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Total Synthesis of the Proposed Structure for Aromin and Its Structural Revision

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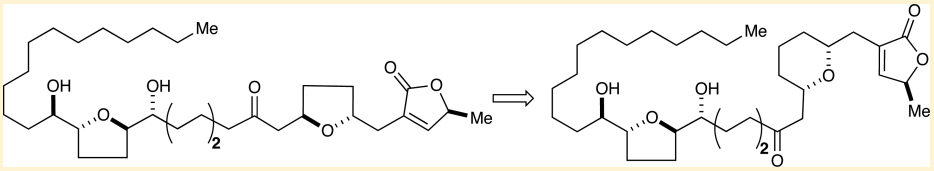
Supporting Information



ABSTRACT: This paper describes the first total synthesis of the proposed structure for aromin, an annonaceous acetogenin possessing an unusual bis-THF ring system, and its 4*S*,7*R*-isomer. The key steps involve an oxidative cyclization of a couple of terminal-diene alcohols and an intermolecular metathesis of an alkenyl tetrahydrofuran with an enone carrying a tetrahydrofuranyl lactone. The spectral data of both samples did not match those of aromin. Re-examination of the NMR data using the CAST/CNMR Structure Elucidator and chemical derivations suggested that the real structure of aromin should be revised to be a tetrahydropyran acetogenin, montanacin D. Cytotoxicities in human solid tumor cell lines for synthetic samples were also evaluated.

INTRODUCTION

The Annonaceous acetogenins from Annonaceae plants comprise a class of almost 420 natural products that exhibit a remarkably broad spectrum of biological properties such as anticancer, antiinfective, immunosuppressive, antifeedant, and pesticidal activities. Structurally, most of these compounds are characterized by a terminal γ-lactone unit at the end of a long aliphatic chain containing one to three tetrahydrofuran (THF) rings or tetrahydropyran (THP) ring or epoxide rings, or other functional groups.[1] Certain acetogenins possess an unusual structure forming a cyclic ether by a 4-hydroxy group adjacent to the γ-lactone ring.[2−4] In 1996, McLaughlin et al. isolated a couple of new acetogenins, aromin and aromicin from the stem bulk of *Xylopia aromatica*.[5] Their structures were elucidated by chemical and spectral means to be **1** and **2** possessing a 4,7-*trans* THF ring along with a 16,19-*trans* THF ring as a common scaffold, respectively (Figure 1). The *trans* configuration of both THF rings in **1** was deduced by the relatively large δ differences between the *gem*-protons in the THF rings and by no cross-peak at H-4/H-7 or at H-16/H-19 in the NOESY spectrum;[6,7] the relative stereochemistry of the C_{15}−C_{20} portion was also confirmed by comparison of their ^{13}C NMR data with those of model compounds.[8] The absolute configurations of C-15 and C-20 in **1** were determined by the Mosher method while the stereochemistries at C-4 and C-34 (C-36 for **2**) were shown to be 4*R*, 34*S* by comparison of the CD curve of **1** with those of several acetogenins previously proven to have 4*R*, 34*S* configurations. Since **1** and **2** differ only by the length of the carbon chain, **2** was assumed to have the same absolute stereochemistry. Both natural products showed significant cytotoxicities among six human tumor cell lines; however, the activity was notably reduced compared to other nonadjacent bis-THF ring acetogenins. We presumed that the reason would be due to a conformational rigidity around the lactone ring, an essential domain for several biological activities. In connection with our synthetic studies on Annonaceous acetogenins,[9] the unique structure stimulated our interest. Described herein is the first total synthesis of aromin that dictates revision of the formula of **1** to **32** (montanacin D).

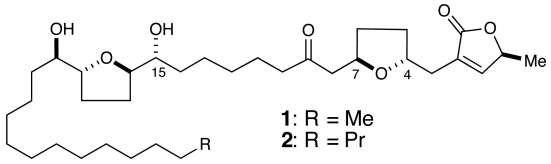


Figure 1. Proposed structures for aromin (**1**) and aromicin (**2**).

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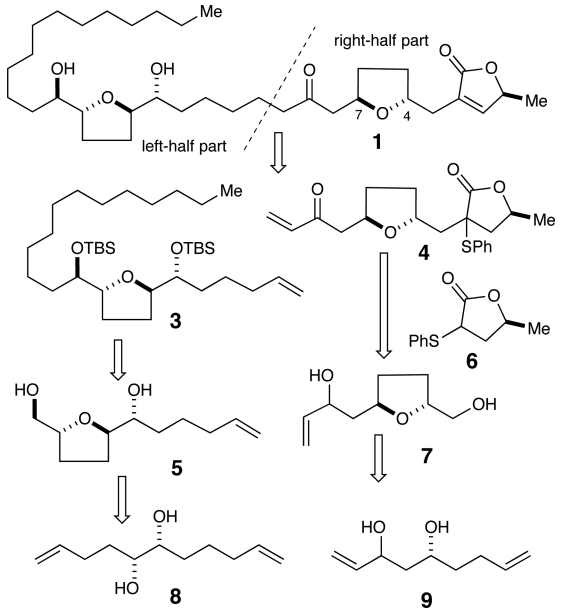
RESULTS AND DISCUSSION

Our synthetic strategy directed toward **1** was based on a convergent process that involved intermolecular metathesis of olefin **3** and enone **4** as illustrated in Scheme 1, and we recently

Scheme 1. Synthetic Plan of 1

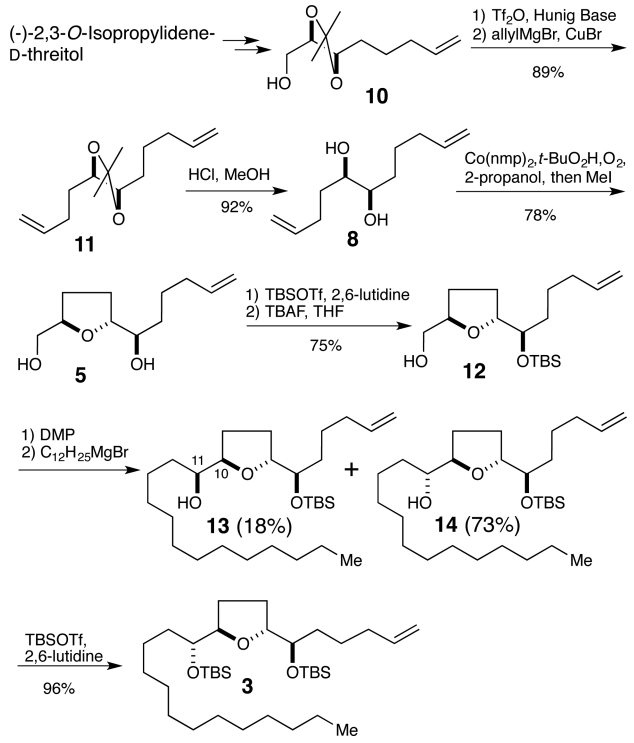


demonstrated the usefulness of this method.[9a,b] The enone **4** might be prepared from γ-lactone **6**[10] and a THF derivative **7** while the left-half segment **3** would be synthesized from a THF alcohol **5**. The presence of the *trans*-THF ring system in both parts made us envisage an oxidative cyclization[11−13] of terminal diene diols **8** and **9**. Since no paper has appeared dealing with the oxidative cyclization of such diene alcohols,[14−16] this strategy might be more challenging.

Synthesis of the left-half segment corresponding to the C_{10}−C_{32} domain began with a chain elongation reaction[17] of **10**[18] (Scheme 2). After hydrolysis of the isopropylidene group in **11**, the resulting diol **8** was treated with 10 mol % of *tert*-butyl hydroperoxide in the presence of $Co(nmp)_2$ (10 mol %) in 2-propanol under an oxygen atmosphere[13] to give a *trans*-THF alcohol **5**[19] in good yield. As expected, a tetrahydropyran[20] or an oxepan derivative and a bicyclic compound including such ring systems were not isolated. Hydroxyl protection of **5** with TBSOTf followed by selective deprotection gave a primary alcohol **12**. After Dess-Martin oxidation, the resulting aldehyde reacted with dodecylmagnesium bromide to provide a desired *threo* alcohol **14** in 73% yield along with its epimer **13** (18%). Each relative stereochemical relationship between the chiral centers at C-10/C-11 was defined based on the NMR data,[7,8] and the stereoselectivity would be explained by an α-chelation controlled reaction pathway. Treatment of **14** with TBSOTf gave the left-half segment **3**.

Having completed the synthesis of the left-half segment, we next turned our attention to preparation of the right-half segment. The fact that the absolute configuration of the THF ring in the segment was not confirmed prompted us to prepare both enantiomers of the part. Prior to the experiment, an oxidative cyclization of 1,3-*anti*-diol **9a** and its *syn* isomer **9b** was considered.[21] Different from the cyclization of **8**, there are 4 types of possible pathways (Scheme 3). In the case of **9a**, we

Scheme 2. Synthesis of the Left-Half Segement of 1



predicted that the Co-olefin complex interacting with a C-3 alkoxy radical would cause a conformational lock of the vinyl moiety, resulting in inhibition of path a. On the other hand, path d leading to **18** from **9b** may be unfavorable because there should be a serious repulsion in the transition state. Therefore, allyl alcohol such as **7a** or **7b** was expected to be a major product in both cases. An initial attempt to prepare the proposed structure **7a** from **9a** was conducted under Mukaiyama's conditions,[12] affording a single product as judged by TLC analysis. However, it was revealed to be an inseparable mixture of two compounds by ^{1}H NMR spectra. Each compound could be separated after acetylation and characterized to be **16** and **17** (Table 1).[19,28] As expected, the major product was **17** through path b. The modified procedure reported by Pagenkopf et al.[13] slightly improved the yield of **17** (57%) but **16** was also obtained in 26% yield. Upon deacetylation, **17** afforded the desired diol **7a**. The cyclization of 1,3-*syn*-diol **9b** also resulted in an inseparable mixture of cyclized products, and after acetylation, THF derivatives **19** and **20** were separated (Table 1). Compound **19** was transformed into **7b** in a similar way. As the regioselectivity in the cyclization resulted in being not as high as expected, we decided to develop a more efficient route to the THF core.[29]

The second approach to the THF core began with Keck's asymmetric allylation[30] of 4-pentenal (Scheme 4). The Mukaiyama's oxidative cyclization of **21**[31] thus obtained (>98% e.e.)[32] proceeded without trouble to give a THF alcohol **22**[33] in good yield.[19] After ozonolysis, the resulting aldehyde underwent vinylation to give a diol **7** as an epimeric mixture. Regioselective sulfonylation and silylation of two hydroxyl groups in **7** were carried out by the previously reported method.[9] Thus, treatment of **7** with 1.1 equiv of triflic anhydride in the presence of 2,6-lutidine at −78 °C followed by addition of TBSOTf afforded **23** in one pot. Lithium enolate generated from γ-lactone **6** reacted with the triflate to give a

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Scheme 3. Oxidative Cyclization of Terminal Diene Diols 9a and 9b

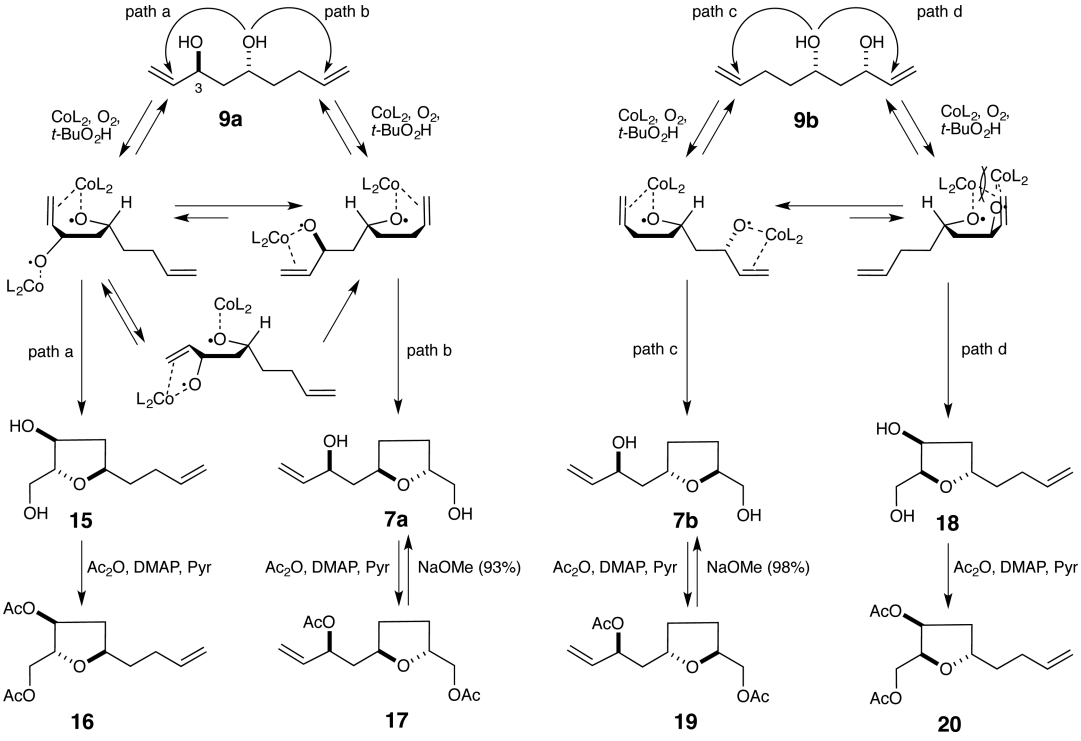
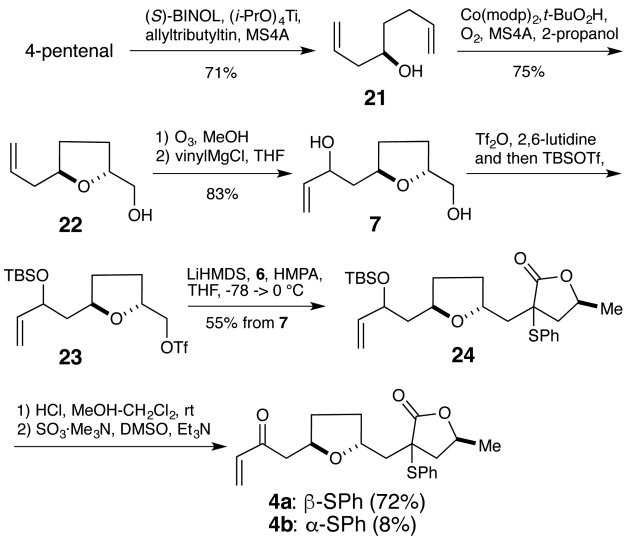


Table 1. Oxidative Cyclization of Diols 9a and 9b

		yield (%)[b]			
entry	conditions[a]	16	17	19	20
1	**9a**, $Co(modp)_2$ (20 mol %), *t*-BuO_2H (100 mol %), O_2, MS4A, 2-propanol, 50−52 °C	20	42	–	–
2	**9a**, $Co(nmp)_2$ (10 mol %), *t*-BuO_2H (10 mol %), O_2, 2-propanol, 50−52 °C, then MeI, 0 °C → rt	26	57	–	–
3	**9b**, $Co(modp)_2$ (20 mol %), *t*-BuO_2H (100 mol %), O_2, MS4A, 2-propanol, 50−52 °C	–	–	50	20
4	**9b**, $Co(nmp)_2$ (10 mol %), *t*-BuO_2H (10 mol %), O_2, 2-propanol, 50−52 °C, then MeI, 0 °C → rt	–	–	55	23

[a] $Co(modp)_2$ = bis(1-morpholinocarbamoyl-4,4-dimethyl-1,3-pentanedionate) cobalt(II).[12] $Co(nmp)_2$ = bis(4,4-dimethyl-1-(4-methylpiperazino)-carbamoyl-1,3-pentanedionate) cobalt(II).[13] [b] Isolated yield after acetylation (Ac_2O, DMAP, pyr, 0 °C → rt, 13 h).

Scheme 4. Preparation of the Right-Half Segment



coupling product **24**.[34] Acidic hydrolysis of the TBS group followed by an allylic oxidation gave **4a** in 72% yield along with the diastereomer **4b** (8%).[35]

The complete carbon skeleton of **1** was assembled by joining **3** and **4a** in the presence of Grubbs' second generation catalyst[36] in dichloromethane to afford an enone **25** (Scheme 5). This was hydrogenated to give **26**. Finally, installation of a butenolide residue and desilylation afforded structure **1**. The spectroscopic and physical properties of synthetic material **1** were found to differ from those reported of the natural aromin. In particular, the natural product contained two multiplets at δ 3.59 (H-4) and 3.84 (H-7), which were observed at 4.21 and 4.36 ppm, respectively, in the ^{1}H NMR spectrum of the synthetic product (Table 2). These results suggested a difference in the structure around the central THF ring. Therefore, we presumed the diastereomer **31** as another possibility of aromin (Figure 2). Synthesis of **31** started from *ent*-**21**[31] obtained by using (*R*)-BINOL in the asymmetric allylation (Scheme 4). By the same sequence of reactions described above, this alcohol was transformed into γ-lactone **27** including the antipodal THF ring and then enone **28**.[37] Cross-metathesis of **28** with **3** followed by reduction of the resulting product **29** yielded **30**, which was converted into **31** through a three-step sequence. Contrary to expectations, the NMR data of **31** were inconsistent with those of the natural product (Table 2). The five signals for C-4−8 of the synthetic compounds **1** and **31** deviated by 0.4−0.8 ppm compared

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Scheme 5. Completion of Total Synthesis of the Proposed Structure 1 for Aromin

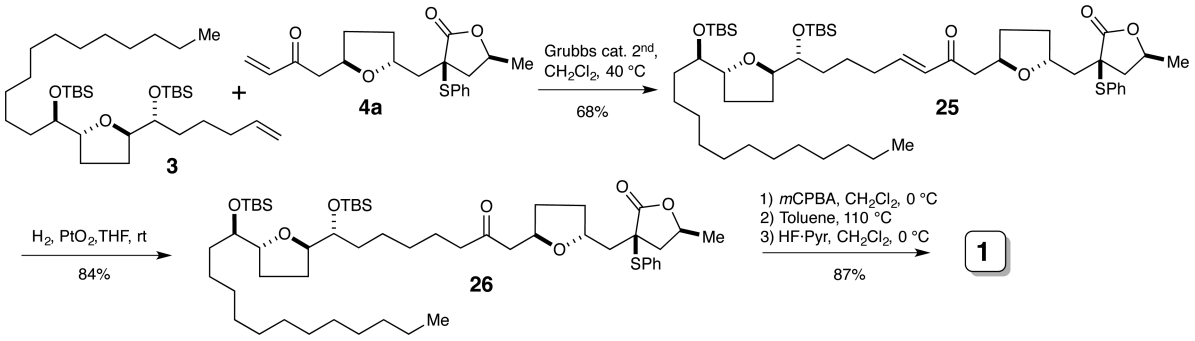

Table 2. NMR Data (δ) for Natural Aromin, Compound 1, and Its Diastereomer 31

	natural aromin[a]		synthetic **1**		synthetic **31**	
Position	^{1}H (J) (500 MHz, $CDCl_3$)	^{13}C[c] ($CDCl_3$)	^{1}H (J) (600 MHz, $CDCl_3$)	^{13}C[d] ($CDCl_3$)	^{1}H (J) (600 MHz, $CDCl_3$)	^{13}C[d] ($CDCl_3$)
1	–	174.2	–	173.9	–	174.0
2	–	130.6	–	130.8	–	130.7
3a	2.36 (m)	31.1–31.9	2.46 (m)	31.1	2.45 (m)	31.1
3b						
4	3.59 (m)	75.6	4.21 (m)	76.4	4.20 (m)	76.4
5a	1.22 (m)	31.1–31.9	1.62 (m)	31.6	1.58 (m)	31.6
5b	1.56 (m)		2.08 (m)		2.06 (m)	
6a	1.22 (m)	31.1–31.9	1.53 (m)	32.0	1.52 (m)	32.0
6b	1.56 (m)		2.14 (m)		2.13 (m)	
7	3.84 (m)	74.1	4.36 (m)	74.8	4.36 (m)	74.7
8a	2.38	49.1	2.59	48.7	2.49	48.7
	(dd, 15.5, 4.0)		(dd, 15.8, 5.5)		(dd, 15.8, 5.5)	
8b	2.63		2.70		2.70	
	(dd, 15.5, 9.0)		(dd, 15.8, 7.2)		(dd, 15.8, 7.2)	
9	–	209.3	–	209.3	–	209.3
10	2.42 (t, 7.0)	43.8	2.43 (t, 7.5)	43.4	2.43 (t, 7.3)	43.4
11	1.3–1.8	29.3–29.7	1.57 (m)	23.4	1.57 (m)	23.4
12	1.3–1.8	25.2–25.6	1.31 (m)	29.2	1.31 (m)	29.2
13	1.3–1.8	25.2[b]	1.38 (m), 1.51 (m)	25.4	1.37 (m), 1.51 (m)	25.4
14	1.39 (m)	33.5[b]	1.39 (m)	33.2	1.39 (m)	33.2
15	3.40 (m)	74.1[b]	3.39 (m)	73.9	3.39 (m)	73.9
16	3.79 (m)	82.7[b]	3.79 (m)	82.6	3.79 (m)	82.6
17a	1.66 (m)	28.7[b]	1.67 (m)	28.7	1.67 (m)	28.7
17b	1.98 (m)		1.97 (m)		1.97 (m)	
18a	1.98 (m)	28.7[b]	1.67 (m)	28.7	1.67 (m)	28.7
18b			1.97 (m)		1.97 (m)	
19	3.79 (m)	82.5[b]	3.79 (m)	82.7	3.79 (m)	82.7
20	3.40 (m)	73.7[b]	3.39 (m)	74.0	3.39 (m)	74.0
21	1.39 (m)	33.3[b]	1.39 (m)	33.5	1.39 (m)	33.5
22	1.3–1.8	25.6[b]	1.37 (m), 1.51 (m)	25.6	1.37 (m), 1.51 (m)	25.6
23	1.3–1.8	29.3–29.7	1.25 (m)	29.6–29.7	1.25 (m)	29.6–29.7
24–30	1.3–1.8	23.3–31.9	1.25 (m)	29.3–31.9	1.25 (m)	29.3–31.9
31	1.3–1.8	22.7	1.27 (m)	22.7	1.27 (m)	22.7
32	0.88 (t, 7.0)	14.1	0.87 (t, 7.2)	14.1	0.87 (t, 6.8)	14.1
33	7.15 (bs)	151.3	7.18 (m)	151.6	7.19 (m)	151.7
34	4.99	77.8	5.01	77.7	5.00	77.7
	(qddd, 6.5, 1.5, 1.5, 1.5)		(br. q. 6.8)		(br. q. 6.9)	
35	1.40 (d, 6.5)	19.1	1.40 (d, 6.8)	19.1	1.41 (q, 6.9)	**19.1**

[a]Reference 5. [b]Interchangeable within the same column. [c]125 MHz. [d]150 MHz.

with the respective signals of the natural compound in the ^{13}C NMR spectrum.

Comparing the NMR data of natural aromin with those of acetogenins having a 4-hydroxyl group, we speculated that the natural product might possess an ether ring at the C4 position.[38] The fact that two signals derived from H-4 and H-7 of the natural product were observed at a high field compared to those of our synthetic samples made us reexamine the ring size of the natural product. Although ^{1}H NMR chemical shifts are very sensitive to neighboring substituents,

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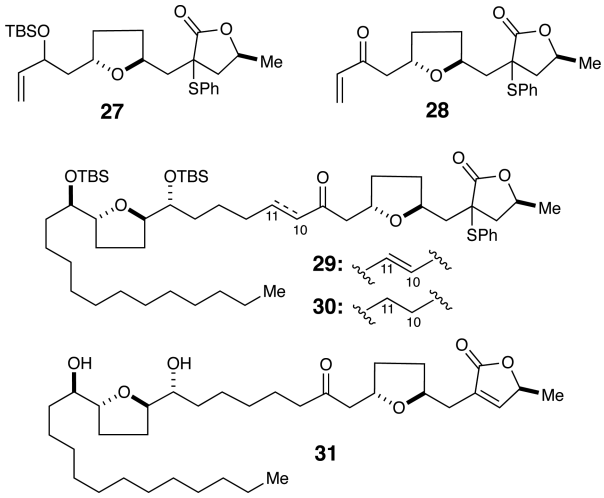

Figure 2. Structures of the diastereomer of **1** and its synthetic intermediates.

the ring size of a cyclic ether could be distinguishable by ^{13}C NMR data in general. To clarify the real structure of natural aromin, we searched similar ^{13}C NMR data from the literature using the CAST (CAnonical-representation of STereochemistry)/CNMR system.[39−41] Recently one of us developed a new system CAST/CNMR Structure Elucidator[42] and successfully revised several natural products.[43,44] The system uses a set of ^{13}C NMR chemical shifts as a query and searches partial structures with similar ^{13}C NMR chemical shifts from the database developed for the CAST/CNMR Chemical Shift Predictor[39,40,45,46] using CAST codes. By applying the CAST/CNMR Structure Elucidator using a query of ^{13}C NMR chemical shift data of natural aromin, montanacin D (**32**) (Figure 3) was found as a structural candidate having a well

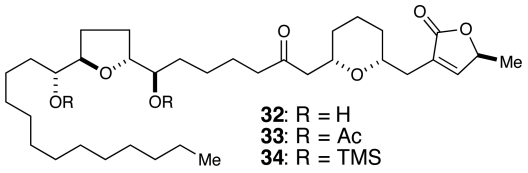

Figure 3. Structures of montanacin D (**32**) and its derivatives.

matched ^{13}C NMR data (Table 3).[47,48] This natural product was isolated from *Annona montana* by Qin et al. in 2000,[3] and its structure was established by our total synthesis.[9a]

In the reported NMR data for natural aromin, assignments of methylene groups were ambiguous, however three high-field shifted methylene carbons at 23.3 (C-6), 23.5 (C12), and 22.7 (C31) ppm of montanacin D were distinguished. Misassignment of C-6 seemed to lead to the incorrectly proposed THF structure for aromin. The ^1H NMR data well matched those reported of aromin. In order to gain further information for the identification, we prepared diacetate **33** and di-TMS ether **34** from **32**. As shown in Table 3, the ^1H data of **33** in C_6D_6 were identical to those reported for aromin diacetate. MS spectral data also supported the structural revision. Aromin di-TMS ether was reported to display a fragment ion at m/z 195 corresponding to the C_1-C_8 part in the EIMS while the di-TMS derivative **35** prepared from the synthetic **1** gave a strong fragment ion at m/z 181 instead of the corresponding fragment ion (Figure 4). The fragment ion can be explained by the cleavage between C-7 and -8 not C-8 and -9. On the other hand, the fragment ion (m/z 195) was observed in the EIMS spectra of montanacin D bis-TMS ether **34**.

These results strongly suggest that the structure of aromin should be revised to be montanacin D (**32**). To clarify this, direct comparison of natural aromin with our authentic sample (montanacin D) is needed. Since aromin and aromicin differ only by the length of the carbon chain, reinvestigation of the proposed structure for aromicin is necessary.[49]

Antitumor activities of synthetic samples **1** and **31** were evaluated, and their data are summarized in Table 4. Both compounds showed significant cytotoxicities against the six human solid tumor cell lines tested *in vitro*. The level of activity was revealed to be relatively strong compared to those of THP acetogenins[9b] such as **32** but not to be comparable to those expected for the usual nonadjacent bis-THF acetogenins.

In summary, the usefulness of a cross-olefin metathesis and a Co-mediated oxidative cyclization of a bis-homoallyl alcohol was demonstrated by the total synthesis of the proposed structure for aromin. Our synthetic studies coupled with a structure search system using the CAST/CNMR Structure Elucidator revealed that aromin possessing an unusual bis-THF ring structure should be revised to a THP acetogenin, montanacin D (**32**). In addition, these results obtained here suggest that the structures of related natural products such as aromicin and aromin-A[4,49] should be reinvestigated.

EXPERIMENTAL SECTION

General Procedures. All reactions were carried out under an argon atmosphere, unless otherwise noted. IR spectra were recorded by the ATR method. The NMR spectra were recorded at 500 or 600 MHz for ^1H and 125 or 150 MHz for ^{13}C. Chemical shifts are reported in ppm downfield from tetramethylsilane with the solvent resonance as the internal standard (δ_H 7.26 ppm or δ_C 77.0 ppm). High-resolution mass spectra (HRMS) were acquired in the electron ionization mode (EI) or the field ionization mode (FI) using a gas chromatography time-of-flight mass spectrometer or electrospray ionization (ESI) hybrid quadrupole/time-of-flight tandem mass spectrometer. The solvent extracts were dried with magnesium sulfate, and the solutions were evaporated under diminished pressure at 35−40 °C.

(4*R*,5*R*)-4-(But-3-en-1-yl)-2,2-dimethyl-5-(pent-4-en-1-yl)-1,3-dioxolane (11). To a stirred solution of **10** (1.0 g, 4.99 mmol) and *N*,*N*-diisopropylethylamine (2.62 mL, 15.0 mmol) in dichloromethane (6.0 mL) was added dropwise a solution of trifluoromethanesulfonic anhydride (1.26 mL, 7.48 mmol) in dichloromethane (84 mL) at −40 °C, and the mixture was stirred at the same temperature for 30 min. After addition of ice−water, the resulting mixture was stirred vigorously for 10 min and then extracted with dichloromethane. The combined organic layers were washed successively with water, saturated aqueous $NaHCO_3$, water, and brine, dried, and concentrated. The residue was passed through a short column of silica gel (*n*-hexane−ethyl acetate = 50:1 → 10:1) to give a syrup (1.55 g). This compound was employed to the next step without further purification. To a stirred suspension of CuBr (273 mg, 1.90 mmol) in ether (15 mL) was added a 1.0 M solution of allylmagnesium bromide in ether (15 mL, 15.0 mmol) at 0 °C, and the mixture was stirred at the same temperature for 20 min. A solution of the above-mentioned syrup (1.55 g) in ether (8 mL) was added dropwise at 0 °C, and the mixture was stirred at 0 °C → rt for 14 h. After addition of saturated aqueous NH_4Cl, the mixture was extracted with dichloromethane−ethyl acetate (1:1). The combined organic layers were washed successively with water and brine, dried, and concentrated. The residue was chromatographed on silica gel (*n*-hexane−ether = 50:1 → 10:1) to give **11** (1.0 g, 89% from **10**) as a light-yellow liquid; $[\alpha]_D^{25}$ +30.3 (*c* 0.44, $CHCl_3$); IR (ZnSe) 3077, 2984, 2932, 1641, 1235, 1087, 908, 875 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 5.86−5.75 (2H, m), 5.06−4.94 (4H, m), 3.63−3.59 (2H,

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Table 3. NMR Data (δ) for Montanacin D (32), Its Diacetate 33, and Natural Aromin-15,20 Diacetates

	montanacin D (**32**)[a]		**33**		aromin-15,20 diacetates[b]
Position	^{1}H (J) (600 MHz, $CDCl_3$)	^{13}C[c] ($CDCl_3$)	^{1}H (J) (600 MHz, C_6D_6)	Position	^{1}H (J) (500 MHz, C_6D_6)
1	–	174.1	–	1	–
2	–	130.6	–	2	–
3a	2.35 (m)	31.8	2.23 (m)	3a	2.22 (dddd, 16.0, 3.5, 1.5, 1.5)
3b	2.35 (m)		2.32 (m)	3b	2.33 (dddd, 16.0, 9.0, 1.5, 1.5)
4	3.58 (m)	75.6	3.33 (m)	4	3.34 (m)
5a	1.25 (m)	31.1	0.98 (m)	5a	0.98 (m)
5b	1.58 (m)		1.19 (m)	5b	1.17 (m)
6a	1.58 (m)	23.3	1.48 (m)	6a	0.93 (m)
6b	1.84 (m)		1.48 (m)	6b	1.20 (m)
7a	1.23 (m)	31.1	0.96 (m)	7	3.66 (m)
7b	1.58 (m)		1.19 (m)	8a	1.93 (dd, 15.5, 3.5)
8	3.82 (m)	74.1	3.66 (m)	8b	2.37 (dd, 15.5, 9.0)
9a	2.37 (dd, 15.9, 8.8)	49.1	1.92 (dd, 15.8, 3.8)	9	–
9b	2.62 (dd, 15.9, 3.9)		2.34 (dd, 15.8, 9.2)		
10	–	209.3	–	10	2.08 (t, 7.0)
11	2.41 (t, 7.2)	43.8	2.08 (m)	11	0.94–1.76
12	1.52 (m), 1.58 (m)	23.5	1.48 (m), 1.56 (m)	12	0.94–1.76
13	1.36 (m), 1.50 (m)	25.2	1.32 (m)	13	0.94–1.76
14	1.39 (m)	33.2	1.51 (m), 1.59 (m)	14	1.5[d]
15	3.38 (m)	73.7	5.02 (m)	15	5.05 (m)
16	3.79 (m)	82.5	3.97 (m)	16	3.97 (m)
17a	1.68 (m)	28.7	1.39 (m)	17a	1.41 (m)
17b	1.98 (m)		1.65 (m)	17b	1.65 (m)
18a	1.68 (m)	28.7	1.39 (m)	18a	1.41 (m)
18b	1.98 (m)		1.65 (m)	18b	1.65 (m)
19	3.79 (m)	82.7	3.98 (m)	19	3.97 (m)
20	3.40 (m)	74.0	5.06 (m)	20	5.05 (m)
21	1.39 (m)	33.5	1.54 (m), 1.63 (m)	21	1.7[d]
22	1.36 (m), 1.50 (m)	25.6	1.39 (m)	22	0.97–1.76
23	1.25 (m)	29.6–29.7	1.30 (m)	23	0.97–1.76
24–30	1.25 (m)	29.6–29.7	1.30 (m)	24–30	0.97–1.76
31	1.28 (m)	22.7	1.30 (m)	31	0.97–1.76
32	0.87 (t, 6.9)	14.1	0.91 (t, 7.0)	32	0.91 (t, 7.0)
33	7.14 (m)	151.3	6.65 (m)	33	6.65 (ddd, 1.5, 1.5, 1.5)
34	4.98 (brq, 6.6)	77.8	4.51 (brq, 6.5)	34	4.51 (qddd, 6.5, 1.5, 1.5, 1.5)
35	1.40 (d, 6.6)	19.1	1.02 (d, 6.5)	35	1.02 (d, 6.5)
15-OAc			1.82 (s)	15-OAc	1.82 (s)[d]
20-OAc			1.83 (s)	20-OAc	1.83 (s)[d]

[a]Reference 9a. [b]Reference 5. [c]150 MHz. [d]Interchangeable within the same column.

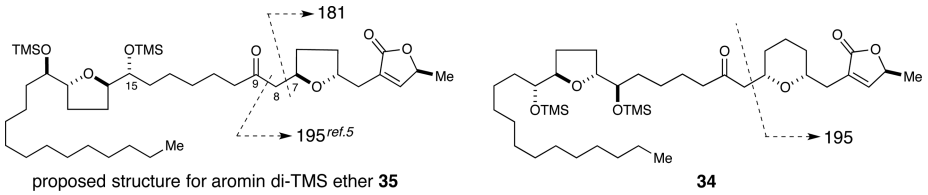

Figure 4. EIMS data of aromin di-TMS ether (**35**) and montanacin D di-TMS ether (**34**).

Table 4. ED_{50} (μg/mL) Values of 1 and 31 against Six Human Solid Tumor Cell Lines[a]

compd	A-549	MCF-7	HT-29	A-498	PC-3	PACA-2
1	2.1	1.1×10^{-1}	2.3	7.3×10^{-1}	5.8×10^{-2}	3.5×10^{-1}
31	1.2	8.6×10^{-2}	1.9	6.0×10^{-1}	3.8×10^{-2}	1.1×10^{-1}
Adr[b]	8.4×10^{-2}	6.6×10^{-2}	1.8×10^{-2}	1.9×10^{-2}	8.4×10^{-2}	9.0×10^{-3}

[a]A-549 (lung carcinoma), MCF-7 (breast carcinoma), HT-29 (colon adenocarcinoma), A-498 (renal carcinoma), PC-3 (prostate adenocarcinoma), PACA (pancreas carcinoma). [b]Adriamycin was used for the standard positive control.

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m), 2.24 (1H, m), 2.14 (1H, m), 2.11−2.05 (2H, m), 1.64−1.42 (6H, m), 1.37 (6H, s); ^{13}C NMR (125 MHz, $CDCl_3$): δ 138.4, 138.0, 114.8, 114.7, 107.9, 80.7, 80.2, 33.7, 32.2, 32.1, 30.2, 27.3, 25.3; HRMS (EI) calcd for $C_{13}H_{21}O_2$ [M − Me]$^+$ 209.1542, found 209.1547.

(5*R*,6*R*)-Undeca-1,10-diene-5,6-diol (8). To a stirred solution of **11** (224 g, 1.0 mmol) in methanol (10 mL) was added a 10% HCl solution in methanol (0.3 mL). The mixture was stirred at 70 °C for 4.5 h, cooled, concentrated *in vacuo*, and then coevaporated with ethanol−benzene (×5). The residue was chromatographed on silica gel (*n*-hexane−ethyl acetate = 10:1 → 4:1) to give **8** (170 mg, 92%) as a syrup; $[\alpha]_D^{26}$ +27.8 (*c* 0.78, $CHCl_3$); IR (ZnSe) 3358, 3076, 2916, 1640, 1070, 992, 906 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 5.86−5.75 (2H, m), 5.06−4.93 (4H, m), 3.39 (2H, m), 2.70 (2H, brs), 2.26 (1H, m), 2.14 (1H, m), 2.11−2.03 (2H, m), 1.61−1.39 (6H, m); ^{13}C NMR (125 MHz, $CDCl_3$): δ 138.5, 138.3, 115.0, 114.7, 74.3, 73.9, 33.6, 32.8, 32.6, 29.9, 24.8; HRMS (ESI) calcd for $C_{11}H_{20}O_2$ Na[M + Na]$^+$ 207.1361, found 207.1366.

(*R*)-1-((2*R*,5*R*)-5-(Hydroxymethyl)tetrahydrofuran-2-yl)hex-5-en-1-ol (5). To a stirred solution of **8** (75 mg, 0.41 mmol) and $Co(nmp)_2$ (23 mg, 0.04 mmol) in 2-propanol (4.0 mL) was added a 5.0−6.0 M solution of *tert*-butyl hydroperoxide in decane (10 μL), and the mixture was stirred at 50−52 °C for 8.5 h under an oxygen atmosphere and then cooled to rt. After addition of iodomethane (25 μL) at 0 °C, the resulting mixture was stirred at 0 °C → rt for 13 h, concentrated, diluted with water, and then extracted with dichloromethane. The combined organic layers were washed with brine, dried, and concentrated. The residue was chromatographed on silica gel (*n*-hexane−ethyl acetate = 10:1 → 4:1 → 1:1) to give **5** (63.6 mg, 78%) as a syrup; $[\alpha]_D^{26}$ +5.7 (*c* 0.34, $CHCl_3$); IR (ZnSe) 3398, 3076, 2915, 1639, 1235, 1085, 878 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 5.80 (1H, ddt, *J* = 17.2, 10.3, 6.7 Hz), 5.00 (1H, ddt, *J* = 17.2, 2.0, 1.5 Hz), 4.94 (1H, brd, *J* = 10.3, 2.0, 1.0 Hz), 4.10 (1H, m), 3.82 (1H, dt, *J* = 7.9, 6.6 Hz), 3.67 (1H, brd, *J* = 11.1 Hz), 3.50 (1H, brdd, *J* = 11.1, 5.1 Hz), 3.42 (1H, m), 2.73 (1H, brs), 2.47 (1H, brs), 2.10−1.95 (4H, m), 1.73−1.62 (3H, m), 1.51−1.40 (3H, m); ^{13}C NMR (125 MHz, $CDCl_3$): δ 138.6, 114.6, 82.9, 79.7, 74.0, 64.7, 33.7, 32.6, 28.5, 27.8, 24.8; HRMS (ESI) calcd for $C_{11}H_{20}O_3Na$ [M + Na]$^+$ 223.1310, found 223.1311.

((2*R*,5*R*)-5-((*R*)-1-((*tert*-Butyldimethylsilyl)oxy)hex-5-en-1-yl)-tetrahydrofuran-2-yl)methanol (12). To a stirred solution of **5** (41 mg, 0.21 mmol) and 2,6-lutidine (0.12 mL, 1.03 mmol) in dichloromethane (1.3 mL) was added *tert*-butyldimethylsilyl trifluoromethanesulfonate (0.12 mL, 0.52 mmol) at 0 °C, and the mixture was stirred at 0 °C → rt for 3 h. After addition of ice−water, the resulting mixture was stirred vigorously for 40 min and then extracted with ether. The combined organic layers were washed successively with cold aqueous HCl, water, saturated aqueous $NaHCO_3$, water, and brine, dried, and concentrated. The residue was passed through a short column of silica gel (*n*-hexane−ether = 100:1 → 10:1) to give a syrup (85 mg) which was dissolved in tetrahydrofuran (1.0 mL). To the solution was added a 1.0 M solution of tetrabutylammonium fluoride in tetrahydrofuran (0.15 mL) at −78 °C, and the mixture was stirred at −78 °C → rt for 23 h, diluted with ethyl acetate, washed with brine, dried, and concentrated. The residue was chromatographed on silica gel (*n*-hexane−ethyl acetate = 10:1 → 4:1) to give **12** (48.1 mg, 75%) as a syrup; $[\alpha]_D^{27}$ +7.4 (*c* 0.80, $CHCl_3$); IR (ZnSe) 3392, 3077, 2927, 2855, 1640, 1250, 1076, 878, 831 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 5.80 (1H, ddt, *J* = 17.1, 10.3, 6.6 Hz), 5.00 (1H, ddt, *J* = 17.3, 2.2, 1.7 Hz), 4.94 (1H, ddt, *J* = 10.3, 2.2, 1.2 Hz), 4.08 (1H, m), 3.91 (1H, dt, *J* = 7.8, 6.1 Hz), 3.64 (1H, ddd, *J* = 11.7, 5.9, 3.2 Hz), 3.58 (1H, m), 3.48 (1H, dt, *J* = 11.7, 5.4 Hz), 2.10 (1H, brs), 2.10−1.98 (2H, m), 1.97−1.88 (2H, m), 1.74−1.61 (2H, m), 1.55−1.32 (4H, m), 0.88 (9H, s), 0.07 (3H, s), 0.06 (3H, s); ^{13}C NMR (150 MHz, $CDCl_3$): δ 138.8, 114.5, 82.0, 79.4, 74.8, 64.9, 33.8, 32.4, 27.8, 27.7, 26.0, 24.9, 18.3, −4.2, −4.6; HRMS (ESI) calcd for $C_{17}H_{34}O_3SiNa$ [M + Na]$^+$ 337.2175, found 337.2179.

(*S*)-1-((2*R*,5*R*)-5-((*R*)-1-((*tert*-Butyldimethylsilyl)oxy)hex-5-en-1-yl)tetrahydrofuran-2-yl)tridecan-1-ol (13) and (*R*)-1-((2*R*,5*R*)-5-((*R*)-1-((*tert*-Butyldimethylsilyl)oxy)hex-5-en-1-yl)tetrahydrofuran-2-yl)tridecan-1-ol (14). To a stirred solution of oxalyl chloride (85 μL, 0.97 mmol) in dichloromethane (2.0 mL) was added dropwise a solution of DMSO (0.15 mL, 1.94 mmol) in dichloromethane (0.5 mL) at −70 °C, and the mixture was stirred at −70 °C for 1 h. A solution of **12** (68 mg, 0.22 mmol) in dichloromethane (0.6 mL) was added dropwise, and the mixture was stirred at the same temperature for 1 h. Triethylamine (0.30 mL, 2.16 mmol) was added, and the resulting mixture was gradually warmed to 0 °C with stirring and then poured into ice−water. The resulting mixture was extracted with ether. The combined organic layers were washed successively with cold aqueous HCl, water, saturated aqueous $NaHCO_3$, water, and brine, dried, and concentrated. The residue was coevaporated with benzene (×5) to give a syrup (72 mg) which was dissolved in ether (1.5 mL). To this stirred solution was added dropwise a 1.0 M solution of dodecylmagnesium bromide (1.76 mL, 1.76 mmol) in ether at −78 °C, and the mixture was stirred at the same temperature for 4.5 h. Saturated aqueous NH_4Cl was added with vigorous stirring, and then the resulting mixture was extracted with ether. The combined organic layers were washed successively with water and brine, dried, and concentrated. The residue was passed through a short column of silica gel (*n*-hexane−ethyl acetate = 10:1 → 4:1) to give a syrup (104 mg), which was purified by preparative TLC (*n*-hexane−ethyl acetate = 10:1, five developments) to afford **13** (19 mg, 18%) and **14** (76 mg, 73%).

13. Syrup; $[\alpha]_D^{27}$ +14.3 (*c* 0.30, $CHCl_3$); IR (ZnSe) 3464, 3073, 2923, 2853, 1640, 1467, 1236, 1087, 883, 834, 774 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 5.80 (1H, ddt, *J* = 17.0, 10.0, 6.6 Hz), 5.00 (1H, ddt, *J* = 17.0, 2.0, 1.7 Hz), 4.94 (1H, ddt, *J* = 10.0, 2.0, 1.2 Hz), 3.91 (1H, dt, *J* = 8.6, 6.3 Hz), 3.84 (1H, m), 3.79 (1H, m), 3.55 (1H, m), 2.08−2.02 (3H, m), 1.92 (1H, m), 1.83−1.78 (2H, m), 1.59 (1H, m), 1.61−1.25 (26H, m), 0.884 (9H, s), 0.876 (3H, t, *J* = 7.4 Hz), 0.07 (3H, s), 0.05 (3H, s); ^{13}C NMR (125 MHz, $CDCl_3$): δ 138.8, 114.4, 82.5, 82.1, 75.2, 71.6, 33.8, 32.5, 32.4, 31.9, 29.73, 29.66, 29.65, 29.63, 29.59, 29.56, 29.3, 28.0, 26.00, 25.97, 25.1, 24.8, 22.7, 18.3, 14.1, −4.1, −4.6; HRMS (ESI) calcd for $C_{29}H_{58}O_3SiNa$ [M + Na]$^+$ 505.4053, found 505.4061.

14. Syrup; $[\alpha]_D^{27}$ +14.7 (*c* 0.63, $CHCl_3$); IR (ZnSe) 3574, 3069, 2923, 2853, 1640, 1465, 1236, 1088, 879, 834, 774 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 5.79 (1H, ddt, *J* = 17.2, 10.3, 6.6 Hz), 4.99 (1H, ddt, *J* = 17.2, 2.0, 1.6 Hz), 4.94 (1H, ddt, *J* = 10.3, 2.0, 1.2 Hz), 3.84 (1H, dt, *J* = 8.0, 6.4 Hz), 3.76 (1H, dt, *J* = 7.8, 6.6 Hz), 3.56 (1H, m), 3.37 (1H, m), 2.39 (1H, d, *J* = 3.9 Hz), 2.07−1.99 (2H, m), 1.95−1.89 (2H, m), 1.70−1.55 (2H, m), 1.52−1.24 (26H, m), 0.88 (9H, s), 0.87 (3H, t, *J* = 7.1 Hz), 0.07 (3H, s), 0.05 (3H, s); ^{13}C NMR (125 MHz, $CDCl_3$): δ 138.7, 114.5, 82.4, 82.2, 75.1, 74.1, 33.8, 33.4, 32.5, 31.9, 29.71, 29.66, 29.65, 29.63, 29.60, 29.57, 29.3, 28.55, 28.45, 25.9, 25.6, 24.6, 22.7, 18.3, 14.1, −4.1, −4.6; HRMS (ESI) calcd for $C_{29}H_{58}O_3SiNa$ [M + Na]$^+$ 505.4053, found 505.4052.

***tert*-Butyl(((*R*)-1-((2*R*,5*R*)-5-((*R*)-1-((*tert*-butyldimethylsilyl)-oxy)hex-5-en-1-yl)tetrahydrofuran-2-yl)tridecyl)oxy)dimethylsilane (3).** To a stirred solution of **14** (35 mg, 72 μmol) and 2,6-lutidine (21 μL, 0.18 mmol) in dichloromethane (0.8 mL) was added *tert*-butyldimethylsilyl trifluoromethanesulfonate (18 μL, 80 μmol) at 0 °C, and the mixture was stirred at 0 °C for 2 h. After addition of ice−water, the resulting mixture was stirred vigorously for 20 min and then extracted with ether. The combined organic layers were washed successively with cold aqueous HCl, water, saturated aqueous $NaHCO_3$, water, and brine, dried, and concentrated. The residue was chromatographed on silica gel (*n*-hexane−ether = 200:1 → 100:1) to give **3** (41 mg, 96%) as a syrup; $[\alpha]_D^{25}$ +20.2 (*c* 0.88, $CHCl_3$); IR (ZnSe) 2924, 2854, 1636, 1471, 1235, 1086, 873, 833, 773 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 5.81 (1H, ddd, *J* = 17.1, 10.0, 6.6 Hz), 5.00 (1H, ddt, *J* = 17.1, 2.0, 1.6 Hz), 4.94 (1H, ddt, *J* = 10.0, 2.0, 1.0 Hz), 3.90 (1H, m), 3.58 (1H, m), 2.04 (1H, m), 1.83 (1H, m), 1.68 (1H, m), 1.51 (1H, m), 1.43−1.22 (28H, m), 0.88 (18H, s), 0.87 (3H, t, *J* = 7.4 Hz), 0.058 (3H, s), 0.054 (3H, s), 0.049 (3H, s), 0.047 (3H, s); ^{13}C NMR (125 MHz, $CDCl_3$): δ 138.9, 114.3, 81.7, 74.7, 74.6, 33.9, 32.6, 32.0, 31.9, 29.8, 29.69, 29.66, 29.65, 29.63, 29.62, 29.4, 27.2, 25.95, 25.87, 25.2, 22.7, 18.2, 14.1, −4.3, −4.55. −4.57; HRMS (ESI) calcd for $C_{35}H_{72}O_3Si_2Na$ [M + Na]$^+$ 619.4918, found 619.4918.

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(3*S*,5*R*)-Nona-1,8-diene-3,5-diol (9a). To a stirred solution of **37** (563 mg, 2.30 mmol) in acetic acid (10 mL) was added water (1.0 mL). The mixture was stirred at 50 °C for 3.5 h, cooled, concentrated, and then coevaporated with toluene (×3). The residue was chromatographed on silica gel (*n*-hexane−ethyl acetate = 3:1 → 2:1) to give **9a** (359 mg, quant.) as a syrup; $[\alpha]_D^{24}$ +1.2 (*c* 0.91, $CHCl_3$); IR (ZnSe) 3345, 3078, 2980, 2936, 1641, 1416, 1078, 991, 910, 825 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 5.84 (1H, ddd, *J* = 17.1, 10.5, 5.3 Hz), 5.76 (1H, ddt, *J* = 17.1, 10.0, 6.7 Hz), 5.21 (1H, ddd, *J* = 17.1, 1.5, 1.5 Hz), 5.05 (1H, ddd, *J* = 10.5, 1.5, 1.2 Hz), 4.98 (1H, ddt, *J* = 17.1, 1.8, 1.6 Hz), 4.91 (1H, brdd, *J* = 10.0, 1.8 Hz), 4.39 (1H, m), 3.88 (1H, brs), 3.86 (1H, m), 3.72 (1H, brs), 2.12 (1H, m), 2.05 (1H, m), 1.65−1.52 (3H, m), 1.47 (1H, m); ^{13}C NMR (125 MHz, $CDCl_3$): δ 140.5, 138.2, 114.6, 114.1, 69.9, 68.2, 42.2, 36.3, 29.8; HRMS (FI) calcd for $C_9H_{16}O_2$ $[M]^+$ 156.1150, found 156.1161.

(2*R*,3*S*,5*R*)-5-(But-3-en-1-yl)-3-acetoxy-2-(acetoxymethyl)-tetrahydrofuran (16) and (2*R*,5*R*)-2-((*S*)-2-acetoxybut-3-en-1-yl)-5-(acetoxymethyl)tetrahydrofuran (17). (i) To a stirred solution of **9a** (110 mg, 0.70 mmol) and $Co(nmp)_2$ (40 mg, 70 μmol) in 2-propanol (6.9 mL) was added a 5.0−6.0 M solution of *tert*-butyl hydroperoxide in decane (14 μL), and the mixture was stirred at 50−52 °C for 7 h under an oxygen atmosphere and then cooled to rt. After addition of iodomethane (80 μL) at 0 °C, the resulting mixture was stirred at 0 °C → rt for 13 h, concentrated, diluted with water, and then extracted with dichloromethane. The combined organic layers were washed with brine, dried, and concentrated. The residue was dissolved in pyridine (1.0 mL). To the solution were added acetic anhydride (0.5 mL) and *N*,*N*-dimethylaminopyridine (7.0 mg), and the mixture was stirred at rt for 14 h. After addition of ice−water, the resulting mixture was stirred vigorously for 3 h and then extracted with ether. The combined organic layers were washed successively with cold aqueous HCl, water, saturated aqueous $NaHCO_3$, water, and brine, dried, and concentrated. The residue was chromatographed on silica gel (dichloromethane−ethyl acetate = 40:1 → 30:1 → 20:1 → 10:1) to give **17** (102 mg, 57%) and **16** (46 mg, 26%).

(ii) To a stirred suspension of **9a** (103 mg, 0.66 mmol), $Co(modp)_2$ (71.1 mg, 0.13 mmol), and MS4A (0.31 g) in 2-propanol (6.2 mL) was added a 5.0−6.0 M solution of *tert*-butyl hydroperoxide in decane (0.13 mL), and the mixture was stirred at 50−52 °C for 4 h under an oxygen atmosphere, cooled to rt, and then filtered through a pad of Celite. After addition of aqueous saturated $Na_2S_2O_3$ to the filtrate, the resulting mixture was stirred at rt for 1 h, concentrated, diluted with ethyl acetate, washed with brine, dried, and concentrated. The residue was submitted to acetylation as described above to give **17** (70.7 mg, 42%) and **16** (33.3 mg, 20%).

16. Syrup; $[\alpha]_D^{22}$ +30.0 (*c* 0.84, $CHCl_3$); IR (ZnSe) 3080, 2934, 1738, 1640, 1438, 1366, 1229, 1041, 906 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 5.82 (1H, ddt, *J* = 17.1, 10.3, 6.6 Hz), 5.09 (1H, ddd, *J* = 7.3, 4.6, 3.4 Hz), 5.03 (1H, ddt, *J* = 17.1, 1.7, 1.7 Hz), 4.97 (1H, ddt, *J* = 10.3, 1.7, 1.2 Hz), 4.19−4.10 (4H, m), 2.47 (1H, dt, *J* = 13.5, 7.1 Hz), 2.16−2.10 (2H, m), 2.09 (3H, s), 2.07 (3H, s), 1.79 (1H, m), 1.70 (1H, ddd, *J* = 13.5, 6.8, 4.6 Hz), 1.59 (1H, m); ^{13}C NMR (125 MHz, $CDCl_3$): δ 170.7, 170.6, 137.9, 114.8, 80.5, 78.2, 75.7, 64.0, 37.5, 34.8, 30.1, 21.0, 20.8; HRMS (FI) calcd for $C_{13}H_{20}O_5$ $[M]^+$ 256.1311, found 256.1327.

17. Syrup; $[\alpha]_D^{22}$ −27.8 (*c* 1.03, $CHCl_3$); IR (ZnSe) 3090, 2938, 1737, 1647, 1435, 1370, 1232, 1086, 1022, 884 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 5.76 (1H, ddd, *J* = 17.3, 10.8, 6.4 Hz), 5.30 (1H, brdd, *J* = 6.4, 5.2 Hz), 5.21 (1H, ddd, *J* = 17.3, 1.2, 1.2 Hz), 5.12 (1H, ddd, *J* = 10.8, 1.2, 1.0 Hz), 4.17 (1H, m), 4.01 (1H, dd, *J* = 11.5, 3.9 Hz), 3.97 (1H, dd, *J* = 11.5, 6.8 Hz), 3.96 (1H, m), 2.06−2.00 (2H, m), 2.05 (3H, s), 2.03 (3H, s), 1.85 (1H, ddd, *J* = 13.9, 7.2, 5.3 Hz), 1.75 (1H, ddd, *J* = 13.9, 8.6, 5.9 Hz), 1.61−1.53 (2H, m); ^{13}C NMR (125 MHz, $CDCl_3$): δ 170.9, 170.0, 136.4, 116.4, 75.8, 75.7, 72.2, 66.4, 39.9, 31.8, 28.2, 21.1, 20.8; HRMS (FI) calcd for $C_{13}H_{20}O_5$ $[M]^+$ 256.1311, found 256.1295.

(*S*)-1-((2*R*,5*R*)-5-(Hydroxymethyl)tetrahydrofuran-2-yl)but-3-en-2-ol (7a). To a stirred solution of **17** (102 mg, 0.39 mmol) in methanol−dichloromethane (10:1, 1.1 mL) was added a 1.0 M solution of sodium methoxide in methanol (50 μL, 0.05 mmol), and the mixture was stirred at rt for 4 h and made neutral with Dowex-50W X-8 (H^+) resin. The mixture was filtered, and the filtrate was evaporated. The residue was chromatographed on silica gel (*n*-hexane−ethyl acetate = 2:1 → 1:1 → 1:5) to give **7a** (57.7 mg, 93%) as a syrup; $[\alpha]_D^{25}$ −10.6 (*c* 1.00, $CHCl_3$); IR (ZnSe) 3346, 2932, 2869, 1646, 1037, 991, 917 cm^{-1}; ^{1} H NMR (500 MHz, $CDCl_3$): δ 5.87 (1H, ddd, *J* = 17.2, 10.3, 5.4 Hz,), 5.25 (1H, dt, *J* = 17.2, 1.5 Hz), 5.07 (1H, dt, *J* = 10.3, 1.5 Hz), 4.34 (1H, brs), 4.20 (1H, m), 4.11(1H, m), 3.60 (1H, dd, *J* = 11.7, 1.9 Hz), 3.52 (1H, brs), 3.46 (1H, dd, *J* = 11.7, 5.9 Hz), 3.08 (1H, brs), 2.03 (1H, m), 1.95 (1H, m), 1.74−1.63 (3H, m), 1.58 (1H, m); ^{13}C NMR (125 MHz, $CDCl_3$): δ 140.8, 114.1, 79.4, 76.1, 70.0, 64.6, 41.6, 32.2, 27.1; HRMS (FI) calcd for $C_9H_{17}O_3$ $[M + H]^+$ 173.1178, found 173.1177.

(3*S*,5*S*)-Nona-1,8-diene-3,5-diol (9b). Compound **38** (488 mg, 1.99 mmol) in acetic acid−water (10:1; 11 mL) was heated at 50−55 °C with stirring for 9.0 h. After being cooled to rt, the resulting mixture was concentrated and then coevaporated with toluene (×3). The residue was chromatographed on silica gel (*n*-hexane−ethyl acetate = 3:1 → 2:1) to give **9b** (210 mg, 67%) and recovered **38** (200 mg). The latter was converted into **9b** (84 mg) by treating with acetic acid−water (10:1; 5.5 mL) at 50−55 °C for 6.0 h, followed by chromatography on silica gel (*n*-hexane−ethyl acetate = 3:1 → 2:1). The total amount of **9b** was 294 mg (94%); $[\alpha]_D^{22}$ +0.5 (*c* 2.01, $CHCl_3$); IR (ZnSe) 3329, 3078, 2977, 2936, 1641, 1421, 1312, 1134, 1078, 990, 909, 846 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 5.87 (1H, ddd, *J* = 17.4, 10.5, 5.9 Hz), 5.83 (1H, ddt, *J* = 17.2, 10.2, 6.7 Hz), 5.24 (1H, ddd, *J* = 17.4, 1.5, 1.2 Hz), 5.09 (1H, ddd, *J* = 10.5, 1.4, 1.2 Hz), 5.04 (1H, ddt, *J* = 17.2, 2.0, 1.5 Hz), 4.97 (1H, ddt, *J* = 10.2, 2.0, 1.2 Hz), 4.36 (1H, m), 3.91 (1H, m), 2.94 (2H, brs), 2.18−2.12 (2H, m), 1.67−1.42 (4H, m); ^{13}C NMR (125 MHz, $CDCl_3$): δ 140.6, 138.3, 114.9, 114.5, 73.7, 71.9, 42.8, 37.0, 29.7; HRMS (FI) calcd for $C_9H_{16}O_2$ $[M]^+$ 156.1150, found 156.1171.

(2*S*,5*S*)-2-((*S*)-2-Acetoxybut-3-en-1-yl)-5-(acetoxymethyl)-tetrahydrofuran (19) and (2*S*,3*S*,5*S*)-5-(But-3-en-1-yl)-3-acetoxy-2-(acetoxymethyl)tetrahydrofuran (20). (i) Treatment of **9b** (144 mg, 0.922 mmol) with $Co(nmp)_2$ (52.1 mg, 0.09 mmol) and *tert*-butyl hydroperoxide in decane (18 μL) as described for preparation of **16** and **17** gave **19** (129.8 mg, 55%) and **20** (55.1 mg, 23%).

(ii) Treatment of **9b** (133 mg, 0.85 mmol) with $Co(modp)_2$ (92 mg, 0.17 mmol) and *tert*-butyl hydroperoxide in decane (0.17 mL) as described for preparation of **16** and **17** gave **19** (109 mg, 50%) and **20** (44.1 mg, 20%).

19. Syrup; $[\alpha]_D^{24}$ +10.8 (*c* 1.50, $CHCl_3$); IR (ZnSe) 3087, 2923, 1736, 1664, 1436, 1370, 1233, 1086, 1039, 887 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 5.80 (1H, ddd, *J* = 17.1, 10.5, 6.4 Hz), 5.38 (1H, dt, *J* = 7.4, 6.3 Hz), 5.27 (1H, ddd, *J* = 17.1, 1.2, 1.2 Hz), 5.18 (1H, ddd, *J* = 10.5, 1.2, 1.2 Hz), 4.23 (1H, m), 4.10 (1H, dd, *J* = 11.5, 3.5 Hz), 4.00 (1H, m), 3.97 (1H, dd, *J* = 11.5, 7.1 Hz), 2.10−2.01 (3H, m), 2.09 (3H, s), 2.06 (3H, s), 1.71 (1H, dt, *J* = 13.9, 6.1 Hz), 1.64−1.52 (2H, m); ^{13}C NMR (125 MHz, $CDCl_3$): δ 171.1, 170.2, 136.1, 116.9, 76.04, 75.97, 72.5, 66.6, 39.9, 32.0, 28.2, 21.3, 21.0; HRMS (FI) calcd for $C_{13}H_{20}O_5$ $[M]^+$ 256.1311, found 256.1325.

20. Syrup; $[\alpha]_D^{23}$ +14.9 (*c* 0.75, $CHCl_3$); IR (ZnSe) 3076, 2973, 2926, 1738, 1640, 1437, 1372, 1228, 1085, 1043, 889 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 5.82 (1H, ddt, *J* = 17.1, 10.3, 6.6 Hz), 5.43 (1H, brt, *J* = 4.2 Hz), 5.03 (1H, ddt, *J* = 17.1, 1.7, 1.7 Hz), 4.97 (1H, ddt, *J* = 10.3, 1.7, 1.3 Hz), 4.26 (1H, dt, *J* = 7.3, 4.2 Hz), 4.21 (1H, dd, *J* = 11.5, 5.6 Hz), 4.20 (1H, m), 4.15 (1H, dd, *J* = 11.5, 7.4 Hz), 2.20−2.06 (3H, m), 2.07 (6H, s), 1.84 (1H, ddd, *J* = 13.5, 9.8, 5.4 Hz), 1.76 (1H, ddt, *J* = 13.5, 9.4, 6.9 Hz), 1.57 (1H, m); ^{13}C NMR (125 MHz, $CDCl_3$): δ 170.8, 170.2, 137.9, 114.9, 77.70, 77.67, 74.7, 62.8, 39.1, 34.7, 30.0, 20.99, 20.91; HRMS (FI) calcd for $C_{13}H_{20}O_5$ $[M]^+$ 256.1311, found 256.1329.

(*S*)-1-((2*S*,5*S*)-5-(Hydroxymethyl)tetrahydrofuran-2-yl)but-3-en-2-ol (7b). Treatment of **19** (130 mg, 0.51 mmol) with a 1.0 M solution of sodium methoxide in methanol (50 μL, 0.05 mmol) as described for preparation of **7a** yielded **7b** (78 mg, 98%) as a syrup; $[\alpha]_D^{22}$ +12.5 (*c* 1.01, $CHCl_3$); IR (ZnSe) 3355, 2926, 2854, 1647, 1420, 1376, 1036, 991, 918 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ

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5.82 (1H, ddd, J = 16.2, 10.3, 5.6 Hz), 5.22 (1H, dt, J = 16.2, 1.5 Hz), 5.05 (1H, dt, J = 10.3, 1.5 Hz), 4.28 (1H, m), 4.16 (1H, m), 4.13 (1H, m), 3.76 (1H, brs), 3.60 (1H, dd, J = 11.7, 3.2 Hz), 3.47 (1H, dd, J = 11.7, 5.9 Hz), 2.80 (1H, brs), 2.09 (1H, m), 1.94 (1H, m), 1.70−1.64 (3H, m), 1.57 (1H, m); ^{13}C NMR (125 MHz, $CDCl_3$): δ 140.4, 114.2, 79.6, 79.0, 72.4, 64.6, 42.4, 32.7, 26.9; HRMS (FI) calcd for $C_9H_{17}O_3$ $[M + H]^+$ 173.1178, found 173.1172.

(*R*)-Octa-1,7-dien-4-ol (21). To a stirred suspension of (*S*)-(+)-l,l′-bi-2-naphthol (1.74 g, 6.1 mmol) and MS4A (14.7 g) in dichloromethane (62 mL) was added $(i\text{-PrO})_4$Ti (1.79 mL, 6.1 mmol), and the mixture was heated at reflux for 1 h and then cooled to rt. A solution of 4-pentenal (2.56 g, 30.4 mmol) in dichloromethane (10 mL) was added. After being stirred for 15 min, the contents were cooled to −78 °C, and allyltributyltin (11.1 g, 33.4 mmol) was added. The mixture was stirred at −78 °C for 15 min and then −23 °C for 120 h. After addition of saturated $NaHCO_3$, the resulting mixture was stirred at rt for 1 h and then filtered through a pad of Celite. The filtrate was extracted with dichloromethane. The combined organic layers were washed with brine, dried, and concentrated. The residue was passed through a short column of silica gel (*n*-hexane−ether = 6:1) to give a syrup, which was distilled under reduced pressure to give **21** (2.72 g, 71%) as a colorless liquid; bp 64 °C/19 mmHg (lit.[31a] 80−83 °C/7 mmHg for *ent*-**21**); $[\alpha]_D^{21}$ +13.9 (c = 3.7, CCl_4) {lit.[31b] $[\alpha]_D^{25}$ +8.3 (c = 4.1, CCl_4), lit.[31c] $[\alpha]_D^{20}$ +12.3 (c = 2.0, CCl_4)}; IR (ZnSe) 3352, 3077, 2978, 2914, 1640, 1434, 1235, 1086, 992, 907 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 5.83 (2H, m), 5.14 (2H, m), 5.05 (1H, ddt, J = 17.1, 1.7, 1.6 Hz), 4.97 (1H, ddt, J = 10.3, 1.7, 1.3 Hz), 3.67 (1H, m), 2.29 (1H, m), 2.26−2.10 (3H, m), 1.61−1.52 (2H, m); ^{13}C NMR (125 MHz, $CDCl_3$): δ 138.4, 134.7, 118.1, 114.8, 70.1, 41.9, 35.8, 30.0; HRMS (FI) calcd for $C_8H_{14}O$ $[M]^+$ 126.1045, found 126.1056.

(*S*)-Octa-1,7-dien-4-ol (*ent*-21). According to the procedure described above, allylation of 4-pentenal (2.56 g, 30.4 mmol) using (*R*)-(+)-l,l′-bi-2-naphthol (1.74 g, 6.08 mmol) instead of the *S*-isomer yielded *ent*-**21** (2.86 g, 75%); $[\alpha]_D^{21}$ −13.9 (c = 4.0, CCl_4) {lit.[31a] $[\alpha]_D^{25}$ −6.02 (c = 4.900, methanol)}; HRMS (FI) calcd for $C_8H_{14}O$ $[M]^+$ 126.1045, found 126.1059.

((2*R*,5*R*)-5-Allyltetrahydrofuran-2-yl)methanol (22). To a stirred suspension of **21** (909 mg, 7.20 mmol), $Co(modp)_2$ (776 mg, 1.44 mmol), and MS4A (0.92 g) in 2-propanol (67 mL) was added a 5.0−6.0 M solution of *tert*-butyl hydroperoxide in decane (1.50 mL), and the mixture was stirred at 50−52 °C for 6 h under an oxygen atmosphere, cooled to rt, and filtered through a pad of Celite. After addition of aqueous saturated $Na_2S_2O_3$ to the filtrate, the resulting mixture was stirred at rt for 1 h, concentrated, diluted with dichloromethane, washed with brine, dried, and concentrated. The residue was chromatographed on silica gel (*n*-hexane−ethyl acetate = 2:1) to give **22** (765 mg, 75%) as a syrup; $[\alpha]_D^{23}$ −7.3 (c 1.8, $CHCl_3$); IR (ZnSe) 3408, 3075, 2972, 2911, 1641, 1235, 1088, 882 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 5.79 (1H, ddt, J = 17.1, 10.1, 6.7 Hz), 5.07 (1H, ddt, J = 17.1, 2.0, 1.7 Hz), 5.04 (1H, ddt, J = 10.1, 2.0, 1.0 Hz), 4.10 (1H, ddd, J = 13.9, 6.4, 3.4 Hz), 4.01 (1H, ddt, J = 13.9, 6.1, 1.7 Hz), 3.61 (1H, dd, J = 11.5, 2.2 Hz), 3.47 (1H, dt, J = 11.5, 6.1 Hz), 2.38−2.32 (2H, m), 2.21 (1H, m), 2.03−1.92 (2H, m), 1.70−1.53 (2H, m); ^{13}C NMR (125 MHz, $CDCl_3$): δ 134.7, 117.0, 79.2, 78.6, 64.9, 40.0, 31.4, 27.4; HRMS (FI) calcd for $C_8H_{15}O_2$ $[M + H]^+$ 143.1072, found 143.1078.

((2*S*,5*S*)-5-Allyltetrahydrofuran-2-yl)methanol (*ent*-22). Treatment of *ent*-**21** (918 mg, 7.27 mmol) as described above yielded *ent*-**22** (733 mg, 71%); $[\alpha]_D^{24}$ +7.1 (c 1.9, $CHCl_3$); HRMS (FI) calcd for $C_8H_{15}O_2$ $[M + H]^+$ 143.1072, found 143.1064.

1-((2*R*,5*R*)-5-(Hydroxymethyl)tetrahydrofuran-2-yl)but-3-en-2-ol (7). To a stirred solution of **22** (470 mg, 3.31 mmol) in methanol (20 mL) was bubbled ozone (O_3) at −78 °C for 35 min. After the excess of O_3 was flushed out by the stream of nitrogen, dimethylsulfide (5.0 mL) was added. After stirring at −78 °C for 2 h and at −78 °C−rt for 4 h, the mixture was concentrated and coevaporated with benzene (×3) to give a syrup which was dissolved in tetrahydrofuran (10 mL). To the solution was added a 1.46 M solution of vinylmagnesium chloride (9.4 mL, 13.7 mmol) at 0 °C with stirring, and the mixture was stirred at 0 °C−rt for 2 h. After being quenched with saturated aqueous NH_4Cl at 0 °C, the mixture was extracted with EtOAc. The combined organic layers were washed with brine, dried, and concentrated. The residue was chromatographed on silica gel (*n*-hexane−ethyl acetate = 2:1 → 1:1 → 0:1) to give **7** (470 mg, 83%) as a syrup; IR (ZnSe) 3340, 2932, 2872, 1647, 1419, 1318, 1218, 1037, 991, 916, 878 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 5.92−5.81 (1H, ms), 5.29−5.20 (1H, m), 5.14−5.03 (1H, m), 4.37−4.29 (1H, m), 4.25−4.09 (2H, m), 3.64−3.60 (1H, m), 3.50−3.45 (1H, m), 3.12 (2H, brs), 2.12−1.98 (2H, m), 1.77−1.54 (4H, m); ^{13}C NMR (125 MHz, $CDCl_3$): δ 140.8, 140.4, 114.3, 114.1, 79.6, 79.3, 79.2, 76.2, 72.5, 70.1, 64.7, 64.6, 42.4, 41.4, 32.7, 32.2, 27.1, 26.9; HRMS (ESI) calcd for $C_9H_{16}O_3Na$ $[M + Na]^+$ 195.0997, found 195.0995.

1-((2*S*,5*S*)-5-(Hydroxymethyl)tetrahydrofuran-2-yl)but-3-en-2-ol (*ent*-7). According to the method described above, *ent*-**22** (237 mg, 1.67 mmol) was transformed into *ent*-**7** (243 mg, 85%); HRMS (ESI) calcd for $C_9H_{16}O_3Na$ $[M + Na]^+$ 195.0997, found 195.1001.

(5*S*)-3-(((2*R*,5*R*)-5-(2-(((*tert*-Butyldimethylsilyl)oxy)but-3-en-1-yl)tetrahydrofuran-2-yl)methyl)-5-methyl-3-(phenylthio)-dihydrofuran-2(3*H*)-one (24). To a stirred mixture of **7** (247 mg, 1.43 mmol) and 2,6-lutidine (1.73 mL, 14.8 mmol) in dichloromethane (10 mL) was added dropwise triflic anhydride (0.25 mL, 1.52 mmol) at −78 °C. After 1 h, *tert*-butyldimethylsilyl trifluoromethanesulfonate (0.43 mL, 1.86 mmol) was added and the reaction mixture was stirred at −78 °C for 1 h and then gradually warmed to 0 °C during 30 min. Crushed ice was added, and the resulting mixture was stirred for 20 min and extracted with ether. The combined organic layers were washed with cold aqueous HCl, water, saturated aqueous $NaHCO_3$, water, and brine, dried, concentrated, and coevaporated with benzene (×3) to give **23** (565 mg) which was employed for the next step without further purification. To a stirred solution of lithium hexamethyldisilazide prepared from a 1.65 M solution of *n*-butyllithium in *n*-hexane (2.6 mL, 4.29 mmol) and hexamethyldisilazane (0.90 mL, 4.29 mmol) in tetrahydrofuran (5.0 mL) was added dropwise a solution of **6** (894 mg, 4.29 mmol) in THF (3.0 mL) at −78 °C. After 7 min, the mixture was gradually warmed to 0 °C with stirring for 1 h. To this solution was added dropwise a solution of **23** (565 mg) in HMPA (2.0 mL) at −78 °C, and the resulting mixture was stirred at −78 → 0 °C for 3 h. After addition of saturated aqueous NH_4Cl, the resulting mixture was extracted with ether. The combined organic layers were washed with water and brine, dried, and concentrated. The residue was chromatographed on silica gel (*n*-hexane−ethyl acetate = 30:1 → 20:1 → 10:1 → 4:1) to give **24** (373 mg, 55% from **7**) as a diastereomeric mixture.

IR (ZnSe) 3064, 2927, 2855, 1767, 1647, 1472, 1439, 1383, 1340, 1250, 1185, 1081, 833 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.57−7.52 (2H, m), 7.43−7.32 (3H, m), 5.86−5.76 (1H, m), 5.24−4.98 (2H, m), 4.66−4.50 (1H, m), 4.38 (0.82H, m), 4.22 (1H, m), 4.12−3.83 (1.18H, m), 2.99 (0.47H, dd, J = 14.2, 7.3 Hz), 2.90 (0.35H, dd, J = 14.2, 7.6 Hz), 2.88 (0.10H, dd, J = 14.1, 10.0 Hz), 2.81 (0.08H, dd, J = 14.0, 10.0 Hz), 2.26 (0.10H, dd, J = 14.1, 5.3 Hz), 2.10−1.42 (8.90H, m), 1.40 (0.30 H, d, J = 6.1 Hz), 1.39 (0.24H, d, J = 6.4 Hz), 1.21 (1.41H, d, J = 6.4 Hz), 1.15 (1.05H, d, J = 6.2 Hz), 0.89−0.88 (9H, m), 0.05−0.02 (12H, m); ^{13}C NMR (125 MHz, $CDCl_3$): δ 177.6, 177.4, 175.22, 175.15, 142.1, 141.0, 140.7, 137.3, 136.99, 136.96, 130.4, 130.3, 130.1, 129.71, 129.69, 129.3, 128.96, 128.94, 128.9, 114.5, 114.2, 113.3, 75.7, 75.6, 75.55, 75.32, 75.28, 74.4, 74.2, 73.8, 73.3, 73.1, 71.84, 71.79, 71.54, 71.52, 55.36, 55.33, 55.30, 55.27, 44.8, 44.4, 44.2, 41.9, 41.4, 41.2, 41.0, 40.9, 39.0, 38.8, 33.6, 33.5, 33.0, 32.7, 32.1, 31.9, 31.8, 29.7, 29.6, 29.3, 25.89, 25.87, 25.83, 21.3, 21.2, 20.73, 20.72, 18.23, 18.18, −4.26, −4.31, −4.41, −4.48, −4.83, −4.88, −4.93; HRMS (ESI) calcd for $C_{26}H_{40}O_4SSiNa$ $[M + Na]^+$ 499.2314, found 499.2317.

(5*S*)-3-(((2*S*,5*S*)-5-(2-(((*tert*-Butyldimethylsilyl)oxy)but-3-en-1-yl)tetrahydrofuran-2-yl)methyl)-5-methyl-3-(phenylthio)-dihydrofuran-2(3*H*)-one (27). According to the procedure described above, *ent*-**7** (244 mg, 1.42 mmol) was transformed into the corresponding lactone **27** (305 mg, 45% from *ent*-**7**).

IR (ZnSe) 3075, 2926, 2855, 1767, 1640, 1472, 1383, 1340, 1234, 1185, 1086, 865, 834 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.56−

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7.48 (2H, m), 7.42−7.31 (3H, m), 5.86−5.75 (1H, m), 5.18−4.97 (2H, m), 4.63−3.85 (4H, m), 3.11−1.40 (10H, m), 1.39−1.11 (3H, m), 0.90−0.87 (9H, m), 0.06−0.015 (6H, m); ^{13}C NMR (125 MHz, $CDCl_3$): δ 177.5, 177.4, 175.7, 141.9, 141.0, 140.9, 137.1, 137.0, 136.9, 130.48, 130,46, 129.9, 129.8, 129.4, 128.99, 128.96, 128.91, 114.22, 114.19, 113.5, 75.8, 75.7, 75.61, 75.57, 75.3, 75.1, 74.4, 74.0, 73.95, 73.87, 71.9, 71.6, 55.73, 55.65, 55.3, 44.8, 44.4, 44.3, 44.2, 43.04, 42.96, 41.9, 39.9, 39.7, 39.6, 33.73, 33.65, 32.7, 32.5, 32.1, 31.93, 31.87, 25.88, 25.87, 25.8, 21.49, 21.45, 20.7, 18.22, 18.19, −4.2, −4.4, −4.5, −4.8, −4.90, −4.93; HRMS (ESI) calcd for $C_{26}H_{40}O_4SSiNa$ [M + Na]$^+$ 499.2314, found 499.2321.

(3*S*,5*S*)-5-Methyl-3-(((2*R*,5*R*)-5-(2-oxobut-3-en-1-yl)-tetrahydrofuran-2-yl)methyl)-3-(phenylthio)dihydrofuran-2(3*H*)-one (4a) and (3*R*,5*S*)-5-Methyl-3-(((2*R*,5*R*)-5-(2-oxobut-3-en-1-yl)tetrahydrofuran-2-yl)methyl)-3-(phenylthio)dihydrofuran-2(3*H*)-one (4b). To a stirred solution of **24** (200 mg, 0.42 mmol) in dichloromethane (4.4 mL) was added a 10% HCl solution in methanol (2.2 mL) at rt. The mixture was stirred at rt for 1.2 h, made neutral by addition of $NaHCO_3$ (powder), filtered through a pad of Celite, and then concentrated. The residue was diluted with ethyl acetate, washed with saturated aqueous $NaHCO_3$, water, and brine, dried, and concentrated. The residue was passed through a short column of silica gel (*n*-hexane−ethyl acetate = 10:1 → 4:1) to give a syrup (143 mg) which was dissolved in dichloromethane−DMSO (1:1; 4.8 mL). Triethylamine (0.55 mL, 3.95 mmol) and a sulfur trioxide trimethylamine complex (274 mg, 1.97 mmol) were sequentially added to the solution at 0 °C, and the mixture was stirred at 0 °C−rt for 39 h, diluted with ether, and then washed with saturated aqueous NH_4Cl, water, and brine, dried, and concentrated. The residue was purified by preparative TLC (*n*-hexane−ethyl acetate = 4:1, 4 developments) to give **4a** (108 mg, 72%) and **4b** (13 mg, 8%).

4a. Syrup; $[\alpha]_D^{25}$ −80.6 (*c* 1.16, $CHCl_3$); IR (ZnSe) 3059, 2971, 2930, 1759, 1676, 1615, 1439, 1383, 1343, 1185, 1079, 974, 884, 753 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.55 (2H, brd, *J* = 7.4 Hz), 7.39 (1H, brt, *J* = 7.4 Hz), 7.33 (2H, brt, *J* = 7.4 Hz), 6.35 (1H, dd, *J* = 17.6, 10.5 Hz), 6.21 (1H, dd, *J* = 17.6, 1.0 Hz), 5.84 (1H, dd, *J* = 10.5, 1.0 Hz), 4.51 (1H, m), 4.44 (1H, m), 4.31 (1H, m), 2.88 (1H, dd, *J* = 14.2, 7.6 Hz), 2.87 (1H, dd, *J* = 15.4, 6.9 Hz), 2.66 (1H, dd, *J* = 15.4, 6.4 Hz), 2.11 (2H, m), 2.00 (1H, dd, *J* = 14.7, 9.8 Hz), 1.88 (1H, dd, *J* = 14.2, 6.8 Hz), 1.87 (1H, dd, *J* = 14.7, 2.7 Hz), 1.54 (2H, m), 1.18 (3H, *d*, *J* = 6.3 Hz); ^{13}C NMR (125 MHz, $CDCl_3$): δ 198.8, 177.4, 136.9, 136.6, 130.2, 129.7, 128.9, 128.7, 74.7, 73.3, 55.0, 45.6, 41.2, 38.8, 32.3, 31.5, 21.2; HRMS (ESI) calcd for $C_{20}H_{24}O_4SNa$ [M + Na]$^+$ 383.1293, found 383.1288.

4b. Syrup; $[\alpha]_D^{25}$ +22.3 (*c* 0.22, $CHCl_3$); IR (ZnSe) 2972, 2919, 1759, 1676, 1384, 1188, 1086, 875, 753 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.52 (2H, brd, *J* = 7.4 Hz), 7.42 (1H, brt, *J* = 7.4 Hz), 7.34 (2H, brt, *J* = 7.4 Hz), 6.35 (1H, dd, *J* = 17.6, 10.5 Hz), 6.21 (1H, dd, *J* = 17.6, 1.0 Hz), 5.85 (1H, dd, *J* = 10.5, 1.0 Hz), 4.60 (1H, m), 4.41 (1H, m), 3.93 (1H, m), 2.88 (1H, dd, *J* = 15.7, 7.3 Hz), 2.74 (1H, dd, *J* = 14.1, 10.2 Hz), 2.60 (1H, dd, *J* = 15.7, 5.4 Hz), 2.23 (1H, dd, *J* = 14.1, 5.6 Hz), 2.13−1.95 (4H, m), 1.58−1.41 (2H, m), 1.34 (3H, d, *J* = 6.1 Hz); ^{13}C NMR (125 MHz, $CDCl_3$): δ 198.9, 175.2, 137.3, 136.9, 130.1, 129.3, 128.9, 128.8, 76.2, 75.1, 74.0, 55.1, 45.5, 41.4, 40.5, 33.3, 31.7, 20.6; HRMS (ESI) calcd for $C_{20}H_{24}O_4SNa$ [M + Na]$^+$ 383.1293, found 383.1289.

(5*S*)-5-Methyl-3-(((2*S*,5*S*)-5-(2-oxobut-3-en-1-yl)tetrahydrofuran-2-yl)methyl)-3-(phenylthio)dihydrofuran-2(3*H*)-one (28). According to the procedure described above, **27** (174 mg, 0.37 mmol) was transformed into the corresponding allyl alcohol (121 mg, 91%). This compound (72 mg, 0.20 mmol) was oxidized as described above to give **28** (57.1 mg, 80%) as a light yellow oil; IR (ZnSe) 3057, 2973, 2919, 1758, 1676, 1615, 1439, 1383, 1342, 1185, 1085, 967, 878, 754 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.55−7.53 (2H, m), 7.49−7.30 (3H, m), 6.38 (0.4H, dd, *J* = 17.6, 10.5 Hz), 6.33 (0.6H, dd, *J* = 17.6, 10.5 Hz), 6.23 (0.4H, dd, *J* = 17.6, 1.0 Hz), 6.19 (0.6H, dd, *J* = 17.6, 1.0 Hz), 5.85 (0.4H, dd, *J* = 10.5, 1.0 Hz), 5.84 (0.6H, dd, *J* = 10.5, 1.0 Hz), 4.65 (0.4H, m), 4.58 (0.4H, m), 4.53 (0.6H, m), 4.41 (0.6H, m), 4.33 (0.4H, m), 3.96 (0.6H, m), 3.01 (0.6H, dd, *J* = 14.0, 7.9 Hz), 2.90 (0.4H, dd, *J* = 15.4, 7.0 Hz), 2.87 (0.6H, dd, *J* = 15.7, 7.6 Hz), 2.67 (0.4H, dd, *J* = 15.4, 5.9 Hz), 2.61 (0.6H, dd, *J* = 15.7, 5.1 Hz), 2.37 (0.4H, dd, *J* = 14.4, 5.3 Hz), 2.23 (0.4H, dd, *J* = 14.4, 10.2 Hz), 2.17−2.05 (2H, m), 2.04−1.93 (1.6H, m), 1.86 (0.6H, dd, *J* = 14.0, 6.6 Hz), 1.72 (0.4H, dd, *J* = 14.9, 10.0 Hz), 1.59−1.44 (2H, m), 1.37 (1.2H, d, *J* = 6.1 Hz), 1.08 (1.8H, d, *J* = 6.7 Hz); ^{13}C NMR (125 MHz, $CDCl_3$): δ 198.9, 198.8, 177.4, 175.6, 137.1, 137.0, 136.8, 136.7, 130.4, 129.9, 129.8, 129.3, 129.0, 128.9, 128.8, 128.6, 76.1, 75.1, 74.7, 74.4, 74.1, 73.9, 55.5, 55.3, 45.7, 45.3, 42.8, 42.6, 39.8, 33.3, 32.2, 31.8, 31.7, 21.4, 20.6; HRMS (ESI) calcd for $C_{20}H_{24}O_4SNa$ [M + Na]$^+$ 383.1293, found 383.1288.

(3*R*,5*S*)-3-(((2*R*,5*R*)-5-((*R*,*E*)-8-((*tert*-Butyldimethylsilyl)oxy)-8-((2*R*,5*R*)-5-((*R*)-1-((*tert*-butyldimethylsilyl)oxy)tridecyl)-tetrahydrofuran-2-yl)-2-oxooct-3-en-1-yl)tetrahydrofuran-2-yl)methyl)-5-methyl-3-(phenylthio)dihydrofuran-2(3*H*)-one (25). To a stirred mixture of lactone **4a** (24.7 mg, 68.5 μmol) and **3** (52.1 mg, 87.2 μmol) in dichloromethane (2.0 mL) was added Grubbs' second-generation catalyst (10 mg, 11.8 μmol). The mixture was stirred at rt for 5 min and at 40 °C for 2 h and then cooled to rt. Florisil was added with stirring, and the resulting mixture was filtered through a pad of Celite. The filtrate was concentrated to give a syrup, which was purified by preparative TLC (*n*-hexane−ethyl acetate = 2:1, 4 developments) to give **25** (43.1 mg, 68%) as a colorless oil; $[\alpha]_D^{26}$ −17.7 (*c* 0.64, $CHCl_3$); IR (ZnSe) 2925, 2853, 1764, 1670, 1625, 1460, 1250, 1184, 1073, 832, 773 cm^{-1}; ^{1} H NMR (500 MHz, $CDCl_3$): δ 7.54 (2H, brd, *J* = 7.1 Hz), 7.39 (1H, brt, *J* = 7.1 Hz), 7.34 (2H, brt, *J* = 7.1 Hz), 6.82 (1H, dt, *J* = 15.9, 6.8 Hz), 6.10 (1H, dt, *J* = 15.9, 1.5 Hz), 4.52 (1H, m), 4.46 (1H, m), 4.30 (1H, m), 3.90 (2H, m), 3.60 (1H, m), 3.56 (1H, m), 2.91 (1H, dd, *J* = 14.2, 7.6 Hz), 2.85 (1H, dd, *J* = 15.4, 6.4 Hz), 2.61 (1H, dd, *J* = 15.4, 6.6 Hz), 2.22 (2H, m), 2.11 (2H, m), 1.99 (1H, brdd, *J* = 14.7, 9.8 Hz), 1.88 (1H, dd, *J* = 14.2, 6.3 Hz), 1.87 (1H, brdd, *J* = 14.7, 2.9 Hz), 1.83 (2H, m), 1.68−1.22 (30H, m), 1.20 (1H, dd, *J* = 6.3 Hz), 0.87 (3H, t, *J* = 6.8 Hz), 0.87 (18H, s), 0.06 (3H, s), 0.05 (3H, s), 0.04 (6H, s); ^{13} C NMR (125 MHz, $CDCl_3$): δ 198.4, 177.4, 147.9, 137.0, 130.5, 130.3, 129.7, 128.9, 81.8, 81.7, 74.9, 74.73, 74.65, 74.4, 73.3, 55.0, 46.0, 41.1, 39.0, 32.71, 32.68, 32.4, 32.2, 31.9, 31.6, 29.8, 29.7, 29.63, 29.62, 29.61, 29.6, 29.3, 27.3, 25.94, 25.93, 25.8, 24.4, 22.7, 21.3, 18.18, 18.17, 14.1, −4.28, −4.30, −4.5, −4.6; HRMS (ESI) calcd for $C_{53}H_{92}O_7SSi_2Na$ [M + Na]$^+$ 951.6000, found 951.6006.

(5*S*)-3-(((2*S*,5*S*)-5-((*R*,*E*)-8-((*tert*-Butyldimethylsilyl)oxy)-8-((2*R*,5*R*)-5-((*R*)-1-((*tert*-butyldimethylsilyl)oxy)tridecyl)tetrahydrofuran-2-yl)-2-oxooct-3-en-1-yl)tetrahydrofuran-2-yl)-methyl)-5-methyl-3-(phenylthio)dihydrofuran-2(3*H*)-one (29). Treatment of lactone **28** (25.0 mg, 69.4 μmol) and **3** (53.1 mg, 88.9 μmol) with Grubbs' second-generation catalyst (10.4 mg, 12.3 μmol) as described for preparation of **25** gave **29** (47.1 mg, 73%) as a colorless oil; IR (ZnSe) 2924, 2853, 1763, 1670, 1625, 1463, 1439, 1386, 1251, 1185, 1073, 833, 773 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.55−7.53 (1.30H, brd, *J* = 7.1 Hz), 7.49−7.47 (0.70H, brd, *J* = 7.1 Hz), 7.41−7.31 (3H, m), 6.83 (0.35H, dt, *J* = 15.9, 6.9 Hz), 6.80 (0.65H, dt, *J* = 15.9, 6.8 Hz), 6.11 (0.35H, brd, *J* = 15.9, 1.5 Hz), 6.07 (0.65H, brd, *J* = 15.9, 1.5 Hz), 4.64 (0.35H, m), 4.58 (0.35H, m), 4.54 (0.65H, m), 4.40 (0.65H, m), 4.31 (0.35H, m), 3.95 (0.65H, m), 3.89 (2H, m), 3.59 (1H, m), 3.57 (1H, m), 3.02 (0.65H, dd, *J* = 14.0, 7.9 Hz), 2.88 (0.35H, dd, *J* = 15.4, 6.8 Hz), 2.82 (0.65H, dd, *J* = 15.7, 7.4 Hz), 2.62 (0.35H, dd, *J* = 15.4, 6.3 Hz), 2.57 (0.65H, dd, *J* = 15.7, 5.6 Hz), 2.38 (0.35H, dd, *J* = 14.4, 5.4 Hz), 2.23−1.22 (39H, m), 1.37 (1.05H, d, *J* = 6.2 Hz), 1.07 (1.95H, d, *J* = 6.4 Hz), 0.89−0.87 (21H, m), 0.06, 0.053, 0.045, 0.041, 0.034, 0.028 (total 12H, each s); ^{13}C NMR (125 MHz, $CDCl_3$): δ 198.5, 198.4, 177.4, 175.6, 148.0, 147.9, 137.1, 137.0, 130.6, 130.5, 129.9, 129.8, 129.4, 129.0, 128.9, 81.8, 81.7, 76.0, 75.2, 74.9, 74.7, 74.4, 74.3, 74.1, 73.9, 55.5, 55.4, 46.1, 45.8, 43.0, 42.7, 39.83, 39.77, 33.3, 32.72, 32.69, 32.3, 32.1, 31.9, 31.8, 31.7, 29.8, 29.7, 29.63, 29.62, 29.61, 29.59, 29.33, 27.3, 27.2, 25.94, 25.91, 25.8, 24.5, 24.4, 22.7, 21.4, 20.6, 18.20, 18.17, 14.1, −4.3, −4.5, −4.6; HRMS (ESI) calcd for $C_{53}H_{92}O_7SSi_2Na$ [M + Na]$^+$ 951.6000, found 951.6025.

(3*R*,5*S*)-3-(((2*R*,5*R*)-5-((*R*)-8-((*tert*-Butyldimethylsilyl)oxy)-8-((2*R*,5*R*)-5-((*R*)-1-((*tert*-butyldimethylsilyl)oxy)tridecyl)-tetrahydrofuran-2-yl)-2-oxooctyl)tetrahydrofuran-2-yl)-methyl)-5-methyl-3-(phenylthio)dihydrofuran-2(3*H*)-one (26).

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A mixture of **25** (20.4 mg, 21.9 μmol) and PtO_2 (5.6 mg) in THF (1.1 mL) was vigorously stirred at rt under a hydrogen atmosphere for 13 h, filtered through a pad of Celite, and concentrated. The residue was purified by preparative TLC (*n*-hexane−ethyl acetate = 10:1, 6 developments) to give **26** (17.1 mg, 84%) as a colorless oil; $[\alpha]_D^{24}$ = −17.7 (*c* 0.66, $CHCl_3$); IR (ZnSe) 2924, 2854, 1767, 1713, 1462, 1250, 1185, 1082, 833, 773 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.56−7.54 (2H, m), 7.41−7.32 (1H, m), 7.37−7.32 (2H, m), 4.51 (1H, m), 4.44 (1H, m), 4.29 (1H, m), 3.90 (2H, m), 3.56 (2H, m), 2.88 (1H, dd, *J* = 14.2, 7.6 Hz), 2.62 (1H, dd, *J* = 15.2, 7.6 Hz), 2.48 (1H, dd, *J* = 15.2, 5.6 Hz), 2.43 (2H, dt, *J* = 7.4, 1.2 Hz), 2.11 (2H, m), 1.99 (1H, dd, *J* = 14.7, 10.0 Hz), 1.88 (1H, dd, *J* = 14.2, 6.8 Hz), 1.87 (1H, dd, *J* = 14.7, 2.2 Hz), 1.82 (2H, m), 1.67−1.25 (34H, m), 1.18 (3H, d, *J* = 6.3 Hz), 0.876 (3H, t, *J* = 6.9 Hz), 0.875 (9H, s), 0.870 (9H, s), 0.049 (3H, s), 0.046 (3H, s), 0.042 (3H, s), 0.03 (3H, s); ^{13}C NMR (125 MHz, $CDCl_3$): δ 209.4, 177.4, 137.0, 130.3, 129.8, 129.0, 81.8, 81.7, 74.8, 74.74, 74.71, 73.3, 55.0, 48.9, 43.1, 41.3, 38.9, 32.6, 32.4, 32.3, 31.9, 31.6, 29.8, 29.7, 29.65, 29.63, 29.62, 29.61, 29.5, 29.3, 27.3, 27.2, 25.95, 25.87, 25.8, 23.6, 22.7, 21.3, 18.2, 14.1, −4.3, −4.6; HRMS (ESI) calcd for $C_{53}H_{94}O_7SSi_2Na$ [M + Na]$^+$ 953.6156, found 953.6166.

(5*S*)-3-(((2*S*,5*S*)-5-((*R*)-8-((*tert*-Butyldimethylsilyl)oxy)-8-((2*R*,5*R*)-5-((*R*)-1-((*tert*-butyldimethylsilyl)oxy)tridecyl)tetrahydrofuran-2-yl)-2-oxooctyl)tetrahydrofuran-2-yl)methyl)-5-methyl-3-(phenylthio)dihydrofuran-2(3*H*)-one (30). Treatment of **29** (24.3 mg, 26.1 μmol) with PtO_2 (6.6 mg) as described for preparation of **26** gave **30** (20.3 mg, 84%) as a colorless oil; IR (ZnSe) 2925, 2854, 1764, 1715, 1463, 1383, 1251, 1185, 1084, 832, 773 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.56−7.54 (1.30H, m), 7.49−7.47 (0.70H, m), 7.42−7.31 (3H, m), 4.64 (0.35H, m), 4.56 (0.35H, m), 4.53 (0.65H, m), 4.36 (0.65H, m), 4.28 (0.35H, m), 3.96 (0.65H, m), 3.89 (2H, m), 3.58 (2H, m), 3.01 (0.65H, dd, *J* = 14.0, 7.8 Hz), 2.66 (0.35H, dd, *J* = 15.4, 7.6 Hz), 2.64 (0.65H, dd, *J* = 15.9, 7.8 Hz), 2.48 (0.35H, dd, *J* = 15.4, 5.4 Hz), 2.46 (0.65H, dd, *J* = 15.9, 5.2 Hz), 2.45 (0.70H, t, *J* = 6.9 Hz), 2.39 (1.30H, t, *J* = 7.1 Hz), 2.36 (0.35H, dd, *J* = 14.2, 5.4 Hz), 2.23 (0.35H, dd, *J* = 14.2, 10.0 Hz), 2.11−1.22 (40.65H, m), 1.37 (1.05H, d, *J* = 6.1 Hz), 1.09 (1.95H, d, *J* = 6.4 Hz), 0.89−0.86 (21H, m), 0.052, 0.048, 0.044, 0.041, 0.038, 0.030 (total 12H, each s); ^{13}C NMR (125 MHz, $CDCl_3$): δ 209.4, 209.2, 177.3, 175.6, 137.1, 137.0, 130.5, 129.9, 129.4, 129.0, 128.9, 81.8, 81.7, 76.1, 76.0, 74.9, 74.8, 74.7, 74.6, 74.5, 74.4, 74.1, 74.0, 73.90, 73.87, 55.5, 55.3, 48.9, 48.6, 43.6, 43.4, 42.8, 42.7, 39.9, 33.3, 32.6, 32.4, 32.3, 31.9, 31.7, 29.8, 29.6, 29.5, 29.3, 27.3, 25.96, 25.94, 23.6, 22.7, 21.5, 21.4, 18.2, 14.1, −4.27, −4.31, −4.5, −4.6; HRMS (ESI) calcd for $C_{53}H_{94}O_7SSi_2Na$ [M + Na]$^+$ 953.6156, found 953.6149.

(*S*)-3-(((2*R*,5*R*)-5-((*R*)-8-Hydroxy-8-((2*R*,5*R*)-5-((*R*)-1-hydroxytridecyl)tetrahydrofuran-2-yl)-2-oxooctyl)tetrahydrofuran-2-yl)methyl)-5-methylfuran-2(5*H*)-one (1). To a stirred solution of **26** (16.3 mg, 17.4 μmol) in dichloromethane (0.9 mL) was added *m*CPBA (70−75% assay; 4.3 mg) at 0 °C. After 30 min, aqueous saturated $NaHCO_3/Na_2S_2O_3$ (1:1) was added, and the resulting mixture was extracted with ether. The combined organic layers were washed with aqueous saturated $NaHCO_3$, water, and brine, dried, and concentrated. The residue (22.4 mg) was dissolved in toluene (0.9 mL). The solution was heated at 100−105 °C for 1.5 h with stirring and concentrated to give a crude butenolide (18.5 mg). To a stirred solution of the butenolide in dichloromethane (0.8 mL) was added HF·pyridine (80 μL) at 0 °C, and the mixture was stirred at 0 °C for 20 min. After addition of aqueous saturated $NaHCO_3$, the resulting mixture was stirred at 0 °C for 10 min and extracted with ethyl acetate. The combined organic layers were washed with aqueous saturated $NaHCO_3$, water, and brine, dried, and concentrated. The residue was purified by preparative TLC (ethyl acetate, 3 developments) to give **1** (9.0 mg, 87% from **26**) as a white powder; mp 72−73 °C (*n*-hexane-ether); $[\alpha]_D^{25}$ = +1.4 (*c* 0.42, $CHCl_3$); IR (ZnSe) 3447, 2917, 2849, 1751, 1734, 1700, 1456, 1404, 1373, 1323, 1270, 1202, 1027 cm^{-1}; HRMS (ESI) calcd for $C_{35}H_{60}O_7Na$ [M + Na]$^+$ 615.4237, found 615.4239.

(*S*)-3-(((2*S*,5*S*)-5-((*R*)-8-Hydroxy-8-((2*R*,5*R*)-5-((*R*)-1-hydroxytridecyl)tetrahydrofuran-2-yl)-2-oxooctyl)tetrahydrofuran-2-yl)methyl)-5-methylfuran-2(5*H*)-one (31). According to the procedure described for preparation of **1** from **26**, compound **30** (18.8 mg, 20.1 μmol) was transformed into **31** (10.4 mg, 87%) as a white powder; mp 58−60 °C (*n*-hexane-ether); $[\alpha]_D^{25}$ = +41.2 (*c* 0.61, $CHCl_3$); IR (ZnSe) 3465, 2915, 2849, 1751, 1734, 1700, 1467, 1413, 1342, 1317, 1197, 1024, 961 cm^{-1}; HRMS (ESI) calcd for $C_{35}H_{60}O_7Na$ [M + Na]$^+$ 615.4237, found 615.4236.

Montanacin D-15,20-Diacetate (33). According to the procedure described in the literature,[5] **32** (1.0 mg, 1.7 μmol) was transformed into **33** (0.9 mg, 79%) as a syrup; $[\alpha]_D^{27}$ +17.5 (*c* 0.09, $CHCl_3$); IR (ZnSe) 2931, 2855, 2922, 1749, 1455, 1369, 1200, 1027 cm^{-1}; HRMS (ESI) calcd for $C_{39}H_{64}O_9Na$ [M + Na]$^+$ 699.4448, found 699.4447.

Bis-TMS Derivative 34 of 32. According to the procedure described in the literature,[5] **32** (0.9 mg, 1.5 μmol) was transformed into **34** (0.9 mg, 81%) as an amorphous solid; ^{1}H NMR (500 MHz, $CDCl_3$): δ 6.66 (1H, m), 4.45 (1H, brq, *J* = 6.8 Hz), 4.01−3.94 (2H, m), 3.66 (1H, m), 3.62 (1H, m), 3.60 (1H, m), 3.33 (1H, m), 2.37 (1H, dd, *J* = 15.6, 8.8 Hz), 2.33−2.23 (2H, m), 2.17−2.13 (2H, m), 1.94 (1H, dd, *J* = 15.6, 3.9 Hz), 1.75−1.17 (38H, m), 0.99 (3H, d, *J* = 6.8 Hz), 0.91 (3H, t, *J* = 6.6 Hz), 0.25, (18H, s); HRMS (EI) calcd for $C_{41}H_{76}O_7Si_2$ [M]$^+$ 736.5130, found 736.5131.

Bis-TMS Derivative 35 of 1. According to the procedure described in the literature,[5] **1** (1.0 mg, 1.7 μmol) was transformed into **35** (1.2 mg, 96%) as an amorphous solid; ^{1}H NMR (500 MHz, $CDCl_3$): δ 6.50 (1H, m), 4.29−4.26 (2H, m), 4.02 (1H, m), 3.98 (2H, m), 3.64 (1H, m), 3.61 (1H, m), 2.41 (1H, dd, *J* = 15.4, 7.3 Hz), 2.34−2.26 (2H, m), 2.13 (2H, t, *J* = 7.3 Hz), 2.07 (1H, dd, *J* = 15.4, 5.6 Hz), 1.78−1.12 (38H, m), 0.91 (3H, t, *J* = 6.9 Hz), 0.86 (3H, d, *J* = 6.9 Hz), 0.244 (9H, s), 0.242, (9H, s); HRMS (EI) calcd for $C_{41}H_{76}O_7Si_2$ [M]$^+$ 736.5130, found 736.5110.

(3*S*)-3-((*tert*-Butyldimethylsilyl)oxy)nona-1,8-dien-5-ol (36). To a stirred solution of (*S*)-3-TBSoxy-4-pentenal (0.79 g, 3.68 mmol) in tetrahydrofuran (20 mL) was added dropwise a 0.5 M solution of 3-butenylmagnesium bromide in ether (10 mL, 5.0 mmol) at −78 °C, and the mixture was stirred at −78 °C for 1.5 h and at 0 °C for 1 h. Saturated aqueous NH_4Cl was added with vigorously stirring, and then the resulting mixture was extracted with ether. The combined organic layers were washed successively with water and brine, dried, and concentrated. The residue was chromatographed on silica gel (*n*-hexane−ether = 30:1 → 10:1) to give **36** (884 mg, 89%) as a syrup; IR (ZnSe) 3441, 3079, 2928, 2857, 1641, 1471, 1254, 1084, 910, 835, 775 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 5.90−5.79 (2H, m), 5.27−4.94 (4H, m), 4.52 (0.44H, m), 4.37 (0.56H, m), 3.92 (0.44H, m), 3.84 (0.56H, m), 3.38 (0.44H, brs), 3.21 (0.56H, brs), 2.22−2.09 (2H, m), 1.75−1.43(4H, m), 0.912 (3.96H, s), 0.906 (5.04H, s), 0.11 (1.32H, s), 010 (1.68H, s), 0.07 (3H, s); ^{13}C NMR (125 MHz, $CDCl_3$): δ 141.4, 140.0, 138.59, 138.57, 114.5, 114.4, 75.0, 72.7, 70.2, 67.9, 44.4, 43.0, 36.8, 36.7, 29.8, 29.6, 25.80, 25.79, 18.1, 18.0, −3.9, −4.6, −4.9, −5.2; HRMS (FI) calcd for $C_{15}H_{31}O_2Si$ [M + H]$^+$ 271.2093, found 271.2090.

(4*R*,6*S*)-4-(But-3-en-1-yl)-2-phenyl-6-vinyl-1,3-dioxane (37) and (4*S*,6*S*)-4-(But-3-en-1-yl)-2-phenyl-6-vinyl-1,3-dioxane (38). To a stirred solution of **36** (1.43 g, 5.28 mmol) in tetrahydrofuran (6.0 mL) was added a 1.0 M solution of tetrabutylammonium fluoride in tetrahydrofuran (6.34 mL) at 0 °C, and the mixture was stirred at 0 °C → rt for 3 h, diluted with ethyl acetate, washed with brine, dried, and concentrated. The residue was passed through a short column of silica gel (*n*-hexane−ethyl acetate = 3:1 → 0:1) to give a syrup (744 mg), which was dissolved in *N*,*N*-dimethylformamide (5.0 mL). To the solution were added benzaldehyde dimethylacetal (0.86 mL, 5.71 mmol) and d-camphorsulfonic acid (55 mg, 0.48 mmol). The mixture was stirred under diminished pressure (~2.6 kPa) at 50 °C for 1 h, cooled, diluted with ether, washed successively with saturated aqueous $NaHCO_3$, water, and brine, dried, and concentrated. The residue was chromatographed on silica gel (*n*-hexane−dichloromethane = 6:1 → 4:1 → 2:1 → *n*-hexane−ethyl acetate = 4:1 and then *n*-hexane−dichloromethane = 8:1 → 7:1 → 6:1) to give **37** (483 mg, 37% from **36**) and **38** (511 mg, 40% from **36**).

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37 (major/minor = ca. 2.3:1). Syrup; IR (ZnSe) 3072, 3032, 2977, 2922, 1639, 1399, 1235, 1088, 991, 903, 743 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 7.53−7.50 (2H, m), 7.38−7.26 (3H, m), 6.11 (0.73H, ddd, J = 17.7, 11.0, 4.0 Hz), 5.96−5.80 (1.27H, m), 5.83 (0.27H, s), 5.82 (0.73H, s), 5.40 (0.73H, dt, J = 11.0, 1.2 Hz), 5.35 (0.27H, dt, J = 17.3, 1.0 Hz), 5.34 (0.73H, dt, J = 17.7, 1.7 Hz), 5.18 (0.27H, dt, J = 10.6, 1.2 Hz), 5.08 (0.27H, dt, J = 17.7, 1.5 Hz), 5.04 (0.73H, dt, J = 17.8, 1.7 Hz), 5.01 (0.27H, dt, J = 10.3, 1.5 Hz), 4.98 (0.73H, dt, J = 10.3, 1.4 Hz), 4.82 (0.73H, brs), 4.55 (0.27H, m), 4.27 (0.27H, m), 3.97 (0.73H, m), 2.34−2.03 (3H, m), 1.81−1.54 (3H, m); ^{13}C NMR (125 MHz, $CDCl_3$): δ 139.0, 138.9, 138.2, 138.1, 137.9, 137.3, 128.7, 128.6, 128.2, 126.1, 126.0, 117.6, 115.6, 115.1, 114.9, 95.1, 93.9, 73.0, 72.7, 72.05, 71.99, 35.1, 33.8, 33.3, 30.0, 29.7, 29.2; HRMS (EI) calcd for $C_{16}H_{20}O_2$ $[M]^+$ 244.1463, found 244.1442.

38. Syrup; $[\alpha]_D^{24}$ −15.7 (c 0.96, $CHCl_3$); IR (ZnSe) 3070, 3032, 2977, 2915, 2844, 1640, 1336, 1149, 1088, 1017, 902, 840, 756 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 7.56 (2H, brd, J = 6.8 Hz), 7.40−7.32 (3H, m), 5.97 (1H, ddd, J = 17.3, 10.3, 5.4 Hz), 5.87 (1H, ddt, J = 17.1, 10.3, 6.6 Hz), 5.60 (1H, s), 5.37 (1H, dt, J = 17.3, 1.4 Hz), 5.20 (1H, dt, J = 10.5, 1.2 Hz), 5.08 (1H, dt, J = 17.1, 1.5 Hz), 5.02 (1H, dt, J = 10.3, 0.8 Hz), 4.37 (1H, m), 3.89 (1H, m), 2.32−2.19 (2H, m), 1.81 (1H, ddd, J = 13.7, 8.8, 5.8 Hz), 1.69 (1H, dt, J = 13.2, 2.4 Hz), 1.66 (1H, m), 1.56 (1H, dt, J = 13.2, 11.3 Hz); ^{13}C NMR (125 MHz, $CDCl_3$): δ 138.7, 138.1, 137.8, 128.6, 128.1, 126.1, 115.4, 114.8, 100.5, 77.2, 75.9, 36.6, 34.9, 29.1; HRMS (EI) calcd for $C_{16}H_{20}O_2$ $[M]^+$ 244.1463, found 244.1476.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b02187.

NMR spectra of **1**, **3**, **4a**, **4b**, **5**, **7**−**9**, **11**−**14**, **16**, **17**, **19**−**22**, **24**−**31**, **33**, and **36**−**38** (PDF)

2D-NMR spectra of **1**, **31**, and **33**; MS spectra of **34** and **35**, CAST/CNMR data (PDF)

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Notes

The authors declare no competing financial interest.

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(28) In the ^{1}H NMR spectra, the splitting pattern of the olefinic methine proton was clearly different between the major and minor compound.
(29) Attempted oxidative cyclization of **36** (*syn*/*anti* = ca. 1.2/1) under Pagenkopf's condition afforded a mixture of four compounds which were separated as the corresponding diacetates: **16** (14% yield from **36**), **17** (15%), **19** (25%), and **20** (13%). Mukaiyama's cyclization also gave a similar result: **16** (13% yield from **36**), **17** (15%), **19** (21%), and **20** (12%).
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(49) The structure of aromin-A (ref 4) should also be reinvestigated because the compound was shown to be the C-20 epimer of aromin. Its absolute configuration at the left-half segment corresponding to C-15−C-32 is not reported.

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