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Insect Pheromone Synthesis Using Mn-Salen Catalyzed Asymmetric Epoxidation as a Key Step

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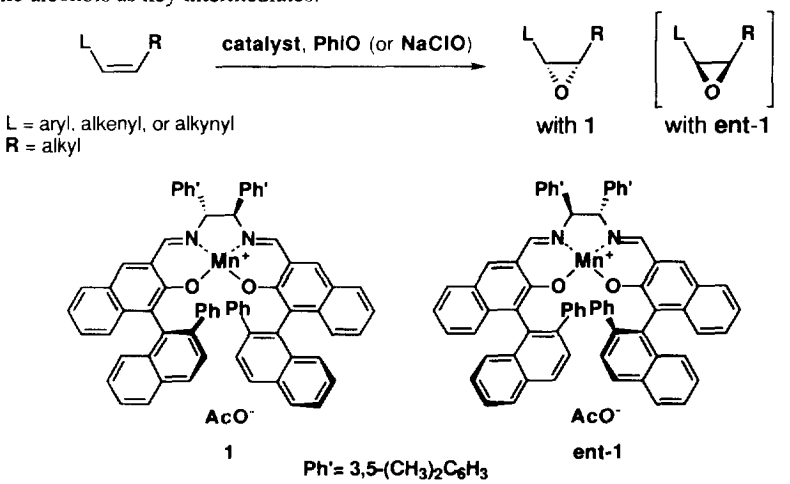
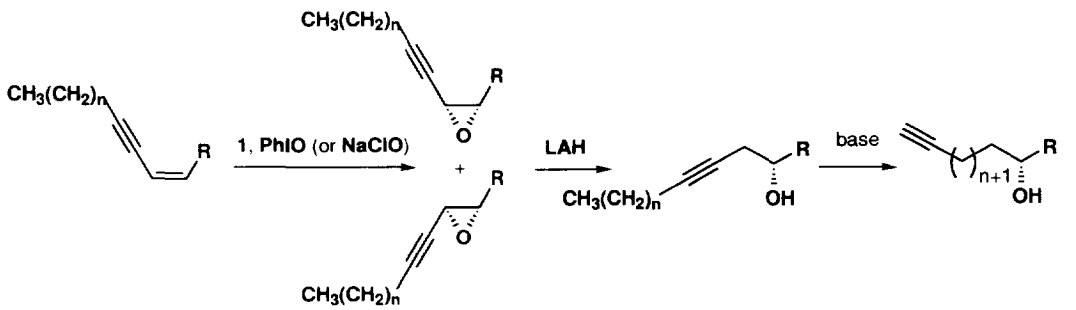
Abstract: Enantioselective synthesis of three insect pheromones, (5*Z*, 13*S*)-5-tetradecen-13-olide, (9*R*)-decan-9-olide, and (*S*)-2-acetoxytridecane, has been achieved by using Mn-salen catalyzed asymmetric epoxidation as a key step.

Since a wide variety of olefins are readily available and optically active epoxides can be converted into various functionalities with high regio- and stereoselectivity, asymmetric epoxidation of olefins is a useful synthetic tool in organic synthesis. Recently we developed an enantioselective epoxidation of simple olefins with Mn-salen catalyst **1** or **ent-1** which proceeded under mild conditions (Scheme 1).[1] In particular, remarkably high enantioselectivity was realized in the epoxidation of conjugated *cis*-disubstituted and trisubstituted olefins. To show the utility of this reaction in organic synthesis, we carried out the synthesis of several optically active insect pheromones using epoxidation of *cis*-enynes as a key step. Although epoxidation of *cis*-enynes with **1** (or **ent-1**) provides a mixture of the corresponding *cis*- and *trans*-epoxides, LAH reduction of these diastereomeric epoxides gives the same homopropargylic alcohol of high enantiomeric purity (Scheme 2). Since the acetylenic group in the homopropargylic alcohols can be transferred to the terminal position without compromising the stereochemistry of the carbinol carbon and the resulting terminal acetylene can be further carbon-extended, these optically active homopropargylic alcohols are considered to serve as useful building blocks for the synthesis of various optically active compounds. In this paper, we describe the synthesis of three insect pheromones **2**, **3**, and **4** by using optically active homopropargylic alcohols as key intermediates.[2]

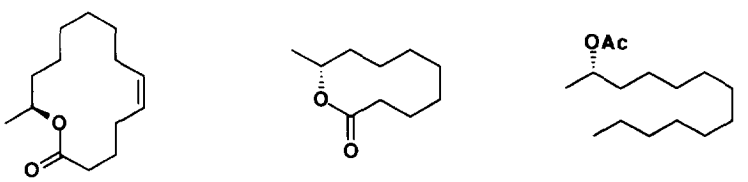


Scheme 1

Dedicated to the memory of Professor Hidemasa Takaya, deceased on 5 October 1995



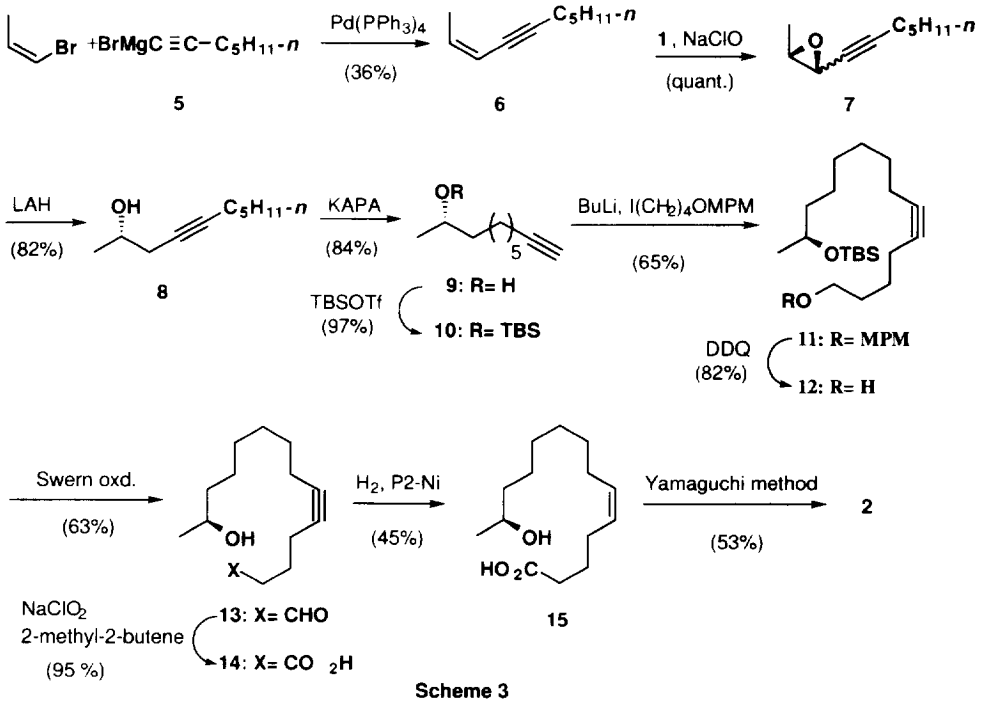
Scheme 2



2 3 4

(5*Z*, 13*S*)-5-Tetradecen-13-olide **2** is a synergist of the aggregation pheromone, (*Z*)-3-dodecen-12-olide, of the flat grain beetle, *Cryptolestes pusillus*.[3] The synthesis of **2** started from the epoxidation of (*Z*)-dec-2-en-4-yne **6** which was easily obtained by cross coupling of (*Z*)-1-bromo-1-propene and the Grignard reagent **5** derived from 1-heptyne, in the presence of a Pd(0) catalyst (Scheme 3).[4] Asymmetric epoxidation of **6** with **1** as a catalyst gave a mixture of *cis*- and *trans*-epoxides **7**, which was directly reduced without separating by lithium aluminum hydride (LAH) to give homopropargylic alcohol **8**. HPLC analysis using an optically active column revealed that the enantiomeric purity of **8** was 86% ee.[5] Compound **8** was treated with potassium 3-aminopropylamide (KAPA) to give terminal acetylene **9**[6] and protected as *t*-butyldimethylsilyl (TBS) ether. The resulting TBS ether **10** was treated successively with *n*-butyllithium and 4-iodobutyl *p*-methoxybenzyl ether to give **11** which had the requisite carbons for the synthesis of **2**. Compound **11** was exposed to aqueous dichlorodicyanoquinone (DDQ)[7] and the resulting alcohol **12** was subjected to Swern oxidation. Under the conditions, TBS ether was also cleaved to give hydroxy aldehyde **13**. Aldehyde **13** was treated with sodium chlorite in the presence of 2-methyl-2-butene[8] to give the corresponding acid **14**. Acid **14** was hydrogenated in the presence of P2-Ni[9] and the resulting seco acid **15** was subjected to Yamaguchi method[10] to give **2**, which gave the satisfactory spectroscopic data. Comparison of the specific rotation with that reported by Mori et al.[3c] indicated that the optical purity of **2** was 88% ee.

Homopropargylic alcohol **18**, a requisite intermediate for the synthesis of **3**, was prepared from (*Z*)-1-bromo-1-propene and 1-hexyne with enantioselectivity of 83% ee in a similar manner to that described for the synthesis of **8**, except that catalyst **ent-1** was used for the epoxidation of **16**, in lieu of **1**. Compound **18** was treated with KAPA[6] to give terminal acetylene **19a**. Compound **19a** was converted into the corresponding 3,5-dinitrobenzoate **19b** and recrystallized from hexane to homochirality. The homochiral **19a** obtained by the hydrolysis of **19b** was converted into (9*R*)-decan-9-olide **3**, the defensive secretion of the Eucarypt longicorn, *Phoracantha synonyma*,[11] as follows (Scheme 4). Compound **19a** was protected as TBS ether **20** and subjected to ethoxycarbonylation to give ester **21**. Ester **21** was converted into seco acid **24** by the



Scheme 3

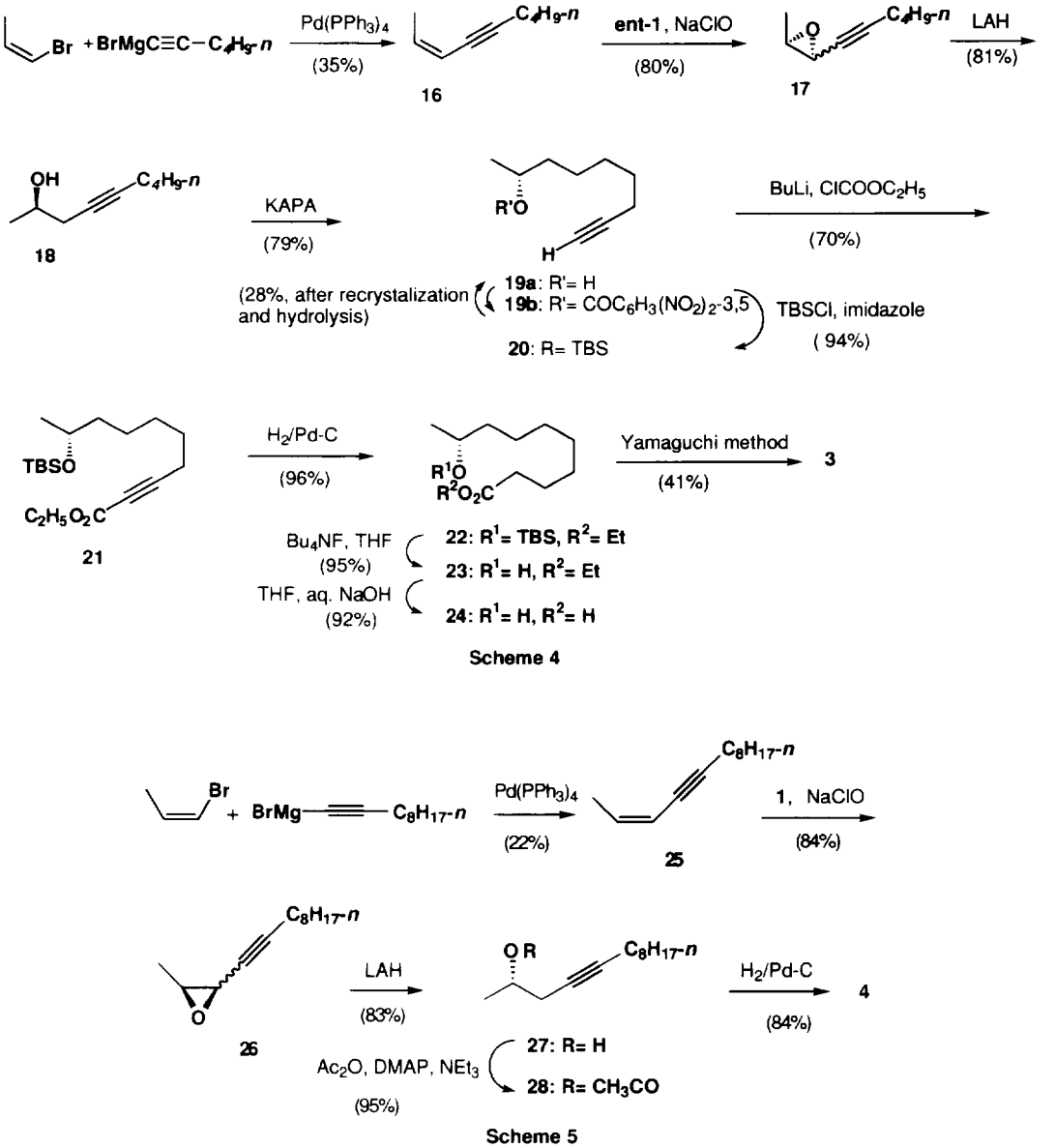
sequence: i) hydrogenation ii) desilylation of the resulting **22**, and iii) hydrolysis of ester **23**. Compound **24** was cyclized by using Yamaguchi method to **3**, which gave the satisfactory spectroscopic data and specific rotation.

Optically active homopropargylic alcohol **27** of 90% ee was also prepared from *cis*-enyne **25** in a similar manner to that described for the synthesis of **8**, by way of **26** (Scheme 5). Compound **27** was converted into (*S*)-2-acetoxytridecane **4**, the aggregation pheromone of *Drosophia mulleri*,[12] by the sequence: i) acetylation and ii) hydrogenation of the resulting **28**.

The examples described above demonstrated the high utility of Mn-salen catalyzed epoxidation in organic synthesis.

Experimental

NMR spectra were recorded at 400 MHz on a JEOL GX-400 or at 270 MHz on a JEOL EX-270 instrument. All signals were expressed as ppm down field from tetramethylsilane used as an internal standard (δ-value in $CDCl_3$). IR spectra were obtained with a SIMADZU FTIR-8600 instrument. Optical rotations were measured with a JASCO DIP-360 automatic digital polarimeter. High-resolution mass spectra were recorded on a JEOL JMS-SX/SX 102A instrument. Column chromatography was conducted on Silica Gel BW-820MH, 70-200 mesh ASTM, available from FUJI SILYSIA CHEMICAL LTD. Preparative thin layer chromatography was performed on 0.5 mm x 20 cm x 20 cm E. Merck silica gel plate (60 F-254). Solvents were dried and distilled shortly before use. Reactions were carried out under an atmosphere of nitrogen if necessary.



(Z)-Dec-2-en-4-yne 6

To a solution of 1-heptyne (3.25 ml, 24.8 mmol) in THF (13.2 ml) was added a solution of methylmagnesium bromide in THF (33.1 ml, 0.90 M) and the resulting mixture was stirred for 3 h at room temperature. To this solution was added a solution of (Z)-1-bromopropene (2.12 ml, 24.8 mmol) and $Pd(PPh_3)_4$ (569 mg, 0.50 mmol) in benzene (33 ml), and the mixture was stirred for 10 h at the same temperature. The reaction mixture was quenched with saturated aqueous NH_4Cl, extracted with ether, dried

over Na_2SO_4, and concentrated. The residue was distilled by Kugelrohr to give *cis*-enyne **6** (1.22 g, 36%) as an oil. ^{1}H NMR (270 MHz): δ 5.87 (dq, *J*= 6.7 and 10.6 Hz, 1H), 5.46 (dtq, *J*= 1.7, 2.0, and 10.6 Hz, 1H), 2.35 (dt, *J*= 2.0 and 7.1 Hz, 2H), 1.85 (dd, *J*= 1.7 and 6.7 Hz, 3H), 1.61-1.26 (m, 6H), 0.91 (t, *J*= 7.1 Hz 3H). IR (KBr): 3449, 2957, 2926, 2855, 1736, 1638, 1061, 1028, 702, 419 cm^{-1}. Anal. Calcd for $C_{10}H_{16}$: C, 88.16; H, 11.84. Found: C, 87.94; H, 11.65.

A mixture of (2*S*,3*R*)- and (2*S*,3*S*)-2,3-epoxy-4-decynes 7

Mn-salen complex **1** (48.1 mg, 0.44 mmol) was added to a solution of *cis*-enyne **4** (300 mg, 2.20 mmol) and 4-phenylpyridine *N*-oxide (75.3 mg, 0.44 mmol) in dichloromethane (13.8 ml) and cooled to 0 °C. To the solution was added aqueous NaOCl adjusted at pH 11.3 with phosphate buffer (18.7 ml, 0.588 M) at the same temperature. The two phase solution was stirred for 1 h, then allowed to warm to room temperature, and separated. The aqueous phase was extracted with dichloromethane and the combined organic layers were dried over Na_2SO_4 and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (pentane-ether= 1:0~19:1) to give a mixture of *cis*- and *trans*-epoxides **7** (335 mg, quant.) as an oil. IR (KBr): 3452, 2932, 2091, 1638, 1508, 1458, 698, 652, 600 cm^{-1}. HREIMS m/z. Calcd. for $C_{10}H_{16}O$: 152.1201. Found: 152.1201.

(*S*)-4-Decyn-2-ol 8

To a mixture of *cis*- and *trans*-epoxides **7** (250 mg, 1.64 mmol) in THF (16.4 ml) was added LAH (62.2 mg, 1.64 mmol) at 0 °C. The solution was gradually raised to room temperature and stirred for 12 h. The reaction mixture was quenched with aqueous KF (0.40 ml, 15.9 N), filtered through a pad of Celite, dried over Na_2SO_4, and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (pentane-ether= 19:1~9:1) to give homopropargylic alcohol **8** (208 mg, 82%) as an oil. The enantiomeric excess of **8** was determined to be 86% by ^{1}H NMR analysis [Eu(hfc)$_3$ in C_6D_6] of the corresponding acetate. $[\alpha]_D^{23}$ +11.7 (*c* 1.08, $CHCl_3$). ^{1}H NMR (270 MHz): δ 3.90 (ddq, *J*= 5.0, 6.3, and 6.8 Hz, 1H), 2.36 (ddt, *J*= 2.3, 5.0, and 16.3 Hz, 1H), 2.29 (ddt, *J*= 2.3, 6.8, and 16.3 Hz, 1H), 2.17 (ddt, *J*= 2.3, 2.3, and 6.9 Hz, 2H), 1.80 (br s, 1H), 1.56-1.17 (m, 6H), 1.24 (d, *J*= 6.3 Hz, 3H), 0.90 (t, *J*= 7.1 Hz, 3H). IR (KBr): 3449, 2957, 2928, 2856, 1639, 1560, 1458, 1115, 1086, 698, 594, 503 cm^{-1}. Anal. Calcd for $C_{10}H_{18}O$: C, 77.87; H, 11.76. Found: C, 77.65; H, 11.73.

(*S*)-9-Decyn-2-ol 9

To potassium hydride (35% suspension in mineral oil, 641 mg, 16.0 mmol) that was washed three times with ether under nitrogen, was added 3-aminopropylamine (31.9 ml, 383 mmol) at room temperature and the mixture was stirred for 1 h at the temperature. The mixture was cooled to 0 °C and slowly added to homopropargylic alcohol **8** (986 mg, 6.39 mmol) at 0 °C. After the addition, the mixture was allowed to warm to room temperature and stirred for 10 h. The reaction mixture was quenched with water at 0 °C and extracted with ether. The ether layer was washed with 4 M HCl and with water successively, dried over Na_2SO_4 and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (pentane-ether= 19:1~9:1~8:2) to give **9** (826 mg, 84%) as an oil. $[\alpha]_D^{25}$ +6.48 (*c* 0.94, $CHCl_3$). ^{1}H NMR (270 MHz): δ 3.80 (br s, 1H), 2.19 (dt, *J*= 2.6 and 6.9 Hz, 2H), 1.94 (t, *J*= 2.6 Hz, 1H), 1.57-1.23 (m, 11H), 1.19 (d, *J*= 6.3 Hz, 3H). IR (KBr): 3422, 3312, 2966, 2934, 2858, 2374, 2345, 1655, 1458, 1375, 1128, 1103, 1055, 667, 633, 405 cm^{-1}. Anal. Calcd for $C_{10}H_{18}O$: C, 77.87; H, 11.76. Found: C, 77.75; H, 11.66.

(*S*)-9-(*t*-Butyldimethylsiloxy)-1-decyne 10

To a solution of **9** (253 mg, 1.64 mmol) in dichloromethane were added 2,6-lutidine (0.23 ml, 1.97 mmol)

and *t*-buthyldimethylsilyl triflate (0.45 ml, 1.97 mmol) at 0 °C. After being stirred for 1 h at the same temperature, the mixture was quenched with water, extracted with dichloromethane, dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (pentane-ether= 1:0~49:1) to give TBS ether **10** (427 mg, 97%) as an oil. $[\alpha]_D^{26}$ +9.69 (*c* 1.26, $CHCl_3$). ^1H NMR (270 MHz): δ 3.80-3.74 (m, 1H), 2.18 (dt, *J*= 2.6 and 6.9 Hz, 2H), 1.94 (t, *J*= 2.6 Hz, 1H), 1.56-1.21 (m, 10H), 1.11 (d, *J*= 6.3 Hz, 3H), 0.89 (s, 9H), 0.04 (s, 6H). IR (KBr): 3449, 3315, 2934, 2858, 2374, 2120, 1638, 1474, 1464, 1375, 1256, 1136, 1105, 1067, 1005, 939, 835, 808, 773, 631 cm^{-1}. Anal. Calcd for $C_{16}H_{32}OSi$: C, 71.57; H, 12.01. Found: C, 71.52; H, 12.00.

(*S*)-1-(*p*-Methoxybenzyloxy)-13-(*t*-butyldimethylsiloxy)-5-tetradecyne 11

To a solution of TBS ether **10** (1.36 g, 5.07 mmol) in THF-HMPA (5.0 ml, 1:1) was added *n*-butyllithium (3.7 ml, 6.1 mmol, 1.63 N in hexane) at 0 °C and the reaction mixture was stirred for 30 min. To the solution was added a pre-cooled (0 °C) solution of 4-iodobutyl *p*-methoxybenzyl ether (1.79 g, 5.58 mmol) in THF-HMPA (5.0 ml, 1:1) via cannula at the same temperature. After being stirred for 7 h, the mixture was quenched with water and extracted with ethyl acetate. The combined organic layers were washed with water twice, dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (pentane-ether= 5:1~3:2~2:3) to give **11** (1.53 g, 65%) as an oil. $[\alpha]_D^{24}$ +5.16 (*c* 0.88, $CHCl_3$). ^1H NMR (270 MHz): δ 7.26 (d, *J*= 8.6 Hz, 2H), 6.82 (d, *J*= 8.6 Hz, 2H), 4.43 (s, 2H), 3.80 (s, 3H), 3.75 (m, 1H), 3.46 (t, *J*= 6.4 Hz, 2H), 2.19-2.09 (m, 4H), 1.73-1.21 (m, 14H), 1.11 (d, *J*= 6.3 Hz, 3H), 0.88 (s, 9H), 0.04 (s, 6H). IR (KBr): 3349, 2934, 2856, 2374, 2345, 2322, 2098, 1616, 1514, 1464, 1362, 1248, 1103, 1040, 835, 775, 667 cm^{-1}. HREIMS m/z. Calcd. for $C_{28}H_{48}O_3Si$: 460.3373. Found: 460.3433.

(*S*)-13-(*t*-Butyldimethylsiloxy)-5-tetradecyn-1-ol 12

To a mixture of MPM ether **11** (1.52 g, 3.29 mmol) in dichloromethane-water (17 ml, 19:1) was added 2,3-dichloro-5,6-dicyanobenzoquinone (896 mg, 3.95 mmol) at 0 °C. After being stirred for 2 h at the same temperature, the mixture was dried over $MgSO_4$, filtered through a pad of Celite, and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (hexane-ethyl acetate= 19:1~9:1) to give **12** (913 mg, 82%) as an oil. $[\alpha]_D^{26}$ +7.67 (*c* 0.44, $CHCl_3$). ^1H NMR (270 MHz): δ 3.80-3.71 (m, 1H), 3.67 (t, *J*= 6.3 Hz, 2H), 2.23-2.10 (m, 4H), 1.73-1.26 (m, 15H), 1.11 (*J*= 5.9 Hz, 3H), 0.89 (s, 9H), 0.05 (s, 6H). IR (KBr): 3450, 3423, 2934, 1638, 1458, 1375, 1256, 1134, 1103, 1065, 835, 808, 773, 706, 429 cm^{-1}. HRFABMS m/z. Calcd. for $C_{20}H_{40}O_2Si$ (M^+ +H): 341.2876. Found: 341.2872.

(*S*)-13-Hydroxy-5-tetradecynal 13

To a solution of oxalyl chloride (0.45 ml, 5.14 mmol) in dichloromethane (10.0 ml) was added dimethylsulfoxide (0.49 ml, 6.84 mmol) at -78 °C. After being stirred for 10 min, a solution of **12** (876 mg, 2.57 mmol) in dichloromethane (1.0 ml) was added to the solution. After being stirred for another 15 min, triethylamine (2.6 ml, 18.8 mmol) was added to this and the reaction mixture was stirred for 2.5 h at the same temperature. Then the reaction temperature was gradually raised to 0 °C. The reaction mixture was quenched with water, extracted with dichloromethane, dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (hexane-ethyl acetate= 1:0~19:1) to give **13** (362 mg, 63%) as an oil. $[\alpha]_D^{24}$ +7.10 (*c* 0.83, $CHCl_3$). ^1H NMR (270 MHz): δ 9.81 (t, *J*= 1.3 Hz 1H), 3.81-3.76 (m, 1H), 2.57 (dt, *J*= 1.3 and 7.3 Hz, 2H), 2.23 (tt, *J*= 2.3 and 6.9 Hz, 2H), 2.14 (tt, *J*= 2.3 and 6.9 Hz, 2H), 1.80 (tt, *J*= 6.9 and 7.3 Hz, 2H), 1.60-1.34 (m, 11 H), 1.19 (d, *J*= 6.3 Hz, 3H). IR (KBr): 3431, 2932, 2856, 1719, 1655,

1458, 1437, 1375, 1340, 1113, 1059, 1028, 696, 667, 594, 503, 421 cm^{-1}. HRFABMS m/z. Calcd. for $C_{14}H_{23}O$ (M^+ -OH): 207.1749. Found: 207.1745.

(*S*)-13-Hydroxy-5-tetradecynoic acid 14

To a mixture of hydroxy aldehyde **13** (5.0 mg, 22 μmol), *t*-butanol (160 μl), water (42 μl), NaH_2PO_4 (2.7 mg, 0.022 mmol), and 2-methyl-2-butene (11.0 ml, 99 μmol) was slowly added $NaClO_2$ (6.9 mg, 0.076 mmol) at room temperature. After 30 min, the reaction mixture was cooled to 0 °C, quenched with 1N HCl, extracted with dichloromethane, dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (hexane-ethyl acetate= 7:3~1:1, the eluate contains 1% of acetic acid) to give **14** (5.1 mg, 95%) as an oil. $[\alpha]_D^{24}$ +4.52 (*c* 1.24, $CHCl_3$). ^1H NMR (270 MHz): δ 5.90 (br s, 2H), 3.85-3.75 (m, 1H), 2.49 (t, *J*= 7.3 Hz, 2H), 2.25 (tt, *J*= 2.3 and 6.8 Hz, 2H), 2.14 (tt, *J*= 2.3 and 6.8 Hz, 2H), 1.81 (tt, *J*= 6.8 and 7.3 Hz, 2H), 1.48-1.23 (m, 10 H), 1.19 (d, *J*= 6.3 Hz, 3H). IR (KBr): 3449, 2934, 2858, 2638, 1713, 1458, 1437, 1412, 1236, 1159, 1128, 1053, 934, 667, 623, 505 cm-1. HRFABMS m/z. Calcd. for $C_{14}H_{23}O_2$ (M^+-OH): 223.1698. Found: 223.1698.

(5*Z*,13*S*)-13-Hydroxy-5-tetradecenoic acid 15

$NaBH_4$ (250 mg, 6.61 mmol) was dissolved in ethanol (6.0 ml) containing 2 N NaOH (0.32 ml). After stirring for a while, the mixture was filtered through absorbent cotton. A portion (0.53 ml) of the filtrate was added dropwise to a vigorously stirred mixture of nickel acetate tetrahydrate (106 mg, 0.43 mmol) in ethanol (8.5 ml) under hydrogen. Ethylendiamine (85 μl, 1.50 mmol) was added to the resulting black suspension to give P-2 nickel catalyst. A solution of hydroxy acid **14** (360 mg, 1.50 mmol) in ethanol (4.2 ml) was then added dropwise to the suspension of P-2 nickel under hydrogen. The mixture was stirred for 4.5 h at room temperature, diluted with brine, acidified with 2 N HCl to pH 3, and extracted with ether. The ethereal solution was washed with brine, dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (hexane-ether= 2:1~1:1, the eluate contains 1% of acetic acid) to give seco acid **15** (163 mg, 57%) as an oil. $[\alpha]_D^{25}$ +5.09 (*c* 1.92, $CHCl_3$). ^1H NMR (270 MHz): δ 5.47 (br s, 1H), 5.47-5.26 (m, 2H), 3.86-3.76 (m, 1H), 2.36 (t, *J*= 7.3 Hz, 2H), 2.10 (dt, *J*= 7.2 and 7.2 Hz, 2H), 2.01 (dt, *J*= 6.6 and 6.6 Hz, 2H), 1.70 (tt, *J*= 7.2 and 7.3 Hz, 2H), 1.43-1.31 (m, 11 H), 1.19 (d, *J*= 6.3 Hz, 3H). IR (KBr): 3447, 3005, 2930, 2856, 2637, 1709, 1458, 1412, 1240, 1128, 1043, 935, 804, 721, 600 cm^{-1}. HREIMS m/z. Calcd. for $C_{14}H_{26}O_3$: 242.1882. Found: 242.1889.

(5*Z*, 13*S*)-5-Tetradecen-13-olide 2

To a mixture of seco acid **15** (80.0 mg, 0.33 mmol) and triethylamine (51 μl, 0.36 mmol) in THF was added 2,4,6-trichlorobenzoyl chloride (52 μl, 0.33 mmol) and the mixture was stirred for 2 h at room temperature. The reaction mixture was filtered through dry absorbent cotton to remove triethylamine hydrochloride and concentrated. The residue was diluted with toluene (165 ml), added under high dilution conditions to a refluxing solution of 4-(*N*,*N*-dimethylamino)pyridine (203 mg, 1.65 mmol) in toluene (33.0 ml) over a period of 5 h and stirred for additional 2 h. The mixture was quenched with 10% phosphoric acid, extracted with ethyl acetate, dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (hexane-ethyl acetate= 1:0~19:1) to give **2** (39.0 mg, 53%) as an oil. $[\alpha]_D^{24}$ +48.1 (*c* 1.35, $CHCl_3$), [Lit. $[\alpha]_D^{32}$ +49.6 (*c* 1.275, $CHCl_3$)[3b] $[\alpha]_D^{23}$ +54.4 (*c* 4.62, $CHCl_3$)[3c]]. ^1H NMR (270 MHz): δ 5.44-5.26 (m, 2H), 5.04-4.92 (m, 1H), 2.48-2.13 (m, 4H), 2.01-1.12 (m, 14H), 1.23 (d, *J*= 6.3 Hz, 3H). IR (KBr): 3445, 3001, 2934, 2858, 2374, 1732, 1655, 1460, 1375, 1246, 1207, 1132, 1043, 806, 706 cm^{-1}. HREIMS m/z. Calcd. for $C_{14}H_{24}O_2$: 224.1776. Found: 224.1751.

(Z)-Non-2-en-4-yne 16

Compound **16** was prepared in 35% yield from 1-hexyne and (Z)-1-bromo-1-propene in a similar manner to that described for the preparation of **6**. **16**: an oil. ^{1}H NMR (270 MHz): δ 5.88 (dq, *J*= 10.6 and 6.6 Hz, 1H), 5.47 (dtq, *J*= 10.6, 2.0, and 1.7 Hz, 1H), 2.36 (dt, *J*= 2.0 and 6.9 Hz, 2H), 1.86 (dd, *J*= 1.7 and 6.6 Hz, 3H), 1.60-1.38 (m, 4H), 0.92 (t, *J*= 6.9 Hz 3H). IR (KBr): 2930, 2950, 2360, 2345, 1701, 1683, 1652, 1508, 1458 cm^{-1}. HREIMS m/z. Calcd. for C_9H_{14}: 122.1096. Found: 122.1100.

A mixture of (2*R*,3*S*)- and (2*R*,3*R*)-2,3-epoxy-4-nonynes 17

Compound **17** was prepared in 80% from (Z)-non-2-en-4-yne in a similar manner to that described for the preparation of **7**, except that Mn-salen catalyst **ent-1** was used, instead of **1**. **17**: an oil. IR (KBr): 2968, 2986, 2873, 2361, 2341, 2241, 1653, 1458, 1379, 1350, 1325, 1144, 1021, 930, 845, 827, 745, 669 cm^{-1}. HREIMS m/z. Calcd. for $C_9H_{14}O$: 138.1045. Found: 138.1042.

(*R*)-4-Nonyn-2-ol 18

Compound **18** was prepared in 81% from **17** in a similar manner to that described for the preparation of **8**. **18**: an oil. $[\alpha]_D^{19}$ -10.0 (*c* 1.07, $CHCl_3$). ^{1}H NMR (270 MHz): δ 3.96-3.83 (m, 1H), 2.35 (ddt, *J*= 2.3, 4.8, and 16.3 Hz, 1H), 2.30 (ddt, *J*= 2.3, 6.8, and 16.3 Hz, 1H), 2.23-2.14 (m, 2H), 1.98 (br s, 1H), 1.54-1.17 (m, 4H), 1.24 (d, *J*= 6.9 Hz, 3H), 0.91 (t, *J*= 6.9 Hz, 3H). IR (KBr): 3422, 2930, 2961, 2860, 2137, 1458, 1377, 1117, 1086, 941 cm^{-1}. HREIMS m/z. Calcd. for $C_9H_{16}O$: 140.1201. Found: 140.1194.

(*R*)-9-Nonyn-2-ol 19a

Compound **19a** was prepared in 79% from **18** in a similar manner to that described for the preparation of **9**. **19a**: an oil. $[\alpha]_D^{23}$ -6.6 (*c* 0.18, $CHCl_3$). ^{1}H NMR (270 MHz): δ 3.80-3.76 (m, 1H), 2.19 (dt, *J*= 6.9 and 2.6 Hz, 2H), 1.94 (t, *J*= 2.6 Hz, 1H), 1.62-1.32 (m, 9H), 1.19 (d, *J*= 5.9 Hz, 3H). IR (KBr): 3422, 3312, 2984, 2964, 2858, 2120, 1654, 1458, 1375, 1130, 1097, 631 cm^{-1}.

(*R*)-1-Methyl-7-octynyl 3,5-dinitrobenzoate 19b

3,5-Dinitrobenzoyl chloride (1.07 g, 4.63 mmol) was added to a solution of 4-(*N*,*N*-dimethylamino)pyridine (cat. amount), triethylamine (1.1 ml, 4.63 mmol), and **19a** (537 mg, 3.86 mmol) in dry dichloromethane (15.4 ml) at room temperature. After being stirred for 2 h, the mixture was quenched with H_2O, extracted with dichloromethane, dried over $MgSO_4$, and concentrated *in vacuo*. Silica gel column chromatography of the residue (hexane-ethyl acetate= 30:1) gave the corresponding dinitrobenzoate **19b** (1.20 g, 93%) as crystals, which was recrystallized from hexane three times to give **19b** (36%) as colorless needles. The enantiomeric excess was determined to be >99% by HPLC analysis (DAICEL CHILARCEL OJ, hexane/*i*-PrOH= 8:2, 0.5 ml/min). M.p. 64.0-64.5°C. $[\alpha]_D^{19}$ -31.8 (*c* 0.27, $CHCl_3$). ^{1}H NMR (270 MHz): δ 9.33 (t, *J*= 2.3 Hz, 1H), 9.25 (d, *J*= 2.3 Hz, 2H), 5.41-5.34 (m, 1H), 2.30 (dt, *J*= 2.6 and 6.6 Hz, 2H), 2.03 (t, *J*= 2.6 Hz, 1H), 1.98-1.54 (m, 8H), 1.52 (d, *J*= 6.3 Hz, 3H). IR (KBr): 3292, 3107, 2939, 2862, 2120, 1717, 1632, 1539, 1346, 1296, 1176, 1128, 1096, 1072, 916, 721, 661, 646 cm^{-1}. Anal. Calcd for $C_{16}H_{18}N_2O_6$: C, 57.48; H, 5.43; N, 8.38. Found: C, 57.31; H, 5.46; N, 8.29.

Homochiral (2*R*)-9-nonyn-2-ol 19a

K_2CO_3 (203 mg, 1.85 mmol) was added to a solution of **19b** (378 mg, 1.13 mmol) in methanol (5.7 ml) at room temperature. After being stirred for 2 h at room temperature, the mixture was diluted with H_2O, extracted with $CHCl_3$, dried over $MgSO_4$, and concentrated *in vacuo*. Silica gel column chromatography of the residue (pentane-ether= 8:2) gave **19a** (157.1 mg, 99%) as an oil. $[\alpha]_D^{24}$ -6.8 (*c* 0.08, $CHCl_3$).

(*R*)-9-(*t*-Butyldimethylsiloxy)-2-nonyne 20

Imidazole (92.3 mg, 1.36 mmol) and *t*-butyldimethylsilyl chloride (204 mg, 1.36 mmol) were successively added at room temperature to a solution of **19a** (157 mg, 1.13 mmol) in dimethylformamide (DMF) (2.3 ml). After being stirred for 3 h, the mixture was quenched with water, extracted with ether, dried over Na_2SO_4, and concentrated *in vacuo*. Silica gel column chromatography of the residue (pentane-ether= 30:1~9:1) gave **20** (268 mg, 94%) as an oil. $[\alpha]_D^{20}$ -14.6 (*c* 0.31, $CHCl_3$). ^1H NMR (270 MHz): δ 3.78-3.74 (m, 1H), 2.18 (dt, *J*= 6.9 and 2.6 Hz, 2H), 1.93 (t, *J*= 2.6 Hz, 1H), 1.55-1.25 (m, 8H), 1.11 (d, *J*= 6.3 Hz, 3H), 0.88 (s, 9H), 0.04 (s, 6H). IR (KBr): 3508, 3315, 2984, 2858, 2119, 1658, 1256, 1136, 1101, 1055, 835 773, 631 cm^{-1}.

Ethyl (*R*)-9-(*t*-butyldimethylsiloxy)-2-decynoate 21

Butyllithium (0.78 ml, 1.25 mmol, 1.6 N in hexane) was added to a solution of **20** (268 mg, 1.06 mmol) in THF (1.1 ml) at -78 °C and stirred for 0.5 h. The mixture was added to ethyl chloroformate (0.20 ml, 2.1 mmol) at the same temperature and the reaction temperature was gradually raised to room temperature. After being stirred for another 1.5 h, the mixture was quenched with saturated $NaHCO_3$, extracted with ether, dried over $MgSO_4$, and concentrated *in vacuo*. Silica gel column chromatography of the residue (hexane-ether= 100:1) gave **21** (241 mg, 70%) as an oil. $[\alpha]_D^{22}$ -10.5 (*c* 0.55, $CHCl_3$). ^1H NMR (270 MHz): δ 4.21 (q, *J*= 7.06 Hz, 2H), 3.82-3.76 (m, 1H), 2.32 (t, *J*= 7.1 Hz, 2H), 1.61-1.33 (m, 8H), 1.30 (t, *J*= 7.1 Hz, 3H), 1.11 (d, *J*= 6.3 Hz, 3H), 0.88 (s, 9H), 0.04 (s, 6H). IR (KBr): 3508, 2934, 2858, 2237, 1715, 1638, 1474, 1366, 1522, 1099, 835, 775 cm^{-1}.

Ethyl (*R*)-9-(*t*-butyldimethylsiloxy)-2-decanoate 22

A mixture of **21** (223 mg, 0.68 mmol) and 10% Pd-C (22.0 mg) in ethyl acetate (5.7 ml) was placed under hydrogen and stirred for 3 h. The mixture was filtered through a pad of Celite and concentrated *in vacuo* to give **22** (140 mg, 95%) as an oil. $[\alpha]_D^{19}$ -7.6 (*c* 0.73, $CHCl_3$). ^1H NMR (270 MHz): δ 4.12 (q, *J*= 7.13 Hz, 2H), 3.79-3.73 (m, 1H), 2.28 (t, *J*= 7.6 Hz, 2H), 1.64-1.17 (m, 15H), 1.11 (d, *J*= 6.3 Hz, 3H), 0.88 (s, 9H), 0.04 (s, 6H). IR (KBr): 3449, 2932, 2858, 1740, 1464, 1373, 1256, 1178, 835, 773 cm^{-1}. Anal. Calcd for $C_{18}H_{38}O_3Si$: C, 65.40; H, 11.59. Found: C, 65.39; H, 11.57.

Ethyl (*R*)-9-hydroxydecanoate 23

A solution (1.0 M) of tetrabutylammonium fluoride in THF (1.4 ml) was added to **22** (223 mg, 0.68 mmol) at room temperature and stirred for 3.5 h. The reaction mixture was quenched with water, extracted with ether, dried over $MgSO_4$, and concentrated *in vacuo*. Silica gel column chromatography of the residue (hexane-ethyl acetate= 9:1~7:3) gave **23** (140 mg, 95%) as an oil. $[\alpha]_D^{19}$ -5.5 (*c* 1.12, $CHCl_3$). ^1H NMR (270 MHz): δ 4.12 (q, *J*= 7.1 Hz, 2H), 3.82-3.76 (m, 1H), 2.29 (t, *J*= 7.4 Hz, 2H), 2.05-1.29 (m, 13H), 1.25 (t, *J*= 7.1 Hz, 3H), 1.18 (d, *J*= 5.9 Hz, 3H). IR (KBr): 3368, 2966, 2934, 2851, 1701, 1464, 1410, 1300, 1231, 1196, 1109, 943, 643 cm^{-1}. HREIMS m/z. Calcd. for $C_{12}H_{25}O_3$ ($M+H^+$): 217.1804. Found: 217.1790.

(*R*)-9-Hydroxydecanoic acid 24

To a solution of **23** (125 mg, 0.58 mmol) in THF (1.2 ml) was added aqueous sodium hydroxide (0.23 ml, 5.0 N) at room temperature. The reaction temperature was gradually raised to 60 °C. After being stirred for 2 h, the mixture was filtered through Dowex 50w x 8 and the filtrate was concentrated *in vacuo*. Silica gel column chromatography of the residue (hexane-ethyl acetate= 8:2~7:3) gave **24** (100 mg, 92%) as an oil. $[\alpha]_D^{20}$ -6.6 (*c* 0.35, $CHCl_3$). ^1H NMR (400 MHz): δ 5.35 (br s, 2H), 3.84-3.74 (m, 1H), 2.34 (t, *J*= 7.4 Hz, 2H), 1.66-1.57 (m, 2H), 1.45-1.22 (m, 10H), 1.18 (d, *J*= 6.3 Hz, 3H). IR (KBr): 3447, 2966, 2982, 2856,

1736, 1458, 1375, 1186, 1061, 1036, 1302, 1115 cm^{-1}. HRFABMS m/z. Calcd. for $C_{10}H_{21}O_3$ ($M+H^+$): 189.1491. Found: 189.1492.

(*R*)-Decan-9-olide 3

To a solution of seco-acid **24** (96.5 mg, 0.52 mmol) and triethylamine (79 µl, 0.57 mmol) in THF (5.2 ml) was added 2,4,6-trichlorobenzoyl chloride (81 µl, 0.52 mmol) at room temperature. After being stirred for 2 h, the mixture was filtered, concentrated, and diluted with benzene (260 ml). The solution was added to a refluxing solution of 4-(*N*,*N*-dimethylamino)pyridine (317 mg, 2.58 mmol) in benzene (51.5 ml) and the whole mixture was stirred for another 2 h at the same temperature. The mixture was cooled to room temperature, quenched with aqueous H_3PO_4 (50.0 ml, 10%), and extracted with ethyl acetate. The extract was dried over $MgSO_4$ and concentrated *in vacuo*. Silica gel column chromatography of the residue (hexane-ethyl acetate= 30:1~19:1) gave **3** (35.6 mg, 41%) as an oil. $[\alpha]_D^{24}$ -37.3 (*c* 0.66, $CHCl_3$), [Lit.[11b] $[\alpha]_D^{22}$ -35.1 (*c* 1.15, $CHCl_3$)]. ^1H NMR (270 MHz): δ 4.99 (ddq, *J*= 2.6, 6.6, and 6.6 Hz, 1H), 2.48 (ddd, *J*= 2.9, 6.3, and 15.1 Hz, 1H), 2.22-1.89 (m, 3H), 1.82-1.68 (m, 1H), 1.63-1.30 (m, 8H), 1.26 (d, *J*= 6.6 Hz, 3H), 1.13-0.98 (m, 1H). IR (KBr): 3491, 2934, 2959, 2868, 1726, 1647, 1467, 1364, 1167, 1146, 1078, 1049, 970 cm^{-1}. HREIMS m/z. Calcd. for $C_{10}H_{18}O_2$: 170.1307 Found: 170.1304.

(*Z*)-Tridec-2-en-4-yne 25

Compound **25** was prepared in 22% from 1-decyne and (*Z*)-1-bromopropene in a similar manner to that described for the preparation of **6**. **25**: a liquid. ^1H NMR (270 MHz): δ 5.88 (dq, *J*= 6.6 and 10.6 Hz 1H), 5.46 (dtq, *J*= 1.7, 2.1, and 10.6 Hz, 1H), 2.34 (dt, *J*= 2.1 and 6.9 Hz, 2H), 1.85 (dd, *J*= 1.7 and 6.6 Hz, 3H), 1.60-1.18 (m, 12H), 0.88 (t, *J*= 6.8 Hz, 3H). IR (KBr): 3445, 3028, 2957, 2928, 1647, 1458, 1362, 721, 667 cm^{-1}. HREIMS m/z. Calcd. for $C_{13}H_{22}$: 178.1722. Found: 178.1720.

A mixture of (2*S*,3*R*)- and (2*S*,3*S*)-2,3-epoxy-4-tridecynes 26

Compound **26** was prepared in 84% from (*Z*)-tridec-2-en-4-yne in a similar manner to that described for the preparation of **7**. **26**: an oil. IR (KBr): 3449, 2957, 2930, 2856, 2239, 1638, 1458, 1379, 1350, 1325, 1144, 1020, 934, 847, 745, 667 cm^{-1}. Anal. Calc. for $C_{13}H_{22}O$: C, 80.35; H, 11.41. Found: C, 80.17; H, 11.17.

(*S*)-4-Tridecyn-2-ol 27

Compound **27** was prepared in 83% from **26** in a similar manner to that described for the preparation of **8**. **8**: an oil. **27**: a liquid. $[\alpha]_D^{26}$ +8.96 (*c* 1.28, $CHCl_3$). ^1H NMR (270 MHz): δ 3.90 (ddq, *J*= 5.0, 6.3, and 6.8 Hz, 1H), 2.36 (ddt, *J*= 2.5, 5.0, and 16.2 Hz, 1H), 2.27 (ddt, *J*= 2.3, 6.8, and 16.2 Hz, 1H), 2.17 (ddt, *J*= 2.3, 2.5, and 6.9 Hz, 2H), 1.68 (br s, 1H), 1.54-1.17 (m, 12H), 1.24 (d, *J*= 6.3 Hz, 3H), 0.88 (t, *J*= 6.6 Hz, 3H). IR (KBr): 3422, 2959, 2928, 2856, 1638, 1458, 1377, 1215, 1117, 1086, 941, 721, 667, 503 cm^{-1}. HREIMS m/z. Calcd. for $C_{13}H_{24}O$: 196.1827. Found: 196.1819.

(*S*)-2-Acetoxy-4-tridecyne 28

To a solution of **27** (160 mg, 0.83 mmol) in dichloromethane (3.3 ml) were added triethylamine (136 µl, 0.98 mmol), 4-(*N*,*N*-dimethylamino)pyridine (cat. amount), and acetic anhydride (92 µl, 0.98 mmol) at 0 °C and gradually raised to room temperature. After being stirred for 5.5 h at the same temperature, the mixture was quenched with water, extracted with dichloromethane, dried over $MgSO_4$, and concentrated. The residue was purified by column chromatography (SiO_2, pentane-ether= 1:0~19:1) to give **28** (186 mg, 95%) as an oil. The enantiomeric excess was determined to be 90% by ^1H NMR analysis [400 MHz, Eu(hfc)$_3$ in C_6D_6]. $[\alpha]_D^{26}$ -18.7 (*c* 1.11, $CHCl_3$). ^1H NMR (270 MHz): δ 4.95 (ddq, *J*= 5.5, 6.3, and 6.6 Hz, 1H), 2.42 (ddt, *J*=

2.6, 5.5, and 16.5 Hz, 1H), 2.39 (ddt, *J*= 2.3, 6.6, and 16.5 Hz, 1H), 2.14 (ddt, *J*= 2.3, 2.6, and 6.9 Hz, 2H), 2.04 (s, 3H), 1.53-1.18 (m, 12H), 1.20 (d, *J*= 6.3 Hz, 3H), 0.88 (t, *J*= 6.6 Hz, 3H). IR (KBr): 3449, 2932, 2856, 1742, 1638, 1458, 1373, 1242, 1132, 1061, 1015, 957, 723, 667, 608 cm^{-1}. HREIMS m/z. Calcd. for $C_{15}H_{27}O_2$ (M+H+): 239.2011. Found: 239.1999.

(*S*)-2-Acetoxytridecane 4

A mixture of **28** (15.0 mg, 0.065 mmol) and 10% Pd/C (3.0 mg) in ether (2.0 ml) was placed under hydrogen and stirred for 15 h at room temperature. The mixture was filtered through a pad of Celite and concentrated. The residue was purified by column chromatography (SiO_2, pentane/ether= 1/0 to 40/1) to give **4** (13.3 mg, 84%) as an oil. $[\alpha]_D^{23}$ +3.42 (*c* 0.94, hexane), [Lit.[12a] $[\alpha]_D^{23}$ +4.6 (*c* 0.57, hexane)]. ^1H NMR (270 MHz): δ 4.94-4.83 (m, 1H), 2.03 (s, 3H), 1.53-1.18 (m, 20H), 1.20 (d, *J*= 6.3 Hz, 3H), 0.88 (t, *J*= 6.8 Hz, 3H). IR (KBr): 3454, 2926, 2856, 2683, 2683, 1740, 1638, 1468, 1373, 1244, 1126, 1022, 953, 721, 667, 610 cm^{-1}. HREIMS m/z. Calcd. for $C_{15}H_{31}O_2$ ($M+H^+$): 243.2324. Found: 243.2330.

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References and Note

1) a) Sasaki, H.; Irie, R.; Katsuki, T. *Synlett*, **1994**, 356-358. b) Sasaki, H.; Irie, R.; Hamada, T.; Suzuki, K.; Katsuki, T. *Tetrahedron*, **1994**, *50*, 11827-11838. c) Fukuda, T.; Irie, R.; Katsuki, T. *Synlett*, **1995**, 197-198.

2) Some preliminary results of this research have been communicated: Hamada, T.; Daikai, K.; Irie, R.; Katsuki, T. *Synlett*, **1995**, 407.

3) Isolation: a) Millar, J. G.; Pierce, Jr., H. D.; Pierce, A. C.; Oehlschlager, A. C.; Borden, J. H.; Barak, A. V. *J. Chem. Ecology*, **1985**, *11*, 1053-1070.
Synthesis: b) Millar, J. G.; Oehlschlager, A. C.; Wong, J. W. *J. Org. Chem.*, **1983**, *48*, 4404-4407. c) Sakai, T.; Hamamoto, H.; Mori, K. *Agric. Biol. Chem.*, **1986**, *50*, 1621-1627.

4) Rossi, R.; Carpita, A.; Lezzi, A. *Tetrahedron*, **1984**, *40*, 2773-2779.

5) Compound **4** was converted into the corresponding 3,5-dinitrobenzoate and recrystallized from various solvents. However, no enhancement of the enantiomeric excess was observed.

6) Brown, C. A.; Yamashita, A. *J. Chem. Soc., Chem. Commun.*, **1976**, 959-960.

7) Oikawa, Y.; Yoshioka, T.; Yonemitsu, O. *Tetrahedron Lett.*, **1982**, *23*, 885-888.

8) Kraus, G. A.; Tashner, M. J. *J. Org. Chem.*, **1980**, *45*, 1175-1176.

9) Brown, C. A.; Ahuja, V. K. *J. Chem. Soc., Chem. Commun.*, **1973**, 553-554.

10) Inanaga, J.; Hirata, K.; Saeki, H.; Katsuki, T.; Yamaguchi, M. *Bull. Chem. Soc. Jpn.*, **1979**, *52*, 1989-1993.

11) Isolation: a) Moore, B. P.; Brown, W. V. *Aust. J. Chem.*, **1976**, *29*, 1365-1374.
Synthesis: b) Kitahara, T.; Koseki, K.; Mori, K. *Agric. Biol. Chem.*, **1983**, *47*, 389-393. c) Jones, G. B.; Chapman, B. J.; Huber, R. S.; Beaty, R. *Tetrahedron: Asymmetry*, **1994**, *5*, 1199-1202.

12) Isolation: a) Bartelt, R. J.; Schander, A. M.; Jackson, L. L. *J. Chem. Ecology*, **1989**, *15*, 399-411.
Synthesis: b) Ender, D.; Plant, A. *Liebigs Ann. Chem.*, **1991**, 1241-1243.

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