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Synthetic Study on a 26-Membered Macrolide, Amphidinolide B: Synthesis of the C_1—C_{13} Fragment

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The C_1—C_{13} fragment of amphidinolide B (**1**) was synthesized from D-erythrose (**3**). The Evans alkylation reaction protocol allowed the introduction of the stereogenic center at the C_{11} position, which was unambiguously confirmed by a single X-ray crystallographic analysis.

Amphidinolide B (**1**) and the related 18 congeners (amphidinolides A, C-S), have been isolated from cultured marine dinoflagellates of the genus *Amphidinium*, which was originally found living inside of Okinawan marine flatworms of the genus *Amphiscolops*. In 1987, Kobayashi et al. reported the first isolation and a 26-membered macrolide structure of amphidinolide B (**1**) (Fig. 1), on the basis of 2D-NMR technics, although their stereochemistry was unsettled.[1] This macrolide family has powerful antitumor activities. In particular, **1** shows IC_{50} values against L1210 (0.00014 μg ml^{-1}) and KB cells (0.0042 μg ml^{-1}). In 1994, the relative stereochemistry of **1** was identified on the basis of the X-ray crystallographic analysis by Shimizu et al.[2] Kobayashi established the absolute configuration by comparison of a degradation product of **1** with synthetic samples.[3]

In addition to the potent cytotoxic activites, the unique structure involving the conjugated exomethylene moiety, prompted us to initiate the synthetic investigation of amphidinolide B (**1**). We describe herein the synthesis of the C_1—C_{13} fragment of **1**.[4,5]

Results and Discussion

In our retrosynthetic analysis, amphidinolide B (**1**) can be divided into a top half and a bottom half **2** segments, and the latter had the vicinal diol at the C_8 and C_9 positions, as an epoxide equivalent. Both segments would be coupled

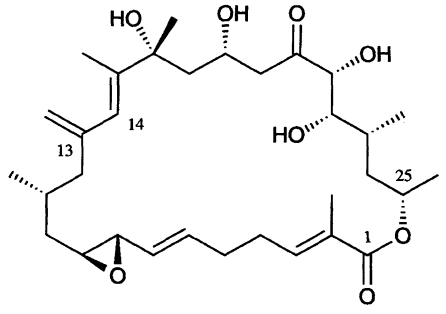
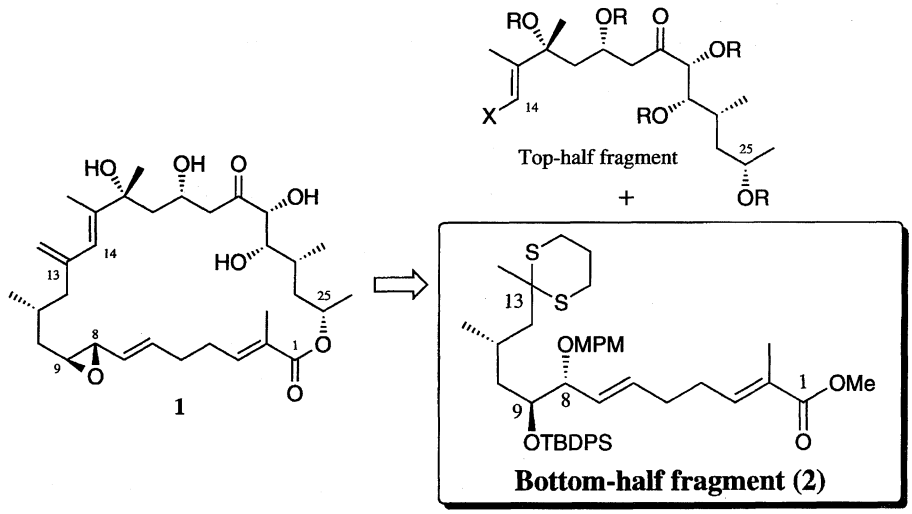


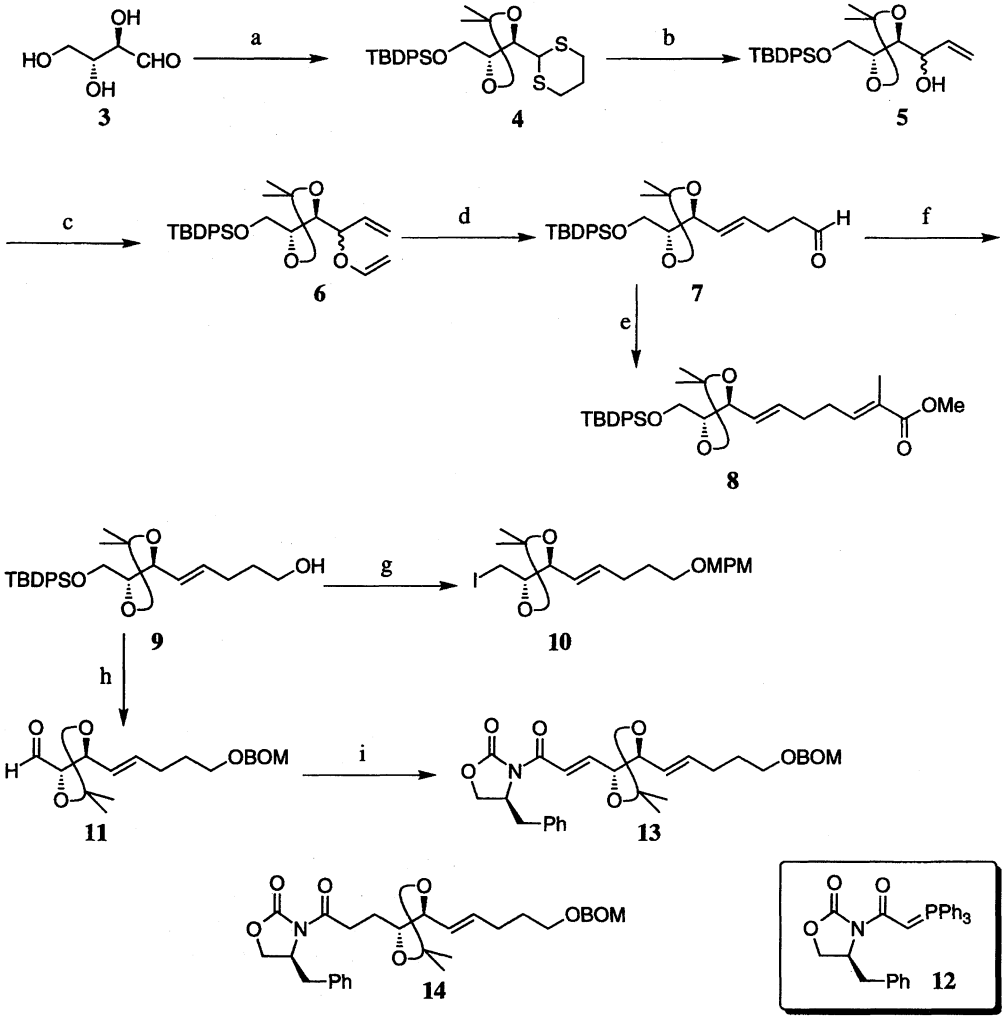
Fig. 1. Stereostructure of amphidinolide B (**1**).

by using Pd(0)-mediated diene synthesis,[6] and esterification (Scheme 1).

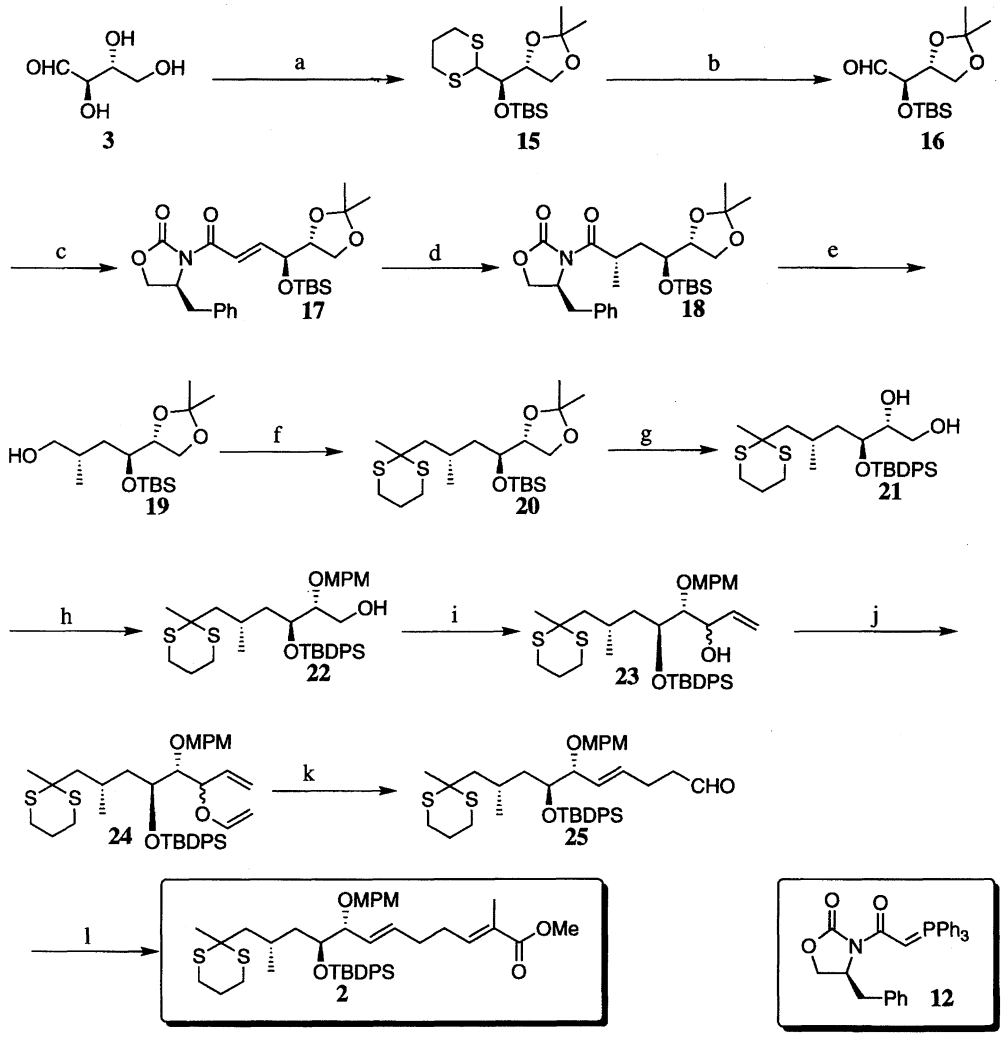
At outset, according to the synthetic plan, the bottom-half fragment was intended to be constructed by the successive coupling of the D-erythrose-derived center core (C_7—C_{10}) with the right unit (C_1—C_7) by the Claisen rearrangement, followed by the left unit (C_{11}—C_{13}) (Scheme 2). Thus, selective deprotection of **4** prepared from D-erythrose (**3**) in 3 steps, with $Hg(ClO_4)_2$ and $CaCO_3$ provided the corresponding aldehyde, which on treatment with vinylmagnesium bromide gave a diastereomeric 1 : 1 mixture of allyl alcohol **5** (76% in 2 steps). Without further separation, this mixture was reacted with ethyl vinyl ether in the presence of $Hg(OAc)_2$ to afford the corresponding vinyl ether **6** in 68% yield. Claisen rearrangement of **6** proceeded in an expected manner, leading to the aldehyde **7** in 97% yield. Upon treatment with the appropriate phosphorane, **7** was converted to the desired α,β-unsaturated ester **8** in 66% yield, with the same C_1—C_9 carbon framework as that of **1**. On the other hand, to introduce the left segment, **7** was reduced with $NaBH_4$, and the alcohol generated was protected as a MPM ether. Successive manipulation in four steps via alcohol **9**, provided the corresponding iodide **10** in good overall yield. Carbon chain homologation of **10** by the Evans oxazolidinone protocol was unsuccessful, probably owing to a repulsion of the bulky acetonide group. Such a stereochemical problem also prevented an alternative route to introduce the chirality at the C_{11} position by using amide **14**. To acquire this amide, the primary alcohol **9** was transformed into aldehyde **11**, which was submitted to the Witting reaction with the phosphorane **12**[7] prepared by coupling of triphenylphosphine with the corresponding bromoacetate in a similar manner to the case of 3-[3-(triphenylylidene)propanoyl]-1,3-oxazolidin-2-one,[8] which gave unsaturated amide **13**. Since selective reduction of the olefin position at the C_{10}—C_{11} positions with such reagents as NaTeH[9] or the Stryker reagent,[10] was sluggish, the C_{11} methyl group would be introduced at an early stage of the synthesis, as can be seen in Scheme 3.



Scheme 1. Retrosynthetic analysis of **1**.



Scheme 2. *reagents*: a. 1) 1,3-propanedithiol, concd HCl (64%): 2) TBDPSCl, imidazole (94%): 3) 2,2-dimethoxypropane, PPTS (97%). b. 1) $Hg(ClO_4)_2$, $CaCO_3$: 2) vinylmagnesium bromide (67% in 2 steps). c. ethyl vinyl ether, $Hg(OAc)_2$ (68%). d. 200 °C/decalin (97%). e. $Ph_3P{=}C(CH_3)COOMe$ (66%). f. $NaBH_4$ (99%). g. 1) MPMCl, NaH (68%): 2) TBAF (74%): 3) *p*-TsCl/pyr.: 4) NaI (85% in 2 steps). h. 1) BOMCl, *i*-Pr_2NEt, NaI: 2) TBAF (86% in 2 steps): 3) Dess–Martin reagent (99%). i. **12**/PhH (76%).



Scheme 3. *reagents*: a. 1) 1,3-propanedithiol, concd HCl: 2) 2,2-dimethoxypropane, *p*-TsCl (64%): 3) TBSOTf, 2,6-lutidine (93%). b. $Hg(ClO_4)_2$, $CaCO_3$. c. **12**/PhH (75% in 2 steps). d. 1) H_2, 10% Pd/C (95%): 2) LDA, then MeI (83%). e. $LiAlH_4$ (88%). f. 1) *p*-TsCl/pyr.: 2) NaI (89% in 2 steps): 3) 2-methyl-1,3-dithiane, *t*-BuLi, HMPA (quant.). g. 1) TBAF (88%): 2) TBDPSCl, imidazole, DMAP: 3) 80% AcOH aq (83% in 2 steps). h. 1) anisaldehyde dimethyl acetal, PPTS: 2) DIBAL-H (73% in 2 steps). i. 1) SO_3·pyr., DMSO, Et_3N: 2) vinylmagnesium bromide (78% in 2 steps). j. ethyl vinyl ether, $Hg(OAc)_2$ (22%). k. 200 °C/decalin (50%). l. $Ph_3P{=}C(CH_3)COOMe$ (74%).

To realize this plan, the aldehyde **16**, prepared from **15**, was coupled with the phosphorane **12** to give α,β-unsaturated amide **17** in 75% yield in 2 steps. With monitoring by TLC, this reaction produced a sole product, the ^1H NMR spectrum of which indicated an *E*-olefinic structure. Catalytic hydrogenation of **17**, followed by methylation under the Evans chiral auxiliary conditions[11] provided **18** in 83% yield. The stereochemistry of the newly introduced methyl group was unambiguously confirmed by a single X-ray crystallographic analysis, as depicted in Fig. 2. After reductive removal of the oxazolidinone moiety of **18**, the resulting primary alcohol **19** was treated by a three-step procedure to afford dithiane **20** in 89% yield from **19**.

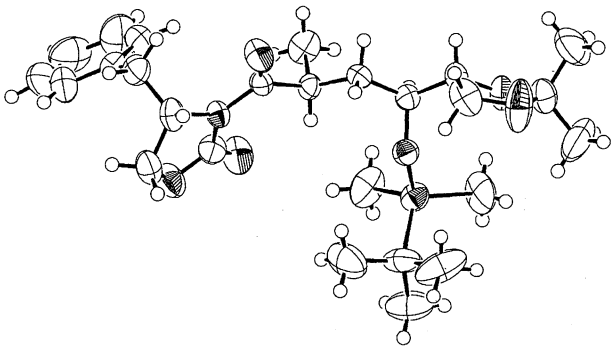


Fig. 2. Ortep drawing of compound **18**.

Exchange of the siloxy protective group, followed by hydrolysis under 80% AcOH aq conditions, effected conversion of **20** to diol **21** in 73% yield. Diol **21** was treated with anisaldehyde dimethyl acetal in the presence of catalytic amounts of PPTS (pyridinium *p*-toluenesulfonate), followed by the regioselective reductive acetal opening with DIBAL-H[12] to give primary alcohol **22** (73% in 2 steps). Oxidation of primary alcohol **22** with SO_3·pyr-DMSO provided the corresponding aldehyde, which was treated with vinylmagnesium bromide to give a diastereomeric 1 : 1 mixture of allyl alco-

hol **23** (78% in 2 steps). Without separation of this mixture, **23** was treated with ethyl vinyl ether in the presence of $Hg(OAc)_2$ to provide the vinyl ether **24** (22%). The low yield of this etherification might be derived from an affinity of $Hg(OAc)_2$ for the thio protective group. Improvement of this reaction is in progress. Claisen rearrangement of **24** provided the corresponding aldehyde **25** (50%), which was treated by the same Wittig reaction as described in the case of **8** to provide the desired α,β-unsaturated ester **2** (74%).

In summary, enantioselective synthesis of the C_1—C_{13} fragment of the antitumor agent, amphidinolide B (**1**), was unambiguously accomplished from D-erythrose (**3**). Further investigation toward a total synthesis of **1** is in progress.

Experimental

IR spectra were recorded on a JASCO Model A-202 spectrophotometer. ^{1}H NMR and ^{13}C NMR spectra were obtained on a JEOL JNM EX-270, a JEOL JNM GX-400 NMR, or a JEOL JNM ALPHA-400 spectrometer in a deuteriochloroform ($CDCl_3$) solution using tetramethylsilane as an internal standard, unless otherwise stated. High resolution mass spectra were obtained on a Hitachi M-80 B GC-MS spectrometer operating at the ionization energy of 70 eV. Optical rotations were recorded on a JASCO DIP-360 digital polarimeter. All of the melting points were obtained on a Yanaco MP-S3 and are uncorrected. Preparative and analytical TLC were done on silica-gel plates (Kieselgel 60 F_{254}, E. Merck A. G., Germany) using UV light and/or 5% phosphomolybdic acid in ethanol for detection. Katayama silica gel (K 070) was used for column chromatography.

(4*S*,5*R*)-4-(*t*-Butyldiphenylsiloxy)-5-(1,3-dithian-2-yl)-2,2-dimethyl-1,3-dioxolane (4). To an ice-cooled suspension of D-erythrose (**3**, 255 mg, 2.13 mmol) in THF (10 ml) were added 1,3-propanedithiol (0.4 ml, 4.25 mmol) and 12 M HCl (10 ml). The mixture was warmed up to ambient temperature and stirred overnight. The resulted mixture was concentrated in vacuo, and the residue was chromatographed on a silica-gel column (10/1 $CHCl_3$/MeOH) to give dithiane triol (286 mg, 64%).

To a solution of the triol (130 mg, 0.62 mmol) in DMF (3 ml) were successively added imidazole (105 mg, 1.60 mmol) and TBDPSCl (*t*-butyldiphenylsilyl chloride) (0.23 ml, 0.87 mmol). After being stirred at ambient temperature for 1 h under an argon atmosphere, the reaction mixture was poured into ice-water, and extracted with EtOAc (3×50 ml). The combined organic layer was washed with 1 M HCl, sat. aq $NaHCO_3$, and brine, dried (Na_2SO_4), then evaporated. The residue was purified by silica-gel column chromatography (3/1 hexane/EtOAc) to give a diol (230 mg, 94%).

The diol (6.07 g, 14 mmol) was dissolved in a mixture of CH_2Cl_2 (135 ml) and 2,2-dimethoxypropane (8.3 ml, 68 mmol) in the presence of catalytic amounts of PPTS. After being stirred at ambient temperature for 24 h, the reaction mixture was poured into sat. aq $NaHCO_3$ and extracted with $CHCl_3$ (3×500 ml). The combined organic layer was washed with brine, dried (Na_2SO_4), then concentrated in vacuo. The residue was purified by silica-gel column chromatography (10/1 hexane/EtOAc) to yield **4** (6.38 g, 97%): IR (film) 1430 cm^{-1}; ^{1}H NMR δ = 1.09 (9H, s), 1.37 (3H, s), 1.52 (3H, s), 1.87—2.05 (2H, complex), 2.64—2.87 (4H, complex), 3.96 (1H, dd, J = 4.6, 10.9 Hz), 4.09 (1H, dd, J = 5.6, 10.9 Hz), 4.32 (1H, dd, J = 5.3, 10.6 Hz), 4.37—4.46 (2H, complex), and 7.36—7.73 (10H, complex).

(4*R*,5*S*)-4-(*t*-Butyldiphenylsiloxymethyl)-2,2-dimethyl-5-(1-vinyloxyallyl)-1,3-dioxolane (5). To a solution of **4** (223 mg, 0.47 mmol) in THF (4 ml) and H_2O (0.8 ml) were added $Hg(ClO_4)_2$ (1.06 g, 2.34 mmol) and $CaCO_3$ (234 mg, 2.34 mmol) at ambient temperature. After being stirred for 45 min, the reaction mixture was diluted with Et_2O (40 ml), and then poured into 1 M aq KI (50 ml). The ethereal layer was removed, and the aqueous layer was extracted with Et_2O (3×50 ml), the combined organic layer was washed with 1 M aq KI, sat. aq $NaHCO_3$, and brine, dried (Na_2SO_4), then evaporated. Purification of the residue by silica-gel column chromatography (7/1 hexane/EtOAc) gave an aldehyde.

To a ice-cooled solution of the aldehyde in THF (4.7 ml) was added 1 M vinylmagnesium bromide solution in THF (0.8 ml, 0.8 mmol) under an argon atmosphere. After being stirred for 60 min, the reaction mixture was poured into aq NH_4Cl (10 ml), and extracted with $CHCl_3$ (3×50 ml). The combined organics were washed with brine, dried (Na_2SO_4), then concentrated in vacuo. The residue was purified by PTLC (10/1 hexane/EtOAc) to give a diastereomeric mixture of **5** (129 mg, 67% in 2 steps) as a colorless syrup. Major product: $[\alpha]_D^{25}$ +1.3° (*c* 2.48, $CHCl_3$); IR (film) 3480 cm^{-1}; ^{1}H NMR δ = 1.07 (9H, s), 1.35 (3H, s), 1.46 (3H, s), 3.78 (1H, dd, J = 4.26, 10.6 Hz), 4.00 (1H, dd, J = 6.6, 10.6 Hz), 4.12 (1H, dd, J = 4.6, 6.6 Hz), 4.26 (1H, ddd, J = 5.0, 6.6, 6.6 Hz), 4.41 (1H, dd, J = 4.6, 6.6 Hz), 5.14 (1H, ddd, J = 1.7, 1.7, 10.6 Hz), 5.33 (1H, ddd, J = 1.7, 1.7, 17.5 Hz), 5.95 (1H, ddd, J = 5.6, 10.6, 17.5 Hz), 7.36—7.70 (10H, complex); ^{13}C NMR δ = 137.6, 135.6, 132.94, 132.89, 129.85, 129.82, 127.7, 116.2, 108.3, 79.6, 77.2, 70.1, 62.6, 27.2, 26.8, 24.9, and 19.2. Found: *m/z* 411.1964. Calcd for $C_{24}H_{31}O_4Si$: M − CH_3, 411.1890. Minor product: $[\alpha]_D^{25}$ −7.4° (*c* 2.07, $CHCl_3$); IR (film) 3480 cm^{-1}; ^{1}H NMR δ = 1.07 (9H, s), 1.30 (3H, s), 1.33 (3H, s), 3.65 (1H, dd, J = 3.6, 10.9 Hz), 3.90 (1H, dd, J = 9.6, 10.6 Hz), 4.12 (1H, dd, J = 5.6, 9.2 Hz), 4.35 (1H, ddd, J = 3.6, 5.6, 9.2 Hz), 4.42 (1H, dd, J = 4.6, 6.6 Hz), 5.28 (1H, dt, J = 1.7, 10.6 Hz), 5.47 (1H, dt, J = 1.7, 17.5 Hz), 6.05 (1H, ddd, J = 5.3, 10.6, 17.2 Hz), and 7.38—7.70 (10H, complex); ^{13}C NMR δ = 137.3, 135.5, 132.0, 131.8, 130.18, 130.14, 127.97, 127.94, 116.3, 108.6, 80.5, 77.0, 70.0, 62.6, 27.8, 26.7, 25.2, and 19.0. The mixture was used for the next step without further separation.

1-[(4*S*,5*R*)-5-(*t*-Butyldiphenylsiloxymethyl)-2,2-dimethyl(1,3-dioxolan-4-yl)]-1-vinyloxyprop-2-ene (6). To a solution of **5** (284 mg, 0.67 mmol) in ethyl vinyl ether (10 ml) was added $Hg(OAc)_2$ (212 mg, 0.67 mmol); the mixture was stirred at refluxing temperature overnight. The resultant mixture was poured into 1 M aq KI (50 ml), and extracted with EtOAc (3×50 ml). The combined organic layer was washed with brine, dried (Na_2SO_4), then concentrated in vacuo. The residue was purified by PTLC (10/1 hexane/EtOAc) to give **6** (205 mg, 68%) as a colorless oil: IR (film) 3072 and 3048 cm^{-1}; ^{1}H NMR δ = 1.07 (9H, s), 1.36 (3H, s), 1.48 (3H, s), 3.80 (1H, dd, J = 5.6, 10.6 Hz), 3.87 (1H, dd, J = 5.9, 10.6 Hz), 4.00 (1H, dd, J = 1.7, 6.6 Hz), 4.18—4.31 (3H, complex), 4.46 (1H, dd, J = 5.6, 5.6 Hz), 5.22 (1H, d, J = 17.2 Hz), 5.25 (1H, d, J = 10.6 Hz), 5.87 (1H, ddd, J = 6.3, 10.9, 17.2 Hz), 6.25 (1H, dd, J = 6.6, 14.2 Hz), and 7.35—7.72 (5H, complex); ^{13}C NMR δ = 150.0, 135.6, 134.5, 133.10, 133.05, 129.78, 129.75, 127.7, 118.6, 109.1, 89.3, 79.2, 77.9, 77.0, 62.8, 27.0, 26.9, 25.5, and 19.2.

(4*E*)-5-[(4*S*,5*R*)-5-(*t*-Butyldiphenylsiloxymethyl)-2,2-dimethyl-1,3-dioxolan-4-yl]pent-4-enal (7). Compound **6** (252 mg, 0.56 mmol) was dissolved in decalin (0.1 ml) and stirred at 200 °C under an argon atmosphere in sealed tube. After being stirred for 15 min, the reaction mixture was purified by PTLC (5/1 hexane/EtOAc) to give **7** (244 mg, 97%) as a colorless oil: IR (film) 3071, 3048, and 1726 cm^{-1}; ^{1}H NMR δ = 1.05 (9H, s), 1.35 (3H, s), 1.43 (3H, s), 2.28—2.49 (4H, complex), 3.62 (1H, dd, J = 5.3, 10.6 Hz), 3.69

(1H, dd, J = 6.6, 10.6 Hz), 4.23 (1H, dd, J = 6.6, 11.5 Hz), 4.61 (1H, dd, J = 6.6, 7.6 Hz), 5.61 (1H, dd, J = 7.6, 15.5 Hz), 5.78 (1H, ddd, J = 6.6, 7.6, 15.5 Hz), 7.26—7.67 (5H, complex), and 9.71 (1H, d, J = 1.3 Hz). Because of its instability, this sample was immediately used in the next reaction.

Methyl (2*E*,6*E*)-7-[(4*S*,5*R*)-5-(*t*-Butyldiphenylsiloxymethyl)-2,2-dimethyl-1,3-dioxolan-4-yl]-2-methylhepta-2,6-dienoate (8). To a solution of **7** (3.9 mg, 0.009 mmol) in CH_2Cl_2 (0.5 ml) was added $Ph_3P{=}C(CH_3)COOMe$ (15 mg, 0.04 mmol); the mixture was stirred for 1 h at ambient temperature. The resulting mixture was concentrated in vacuo, and the residue was purified by PTLC (5/1 hexane/EtOAc) to give **8** (3 mg, 66%) as an amorphous solid: ^{1}H NMR δ = 1.04 (9H, s), 1.36 (3H, s), 1.43 (3H, s) 2.05—2.23 (4H, complex), 3.63 (1H, dd, J = 5.3, 10.6 Hz), 3.71 (1H, dd, J = 6.6, 11.6 Hz), 3.72 (3H, s), 4.23 (1H, dd, J = 6.6, 11.6 Hz), 4.63 (1H, dd, J = 6.6, 7.4 Hz), 5.63 (1H, dd, J = 7.6, 15.6 Hz), 5.80 (1H, ddd, J = 5.9, 5.9, 15.2 Hz), 6.72 (1H, dd, J = 5.6, 6.9 Hz), and 7.26—7.68 (5H, complex); ^{13}C NMR δ = 168.6, 141.3, 135.6, 135.5, 134.0, 129.7, 126.7, 126.1, 108.3, 78.5, 78.4, 77.2, 62.9, 51.7, 31.2, 29.7, 28.2, 27.8, 26.8, 25.4, 19.2, and 12.4. Found: m/z 522.2765. Calcd for $C_{31}H_{42}O_5Si$: M, 522.2798.

(4*E*)-5-[(4*S*,5*R*)-5-(*t*-Butyldiphenylsiloxymethyl)-2,2-dimethyl-1,3-dioxolan-4-yl]pent-4-en-1-ol (9). To a solution of **7** (74 mg, 0.16 mmol) in EtOH (1.6 ml) was added $NaBH_4$ (5 mg, 0.13 mmol) at 0 °C; the mixture was stirred at the same temperature for 10 min. Several drops of H_2O were added, and the reaction mixture was concentrated in vacuo. The residue was purified by PTLC (2/1 hexane/EtOAc) to give **9** (74.5 mg, 99%) as a colorless syrup: IR (film) 3450 cm^{-1}; ^{1}H NMR δ = 1.05 (9H, s), 1.36 (3H, s), 1.44 (3H, s), 1.62 (2H, dd, J = 6.6, 14.2 Hz), 2.13 (2H, dd, J = 6.9, 14.2 Hz), 3.58 (2H, dd, J = 6.6, 6.9 Hz), 3.69 (2H, dd, J = 6.3, 11.2 Hz), 4.23 (1H, t, J = 6.6, 7.6 Hz), 5.59 (1H, dd, J = 7.9, 15.5 Hz), 5.78 (1H, ddd, J = 6.6, 6.6, 15.2 Hz), and 7.35—7.69 (10H, complex); ^{13}C NMR δ = 135.6, 135.5, 134.7, 133.3, 133.2, 129.9, 129.7, 127.8, 127.6, 125.8, 108.3, 78.6, 78.4, 74.0, 73.5, 62.3, 31.8, 31.7, 28.9, 28.6, 27.8, 26.8, 25.4, 19.2.

(4*S*,5*S*)-4-(Iodomethyl)-5-[5-(1*E*)-(4-methoxybenzyloxy)pent-1-enyl]-2,2-dimethyl-1,3-dioxolane (10). To an ice-cooled solution of **9** (234 mg, 0.51 mmol) in DMF (2.6 ml) was added NaH (51.3 mg, 1.3 mmol, 60% dispersion in mineral oil); the mixture was stirred for 30 min. MPMCl (4-methoxybenzyl chloride) (0.75 ml, 5.1 mmol) was added, and the mixture was warmed up to ambient temperature, during 3 h. The reaction mixture was poured into aq NH_4Cl (20 ml), and extracted with EtOAc (3×50 ml). The combined organic layer was washed with brine, dried (Na_2SO_4), then evaporated. The residue was purified by PTLC (5/1 hexane/EtOAc) to give a MPM ether (186 mg, 63%) as a colorless oil.

To a solution of the MPM ether (186 mg, 0.32 mmol) in THF (3 ml) was added 1 M n-Bu_4NF in THF (0.5 ml, 0.5 mmol) at 0 °C; the mixture was warmed up to ambient temperature. After being stirred for 1 h, the reaction mixture was poured into aq NH_4Cl (20 ml), and extracted with EtOAc (3×20 ml). The combined organic layer was washed with brine, dried (Na_2SO_4), then concentrated in vacuo. The residue was purified by PTLC (1/1 hexane/EtOAc) to give an alcohol (81 mg, 74%) as a colorless syrup.

To a solution of the alcohol (81 mg, 0.24 mmol) in pyridine (1 ml) at 0 °C was added TsCl (92 mg, 0.48 mmol); the mixture was slowly warmed up to ambient temperature. After being stirred at the same temperature overnight, the reaction mixture was poured into ice-water, and the mixture was extracted with EtOAc (3×20 ml). The combined organic extracts were washed with 1 M HCl, sat. aq $NaHCO_3$, and brine, and dried (Na_2SO_4), then concentrated in vacuo. The residue was purified by PTLC (2/1 hexane/EtOAc) to give a tosylate (113 mg) as a colorless oil.

To a solution of the tosylate (113 mg, 0.24 mmol) in acetone (5 ml) was added NaI (361 mg, 2.4 mmol). After being stirred at refluxing temperature overnight, the reaction mixture was cooled, and poured into ice-water, then the mixture was extracted with EtOAc (3×20 ml). The combined organic layer was washed with brine, dried (Na_2SO_4), then concentrated in vacuo. The residue was purified by PTLC (3/1 hexane/EtOAc) to give **10** (96 mg, 85% yield in 2 steps) as a colorless oil: ^{1}H NMR δ = 1.38 (3H, s), 1.50 (3H, s), 1.69 (2H, complex), 2.16 (2H, dd, J = 6.6, 14.2 Hz), 4.44 (2H, t, J = 6.6 Hz), 3.54 (2H, d, J = 5.61 Hz), 3.80 (3H, s),4.20 (1H, dd, J = 5.9, 12.5 Hz), 4.42 (2H, s), 4.60 (1H, dd, J = 6.0, 7.6 Hz), 5.49 (1H, dd, J = 7.9, 15.2 Hz), 5.80 (1H, ddd, J = 6.6, 6.9, 15.2 Hz), and 7.25 (2H, d, J = 8.9 Hz).

5-{(1*E*)-5-[(Benzyloxy)methoxy]pent-1-enyl}(4*S*,5*S*)-2,2-dimethyl-1,3-dioxolane-4-carbaldehyde (11). To a solution of **9** (180 mg, 0.4 mmol) in THF (4 ml) were added i-Pr_2NEt (0.11 ml, 0.64 mmol), BOMCl (benzyloxymethyl chloride) (0.09 ml, 0.6 mmol), and NaI (6 mg, 0.04 mmol) at ambient temperature. After being stirred for 2 d, the reaction mixture was poured into ice-water, and the mixture was extracted with EtOAc (3×50 ml). The combined organic layer was successively washed with 1 M HCl, sat. aq $NaHCO_3$, and brine, dried (Na_2SO_4), then evaporated. The residue was purified by silica-gel column chromatography (8/1 hexane/EtOAc) to give an ether (228 mg) as a colorless oil.

To a solution of the ether (228 mg, 0.4 mmol) in THF (4 ml) was added 1 M n-Bu_4NF in THF (0.64 ml, 0.64 mmol) at 0 °C; the mixture was warmed up to ambient temperature. After being stirred for 1 h, the reaction mixture was poured into aq NH_4Cl (20 ml), and extracted with EtOAc (3×20 ml). The combined organic layer was washed with brine, dried (Na_2SO_4), then evaporated. The residue was purified by silica-gel column chromatography (1/1 hexane/EtOAc) to give an alcohol (114 mg, 86% yield in 2 steps) as a colorless syrup.

To a solution of the alcohol (50 mg, 0.15 mmol) in CH_2Cl_2 (1.5 ml) at ambient temperature were added pyridine (0.04 ml) and Dess–Martin reagent (102 mg, 0.23 mmol). After being stirred for 5 min, the reaction mixture was poured into aq $Na_2S_2O_3$ (20 ml), and extrated with EtOAc (3×20 ml). The combined organic layer was washed with brine, dried (Na_2SO_4), then evaporated. The residue was purified by PTLC (1/1 hexane/EtOAc) to give **11** (50 mg, 99%) as a colorless oil: IR (film) 1733 cm^{-1}; ^{1}H NMR δ = 1.43 (3H, s), 1.61 (3H, s), 1.68 (2H, tt, J = 6.6, 6.6 Hz), 2.16 (2H, dt, J = 6.9, 6.6 Hz), 3.57 (2H, t, J = 6.6 Hz), 4.35 (1H, dd, J = 3.0, 7.6 Hz), 4.59 (2H, s), 4.74 (2H, s), 4.81 (1H, dd, J = 7.6, 7.6 Hz), 5.39 (1H, dd, J = 7.6, 15.1 Hz), 5.90 (1H, dt, J = 15.1, 6.9 Hz), 7.26—7.36 (5H, complex), and 9.55 (1H, d, J = 3.0 Hz).

(4*S*)-4-Benzyl-3-[(2*E*)-3-(5-{(1*E*)-5-[(benzyloxy)methoxy]-pent-1-enyl}(4*R*,5*S*)-2,2-dimethyl-1,3-dioxolan-4yl)prop-2-enoyl]-1,3-oxazolidin-2-one (13). To a solution of **11** (50 mg, 0.15 mmol) in CH_2Cl_2 (1.5 ml) was added phosphorane **12**[7,8] (216 mg, 0.45 mmol); the mixture was stirred at ambient temperature overnight. The resulted mixture was concentrated in vacuo, and the residue was purified by PTLC (2/1 hexane/EtOAc) to give **13** (61 mg, 76%, E/Z = 3/1) as an amorphous solid. A part of the sample was further separated to get the physical data.

Z isomer: IR (film) 3030, 1783, 1681, and 1634 cm^{-1}; ^{1}H NMR δ = 1.41 (3H, s), 1.55 (3H, s), 1.65 (2H, m), 2.10 (2H, m), 2.74 (1H, dd, J = 9.6, 13.5 Hz), 3.30 (1H, dd, J = 3.3, 13.5 Hz), 3.55 (2H, t, J = 6.6 Hz) 4.17 (2H, complex), 4.57 (2H, s), 4.67 (1H, m),

4.72 (2H, s), 4.93 (1H, dd, J = 7.9, 7.9 Hz), 5.39 (1H, dd, J = 7.9, 15.5 Hz), 5.52 (1H, dt, J = 1.3, 7.9 Hz), 5.76 (1H, dt, J = 15.5, 6.6 Hz), 6.05 (1H, dd, J = 7.6, 11.9 Hz), and 7.19 —7.33 (11H, complex); ^{13}C NMR δ = 163.9, 153.1, 148.4, 137.9, 135.1, 134.1, 129.3, 128.9, 128.4, 127.6, 127.4, 126.2, 120.3, 109.0, 94.5, 79.8, 69.2, 67.2, 66.0, 55.0, 37.7, 29.1, 28.8, 27.9, and 25.1.

E isomer: IR (film) 3029, 1779, 1682, and 1643 cm^{-1}; ^{1}H NMR δ = 1.42 (3H, s), 1.59 (3H, s), 1.66 (2H, m), 2.16 (2H, m), 2.77 (1H, dd, J = 9.6, 13.5 Hz), 3.34 (1H, dd, J = 3.3, 13.5 Hz), 3.56 (2H, t, J = 6.6 Hz), 4.17 (2H, complex), 4.58 (2H, s), 4.66—4.82 (3H, complex), 4.73 (2H, s), 5.41 (1H, dd, J = 8.3, 15.1 Hz), 5.84 (1H, dt, J = 15.1, 6.3 Hz), 7.03, (1H, dd, J = 6.3, 15.5 Hz), 7.19—7.34 (10H, complex), and 7.48 (1H, dd, J = 1.3, 15.5 Hz); ^{13}C NMR δ = 164.2, 153.2, 146.1, 137.9, 135.9, 135.3, 129.4, 128.9, 127.8, 127.6, 127.3, 125.3, 121.8, 109.5, 94.5, 79.7, 78.0, 69.2, 67.1, 66.1, 55.3, 37.8, 28.9, 27.8, and 25.4. Found: *m/z* 536.2644. Calcd for $C_{31}H_{38}NO_7$: M+H, 536.2643.

(1*R*)-*t*-Butyldimethylsiloxy[(4*R*)-2,2-dimethyl-1,3-dioxolan-4-yl]-1,3-dithian-2-ylmethane (15). A crude dithiane derivative obtained from **3** (9.0 g, 75 mmol) by the same procedure as in the case of **4**, was dissolved in a mixture of acetone (135 ml) and 2,2-dimethoxypropane (4.25 ml, 38 mmol) in the presence of catalytic amounts of TsOH. After being stirred for 24 h at ambient temperature, the reaction mixture was poured into sat. aq $NaHCO_3$, and extracted with $CHCl_3$ (3×500 ml). The combined organic layer was washed with brine, dried (Na_2SO_4), then concentrated in vacuo. The residue was purified by silica-gel column chromatography (3/1 hexane/EtOAc) to yield dithiane alcohol (9.73 g, 58% yield from **3**).

To a solution of the alcohol in CH_2Cl_2 (75 ml) were successively added 2,6-lutidine (5.90 ml, 50.6 mmol) and TBSOTf (*t*-butyldimethylsilyl triflate) (11.6 ml, 50.6 mmol). After being stirred at ambient temperature under an argon atmosphere overnight, the reaction mixture was poured into ice-water, and the mixture was extracted with EtOAc (3×300 ml). The combined organic layer was successively washed with 1 M HCl, sat. aq $NaHCO_3$, and brine, and dried (Na_2SO_4), then concentrated in vacuo. The residue was purified by silica-gel column chromatography (10/1 hexane/EtOAc) to give **15** (13.1 g, 93%) as a colorless oil: $[\alpha]_D^{23}$ +13.9° (*c* 2.30, $CHCl_3$); IR (film) 2950 cm^{-1}; ^{1}H NMR δ = 0.15 (3H, s), 0.27 (3H, s), 0.96 (9H, s), 1.38 (3H, s), 1.45 (3H, s), 1.90 (1H, m), 2.15 (1H, m), 2.82—2.99 (4H, complex), 3.90—3.95 (2H, complex), 4.07 (1H, dd, J = 6.3, 8.3 Hz), 4.30 (1H, dd, J = 6.3, 12.2 Hz), and 4.44 (1H, d, J = 2.3 Hz); ^{13}C NMR δ = 108.8, 76.4, 75.8, 66.2, 53.3, 31.4, 30.9, 26.7, 26.4, 25.9, 18.3, −3.9, and −4.3. Found: *m/z* 349.1315. Calcd for $C_{15}H_{29}O_3S_2Si$: M − Me, 349.1325.

(4*S*)-4-Benzyl-3-{(2*E*,4*S*)-4-(*t*-butyldimethylsiloxy)-4-[(4*R*)-2,2-dimethyl-1,3-dioxolan-4-yl]but-2-enoyl}-1,3-oxazolidin-2-one (17). To a solution of **15** (8.04 g, 22 mmol) in THF (150 ml) and H_2O (30 ml) were added $Hg(ClO_4)_2$ (37.6 g, 88 mmol) and $CaCO_3$ (8.80 g, 88 mmol) at ambient temperature. After being stirred for 45 min, the reaction mixture was diluted with Et_2O (300 ml), and poured into 1 M aq KI (600 ml). The mixture was extracted with Et_2O (3×400 ml), and the combined organic layer was washed with 1 M aq KI, sat. aq $NaHCO_3$, and brine, dried (Na_2SO_4), then concentrated in vacuo. Purification of the residue by silica-gel column chromatography (5/1 hexane/EtOAc) gave **16** (6.05 g) as a colorless oil.

To a solution of **16** (6.05 g, 22 mmol) in benzene (200 ml) was added phosphorane **12** (17 g, 35 mmol); the mixture was stirred overnight at 50 °C. The resulted mixture was concentrated in vacuo, and residue was purified by silica-gel column chromatography (5/1 hexane/EtOAc), followed by 5% (w/w) $AgNO_3$–silica-gel column chromatography (3/1 hexane/EtOAc) to give **17** (7.72 g, 75% yield from **15**) as an amorphous solid: $[\alpha]_D^{23}$ +37.8° (*c* 1.43, $CHCl_3$); IR (film) 1780, 1680, and 1635 cm^{-1}; ^{1}H NMR δ = 0.09 (3H, s), 0.12 (3H, s), 0.94 (9H, s), 1.35 (3H, s), 1.45 (3H, s), 2.82 (1H, dd, J = 9.6, 13.5 Hz), 3.35 (1H, dd, J = 3.3, 13.5 Hz), 3.90—4.06 (3H, complex), 4.15—4.25 (2H, complex), 4.40 (1H, m), 4.73 (1H, ddd, J = 3.3, 9.6, 12.9 Hz), 7.17—7.36 (6H, complex), and 7.50 (1H, dd, J = 1.7, 15.5 Hz); ^{13}C NMR δ = 164.6, 153.1, 149.8, 135.3, 129.4, 128.9, 127.3, 120.7, 109.7, 93.5, 78.4, 77.2, 72.6, 66.1, 66.0, 55.3, 37.8, 26.7, 25.8, 25.5, 25.3, 18.1, −4.3, and −4.9. Found: *m/z* 476.2458. Calcd for $C_{25}H_{38}NO_6Si$: M+H, 476.2465.

(4*S*)-4-Benzyl-3-{(2*S*,4*S*)-4-(*t*-butyldimethylsiloxy)-[(4*R*)-2,2-dimethyl-1,3-dioxolan-4-yl]-2-methylbutanoyl}-1,3-oxazolidin-2-one (18). A solution of **17** (10.6 g, 23 mmol) in EtOH (200 ml) in the presence of catalytic amounts of Pd/C was stirred for 5 h at ambient temperature in a hydrogen atmosphere. The reaction mixture was filtered, and the solid was washed with EtOH (200 ml). The filtrate and washings were combined and evaporated. Purification of the residue by silica-gel column chromatography (3/1 hexane/EtOAc) gave an amide (10.6 g, 99%) as an amorphous solid.

To a solution of the amide (72 mg, 0.15 mmol) in THF (1.5 ml) at −78 °C was added 2 M LDA in THF (0.15 ml, 0.3 mmol); the mixture was stirred at the same temperature for 30 min in an argon atmosphere. After the addition of MeI (0.25 ml, 4.5 mmol), the reaction mixture was warmed up to −30 °C, and the stirring was continued for another 1 h. The reaction mixture was poured into aq NH_4Cl (20 ml), and extracted with EtOAc (3×20 ml). The combined organic layer was washed with brine, dried (Na_2SO_4), then evaporated. The residue was purified by PTLC (5/1 hexane/EtOAc) to give **18** (62 mg, 83%): Mp 93—94 °C (colorless needles from *i*-PrOH); $[\alpha]_D^{22}$ +52.0° (*c* 0.74, $CHCl_3$); IR (film) 1780 and 1695 cm^{-1}; ^{1}H NMR δ = 0.11 (3H, s), 0.16 (3H, s), 0.89 (9H, s), 1.25 (3H, d, J = 6.9 Hz), 1.31 (3H, s), 1.33 (3H, s), 2.10 (1H, m), 2.78 (1H, dd, J = 9.6, 13.2 Hz), 3.23 (1H, dd, J = 3.3, 13.5 Hz), 3.74 (2H, complex), 3.97 (3H, complex), 4.16 (2H, d, J = 5.3 Hz), 4.68 (1H, m), and 7.20—7.36 (5H, complex); ^{13}C NMR δ = 176.7, 152.6, 135.2, 129.5, 128.9, 127.3, 109.0, 79.2, 77.2, 70.5, 67.0, 65.8, 55.0, 39.1, 37.9, 33.9, 26.4, 25.8, 25.3, 18.8, 18.0, −4.1, and −4.6. Found: *m/z* 476.2469. Calcd for $C_{25}H_{38}NO_6Si$: M − Me, 476.2467. Found: C, 63.27; H, 8.46; N, 2.77%. Calcd for $C_{26}H_{41}NO_6Si$: C, 63.51; H, 8.40; H, 2.85%.

The relative stereochemistry has been identified by X-ray structure analysis. Crystal data: $C_{26}H_{41}NO_6Si$ (FW = 491.70), orthorhombic, $P2_12_12_1$, a = 10.901(5), b = 39.461(6), c = 6.592(5) Å, V = 2836(3) Å^3, Z = 4, D_x = 1.152 Mg m^{-3}, T = 298 K. X-ray intensities were measured on a Rigaku AFC-5 diffractometer with Mo $K\alpha$ radiation (λ = 0.71073 Å), and final R = 0.065 for 1806 observed reflections. Tables of the atomic parameters, bond lengths and bond angles, and the structure factors and deposited as Document No. 71050 at the Office of the Editor of Bull. Chem. Soc. Jpn.

(2*S*,4*S*)-4-(*t*-Butyldimethylsiloxy)-4-[(4*R*)-2,2-dimethyl-1,3-dioxolan-4-yl]-2-methylbutan-1-ol (19). To a solution of **18** (888 mg, 1.81 mmol) in THF (18 ml) at 0 °C under an argon atmosphere was added 1 M $LiAlH_4$ in THF (2.70 ml, 2.70 mmol). After being stirred for 1 h, the reaction was quenched by the addition of aq Et_2O and 4 M aq NaOH. The suspension was filtered through Celite pad, and the residue was washed with EtOAc (100 ml). The filtrate and washings were combined, and evaporated. Purification of the residue by silica-gel column chromatography (5/1 hexane/EtOAc)

gave **19** (505 mg, 88%) as a colorless oil: $[\alpha]_D^{24}$ +6.3° (*c* 0.89, $CHCl_3$); IR (film) 3400 cm^{-1}; ^1H NMR δ = 0.08 (3H, s), 0.09 (3H, s), 0.88 (9H, s), 0.94 (3H, d, *J* = 6.6 Hz), 1.28—1.38 (1H, m), 1.34 (3H, s), 1.40 (3H, s), 1.60 (1H, ddd, *J* = 5.9, 6.9, 13.9 Hz), 1.68 (1H, s), 1.89 (1H, m), 3.47 (2H, d, *J* = 5.9 Hz), 3.76—3.87 (2H, complex), and 3.99 (2H, complex); ^{13}C NMR δ = 109.0, 70.8, 68.7, 66.6, 38.6, 31.5, 26.5, 25.8, 25.3, 18.1, 17.2, −4.1, and −4.2. Found: *m/z* 303.2010. Calcd for $C_{15}H_{31}O_4Si$: M − Me, 303.2030.

(1*S*,3*S*)-1-(*t*-Butyldimethylsiloxy)-1-[(4*R*)-2,2-dimethyl-1,3-dioxolan-4-yl]-3-methyl-4-(2-methyl-1,3-dithian-2-yl)butane (20). To a solution of **19** (505 mg, 1.6 mmol) in pyridine (3 ml) at 0 °C was added TsCl (610 mg, 3.2 mmol); the mixture was warmed up to ambient temperature slowly. After being stirred overnight at the same temperature, the reaction mixture was poured into ice-water, and the mixture was extracted with EtOAc (3×300 ml). The combined organic layer was washed with 1 M HCl, sat. aq $NaHCO_3$ and brine, dried (Na_2SO_4), then concentrated in vacuo. The residue was purified by silica-gel column chromatography (3/1 hexane/EtOAc) to give a tosylate (806 mg, quant.) as a colorless oil.

To a solution of the tosylate (750 mg, 1.6 mmol) in acetone (15 ml) was added NaI (950 mg, 6.4 mmol). After being stirred at refluxing temperature overnight, the reaction mixture was cooled to ambient temperature and poured into ice-water, and the mixture was extracted with EtOAc (3×300 ml). The combined organic layer was washed with brine, dried (Na_2SO_4), and evaporated. The residue was purified by silica-gel column chromatography (50/1 hexane/EtOAc) to give an iodide (603 mg, 89%) as a colorless oil.

To a solution of 2-methyl-1,3-dithiane (0.34 ml, 2.8 mmol) in THF (15 ml) and HMPA (0.49 ml, 2.8 mmol) was added 1.6 M *t*-BuLi in pentane (1.74 ml, 2.8 mmol) at −78 °C under an argon atmosphere; the mixture was stirred at the same temperature for 45 min. After the addition of THF solution (3 ml) of the iodide (663 mg, 1.4 mmol), the stirring was continued for another 1 h. The reaction mixture was poured into aq NH_4Cl (50 ml), and extracted with EtOAc (3×100 ml). The combined organic layer was washed with brine, dried (Na_2SO_4), then concentrated in vacuo. The residue was purified by silica-gel column chromatography (20/1 hexane/EtOAc) to give **20** (806 mg, quant.) as a light yellow oil: $[\alpha]_D^{26}$ +2.8° (*c* 0.98, $CHCl_3$); IR (film) 2930 cm^{-1}; ^1H NMR δ = 0.10 (3H, s), 0.11 (3H, s), 0.89 (9H, s), 1.03 (3H, d, *J* = 6.3 Hz), 1.33 (3H, s), 1.35 (1H, m), 1.41 (3H, s), 1.54 (1H, ddd, *J* = 3.7, 8.4, 12.6 Hz), 1.66 (3H, s), 1.85—2.31 (4H, complex), 2.83 (4H, complex), and 3.77—3.99 (4H, complex); ^{13}C NMR δ = 108.7, 79.3, 77.2, 70.1, 65.7, 49.6, 49.5, 44.0, 43.2, 31.2, 28.1, 26.7, 26.5, 26.0, 25.7, 25.3, 25.2, 21.7, 18.1, −3.9, and −4.1. Found: *m/z* 420.2186. Calcd for $C_{20}H_{40}O_3S_2Si$: M+H − Me, 420.2186.

(2*R*,3*S*,5*S*)-3-(*t*-Butyldiphenylsiloxy)-5-methyl-6-(2-methyl-1,3-dithian-2-yl)hexan-1,2-diol (21). To a solution of **20** (611 mg, 1.4 mmol) in THF (14 ml) was added 1 M *n*-Bu_4NF in THF (3.56 ml, 3.53 mmol) at 0 °C; the mixture was warmed up to ambient temperature. After being stirred overnight, the reaction mixture was poured into aq NH_4Cl (50 ml), and extracted with EtOAc (3×100 ml). The combined organic layer was washed with brine, dried (Na_2SO_4), then concentrated in vacuo. The residue was purified by silica-gel column chromatography (5/1 hexane/EtOAc) to give an alcohol (396 mg, 88%) as a light yellow syrup.

To a solution of the alcohol (396 mg, 1.2 mmol) in DMF (4 ml) were added imidazole (340 mg, 5.0 mmol), TBDPSCl (1.31 ml, 5.0 mmol) and catalytic amounts of DMAP (4-dimethylaminopyridine) at ambient temperature. After being stirred at 50 °C overnight, the reaction mixture was poured into ice-water, and the slurry was extracted with EtOAc (3×50 ml). The combined organics were washed with 1 M HCl, sat. aq $NaHCO_3$, and brine, dried (Na_2SO_4), then evaporated. The residue was purified by silica-gel column chromatography (10/1 hexane/EtOAc) to give a siloxy ether (550 mg, quant.) as a colorless oil.

The siloxy ether (699 mg, 1.2 mmol) was dissolved in 80% aq AcOH (12 ml) and stirred at 40 °C for 20 min. The resultant mixture was concentrated in vacuo. The residue was purified by silica-gel column chromatography (2/1 hexane/EtOAc) to give **21** (539 mg, 83%) as a colorless syrup: $[\alpha]_D^{23}$ +15.6° (*c* 1.89, $CHCl_3$); IR (film) 3440 cm^{-1}; ^1H NMR δ = 0.71 (3H, d, *J* = 6.3 Hz), 1.07 (9H, s), 1.21—1.31 (1H, m), 1.39—1.71 (4H, complex), 1.47 (3H, s), 1.82—1.94 (2H, complex), 2.57—2.82 (4H, complex), 3.61 (1H, m), 3.75 (2H, ddd, *J* = 2.3, 6.3, 11.2 Hz), 3.92, (1H, dt, *J* = 2.6, 6.6 Hz), 7.42 (6H, complex), and 7.72 (4H, complex); ^{13}C NMR δ = 136.05, 135.96, 133.2, 133.0, 130.0, 129.9, 127.9, 127.7, 74.0, 63.1, 49.2, 48.6, 42.1, 28.3, 27.1, 26.6, 26.1, 25.1, 22.4, and 19.4. Found: *m/z* 519.2448. Calcd for $C_{28}H_{43}O_3S_2Si$: M+H, 519.2421.

(2*R*,3*S*,5*S*)-3-(*t*-Butyldiphenylsiloxy)-2-(4-methoxybenzyloxy)-5-methyl-6-(2-methyl-1,3-dithian-2-yl)hexan-1-ol (22). To a solution of **21** (371 mg, 0.71 mmol) in CH_2Cl_2 (7 ml) were added anisaldehyde dimethyl acetal (0.38 ml, 2.1 mmol) and catalytic amounts of PPTS. After being stirred overnight, the reaction mixture was poured into sat. aq $NaHCO_3$ (50 ml), and extracted with $CHCl_3$ (3×100 ml). The combined organic layer was washed with brine, dried (Na_2SO_4), then evaporated. The residue was purified by silica-gel column chromatography (10/1 hexane/EtOAc) to give an acetal (396 mg, quant.) as a pale yellow syrup.

To a solution of the acetal (16 mg, 0.024 mmol) in toluene (0.5 ml) was added 1 M DIBAL-H solution in toluene (0.16 ml, 0.16 mmol) at −78 °C under an argon atmosphere. After being stirred at the same temperature for 30 min, the reaction was quenched by the addition of aq Et_2O and 4 M aq NaOH. The suspension was filtered through a Celite pad, and the residue was washed with EtOAc (100 ml). The filtrate and washings were combined and evaporated. Purification of the residue by PTLC (3/1 hexane/EtOAc) gave **22** (12 mg, 73%) as a colorless oil: $[\alpha]_D^{26}$ +0.38° (*c* 1.81, $CHCl_3$); IR (film) 3460 cm^{-1}; ^1H NMR δ = 0.65 (3H, d, *J* = 5.9 Hz), 1.05 (9H, s), 1.26—1.37 (2H, complex), 1.40 (3H, s), 1.57 (3H, complex), 1.85 (2H, complex), 2.51—2.78 (4H, complex), 3.53 (1H, m), 3.72 (1H, dd, *J* = 3.6, 11.6 Hz), 4.00 (1H, m), 4.43 (1H, d, *J* = 11.2 Hz), 4.58 (1H, d, *J* = 11.2 Hz), 6.86 (2H, complex), 7.19—7.44 (8H, complex), and 7.74 (4H, complex); ^{13}C NMR δ = 159.1, 136.3, 136.1, 133.9, 133.1, 130.6, 129.7, 129.2, 127.61, 127.56, 113.7, 82.0, 77.2, 72.2, 71.4, 61.3, 55.3, 49.1, 48.7, 43.3, 28.1, 27.0, 26.6, 26.5, 26.4, 25.1, 22.2, and 19.5. Found: *m/z* 607.2739. Calcd for $C_{35}H_{47}O_3S_2Si$: M − OMe, 607.2733.

(4*R*,5*S*,7*S*)-5-(*t*-Butyldiphenylsiloxy)-4-(4-methoxybenzyloxy)-7-methyl-8-(2-methyl-1,3-dithian-2-yl)oct-1-en-3-ol (23). To a solution of **22** (77 mg, 0.12 mmol) in the mixture of DMSO (1 ml) and Et_3N (0.3 ml) was added SO_3–pyridine complex (66 mg, 0.41 mmol) at ambient temperature under an argon atmosphere. After being stirred for 60 min, the reaction mixture was poured into ice-water, and extracted with EtOAc (3×50 ml). The combined organic layer was washed with 1 M HCl, sat. aq $NaHCO_3$ and brine, dried (Na_2SO_4), then concentrated in vacuo. The residue was purified by silica-gel column chromatography (3/1 hexane/EtOAc) to give an aldehyde (77 mg) as a colorless oil.

To a ice-cooled solution of the aldehyde (77 mg, 0.12 mmol) in THF (1 ml) was added 1 M vinylmagnesium bromide solution in THF (0.24 ml, 0.24 mmol) under an argon atmosphere. After being stirred for 15 min, the reaction mixture was poured into

aq NH_4Cl (10 ml), and extracted with $CHCl_3$ (3×20 ml). The combined organic layer was washed with brine, dried (Na_2SO_4), then evaporated. The residue was purified by PTLC (3/1 hexane/EtOAc) to give a diastereomeric mixture of **23** (62 mg, 78% yield in 2 steps) as a pale yellow syrup. Found: *m/z* 650.2914. Calcd for $C_{37}H_{50}O_4S_2Si$: M+H−Me, 650.2916.

(4*S*,5*S*,7*S*)-5-(*t*-Butyldiphenylsiloxy)-4-(4-methoxylbenzyloxy)-7-methyl-8-(2-methyl-1,3-dithian-2-yl)-3-vinyloxyoct-1-ene (24). To a solution of **23** (62 mg, 0.09 mmol) in ethyl vinyl ether (1 ml) was added $Hg(OAc)_2$ (44 mg, 0.14 mmol); the mixture was stirred at refluxing temperature overnight. The resultant mixture was poured into 1 M aq KI (20 ml), and extracted with EtOAc (3×20 ml). The combined organic layer was washed with brine, dried (Na_2SO_4), then concentrated in vacuo. The residue was purified by PTLC (8/1 hexane/EtOAc) to give a diastereomeric mixture of **24** (14 mg, 22%) as a colorless oil. Found: *m/z* 633.2889. Calcd for $C_{37}H_{49}O_3S_2Si$: M−C_3H_5O, 633.2889.

(4*E*,6*R*,7*S*,9*S*)-7-(*t*-Butyldiphenylsiloxy)-6-(4-methoxybenzyloxy)-9-methyl-10-(2-methyl-1,3-dithian-2-yl)dec-4-enal (25). Compound **24** (14 mg, 0.02 mmol) was dissolved in decalin (1.0 ml) and stirred at 200 °C under an argon atmosphere in a sealed tube. After being stirred for 14 min, the reaction mixture was purified by PTLC (5/1 hexane/EtOAc) to give **25** (7 mg, 50%) as a colorless oil: ^{1}H NMR δ = 0.73 (3H, d, J = 6.6 Hz), 1.04 (9H, s), 1.48 (3H, s), 1.43—1.90 (7H, complex), 2.30—2.51 (4H, complex), 2.62—2.75 (4H, complex), 3.67 (1H, dd, J = 2.3, 6.9 Hz), 3.79—3.81 (4H, complex), 4.13 (1H, d, J = 11.6 Hz) 4.34 (1H, d, J = 11.6 Hz), 5.34—5.54 (2H, complex), 6.83 (2H, d, J = 8.6 Hz), 7.01 (1H, d, J = 8.5 Hz), 7.15 (2H, d, J = 8.6 Hz), 7.27—7.41 (6H, complex), 7.68—7.75 (4H, complex), 7.85 (1H, d, J = 8.5 Hz), and 9.76 (1H, t, J = 1.5 Hz). For its unstable property, **25** was submitted to the next reaction without further characterization.

Bottom-Half Fragment (2). To a solution of **25** (7 mg, 0.01 mmol) in CH_2Cl_2 (0.5 ml) was added Ph_3P=$C(CH_3)COOMe$ (10 mg, 0.03 mmol); the mixture was stirred for 2.5 h at ambient temperature. The resulting mixture was concentrated in vacuo, and the residue was purified by PTLC (5/1 hexane/EtOAc) to give **2** (6 mg, 74%) as an amorphous solid: $[\alpha]_D^{27}$ −25.2° (*c* 0.58, $CHCl_3$); IR (film) 1710 cm^{-1}; ^{1}H NMR δ = 0.73 (3H, d, J = 7.3 Hz), 1.04 (9H, s), 1.47 (3H, s), 1.83 (3H, d, J = 1.3 Hz), 1.46—1.91 (7H, complex), 2.13—2.28 (4H, complex), 2.62—2.77 (4H, complex), 3.67 (1H, dd, J = 2.4, 7.3 Hz), 3.70 (3H, s), 3.79—3.81 (4H, complex), 4.26 (1H, d, J = 11.6 Hz), 4.36 (1H, d, J = 11.6 Hz), 5.37 (1H, dt, J = 5.6, 15.8 Hz), 5.46 (1H, dd, J = 7.3, 15.8 Hz), 6.73 (1H, dt, J = 1.3, 5.6 Hz), 6.83 (2H, d, J = 8.6 Hz), 7.15 (2H, d, J = 8.6 Hz), 7.27—7.41 (6H, complex), and 7.68—7.75 (4H, complex); ^{13}C NMR δ = 168.5, 158.7, 149.5, 141.6, 136.3, 136.2, 134.3, 134.2, 134.0, 131.2, 129.4, 129.3, 128.9, 128.3, 127.9, 127.5, 127.3, 113.5, 83.3, 77.2, 74.1, 69.5, 55.3, 51.7, 49.3, 48.2, 42.1, 31.3, 28.3, 28.0, 27.1, 26.6, 26.2, 25.2, 22.0, 19.6, and, 12.5. Found: *m/z* 703.2934. Calcd for $C_{40}H_{51}O_5S_2Si$: M−C_4H_9, 703.2943.

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