHCl_3$), corresponding to 15% ee. (2*R*,3*R*)-**16**; t_R=12.6 min, $[\alpha]_D^{28}$ −1.47° (c=1.00, $CHCl_3$), corresponding to 74% ee.

3) Using 100 mg of Substrate (±)-**5**: A mixture of (±)-**5** (*ca.* 100 mg), lipase (100 mg) or the above-mentioned immobilized lipase "Amano P" and isopropenyl acetate (100 mg) in isopropyl ether (20 ml) was incubated at 33 °C for a suitable time. When spots of the starting material and product on TLC showed an approximately 1 : 1 ratio, the reaction mixture was filtered and the filter was washed with ether. The combined filtrate and washings were evaporated to give a crude product, which was chromatographed on silica gel (10 g) to afford (2*R*,3*R*)-**15** from the *n*-hexane–ethyl acetate (4 : 1) eluate and (2*S*,3*S*)-**5** from the *n*-hexane–ethyl acetate (1 : 1) eluate. Enantiomeric excess values of the alcohol **5** and acetate **15** were analyzed by HPLC and the results are shown in Table 3. The recovered immobilized lipase was repeatedly employed for enantioselective esterification. (2*S*,3*S*)-**15**; t_R=16.5 min, $[\alpha]_D^{30}$ +9.07° (c=1.08, $CHCl_3$), corresponding to 93% ee (entry 10). (2*R*,3*R*)-**5**; t_R=12.4 min, corresponding to 15% ee.

4) Repeated Enantioselective Acetylation: A mixture of (2*S*,3*S*)-**5** (27% ee, 300 mg), isopropenyl acetate (300 mg) and the recovered immobilized lipase in isopropyl ether (30 ml) was incubated at 33 °C for 24 h. The reaction mixture was filtered and the filter was washed with ether. The combined filtrate and washings were evaporated and the residue was separated to afford (2*S*,3*S*)-**5** (147 mg, 49% recovery, 88% ee) and (2*R*,3*R*)-**15** (157 mg, 44% yield, 41% ee) in the same way as in the case of 3). Recrystallization of (2*S*,3*S*)-**5** (88% ee) from *n*-hexane–ether gave (2*S*,3*S*)-**5** with more than 99% ee. (2*S*,3*S*)-**5**; $[\alpha]_D^{26}$ +17.6° (c=1.00, $CHCl_3$), corresponding to 99% ee.

Determination of Absolute Structure of Enzymatic Resolution Products 1) TBDMSCl (299 mg) in DMF (7.5 ml) was added to a solution of (2*S*,3*S*)-**5** (419 mg) and imidazole (257 mg) in DMF (7.5 ml) for 1 h under ice-H_2O cooling with stirring. The reaction mixture was worked up and purified in the same way as in the case of conversion of (±)-**5** into (±)-**6** to afford (2*S*,3*S*)-**6** (634 mg, 99% yield) as a colorless oil. (2*S*,3*S*)-**6**; $[\alpha]_D^{27}$ +17.4° (c=0.54, $CHCl_3$).

2) A suspension of KH (35% in mineral oil, 624 mg) in THF (5 ml) was added to a solution of (2*S*,3*S*)-**6** (610 mg) in THF (10 ml) under an argon atmosphere at 0 °C, and then a solution of MeI (1.159 g) in THF (5 ml) was further added. The reaction mixture was stirred for 3 h at room temperature, then worked up in the same way as in the case of conversion of (±)-**6** into (±)-**7** to afford (2*S*,3*S*)-**7** (623 mg, 98% yield). (2*S*,3*S*)-**7**; $[\alpha]_D^{27}$ +1.45° (c=0.69, $CHCl_3$).

3) TBAF (790 mg) was added to a solution of (2*S*,3*S*)-**7** (584 mg) in THF (10 ml) with stirring at room temperature and the reaction mixture was stirred for 1 h at the same temperature, then worked up and purified in the same way as in the case of conversion of (±)-**7** into (±)-**8**, to give (2*S*,3*S*)-**8** (394 mg, 99% yield) as colorless crystals. (2*S*,3*S*)-**8**; mp 52—53 °C. $[\alpha]_D^{26}$ +43.2° (c=1.00, $CHCl_3$).

4) Ph_3P (571 mg) was added to a solution of CBr_4 (722 mg) in THF (4 ml) under an argon atmosphere at 0 °C with stirring for 10 min, then (2*S*,3*S*)-**9** (257 mg) was added. The reaction mixture was stirred for 10 min at 0 °C and for 40 min at room temperature, then DMSO (15 ml) and NaCN (0.7 g) were added at room temperature with stirring for 10 min and stirring was continued for 1 h at 60 °C. The reaction mixture was worked up and purified in the same way as in the case of conversion of (±)-**8** into (±)-**9** to afford (3*S*,4*R*)-**9** (242 mg, 91% yield) as colorless crystals. (3*S*,4*R*)-**9**; mp 62—63 °C. $[\alpha]_D^{24}$ −35.4° (c=1.00, $CHCl_3$). The NMR data of (3*S*,4*R*)-**9** was identical with those reported for (3*S*,4*R*)-**9**.

5) A solution of (2*R*,3*R*)-**16** (21 mg, 74% ee) and K_2CO_3 (2 mg) in MeOH (0.7 ml) was stirred for 30 min at room temperature. The reaction mixture was diluted with H_2O and extracted with ether. The ether layer was evaporated to give a crude residue, which was chromatographed on silica gel (20 g) to afford (2*R*,3*R*)-**8** (17 mg, 96% yield) from the *n*-hexane–ethyl acetate (1 : 1) eluate. (2*R*,3*R*)-**8**; $[\alpha]_D^{24}$ −30.2° (c=1.6, $CHCl_3$), corresponding to 73% ee. The NMR data of (2*R*,3*R*)-**8** were identical with those of the above-mentioned (2*S*,3*S*)-**8**.

Methyl (3*S*,4*R*)-4-Methoxy-6-(4-methoxyphenyl)-3-methyl-(5*E*)-hexenoate (10) A mixture of (3*S*,4*R*)-**9** (178 mg), NaOH (3.7 g), H_2O (3.7 ml), and ethanol (10 ml) was refluxed with stirring for 3 h. The reaction mixture was diluted with H_2O, acidified with aqueous 2 N HCl and extracted with CH_2Cl_2. The CH_2Cl_2 layer was evaporated to provide the crude acid (190 mg, 99% yield), which was treated with CH_2N_2–ether solution to give (3*S*,4*R*)-**10** as a homogeneous oil (168 mg, 83% yield from (3*S*,4*R*)-**9**) in the same way as described for the conversion of (±)-**9** into (±)-**10**. (3*S*,4*R*)-**10**: *Anal.* HRMS Calcd for $C_{16}H_{22}O_4$ (M^+; *m/z*): 278.151. Found; 278.150. $[\alpha]_D^{25}$ +10.98° (c=1.42, $CHCl_3$). The NMR data of (3*S*,4*R*)-**10** were identical with those reported for (3*S*,4*R*)-**10**.[3b]

(−)-Oudemansin X (1) The methyl ester (3*S*,4*R*)-**10** (132 mg) was finally converted into (−)-oudemansin X (**1**) (49 mg, 32% overall yield

from (3*S*,4*R*)-**10**) in the same way as described for the synthesis of (±)-**1** from (±)-**10**. (−)-**1**: mp 55—56 °C. *Anal.* HRMS Calcd for $C_{18}H_{24}O_5$ (M^+; *m/z*): 320.162. Found; 320.162. $[\alpha]_D^{25}$ −20° (*c*=1.0, EtOH). The NMR data of the present synthesized (−)-**1** were identical with those reported for (−)-**1**.[2,3]

(2*R*,3*R*)-5-(4-Methoxyphenyl)-2-methyl-(4*E*)-penten-1,3-diol (5) A mixture of (2*R*,3*R*)-1-acetoxy-3-hydroxy-5-(4-methoxyphenyl)-2-methyl-(4*E*)-pentene **15** (450 mg, 93% ee, (Table 3, entry 10)), K_2CO_3 (560 mg), and H_2O (0.5 ml) in MeOH (5 ml) was stirred for 2 h at room temperature. The reaction mixture was diluted with H_2O and extracted with ether. The ether layer was evaporated to give a crude residue, which was chromatographed on silica gel (20 g) to afford the diol (2*R*,3*R*)-**5** from the *n*-hexane–ethyl acetate (1 : 1) eluate. Recrystallization of (2*R*,3*R*)-**5** from *n*-hexane–ether gave (2*R*,3*R*)-**5** as colorless crystals (335 mg, 89% yield). The optical purity was found to be more than 99% ee by HPLC analysis. (2*R*,3*R*)-**5**; mp 65—66 °C. *Anal.* Calcd for $C_{13}H_{16}O_3 \cdot 1/2H_2O$: C, 67.51, H, 8.28. Found: C, 67.23, H, 8.24. MS *m/z*: 222 (M^+). $[\alpha]_D^{26}$ −18.6° (*c*=1.0, $CHCl_3$). The NMR data of (2*R*,3*R*)-**5** were identical with those of (±)-**5**.

(+)-Oudemansin X (1) The diol (2*R*,3*R*)-**5** (138 mg) was finally converted into (+)-oudemansin X (**1**) (28 mg, 14% overall yield from (2*R*,3*R*)-**5**) in the same way as described for the synthesis of (±)-**1** from (±)-**5**. (+)-**1**: mp 54 °C. *Anal.* HRMS Calcd for $C_{18}H_{24}O_5$ (M^+; *m/z*): 320.162. Found; 320.164. $[\alpha]_D^{25}$ +20.2° (*c*=0.75, EtOH). The NMR data of (+)-**1** were identical with those reported for (±)-**1**.

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