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Absolute stereochemistry of amphidinolide C: synthesis of C-1–C-10 and C-17–C-29 segments

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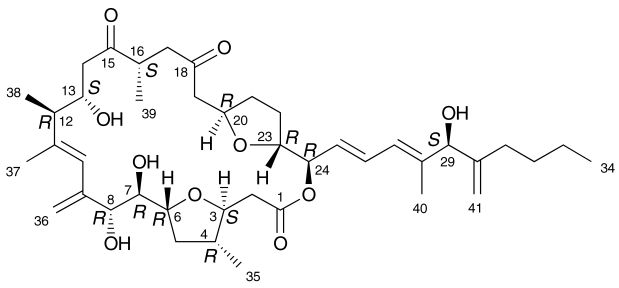
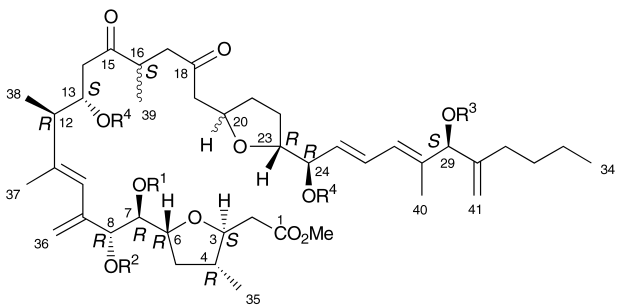
Abstract—Two of each diastereomers of the C-1–C-10 and C-17–C-29 segments of amphidinolide C (**1**) were synthesized. Comparing the ^{1}H NMR chemical shifts of its MTPA esters with those of linear methyl ester of **1**, the absolute configurations at C-7, C-8, C-20, C-23, and C-24 in amphidinolide C (**1**) were confirmed to be all *R*.

1. Introduction

Amphidinolides are a series of cytotoxic macrolides possessing unique structural features isolated from laboratory-cultured marine dinoflagellates *Amphidinium* sp.[1] Amphidinolide C (**1**), obtained from the marine dinoflagellate *Amphidinium* sp. (Y-5), is unique 25-membered macrolides having two tetrahydrofuran rings and vicinally-located one-carbon branches, of which the gross structure has been elucidated by 2D NMR data.[2] An *erythro* relationship for the C-7–C-8 bond was deduced from analysis of the NOESY spectrum of the 7,8-*O*-isopropylidene derivative of **1**.[3] On the other hand, the relative stereochemistry of H-20/H-23 and H-23/H-24 was assigned to be *anti* and *threo*, respectively, from analysis of the NOESY spectrum of **1**.[4] Recently, relatively large amounts of amphidinolide C (**1**) have been isolated from three strains (Y-56, Y-59, and Y-71) of the genus *Amphidinium*, which were separated from the inside cells of the marine acoel flatworms *Amphiscolops* sp. This sample allowed us to apply the elucidation of the absolute configurations of 12 chiral centers in **1**.[5] The absolute configurations at C-12, C-13, C-20, C-23, and C-29 were assigned as *R*, *S*, and *S* by *J*-based configuration analysis[6] and the modified Mosher's method.[7] 3*S*, 4*R*, 6*R*, and 16*S*-configurations were determined by comparison of the ^{1}H NMR spectra of the C-1–C-7 and C16–C-18 segments obtained by oxidative degradation of **1** with those of the synthetic segments. For the absolute stereochemistry of C-7 and C-8, the Mosher's method for *erythro*-glycol proposed by Kusumi et al.[8] was applied.



1



2: $R^1 = R^2 = R^3 = R^4 = (S)$-MTPA

3: R^1, $R^2 = C(CH_3)_2$, $R^3 = C(CH_3)_2OCH_3$, $R^4 = (S)$-MTPA

Here, we synthesized two of each diastereomers of the C-1–C-10 (**4a** and **4b**) and C-17–C-29 segments (**6a** and **6b**) of amphidinolide C (**1**) and compared the ^{1}H NMR chemical shifts of their α-methoxy-α-trifluoromethylphenylacetyl (MTPA) esters with those of pentakis- and bis-MTPA esters (**2** and **3**, respectively) of the linear methyl ester of **1**.

Keywords: amphidinolide C; α-methoxy-α-trifluoromethylphenylacetyl; acetonide.

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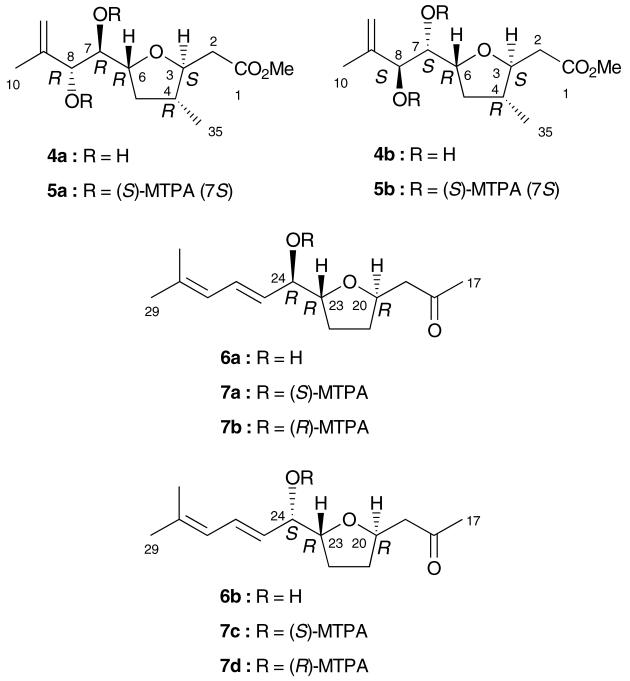
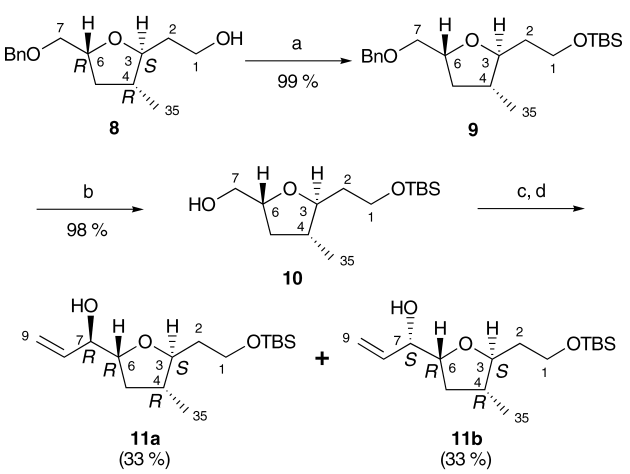


2. Results and discussion

The C-1–C-10 segments (**4a** and **4b**) were synthesized from tetrahydrofuran **8**,[5] which was prepared from D-glutamic acid. The hydroxyl group of **8** was protected with TBDMS group, and then the benzyl group in **9** was removed by hydrogenolysis to afford alcohol **10** (Scheme 1). Oxidation of **10** with Dess–Martin periodinane[9] followed by treatment of the corresponding aldehyde with vinylmagnesium bromide (vinylMgBr) afforded 1:1 mixture of **11a** and **11b**, which was separated by silica gel column chromatography. The absolute configurations at C-7 in **11b** was determined as *S* by a modified Mosher's method (selective $\Delta\delta$ values; H_2-5: +0.10 and +0.04, H-6: +0.07, H-8: −0.08, H_2-9: −0.10 and −0.06). Thus, **11a** possessed 7*R*-configuration. The 7*R*-alcohol **11a** were converted into a



Scheme 1. *Reagents and conditions*: (a) TBSCl, imidazole, DMF, rt, 1 h; (b) H_2, Pd–C, EtOH, rt, 6 h; (c) Dess–Martin periodinane, $NaHCO_3$, CH_2Cl_2, rt, 30 min; (d) vinylMgBr, THF, 0°C, 1 h.

TES ester **12a**, and treatment of the terminal olefin in **12a** with OsO_4 and then $NaIO_4$ afforded an aldehyde, which was subjected to Grignard reaction with isopropenylmagnesium bromide (isopropenylMgBr) to afford 7,8-*erythro* and *threo* diols (**13a** and **13b**, respectively) (Scheme 2). The absolute configuration at C-8 in major isomer **13a** was determined as *R* by a modified Mosher's method (selective $\Delta\delta$ values; H-6: −0.11, H_3-10: +0.14, H_2-36:+0.14 and +0.08) as well as NOE data of its 7,8-*O*-isopropylidene acetal **15a**. Two-step oxidation of **14a** and then methylation with trimethylsilyldiazomethane ($TMSCHN_2$) afforded methyl ester **15a**. Finally acetonide of **15a** was hydrolyzed to afford the (7*R*,8*R*)-C-1–C-10 segment (**4a**), which was then transformed into the bis-(*S*)-MTPA ester (**5a**) with 3*S*-, 4*R*-, 6*R*-, 7*S*-, and 8*R*-configurations. The (7*S*,8*S*)-C-1–C-10 segment (**4b**) and its (*S*)-MTPA ester **5b** were also synthesized from **12b** by the same procedures as describe above.

The proton chemical shifts of the two diastereomers **5a** and **5b** were compared with those of the corresponding portion in **2**. Subtraction of the chemical shift values of synthetic segments from those of **2** shown in Figure 1. Though they were similar to each other, differences were observed for the chemical shifts for signals due to H-5, H-6, and H-7. The ^1H NMR profile of the C-1–C-10 portion in **2** was close to that of **5a** possessing 7*S*- and 8*R*-configurations rather than that of (7*R*,8*S*)-**5b**. Therefore, the absolute configurations at C-7 and C-8 in amphidinolide C (**1**) were demonstrated to be both *R*, corresponding to the previous results.

The C-17–C-29 segments of **1** were synthesized from (*R*)-5-benzyloxymethyl-γ-butyrolactone (**16**), which was prepared from D-glutamic acid.[5] Two-carbon elongation of **16** with Wittig reaction afforded *E*-olefin **17** in two steps (Scheme 3). The unsaturated ester **17** was converted into a tetrahydrofuran by treatment with TBAF in THF through Michael addition.[10] After the ester carbonyl group was reduced by DIBAL-H, protection of the hydroxyl group with TBDMSCl and deprotection of the benzyloxy group by hydrogenation using palladium–charcoal (Pd–C) in EtOH afforded a 1:1 mixture of **18a** and its 20*R*-isomer **18b**, which was separated by silica gel column chromatography. Relative stereochemistry between H-20 and H-23 of **18a** and **18b** was elucidated to be *anti* and *syn*, respectively, by NOESY correlations (**18a**: H_2-19/H-23 and H-20/H_2-24, **18b**: H-20/H-22). The alcohol **18a** was then subjected to Parikh–Doering oxidation[11] and the resultant aldehyde was treated with vinylmagnesium bromide to afford a 1:1 mixture of **19a** and **19b**, which was separated by silica gel column chromatography. Absolute configuration at C-24 in

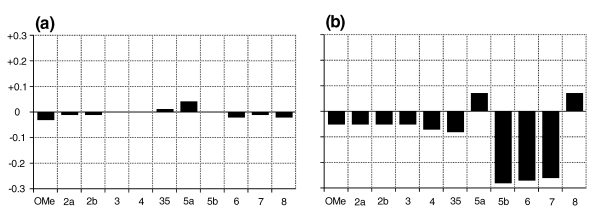
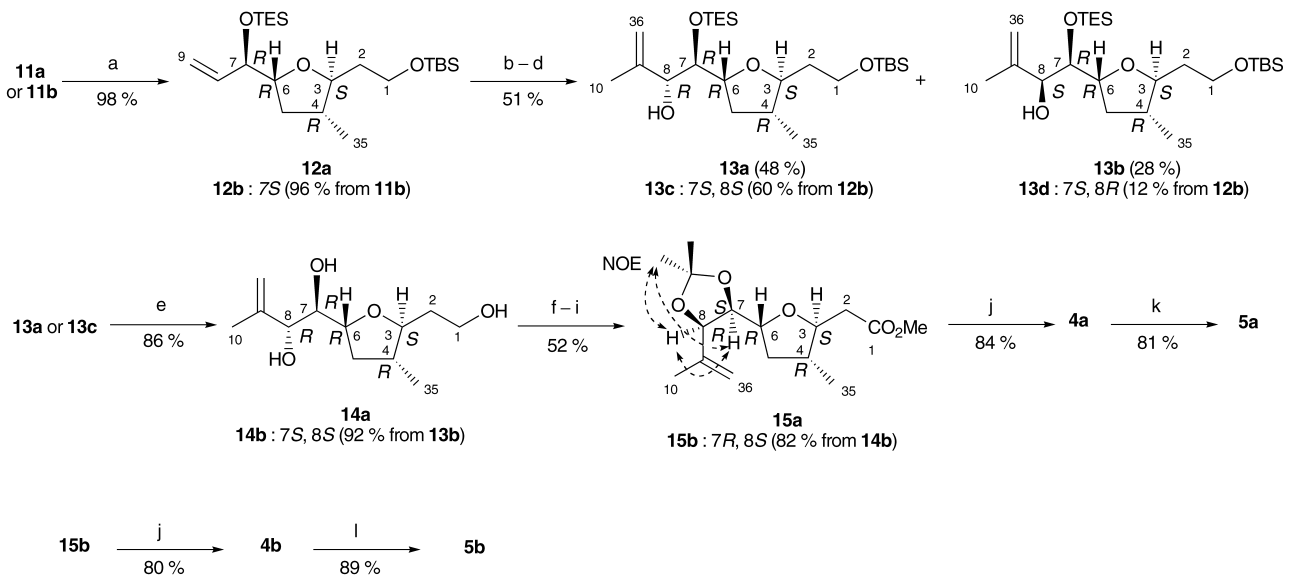


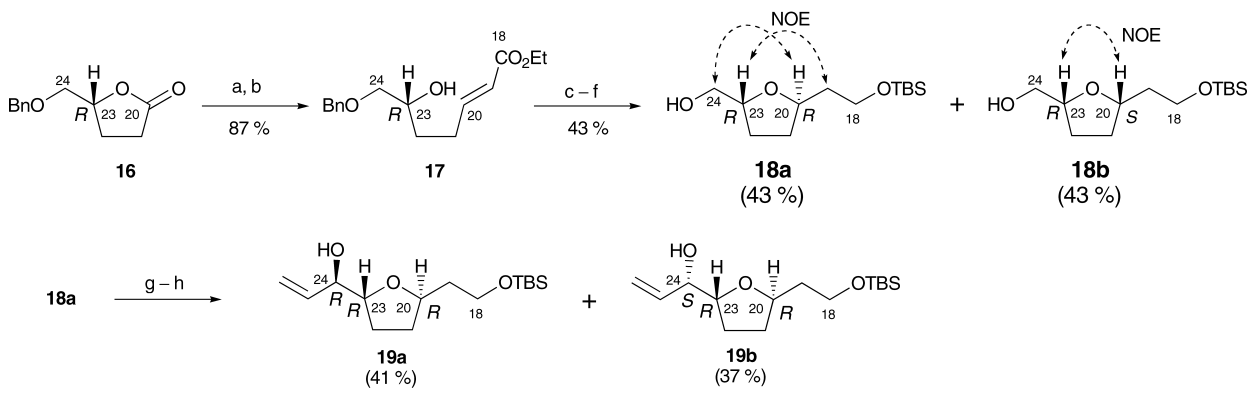
Figure 1. Graphs for differences between proton chemical shifts of pentakis-(*S*)-MTPA ester (**2**) derived from amphidinolide C (**1**) and those of synthetic (a) (7*S*,8*R*)- and (b) (7*R*,8*S*)-C-1–C-10 segments [**5a** and **5b**, respectively]. The *x* and *y* axes represent proton number and $\Delta\delta$ [δ(**2**)−δ(synthetic segments) in ppm], respectively.



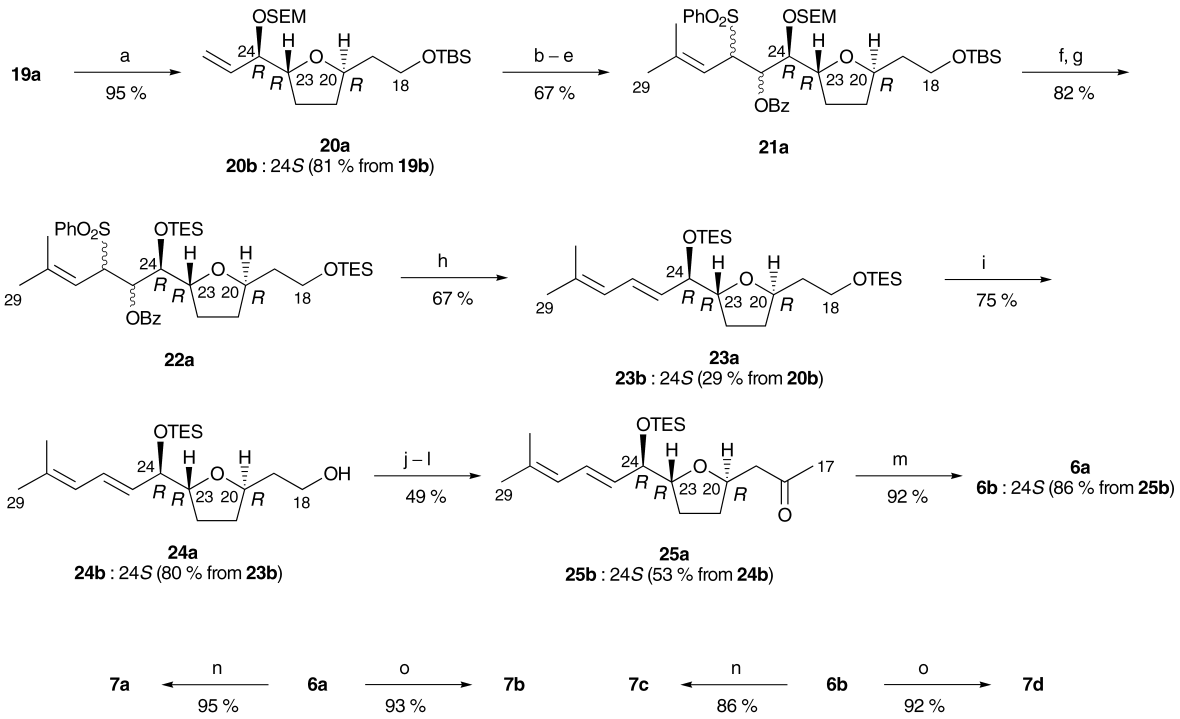
Scheme 2. *Reagents and conditions*: (a) TESCl, imidazole, DMF, rt, 3 h; (b) OsO_4, NMO, acetone, H_2O, rt, 16 h; (c) $NaIO_4$, THF–phosphate buffer (1:1), 0°C, 1 h; (d) isopropenylMgBr, THF, −78°C, 30 min; (e) AcOH–H_2O–THF (3:1:1), rt, 6 h; (f) 2,2-dimethoxypropane, PPTS, acetone, rt, 1 h; (g) DMSO, SO_3–pyridine, Et_3N, CH_2Cl_2, rt, 1 h; (h) $NaClO_2$, NaH_2PO_4, 2-methyl-2-butene, *t*-BuOH–H_2O (4:1), 0°C, 1 h; (i) $TMSCHN_2$, MeOH, 0°C, 1 h; (j) PPTS, MeOH, 55°C, 5 h; (k) (*R*)-MTPACl, DMAP, Et_3N, CH_2Cl_2, rt, 1 h; (l) (*S*)-MTPACl, DMAP, Et_3N, CH_2Cl_2, rt, 1 h.

19a was determined as *R* by modified Mosher's method (selective $\Delta\delta$ values; H_2-22: −0.07 and −0.06, H-23: −0.01, H-25: +0.17, H_2-26: +0.14 and +0.08). The hydroxyl group of **19a** was converted into 2-(trimethylsilyl)ethoxymethyl (SEM) ethers **20a** (Scheme 4). Treatment of the terminal olefin in **20a** with OsO_4 and then $NaIO_4$ resulted in generation of an aldehyde, which was condensed with (3-methyl-2-butene-1-sulfonyl)benzene[12] using Julia coupling[13] to afford a diastereomeric mixture of β-hydroxy sulfones. Protection of the resultant hydroxyl group with benzoyl chloride (BzCl) converted the mixture of alcohols into a mixture of β-benzoyloxy sulfones **21a**. In this stage, SEM and TBDMS groups were deprotected by treatment of **21a** with trifluoroacetic acid in CH_2Cl_2 at 0°C, and then two hydroxyl groups were protected by triethylsilyl chloride (TESCl) to afford a bis-TES ether **22a**, since removal of the SEM group was troublesome in later steps. To form a diene unit, the resultant bis-TES ether **22a** was treated with sodium amalgam [Na(Hg)] to afford an *E*-olefin **23a**. In this stage, the *Z*-isomer of **23a** was not obtained. The TES group on C-18 of **23a** was removed selectively by treatment with AcOH–THF–H_2O (1:20:20) at 0°C to afford **24a**. The hydroxyl group of **24a** was oxidized by Parikh–Doering procedure and then the resultant aldehyde was treated with MeMgBr to afford an alcohol with the terminal carbon elongation, which was oxidized again to afford ketone **25a**. The TES group at C-24 of **25a** was carefully deprotected by treatment with AcOH–THF–H_2O (1:10:10) at 0°C to afford the (20*R*,23*R*,24*R*)-C-17–C-29 segment (**6a**). Finally, the segment **6a** was transformed into (*R*)- and (*S*)-MTPA esters (**7a** and **7b**, respectively). The (20*R*,23*R*,24*S*)-C-17–C-29 segment (**6b**) and its (*R*)- and (*S*)-MTPA esters (**7c** and **7d**, respectively) were also synthesized by similar procedures from the 24*S*-isomer (**19b**) of **19a**.

The ^1H NMR profiles of four diastereomers (**7a**–**d**) were compared with that of the corresponding portion in **3**, which was derived by four-step conversion of amphidinolide C (**1**): actonization of C-7 and C-8 and protection of C-29, hydrolysis of a ester carbonyl group, and esterification of hydroxyl groups at C-13 and C-24 with (*R*)-MTPACl. The ^1H NMR profiles of the C-17–C-29 portion in **3** were close



Scheme 3. *Reagents and conditions*: (a) DIBAL-H, CH_2Cl_2, −78°C, 1 h; (b) $Ph_3P{=}CHCO_2Et$, benzene, 55°C, 16 h; (c) TBAF, THF, rt, 1 h; (d) DIBAL-H, CH_2Cl_2, −78°C, 1 h; (e) TBDMSCl, imidazole, DMF, rt, 3.5 h; (f) H_2, Pd–C, EtOH, rt, 6 h; (g) SO_3-pyridine, DMSO, Et_3N, CH_2Cl_2, 0°C then rt, 20 min; (h) vinylMgBr, THF, 0°C, 1 h.



Scheme 4. *Reagents and conditions*: (a) (i) SEMCl, *i*-Pr_2NEt, CH_2Cl_2, rt, 4 h; (b) OsO_4, NMO, acetone–H_2O (8:1), rt, 19 h; (c) $NaIO_4$, THF–phosphate buffer (1:1), 0°C then rt, 1 h; (d) $(CH_3)_2C{=}CHCH_2SO_2Ph$, BuLi, THF, −78°C, 2 h, then rt, 1 h; (e) BzCl, DMAP, Et_3N, CH_2Cl_2, rt, 20 h; (f) TFA, CH_2Cl_2, 0°C, 30 min; (g) TESCl, imidazole, DMF, rt, 3 h; (h) Na(Hg), Na_2HPO_4, THF–MeOH (3:1), −20°C, 1 h; (i) AcOH–H_2O–THF (1:20:20), 0°C, 1 h; (j) SO_3–pyridine, DMSO, Et_3N, CH_2Cl_2, 0°C then rt, 30 min; (k) MeMgBr, THF, 0°C, 1 h; (l) SO_3-pyridine, DMSO, Et_3N, CH_2Cl_2, rt, 30 min; (m) AcOH–H_2O–THF (1:10:10), 0°C, 4 h; (n) (*R*)-MTPACl, DMAP, Et_3N, CH_2Cl_2, rt, 16 h; (o) (*S*)-MTPACl, DMAP, Et_3N, CH_2Cl_2, rt, 16 h.

to those of **7a** rather than those of **7b**–**d**, suggesting that **3** possessed 20*R*-, 23*R*-, and 24*R*-configurations. Therefore, the absolute configurations at C-20, C-23 and C-24 in amphidinolide C (**1**) were concluded as *R*, *R*, and *R*, respectively as estimated previously (Fig. 2).

In conclusion, the absolute configurations at C-7, C-8, C-20, C-23, and C-24 in amphidinolide C (**1**) were reinvestigated on the basis of synthesis of the diastereomers corresponding to the C-1–C-10 and C-17–C-29 portions in the derivatives (**2** and **3**, respectively) of **1** and comparison of their ^1H NMR chemical shifts with those of **2a** and **2b**. As a result, the absolute configurations at C-7, C-8, C-20, C-23, and C-24 in amphidinolide C (**1**) were concluded as all *R* unambiguously.

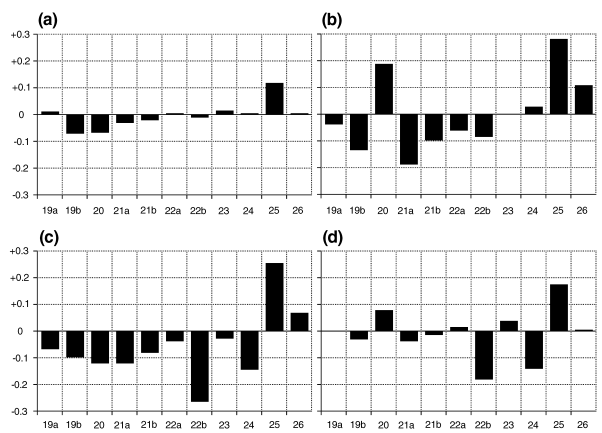


Figure 2. Graphs for differences between proton chemical shifts of bis-(*S*)-MTPA ester (**3**) derived from amphidinolide C (**1**) and those of synthetic (a) (*S*)- and (b) (*R*)-MTPA ester of (24*S*)- and (c) (*S*)- and (d) (*R*)-MTPA ester of (24*R*)-C-17–C-29 segments [**7a**–**d**, respectively]. The *x* and *y* axes represent proton number and $\Delta\delta$ [δ(**3**)−δ(synthetic segments) in ppm], respectively.

3. Experimental

3.1. General experimental procedures

^1H, ^{13}C, and 2D NMR spectra were recorded on a Bruker AMX-500 and 600 spectrometers at 300 K. FABMS spectra were recorded on a JEOL JMS-HX110 using *p*-nitrobenzyl alcohol as matrix in positive mode. Positive mode electrospray ionization (ESI) mass spectra were measured on a JEOL JMS-700TZ using samples dissolved in MeOH with flow rate of 0.1 mL/min. Column chromatography (CC) was performed on silica gel (Wakogel C-200).

3.1.1. (2*S*,3*R*,5*R*)-2-[2-(*tert*-Butyldimethylsilyloxy)ethyl]-5-benzyloxymethyl-3-methyltetrahydrofuran (9). (2*S*,3*R*,5*R*)-2-(5-Benzyloxymethyl-3-methyltetrahydrofuran-2-yl)-ethanol[5] (**8**, 1.20 g, 4.79 mmol) dissolved in dry DMF (18.5 mL) was treated with TBDMSCl (1.10 g, 7.30 mmol) and imidazole (635 mg, 9.33 mmol) at rt for 1 h. After addition of saturated aqueous NH_4Cl, the mixture was extracted with Et_2O. The organic layer was washed with H_2O and brine, dried, and concentrated. The residue was purified by CC (hexane–EtOAc, 15:1) to afford compound **9** (1.72 g, 4.73 mmol, 99%) as colorless oil; $[\alpha]_D^{20}=-8°$ (*c* 1.0, $CHCl_3$); IR (neat) ν_{max} 3064, 3030, 2955, 2928, 2857, 1496, 1461, 1360, 1095, 734, and 697 cm^{-1}; ^1H NMR (500 MHz; $CDCl_3$) δ_H 0.06 (6H, s), 0.90 (9H, s), 1.02

(3H, d, J=6.6 Hz), 1.33 (1H, m), 1.67 (1H, m), 1.80 (1H, m), 1.90 (1H, m), 2.14 (1H, m), 3.44 (1H, dd, J=10.0, 4.4 Hz), 3.49 (1H, dd, J=10.0, 5.6 Hz), 3.53 (1H, m), 3.73 (1H, m), 3.80 (1H, m), 4.17 (1H, m), 4.56 (1H, d, J=12.3 Hz), 4.60 (1H, d, J=12.3 Hz), and 7.25–7.35 (5H, m); ^{13}C NMR (125 MHz; $CDCl_3$) δ_C −5.3 (2C, q), 16.4 (q), 18.3 (s), 25.9 (3C, q), 37.3 (t), 37.9 (t), 39.7 (d), 60.5 (t), 73.2 (t), 73.3 (t), 77.0 (d), 82.1 (d), 127.4 (d), 127.6 (2C, d), 128.3 (2C, d), and 138.5 (s); FABMS m/z 365 $(M+H)^+$; HRFABMS m/z 365.2483 [$(M+H)^+$, calcd for $C_{21}H_{37}O_3Si$: 365.2512].

3.1.2. {(2*R*,4*R*,5*S*)-5-[2-(*tert*-Butyldimethylsilyloxy)ethyl]-4-methyltetrahydrofuran-2-yl}-methanol (10). Compound **9** (1.70 g, 4.67 mmol) was treated with 10% Pd–C (170 mg) in EtOH (47 mL) under hydrogen atmosphere at rt for 6 h. After filtration of the catalyst, the filtrate was evaporated to afford compound **10** (1.26 g, 4.59 mmol, 98%) as colorless oil; $[\alpha]_D^{20}$=−6° (c 1.0, $CHCl_3$); IR (neat) ν_{max} 3433, 3063, 3029, 2929, 2872, 1496, 1454, 1378, 1052, 737, and 699 cm^{-1}; ^{1}H NMR (500 MHz; $CDCl_3$) δ_H 0.04 (6H, s), 0.88 (9H, s), 1.00 (3H, d, J=6.6 Hz), 1.33 (1H, m), 1.61 (1H, m), 1.79 (1H, m), 1.90 (1H, m), 2.06 (1H, m), 3.46 (1H, dd, J=11.8, 6.4 Hz), 3.49 (1H, m), 3.60 (1H, dd, J=11.8, 2.5 Hz), 3.70 (1H, m), 3.76 (1H, m), and 4.06 (1H, m); ^{13}C NMR (125 MHz; $CDCl_3$) δ_C −5.4 (2C, q), 16.3 (q), 18.2 (s), 25.9 (3C, q), 36.6 (t), 37.3 (t), 40.0 (d), 60.4 (t), 65.2 (t), 78.4 (d), and 82.0 (d); FABMS m/z 275 $(M+H)^+$; HRFABMS m/z 275.2036 [$(M+H)^+$, calcd for $C_{14}H_{31}O_3Si$: 275.2042].

3.1.3. (1*R*)- and (1*S*)-1-{(2*R*,4*R*,5*S*)-5-[2-(*tert*-Butyldimethylsilyloxy)ethyl]-4-methyltetrahydrofuran-2-yl}-2-propen-1-ol (11a and 11b). To a solution of **10** (511.2 mg, 1.86 mmol) in CH_2Cl_2 (30 mL) were added $NaHCO_3$ (950 mg) and Dess–Martin periodinane (950.5 mg, 2.24 mmol), and the mixture was stirred at rt for 30 min. The reaction was quenched by addition of saturated aqueous $Na_2S_2O_3$ (10 mL), and then the mixture was extracted with Et_2O. The organic layer was washed with H_2O and brine, dried, and concentrated. The residue was purified by CC (hexane–EtOAc, 15:1 to 10:1) to afford an aldehyde (474 mg, 1.74 mmol, 93%) as colorless oil. To a stirred solution of the aldehyde (474 mg, 1.74 mmol) in THF (5.0 mL) was added vinylMgBr (1.06 M, 5.0 mL, 5.3 mmol) in Et_2O at 0°C. After stirring for 1 h, the reaction was quenched by addition of saturated aqueous NH_4Cl, and then the mixture was extracted with Et_2O. The organic layer was washed with H_2O and brine, dried, and concentrated. The residue was purified by CC (hexane–EtOAc, 8:1 to 3:1) to afford compounds **11a** (181.4 mg, 605 μmol, 35%) and **11b** (185.2 mg, 617 μmol, 35%).

Compound **11a**. Colorless oil; $[\alpha]_D^{20}$=−23° (c 1.0, $CHCl_3$); IR (neat) ν_{max} 3459, 2956, 2930, 2857, 1462, and 1095 cm^{-1}; ^{1}H NMR (500 MHz; $CDCl_3$) δ_H 0.00 (6H, s), 0.84 (9H, s), 0.96 (3H, d, J=6.2 Hz), 1.28 (1H, m), 1.56 (1H, m), 1.75 (1H, m), 1.85 (1H, m), 2.01 (1H, m), 3.46 (1H, m), 3.63–3.74 (2H, m), 3.77 (1H, m), 3.87 (1H, m), 5.12 (1H, m), 5.30 (1H, m), and 5.72 (1H, m); ^{13}C NMR (125 MHz; $CDCl_3$) δ_C −5.4 (2C, q), 16.1 (q), 18.2 (s), 25.8 (3C, q), 37.0 (t), 37.2 (t), 40.1 (d), 60.2 (t), 75.9 (d), 80.8 (d), 81.9 (d), 116.6 (t), and 136.6 (d); FABMS m/z 301 $(M+H)^+$; HRFABMS m/z 301.2186 [$(M+H)^+$, calcd for $C_{16}H_{33}O_3Si$: 301.2199].

Compound **11b**. Colorless oil; $[\alpha]_D^{20}$=−24° (c 1.0, $CHCl_3$); IR (neat) ν_{max} 3451, 2954, 2929, 2856, 1458, and 1095 cm^{-1}; ^{1}H NMR (500 MHz; $CDCl_3$) δ_H 0.03 (6H, s), 0.87 (9H, s), 0.99 (3H, d, J=6.2 Hz), 1.53 (1H, m), 1.58 (1H, m), 1.77 (1H, m), 1.83–1.93 (2H, m), 3.53 (1H, m), 3.66–3.78 (2H, m), 3.95 (1H, m), 4.25 (1H, m), 5.14 (1H, m), 5.29 (1H, m), and 5.76 (1H, m); ^{13}C NMR (125 MHz; $CDCl_3$) δ_C −5.4 (2C, q), 16.1 (q), 18.2 (s), 25.9 (3C, q), 34.5 (t), 37.5 (t), 39.9 (d), 60.3 (t), 73.4 (d), 80.7 (d), 83.0 (d), 116.1 (t), and 136.4 (d); FABMS m/z 301 $(M+H)^+$; HRFABMS m/z 301.2211 [$(M+H)^+$, calcd for $C_{16}H_{33}O_3Si$: 301.2199].

3.1.4. (*S*)-MTPA ester of 11b. To a solution of **11b** (0.5 mg, 1.67 μmol) in CH_2Cl_2 (60 μL) were added DMAP (30 μg), Et_3N (0.13 μL), and (*R*)-(−)-MTPACl (0.23 μL) at rt, and stirring was continued for 18 h. *N*,*N*-Dimethyl-1,3-propanediamine (0.23 μL) was added, and the reaction mixture was stirred for 10 min. After addition of phosphate buffer (pH 6.85), the reaction mixture was extracted with $CHCl_3$, and then the organic layer was evaporated. The residue was purified by CC (hexane–EtOAc, 1:0 to 2:1) to afford an (*S*)-MTPA ester of **11a** (0.8 mg, 1.55 μmol, 93%) as colorless oil; ^{1}H NMR (600 MHz; $CDCl_3$) δ_H 0.05 (6H, s), 0.89 (9H, s), 0.97 (3H, d, J=6.2 Hz, H-35), 1.50 (1H, m, H-5), 1.62 (1H, m, H-2), 1.78 (1H, m, H-2), 1.89 (1H, m, H-4), 2.03 (1H, m, H-5), 3.46 (1H, brdt, J=3.1, 8.7 Hz, H-3), 3.56 (3H, s, OMe), 3.67 (1H, m, H-1), 3.77 (1H, m, H-1), 4.12 (1H, m, H-6), 5.27 (1H, brd, J=10.6 Hz, H-9), 5.31 (1H, brd, J=16.8 Hz, H-9), 5.57 (1H, dd, J=6.9, 3.7 Hz, H-7), 5.74 (1H, ddd, J=16.8, 10.6, 6.9 Hz, H-8), and 7.35–7.61 (5H, m, ph); FABMS m/z 517 $(M+H)^+$; HRFABMS m/z 517.2603 [$(M+H)^+$, calcd for $C_{26}H_{40}O_5F_3Si$: 517.2597].

3.1.5. (*R*)-MTPA ester of 11b. The (*R*)-MTPA ester of **11b** (1.5 mg, 1.5 μmol) was obtained from **11b** (0.5 mg, 1.6 μmol) in 92% yield through the same procedure as described for preparation of the (*S*)-MTPA ester of **11a**. (*R*)-MTPA ester of **11b**. ^{1}H NMR (600 MHz; $CDCl_3$) δ_H 0.04 (6H, s), 0.89 (9H, s), 0.94 (3H, d, J=6.2 Hz, H-35), 1.40 (1H, m, H-5), 1.57 (1H, m, H-2), 1.73 (1H, m, H-2), 1.83 (1H, m, H-4), 1.99 (1H, m, H-5), 3.39 (1H, brdt, J=3.1, 8.7 Hz, H-3), 3.55 (3H, s, OMe), 3.64 (1H, m, H-1), 3.71 (1H, m, H-1), 4.05 (1H, m, H-6), 5.33 (1H, brd, J=10.6 Hz, H-9), 5.41 (1H, brd, J=16.8 Hz, H-9), 5.55 (1H, dd, J=6.9, 3.7 Hz, H-7), 5.82 (1H, ddd, J=16.8, 10.6, 6.9 Hz, H-8), and 7.34–7.57 (5H, m, ph); FABMS m/z 517 $(M+H)^+$; HRFABMS m/z 517.2605 [$(M+H)^+$, calcd for $C_{26}H_{40}O_5F_3Si$: 517.2597].

3.1.6. (2*S*,3*R*,5*R*)-2-[2-(*tert*-Butyldimethylsilyloxy)ethyl]-3-methyl-5-[(1*R*)-1-(triethylsilyloxy)-2-propenyl]-tetrahydrofuran (12a). Compound **11a** (176.2 mg, 587 μmol) dissolved in dry DMF (2.0 mL) was treated with TESCl (160 μL, 0.9 mmol) and imidazole (82.6 mg, 1.21 mmol) at rt for 3 h. After evaporation of the solvent, the reaction mixture was purified by CC (hexane–EtOAc, 15:1) to afford **12a** (238.2 mg, 575 μmol, 98%). Colorless oil; $[\alpha]_D^{20}$=−3° (c 1.0, $CHCl_3$); IR (neat) ν_{max} 2955, 2876, 1457 and 1095 cm^{-1}; ^{1}H NMR (500 MHz; $CDCl_3$) δ_H 0.04 (6H, s),

0.60 (6H, q, J=8.1 Hz), 0.89 (9H, s), 0.94 (9H, t, J=8.1 Hz), 0.97 (3H, d, J=6.2 Hz), 1.34 (1H, m), 1.59 (1H, m), 1.73–1.86 (2H, m), 1.97 (1H, m), 3.41 (1H, m), 3.68 (1H, m), 3.78 (1H, m), 3.89 (1H, m), 4.10 (1H, m), 5.12 (1H, m), 5.27 (1H, m), and 5.83 (1H, m); ^{13}C NMR (125 MHz; $CDCl_3$) δ_C −5.3 (2C, q), 5.0 (3C, t), 6.7 (3C, q), 15.9 (q), 18.3 (s), 26.0 (3C, q), 36.7 (t), 37.3 (t), 39.9 (d), 60.7 (t), 76.0 (d), 81.1 (d), 82.0 (d), 115.5 (t), and 137.8 (d); FABMS m/z 415 $(M+H)^+$; HRFABMS m/z 415.3069 [$(M+H)^+$, calcd for $C_{22}H_{47}O_3Si_2$: 415.3064].

3.1.7. (2*S*,3*R*,5*R*)-2-[2-(*tert*-Butyldimethylsilyloxy)ethyl]-3-methyl-5-[(1*S*)-1-(triethylsilyloxy)-2-propenyl]-tetrahydrofuran (12b). Compound **12b** (239.5 mg, 577 μmol) was obtained from **11b** (180.1 mg, 600 μmol) in 96% yield through the same procedure as described for preparation of **12a**.

Compound **12b**. Colorless oil; $[\alpha]_D^{20}$=−21° (c 1.0, $CHCl_3$); IR (neat) ν_{max} 2956, 2863, 1458, and 1094 cm^{-1}; ^{1}H NMR (500 MHz; $CDCl_3$) δ_H 0.04 (6H, s), 0.60 (6H, q, J=8.1 Hz), 0.88 (9H, s), 0.95 (9H, t, J=8.1 Hz), 0.99 (3H, d, J=6.2 Hz), 1.35 (1H, m), 1.59 (1H, m), 1.72–1.85 (2H, m), 1.92 (1H, m), 3.47 (1H, m), 3.67 (1H, m), 3.77 (1H, m), 3.87 (1H, m), 4.23 (1H, m), 5.07 (1H, m), 5.22 (1H, m), and 5.77 (1H, m); ^{13}C NMR (125 MHz; $CDCl_3$) δ_C −5.4 (2C, q), 4.9 (3C, t), 6.8 (3C, q), 15.9 (q), 18.3 (s), 26.0 (3C, q), 34.9 (t), 37.6 (t), 39.9 (d), 60.8 (t), 75.5 (d), 81.2 (d), 82.6 (d), 114.9 (t), and 138.7 (d); FABMS m/z 415 $(M+H)^+$; HRFABMS m/z 415.3058 [$(M+H)^+$, calcd for $C_{22}H_{47}O_3Si_2$: 415.3064].

3.1.8. (1*R*,2*R*)- and (1*R*,2*S*)-1-{(2*R*,4*R*,5*S*)-5-[2-(*tert*-Butyldimethylsilyloxy)ethyl]-4-methyltetrahydrofuran-2-yl}-3-methyl-1-triethylsilyloxy-3-buten-2-ol (13a and 13b). Compound **12a** (233.4 mg, 564 μmol) was dissolved in an 8:1 mixture (6.5 mL) of acetone and H_2O, and to this mixture were added 1% OsO_4 in t-BuOH (720 μL, 28 μmol) and NMO (132.2 mg, 1.13 mmol). After stirring at rt for 16 h, the reaction was quenched by addition of saturated aqueous $NaHSO_3$, and then the mixture was extracted with EtOAc. The organic layer was washed with brine, dried, and concentrated. The residue was purified by CC (hexane–EtOAc, 5:1 to 3:1) to afford a mixture of diols (245.7 mg, 547 μmol, 97%) as colorless oil. To a stirring solution of the mixture of diols (79.5 mg, 177 μmol) in a 1:1 mixture (1.6 mL) of THF and potassium phosphate buffer (pH 6.8) was added $NaIO_4$ (56.8 mg, 404 μmol) at 0°C. After stirring at 0°C for 1 h, the mixture was extracted with Et_2O. The organic layer was washed with brine, dried, and concentrated. The residue was purified by CC (hexane–EtOAc, 20:1 to 10:1) to afford an aldehyde (71.3 mg, 171 μmol, 97%) as colorless oil. To a stirred solution of the aldehyde (71.3 mg, 171 μmol) in THF (0.8 mL) was added isopropenylMgBr (0.675 M, 1.6 mL, 1.08 mmol) in THF at −78°C. After stirring for 30 min, the reaction was quenched by addition of saturated aqueous NH_4Cl and then the mixture was extracted with Et_2O. The organic layer was washed with H_2O and brine, dried, and concentrated. The residue was purified by CC (hexane–EtOAc, 8:1 to 3:1) to afford **13a** (40.3 mg, 88.0 μmol, 51%) and **13b** (23.8 mg, 52.0 μmol, 30%).

Compound **13a**. Colorless oil; $[\alpha]_D^{20}$=−25° (c 1.0, $CHCl_3$); IR (neat) ν_{max} 3480, 2955, 2877, 1456, 1378, and 1096 cm^{-1}; ^{1}H NMR (500 MHz; $CDCl_3$) δ_H 0.05 (6H, s), 0.65 (6H, q, J=8.1 Hz), 0.88 (9H, s), 0.98 (9H, t, J=8.1 Hz), 1.00 (3H, d, J=6.2 Hz), 1.53–1.63 (2H, m), 1.74 (3H, s), 1.75–1.84 (2H, m), 1.97 (1H, dt, J=11.8, 6.5 Hz), 3.54 (1H, dt, J=2.4, 9.3 Hz), 3.68 (2H, m), 3.76 (1H, ddd, J=10.0, 8.1, 5.0 Hz), 4.06 (1H, ddd, J=9.3, 6.2, 3.1 Hz), 4.14 (1H, d, J=3.7 Hz), 4.92 (1H, s), and 5.09 (1H, s); ^{13}C NMR (125 MHz; $CDCl_3$) δ_C 5.4 (2C, q), 5.2 (3C, t), 6.9 (3C, q), 15.9 (s), 18.3 (q), 19.4 (q), 25.9 (3C, q), 36.9 (t), 37.3 (t), 39.4 (d), 60.6 (t), 73.9 (d), 78.1 (d), 78.5 (d), 82.9 (d), 112.3 (t), and 145.0 (s); FABMS m/z 459 $(M+H)^+$; HRFABMS m/z 459.3346 [$(M+H)^+$, calcd for $C_{24}H_{51}O_4S_2$: 459.3326].

Compound **13b**. Colorless oil; $[\alpha]_D^{20}$=−10° (c 1.0, $CHCl_3$); IR (neat) ν_{max} 3484, 2955, 2875, 1453, 1376, and 1093 cm^{-1}; ^{1}H NMR (500 MHz; $CDCl_3$) δ_H 0.05 (6H, s), 0.62 (6H, q, J=8.1 Hz), 0.89 (9H, s), 0.94 (9H, t, J=8.1 Hz), 1.02 (3H, d, J=6.2 Hz), 1.30 (1H, m), 1.53 (1H, m), 1.72 (3H, s), 1.78 (1H, m), 1.88 (1H, m), 1.97 (1H, ddd, J=12.2, 6.3 Hz), 3.45 (1H, brt, J=8.9 Hz), 3.58 (1H, brd, J=6.9 Hz), 3.67 (1H, dt, J=9.6, 7.3 Hz), 3.80 (1H, ddd, J=9.9, 9.6, 7.3 Hz), 3.86 (1H, brs), 4.06 (1H, dt, J=10.0, 6.5 Hz), 4.90 (1H, s), and 5.02 (1H, s); ^{13}C NMR (125 MHz; $CDCl_3$) δ_C −5.4 (1C, q), −5.3 (1C, q), 5.2 (3C, t), 6.9 (3C, q), 16.0 (s), 18.3 (q), 19.2 (q), 25.9 (3C, q), 37.5 (t), 37.9 (t), 40.0 (d), 60.8 (t), 74.1 (d), 75.9 (d), 80.0 (d), 82.1 (d), 111.2 (t), and 145.1 (s); FABMS m/z 459 $(M+H)^+$; HRFABMS m/z 459.3308 [$(M+H)^+$, calcd for $C_{24}H_{51}O_4S_2$: 459.3326].

3.1.9. (*S*)-MTPA ester of 13a. The (*S*)-MTPA ester of **13a** (0.6 mg, 0.8 μmol) was obtained from **13a** (0.5 mg, 1.1 μmol) in 72% yield through the same procedure as described for preparation of the (*S*)-MTPA ester of **11b**. (*S*)-MTPA ester of **13a**. Colorless oil; ^{1}H NMR (600 MHz; $CDCl_3$) δ_H 0.05 (6H, s), 0.49 (6H, m), 0.86 (9H, t, J=8.1 Hz), 0.89 (9H, s), 0.97 (3H, d, J=6.9 Hz, H-35), 1.19–1.39 (2H, m), 1.50–1.65 (1H, m), 1.77 (1H, m), 1.84 (3H, s, H-10), 1.90 (1H, m, H-5), 3.37 (1H, brdt, J=2.5, 9.3 Hz, H-3), 3.56 (3H, s, OMe), 3.63–3.73 (3H, m), 3.78 (1H, m, H-6), 5.04 (1H, brs, H-36), 5.08 (1H, s, H-36), 5.41 (1H, d, J=4.4 Hz, H-8), and 7.34–7.59 (5H, m, ph); FABMS m/z 675 $(M+H)^+$; HRFABMS m/z 675.3722 [$(M+H)^+$, calcd for $C_{34}H_{58}O_6F_3Si_2$: 675.3724].

3.1.10. (*R*)-MTPA ester of 13a. The (*R*)-MTPA ester of **13a** (0.7 mg, 1.0 μmol) was obtained from **13a** (0.5 mg, 1.1 μmol) in 95% yield through the same procedure as described for preparation of the (*S*)-MTPA ester of **11b**. (*R*)-MTPA ester of **13a**. Colorless oil; ^{1}H NMR (600 MHz; $CDCl_3$) δ_H 0.05 (6H, s), 0.58 (6H, m), 0.88 (9H, s), 0.91 (9H, t, J=8.1 Hz), 0.98 (3H, d, J=6.2 Hz, H-35), 1.21–1.41 (2H, m), 1.70 (3H, s, H-10), 1.50–1.65 (1H, m), 1.74–1.88 (1H, m), 1.97 (1H, m, H-5), 3.39 (1H, brdt, J=2.5, 9.3 Hz, H-3), 3.57 (3H, s, OMe), 3.67 (1H, dt, J=10.0, 7.5 Hz, H-7), 3.74–3.82 (2H, m), 3.89 (1H, dd, J=10.0, 5.6 Hz, H-6), 4.93 (1H, s, H-36), 4.96 (1H, brs, H-36), 5.41 (1H, d, J=4.4 Hz, H-8), and 7.33–7.63 (5H, m, ph); FABMS m/z 675 $(M+H)^+$; HRFABMS m/z 675.3726 [$(M+H)^+$, calcd for $C_{34}H_{58}O_6F_3Si_2$: 675.3724].

3.1.11. (1*S*,2*S*)- and (1*S*,2*R*)-1-{(2*R*,4*R*,5*S*)-5-[2-(*tert*-Butyldimethylsilyloxy)ethyl]-4-methyltetrahydrofuran-2-yl}-3-methyl-1-triethylsilyloxy-3-buten-2-ol (13c and

13d). Compound **13c** (138.2 mg, 302 μmol) and **13d** (24.6 mg, 53.7 μmol) were obtained from **12b** (235.1 mg, 568 μmol) in 60 and 12% yield, respectively, through the same procedure as described for preparation of **13a** and **13b**.

Compound **13c**. Colorless oil; $[\alpha]_D^{20}=-12°$ (*c* 1.0, $CHCl_3$); IR (neat) ν_{max} 3470, 2955, 2930, 2867, 1472 and 1095 cm^{-1}; ^1H NMR (500 MHz; $CDCl_3$) δ_H 0.04 (6H, s), 0.64 (6H, q, *J*=8.1 Hz), 0.88 (9H, s), 0.97 (9H, t, *J*=8.1 Hz), 1.00 (3H, d, *J*=6.2 Hz), 1.59 (2H, m), 1.74 (3H, s), 1.71–1.87 (2H, m), 2.00 (1H, ddd, *J*=12.5, 6.2, 5.6 Hz), 3.43 (1H, ddd, *J*=9.0, 9.0, 3.1 Hz), 3.65 (1H, ddd, *J*=10.0, 6.9, 6.9 Hz), 3.75 (1H, ddd, *J*=10.0, 8.1, 5.0 Hz), 3.90 (1H, ddd, *J*=10.0, 5.6, 3.7 Hz), 3.94 (1H, dd, *J*=5.0, 3.7 Hz), 4.08 (1H, d, *J*=5.0 Hz), 4.88 (1H, s), and 5.07 (1H, s); ^{13}C NMR (125 MHz; $CDCl_3$) δ_C −5.3 (2C, q), 5.1 (3C, t), 6.9 (3C, q), 16.2 (s), 18.3 (q), 19.3 (q), 25.9 (3C, q), 36.4 (t), 37.7 (t), 40.1 (d), 60.7 (t), 74.3 (d), 77.5 (d), 78.4 (d), 82.0 (d), 111.8 (t), and 143.2 (s); FABMS *m/z* 459 $(M+H)^+$; HRFABMS *m/z* 459.3308 [$(M+H)^+$, calcd for $C_{24}H_{51}O_4Si_2$: 459.3326].

Compound **13d**. Colorless oil; $[\alpha]_D^{20}=-8°$ (*c* 1.0, $CHCl_3$); IR (neat) ν_{max} 3478, 2955, 2872, 1468 and 1093 cm^{-1}; ^1H NMR (500 MHz; $CDCl_3$) δ_H 0.05 (6H, s), 0.64 (6H, q, *J*=8.1 Hz), 0.89 (9H, s), 0.97 (9H, t, *J*=8.1 Hz), 1.02 (3H, d, *J*=6.2 Hz), 1.55–165 (2H, m), 1.75 (3H, s), 1.78 (1H, m), 1.84 (1H, m), 1.97 (1H, m), 3.49 (1H, brt, *J*=9.0 Hz), 3.62–3.70 (2H, m), 3.75 (1H, m), 3.88 (1H, m), 4.13 (1H, m), 4.92 (1H, s), and 5.00 (1H, s); ^{13}C NMR (125 MHz; $CDCl_3$) δ_C −5.4 (1C, q), −5.3 (1C, q), 5.2 (3C, t), 6.9 (3C, q), 16.0 (s), 16.4 (q), 18.9 (q), 25.9 (3C, q), 36.3 (t), 37.9 (t), 40.0 (d), 60.6 (t), 74.8 (d), 75.9 (d), 79.7 (d), 82.9 (d), 112.5 (t), and 144.6 (s); FABMS *m/z* 459 $(M+H)^+$; HRFABMS *m/z* 459.3313 [$(M+H)^+$, calcd for $C_{24}H_{51}O_4S_2$: 459.3326].

3.1.12. (*S*)-MTPA ester of 13c. The (*S*)-MTPA ester of **13c** (0.6 mg, 0.8 μmol) was obtained from **13c** (0.5 mg, 1.1 μmol) in 72% yield through the same procedure as described for preparation of the (*S*)-MTPA ester of **11b**. (*S*)-MTPA ester of **13c**. As colorless oil; ^1H NMR (600 MHz; $CDCl_3$) δ_H 0.04 (6H, s), 0.61 (6H, q, *J*=8.1 Hz), 0.87 (9H, s), 0.91 (9H, t, *J*=8.1 Hz), 0.98 (3H, d, *J*=6.2 Hz, H-35), 1.45–1.82 (5H, m), 1.71 (3H, s, H-10), 3.41 (1H, brdt, *J*=2.5, 8.7 Hz, H-3), 3.58 (3H, s, OMe), 3.64 (1H, dt, *J*=10.0, 7.5 Hz, H-1), 3.74 (1H, m, H-1), 3.90 (1H, m, H-6), 4.11 (1H, brt, *J*=3.7 Hz, H-7), 4.72 (1H, s, H-36), 4.86 (1H, brs, H-36), 5.36 (1H, d, *J*=4.4 Hz, H-8), and 7.34–7.60 (5H, m, ph); FABMS *m/z* 675 $(M+H)^+$; HRFABMS *m/z* 675.3712 [$(M+H)^+$, calcd for $C_{34}H_{58}O_6F_3Si_2$: 675.3724].

3.1.13. (*R*)-MTPA ester of 13c. The (*R*)-MTPA ester of **13c** (0.7 mg, 1.0 μmol) was obtained from **13c** (0.5 mg, 1.1 μmol) in 91% yield through the same procedure as described for preparation of the (*S*)-MTPA ester of **11b**. (*R*)-MTPA ester of **13c**. Colorless oil; ^1H NMR (600 MHz; $CDCl_3$) δ_H 0.04 (6H, s), 0.55 (6H, q, *J*=8.1 Hz), 0.87 (9H, s), 0.91 (9H, t, *J*=8.1 Hz), 0.98 (3H, d, *J*=6.2 Hz, H-35), 1.38 (1H, m), 1.43–1.73 (4H, m), 1.80 (3H, s, H-10), 3.36 (1H, brdt, *J*=2.5, 8.7 Hz, H-3), 3.55 (3H, s, OMe), 3.62 (1H, dt, *J*=10.0, 7.5 Hz, H-1), 3.72 (2H, m), 4.01 (1H, dd, *J*=5.6, 3.1 Hz, H-7), 5.01 (1H, brs, H-36), 5.06 (1H, s, H-36), 5.31 (1H, d, *J*=5.6 Hz, H-8), and 7.34–7.56 (5H, m, ph); FABMS *m/z* 675 $(M+H)^+$; HRFABMS *m/z* 675.3719 [$(M+H)^+$, calcd for $C_{34}H_{58}O_6F_3Si_2$: 675.3724].

3.1.14. (1*R*,2*R*)-1-[(2*R*,4*R*,5*S*)-5-(2-Hydroxyethyl)-4-methyltetrahydrofuran-2-yl]-3-methyl-3-butene-1,2-diol (14a). Compound **13a** (36.0 mg, 78.6 μmol) was dissolved in a 3:1:1 mixture (4.0 mL) of AcOH, H_2O, and THF. After stirring at rt for 6 h, the reaction was quenched by addition of $NaHCO_3$. After filtration of the insoluble material, the filtrate was concentrated. The residue was purified by CC ($CHCl_3$–MeOH, 9:1) to afford a triol **14a** (15.5 mg, 67.4 μmol, 86%). Colorless oil; $[\alpha]_D^{20}=-21°$ (*c* 1.0, $CHCl_3$); IR (neat) ν_{max} 3420, 2957, 1455, and 1053 cm^{-1}; ^1H NMR (500 MHz; $CDCl_3$) δ_H 1.03 (3H, d, *J*=6.2 Hz), 1.62 (1H, m), 1.73 (1H, m), 1.75 (3H, s), 1.83–1.95 (2H, m), 2.03 (1H, ddd, *J*=11.8, 6.2, 6.2 Hz), 3.56 (1H, dd, *J*=5.0, 2.5 Hz), 3.64 (1H, ddd, *J*=9.0, 9.0, 2.5 Hz), 3.72–3.83 (2H, m), 4.18 (1H, m), 4.97 (1H, brs), and 5.07 (1H, brs); ^{13}C NMR (125 MHz; $CDCl_3$) δ_C 15.8 (q), 18.7 (q), 36.7 (t), 36.9 (t), 39.7 (d), 60.9 (t), 72.1 (d), 77.5 (d), 77.5 (d), 85.3 (d), 112.5 (t), and 144.6 (s); FABMS *m/z* 231 $(M+H)^+$; HRFABMS *m/z* 231.1589 [$(M+H)^+$, calcd for $C_{12}H_{23}O_4$: 231.1596].

3.1.15. (1*S*,2*S*)-1-[(2*R*,4*R*,5*S*)-5-(2-Hydroxyethyl)-4-methyltetrahydrofuran-2-yl]-3-methyl-3-butene-1,2-diol (14b). Compound **14b** (59.9 mg, 260 μmol) was obtained from **13b** (130.2 mg, 284 μmol) in 92% yield through the same procedure as described for preparation of **14a**.

Compound **14b**. Colorless oil; $[\alpha]_D^{20}=-4°$ (*c* 1.0, $CHCl_3$); IR (neat) ν_{max} 3425, 2956, 2930, 2860, 1460, and 1054 cm^{-1}; ^1H NMR (500 MHz; $CDCl_3$) δ_H 1.05 (3H, d, *J*=6.2 Hz), 1.57–1.70 (2H, m), 1.79 (3H, s), 1.87 (1H, m), 1.93 (1H, m), 2.22 (1H, m), 3.63 (1H, dt, *J*=2.5, 9.3 Hz), 3.65 (1H, brt, *J*=6.5 Hz), 3.78 (2H, m), 4.07 (1H, dt, *J*=9.3, 6.2 Hz), 4.12 (1H, d, *J*=6.9 Hz), 5.01 (1H, s), and 5.06 (1H, s); ^{13}C NMR (125 MHz; $CDCl_3$) δ_C 16.0 (q), 17.9 (q), 35.7 (t), 37.0 (t), 39.9 (d), 61.3 (t), 72.6 (d), 77.9 (d), 79.9 (d), 85.4 (d), 114.0 (t), and 144.3 (s); FABMS *m/z* 231 $(M+H)^+$; HRFABMS *m/z* 231.1602 [$(M+H)^+$, calcd for $C_{12}H_{23}O_4$ 231.1596].

3.1.16. Methyl {(2*S*,3*R*,5*R*)-5-[(1*S*,2*R*)-1,2-isopropylidenedioxy-3-methyl-3-butenyl]-3-methyltetrahydrofuran-2-yl}-acetate (15a). Compound **14a** (10.3 mg, 44.8 μmol) was dissolved in acetone (1.5 mL) and treated with 2,2-dimethoxypropane (0.5 mL) and PPTS (12 mg) at rt for 1 h. After addition of H_2O, the reaction mixture was extracted with EtOAc. The organic layer was washed with brine, dried, and evaporated to afford an acetonide (9.7 mg, 35.9 μmol, 80%): ^1H NMR (500 MHz; $CDCl_3$) δ_H 1.01 (3H, d, *J*=6.2 Hz), 1.35 (1H, m), 1.39 (3H, s), 1.54 (3H, s), 1.64 (1H, m), 1.77 (3H, s), 1.82–1.93 (2H, m), 2.08 (1H, ddd, *J*=12.5, 6.2, 6.2 Hz), 3.61 (1H, ddd, *J*=8.7, 8.7, 3.1 Hz), 3.73–3.83 (2H, m), 4.00 (1H, ddd, *J*=9.3, 5.6, 5.6 Hz), 4.09 (1H, dd, *J*=6.9, 5.6 Hz), 4.57 (1H, d, *J*=6.9 Hz), 4.98 (1H, s), and 5.09 (1H, s); ^{13}C NMR (125 MHz; $CDCl_3$) δ_C 9.1 (q), 13.3 (q), 18.6 (q), 20.0 (q), 28.3 (t), 31.1 (t), 32.9 (d), 54.8 (t), 69.8 (d), 73.4 (d), 73.9 (d), 79.3 (d), 102.0 (s), 106.8 (t), and 134.1 (s); FABMS *m/z* 271 $(M+H)^+$; HRFABMS *m/z* 271.1918 [$(M+H)^+$, calcd for $C_{14}H_{24}O_4$ 271.1909].

To a solution of the acetonide (6.0 mg, 22.2 μmol) dissolved in a mixture of DMSO (74.5 μL), CH_2Cl_2 (451 μL) and Et_3N (25.9 μL) was added SO_3-pyridine complex (20.5 mg, 129 μmol) at 0°C. After stirring at rt for 1 h, the solution was poured into H_2O and the aqueous layer was extracted with Et_2O. The combined organic layer was washed with H_2O and brine, dried, and concentrated to afford a crude aldehyde (6.0 mg, 22.2 μmol, quant.). To a solution of the crude aldehyde (6.0 mg) in a mixture of *t*-BuOH (1.56 mL) and H_2O (388 μL) were added 2-methyl-2-butene (2 M, 107.3 μL, 214 μmol) in THF, NaH_2PO_4 (17.4 mg), and $NaClO_2$, (15.6 mg). After stirring at 0°C for 1 h, saturated aqueous $NaHSO_3$ was added, and the mixture was extracted with EtOAc. The organic layer was washed with brine, dried, and concentrated to afford a crude carboxylic acid (5.7 mg, 20.1 μmol, 91%). To a solution of the crude carboxylic acid in MeOH (1.0 mL) was added trimethylsilyldiazomethane ($TMSCHN_2$, 2 M, 125 μL, 250 μmol) in hexanes at 0°C. After stirring at 0°C for 1 h, the solution was evaporated. The residue was purified by CC (hexane–EtOAc, 15:1) to afford a methyl ester **15a** (4.3 mg, 14.4 μmol, 72%).

Compound **15a**. Colorless oil; $[\alpha]_D^{20}=-21°$ (*c* 0.5, $CHCl_3$); IR (neat) ν_{max} 2956, 2931, 1743, 1456, and 1044 cm^{-1}; ^1H NMR (500 MHz; $CDCl_3$) δ_H 1.01 (3H, d, *J*=6.6 Hz), 1.27 (1H, m), 1.39 (3H, s), 1.54 (3H, s), 1.77 (3H, s), 1.97 (1H, m), 2.15 (1H, ddd, *J*=12.3, 6.6, 6.6 Hz), 2.51 (1H, dd, *J*=14.9, 5.7 Hz), 2.60 (1H, dd, *J*=14.9, 6.4 Hz), 3.66 (3H, s), 3.89 (1H, ddd, *J*=8.5, 6.1, 6.1 Hz), 3.97 (1H, m), 4.13 (1H, brt, *J*=7.2 Hz), 4.54 (1H, d, *J*=6.8 Hz), 4.96 (1H, s), and 4.97 (1H, s); FABMS *m/z* 299 $(M+H)^+$; HRFABMS *m/z* 299.1860 $[(M+H)^+$, calcd for $C_{15}H_{27}O_4$: 299.1859].

3.1.17. Methyl {(2*S*,3*R*,5*R*)-5-[(1*R*,2*S*)-1,2-isopropylidenedioxy-3-methyl-3-butenyl]-3-methyltetrahydrofuran-2-yl}-acetate (15b). Compound **15b** (5.3 mg, 17.7 μmol) was obtained from **14b** (5.0 mg, 21.6 μmol) in 82% yield by 4 steps through the same procedure as described for preparation of **15a**.

Compound **15b**. Colorless oil; $[\alpha]_D^{20}=+1°$ (*c* 1.0, $CHCl_3$); IR (neat) ν_{max} 2956, 2930, 2857, 1457, and 1055 cm^{-1}; ^1H NMR (500 MHz; $CDCl_3$) δ_H 1.02 (3H, d, *J*=6.4 Hz), 1.36 (3H, S), 1.45 (3H, s), 1.54 (1H, ddd, *J*=12.5, 10.9, 9.0 Hz), 1.74 (3H, s), 1.86 (1H, m), 2.17 (1H, ddd, *J*=12.7, 6.6, 6.6 Hz), 2.39 (1H, dd, *J*=14.7, 8.6 Hz), 2.48 (1H, dd, *J*=14.7, 4.0 Hz), 3.66 (3H, s), 3.81 (1H, ddd, *J*=8.6, 4.0, 4.0 Hz), 3.89 (1H, m), 4.05 (1H, dd, *J*=7.9, 6.3 Hz), 4.56 (1H, d, *J*=6.3 Hz), 4.93 (1H, s), and 5.12 (1H, s); *m/z*; FABMS *m/z* 299 $(M+H)^+$; HRFABMS *m/z* 299.1849 $[(M+H)^+$, calcd for $C_{15}H_{27}O_4$: 299.1859].

3.1.18. Methyl {(2*S*,3*R*,5*R*)-5-[(1*R*,2*R*)-1,2-dihydroxy-3-methyl-3-butenyl]-3-methyltetrahydrofuran-2-yl}-acetate (4a). To a solution of **15a** (3.3 mg, 11.1 μmol) dissolved in MeOH (504 μL) was added PPTS (3.75 mg, 0.02 mmol). After stirring at 55°C for 5 h, the solvent was evaporated. The residue was purified by CC (hexane–EtOAc, 2:1) to afford **4a** (2.4 mg, 9.3 μmol, 84%). Colorless oil; $[\alpha]_D^{20}=-42°$ (*c* 0.5, $CHCl_3$); IR (neat) ν_{max} 3433, 2957, 2922, 1732, 1456, and 1033 cm^{-1}; ^1H NMR (500 MHz; $CDCl_3$) δ_H 1.05 (3H, d, *J*=6.4 Hz), 1.74 (3H, s), 1.79 (1H, m), 1.91 (1H, m), 2.04 (1H, ddd, *J*=12.0, 6.6, 6.6 Hz), 2.43 (1H, dd, *J*=15.3, 8.6 Hz), 2.55 (1H, dd, *J*=15.3, 3.7 Hz), 3.57 (1H, dd, *J*=4.8, 2.4 Hz), 3.69 (3H, s), 3.87 (1H, ddd, *J*=8.8, 8.8, 3.7 Hz), 4.15 (1H, ddd, *J*=9.7, 6.1, 2.3 Hz), 4.20 (1H, d, *J*=4.8 Hz), 4.97 (1H, brs), and 5.07 (1H, s); FABMS *m/z* 259 $(M+H)^+$; HRFABMS *m/z* 259.1558 $[(M+H)^+$, calcd for $C_{13}H_{23}O_5$: 259.1546].

3.1.19. Methyl {(2*S*,3*R*,5*R*)-5-[(1*S*,2*S*)-1,2-dihydroxy-3-methyl-3-butenyl]-3-methyltetrahydrofuran-2-yl}-acetate (4b). Compound **4b** (2.1 mg, 8.1 μmol) was obtained from **15b** (3.0 mg, 10.1 μmol) in 80% yield through the same procedure as described for preparation of **4a**.

Compound **4b**. Colorless oil; $[\alpha]_D^{20}=-6°$ (*c* 0.5, $CHCl_3$); IR (neat) ν_{max} 3461, 2957, 2925, 1457, and 1033 cm^{-1}; ^1H NMR (500 MHz; $CDCl_3$) δ_H 1.06 (3H, d, *J*=6.6 Hz), 1.64 (1H, ddd, *J*=12.8, 11.2, 9.4 Hz), 1.79 (3H, s), 1.95 (1H, m), 2.30 (1H, ddd, *J*=12.8, 6.6, 6.6 Hz), 2.46 (1H, dd, *J*=15.4, 8.8 Hz), 2.56 (1H, dd, *J*=15.4, 3.5 Hz), 3.55 (1H, brt, *J*=7.08 Hz), 3.69 (3H, s), 3.89 (1H, ddd, *J*=8.9, 8.9, 3.5 Hz), 4.03 (1H, ddd, *J*=9.4, 6.3, 6.3 Hz), 4.15 (1H, d, *J*=7.5 Hz), 5.02 (1H, brs), and 5.05 (1H, s); FABMS *m/z* 259 $(M+H)^+$; HRFABMS *m/z* 259.1553 $[(M+H)^+$, calcd for $C_{13}H_{23}O_5$: 259.1546].

3.1.20. Bis-(*S*)-MTPA ester (5a) of 4a. Compound **5a** (1.5 mg, 2.2 μmol) was obtained from **4a** (0.7 mg, 2.7 μmol) in 81% yield through the same procedure as described for preparation of the (*S*)-MTPA ester of **11a**.

Compound **5a**. Colorless oil; ^1H NMR (600 MHz; $CDCl_3$) δ_H 0.86 (3H, d, *J*=6.4 Hz, H-35), 1.22 (1H, brdt, *J*=9.7, 11.4 Hz, H-5), 1.72 (3H, s, H-10), 1.81 (1H, m, H-4), 1.92 (1H, brdt, *J*=12.3, 6.6 Hz, H-5), 2.36 (1H, dd, *J*=14.7, 7.9 Hz, H-2), 2.46 (1H, dd, *J*=14.7, 4.4 Hz, H-2), 3.40 (3H, s, OMe), 3.51 (3H, s, OMe), 3.66 (3H, s, OMe), 3.71 (1H, brdt, *J*=4.4, 9.0 Hz, H-3), 3.81 (1H, brdt, *J*=9.7, 5.7 Hz, H-6), 5.04 (1H, brs, H-36), 5.10 (1H, s, H-36), 5.30 (1H, brt, *J*=6.0 Hz and H-7), 5.61 (1H, d, *J*=6.8 Hz, H-8), and 7.32–7.54 (10H, m, Ph); FABMS *m/z* 691 $(M+H)^+$; HRFABMS *m/z* 691.2353 $[(M+H)^+$, calcd for $C_{33}H_{37}O_9F_6$: 691.2342].

3.1.21. Bis-(*S*)-MTPA ester (5b) of 4b. Compound **5b** (1.2 mg, 1.7 μmol) was obtained from **4b** (0.5 mg, 1.9 μmol) in 89% yield through the same procedure as described for preparation of **11a**.

Compound **5b**. Colorless oil; ^1H NMR (600 MHz; $CDCl_3$) δ_H 0.86 (3H, d, *J*=6.4 Hz, H-35), 1.22 (1H, brdt, *J*=9.7, 11.4 Hz, H-5), 1.72 (3H, s, H-10), 1.81 (1H, m, H-4), 1.92 (1H, brdt, *J*=12.3, 6.6 Hz, H-5), 2.36 (1H, dd, *J*=14.7, 7.9 Hz, H-2), 2.46 (1H, dd, *J*=14.7, 4.4 Hz, H-2), 3.40 (3H, s, OMe), 3.51 (3H, s, OMe), 3.66 (3H, s, OMe), 3.71 (1H, brdt, *J*=4.4, 9.0 Hz, H-3), 3.81 (1H, brdt, *J*=9.7, 5.7 Hz, H-6), 5.04 (1H, brs, H-36), 5.10 (1H, s, H-36), 5.30 (1H, brt, *J*=6.0 Hz and H-7), 5.61 (1H, d, *J*=6.8 Hz, H-8), and 7.32–7.54 (10H, m, Ph); FABMS *m/z* 691 $(M+H)^+$; HRFABMS *m/z* 691.2353 $[(M+H)^+$, calcd for $C_{33}H_{37}O_9F_6$: 691.2342].

3.1.22. Ethyl (2*E*,6*R*)-7-benzyloxy-6-hydroxy-2-heptenoate (17). To a solution of (*R*)-5-benzyloxymethyl-γ-butyrolactone (**16**, 9.27 g, 45.0 mmol) in CH_2Cl_2

(100 mL) was added DIBAL-H (1.01 M, 56 mL, 56.6 mmol) in toluene at −78°C, and the mixture was stirred for 1 h. After addition of MeOH and saturated aqueous potassium sodium tartrate, the mixture was allowed to warm to rt, and stirred vigorously for 1 h. The reaction mixture was extracted with EtOAc, and the organic layer was washed with H_2O and brine, dried, and evaporated to afford a crude acetal (9.36 g, 45.0 mmol, quant.). To a solution of the crude acetal (9.36 g, 45.0 mmol) in benzene (200 mL) was added (ethoxycarbonylmethylene)triphenyl phosphorane (22.7 g, 67.5 mmol), and stirring was continued at 55°C for 16 h. After evaporation of the solvent, the residue was subjected to CC (hexane–EtOAc, 5:1) to afford **17** (11.0 g, 39.6 mmol, 87%). Colorless oil; $[\alpha]_D^{20}=+0.4°$ (*c* 1.0, $CHCl_3$); IR (neat) ν_{max} 3478, 3030, 2981, 2931, 2860, 1716, 1653, 1454, 1368, 1045, 738, and 699 cm^{-1}; ^1H NMR (500 MHz; $CDCl_3$) δ_H 1.25 (3H, t, *J*=6.9 Hz), 1.56 (2H, m), 2.25 (1H, m), 2.34 (1H, m), 3.32 (1H, m), 3.44 (1H, m), 3.77 (1H, m), 4.15 (2H, m), 4.51 (2H, m), 5.81 (1H, d, *J*=15.6 Hz), 6.94 (1H, m), and 7.22–7.37 (5H, m); ^{13}C NMR (125 MHz; $CDCl_3$) δ_C 14.1 (q), 28.0 (t), 31.3 (t), 60.0 (t), 69.3 (d), 73.1 (t), 74.2 (t), 121.5 (d), 127.5 (2C, d), 127.6 (d), 128.3 (2C, d), 137.7 (s), 148.4 (d), and 166.4 (s); FABMS *m/z* 279 $(M+H)^+$; HRFABMS *m/z* 279.1602 [$(M+H)^+$, calcd for $C_{16}H_{23}O_4$: 279.1596].

3.1.23. {(2*R*,5*R*)- and {(2*S*,5*R*)-5-[2-(*tert*-Butyldimethylsilyloxy)ethyl]-tetrahydrofuran-2-yl}-methanol (18a and 18b). To a solution of **17** (6.82 g, 24.5 mmol) in THF (100 mL) was added TBAF (1.00 M, 30 mL, 30 mmol) in THF, and the mixture was stirred at rt for 1 h. After evaporation of the solvent, the residue was subjected to CC (hexane–EtOAc, 10:0 to 4:1) to afford a tetrahydrofuran (6.53 g, 23.5 mmol, 96%). To a solution of the tetrahydrofuran (6.48 g, 23.3 mmol) in CH_2Cl_2 (85 mL) was added DIBAL-H (1.01 M, 69 mL, 69.7 mmol) in toluene at −78°C, and the mixture was stirred for 1 h. After addition of MeOH and saturated aqueous potassium sodium tartrate, the mixture was allowed to warm to rt, and stirred vigorously for 1 h. The reaction mixture was extracted with EtOAc, and the organic layer was washed with H_2O and brine, dried, and evaporated to afford a crude alcohol (5.5 g, 23.3 mmol, 99%). The crude alcohol (5.5 g, 23.3 mmol) in dry DMF (90 mL) was treated with TBDMSCl (5.2 g, 33.1 mmol) and imidazole (3.1 g, 46.6 mmol) at rt for 3.5 h. After addition of saturated aqueous NH_4Cl, the mixture was extracted with Et_2O. The organic layer was washed with H_2O and brine, dried, and concentrated. The residue was purified by CC (hexane–EtOAc, 15:1) to afford a TBDMS ether (7.81 g, 22.3 mmol, 96%) as colorless oil. The TBDMS ether (7.81 g, 22.3 mmol) in EtOH (100 mL) was treated with 10% Pd–C (385 mg) under a hydrogen atmosphere at rt for 6 h. After filtration of the catalyst, the filtrate was evaporated to afford **18a** (2.50 g, 9.61 mmol, 43%) and **18b** (2.51 g, 9.65 mmol, 43%).

Compound **18a**. Colorless oil; $[\alpha]_D^{20}=-14°$ (*c* 1.0, $CHCl_3$); IR (neat) ν_{max} 3444, 2954, 2930, 2857, 1463, and 1095 cm^{-1}; ^1H NMR (500 MHz; $CDCl_3$) δ_H 0.05 (6H, s), 0.89 (9H, s), 1.52–1.71 (3H, m), 1.78 (1H, m), 1.96 (1H, m), 2.05 (1H, m), 3.47 (1H, dd, *J*=11.2, 6.2 Hz), 3.61 (1H, dd, *J*=11.2, 3.1 Hz), 3.71 (2H, t, 6.2), and 4.02–4.14 (2H, m); ^{13}C NMR (125 MHz; $CDCl_3$) δ_C −5.4 (2C, q), 18.3 (s), 25.9 (3C, q), 27.5 (t), 32.2 (t), 38.8 (t), 60.4 (t), 65.1 (t), 76.4 (d), and 78.7 (d); FABMS *m/z* 261 $(M+H)^+$; HRFABMS *m/z* 261.1894 [$(M+H)^+$, calcd for $C_{13}H_{29}O_3Si$: 261.1886].

Compound **18b**. Colorless oil; $[\alpha]_D^{20}=+4°$ (*c* 1.0, $CHCl_3$); IR (neat) ν_{max} 3438, 2957, 2929, 2858, 1471, and 1095 cm^{-1}; ^1H NMR (500 MHz; $CDCl_3$) δ_H 0.05 (6H, s), 0.89 (9H, s), 1.55 (1H, m), 1.67–1.77 (2H, m), 1.79 (1H, m), 1.91 (1H, m), 1.99 (1H, m), 3.46 (1H, dd, *J*=11.2, 5.6 Hz), 3.69 (1H, dd, *J*=11.2, 3.1 Hz), 3.72 (2H, t, 6.2), and 3.97–4.04 (2H, m); ^{13}C NMR (125 MHz; $CDCl_3$) δ_C −5.4 (2C, q), 18.3 (s), 25.9 (3C, q), 27.0 (t), 31.6 (t), 39.0 (t), 60.6 (t), 65.2 (t), 77.4 (d), and 79.2 (d); FABMS *m/z* 261 $(M+H)^+$; HRFABMS *m/z* 261.1876 [$(M+H)^+$, calcd for $C_{13}H_{29}O_3Si$: 261.1886].

3.1.24. (1*R*)- and (1*S*)-1-{(2*R*,5*R*)-5-[2-(*tert*-Butyldimethylsilyloxy)ethyl]-tetrahydrofuran-2-yl}-2-propen-1-ol (19a and 19b). To a solution of **18a** (1.00 g, 3.85 mmol) in a mixture of DMSO (11 mL), CH_2Cl_2 (67.1 mL) and Et_3N (3.85 mL) was added SO_3-pyridine complex (3.05 g, 19.2 mmol) at 0°C. After stirring at rt for 20 min, the solution was poured into H_2O and the mixture was extracted with Et_2O. The organic layer was washed with H_2O and brine, dried, and concentrated to afford a crude aldehyde (832.8 mg), which was used for the following reaction without purification. To a stirred solution of the crude aldehyde (832.8 mg) in THF (9.0 mL) was added vinylMgBr (1.06 M, 12.0 mL, 12.7 mmol) in THF at 0°C. After stirring for 1 h, the reaction was quenched by addition of saturated aqueous NH_4Cl and then the mixture was extracted with Et_2O. The organic layer was washed with H_2O and brine, dried, and concentrated. The residue was purified by CC ($CHCl_3$–acetone, 10:0 to 9:1) to afford **19a** (376.1 mg, 1.32 mmol, 41%) and **19b** (339.9 mg, 1.19 mmol, 37%).

Compound **19a**. $[\alpha]_D^{20}=-6.1°$ (*c* 1.00, $CHCl_3$); IR (neat) ν_{max} 3446, 2954, 2929, 2857, 1472, and 1092 cm^{-1}; ^1H NMR (500 MHz; $CDCl_3$) δ_H 0.05 (6H, s), 0.89 (9H, s), 1.58 (1H, m), 1.69 (2H, m), 1.78 (1H, m), 1.96 (1H, m), 2.06 (1H, m), 3.71 (2H, m), 3.84 (1H, m), 3.91 (1H, m), 4.07 (1H, m), 5.20 (1H, d, *J*=10.6 Hz), 5.36 (1H, d, *J*=17.4 Hz), and 5.79 (1H, ddd, *J*=17.4, 10.6, 6.2 Hz); ^{13}C NMR (125 MHz; $CDCl_3$) δ_C −5.4 (2C, q), 18.3 (s), 25.9 (3C, q), 27.9 (t), 32.3 (t), 38.7 (t), 60.4 (t), 75.6 (d), 76.5 (d), 81.4 (d), 117.0 (t), and 136.8 (d); FABMS *m/z* 287 $(M+H)^+$; HRFABMS *m/z* 287.2044 [$(M+H)^+$, calcd for $C_{15}H_{31}O_3Si$: 287.2042].

Compound **19b**. $[\alpha]_D^{20}=-5.7°$ (*c* 1.00, $CHCl_3$); IR (neat) ν_{max} 3446, 2954, 2929, 2857, 1472, and 1092 cm^{-1}; ^1H NMR (500 MHz; $CDCl_3$) δ_H 0.05 (6H, s), 0.89 (9H, s), 1.55 (1H, m), 1.67 (1H, m), 1.78 (1H, m), 1.84 (2H, m), 2.06 (1H, m), 3.71 (2H, m), 3.99 (1H, m), 4.12 (1H, m), 4.29 (1H, m), 5.19 (1H, d, *J*=10.6 Hz), 5.33 (1H, d, *J*=17.4 Hz), and 5.81 (1H, ddd, *J*=17.4, 10.6, 6.2 Hz); ^{13}C NMR (125 MHz; $CDCl_3$) δ_C −5.3 (2C, q), 18.3 (s), 25.5 (t), 25.9 (3C, q), 32.3 (t), 39.0 (t), 60.4 (t), 73.6 (d), 77.4 (d), 81.0 (d), 116.3 (t), and 136.4 (d); FABMS *m/z* 287 $(M+H)^+$; HRFABMS *m/z* 287.2044 [$(M+H)^+$, calcd for $C_{15}H_{31}O_3Si$: 287.2042].

3.1.25. (*S*)-MTPA ester of 19a. The (*S*)-MTPA ester of **19a** (0.7 mg, 1.4 μmol) was obtained from **19a** (0.5 mg,

1.7 μmol) in 82% yield through the same procedure as described for preparation of the (*S*)-MTPA ester of **11a**. (*S*)-MTPA ester of **19a**. Colorless oil; ^{1}H NMR (600 MHz; $CDCl_3$) δ_H 0.03 (6H, s), 0.88 (9H, s), 1.47 (1H, m), 1.59 (1H, m), 1.63 (1H, m), 1.73 (1H, m), 1.90 (1H, m), 1.93 (1H, m), 3.55 (3H, s), 3.66 (2H, m), 3.96 (1H, m), 4.07 (1H, m), 5.33 (1H, d, *J*=10.6 Hz), 5.42 (1H, d, *J*=17.4 Hz), 5.45 (1H, m), 5.87 (1H, d, *J*=17.4, 10.6, 7.5 Hz), 7.36–7.42 (3H, m), and 7.54–7.60 (2H, m); FABMS *m/z* 503 $(M+H)^+$; HRFABMS *m/z* 503.2443 [$(M+H)^+$, calcd for $C_{25}H_{38}O_5F_3Si$: 503.2441].

3.1.26. (*R*)-MTPA ester of 19a. The (*R*)-MTPA ester of **19a** (0.8 mg, 1.6 μmol) was obtained from **19a** (0.5 mg, 1.7 μmol) in 94% yield through the same procedure as described for preparation of the (*S*)-MTPA ester of **11a**. (*R*)-MTPA ester of **19a**. Colorless oil; ^{1}H NMR (600 MHz; $CDCl_3$) δ_H 0.02 (6H, s), 0.88 (9H, s), 1.55 (1H, m), 1.65 (1H, m), 1.70 (1H, m), 1.76 (1H, m), 1.97 (1H, m), 2.06 (1H, m), 3.62 (3H, s), 3.66 (2H, m), 4.04 (1H, m), 4.08 (1H, m), 5.24 (1H, d, *J*=10.6 Hz), 5.29 (1H, d, *J*=17.4 Hz), 5.41 (1H, m), 5.70 (1H, d, *J*=17.4, 10.6, 6.9 Hz), 7.34–7.42 (3H, m), and 7.56–7.63 (2H, m); FABMS *m/z* 503 $(M+H)^+$; HRFABMS *m/z* 503.2445 [$(M+H)^+$, calcd for $C_{25}H_{38}O_5F_3Si$: 503.2441].

3.1.27. (2*R*,5*R*)-2-[2-(*tert*-Butyldimethylsilyloxy)ethyl]-5-{(1*R*)-1-[2-(trimethylsilyl)ethoxymethoxy]-2-propenyl}-tetrahydrofuran (20a). Compound **19a** (335.3 mg, 1.17 mmol) dissolved in dry CH_2Cl_2 (7.0 mL) was treated with SEMCl (0.37 mL, 2.32 mmol) and *i*-Pr_2NEt (0.61 mL, 3.48 mmol) at rt for 4 h. The reaction was quenched by addition of saturated aqueous $NaHCO_3$ and then the mixture was extracted with Et_2O. The organic layer was dried and concentrated. The residue was purified by CC (hexane–EtOAc, 10:0 to 8:2) to afford **20a** (462.8 mg, 1.11 mmol, 95%).

Compound **20a**. Colorless oil; $[\alpha]_D^{20}=-33°$ (*c* 1.0, $CHCl_3$); IR (neat) ν_{max} 2954, 2858, 1716, 1473, and 1096 cm^{-1}; ^{1}H NMR (500 MHz; $CDCl_3$) δ_H 0.01 (9H, s), 0.04 (6H, s), 0.88 (9H, s), 0.92 (2H, m), 1.52 (1H, m), 1.60 to 1.75 (2H, m), 1.83 (1H, m), 1.91 (1H, m), 2.01 (1H, m), 3.55 (1H, m), 3.69 (2H, m), 3.75 (1H, m), 3.98–4.08 (3H, m), 4.71 (2H, m), 5.25 (1H, d, *J*=10.6 Hz), 5.29 (1H, d, *J*=17.4 Hz), and 5.72 (1H, ddd, *J*=17.4, 10.6, 6.9 Hz); ^{13}C NMR (125 MHz; $CDCl_3$) δ_C −5.3 (2C, q), −1.4 (3C, q), 18.1 (t), 18.3 (s), 26.0 (3C, q), 28.1 (t), 32.1 (t), 38.9 (t), 60.6 (t), 65.0 (t), 76.9 (d), 79.5 (d), 80.3 (d), 92.5 (t), 118.6 (t), and 135.1 (d); FABMS *m/z* 417 $(M+H)^+$; HRFABMS *m/z* 417.2859 [$(M+H)^+$, calcd for $C_{21}H_{45}O_4Si_2$: 417.2856].

3.1.28. (2*R*,5*R*)-2-[2-(*tert*-Butyldimethylsilyloxy)ethyl]-5-{(1*S*)-1-[2-(trimethylsilyl)ethoxymethoxy]-2-propenyl}-tetrahydrofuran (20b). Compound **20b** (274.6 mg, 660 mmol) was obtained from **19b** (227.0 mg, 794 mmol) in 81% yield through the same procedure as described for preparation of **20a**.

Compound **20b**. Colorless oil; $[\alpha]_D^{20}=-50°$ (*c* 1.0, $CHCl_3$); IR (neat) ν_{max} 2954, 2868, 1718, 1463, and 1096 cm^{-1}; ^{1}H NMR (500 MHz; $CDCl_3$) δ_H 0.01 (9H, s), 0.04 (6H, s), 0.88 (9H, s), 0.93 (2H, m), 1.53 (1H, m), 1.64 (1H, m), 1.81 (2H, m), 1.93–2.06 (2H, m), 3.54 (1H, m), 3.64–3.78 (3H, m), 4.03 (3H, m), 4.67 (1H, d, *J*=6.9 Hz), 4.71 (1H, d, *J*=6.9 Hz), 5.27 (2H, d, *J*=17.4 Hz), and 5.75 (1H, m); ^{13}C NMR (125 MHz; $CDCl_3$) δ_C −5.4 (q), −5.3 (q), −1.4 (3C, q), 18.0 (t), 18.3 (s), 25.9 (3C, q), 27.5 (t), 32.0 (t), 38.8 (t), 60.5 (t), 65.0 (t), 77.2 (d), 79.4 (d), 80.4 (d), 92.4 (t), 118.8 (t), and 135.2 (d); FABMS *m/z* 417 $(M+H)^+$; HRFABMS *m/z* 417.2863 [$(M+H)^+$, calcd for $C_{21}H_{45}O_4Si_2$: 417.2856].

3.1.29. (2*R*,5*R*)-2-[(1*R*,2*E*)-5-Methyl-1-(triethylsilyloxy)-2,4-hexadienyl]-5-[2-(triethylsilyloxy)ethyl]-tetrahydrofuran (23a). Compound **20a** (251.2 mg, 604 μmol) was dissolved in a 8:1 mixture of acetone and H_2O (6.9 mL), and to this mixture were added OsO_4 (1%, 764 μL, 30 μmol) in *t*-BuOH and NMO (143.2 mg, 1.22 mmol). After stirring at rt for 19 h, the reaction was quenched by addition of saturated aqueous $NaHSO_3$, and then the mixture was extracted with EtOAc. The organic layer was washed with brine, dried, and concentrated. The residue was purified by CC (hexane–EtOAc, 5:1 to 2:1) to afford a mixture of diols (243.7 mg, 542 μmol, 90%) as colorless oil. To a stirring solution of the mixture (243.7 mg, 542 μmol) in a 1:1 mixture (5 mL) of THF and phosphate buffer (pH 6.8) was added $NaIO_4$ (159.3 mg, 1.13 mmol) at 0°C. After stirring at rt for 1 h, the mixture was extracted with Et_2O, washed with brine, dried, and concentrated. The residue was purified by CC (hexane–EtOAc, 10:0 to 9:1) to afford an aldehyde (198.8 mg, 476 μmol, 88%) as colorless oil.

A solution of BuLi (2.46 M, 830 μL, 2.04 mmol) in hexane was added to a solution of (3-methyl-2-butene-1-sulfonyl)-benzene[12] (453 mg, 2.16 mmol) in THF (28 mL) at −78°C. After stirring for 20 min, a solution of the aldehyde (198.8 mg, 476 μmol) in THF (3.5 mL) was added to the mixture at −78°C. Stirring was continued at −78°C for 2 h, and then the reaction mixture was allowed to warm to rt over 1 h. The reaction was quenched by addition of saturated aqueous NH_4Cl, and then the mixture was extracted with Et_2O, washed with brine, dried, and concentrated. The residue was purified by CC (hexane–EtOAc, 10:0 to 8:2) to afford a diastereomeric mixture of the β-hydroxy sulfone (260.8 mg, 415 μmol, 87%) as colorless oil. The β-hydroxy sulfone (260.8 mg, 415 μmol) in CH_2Cl_2 (20 mL) was treated with Et_3N (115 μL), DMAP (275 mg), and BzCl (130 μL), and stirring was continued at rt for 20 h. The reaction was quenched by addition of saturated aqueous NH_4Cl, and then the mixture was extracted with Et_2O. The organic layer was washed with brine, dried, and concentrated. The residue was purified by CC (hexane–EtOAc, 10:0 to 8:2) to afford a diastereomeric mixture of the β-benzoyloxy sulfone **21a** (295.0 mg, 403 μmol, 97%) as colorless oil.

Compound **21a** (198.6 mg, 271 μmol) in CH_2Cl_2 (12 mL) was treated with TFA (4 mL) at 0°C for 30 min. The reaction mixture was partitioned between CH_2Cl_2 and H_2O. The organic layer was washed with brine, dried, and evaporated. The residue was purified by CC (CH_2Cl_2–MeOH, 10:0 to 9:1) to afford a diastereomeric mixture of 18,24-diols (116.4 mg, 238 μmol, 87%) as colorless oil. The mixture (60.5 mg, 124 μmol) dissolved in dry DMF (0.4 mL) was treated with TESCl (63.5 μL, 378 μmol) and

imidazole (50.3 mg, 746 μmol) at rt for 3 h. After evaporation of the solvent, the reaction mixture was purified with CC (hexane–EtOAc, 10:0 to 9:1) to afford a diastereomer mixture (**22a**) of 18,24-bis-TES ethers (83.1 mg, 116 μmol, 94%) as colorless oil.

A solution of **22a** (83.1 mg, 116 μmol) in a 3:1 mixture (7.2 mL) of THF and MeOH was treated with Na(Hg) (700.0 mg) and Na_2HPO_4 (701.2 mg) at −20°C for 1 h. The reaction was quenched by addition of H_2O, and then the mixture was extracted with Et_2O. The organic layer was washed with brine, dried, and concentrated. The residue was subjected to CC (hexane–EtOAc, 10:0 to 4:1) to afford **23a** (35.3 mg, 77.8 μmol, 67%). Colorless oil; $[\alpha]_D^{20}=+13°$ (*c* 1.0, $CHCl_3$); UV (cyclohexane) λ_{max} 240 nm (ε 24000); IR (neat) ν_{max} 2955, 2876, 1457, and 1070 cm^{-1}; ^1H NMR (500 MHz; $CDCl_3$) δ_H 0.55–0.65 (12H, m), 0.95 (18H, t, *J*=8.1 Hz), 1.46 (1H, m), 1.60–1.74 (2H, m), 1.75 (3H, s), 1.77 (3H, s), 1.78–1.91 (2H, m), 1.95 (1H, m), 3.64–3.76 (2H, m), 3.92 (1H, m), 3.97 (1H, m), 4.17 (1H, brt, *J*=5.6 Hz), 5.53 (1H, dd, *J*=15.0, 5.6 Hz), 5.82 (1H, d, *J*=11.2 Hz), and 6.45 (1H, dd, *J*=15.0, 11.2 Hz); ^{13}C NMR (125 MHz; $CDCl_3$) δ_C 4.4 (3C, t), 5.0 (3C, t), 6.7 (3C, q), 6.8 (3C, q), 18.2 (q), 25.9 (q), 27.3 (t), 32.3 (t), 39.0 (t), 60.4 (t), 75.4 (d), 76.6 (d), 82.0 (d), 124.8 (d), 127.4 (d), 130.0 (d), and 134.8 (s); FABMS *m/z* 455 $(M+H)^+$; HRFABMS *m/z* 455.3369 $[(M+H)^+$, calcd for $C_{25}H_{51}O_3Si_2$: 455.3377].

3.1.30. (2*R*,5*R*)-2-[(1*S*,2*E*)-5-Methyl-1-(triethylsilyloxy)-2,4-hexadienyl]-5-[2-(triethylsilyloxy)ethyl]-tetrahydrofuran (23b). Compound **23b** (50.3 mg, 111 μmol) was obtained from **20b** 159.6 mg, 383 mmol) in 29% yield by 7 steps through the same procedure as described for preparation of **23a**.

Compound **23b**. Colorless oil; $[\alpha]_D^{20}=+4°$ (*c* 1.0, $CHCl_3$); UV (cyclohexane) λ_{max} 238 nm (ε 23500); IR (neat) ν_{max} 2954, 2876, 1463, and 1069 cm^{-1}; ^1H NMR (500 MHz; $CDCl_3$) δ_H 0.54–0.64 (12H, m), 0.95 (18H, dt, *J*=8.1 Hz), 1.46 (1H, m), 1.64 (1H, m), 1.74 (3H, s), 1.76 (3H, s), 1.77–1.93 (3H, m), 2.00 (1H, m), 3.69 (2H, m), 3.88 (1H, m), 4.04 (1H, m), 4.25 (1H, brt, *J*=5.0 Hz), 5.48 (1H, dd, *J*=15.6, 6.2 Hz), 5.80 (1H, d, *J*=11.2 Hz) and 6.40 (1H, dd, 15.6 and 11.2); ^{13}C NMR (125 MHz; $CDCl_3$) δ_C 4.4 (3C, t), 5.0 (3C, t), 6.7 (3C, q), 6.8 (3C, q), 18.2 (q), 25.9 (q), 26.1 (t), 32.3 (t), 39.1 (t), 60.4 (t), 75.4 (d), 77.0 (d), 82.1 (d), 124.7 (d), 127.0 (d), 130.9 (d), and 134.9 (s); FABMS *m/z* 55 $(M+H)^+$; HRFABMS *m/z* 455.3373 $[(M+H)^+$, calcd for $C_{25}H_{51}O_3Si_2$: 455.3377].

3.1.31. 2-{(2*R*,5*R*)-5-[(1*R*,2*E*)-5-Methyl-1-(triethylsilyloxy)-2,4-hexadienyl]-tetrahydrofuran-2-yl}-ethanol (24a). To **23a** (32.3 mg, 71.1 μmol) was added a mixture (8.2 mL) of AcOH–H_2O–THF (1:20:20), and the reaction mixture was stirred at 0°C for 1 h. The reaction was quenched by addition of saturated aqueous $NaHCO_3$ and then the mixture was extracted with $CHCl_3$. The organic layer was dried, and evaporated. The residue was purified by CC (hexane–EtOAc, 10:0 to 9:1) to afford **24a** (18.2 mg, 53.5 μmol, 75%). Colorless oil; $[\alpha]_D^{20}=+8°$ (*c* 1.0, $CHCl_3$); ^1H NMR (500 MHz; $CDCl_3$) δ_H 0.60 (6H, q, *J*=8.1 Hz), 0.95 (9H, t, *J*=8.1 Hz), 1.54 (1H, m), 1.64–1.92 (4H, m), 1.75 (3H, s), 1.77 (3H, s), 1.99 (1H, m), 3.77 (2H, m), 3.97 (1H, m), 4.11 (1H, m), 4.14 (1H, m), 5.51 (1H, dd, *J*=15.0, 6.2 Hz), 5.81 (1H, d, *J*=11.2 Hz), and 6.44 (1H, dd, *J*=15.0, 11.2 Hz); ^{13}C NMR (125 MHz; $CDCl_3$) δ_C 5.0 (3C, t), 6.8 (3C, q), 18.2 (q), 26.0 (q), 27.2 (t), 32.4 (t), 37.2 (t), 61.8 (t), 75.5 (d), 79.8 (d), 82.5 (d), 124.6 (d), 127.8 (d), 129.7 (d), and 135.3 (s); FABMS *m/z* 341 $(M+H)^+$; HRFABMS *m/z* 341.2515 $[(M+H)^+$, calcd for $C_{19}H_{36}O_3Si$: 341.2512].

3.1.32. 2-{(2*R*,5*R*)-5-[(1*S*,2*E*)-5-Methyl-1-(triethylsilyloxy)-2,4-hexadienyl]-tetrahydrofuran-2-yl}-ethanol (24b). Compound **24b** (25.2 mg, 74.1 μmol) was obtained from **23b** (42.3 mg, 93.2 μmol) in 80% yield through the same procedure as described for preparation of **24a**.

Compound **24b**. Colorless oil; $[\alpha]_D^{20}=+3°$ (*c* 1.0, $CHCl_3$); ^1H NMR (500 MHz; $CDCl_3$) δ_H 0.59 (6H, q, *J*=8.1 Hz), 0.95 (9H, t, *J*=8.1 Hz), 1.52 (1H, m), 1.68–1.78 (2H, m), 1.75 (3H, s), 1.76 (3H, s), 1.80–1.94 (2H, m), 2.03 (1H, m), 3.76 (2H, m), 3.94 (1H, m), 4.15 (1H, m), 4.26 (1H, m), 5.45 (1H, dd, *J*=15.6, 6.2 Hz), 5.79 (1H, d, *J*=11.2 Hz), and 6.40 (1H, dd, *J*=15.6, 11.2 Hz); ^{13}C NMR (125 MHz; $CDCl_3$) δ_C 5.0 (3C, t), 6.8 (3C, q), 18.2 (q), 25.7 (t), 25.9 (q), 32.5 (t), 37.3 (t), 61.9 (t), 75.2 (d), 80.4 (d), 82.6 (d), 124.5 (d), 127.3 (d), 130.4 (d), and 135.3 (s); FABMS *m/z* 341 $(M+H)^+$; HRFABMS *m/z* 341.2512 $[(M+H)^+$, calcd for $C_{19}H_{36}O_3Si$: 341.2512].

3.1.33. 1-{(2*R*,5*R*)-5-[(1*R*,2*E*)-5-Methyl-1-(triethylsilyloxy)-2,4-hexadienyl]-tetrahydrofuran-2-yl}-propan-2-one (25a). To a solution of **24a** (22.7 mg, 66.8 μmol) in a mixture of DMSO (197 μL), CH_2Cl_2 (1.2 mL), and Et_3N (67 μL) was added SO_3-pyridine complex (53.7 mg, 338 μmol) at 0°C. After stirring at rt for 30 min, the solution was poured into H_2O, and the mixture was extracted with Et_2O. The organic layer was washed with brine, dried, and concentrated to afford a crude aldehyde (22.5 mg, 66.6 μmol, 99%). To a stirred solution of the aldehyde (22.5 mg, 66.6 μmol) in THF (9.0 mL) was added MeMgBr (0.87 M, 386 μL, 0.34 mmol) in THF at 0°C. After stirring for 1 h, the reaction was quenched by addition of saturated aqueous NH_4Cl, and then the mixture was extracted with Et_2O. The organic layer was washed with H_2O and brine, dried, and concentrated to afford a diastereomeric mixture of alcohols (17.6 mg, 47.9 μmol, 72%). The diastereomeric mixture (17.6 mg, 47.9 μmol) of alcohols in a mixture of DMSO (197 μL), CH_2Cl_2 (1.2 mL) and Et_3N (67 μL) was treated with SO_3–pyridine complex (32.5 mg, 204 μmol) at rt for 30 min. The solution was poured into H_2O, and the mixture was extracted with Et_2O. The organic layer was washed with brine, dried, and concentrated to afford **25a** (11.7 mg, 33.2 μmol, 69%). Colorless oil; $[\alpha]_D^{20}=+10°$ (*c* 0.5, $CHCl_3$); UV (cyclohexane) λ_{max} 240 nm (ε 21000); IR (neat) ν_{max} 2954, 2911, 2876, 1718, 1458, and 1085 cm^{-1}; ^1H NMR (500 MHz; $CDCl_3$) δ_H 0.59 (6H, q, *J*=8.1 Hz), 0.94 (9H, t, *J*=8.1 Hz), 1.45 (1H, m), 1.68–1.80 (1H, m), 1.75 (3H, s), 1.77 (3H, s), 1.88 (1H, m), 2.06 (1H, m), 2.18 (3H, s), 2.49 (1H, dd, *J*=15.6, 5.6 Hz), 2.72 (1H, dd, *J*=15.6, 6.9 Hz), 3.95 (1H, m), 4.17 (1H, m), 4.28 (1H, m), 5.52 (1H, dd, *J*=15.0, 6.2 Hz), 5.82 (1H, d, *J*=11.2 Hz) and 6.44 (1H, dd, *J*=15.0, 11.2 Hz); ^{13}C NMR (125 MHz; $CDCl_3$) δ_C 5.0 (3C, t), 6.8 (3C, q), 18.2 (q), 26.0 (q), 27.1 (t), 30.7 (q), 32.3 (t), 49.7 (t), 75.3 (d), 75.4 (d), 82.3 (d), 124.7 (d), 127.7 (d), 129.7 (d),

135.2 (s), and 207.5 (s); FABMS *m/z* 353 $(M+H)^+$; HRFABMS *m/z* 353.2502 $[(M+H)^+$, calcd for $C_{20}H_{37}O_3S$: 353.2512].

3.1.34. 1-{(2*R*,5*R*)-5-[(1*S*,2*E*)-5-Methyl-1-(triethylsilyloxy)-2,4-hexadienyl]-tetrahydrofuran-2-yl}-propan-2-one (25b). Compound **25b** (17.2 mg, 48.9 μmol) was obtained from **23b** (31.6 mg, 92.9 μmol) in 53% yield by 3 steps through the same procedure as described for preparation of **25a**.

Compound **25b**. Colorless oil; $[\alpha]_D^{20}=+6°$ (*c* 0.5, $CHCl_3$); UV (cyclohexane) λ_{max} 240 nm (ε 22000); IR (neat) ν_{max} 2954, 2910, 2876, 1720, 1458, and 1085 cm^{-1}; ^1H NMR (500 MHz; $CDCl_3$) δ_H 0.59 (6H, q, *J*=8.1 Hz), 0.94 (9H, t, *J*=8.1 Hz), 1.45 (1H, m), 1.74 (3H, s), 1.76 (3H, s), 1.80–1.97 (2H, m), 2.11 (1H, m), 2.17 (3H, s), 2.49 (1H, dd, *J*=15.6, 6.2 Hz), 2.70 (1H, dd, *J*=15.6, 6.9 Hz), 3.91 (1H, brdt, *J*=4.4, 6.9 Hz), 4.23 (1H, m), 4.33 (1H, m), 5.46 (1H, dd, *J*=15.0, 6.2 Hz), 5.79 (1H, d, *J*=10.6 Hz), and 6.39 (1H, dd, *J*=15.0, 10.6 Hz); ^{13}C NMR (125 MHz; $CDCl_3$) δ_C 5.0 (3C, t), 6.8 (3C, q), 18.2 (q), 25.9 (t), 25.9 (q), 30.6 (q), 32.3 (t), 49.9 (t), 75.2 (d), 75.8 (d), 82.5 (d), 124.5 (d), 127.2 (d), 130.6 (d), 135.2 (s), and 207.5 (s); FABMS *m/z* 353 $(M+H)^+$; HRFABMS *m/z* 353.2498 $[(M+H)^+$, calcd for $C_{20}H_{37}O_3Si$: 353.2512].

3.1.35. 1-{(2*R*,5*R*)-5-[(1*R*,2*E*)-1-Hydroxy-5-methyl-2,4-hexadienyl]-tetrahydrofuran-2-yl}-propan-2-one (6a). Compound **25a** (5.03 mg, 14.3 μmol) was dissolved in the mixture (1.7 mL) of AcOH–H_2O–THF (1:10:10), and the solution was stirred at 0°C for 4 h. The reaction was quenched by addition of saturated aqueous $NaHCO_3$, and then the mixture was extracted with $CHCl_3$. The organic layer was dried, evaporated. The residue was purified with CC (hexane–EtOAc, 2:1 to 1:1) to afford **6a** (3.12 mg, 13.1 mmol, 92%). Colorless oil; $[\alpha]_D^{20}=+15°$ (*c* 1.0, $CHCl_3$); UV (cyclohexane) λ_{max} 240 nm (ε 24000); IR (neat) ν_{max} 3446, 2971, 2926, 1716, 1458, and 1068 cm^{-1}; ^1H NMR (500 MHz; $CDCl_3$) δ_H 1.54 (1H, m), 1.69 (1H, m), 1.76 (3H, s), 1.78 (3H, s), 1.96 (1H, m), 2.15 (1H, m), 2.18 (3H, s), 2.55 (1H, dd, *J*=15.6, 5.6 Hz), 2.79 (1H, dd, *J*=15.6, 6.9 Hz), 3.87 (1H, m), 3.96 (1H, brt, *J*=7.2 Hz), 4.36 (1H, m), 5.45 (1H, dd, *J*=15.0, 6.9 Hz), 5.81 (1H, d, *J*=11.2 Hz), and 6.52 (1H, dd, *J*=15.0, 11.2 Hz); ^{13}C NMR (125 MHz; $CDCl_3$) δ_C 18.3 (q), 26.0 (t), 27.9 (q), 30.8 (q), 32.2 (t), 49.3 (t), 75.1 (d), 75.5 (d), 82.2 (d), 124.4 (d), 128.0 (d), 129.4 (d), 136.6 (s), and 207.0 (s); FABMS *m/z* 239 $(M+H)^+$; HRFABMS *m/z* 239.1658 $[(M+H)^+$, calcd for $C_{14}H_{23}O_3$: 239.1647].

3.1.36. 1-{(2*R*,5*R*)-5-[(1*S*,2*E*)-1-Hydroxy-5-methylhexa-2,4-dienyl]-tetrahydrofuran-2-yl}-propan-2-one (6b). Compound **6b** (2.93 mg, 12.3 μmol) was obtained from **25b** (5.05 mg, 14.3 μmol) in 86% yield through the same procedure as described for preparation of **6a**.

Compound **6b**. Colorless oil; $[\alpha]_D^{20}=+3°$ (*c* 1.0, $CHCl_3$); UV (cyclohexane) λ_{max} 240 nm (ε 23000); IR (neat) ν_{max} 3450, 2970, 2925, 1714, 1458, and 1069 cm^{-1}; ^1H NMR (500 MHz; $CDCl_3$) δ_H 1.53 (1H, m), 1.76 (3H, s), 1.78 (3H, s), 1.84–1.92 (2H, m), 2.14 (1H, m), 2.18 (3H, s), 2.54 (1H, dd, *J*=16.2, 5.2 Hz), 2.75 (1H, dd, *J*=16.2, 7.5 Hz), 4.01 (1H, m), 4.31 (1H, m), 4.40 (1H, m), 5.47 (1H, dd, *J*=15.0, 6.9 Hz), 5.82 (1H, d, *J*=11.2 Hz) and 6.49 (1H, dd, *J*=15.0, 11.2 Hz); ^{13}C NMR (125 MHz; $CDCl_3$) δ_C 18.3 (q), 25.5 (t), 26.0 (q), 30.7 (q), 32.3 (t), 49.7 (t), 73.6 (t), 76.0 (t), 81.8 (t), 124.4 (d), 127.9 (d), 128.8 (d), 136.3 (s), and 207.1 (s); FABMS *m/z* 239 $(M+H)^+$; HRFABMS *m/z* 239.1649 $[(M+H)^+$, calcd for $C_{14}H_{23}O_3$: 239.1647].

3.1.37. (*S*)-MTPA ester (7a) of 6a. The (*S*)-MTPA ester **7a** (0.90 mg, 1.98 μmol) was obtained from **6a** (0.50 mg, 2.09 μmol) in 95% yield through the same procedure as described for preparation of the (*S*)-MTPA ester of **11a**.

Compound **7a**. Colorless oil; ^1H NMR (600 MHz; $CDCl_3$) δ_H 1.44 (1H, m, H-21), 1.60 (1H, m, H-22), 1.76 (3H, s, H-40), 1.79 (3H, s, H-29), 1.93 (1H, m, H-22), 2.01 (1H, m, H-21), 2.13 (3H, s, H-17), 2.48 (1H, dd, *J*=15.6, 5.7 Hz, H-19), 2.63 (1H, dd, *J*=15.6, 7.2 Hz, H-19), 3.54 (3H, s, OMe), 4.10 (1H, m, H-23), 4.24 (1H, m, H-20), 5.45 (1H, brt, *J*=8.4 Hz, H-24), 5.51 (1H, dd, *J*=14.1, 8.4 Hz, H-25), 5.81 (1H, d, *J*=11.1 Hz, H-27), 6.60 (1H, dd, *J*=14.1, 11.1 Hz, H-26), and 7.30–7.60 (5H, m, Ph); FABMS *m/z* 455 $(M+H)^+$; HRFABMS *m/z* 455.2039 $[(M+H)^+$, calcd for $C_{24}H_{30}O_5F_3$: 455.2045].

3.1.38. (*R*)-MTPA ester (7b) of 6a. The (*R*)-MTPA ester **7b** (0.88 mg, 1.94 μmol) was obtained from **6a** (0.50 mg, 2.09 μmol) in 93% yield through the same procedure as described for preparation of the (*S*)-MTPA ester of **11a**.

Compound **7b**. Colorless oil; ^1H NMR (600 MHz; $CDCl_3$) δ_H 1.52 (1H, m, H-21), 1.67 (1H, m, H-22), 1.70 (3H, s, H-40), 1.77 (3H, s, H-29), 1.99 (1H, m, H-22), 2.14 (3H, s, H-17), 2.16 (1H, m, H-21), 2.54 (1H, dd, *J*=15.6, 5.3 Hz, H-19), 2.68 (1H, dd, *J*=15.6, 7.6 Hz, H-19), 3.59 (3H, s, OMe), 4.11 (1H, m, H-23), 4.36 (1H, m, H-20), 5.34 (1H, dd, *J*=15.3, 7.6 Hz, H-25), 5.45 (1H, brt, *J*=7.8 Hz, H-24), 5.76 (1H, d, *J*=11.1 Hz, H-27), 6.50 (1H, dd, *J*=14.9, 11.1 Hz, H-26), and 7.30–7.60 (5H, m, Ph); FABMS *m/z* 455 $(M+H)^+$; HRFABMS *m/z* 455.2037 $[(M+H)^+$, calcd for $C_{24}H_{30}O_5F_3$: 455.2045].

3.1.39. (*S*)-MTPA ester (7c) of 6b. The (*S*)-MTPA ester **7c** (0.85 mg, 1.87 μmol) was obtained from **6b** (0.52 mg, 2.17 μmol) in 86% yield through the same procedure as described for preparation of the (*S*)-MTPA ester of **11a**.

Compound **7c**. Colorless oil; ^1H NMR (600 MHz; $CDCl_3$) δ_H 1.50 (1H, m, H-21), 1.85 (1H, m, H-22), 1.73 (3H, s, H-40), 1.78 (3H, s, H-29), 1.98 (1H, m, H-22), 2.10 (1H, m, H-21), 2.16 (3H, s, H-17), 2.50 (1H, dd, *J*=15.6, 5.7 Hz, H-19), 2.71 (1H, dd, *J*=15.6, 7.2 Hz, H-19), 3.54 (3H, s, OMe), 4.14 (1H, m, H-23), 4.29 (1H, m, H-20), 5.37 (1H, dd, *J*=15.3, 7.6 Hz, H-25), 5.62 (1H, dd, *J*=7.6, 3.8 Hz, H-24), 5.78 (1H, d, *J*=11.1 Hz, H-27), 6.54 (1H, dd, *J*=15.3, 11.1 Hz, H-26), and 7.30–7.70 (5H, m, Ph); FABMS *m/z* 455 $(M+H)^+$; HRFABMS *m/z* 455.2042 $[(M+H)^+$, calcd for $C_{24}H_{30}O_5F_3$: 455.2045].

3.1.40. (*R*)-MTPA ester (7d) of 6b. The (*R*)-MTPA ester **7d** (0.89 mg, 1.96 μmol) was obtained from **6b** (0.51 mg, 2.13 μmol) in 92% yield through the same procedure as described for preparation of the (*S*)-MTPA ester of **11a**.

Compound **7d**. Colorless oil; ^{1}H NMR (600 MHz; $CDCl_3$) δ_H 1.43 (1H, m, H-21), 1.77 (1H, m, H-22), 1.76 (3H, s, H-40), 1.79 (3H, s, H-29), 1.92 (1H, m, H-22), 2.02 (1H, m, H-21), 2.12 (3H, s, H-17), 2.44 (1H, dd, J=15.6, 6.1 Hz, H-19), 2.64 (1H, dd, J=15.6, 6.9 Hz, H-19), 3.55 (3H, s, OMe), 4.07 (1H, m, H-23), 4.10 (1H, m, H-20), 5.45 (1H, dd, J=15.3, 8.0 Hz, H-25), 5.62 (1H, dd, J=8.4, 4.2 Hz, H-24), 5.82 (1H, d, J=11.1 Hz, H-27), 6.61 (1H, dd, J=15.3, 11.1 Hz, H-26), and 7.30–7.70 (5H, m, Ph); FABMS m/z 455 $(M+H)^+$; HRFABMS m/z 455.2033 [$(M+H)^+$, calcd for $C_{24}H_{30}O_5F_3$: 455.2045].

3.1.41. Linear methyl ester 3 of amphidinolide C (1). Amphidinolide C (**1**, 0.9 mg) dissolved in acetone (30 μL) was treated with 2,2-dimethoxypropane (10 μL) and PPTS (0.24 mg) at rt for 1 h. After addition of Et_3N (0.24 μL) and evaporation of the solvent, the residue was subjected to CC (hexane–EtOAc, 3:1) to afford a 7,8-acetonide derivative[5] (1.2 mg) and 29-(1′-methoxy)isopropyl-7,8-acetonide derivative (0.4 mg) of **1**. To a solution of 29-(1′-methoxy)-isopropyl derivative (0.4 mg) in MeOH (30 μL) was added K_2CO_3 (0.14 mg), and the mixture was stirred at 4°C for 40 h. After filtration and evaporation, a mixture (0.4 mg) of four diastereomers of linear methyl ester was obtained. The mixture was subjected to C_{18} HPLC (Develosil ODS-HG-5, Nomura Chemical Co., Ltd., 10×250 mm; eluent, CH_3CN–H_2O, 65:35; flow rate, 2.5 mL/min; UV detection at 240 nm) to afford two linear methyl esters (0.08 mg, t_R 16.0 min; 0.08 mg, t_R 17.3 min) and a mixture of two other diasteromers (0.12 mg, t_R 16.6 min).

To the linear methyl ester eluted at 16.0 min (0.08 mg) in CH_2Cl_2 (15 μL) were added DMAP (0.015 μg), Et_3N (0.4 μL), and (*R*)-(−)-MTPACl (0.2 μL), and stirring was continued at rt for 6 h. After addition of *N*,*N*-dimethyl-1,3-propanediamine (0.2 μL), the reaction mixture was partitioned between CH_2Cl_2 and phosphate buffer. The organic layer was evaporated and the residue was purified by C_{18} HPLC (Develosil ODS-HG-5, 10×250 mm; eluent, CH_3CN–H_2O, 95:5; flow rate, 2.5 mL/min; UV detection at 240 nm) to afford **3** (0.08 mg): ^{1}H NMR (600 MHz; $CDCl_3$) δ_H 0.79 (3H, d, J=6.1 Hz, H_3-39), 0.88 (3H, J=7.4 Hz, H_3-34), 0.99 (3H, d, J=6.4 Hz, H_3-35), 1.08 (3H, d, J=7.2 Hz, H_3-38), 1.24 (1H, m, H-5b), 1.29 (2H, m, H_2-33), 1.29 (3H, s, Me), 1.32 (3H, s, Me), 1.38 (3H, s, Me), 1.40 (2H, m, H_2-32), 1.42 (1H, m, H-21b), 1.55 (3H, s, Me), 1.59 (1H, m, H-22b), 1.63 (3H, s, H_3-40), 1.86 (3H, s, H_3-37), 1.87 (2H, s, H_2-31), 1.89 (1H, m, H-4), 1.93 (1H, m, H-22a), 1.98 (1H, m, H-21a), 2.09 (1H, dt, J=12.3, 6.8 Hz, H-5a), 2.30 (1H, m, H-17b), 2.41 (1H, dd, J=15.4, 6.1 Hz, H-19b), 2.47 (1H, dd, J=15.3, 5.3 Hz, H-2b), 2.58 (1H, dd, J=15.3, 6.4 Hz, H-2a), 2.64 (1H, m, H-12), 2.64 (1H, m, H-19a), 2.68 (1H, m, H-14b), 2.83 (1H, m, H-16), 2.84 (1H, m, H-17a), 2.85 (1H, m, H-14a), 3.10 (3H, s, MeO), 3.49 (3H, s, MeO), 3.52 (3H, s, MeO), 3.66 (3H, s, MeO), 3.88 (1H, m, H-3), 3.92 (1H, m, H-6), 4.11 (1H, m, H-23), 4.12 (1H, m, H-7), 4.17 (1H, m, H-20), 4.47 (1H, s, H-29), 4.53 (1H, d, J=7.0 Hz, H-8), 4.93 (1H, s, H-41b), 4.95 (1H, s, H-41a), 5.08 (1H, s, H-36b), 5.35 (1H, s, H-36a), 5.48 (1H, brt, J=7.2 Hz, H-24), 5.62 (1H, dd, J=15.3, 7.9 Hz, H-25), 5.73 (1H, m, H-13), 5.81 (1H, s, H-10), 6.10 (1H, d, J=11.0 Hz, H-27), 6.61 (1H, dd, J=15.2, 11.0 Hz, H-26), and 7.32–7.57 (10H, m, Ph); m/z ESIMS m/z 1313 $(M+Na)^+$; HRESIMS m/z 1313.6199 [$(M+Na)^+$, calcd for $C_{69}H_{92}O_{16}F_6Na$: 1313.6187].

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