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# Total synthesis of (4*S*,10*R*)-4-hydroxy-10-methyl-11-oxododec-2-en-1,4-olide and related bioactive marine butenolides

Wei-Min Dai *, Lei Shi, Yannian Li

*Center for Cancer Research and Department of Chemistry, The Hong Kong University of Science and Technology, Clear Water Bay, Kowloon, Hong Kong SAR, China*

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ABSTRACT

Marine-derived microorganisms produce structurally diverse butenolides possessing a variety of bioactivities. Described here is the total synthesis of (4*S*,10*R*)-4-hydroxy-10-methyl-11-oxododec-2-en-1,4-olide and a related butenolide containing *anti* stereochemistry at C10–C11. A three-module coupling strategy has been established for synthesis of the stereoisomers of the naturally occurring butenolides by assembling the C3–C7 and C9–C12 fragments via double alkylation of a 1,3-dithiane. The C10–C11 stereochemistry could be easily controlled by an asymmetric aldol condensation, while the butenolide unit was efficiently constructed according to the ring-closing metathesis protocol.



## 1. Introduction

Marine microorganisms are reported to produce a variety of butenolides (or furanones) which are capable of disrupting bacterial communication systems (quorum sensing systems)[1] and prevention of bacterial colonization and infection. The butenolide-based quorum sensing inhibitors are believed to block *N*-acyl-homoserine lactone (AHL) signal reception, leading to modulation on expression of quorum sensing-regulated genes. Since quorum sensing systems play a central role in regulating virulence and biofilms formation in many pathogenic bacteria, they have emerged as attractive targets for developing novel therapeutics for treatment of chronic biofilms infections.[1a] Recently, three teams reported the butenolides **1**,[2a,c,3] **2**,[2a,b,4] and their related structures (Fig. 1)[2] produced by marine microorganisms isolated from the sediments, which were collected from North Atlantic Ocean, and sea water of New Zealand, Korea, and China. Butenolides **1** were reported as a mixture of two inseparable diastereomers.[3] The absolute stereochemistry at C4 has been established by CD measurement, while the stereogenic centers at C10 (for **1** and **2**) and C11 (for **1**) remain undetermined. Gu, Zhu et al. reported cytotoxicity for a mixture of **1** with $IC_{50}$ values in the range of 0.18–1.05 μmol/mL against murine lymphoma P388 and human leukemia K562 cell lines, respectively.[2c] In 2007, Hedenström et al. disclosed the synthesis of the four diastereomers of **1** by using double 1,3-dithiane alkylation at C6 and ring-closing metathesis (RCM) for assembling the butenolide unit.[5,6] The C4 chiral center was carried from (*R*)-vinyloxirane and the C10 and C11 stereogenic centers originated from the enantiomeric building block formed by the asymmetric 1,3-dipolar cycloaddition of a thiocarbonyl ylide with a benzyloxy-substituted dipolarophile appended on a camphorsultam.[5] Herein, we report the total synthesis of the butenolides (4*S*,10*R*,11*S*)-**1** and (4*S*,10*R*)-**2** by a module approach as illustrated in Figure 1.

## 2. Results and discussion

We decided to establish a synthetic strategy for access to a library of stereoisomers of the butenolides **1** and **2** including the (*R*)-configuration at C4. As shown in Figure 1, the C3–C7 fragment **3** and its (4*R*)-enantiomer are easily available by asymmetric dihydroxylation of 4-penten-1-yl 4-methoxybenzoate.[7] All four stereomers of the C9–C12 fragment **5** can be readily prepared by the *anti*- and *syn*-selective aldol condensations of the *E*- and *Z*-boron enolates derived from the Abiko's chiral propionates such as **6** (Scheme 1).[8,9] By employing 1,3-dithiane chemistry,[10] the two chiral building blocks **3** and **5** can be joined at C8 via a double alkylation of 1,3-dithiane **4**. Therefore, our synthetic strategy is flexible and applicable to the synthesis of stereoisomers of the butenolides **1** and **2**. As a proof of concept, we describe the synthesis of (4*S*,10*R*,11*S*)-**1** and (4*S*,10*R*)-**2**.

Scheme 1 shows the synthesis of the functionalized C9–C12 fragment **9**[11] starting from the known *anti*-aldol product **7** (dr = 97:3).[8b] Protection of alcohol **7** as the THP ether was followed by reduction of the ester moiety by Dibal-H at −78 °C to form the primary alcohol **8** in 93% overall yield. Treatment of **8** with $I_2$–$PPh_3$ in the presence of imidazole furnished iodide **9** in 87% yield.

The protected C3–C7 fragment **14** was synthesized from the known chiral 1,2-diol **11**[7] as outlined in Scheme 2.[11] Diol **11** was prepared from the 4-methoxybenzoate **10** on a three-gram scale by using AD-mix-α (*t*-BuOH–$H_2O$, 1:1, 0 °C, 4 h) in 82% isolated yield and in 82% ee. Diol **11** was first converted into the bis-TBS

* Corresponding author. Tel.: +852 23587365; fax: +852 23581594.
*E-mail address:* chdai@ust.hk (W.-M. Dai).

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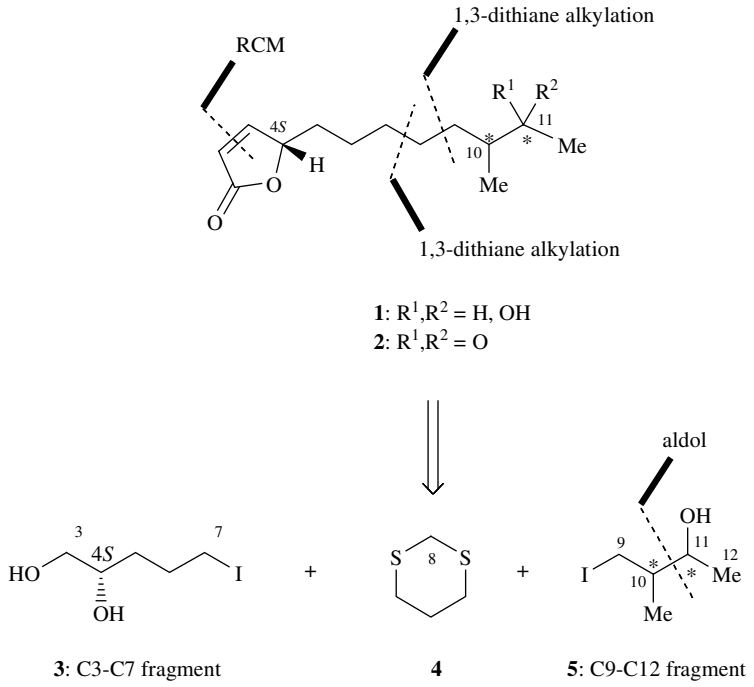
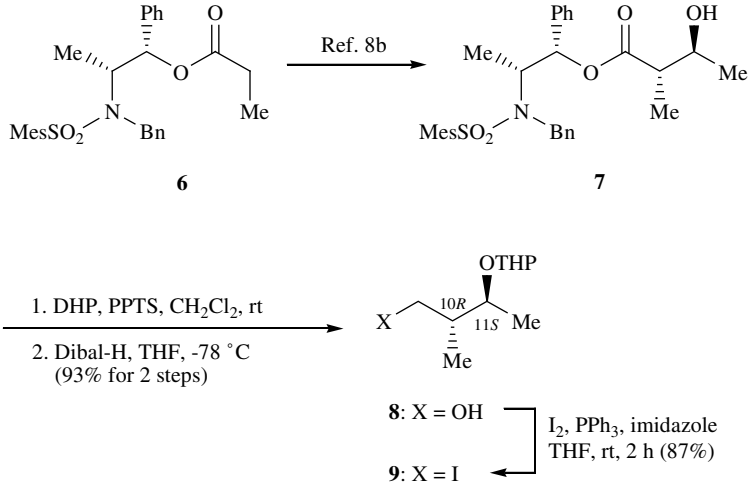



**Figure 1.** Structures of the butenolides **1** and **2** and the retrosynthetic bond disconnections according to a module approach to all stereoisomers.

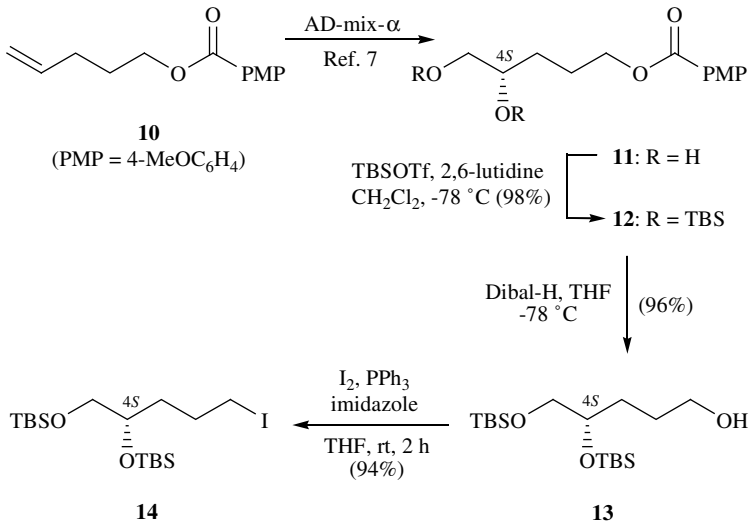



**Scheme 1.** Synthesis of the functionalized C9–C12 fragment **9**.

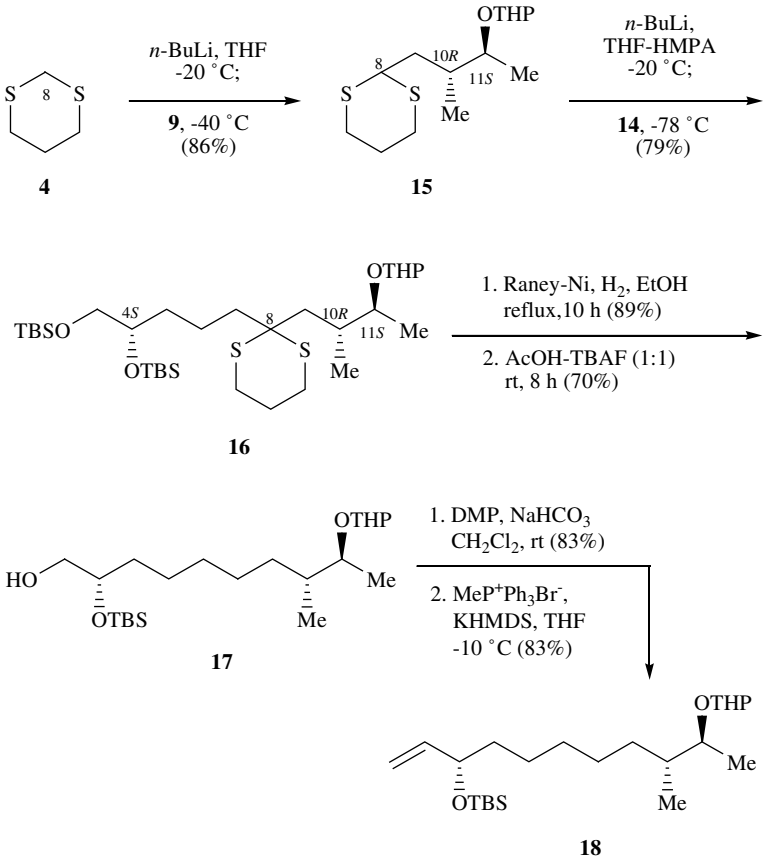
ether **12** in 98% yield. Reduction of the ester moiety in **12** using Dibal-H gave alcohol **13** (96%), which was further transformed into iodide **14** in 94% yield upon exposure to $I_2$–$PPh_3$ in the presence of imidazole.

Next, a three-module coupling process was used to build up the carbon chain of the target butenolides (Scheme 3). 1,3-Dithiane **4** (3 equiv) was deprotonated by *n*-BuLi (3 equiv) in THF at −20 °C, and the resulting carbanion was subjected to alkylation with the iodide **9** (−40 °C, 3 h) to afford **15**[11] in 86% yield. The use of an excess amount of **4** was found beneficial for the high yield of the alkylation. Deprotonation of **15** by *n*-BuLi (1.1 equiv) was carried out in THF–HMPA (10:1) at −20 °C, while the alkylation with iodide **14** was performed at −78 °C for 2 h to furnish **16** with a fully extended carbon chain in 79% yield. The Raney nickel-mediated reduction of the 1,3-dithiane moiety in **16** was carried out in refluxing EtOH under a hydrogen atmosphere[12] to afford cleanly the desired product in 89% yield. The latter was subjected to selective desilylation of the primary TBS ether in 1:1 AcOH–TBAF media, giving the primary alcohol **17** in 70% yield. At this stage, the allylic double bond was introduced via oxidation of **17** with DMP and subsequent Wittig olefination of the aldehyde to produce **18** in 69% overall yield over the two steps.

In order to install the butenolide core, the TBS protecting group in **18** was removed by treating with TBAF (87%), and the obtained alcohol was converted into the acrylate **19** in 81% yield (Scheme 4). The ring-closing metathesis within diene **19** took place smoothly by applying 10 mol % of the Grubbs' second generation initiator **20**[5,13] in refluxing $CH_2Cl_2$ for 1 h. After removal of the protecting group at C11 (PPTS, MeOH, 40 °C), the butenolide (4*S*,10*R*,11*S*)-**1** was isolated in 76% overall yield from **19**. Finally, DMP oxidation

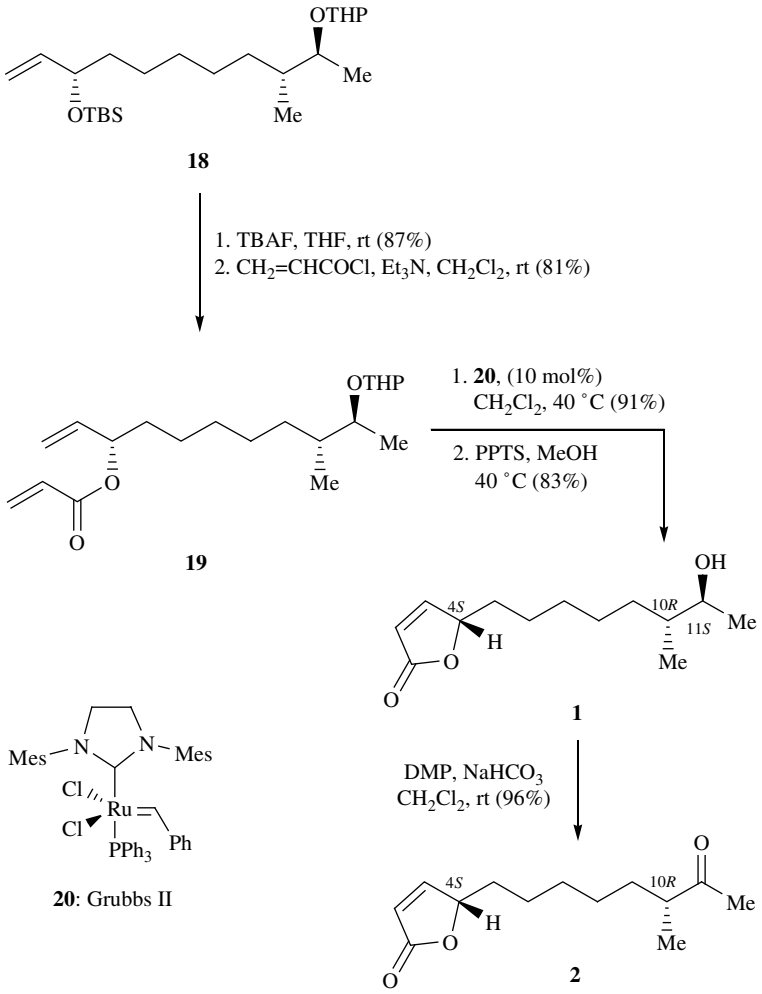



**Scheme 2.** Synthesis of the functionalized C3–C7 fragment **14**.




**Scheme 3.** Synthesis of the allyl silyl ether **18**.

of **1** furnished the keto butenolide (4*S*,10*R*)-**2** in 96% yield. The $^{13}C$ NMR data of the synthesized **1** and **2** along with those reported in the literature are given in Table 1. The specific rotation data for (4*S*,10*R*,11*S*)-**1** {$[\alpha]_D^{20} = +78.0$ (*c* 0.100, MeOH)} agree with those {$[\alpha]_D^{22} = +70.9$ (*c* 0.115, MeOH)} reported by Hedenström et al.[5] Moreover, a comparison of specific rotation data of our synthetic (4*S*,10*R*)-**2** {$[\alpha]_D^{20} = +32.0$ (*c*, 0.100, MeOH)} with those of naturally occurring **2** {$[\alpha]_D^{22} = +45$ (*c* 0.119, MeOH)[2a] and $[\alpha]_D^{22} = +18.4$ (*c* 0.18, MeOH)[2b]} suggests the 10*R* configuration for the sample of **2** isolated from the *Streptomycete* strain B3497.[2a] However, it needs to be confirmed by synthesizing other stereomers.




**Scheme 4.** Synthesis of the butenolides **1** and **2**.

**Table 1**
$^{13}C$ NMR data for the butenolides **1** and **2** in $CDCl_3$

| | Atom | (4*S*,10*R*,11*S*)-**1** (100 MHz) | (4*S*,10*R*,11*S*)-**1** (125 MHz)[5] | (4*S*,10*R*)-**2** (100 MHz) | **2** (75 or 125 MHz)[2a] | **2** (125 MHz)[2b] |
|---|---|---|---|---|---|---|
| 1 | CO | 173.14 | 173.19 | 173.08 | 173.0 | 173.1 |
| 2 | CH | 121.48 | 121.54 | 121.57 | 121.4 | 121.4 |
| 3 | CH | 156.27 | 156.30 | 156.17 | 156.2 | 156.2 |
| 4 | CH | 83.36 | 83.41 | 83.28 | 83.2 | 83.2 |
| 5 | $CH_2$ | 33.09 | 33.15 | 33.03 | 32.9 | 32.9 |
| 6 | $CH_2$ | 24.88 | 24.95 | 24.79 | 24.7 | 24.7 |
| 7 | $CH_2$ | 29.54 | 29.60 | 29.27 | 29.2 | 29.2 |
| 8 | $CH_2$ | 26.92 | 26.98 | 26.92 | 26.8 | 26.8 |
| 9 | $CH_2$ | 32.30 | 32.34 | 32.59 | 32.5 | 32.5 |
| 10 | CH | 39.92 | 39.97 | 47.08 | 47.0 | 47.0 |
| 11 | CH/CO | 71.76 | 71.70 | 212.77 | 212.6 | 212.8 |
| 12 | $CH_3$ | 19.42 | 19.49 | 27.97 | 27.9 | 27.9 |
| 13 | $CH_3$ | 14.52 | 14.57 | 16.25 | 16.1 | 16.2 |

## 3. Conclusion

In conclusion, we have established a three-module coupling approach to butenolides **1** and **2** via double alkylation of 1,3-dithiane **4**[10] by using the stereochemically defined C3–C7 and C9–C12 fragments **3** and **5**. The butenolide core could be easily assembled by employing the ring-closing metathesis[5,13] catalyzed by the Grubbs' second generation initiator **20**. Our approach is flexible and should be applicable to the general synthesis of a library of stereomers of the butenolides **1** and **2** by using the appropriate C3–C7 and C9–C12 fragments **3** and **5** with defined stereogenic centers at C4, C10, and C11. Synthetic work toward this goal is currently in progress in our laboratory.

## 4. Experimental

$^1H$ and $^{13}C$ NMR spectra were recorded in $CDCl_3$ (400 MHz for $^1H$ and 100 MHz for $^{13}C$, respectively) with $CHCl_3$ as the internal reference. IR spectra were taken on a FT-IR spectrophotometer. High-resolution mass spectra (HRMS) were measured by the CI+ method. All reactions were carried out under a nitrogen atmosphere and monitored by thin layer chromatography on 0.25-mm E. Merck silica gel plates (60 F-254) using UV light, or 7% ethanolic phosphomolybdic acid and heating as the visualizing methods. E. Merck Silica Gel (60, particle size 0.040–0.063 mm) was used for flash column chromatography. Yields refer to chromatographically and spectroscopically ($^1H$ NMR) homogeneous materials. All reagents were obtained commercially and used as received. Room temperature is around 23 °C.

### 4.1. (2*R*,3*S*)-2-Methyl-3-((tetrahydropyran-2′-yl)oxy)butan-1-ol 8

To a solution of the known *anti*-aldol **7**[8b] (2.900 g, 5.55 mmol) and PPTS (140 mg, 0.56 mmol) in dry $CH_2Cl_2$ (40 mL) was added

3,4-dihydro-2*H*-pyran (0.79 mL, 8.32 mmol). The resultant mixture was stirred for 2.5 h at room temperature. The reaction mixture was diluted with $Et_2O$ and washed once with saturated brine. The organic layer was dried over anhydrous $Na_2SO_4$, filtered, and concentrated under reduced pressure to give a 1:1 diastereomeric mixture of the THP-protected **7** as a white amorphous solid.

To a solution of the above THP ether in dry $CH_2Cl_2$ (50 mL) cooled at −78 °C was added Dibal-H (1.5 M in toluene, 8.88 mL, 13.32 mmol) dropwise. The resultant mixture was stirred at the same temperature for 10 min, and then allowed to warm to room temperature slowly. The reaction mixture was quenched by the careful addition of a 3:1 (v/v) solution of MeOH and pH 7 buffer (8 mL). A saturated aqueous solution of sodium potassium tartrate (40 mL) was added, and the mixture was stirred for another 1 h. The mixture was diluted with water and $CH_2Cl_2$. The aqueous layer was extracted with $CH_2Cl_2$ (20 mL × 2), and the combined organic layer was dried over anhydrous $Na_2SO_4$, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, eluting with 17% EtOAc in hexane) to give **8** (0.970 g, 93% from **7**) as a colorless oil; IR (film) 3422 (br), 2942, 1454, 1380, 1116, 1024 $cm^{-1}$; HRMS (CI+) calcd for $C_{10}H_{21}O_3$ ($M+H^+$): 189.1491; found, 189.1492.

The two diastereomers of **8** are separable over silica gel column chromatography and analytic samples of pure diastereomers were obtained.

#### 4.1.1. Less polar diastereomer 8a

$R_f$ = 0.23 (17% EtOAc in hexane); $^1H$ NMR (400 MHz, $CDCl_3$) 4.60–4.55 (m, 1H), 3.98–3.92 (m, 1H), 3.87 (dd, *J* = 11.6, 3.0 Hz, 1H), 3.75–3.66 (m, 1H), 3.54–3.48 (m, 1H), 3.46 (dd, *J* = 11.6, 5.0 Hz, 1H), 1.80–1.40 (m, 8H), 1.22 (d, *J* = 6.4 Hz, 3H), 0.95 (d, *J* = 6.4 Hz, 3H); $^{13}C$ NMR (100 MHz, $CDCl_3$) 97.5, 75.3, 65.4, 64.3, 41.2, 31.2, 24.9, 20.8, 17.7, 14.2.

#### 4.1.2. More polar diastereomer 8b

$R_f$ = 0.17 (17% EtOAc in hexane); $^1H$ NMR (400 MHz, $CDCl_3$) 4.67–4.62 (m, 1H), 3.94–3.86 (m, 1H), 3.69–3.60 (m, 2H), 3.52 (dd, *J* = 10.8, 6.2 Hz, 1H), 3.49–3.44 (m, 1H), 2.69 (br s, 1H), 1.80–1.67 (m, 3H), 1.67–1.49 (m, 4H), 1.24 (d, *J* = 6.0 Hz, 3H), 0.89 (d, *J* = 6.8 Hz, 3H); $^{13}C$ NMR (100 MHz, $CDCl_3$) 100.1, 79.6, 65.7, 62.6, 40.7, 30.9, 25.1, 19.7, 19.3, 13.4.

### 4.2. (2′*S*,3′*S*)-2-(1′-Iodo-2′-methyl-3′-butyloxy)tetrahydropyrane 9

To a solution of a diastereomer mixture of the alcohol **8** (50.0 mg, 0.26 mmol) in dry THF (5 mL) were added $PPh_3$ (174.0 mg, 0.66 mmol), imidazole (45.0 mg, 0.66 mmol), and $I_2$ (151.0 mg, 0.60 mmol) at 0 °C followed by stirring at room temperature for 2.5 h. The reaction mixture was quenched by the addition of aqueous $Na_2S_2O_3$. The mixture was diluted with water and $CH_2Cl_2$. The aqueous layer was extracted with $CH_2Cl_2$ (20 mL × 2), and the combined organic layer was dried over anhydrous $Na_2SO_4$, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, eluting with 6% EtOAc in hexane) to give an inseparable mixture of **9** (69.0 mg, 87%) as a colorless oil; $R_f$ = 0.50 (6% EtOAc in hexane); IR (film) 2941, 1453, 1380, 1077, 1023 $cm^{-1}$; HRMS (CI+) calcd for $C_{10}H_{19}IO_2$ ($M^+-H$): 297.0352; found, 297.0352.

Analytic samples of pure diastereomers **9a** and **9b** were prepared from the pure diastereomers **8a** and **8b**, respectively.

#### 4.2.1. Diastereomer 9a (prepared from the less polar diastereomer 8a)

$^1H$ NMR (400 MHz, $CDCl_3$) 4.71–4.68 (m, 1H), 3.92–3.86 (m, 1H), 3.65 (quintet, *J* = 6.4 Hz, 1H), 3.52–3.47 (m, 1H), 3.45 (dd, *J* = 9.6, 4.4 Hz, 1H), 3.22 (dd, *J* = 9.6, 7.6 Hz, 1H), 1.81–1.67 (m, 3H), 1.54–1.51 (m, 4H), 1.10 (d, *J* = 6.4 Hz, 3H), 1.02 (d, *J* = 6.4 Hz, 3H); $^{13}C$ NMR (100 MHz, $CDCl_3$) 95.2, 73.4, 62.6, 41.1, 30.9, 25.2, 19.5, 17.0, 15.6, 13.5.

#### 4.2.2. Diastereomer 9b (prepared from the more polar diastereomer 8b)

$^1H$ NMR (400 MHz, $CDCl_3$) 4.67–4.65 (m, 1H), 3.94–3.88 (m, 1H), 3.55–3.45 (m, 2H), 3.32 (dd, *J* = 9.6, 6.0 Hz, 1H), 3.23 (dd, *J* = 9.6, 4.0 Hz, 1H), 1.82–1.69 (m, 3H), 1.60–1.46 (m, 4H), 1.23 (d, *J* = 6.0 Hz, 3H), 0.94 (d, *J* = 6.4 Hz, 3H); $^{13}C$ NMR (100 MHz, $CDCl_3$) 100.4, 78.0, 62.8, 40.1, 30.9, 25.2, 19.9, 18.3, 16.5, 14.4.

### 4.3. (*S*)-4,5-Bis((*tert*-butyldimethylsilyl)oxy)pent-1-yl 4-methoxybenzoate 12

To a solution of the known chiral diol **11**[7] (1.270 g, 5.0 mmol) in dry $CH_2Cl_2$ (30 mL) cooled at −78 °C were sequentially added 2,6-lutidine (1.285 g, 12.0 mmol) and TBSOTf (2.900 g, 11.0 mmol) under a nitrogen atmosphere. The resultant mixture was stirred at the same temperature for 1 h, and the reaction mixture was quenched by adding saturated aqueous $NaHCO_3$ (10 mL). The reaction mixture was extracted with ethyl acetate (30 mL × 2). The combined organic phase was washed with brine, dried over anhydrous $Na_2SO_4$, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, eluting with 5% EtOAc in hexane) to give **12** (2.360 g, 98%) as a colorless oil; $R_f$ = 0.29 (5% EtOAc in hexane); IR (film) 2955, 2930, 2858, 1717, 1608, 1275, 1255, 1103, 1035 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) 8.10–7.98 ($A'_2B'_2$, 2H), 6.92–6.89 ($A'_2B'_2$, 2H), 4.31–4.28 (m, 2H), 3.82 (s, 3H), 3.74–3.71 (m, 1H), 3.55 (dd, *J* = 10.0, 5.4 Hz, 1H), 3.42 (dd, *J* = 10.0, 6.6 Hz, 1H), 1.92–1.45 (m, 4H), 0.89 (s, 9H), 0.88 (s, 9H), 0.07–0.04 (m, 12H); $^{13}C$ NMR (100 MHz, $CDCl_3$) 166.4, 163.2, 131.5 (×2), 123.0, 113.5 (×2), 72.6, 67.1, 64.9, 55.4, 30.7, 25.9 (×3), 25.9 (×3), 24.4, 18.3, 18.1, −4.3, −4.8, −5.3, −5.4; HRMS (CI+) calcd for $C_{25}H_{47}O_5Si_2$ ($M+H^+$): 483.2962; found, 483.2961.

### 4.4. (*S*)-4,5-Bis((*tert*-butyldimethylsilyl)oxy)pentan-1-ol 13

To a solution of **12** (1.000 g, 2.07 mmol) in dry $CH_2Cl_2$ (50 mL) cooled at −78 °C was added Dibal-H (1.5 M in toluene, 3.50 mL, 5.2 mmol) dropwise. The resultant mixture was stirred at the same temperature for 10 min, and then allowed to warm to room temperature slowly. The reaction mixture was quenched by careful addition of a 3:1 (v/v) solution of MeOH and pH 7 buffer (8 mL). A saturated aqueous solution of sodium potassium tartrate (40 mL) was added, and the mixture was stirred for another hour. The mixture was diluted with water and $CH_2Cl_2$. The aqueous layer was extracted with $CH_2Cl_2$ (20 mL × 2), and the combined organic layer was dried over anhydrous $Na_2SO_4$, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, eluting with 20% EtOAc in hexane) to give **13** (0.690 g, 96%) as a colorless oil; $R_f$ = 0.45 (20% EtOAc in hexane); IR (film) 3342 (br), 2954, 2930, 2858, 1256, 1101, 1058 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) 3.76–3.72 (m, 1H), 3.68–3.60 (m, 2H), 3.55 (dd, *J* = 10.0, 5.6 Hz, 1H), 3.44 (dd, *J* = 10.0, 6.8 Hz, 1H), 1.75–1.50 (m, 5H), 0.89 (s, 18H), 0.08 (s, 3H), 0.07 (s, 3H), 0.05 (s, 3H), 0.05 (s, 3H); $^{13}C$ NMR (100 MHz, $CDCl_3$) 72.8, 66.7, 63.3, 30.8, 28.1, 26.0 (×3), 25.9 (×3), 18.3, 18.1, −4.4, −4.8, −5.3, −5.4; HRMS (CI+) calcd for $C_{17}H_{41}O_3Si_2$ ($M+H^+$): 349.2594; found, 349.2591.

### 4.5. (*S*)-4,5-Bis((*tert*-butyldimethylsilyl)oxy)-1-iodo-pentane 14

To a solution of alcohol **13** (1.680 g, 4.84 mmol) in dry THF (50 mL) were sequentially added $PPh_3$ (3.170 g, 12.1 mmol), imid-

azole (0.823 g, 12.1 mmol), and $I_2$ (2.760 g, 10.9 mmol) at 0 °C. The resultant mixture was stirred at room temperature for 2.5 h. The reaction mixture was quenched by addition of aqueous saturated solution of $Na_2S_2O_3$. The mixture was diluted with water and $CH_2Cl_2$. The organic layer was separated and the aqueous layer was extracted with $CH_2Cl_2$ (40 mL × 2), and the combined organic layer was dried over anhydrous $Na_2SO_4$, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, eluting with 9.1% $CH_2Cl_2$ in hexane) to give **14** (2.090 g, 94%) as a colorless oil; $R_f$ = 0.50 (9.1% $CH_2Cl_2$ in hexane); IR (film) 2955, 2929, 2858, 1256, 1119, 1084 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) 3.70–3.66 (m, 1H), 3.53 (dd, $J$ = 9.6, 5.2 Hz, 1H), 3.38 (dd, $J$ = 10.0, 6.8 Hz, 1H), 2.00–1.40 (m, 4H), 0.89 (s, 9H), 0.88 (s, 9H), 0.05 (s, 6H), 0.05 (s, 6H); $^{13}C$ NMR (100 MHz, $CDCl_3$) 72.1, 67.1, 35.2, 29.2, 26.0 (×3), 25.9 (×3), 18.3, 18.1, 7.5, −4.3, −4.7, −5.3, −5.4; HRMS (CI+) calcd for $C_{17}H_{40}IO_2Si_2$ ($M+H^+$): 459.1612; found, 459.1591.

### 4.6. (2′*R*,3′*S*)-2-[2′-Methyl-3′-((tetrahydropyran-2″-yl)oxy)-butyl]-1,3-dithiane 15

To a solution of 1,3-dithiane **4** (1.080 g, 9.00 mmol) in dry THF (30 mL) cooled at −78 °C was added *n*-BuLi (5.625 mL, 1.6 M in hexanes, 9.00 mmol). The resultant mixture was stirred for 10 min at −78 °C and for 3 h at −20 °C. To the solution, the resultant lithium anion cooled at −40 °C in an $CH_3CN$-dry ice bath was added a solution of iodide **9** (894.0 mg, 3.00 mmol) in dry THF (5 mL) dropwise. The mixture was stirred for another 3 h at −40 °C. The reaction mixture was quenched with saturated aqueous $NH_4Cl$ (10 mL), and the aqueous layer was separated and extracted with ethyl acetate (50 mL × 3). The combined organic layer was dried over anhydrous $Na_2SO_4$, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, eluting with 9.1% EtOAc in hexane) to give **15** (752.0 mg, 86%) as a colorless oil. The excess **4** used in the reaction could not be separated out by column chromatography but it was removed after thorough drying under vacuum. $^1H$ NMR spectrum of **15** shows a mixture of 72:28 due to the chirality of THP, indicating a moderate kinetic resolution during the alkylation of 1,3-dithiane **4** with the diastereomeric iodide **9**.

*Compound* **15**: $R_f$ = 0.43 (9.1% EtOAc in hexane); IR (film) 2939, 1379, 1076, 1022 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) 4.69–4.66 (m, 0.28H for the minor diastereomer), 4.61–4.57 (m, 0.72H for the major diastereomer), 4.10–4.02 (m, 1H), 3.92–3.81 (m, 1H), 3.66–3.55 (m, 1H), 3.50–3.41 (m, 1H), 2.88–2.77 (m, 4H), 2.20–1.40 (m, 11H), 1.13 (d, $J$ = 6.8 Hz, 2.16H for the major diastereomer), 1.03 (d, $J$ = 6.4 Hz, 0.84H for the minor diastereomer), 0.95 (d, $J$ = 6.8 Hz, 0.84H for the minor diastereomer), 0.88 (d, $J$ = 6.8 Hz, 2.16H for the major diastereomer); $^{13}C$ NMR (100 MHz, $CDCl_3$) 99.1, 77.3, 62.7, 45.6, 38.3, 34.4, 31.1, 30.4, 30.1, 26.0, 25.4, 19.9, 17.4, 14.5 (for the major diastereomer) and 95.1, 74.0, 62.2, 45.8, 38.2, 35.6, 31.0, 30.4, 30.1, 26.1, 25.5, 19.4, 15.4, 15.2 (for the minor diastereomer).

### 4.7. (4′*S*,2″*R*,3″*S*)-2-[4′,5′-Bis((*tert*-butyldimethylsilyl)oxy)-pentyl]-2-[2″-methyl-3″-((tetrahydropyran-2‴-yl)oxy)butyl]-1,3-dithiane 16

To a solution of dithiane **15** (90.0 mg, 0.31 mmol) in dry THF (2 mL) and HMPA (0.2 mL) was added *n*-BuLi (0.21 mL, 1.6 M in hexanes, 0.34 mmol) at −78 °C under a nitrogen atmosphere. The resultant solution was stirred at −78 °C for 30 min and then at −20 °C for 2 h. The mixture was cooled to −78 °C again, and a solution of iodide **9** (142.0 mg, 0.31 mmol) in dry THF (0.5 mL) was added dropwise. The resultant mixture was stirred at −78 °C for 2 h, and was allowed to warm to room temperature. The reaction mixture was quenched with the saturated aqueous $NH_4Cl$. The mixture was extracted with ethyl acetate (10 mL × 3). The combined organic layer was washed with brine, dried over anhydrous $Na_2SO_4$, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, eluting with 9.1% EtOAc in hexane) to give a 74:26 mixture of diastereomers of **16** (152.0 mg, 79%) as a colorless oil; $R_f$ = 0.53 (9.1% EtOAc in hexane); IR (film) 2930, 2952, 2857, 1255, 1115, 1022 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) 4.69–4.67 (m, 1H), 3.93–3.87 (m, 1H), 3.75–3.60 (m, 2H), 3.55–3.45 (m, 3H), 2.90–2.70 (m, 4H), 2.10–1.28 (m, 17H), 1.14 (d, $J$ = 6.4 Hz, 2.22H for the major diastereomer), 1.06 (d, $J$ = 6.4 Hz, 0.78H for the minor diastereomer), 1.05 (d, $J$ = 6.8 Hz, 0.78H for the minor diastereomer), 0.99 (d, $J$ = 7.2 Hz, 2.22H for the major diastereomer), 0.89 (s, 9H), 0.88 (s, 9H), 0.06–0.40 (m, 12H); $^{13}C$ NMR (100 MHz, $CDCl_3$) 98.3, 77.3, 73.1, 67.2, 62.9, 54.4, 41.5, 39.3, 34.5, 33.0, 31.2, 26.2, 26.2, 26.0, (×3), 25.9 (×3), 25.5, 25.3, 20.3, 20.1, 18.4, 18.1, 16.5, 16.3, −4.2, −4.6, −5.3 (×2) (for the major diastereomer) and 96.0, 75.4, 73.1, 67.2, 62.5, 54.2, 41.4, 39.2, 35.0, 33.0, 31.2, 26.3, 26.2, 26.0, (×3), 25.9 (×3), 25.6, 25.4, 20.5, 19.7, 18.4, 18.1, 17.5, 14.9, −4.2, −4.6, −5.3 (×2) (for the minor diastereomer); HRMS (CI+) calcd for $C_{31}H_{64}O_4S_2Si_2$ ($M^+$): 620.3785; found, 620.3788.

### 4.8. (2*S*,8*R*,9*S*)-2-((*tert*-Butyldimethylsilyl)oxy)-8-methyl-9-((tetrahydropyran-2′-yl)oxy)octan-1-ol 17

Raney-Ni was washed with excess absolute ethanol before use. To a solution of **16** (380.0 mg, 0.61 mmol) in absolute ethanol (10 mL) was added Raney-Ni (2.0 g) followed by refluxing under a hydrogen atmosphere (1.0 atm) for 10 h. The reaction mixture was filtrated through Celite, and the filtrate was concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, eluting with 5% EtOAc in hexane) to give a 70:30 mixture of diastereomers (280.0 mg, 89%) as an oil; $R_f$ = 0.41 (5% EtOAc in hexane); IR (film) 2955, 2930, 2858, 1255, 1115 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) 4.71–4.67 (m, 0.3H for the minor diastereomer), 4.63–4.58 (m, 0.7H for the major diastereomer), 3.96–3.85 (m, 1H), 3.68–3.58 (m, 2H), 3.49 (dd, $J$ = 15.2, 10.0 Hz, 1H), 3.51–3.44 (m, 1H), 3.39 (dd, $J$ = 10.4, 6.4 Hz, 1H), 1.87–1.17 (m, 17H), 1.12 (d, $J$ = 6.4 Hz, 2.1H for the major diastereomer), 1.01 (d, $J$ = 6.4 Hz, 0.9H for the minor diastereomer), 0.89–0.85 (m, 18H + 0.9H for the minor diastereomer), 0.83 (d, $J$ = 6.8 Hz, 2.1H for the major diastereomer), 0.05 (s, 6H), 0.04 (s, 3H), 0.04 (s, 6H); $^{13}C$ NMR (100 MHz, $CDCl_3$) 98.7, 77.0, 73.2, 67.5, 62.9, 37.1, 34.3, 33.0, 31.2, 30.2, 27.4, 26.0 (×3), 25.9 (×3), 25.5, 25.1, 20.1, 18.4, 18.2, 16.8, 13.9, −4.3, −4.7, −5.3, −5.4 (for the major diastereomer) and 95.9, 74.7, 73.2, 67.5, 62.5, 38.5, 34.4, 33.1, 31.3, 30.2, 27.3, 26.0 (×3), 25.9 (×3), 25.6, 25.1, 19.8, 18.4, 18.2, 14.5 (×2), −4.3, −4.7, −5.3, −5.4 (for the minor diastereomer); HRMS (CI+) calcd for $C_{28}H_{60}O_4Si_2$ ($M^+$): 516.4030; found, 516.3990.

To a solution of the above oil (55.0 mg, 0.11 mmol) in THF (2 mL) was added a mixed solution of TBAF–AcOH (50 mol %: 50 mol %, 2.34 mL, 2.34 mmol). The solution was stirred for 8 h at room temperature, and then the reaction mixture was quenched by the addition of saturated aqueous $NaHCO_3$. The resultant mixture was extracted with ethyl acetate (5 mL × 3), and the combined organic layer was washed with brine, dried over anhydrous $Na_2SO_4$, filtered, and concentrated under reduced pressure. The crude product was purified by column chromatography (silica gel, eluting with 17% EtOAc in hexane) to give a 70:30 mixture of diastereomers of **17** (30.0 mg, 70%) as a colorless oil; $R_f$ = 0.44 (17% EtOAc in hexane); IR (film) 3455 (br), 2930, 2857, 1255, 1114, 1022 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) 4.70–4.67 (m, 0.3H for the minor diastereomer), 4.63–4.58 (m, 0.7H for the major diastereomer), 3.95–3.88 (m, 1H), 3.80–3.68 (m, 1H), 3.68–3.56 (m,

1H), 3.56 (dd, $J$ = 10.8, 4.0 Hz, 1H), 3.50–3.45 (m, 1H), 3.44 (dd, $J$ = 10.8, 5.2 Hz, 1H), 1.90–1.20 (m, 18H), 1.12 (d, $J$ = 6.8 Hz, 2.1H for the major diastereomer), 1.01 (d, $J$ = 6.4 Hz, 0.9H for the minor diastereomer), 0.90 (s, 9H), 0.88 (d, $J$ = 6.4 Hz, 0.9H for the minor diastereomer), 0.83 (d, $J$ = 6.8 Hz, 2.1H for the major diastereomer), 0.08 (s, 6H); $^{13}$C NMR (100 MHz, $CDCl_3$) 98.6, 77.3, 72.9, 66.3, 62.9, 37.0, 33.9, 32.9, 31.2, 30.1, 27.3, 25.8 (×3), 25.5, 25.3, 20.1, 18.1, 16.9, 14.0, −4.5, −4.6 (for the major diastereomer) and 95.9, 77.2, 74.8, 66.3, 62.5, 38.5, 33.9, 33.0, 31.3, 30.1, 27.2, 25.8 (×3), 25.6, 25.3, 19.8, 18.1, 14.6, 14.5, −4.5, −4.6 (for the minor diastereomer); HRMS (CI+) calcd for $C_{22}H_{47}O_4Si$ ($M+H^+$): 403.3244; found, 403.3242.

### 4.9. (3*S*,9*R*,10*S*)-3-((*tert*-Butyldimethylsilyl)oxy)-9-methyl-10-((tetrahydropyran-2′-yl)oxy)undec-1-ene 18

To a solution of alcohol **17** (100.0 mg, 0.25 mmol) in $CH_2Cl_2$ (3 mL) were sequentially added $NaHCO_3$ (200 mg, 2.49 mmol) and Dess–Martin periodinane (1.24 mL, 0.3 M in $CH_2Cl_2$, 0.37 mmol) followed by stirring at room temperature for 2 h. The reaction mixture was quenched by the addition of aqueous $Na_2S_2O_3$. The resultant mixture was extracted with ethyl acetate (10 mL × 3). The combined organic layer was washed with brine, dried over anhydrous $Na_2SO_4$, filtered, and concentrated under reduced pressure. The crude product was purified by column chromatography (silica gel, eluting with 17% EtOAc in hexane) to give a 70:30 mixture of diastereomeric aldehyde (83.0 mg, 83%) as an oil; $R_f$ = 0.68 (17% EtOAc in hexane); IR (film) 2932, 2858, 1737, 1254, 1115, 1022 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) 9.59 (d, $J$ = 2.0 Hz, 1H), 4.70–4.67 (m, 0.3H for the minor diastereomer), 4.62–4.58 (m, 0.7H for major diastereomer), 3.98–3.85 (m, 2H), 3.68–3.57 (m, 1H), 3.52–3.44 (m, 1H), 1.88–1.12 (m, 17H), 1.13 (d, $J$ = 6.4 Hz, 2.1H for the major diastereomer), 1.01 (d, $J$ = 6.0 Hz, 0.9H for the minor diastereomer), 0.92 (s, 9H), 0.88 (d, $J$ = 7.2 Hz, 0.9H for the minor diastereomer), 0.83 (d, $J$ = 6.8 Hz, 2.1H for the major diastereomer), 0.08 (s, 3H), 0.07 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) 204.4, 98.7, 77.7, 76.5, 62.9, 37.1, 32.9, 32.6, 31.2, 29.8, 27.2, 25.7 (×3), 25.5, 24.9, 20.1, 18.2, 16.9, 14.0, −4.6, −4.9 (for the major diastereomer) and 204.4, 96.0, 77.2, 74.7, 62.6, 38.5, 32.9, 32.6, 31.3, 29.8, 27.2, 25.7 (×3), 25.6, 24.6, 19.8, 18.2, 14.6, 14.6, −4.6, −4.9 (for the minor diastereomer); HRMS (CI+) calcd for $C_{22}H_{43}O_4Si$ ($M^+-H$): 399.2931; found, 399.2948.

Methyltriphenylphosphonium bromide was completely dried under high vacuum for 20 h at 110 °C before use. To a suspension of methyltriphenylphosphonium bromide (72.0 mg, 0.20 mmol) in dry THF (2 mL) cooled at 0 °C was added dropwise KHDMS (0.32 mL, 0.5 M in toluene, 0.16 mmol) followed by stirring for 30 min at the same temperature. The resultant yellow solution of the ylide was cooled to −10 °C, and a solution of the above aldehyde (40.0 mg, 0.10 mmol) in dry THF (1 mL) was added dropwise. After being stirred for 30 min at −10 °C, the reaction mixture was allowed to warm to room temperature and then quenched by the addition of water (2 mL). The mixture was extracted with ethyl acetate (10 mL × 3), and the combined organic layer was washed with brine, dried over anhydrous $Na_2SO_4$, filtered, and concentrated under reduced pressure. The crude product was purified by column chromatography (silica gel, 5% EtOAc in hexane) to give a 70:30 mixture of diastereomers of **18** (33.0 mg, 83%) as an oil; $R_f$ = 0.37 (5% EtOAc in hexane); $[\alpha]_D^{20} = -6.1$ ($c$ 1.65, $CH_2Cl_2$); IR (film) 2931, 2856, 1253, 1078, 1023 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) 5.79 (ddd, $J$ = 16.8, 10.4, 6.0 Hz, 1H), 5.12 (br d, $J$ = 17.2 Hz, 1H), 5.00 (br d, $J$ = 10.0 Hz, 1H), 4.70–4.66 (m, 0.3H for the minor diastereomer), 4.63–4.57 (m, 0.7H for the major diastereomer), 4.06 (dt, $J$ = 6.0, 6.0 Hz, 1H), 4.96–4.85 (m, 1H), 3.69–3.57 (m, 1H), 3.52–3.44 (m, 1H), 1.90–1.17 (m, 17H), 1.12 (d, $J$ = 6.4 Hz, 2.1H for the major diastereomer), 1.01 (d, $J$ = 6.0 Hz, 0.9H for the minor diastereomer), 0.89 (s, 9H), 0.88 (d, $J$ = 6.4 Hz, 0.9H for the minor diastereomer), 0.83 (d, $J$ = 6.8 Hz, 2.1H for the major diastereomer), 0.04 (s, 3H), 0.03 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) 141.9, 113.4, 98.7, 77.0, 73.9, 62.9, 38.1, 37.0, 32.9, 31.2, 29.9, 27.4, 25.9 (×3), 25.5, 25.1, 20.1, 18.2, 16.8, 14.0, −4.4, −4.8 (for the major diastereomer) and 141.9, 113.3, 95.9, 74.7, 73.9, 62.5, 38.5, 37.0, 33.0, 31.3, 29.9, 27.3, 25.9 (×3), 25.6, 25.2, 19.8, 18.2, 14.5 (×2), −4.4, −4.8 (for the minor diastereomer); HRMS (CI+) calcd for $C_{23}H_{47}O_3Si$ ($M+H^+$): 399.3294; found, 399.3286.

### 4.10. (3*S*,9*R*,10*S*)-9-Methyl-10-((tetrahydropyran-2′-yl)-oxy)undec-1-en-3-yl acrylate 19

To a solution of olefin **18** (50.0 mg, 0.13 mmol) in THF (2 mL) was added TBAF (0.19 mL, 1 M in THF, 0.19 mmol) dropwise followed by stirring for 6 h at room temperature. The reaction mixture was quenched by the addition of water (1 mL). The resultant mixture was extracted with ethyl acetate (5 mL × 3), and the combined organic layer was washed with brine, dried over anhydrous $Na_2SO_4$, filtered, and concentrated under reduced pressure. The crude product was purified by column chromatography (silica gel, eluting with 25% EtOAc in hexane) to give a 70:30 mixture of diastereomeric alcohol (31.5 mg, 87%) as an oil; $R_f$ = 0.31 (25% EtOAc in hexane); $[\alpha]_D^{20} = -12.0$ ($c$ 1.55, $CH_2Cl_2$); IR (film) 3422 (br), 2932, 2856, 1379, 1115, 1022 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) 5.85 (ddd, $J$ = 17.2, 10.4, 6.4 Hz, 1H), 5.20 (d, $J$ = 17.2 Hz, 1H), 5.08 (d, $J$ = 10.4 Hz, 1H), 4.68–4.66 (m, 0.3H for the minor diastereomer), 4.61–4.58 (m, 0.7H for the major diastereomer), 4.07 (dt, $J$ = 6.4, 6.4 Hz, 1H), 3.95–3.83 (m, 1H), 3.67–3.55 (m, 1H), 3.50–3.41 (m, 1H), 1.90–1.20 (m, 18H), 1.10 (d, $J$ = 6.8 Hz, 2.1H for the major diastereomer), 1.00 (d, $J$ = 6.4 Hz, 0.9H for the minor diastereomer), 0.87 (d, $J$ = 6.8 Hz, 0.9H for the minor diastereomer), 0.81 (d, $J$ = 6.8 Hz, 2.1H for the major diastereomer); $^{13}$C NMR (100 MHz, $CDCl_3$) 141.3, 114.5, 98.6, 77.2, 73.2, 62.8, 37.0, 36.9, 32.9, 31.2, 29.8, 27.3, 25.5, 25.3, 20.1, 16.8, 13.9 (for the major diastereomer) and 141.3, 114.5, 95.9, 74.7, 73.2, 62.5, 38.5, 36.9, 33.0, 31.3, 29.8, 27.2, 25.6, 25.3, 19.7, 14.6, 14.5 (for the minor diastereomer).

To a solution of the above alcohol (31.0 mg, 0.11 mmol) in dry $CH_2Cl_2$ (2 mL) cooled at 0 °C were sequentially added triethylamine (22 mg, 0.22 mmol) and acryloyl chloride (15 mg, 0.16 mmol) followed by stirring for 4 h at room temperature. The reaction mixture was diluted with water and $CH_2Cl_2$. The aqueous layer was extracted with $CH_2Cl_2$ (5 mL × 2), and the combined organic layer was dried over anhydrous $Na_2SO_4$, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, 9.1% EtOAc in hexane) to give a 69:31 mixture of diastereomers of **19** (30.0 mg, 81%) as a colorless oil; $R_f$ = 0.40 (9.1% EtOAc in hexane); IR (film) 2937, 1726, 1404, 1267, 1192, 1023 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) 6.40 (dd, $J$ = 17.2, 1.6 Hz, 1H), 6.12 (dd, $J$ = 17.2, 10.4 Hz, 1H), 5.83–5.74 (m, 2H), 5.29 (dt, $J$ = 6.4, 6.4 Hz, 1H), 5.23 (br d, $J$ = 17.6 Hz, 1H), 5.15 (dd, $J$ = 10.8, 0.8 Hz, 1H), 4.69–4.65 (m, 0.31H for the minor diastereomer), 4.63–4.53 (m, 0.69H for the major diastereomer), 3.95–3.83 (m, 1H), 3.66–3.55 (m, 1H), 3.50–3.43 (m, 1H), 1.90–1.20 (m, 17H), 1.11 (d, $J$ = 6.8 Hz, 2.07H for the major diastereomer), 1.00 (d, $J$ = 6.0 Hz, 0.93H for the minor diastereomer), 0.87 (d, $J$ = 6.8 Hz, 0.93H for the minor diastereomer), 0.81 (d, $J$ = 6.8 Hz, 2.07H for the major diastereomer); $^{13}$C NMR (100 MHz, $CDCl_3$) 165.5, 136.4, 130.5, 128.8, 116.6, 98.6, 77.2, 74.9, 62.9, 37.0, 34.1, 32.8, 31.2, 29.6, 27.3, 25.5, 25.0, 20.1, 16.9, 14.0 (for the major diastereomer) and 165.5, 136.5, 130.5, 128.8, 116.6, 95.9, 75.0, 74.7, 62.5, 38.5, 34.1, 32.9, 31.3, 29.6, 27.2, 25.6, 25.0, 19.8, 14.6, 14.5 (for the minor diastereomer).

### 4.11. (4*S*,10*R*,11*S*)-4,11-Dihydroxy-10-methyldodec-2-en-1,4-olide 1

To a solution of acrylate **19** (18.0 mg, $5.3 \times 10^{-2}$ mmol) in dry and degassed $CH_2Cl_2$ (40 mL) was added a solution of Grubb's II catalyst **20** (4.0 mg) in dry $CH_2Cl_2$ (2 mL). After being refluxed for 1 h, the reaction mixture was concentrated under reduced pressure, and the residue was purified by column chromatography (silica gel, eluting with 25% EtOAc in hexane) to give a 68:32 mixture of the diastereomers of the butenolide (15.0 mg, 91%) as a colorless oil; $R_f = 0.13$ (25% EtOAc in hexane); IR (film) 2936, 1758, 1162, 1022 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) 7.44 (dd, $J = 6.0$, 1.6 Hz, 1H), 6.09 (dd, $J = 6.0$, 2.4 Hz, 1H), 5.05–5.00 (m, 1H), 4.69–4.65 (m, 0.32H for the minor diastereomer), 4.60–4.56 (m, 0.68H for the major diastereomer), 3.95–3.82 (m, 1H), 3.68–3.55 (m, 1H), 3.52–3.42 (m, 1H), 1.90–1.20 (m, 17H), 1.11 (d, $J = 6.0$ Hz, 2.04H for the major diastereomer), 1.01 (d, $J = 6.4$ Hz, 0.96H for the minor diastereomer), 0.87 (d, $J = 6.8$ Hz, 0.96H for the minor diastereomer), 0.82 (d, $J = 6.8$ Hz, 2.04H for the major diastereomer); $^{13}C$ NMR (100 MHz, $CDCl_3$) 173.1, 156.3, 121.5, 98.7, 83.4, 77.2, 62.9, 37.0, 33.1, 32.7, 31.2, 29.6, 27.2, 25.5, 24.9, 20.1, 16.9, 14.0 (for the major diastereomer) and 173.1, 156.3, 121.5, 96.0, 83.4, 74.7, 62.7, 38.5, 33.1, 32.8, 31.3, 29.5, 27.0, 25.6, 24.9, 19.9, 14.7, 14.6 (for the minor diastereomer).

A solution of the above butenolide (23.0 mg, $7.4 \times 10^{-2}$ mmol) and PPTS (2.0 mg, $0.8 \times 10^{-2}$ mmol) in MeOH (1 mL) was stirred at 40 °C (bath temperature) for 2 h. The reaction mixture was concentrated under reduced pressure, and the residue was purified by column chromatography (silica gel, eluting with 50% EtOAc in hexane) to give alcohol **1** (14.0 mg, 83%) as a colorless oil; $R_f = 0.20$ (50% EtOAc in hexane); $[\alpha]_D^{20} = +78.0$ (*c* 0.100, MeOH); IR (film) 3442 (br), 2929, 1749, 1462, 1166, 1102 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) 7.44 (dd, $J = 5.2$, 0.8 Hz, 1H), 6.09 (dd, $J = 5.6$, 1.6 Hz, 1H), 5.04–5.00 (m, 1H), 3.63 (quintet, $J = 5.8$ Hz, 1H), 1.80–1.70 (m, 1H), 1.70–1.57 (m, 2H), 1.50–1.20 (m, 8H), 1.10 (d, $J = 6.0$ Hz, 3H), 1.10–1.00 (m, 1H), 0.84 (d, $J = 6.8$ Hz, 3H); $^{13}C$ NMR data are found in Table 1; HRMS (CI+) calcd for $C_{13}H_{23}O_3^+$ ($M+H^+$): 227.1647; found, 227.1650.

### 4.12. (4*S*,10*R*)-4-Hydroxy-10-methyl-11-oxododec-2-en-1,4-olide 2

To a solution of **1** (10.0 mg, $4.4 \times 10^{-2}$ mmol) in $CH_2Cl_2$ (1 mL) were sequentially added $NaHCO_3$ (30.0 mg, 0.36 mmol) and Dess–Martin periodinane (0.17 mL, 0.3 M in $CH_2Cl_2$, $5.1 \times 10^{-2}$ mmol). After stirring for 2 h, the reaction mixture was condensed and the residue was purified by column chromatography (silica gel, eluting with 50% EtOAc in hexane) to give **2** (9.6 mg, 96%) as a colorless oil; $R_f = 0.34$ (50% EtOAc in hexane); $[\alpha]_D^{20} = +32.0$ (*c* 0.100, MeOH); IR (film) 2934, 1755, 1709, 1461, 1358, 1164, 1106 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) 7.43 (dd, $J = 5.6$, 1.2 Hz, 1H), 6.10 (dd, $J = 6.0$, 2.0 Hz, 1H), 5.03–5.00 (m, 1H), 2.51–2.45 (m, 1H), 2.12 (s, 3H), 1.80–1.60 (m, 3H), 1.50–1.20 (m, 7H), 1.07 (d, $J = 6.8$ Hz, 3H); $^{13}C$ NMR data are found in Table 1; HRMS (+CI) calcd for $C_{13}H_{21}O_3^+$ ($M+H^+$): 225.1491; found, 225.1497.

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