JOC The Journal of Organic Chemistry

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Total Synthesis and Structure Determination of JBIR-108—A 2-Hydroxy-2-(1-hydroxyethyl)-2,3-dihydro-3(2*H*)-furanone Isolated from *Streptomyces gramineus* IR087Pi-4

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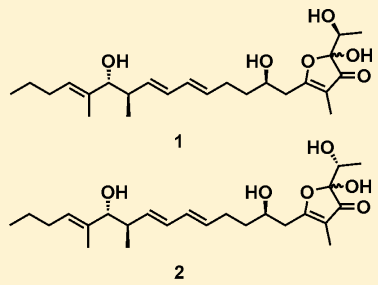
Supporting Information

ABSTRACT: The planar and stereostructures of JBIR-108 isolated from *Streptomyces gramineus* IR087Pi-4 were determined partly by spectral analysis, and these structural assignments were confirmed and completed by the total synthesis of both 1-epimers. The key stereocenters in JBIR-108 were constructed via a Corey–Bakshi–Shibata (CBS) reduction (C-1), vinylogous Mukaiyama aldol reaction (C-7), and Brown crotylation (C-14 and C-15). Although it was difficult to determine the stereochemistries at the C-1 and C-7 positions in the natural product using the modified Mosher's method, the synthesis of two possible C-1 diastereomers enabled the identification of the configurations at the hitherto unknown stereocenters.



JBIR-108 (1) and (2)

INTRODUCTION

Members of the class *Actinobacteria* have been extensively studied owing to their tendency to produce pharmaceutically useful compounds. However, the discovery rate of new compounds from these strains has decreased significantly. It has been proposed that the strains obtained using a variety of microbial isolation protocols, such as moist incubation and desiccation methods,[1] may lead to the production of unique metabolites. Thus, unique actinomycetes, including new species, were isolated from various samples, such as soils, plants, lichens, and marine organisms, and secondary metabolite formation in the cultures of those strains was investigated. As a result, new compounds such as angucycline JBIR-88,[2] butenolide JBIR-89,[2] phenylacetylated peptide JBIR-96,[3] tetraene macrolide JBIR-100,[4] and JBIR-120,[5] were isolated from the new species of actinomycetes. Further screening of a culture of *Streptomyces gramineus* IR087Pi-4 obtained from a bark sample collected in Okinawa Prefecture, Japan, resulted in the isolation of 2-hydroxy-2-(1-hydroxyethyl)-2,3-dihydro-3(2*H*)-furanones, including a known compound E-975[6] and designated JBIR-108 (Figure 1), as a cytotoxic compound. JBIR-108 exhibited moderate cytotoxic activities against SKOV-3, Meso-1, and Jurkat cells with IC_{50} values of 2.3, 2.5, and 1.0 μM, respectively, whereas E-975 showed weaker cytotoxicities with corresponding IC_{50} values of 33.5, 18.5, and 6.6 μM. In this paper, the planar and stereostructures of JBIR-108 isolated from *Streptomyces gramineus* IR087Pi-4 were determined partly by spectral analysis and these structural assignments were confirmed and completed by the total synthesis of both 1-epimers.

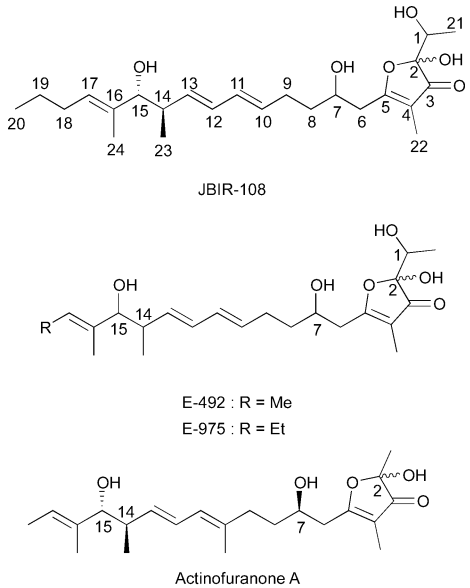


Figure 1. Structures of JBIR-108 and its analogues.

Received: September 24, 2014
Published: December 1, 2014

   dx.doi.org/10.1021/jo502198y | *J. Org. Chem.* 2015, 80, 114–132

RESULTS AND DISCUSSION

Planar Structure Elucidation of JBIR-108. Compound JBIR-108 (this compound was isolated as a mixture of the major and minor components (5:1); see the Experimental Section)[7] was obtained as a colorless amorphous powder: UV λ_{max} (ε) in MeOH: 241 (15 200) and 284 (7200) nm. The molecular formula of both the components was determined via high-resolution electrospray ionization-mass spectrometry to be $C_{24}H_{38}O_6$ (found: 421.2599 $[M - H]^-$, calculated for $C_{24}H_{37}O_6$: 421.2590). The presence of hydroxy (3351 cm^{-1}) and α,β-unsaturated carbonyl (1646 cm^{-1}) functionalities was identified from the infrared (IR) spectrum ν_{max} (attenuated total reflection) of the mixture. These results indicated that the major and minor components were isomers.

In the proton nuclear magnetic resonance (^{1}H NMR) spectrum recorded in CD_3OD, at least three sets of individual signals were observed with an intensity ratio of approximately 1:0.5:0.1 (as explained later, an additional minor set nearly overlapped these signals completely).[8] Therefore, the major component was employed for planar structure elucidation. The ^{13}C and ^{1}H NMR spectroscopic data for the major component are listed in Table 1. The direct connectivity of the protons and carbons in the major component was established through analysis of its heteronuclear single-quantum coherence spectrum, and its structure was established on the basis of the signals observed in the double-quantum-filtered (DQF)-COSY and constant-time heteronuclear multiple-bond correlation (CT-HMBC)[9] spectra.

Table 1. ^{13}C (150 MHz) and ^{1}H (600 MHz) NMR Data for the Major Component of JBIR-108[a]

position	δ_C[b]	δ_H[b], multiplicity [J in Hz]
1	70.0 (70.9)	3.90 (3.92), q [6.5]
2	105.5 (105.6)	
3	205.7 (204.3)	
4	112.1 (112.5)	
5	188.4 (188.0)	
6	38.3	2.76, dd [14.2, 7.9]
		2.71, dd [14.2, 11.2]
7	69.4	4.06, m
8	38.1	1.70, m
		1.62, m
9	29.7	2.26, m
		2.19, m
10	132.4	5.61, ddd [12.0, 6.8, 2.4]
11	131.6	6.08, dd [12.0, 1.8]
12	132.7	6.04, dd [14.1, 1.8]
13	137.3	5.58, dd [14.1, 7.9]
14	41.5	2.34, ddq [8.5, 7.9, 6.7]
15	83.4	3.64, d [8.5]
16	136.3	
17	128.8	5.36, t [7.0]
18	30.6	2.03, dt [7.3, 7.0]
19	23.8	1.40, s
20	14.2	0.92, t [7.3]
21	16.7 (16.3)	1.30 (1.18), d [6.5]
22	5.7	1.66 (1.65), s
23	17.9	0.86, d [6.7]
24	11.4	1.59, s

[a]NMR spectra were obtained in CD_3OD, and the solvent peak was used as an internal standard (δ_H 3.31 ppm and δ_C 49.0 ppm). [b]The chemical shifts in parentheses belong to the C-2 epimer.

Three substructures were established through the analysis of the DQF-COSY spectrum, and the connectivity of those three units was established using the CT-HMBC spectrum. The ^{1}H−^{13}C long-range couplings from oxymethine proton H-1 (δ_H 3.90), which was ^{1}H coupled to methyl protons H_3-21 (δ_H 1.30), to quaternary hemiketal carbon C-2 (δ_C 105.5) and carbonyl carbon C-3 (δ_C 205.7) were observed in the CT-HMBC spectrum. Moreover, the ^{1}H−^{13}C long-range couplings from the singlet methyl protons H_3-22 (δ_H 1.66) to carbonyl carbon C-3, olefinic quaternary carbon C-4 (δ_C 112.1), and oxygenated olefinic quaternary carbon C-5 (δ_C 188.4) established the sequence from C-21 to C-5. The sequence from methylene protons H_2-6 (δ_H 2.76, 2.71) to oxymethine proton H-15 (δ_H 3.64) through oxymethine proton H-7 (δ_H 4.06); methylene protons H_2-8 (δ_H 1.70, 1.62) and H_2-9 (δ_H 2.26, 2.19); olefinic protons H-10 (δ_H 5.61), H-11 (δ_H 6.08), H-12 (δ_H 6.04), and H-13 (δ_H 5.58); and methine proton H-14 (δ_H 2.34), which was ^{1}H−^{1}H spin-coupled with doublet methyl protons H_3-23 (δ_H 0.86), was revealed by analyzing the DQF-COSY spectrum. The remaining ^{1}H sequence from olefinic proton H-17 (δ_H 5.36) to methyl protons H_3-20 (δ_H 0.92) through methylene protons H_2-18 (δ_H 2.03) and H_2-19 (δ_H 1.40) was also constructed by evaluating the DQF-COSY spectrum. The ^{1}H−^{13}C long-range couplings from singlet methyl protons H_3-24 (δ_H 1.59) to oxymethine carbon C-15 (δ_C 83.4), quaternary olefinic carbon C-16 (δ_C 136.3), and olefinic methine carbon C-17 (δ_C 128.8) established the connectivity between the two sequences C6−C15 and C17−C20. Finally, the ^{1}H−^{13}C long-range couplings from the methylene protons H_2-6 to quaternary carbons C-4 and C-5 enabled the determination of the positions of all of the ^{13}C units, as shown in Figure 2. According to the molecular formula of the major component, this compound should possess a cyclic moiety. By taking into consideration the dehydration at C-7, which was confirmed using MTPA derivatization (*vide infra*), a five-membered 4-methyl-3(2*H*)-furanone moiety was established. NMR analyses of the C-2 epimer and the minor component revealed that the planar structures of these isomers were the same as that of the major component. Consequently, JBIR-108 was demonstrated to exist as two pairs of tautomers.

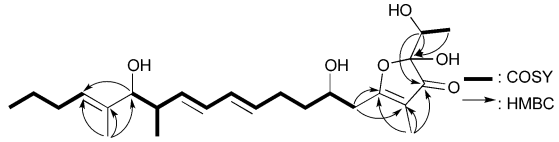


Figure 2. Correlations in the DQF-COSY (bold lines) and CT-HMBC (arrows) spectra of the JBIR-108 major component.

The relative configuration was assigned on the basis of the coupling constants and analysis of the differential NOE (NOESY) spectrum. The configurations of the C-10 and C-12 positions were assigned as 10*E* and 12*E* on the basis of their coupling constants (12.0 and 14.1 Hz, respectively). The NOESY H-15/H-17 correlations indicated that the major component possesses a 16*E* double bond (Figure 3). The high-field shift of the signal for the 16-Me carbon (C-24, δ_C 11.4) due to the γ-effect also supported the *E*-configuration at C-16.

The absolute configuration at C-15 in the major component was revealed using the modified Mosher's method.[10] The proton chemical shifts of the methine proton H-15, olefinic proton

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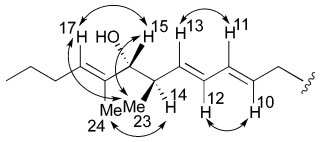


Figure 3. Key NOESY correlations for the JBIR-108 major component.

H-17, methylene protons H_2-18 and H_2-19, and methyl protons H_3-20 and H_3-24 in the (*S*)-MTPA ester derivative of the major component appeared at higher fields than those of the (*R*)-MTPA ester derivative (Figure 4). On the other hand, the

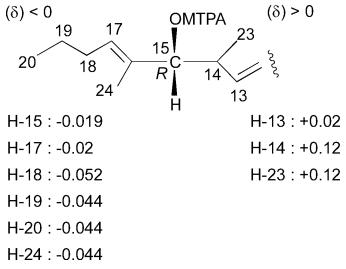
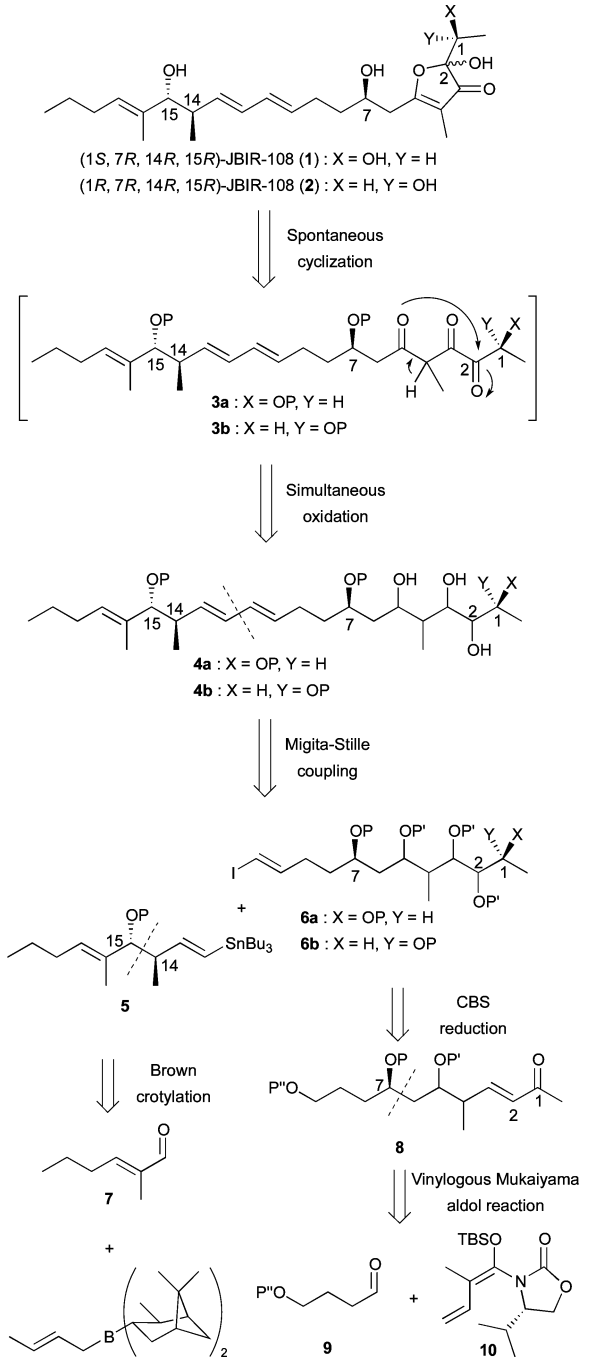


Figure 4. Absolute configuration of C-15 in the JBIR-108 major component as determined using the modified Mosher's method. The differences in the chemical shift values were obtained by subtracting the signal values for the (*R*)-MTPA ester from those for the (*S*)-MTPA ester ($\delta\Delta = \delta(S)$-MTPA $- \delta(R)$-MTPA).

proton chemical shifts of the olefinic proton H-13, methine proton H-14, and methyl proton H_3-23 in the (*S*)-MTPA ester derivative were observed at lower fields than those of the (*R*)-MTPA ester derivative. Thus, the absolute configuration at the C-15 position was confirmed to be *R*. From the magnitude of the $^3J_{H,H}$ vicinal coupling constant (8.5 Hz) for H-14 and H-15, these two protons were assigned an *anti* orientation.[11] In addition, NOESY correlations were observed between H-14 and H_3-24, H-15 and H_3-23, and H-17 and H_3-23 (Figure 3). These results indicated that H-15 and the methyl group H_3-23 are in the *gauche* orientation. Thus, the absolute configuration at C-14 was also found to be *R*. However, Mosher's method[10] by itself could not be used to determine the stereochemistries at C-1 and C-7 owing to the lack of protons in the furanone moiety and the fact that the 7-hydroxy group was dehydrated during MTPA condensation, respectively. Therefore, synthetic studies were required to complete the total structure determination of JBIR-108.

Total Synthesis of JBIR-108. The syntheses of both (1*S*, 7*R*, 14*R*, 15*R*)-JBIR-108 (**1**) and (1*R*, 7*R*, 14*R*, 15*R*)-JBIR-108 (**2**) were planned assuming that the stereochemistries at C-7, C-14, and C-15 are identical to those of actinofuranone A (Figure 1).[12] The retrosynthetic strategy is shown in Scheme 1. The 2-hydroxy-3(2*H*)-furanone core in **1** and **2** would be constructed via spontaneous cyclization of the corresponding triketones **3a**–**3b**. Although this approach has been employed for the synthesis of the same moiety in aurafuron A,[13] the adjacent C-1 stereochemistry, a key feature of JBIR-108, makes the synthesis more challenging. It is necessary to generate all three ketone functions of **3a**–**3b** simultaneously without the loss of the C-1 stereocenter through considerable enolization of the 1,2-diketone moiety. For this purpose, triols **4a**–**4b** were chosen as precursors for simultaneous oxidation.[14] The 1,3-diene moiety in triols **4a**–**4b** would be generated via a Migita–Stille

Scheme 1. Retrosynthesis of JBIR-108

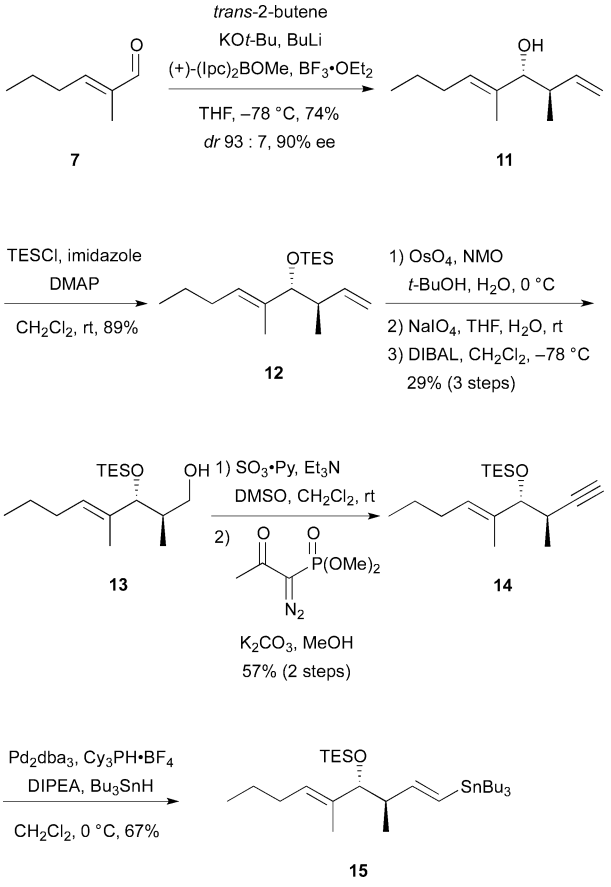


coupling reaction[15] between alkenylstannane **5** and alkenyl iodides **6a**–**6b**. Alkenylstannane **5** would be constructed via Brown crotylation[16] of aldehyde **7**. Alkenyl iodides **6a**–**6b** would be prepared via the vinylogous Mukaiyama aldol reaction[17] of aldehyde **9** with vinylketene silyl *N*,*O*-acetal **10**, followed by the formation of enone **8** and Corey–Bakshi–Shibata reduction.[18] Importantly, this synthetic route would allow the preparation of all diastereomers of JBIR-108 through the selection of matched chiral reagents.

Our synthesis commenced with the preparation of alkenylstannane **15** from aldehyde **7** (Scheme 2). Asymmetric crotylation[16] of **7**[19] provided alcohol **11** in good diastereo- and enantioselectivities (93:7, 90% ee).[20] After the triethylsilyl ether (TES) protection of the hydroxy group, the oxidative cleavage

dx.doi.org/10.1021/jo502198y | J. Org. Chem. 2015, 80, 114–132

Scheme 2. Synthesis of Alkenylstannane 15



of terminal alkene in **12**, followed by the reduction of the resulting aldehyde, afforded alcohol **13**. The minor diastereomer of alcohol **13** generated during the Brown crotylation was removed by column chromatography. Oxidation of **13**, followed by the treatment of the resulting aldehyde with the Ohira–Bestmann reagent,[21] gave alkyne **14**. Regioselective hydrostannylation[22] of **14** then afforded alkenylstannane **15**.

We next prepared alkenyl iodides **29a–29b** (Scheme 3). Vinylogous Mukaiyama aldol reaction[17] of aldehyde **16**[23] with vinylketene silyl *N,O*-acetal **10** provided the desired alcohol **17** in high diastereoselectivity (>95:5).[20] After the *p*-methoxybenzyl ether (PMB) protection of the resulting hydroxy group and reduction of the imide moiety, Katsuki–Sharpless asymmetric epoxidation[24,25] of allylic alcohol **18** afforded epoxide **19**. The oxidation of the primary alcohol in **19**, followed by the Horner–Wadsworth–Emmons reaction[26] of aldehyde **20**, gave ester **21**. Regioselective and stereoselective reductive ring opening of the enoxide in **21** was achieved under Pd catalysis,[27] and then the TES protection of the resulting hydroxy group afforded ester **22**, which was converted to enone **23** in four steps. The asymmetric reduction of **23** with a stoichiometric amount of the (*R*)-Me-CBS reagent[18,28] afforded alcohol **24a** in high diastereoselectivity (*dr* > 95:5).[20] After PMB protection and removal of the TES group, the dihydroxylation of homoallylic alcohol **25a**, followed by the protection of triol **26a** with acetyl groups and removal of the *tert*-butyldiphenylsilyl ether (TBDPS) group, provided alcohols **27a** as a mixture of diastereomers. Because the stereochemistries between C-3 and C-6 in **27a** would be lost during simultaneous oxidation at a later stage, the diastereomeric mixture was used without separation for further reactions. Oxidation of alcohol **27a** gave the aldehyde, which was then converted to alkenyl iodide **28a** via Takai olefination.[29] The removal of the PMB group and TES protection of the two hydroxy groups provided **29a**. The diastereomeric iodide **29b** was also obtained through a similar reaction sequence, except the asymmetric reduction of **23** was achieved using the (*S*)-Me-CBS reagent.

With alkenylstannane **15** and alkenyl iodides **29a–29b** in hand, we investigated the Migita–Stille coupling reaction[15] (Scheme 4). After the screening of Pd catalysts ($Pd_2(dba)_3$, $Pd(PPh_3)_4$, $PdCl_2(dppf)$, and $PdCl_2(MeCN)_2$), as well as additives ($AsPh_3$, LiCl, CuI, CuCl, CuTC, and $[Bu_4N^+][Ph_2P(O)O^-]$[30]), the desired dienes **30a–30b** were obtained in high yield using $PdCl_2(MeCN)_2$, $[Bu_4N^+][Ph_2P(O)O^-]$, and NMP.[31] The removal of all of the acetyl groups in **30a–30b**, simultaneous oxidation[14] of triols **31a–31b**, and spontaneous cyclization of triketones **32a–32b** provided 2-hydroxy-3(2*H*)-furanones **33a–33b**. We confirmed that this spontaneous cyclization proceeded without epimerization at C-1 by using model compounds and chiral HPLC analysis (Scheme 5; see Figures S9 and S10, Supporting Information[20]). Finally, we accomplished the synthesis of (1*S*,7*R*,14*R*,15*R*)-JBIR-108 (**1**) and (1*R*,7*R*,14*R*,15*R*)-JBIR-108 (**2**) by desilylation of **33a–33b**, respectively.

Structure Determination of JBIR-108. In order to determine the relative configuration of natural JBIR-108, ultra performance liquid chromatography (UPLC) peaks for the natural product were compared with those of synthetic products **1** and **2**. It was found that the retention times of the major and minor components of JBIR-108 were identical to those of synthetic **1** and **2**, respectively (see Figure S7, Supporting Information[20]). The ^{1}H NMR spectrum of JBIR-108 was also compared to those of **1** and **2**. The ^{1}H NMR spectra of both **1** and **2** in CD_3OD indicated that these compounds exist as a mixture of C-2 epimers in a ratio of 2:1 (see S105 and S107, Supporting Information[20]). This ratio was determined by comparing the doublet for the methyl protons H_3-21 (δ_H 1.30 (major) and δ_H 1.18 (minor) for **1** and δ_H 1.30 (major) and δ_H 1.17 (minor) for **2**). These ^{1}H NMR spectra were in agreement with one another except for the chemical shifts for the proton at C-21 in the minor C-2 epimers of **1** (δ_H 1.18) and **2** (δ_H 1.17). Magnified ^{1}H NMR spectra are shown in Figure 5, and the difference in the spectra for **1** and **2** is marked using a red arrow. Interestingly, natural JBIR-108 was found to be a diastereomeric mixture of **1** and **2**. It was also revealed that the major and minor components of natural JBIR-108 corresponded to synthetic **1** and **2**, respectively.

However, the above data can only reveal that the relative configuration of C-1 and C-7 in natural JBIR-108 is *syn* for the major component and *anti* for the minor component, respectively (Figure 6). It is considered that the stereogenic centers at C-1 and C-7, C-14 and C-15 may not influence each other because the stereogenic centers at C-1 and C-7 are distal from those at C-14 and C-15. Therefore, (1*R*,7*S*,14*R*,15*R*)-**36** and (1*S*,7*S*,14*R*,15*R*)-**37** can be regarded as a pseudoenantiomer of **1** and **2** around the furanone moiety and may be an alternative structure for the major component and the minor component, respectively. Then, if the absolute configuration at C-1 of the major component of the natural product is determined, the absolute configuration at C-7 can also be determined because the relative configuration of C-1 and C-7 in the natural JBIR-108 major component is *syn*.

Thus, tri-(*R*)-MTPA esters of natural JBIR-108, **1**, and **2** were prepared in order to assign the absolute configuration at C-1 of the major component of the natural product. The

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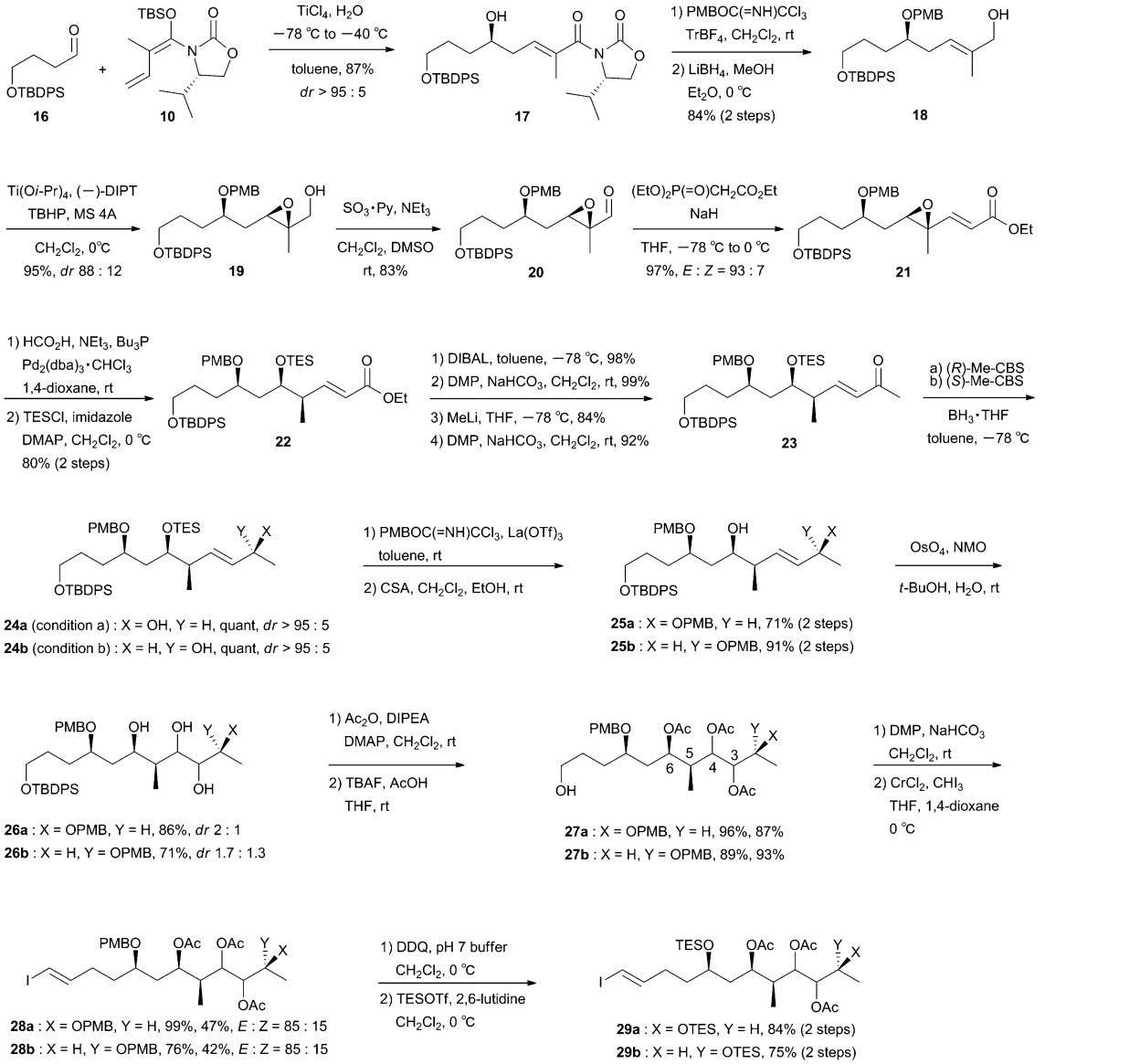
Scheme 3. Synthesis of Alkenyl Iodides 29a−29b



formation of the tri-(*R*)-MTPA esters of the two hydroxy groups at both C-1 and C-2 was accompanied by dehydration at C-6 and C-7, as mentioned above. The ^{1}H NMR spectrum of the tri-(*R*)-MTPA ester of natural JBIR-108 was better matched to that of **38**, which was derived from (1*S*,7*R*,14*R*,15*R*)-JBIR-108 (**1**), rather than that of **39**, which was derived from (1*R*,7*R*,14*R*,15*R*)-JBIR-108 (**2**), as shown in Figure 7. In light of these results, the C-1 and C-7 stereochemistries of the major component are assigned as (1*S*,7*R*). On the basis of all of the above results, therefore, natural JBIR-108 was determined to be a mixture of major (1*S*,7*R*,14*R*,15*R*)-JBIR-108 (**1**) and minor (1*R*,7*R*,14*R*,15*R*)-JBIR-108 (**2**).

■ CONCLUSIONS

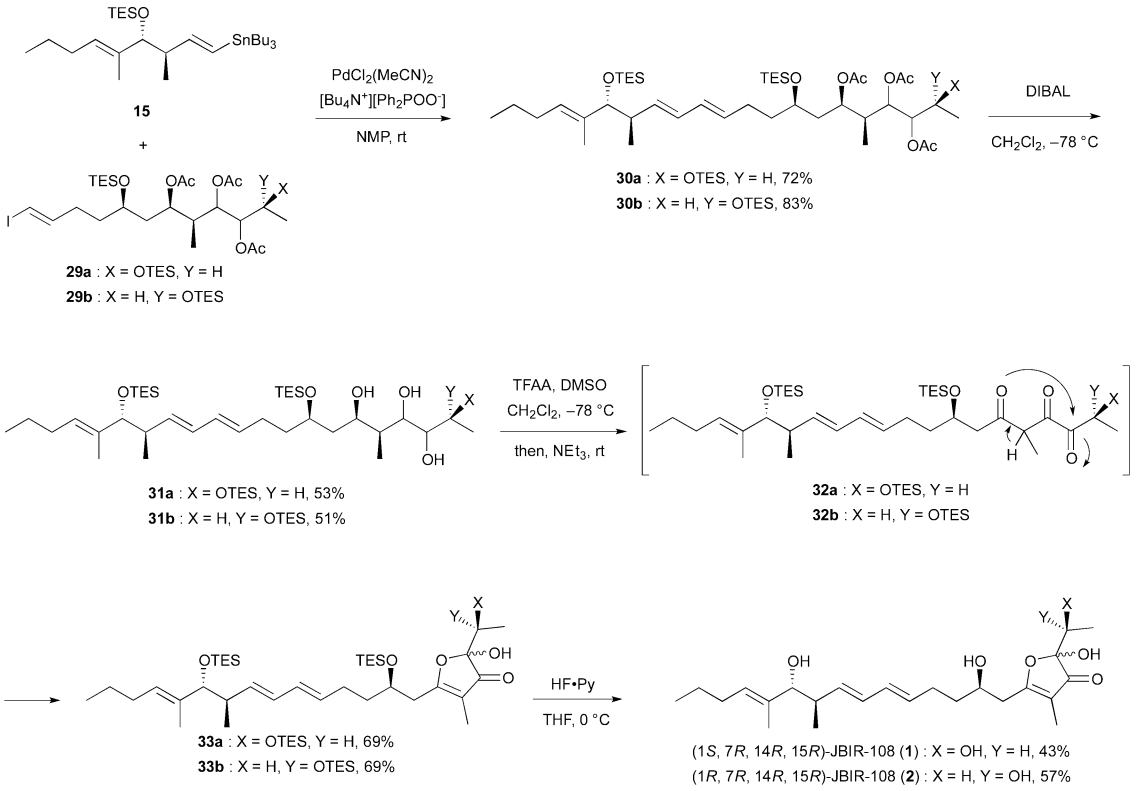
We have described the fermentation, isolation, total synthesis, and structure determination of JBIR-108 (**1**) and (**2**). The first total synthesis of both (1*S*,7*R*,14*R*,15*R*)-(**1**) and (1*R*,7*R*,14*R*,15*R*)-(**2**) was accomplished, individually, by forming the unique structure 2-hydroxy-2-(1-hydroxyethyl)-2,3-dihydro-3(2*H*)-furanone utilizing the spontaneous cyclization of 2-alkoxy-3,4,6-alkanetrione **32** without epimerization, which was generated *in situ* via the oxidation of the corresponding triol **31**. The comparison of the ^{1}H NMR spectra of natural JBIR-108 and those of the synthetic compounds **1** and **2** revealed that JBIR-108 is a 5:2 mixture of diastereomers at C-1, as well as a mixture of C-2 epimers (2:1 in CD_3OD). In biological evaluations, JBIR-108 exhibited potent cytotoxicities against SKOV-3, Meso-1, and Jurkat cells with IC_{50} values of 2.3, 2.5, and 1.0 μM, respectively. These results indicate that JBIR-108 is more potent than E-975 despite only minor structural differences. The development of an efficient synthetic route suitable for structure−activity relationship studies is currently under investigation.

■ EXPERIMENTAL SECTION

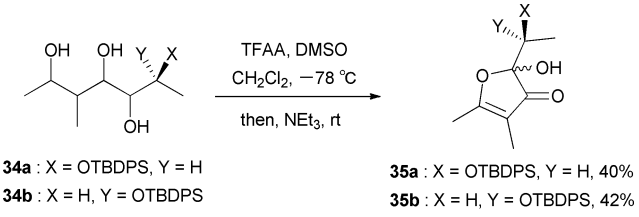
General Procedures. ^{1}H NMR spectra (400 and 600 MHz) and ^{13}C NMR spectra (100 and 150 MHz) were recorded in indicated solvent. For ^{1}H NMR spectra, chemical shifts (δ) are given from TMS (0.00 ppm) in $CDCl_3$ and CD_3OD as internal standards. For ^{13}C NMR spectra, chemical shifts (δ) are given from $CDCl_3$ (77.0 ppm) or CD_3OD (49.0 ppm) as internal standards. The following abbreviations are used: s (singlet), brs (broad singlet), d (doublet), t (triplet),

dx.doi.org/10.1021/jo502198y | J. Org. Chem. 2015, 80, 114−132

Scheme 4. Total Synthesis of (1*S*,7*R*,14*R*,15*R*)-JBIR-108 (1) and (1*R*,7*R*,14*R*,15*R*)-JBIR-108 (2)



Scheme 5. Spontaneous Cyclization of Model Compounds



34a : X = OTBDPS, Y = H
34b : X = H, Y = OTBDPS

35a : X = OTBDPS, Y = H, 40%
35b : X = H, Y = OTBDPS, 42%

q (quartet), m (multiplet), *J* (coupling constants). Only the strongest and/or structurally important absorptions of IR spectra were reported in wavenumbers (cm^{-1}). The optical rotations were measured on a polarimeter. High-resolution mass spectra were measured on a TOF-MS with EI, FAB, or ESI probe. High-performance liquid chromatography (HPLC) was performed with a UV detector and a refractive index detector. Reversed-phase HPLC and reversed-phase ultra performance liquid chromatography (UPLC) were performed with a UV/Visible detector. Gel permeation chromatography (GPC) was performed with a refractive index detector and a UV/visible detector.

Fermentation and Isolation of JBIR-108. The strain *Streptomyces gramineus* IR087Pi-4 was isolated from a bark collected in Okinawa Prefecture, Japan, according to a previously reported method.[1] The strain was cultivated in 50 mL test tubes, each containing 15 mL of a seed medium consisting of 1.0% starch, 1.0% Polypepton, 1.0% molasses, and

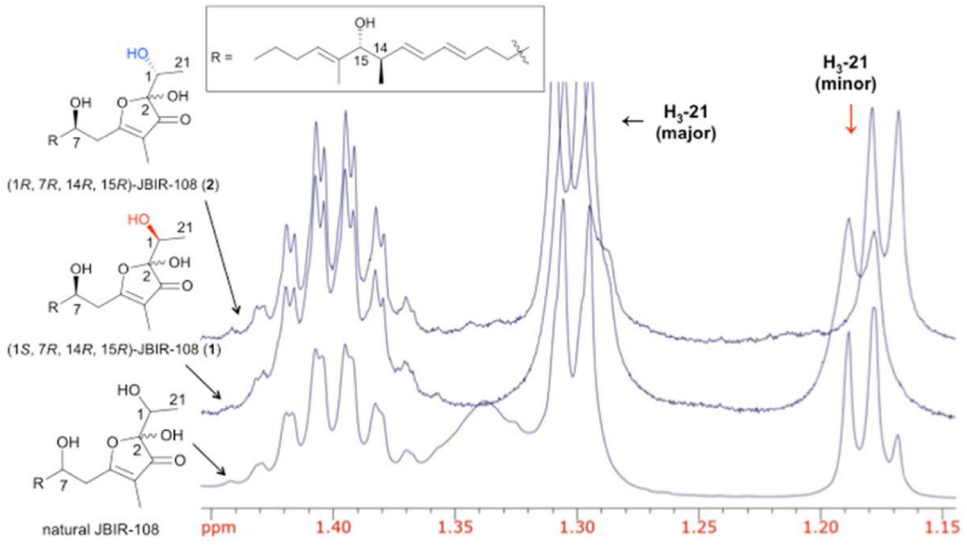


Figure 5. Magnified ^{1}H NMR spectra of JBIR-108 and synthetic **1** and **2**.

dx.doi.org/10.1021/jo502198y | *J. Org. Chem.* 2015, 80, 114−132

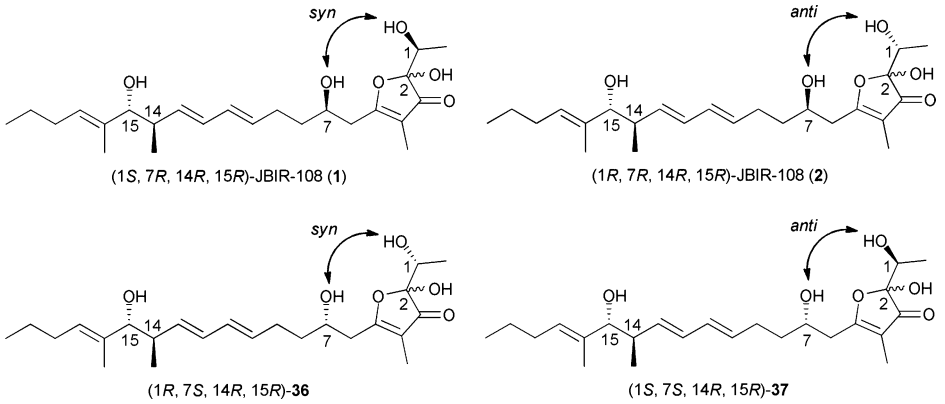


Figure 6. Another potential structure for natural JBIR-108.

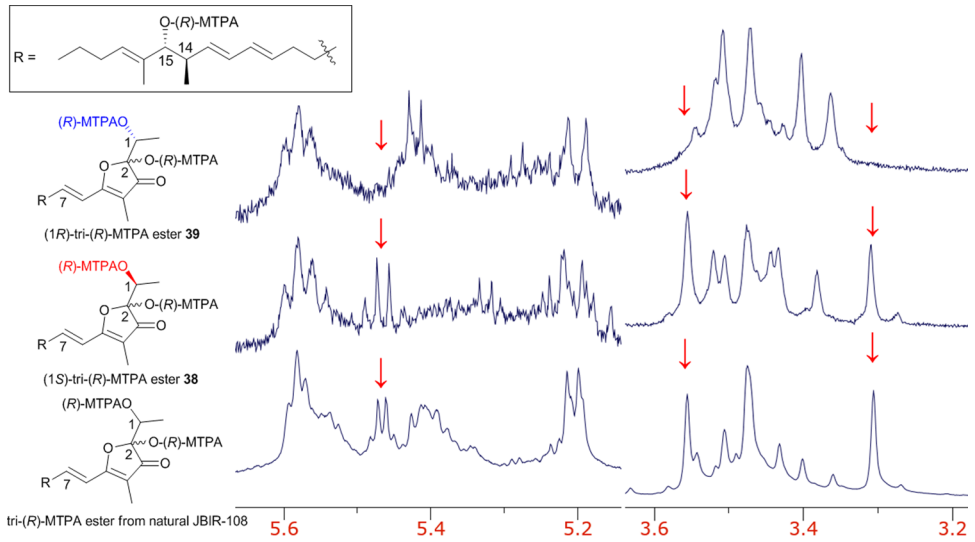


Figure 7. Magnified spectra of the tri-(*R*)-MTPA esters of JBIR-108, **38**, and **39**.

1.0% meat extract at pH 7.2 (adjusted before sterilization). The test tubes were shaken using a reciprocal shaker (320 rpm) at 27 °C for 2 days. Aliquots (2.5 mL) of the culture were then transferred into 500 mL baffled Erlenmeyer flasks filled with 100 mL of a production medium consisting of 4.0% β-cyclodextrin, 0.5% glycerol, 2.0% Pharmamedia, $CuSO_4$ (5 mg), $MnCl_2$ (5 mg), and $ZnSO_4$ (5 mg) and cultured on a rotary shaker (180 rpm) at 27 °C for 5 days.

The fermentation broth (2 L) was centrifuged, and the collected supernatant was extracted with EtOAc (1,800 mL × 2). The combined organic layers were then dried over Na_2SO_4 and concentrated *in vacuo*. The dried residue (267 mg) was applied on a normal-phase medium-pressure liquid column, and the column was successively eluted using a hexane−EtOAc solvent system (0, 5, 10, 20, and 25% EtOAc), followed by a $CHCl_3$−MeOH solvent system (0, 2, 5, 10, and 20% MeOH). The target eluate (5% MeOH, 11 mg) was further purified via preparative reversed-phase high-performance liquid chromatography (HPLC) on a C18 column (5.0 μm, 20 i.d. × 150 mm) with a photodiode array detector and a mass detector using 68% aqueous MeOH containing 0.1% formic acid (flow rate, 10 mL min^{-1}) to yield JBIR-108 (3.4 mg, retention time (R_t) = 20.3 min, major component) and (1.5 mg, R_t = 22.6 min, minor component) together with known compound E-975[6] (1.2 mg, R_t = 13.0 min) and its isomer (0.6 mg, R_t = 15.2 min). After the concentration of the major component of JBIR-108 was purified by reversed-phase HPLC, both the major and the minor components were observed in a ratio of 5:1.[7]

Cytotoxicity Assay. SKOV-3 cells were cultured in DMEM medium supplemented with 10% fetal bovine serum, penicillin (50 U/mL), and streptomycin (50 g/mL). MESO-1 cells were cultured in RPMI1640 medium supplemented with 10% fetal bovine serum, penicillin (50 U/mL), and streptomycin (50 g/mL). Jurkat cells were cultured in DMEM medium supplemented with 10% fetal bovine serum, penicillin (50 U/mL), streptomycin (50 g/mL), and glutamax (2 mM).

All cell lines were seeded in a 384-well plate at a density of 1000 cells/20 μL/well and incubated at 37 °C in a humidified incubator with 5% CO_2. After 4 h, cells were treated with various concentrations of compounds for 72 h. The vehicle solvent (DMSO) was used as a control. Cell viabilities were measured using a Cell Counting Kit-8.

Synthesis of JBIR-108. *(E)-2-Methyl-2-hexenal (7).* To a stirred solution of butanal (7.21 g, 100 mmol) in methyl acrylate (14 mL, 0.15 mol) was added DABCO (1.68 g, 15.0 mmol) at room temperature. The resulting mixture was stirred at the same temperature for 11 days. The mixture was concentrated *in vacuo*, and the residue was washed with 1 M HCl, H_2O, and brine, dried over $MgSO_4$, filtered, and concentrated *in vacuo* to yield methyl 3-hydroxy-2-methylidenehexanoate (**S1**) (14.0 g, 88.5 mmol, 89%), which was used for the next reaction without further purification. To a stirred solution of the above 3-hydroxy-2-methylidenehexanoate (**S1**) (14.0 g, 88.5 mmol) in dry toluene (88 mL) were added DMAP (1.08 g, 8.80 mmol) and Ac_2O (10 mL, 0.11 mol) successively at 0 °C. The resulting mixture was stirred at room temperature for 22 h. To the mixture was added 1 M HCl to quench the reaction. The resulting mixture was washed with H_2O, saturated aqueous $NaHCO_3$ solution, and brine, dried over Na_2SO_4, filtered, and concentrated *in vacuo* to yield methyl 3-acetyloxy-2-methylidenehexanoate (**S2**) (16.8 g, 83.9 mmol, 95%), which was used for the next reaction without further purification. To a stirred suspension of $LiAlH_4$ (2.82 g, 74.4 mmol) in dry Et_2O

dx.doi.org/10.1021/jo502198y | J. Org. Chem. 2015, 80, 114−132

(155 mL) were added EtOH (4.3 mL, 74 mmol) and a solution of methyl 3-(acetyloxy)-2-methylidenehexanoate (**S2**) (6.20 g, 31.0 mmol) in dry Et_2O (30 mL) dropwise successively at −78 °C. The resulting mixture was stirred at the same temperature for 20 min. To the mixture was added H_2O to quench the reaction. The resulting mixture was filtered through a pad of Celite, dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The residue was purified by column chromatography (EtOAc:hexane = 1:4) to yield (*E*)-2-methyl-2-hexen-1-ol (**S3**) (2.93 g, 25.7 mmol, 83%, *E*:*Z* > 95:5) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.91 (3H, t, J = 7.3 Hz), 1.38 (2H, tq, J = 7.3, 7.3 Hz), 1.66 (3H, brs), 1.79 (1H, brs), 2.01 (2H, dt, J = 7.3, 7.3 Hz), 3.99 (2H, brs), 5.41 (1H, tq, J = 7.3, 1.2 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.6, 13.7, 22.6, 29.6, 68.9, 126.2, 134.7. IR (neat): 3336, 2960, 2930, 2873, 1458, 1010 cm^{-1}. LRMS (EI) *m*/*z*: 114 ([M]$^+$). HRMS (EI, [M]$^+$): calcd for $C_7H_{14}O$, 114.1045: found, 114.1031. To a stirred solution of DMSO (8.5 mL, 0.16 mol) in dry CH_2Cl_2 (200 mL) was added $(COCl)_2$ (8.8 mL, 0.10 mol) at −78 °C, and the resulting mixture was stirred at the same temperature for 15 min. Then, a solution of (*E*)-2-methyl-2-hexen-1-ol (**S3**) (5.90 g, 51.7 mmol) in dry CH_2Cl_2 (60 mL) was added to the mixture. After being stirred at −78 °C for 30 min, the reaction mixture was treated with triethylamine (36 mL, 0.26 mol) and then warmed to room temperature. The mixture was stirred for another 30 min, before saturated aqueous NH_4Cl solution was added to the solution at 0 °C. The resulting mixture was extracted with CH_2Cl_2 twice. The combined organic phases were washed with brine, dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The residue was purified by flash column chromatography (EtOAc:hexane = 1:9) to yield (*E*)-2-methyl-2-hexenal (**7**) (5.36 g, 47.8 mmol, 92%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.98 (3H, t, J = 7.3 Hz), 1.55 (2H, tq, J = 7.3, 7.3 Hz), 1.75 (3H, d, J = 1.2 Hz), 2.34 (2H, dt, J = 7.3, 7.3 Hz), 6.49 (1H, tq, J = 7.3, 1.2 Hz), 9.41 (1H, s). ^{13}C NMR (100 MHz, $CDCl_3$): δ 9.2, 13.8, 21.7, 30.9, 139.5, 154.6, 195.3. IR (neat): 2962, 2931, 1685, 1646 cm^{-1}. LRMS (EI) *m*/*z*: 112 ([M]$^+$). HRMS (EI, [M]$^+$): calcd for $C_7H_{12}O$, 112.0888: found, 112.0870.

*(3R,4R,E)-3,5-Dimethylnona-1,5-dien-4-ol (**11**).* To a stirred solution of KO*t*-Bu (754 mg, 6.72 mmol) in dry THF (10 mL) were added *trans*-2-butene (0.84 mL, 10 mmol) and *n*-BuLi (2.6 mL, 6.7 mmol, 2.6 M in hexane) dropwise at −78 °C, and the resulting mixture was stirred at −60 °C for 30 min. Then, a solution of (+)-$(Ipc)_2$BOMe (2.13 g, 6.72 mmol) in dry THF (2.0 mL) was added to the mixture dropwise at −78 °C. After being stirred at the same temperature for 30 min, $BF_3{\cdot}OEt_2$ (1.1 mL, 9.1 mmol) was added to the mixture dropwise. The resulting mixture was stirred at the same temperature for 30 min. A solution of (*E*)-2-methyl-2-hexenal (**7**) (566 mg, 5.05 mmol) in dry THF (2.0 mL) was added to the mixture dropwise at −78 °C. The mixture was stirred at the same temperature for 10 min, before 2.5 M NaOH (7.0 mL) and H_2O_2 (6.5 mL, 30% aq.) were added to the solution at −78 °C. The resulting mixture was warmed to room temperature and then extracted with EtOAc twice. The combined organic phases were washed with saturated aqueous $Na_2S_2O_3$ solution and brine, dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The residue was purified by column chromatography (EtOAc:hexane = 1:19) to yield (3*R*,4*R*,*E*)-3,5-dimethylnona-1,5-dien-4-ol (**11**) (628 mg, 3.73 mmol, 74%) as a colorless oil. The diastereomeric ratio (93:7) was determined by ^{1}H NMR before HPLC purification. The absolute configuration of C14, 15 and enantiomeric excess were determined by synthesizing (3*R*,4*R*,*E*)-3,5-dimethylnona-1,5-dien-4-yl (*S*)-3,3,3-trifluoro-2-methoxy-2-phenylpropanoate (**S4**), (3*R*,4*R*,*E*)-3,5-dimethylnona-1,5-dien-4-yl (*R*)-3,3,3-trifluoro-2-methoxy-2-phenylpropanoate (**S5**), and (4*R*,5*R*)-4-[(*E*)-hex-2-en-2-yl]-2,2,5-trimethyl-1,3-dioxane (**S9**) (Figures S1 and S2, Supporting Information[20]). The analytical sample was obtained by HPLC (column: 8ϕ × 300 mm, IPA:hexane = 1:19, 1 mL/min, R_t = 16.3 min (major), 16.9 min (minor)). ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.88 (3H, d, J = 6.8 Hz), 0.91 (3H, t, J = 7.3 Hz), 1.33−1.46 (2H, m), 1.61 (3H, s), 1.73 (1H, d, J = 1.7 Hz), 2.03 (2H, dt, J = 7.1, 7.3 Hz), 2.27−2.36 (1H, m), 3.64 (1H, dd, J = 1.7, 8.8 Hz), 5.12−5.19 (2H, m), 5.40 (1H, t, J = 7.1 Hz), 5.75 (1H, ddd, J = 8.3, 10.2, 17.3 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ 10.9, 13.8, 16.8, 22.6, 29.7, 42.2, 81.5, 116.4, 129.2, 134.8, 141.4. IR (neat): 3439, 2961, 2930, 2872, 1457, 1006, 908 cm^{-1}. LRMS (EI) *m*/*z*: 168 ([M]$^+$). HRMS (EI, [M]$^+$): calcd for $C_{11}H_{20}O$, 168.1514: found, 168.1494. $[\alpha]_D^{26}$: +5.5 (*c* 0.72, $CHCl_3$).

*(3R,4R,E)-3,5-Dimethyl-4-triethylsilanyloxynona-1,5-diene (**12**).* To a stirred solution of (3*R*,4*R*,*E*)-3,5-dimethylnona-1,5-dien-4-ol (**11**) (1.00 g, 5.94 mmol) in dry CH_2Cl_2 (10 mL) were added imidazole (1.21 g, 17.8 mmol), DMAP (145 mg, 1.19 mmol), and TESCl (1.5 mL, 8.9 mmol) successively at 0 °C. The resulting mixture was stirred at the same temperature for 13 h. To the mixture was added saturated aqueous NH_4Cl solution to quench the reaction. The resulting mixture was extracted with EtOAc twice. The combined organic phases were washed with brine, dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The residue was purified by column chromatography eluted with hexane to yield (3*R*,4*R*,*E*)-3,5-dimethyl-4-triethylsilanyloxynona-1,5-diene (**12**) (1.49 g, 5.27 mmol, 89%) as a colorless oil. The major diastereomer was slightly lost by column chromatography (*dr* 85:15). ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.55 (6H, q, J = 7.8 Hz), 0.81−0.95 (15H, m), 1.33−1.42 (2H, m), 1.53 (0.45H, s), 1.55 (2.55H, s), 1.94−2.01 (2H, m), 2.23−2.32 (1H, m), 3.64 (1H, d, J = 8.0 Hz), 4.85−4.92 (0.3H, m), 4.94−5.01 (1.7H, m), 5.27 (1H, t, J = 7.1 Hz), 5.63 (0.15H, ddd, J = 7.6, 10.2, 17.3 Hz), 5.88 (0.85H, ddd, J = 7.1, 10.2, 17.3 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ 4.9, 6.9, 11.2, 13.9, 16.4, 22.6, 29.6, 41.8, 83.3, 113.4, 127.3, 136.4, 142.4. IR (neat): 2958, 2876, 1458, 1415, 1239, 1067, 1006 cm^{-1}. LRMS (EI) *m*/*z*: 253 ([M − Et]$^+$). HRMS (EI, [M − Et]$^+$): calcd for $C_{15}H_{29}OSi$, 253.1982: found, 253.1981. $[\alpha]_D^{27}$: +2.1 (*c* 1.05, $CHCl_3$).

*(2R,3R,E)-2,4-Dimethyl-4-triethylsilanyloxyoct-4-en-1-ol (**13**).* To a stirred solution of (3*R*,4*R*,*E*)-3,5-dimethyl-4-triethylsilanyloxynona-1,5-diene (**12**) (100 mg, 0.354 mmol) in *t*-BuOH (1.8 mL) and H_2O (1.8 mL) were added NMO (132 mg, 1.13 mmol) and OsO_4 (0.71 mL, 0.035 mmol, 0.05 M in THF) at 0 °C, and the resulting mixture was stirred at the same temperature for 4 h. To the mixture was added saturated aqueous $Na_2S_2O_3$ solution to quench the reaction at 0 °C. The resulting mixture was extracted with EtOAc twice. The combined organic phases were washed with brine, dried over Na_2SO_4, filtered, and concentrated *in vacuo* to yield a diol, which was used for the next reaction without further purification. To a stirred solution of the resulting diol in THF (0.90 mL) and H_2O (0.90 mL) was added $NaIO_4$ (151 mg, 0.708 mmol) at 0 °C, and the resulting mixture was stirred at the same temperature for 30 min. The resulting mixture was filtered and then extracted with Et_2O twice. The combined organic phases were washed with brine, dried over $MgSO_4$, filtered, and concentrated *in vacuo* to yield an aldehyde, which was used for the next reaction without further purification. To a stirred solution of the resulting aldehyde in dry CH_2Cl_2 (3.5 mL) was added DIBAL (0.53 mL, 0.53 mmol, 1.0 M in toluene) at −78 °C. After being stirred at the same temperature for 30 min, the reaction mixture was poured into saturated aqueous Rochell salt solution (4.0 mL), and the mixture was stirred at room temperature until the mixture turned into a clear solution. The resulting mixture was extracted with EtOAc twice. The combined organic phases were washed with brine, dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The residue was purified by column chromatography (EtOAc:hexane = 1:19) to yield (2*R*,3*R*,*E*)-2,4-dimethyl-4-triethylsilanyloxyoct-4-en-1-ol (**13**) (29.6 mg, 0.103 mmol, 29% from (3*R*,4*R*,*E*)-3,5-dimethyl-4-triethylsilanyloxynona-1,5-diene (**12**)) as a brown oil. The minor diastereomer was separated by column chromatography. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.60 (6H, q, J = 7.8 Hz), 0.72 (3H, d, J = 7.1 Hz), 0.92 (3H, t, J = 7.3 Hz), 0.95 (9H, t, J = 7.8 Hz), 1.36−1.42 (2H, m), 1.57 (3H, s), 1.82−1.89 (1H, m), 2.00 (2H, dt, J = 7.1, 7.1 Hz), 3.25 (1H, brs), 3.61 (2H, d, J = 5.1 Hz), 3.83 (1H, d, J = 8.8 Hz), 5.33 (1H, t, J = 7.1 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ 4.7, 6.7, 11.1, 13.9, 14.1, 22.5, 29.6, 38.1, 67.8, 85.8, 128.3, 135.8. IR (neat): 3450, 2958, 2876, 1458, 1415, 1378, 1239, 1048, 1005 cm^{-1}. LRMS (EI) *m*/*z*: 286 ([M]$^+$). HRMS (EI, [M]$^+$): calcd for $C_{16}H_{34}O_2Si$, 286.2328: found, 286.2332. $[\alpha]_D^{25}$: +7.1 (*c* 0.99, $CHCl_3$).

*(3R,4R,E)-3,5-Dimethyl-4-triethylsilanyloxynon-5-en-1-yne (**14**).* To a stirred solution of (2*R*,3*R*,*E*)-2,4-dimethyl-4-triethylsilanyloxyoct-4-en-1-ol (**13**) (99.1 mg, 0.346 mmol) in dry CH_2Cl_2 (1.5 mL) and dry DMSO (0.30 mL) were added NEt_3 (0.30 mL, 2.1 mmol) and

dx.doi.org/10.1021/jo502198y | *J. Org. Chem.* 2015, 80, 114−132

SO_3·Py (166 mg, 1.04 mmol) successively at 0 °C. The resulting mixture was stirred at room temperature for 40 min. To the mixture was added saturated aqueous NH_4Cl solution to quench the reaction at 0 °C. The resulting mixture was extracted with EtOAc twice. The combined organic phases were washed with brine, dried over $MgSO_4$, filtered, and concentrated *in vacuo* to yield an aldehyde, which was used for the next reaction without further purification. To a stirred solution of the above aldehyde in dry MeOH (1.1 mL) were added K_2CO_3 (71.7 mg, 0.519 mmol) and dimethyl (1-diazo-2-oxopropyl)phosphonate (77.9 μL, 0.519 mmol) successively at 0 °C. The resulting mixture was stirred at room temperature for 50 min. To the mixture was added saturated aqueous NH_4Cl solution to quench the reaction at 0 °C. The resulting mixture was extracted with EtOAc twice. The combined organic phases were washed with brine, dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The residue was purified by column chromatography eluted with hexane to yield (3*R*,4*R*,*E*)-3,5-dimethyl-4-triethylsilanyloxynon-5-en-1-yne (**14**) (55.1 mg, 0.196 mmol, 57% from (2*R*,3*R*,*E*)-2,4-dimethyl-4-triethylsilanyloxyoct-4-en-1-ol (**13**)) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.60 (6H, q, *J* = 7.8 Hz), 0.89−1.00 (15H, m), 1.34−1.43 (2H, m), 1.55 (3H, s), 1.94−2.02 (2H, m), 2.00 (1H, d, *J* = 2.4 Hz), 2.52−2.60 (1H, m), 3.85 (1H, d, *J* = 8.3 Hz), 5.34 (1H, t, *J* = 7.1 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ 4.9, 6.9, 10.8, 13.9, 17.5, 22.5, 29.6, 31.6, 68.6, 82.2, 88.0, 128.6, 135.2. IR (neat): 3314, 2957, 2876, 1458, 1239, 1075, 1006 cm^{-1}. LRMS (EI) *m*/*z*: 251 ([M − Et]$^+$). HRMS (EI, [M − Et]$^+$): calcd for $C_{15}H_{27}OSi$, 251.1826: found, 251.1796. $[\alpha]_D^{25}$: −15.8 (*c* 1.00, $CHCl_3$).

*(1E,3R,4R,5E)-3,5-Dimethyl-1-tributylstannyl-4-triethylsilanyloxynona-1,5-diene (**15**).* To a stirred solution of Pd_2dba_3 (0.8 mg, 0.9 μmol) in dry CH_2Cl_2 (1.0 mL) were added $Cy_3PH{\cdot}BF_4$ (1.4 mg, 3.7 μmol) and DIPEA (1.3 μL, 7.4 μmol) at room temperature. After being stirred at the same temperature for 10 min, the mixture was treated with (3*R*,4*R*,*E*)-3,5-dimethyl-4-triethylsilanyloxynon-5-en-1-yne (**14**) (51.5 mg, 0.184 mmol) in dry CH_2Cl_2 (0.80 mL) and Bu_3SnH (59 μL, 0.22 mmol) successively at 0 °C. The resulting mixture was stirred at the same temperature for 1.5 h. The mixture was concentrated *in vacuo*, and the residue was purified by column chromatography eluted with hexane to yield (1*E*,3*R*,4*R*,5*E*)-3,5-dimethyl-1-tributylstannyl-4-triethylsilanyloxynona-1,5-diene (**15**) (71.0 mg, 0.124 mmol, 67%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.55 (6H, q, *J* = 8.0 Hz), 0.79−0.94 (30H, m), 1.26−1.40 (8H, m), 1.45−1.55 (9H, m), 1.98 (2H, dt, *J* = 7.1, 7.1 Hz), 2.25−2.34 (1H, m), 3.66 (1H, d, *J* = 8.3 Hz), 5.26 (1H, t, *J* = 7.1 Hz), 5.88 (1H, d, *J* = 19.0 Hz), 6.04 (1H, dd, *J* = 6.3, 19.0 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ 5.0, 7.0, 9.3, 11.1, 13.7, 13.9, 16.5, 22.7, 27.3, 29.1, 29.6, 45.1, 83.4, 125.7, 127.2, 136.6, 152.8. IR (neat): 2957, 2927, 2874, 1457, 1376, 1070, 1004, 740, 725 cm^{-1}. LRMS (ESI) *m*/*z*: 595 ([M + Na]$^+$). HRMS (ESI, [M + Na]$^+$): calcd for $C_{29}H_{60}ONaSiSn$, 595.3328: found, 595.3320. $[\alpha]_D^{28}$: −6.3 (*c* 1.00, $CHCl_3$).

*(S)-3-[(R,E)-8-(tert-Butyldiphenylsilanyloxy)-5-hydroxy-2-methyloct-2-enoyl]-4-(propan-2-yl)-1,3-oxazolidin-2-one (**17**).* To a stirred solution of 4-(*tert*-butyldiphenylsilanyloxy)butanal (**16**)[22] (71.5 g, 217 mmol) in dry toluene (166 mL) were added H_2O (0.19 mL, 11 mmol), $TiCl_4$ (1.0 M in CH_2Cl_2, 108 mL), and vinylketene silyl *N*,*O*-acetal **10** (35.0 g, 108 mmol) successively at −78 °C. The resulting mixture was stirred at −40 °C for 14 h. To the mixture were added saturated aqueous $NaHCO_3$ solution and saturated aqueous Rochell salt solution. The mixture was stirred at room temperature until the mixture turned into a clear solution and then extracted with EtOAc twice. The combined organic phases were washed with brine, dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The residue was purified by column chromatography (EtOAc:hexane = 1:1) to yield (*S*)-3-[(*R*,*E*)-8-(*tert*-butyldiphenylsilanyloxy)-5-hydroxy-2-methyloct-2-enoyl]-4-(propan-2-yl)-1,3-oxazolidin-2-one (**17**) (50.3 g, 93.5 mmol, 87%, *dr* > 95:5) as a colorless oil. The absolute configuration was determined by Mosher's method (Figure S3, Supporting Information[20]). ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.91 (3H, d, *J* = 6.1 Hz), 0.93 (3H, d, *J* = 6.1 Hz), 1.05 (9H, s), 1.56−1.81 (4H, m), 1.94 (3H, brs), 2.25−2.41 (3H, m), 3.07 (1H, brs), 3.66−3.75 (3H, m), 4.18 (1H, dd, *J* = 5.6, 9.0 Hz), 4.32 (1H, dd, *J* = 9.0, 9.0 Hz), 4.55 (1H, tt, *J* = 4.4, 4.4 Hz), 6.03 (1H, tq, *J* = 7.8, 1.5 Hz), 7.35−7.44 (6H, m), 7.67 (4H, dd, *J* = 1.7, 7.8 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.7, 15.1, 17.8, 19.2, 26.8, 28.4, 28.9, 33.4, 36.7, 58.1, 63.4, 63.9, 70.4, 127.6, 129.5, 132.9, 133.8, 133.9, 135.2, 135.5, 154.2, 171.5 (one carbon of benzene ring was nonequivalence). IR (neat): 3517, 2930, 2858, 1779, 1687, 1111 cm^{-1}. LRMS (ESI) *m*/*z*: 560 ([M + Na]$^+$). HRMS (ESI, [M + Na]$^+$): calcd for $C_{31}H_{43}NNaO_5Si$, 560.2803: found, 560.2794. $[\alpha]_D^{23}$: +14.0 (*c* 1.06, $CHCl_3$).

*(R,E)-8-(tert-Butyldiphenylsilanyloxy)-5-(4-methoxybenzyloxy)-2-methyloct-2-en-1-ol (**18**).* To a stirred solution of (*S*)-3-[(*R*,*E*)-8-(*tert*-butyldiphenylsilanyloxy)-5-hydroxy-2-methyloct-2-enoyl]-4-(propan-2-yl)-1,3-oxazolidin-2-one (**17**) (3.00 g, 5.58 mmol) in dry CH_2Cl_2 (73 mL) were added PMBOC(=NH)CCl_3 (3.2 mL, 16 mmol) and $TrBF_4$ (61 mg, 0.19 mmol) successively at 0 °C. The resulting mixture was stirred at room temperature for 30 min. The mixture was concentrated *in vacuo*, and the residue was purified by column chromatography (EtOAc:hexane = 1:4) to afford PMB ether, which was used for the next reaction without further purification. To a stirred solution of PMB ether in dry Et_2O (56 mL) were added MeOH (0.54 mL, 13 mmol) and $LiBH_4$ (0.32 g, 13 mmol, 90% assay) successively at 0 °C. The resulting mixture was stirred at the same temperature for 10 min. To the mixture was added saturated aqueous NH_4Cl solution to quench the reaction. The resulting mixture was extracted with EtOAc twice. The combined organic phases were washed with brine, dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The residue was purified by column chromatography (EtOAc:hexane = 1:8) to yield (*R*,*E*)-8-(*tert*-butyldiphenylsilanyloxy)-5-(4-methoxybenzyloxy)-2-methyloct-2-en-1-ol (**18**) (2.51 g, 4.70 mmol, 84% from (*S*)-3-[(*R*,*E*)-8-(*tert*-butyldiphenylsilanyloxy)-5-hydroxy-2-methyloct-2-enoyl]-4-(propan-2-yl)-1,3-oxazolidin-2-one (**17**)) as a pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.04 (9H, s), 1.27 (1H, brs), 1.52−1.73 (4H, m), 1.67 (3H, s), 2.22−2.35 (2H, m), 3.39−3.44 (1H, m), 3.65 (2H, t, *J* = 5.6 Hz), 3.79 (3H, s), 3.99 (2H, s), 4.40 (1H, d, *J* = 11.2 Hz), 4.46 (1H, d, *J* = 11.2 Hz), 5.44 (1H, t, *J* = 7.3 Hz), 6.85 (2H, d *J* = 8.8 Hz), 7.23 (2H, d, *J* = 8.8 Hz), 7.35−7.44 (6H, m), 7.66 (4H, dd, *J* = 1.5, 7.8 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.9, 19.2, 26.8, 28.4, 30.1, 32.0, 55.3, 63.8, 68.9, 70.5, 78.1, 113.7, 122.1, 127.6, 129.3, 129.5, 130.9, 134.0, 134.0, 135.5, 136.5, 159.1 (one carbon of benzene ring was nonequivalence). IR (neat): 3421, 2930, 2857, 1513, 1248 cm^{-1}. LRMS (ESI) *m*/*z*: 555 ([M + Na]$^+$). HRMS (ESI, [M + Na]$^+$): calcd for $C_{33}H_{44}O_4NaSi$, 555.2901: found, 555.2887. $[\alpha]_D^{25}$ +8.2 (*c* 0.57, $CHCl_3$).

*(2R,3R,5R)-8-(tert-Butyldiphenylsilanyloxy)-2.3-epoxy-5-(4-methoxybenzyloxy)-2-methyloctan-1-ol (**19**).* To a stirred suspension of activated MS 4A (130 g) in dry CH_2Cl_2 (500 mL) were added $Ti(Oi\text{-}Pr)_4$ (6.9 mL, 23 mmol), (−)-DIPT (5.8 mL, 28 mmol), TBHP (39 mL, 0.23 mol), and (2*E*,5*R*)-8-(*tert*-butyldiphenylsilanyloxy)-5-(4-methoxybenzyloxy)-2-methyloct-2-en-1-ol (**18**) (62.0 g, 116 mmol) in dry CH_2Cl_2 (100 mL) successively at 0 °C. The resulting mixture was stirred at the same temperature for 1 h. To the mixture was added saturated aqueous $Na_2S_2O_3$ solution to quench the reaction. The resulting mixture was filtered through a pad of Celite, dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The residue was purified by column chromatography (EtOAc:hexane = 1:4) to yield (2*R*,3*R*,5*R*)-8-(*tert*-butyldiphenylsilanyloxy)-2.3-epoxy-5-(4-methoxybenzyloxy)-2-methyloctan-1-ol (**19**) (60.7 g, 111 mmol, 95%) as a pale yellow oil. The diastereomer was not separated because stereocenters of C4 and C5 will be lost by oxidation of (2*S*,5*S*,6*R*,8*R*,11*E*,13*E*,15*R*,16*R*,17*E*)-and (2*R*,5*S*,6*R*,8*R*,11*E*,13*E*,15*R*,16*R*,17*E*)-5,15,17-trimethyl-2,8,16-tris(triethylsilanyloxy)henicosa-11,13,17-trien-3,4,6-triol (**31a−b**). The diastereomeric ratio (88:12) was revealed in the next reaction. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.05 (9H, s), 1.26 (3H, s), 1.58−1.87 (7H, m), 3.14 (1H, t, *J* = 6.3 Hz), 3.51−3.58 (2H, m), 3.62−3.68 (3H, m), 3.79 (3H, s), 4.44 (2H, s), 6.85 (2H, d, *J* = 8.5 Hz), 7.24 (2H, d, *J* = 8.5 Hz), 7.35−7.44 (6H, m), 7.66 (4H, dd, *J* = 1.5, 7.8 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.4, 19.2, 26.9, 28.3, 30.2, 32.6, 55.3, 57.3, 60.3, 63.7, 65.4, 70.4, 76.2, 113.8, 127.6, 129.3, 129.5, 130.7, 134.0, 135.6, 159.1. IR (neat): 3442, 2953, 2931, 2858, 1612, 1513, 1248 cm^{-1}. LRMS (ESI) *m*/*z*: 571 ([M + Na]$^+$). HRMS (ESI, [M + Na]$^+$): calcd for $C_{33}H_{44}O_5NaSi$, 571.2850: found, 571.2835. $[\alpha]_D^{25}$: +2.6 (*c* 1.03, $CHCl_3$).

dx.doi.org/10.1021/jo502198y | *J. Org. Chem.* 2015, 80, 114−132

*(2S,3R,5R)-8-(tert-Butyldiphenylsilanyloxy)-2.3-epoxy-5-(4-methoxybenzyloxy)-2-methyloctan-1-al (**20**).* To a stirred solution of (2*R*,3*R*,5*R*)-8-(*tert*-butyldiphenylsilanyloxy)-2.3-epoxy-5-(4-methoxybenzyloxy)-2-methyloctan-1-ol (**19**) (60.7 g, 111 mmol) in dry CH_2Cl_2 (420 mL) and dry DMSO (83 mL) were added NEt_3 (93 mL, 0.67 mol) and SO_3·Py (53 g, 0.33 mol) successively at 0 °C. The resulting mixture was stirred at room temperature for 20 min. To the mixture was added saturated aqueous NH_4Cl solution to quench the reaction at 0 °C. The resulting mixture was extracted with CH_2Cl_2 twice. The combined organic phases were washed with brine, dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by column chromatography (EtOAc:hexane = 1:4) to yield (2*S*,3*R*,5*R*)-8-(*tert*-butyldiphenylsilanyloxy)-2.3-epoxy-5-(4-methoxybenzyloxy)-2-methyloctan-1-al (**20**) (50.4 g, 92.2 mmol, 83%) as a pale yellow oil. The diastereomeric ratio (88:12) was revealed by ^{1}H NMR. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.05 (9H, s), 1.36 (2.64H, s), 1.39 (0.36H, s), 1.59−1.87 (6H, m), 3.26 (1H, dd, J = 4.9, 6.6 Hz), 3.57 (1H, tt, J = 5.6, 5.6 Hz), 3.68 (2H, t, J = 6.1 Hz), 3.80 (3H, s), 4.40 (1H, d, J = 11.2 Hz), 4.47 (1H, d, J = 11.2 Hz), 6.85 (2H, d, J = 8.5 Hz), 7.22 (2H, d, J = 8.5 Hz), 7.35−7.45 (6H, m), 7.66 (4H, dd, J = 1.5, 7.8 Hz), 8.80 (0.88H, s), 8.83 (0.12H, s). ^{13}C NMR (100 MHz, $CDCl_3$): δ 10.1, 19.2, 26.9, 28.2, 30.0, 32.3, 55.3, 57.1, 61.6, 63.6, 70.5, 75.8, 113.8, 127.6, 129.3, 129.6, 130.3, 133.9, 135.6, 159.2, 200.0. IR (neat): 2931, 2858, 1728, 1513, 1248, 1112 cm^{-1}. LRMS (ESI) m/z: 569 ([M + Na]$^+$). HRMS (ESI, [M + Na]$^+$): calcd for $C_{33}H_{42}O_5NaSi$, 569.2694: found, 569.2681. $[\alpha]_D^{25}$: −25.1 (c 0.75, $CHCl_3$).

*Ethyl (4R,5R,7R,E)-10-(tert-butyldiphenylsilanyloxy)-4,5-epoxy-7-(4-methoxybenzyloxy)-4-methyldec-2-enoate (**21**).* To a stirred solution of triethyl phosphonoacetate (1.7 mL, 8.3 mmol) in dry THF (42 mL) was added NaH (0.31 g, 7.8 mmol, 60% assay) at 0 °C, and the resulting mixture was stirred at the same temperature for 30 min. Then, a solution of (2*S*,3*R*,5*R*)-8-(*tert*-butyldiphenylsilanyloxy)-2.3-epoxy-5-(4-methoxybenzyloxy)-2-methyloctan-1-al (**20**) (3.04 g, 5.56 mmol) in dry THF (14 mL) was added to the mixture at −78 °C. After being stirred at the same temperature for 30 min, the resulting mixture was warmed up to 0 °C and stirred for another 30 min. To the mixture was added saturated aqueous NH_4Cl solution to quench the reaction at 0 °C. The resulting mixture was extracted with EtOAc twice. The combined organic phases were washed with brine, dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by column chromatography (EtOAc:hexane = 1:4) to yield ethyl (4*R*,5*R*,7*R*,*E*)-10-(*tert*-butyldiphenylsilanyloxy)-4,5-epoxy-7-(4-methoxybenzyloxy)-4-methyldec-2-enoate (**21**) (3.33 g, 5.40 mmol, 97%, *E*:*Z* = 93:7) as a pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.05 (9H, s), 1.29 (3H, t, J = 7.1 Hz), 1.39 (3H, s), 1.57−1.73 (4H, m), 1.78−1.88 (2H, m), 2.96 (1H, t, J = 5.9 Hz), 3.52−3.58 (1H, m), 3.65−3.68 (2H, m), 3.79 (3H, s), 4.20 (2H, q, J = 7.1 Hz), 4.43 (2H, s), 5.81 (0.07H, d, J = 11.5 Hz), 6.00 (0.93H, d, J = 15.6 Hz), 6.36 (0.07H, d, J = 11.5 Hz), 6.72 (0.93H, d, J = 15.6 Hz), 6.84 (2H, d, J = 8.5 Hz), 7.22 (2H, d, J = 8.5 Hz), 7.35−7.44 (6H, m), 7.66 (4H, d, J = 6.3 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.2, 15.4, 19.2, 26.9, 28.2, 30.1, 32.9, 55.2, 58.0, 60.5, 63.0, 63.7, 70.4, 76.0, 113.8, 121.6, 127.6, 129.3, 129.6, 130.5, 133.9, 135.5, 149.7, 159.2, 166.0. IR (neat): 2932, 2858, 1719, 1513, 1248, 1111 cm^{-1}. LRMS (ESI) m/z: 639 ([M + Na]$^+$). HRMS (ESI, [M + Na]$^+$): calcd for $C_{37}H_{48}O_6NaSi$, 639.3112: found, 639.3097. $[\alpha]_D^{22}$: −6.5 (c 1.04, $CHCl_3$).

*Ethyl (4R,5R,7R,E)-10-(tert-Butyldiphenylsilanyloxy)-7-(4-methoxybenzyloxy)-4-methyl-5-triethylsilanyloxydec-2-enoate (**22**).* To a stirred solution of $Pd_2(dba)_3$·$CHCl_3$ (1.1 g, 1.1 mmol) in dry 1,4-dioxane (250 mL) were added Bu_3P (0.27 mL, 1.1 mmol), a solution of HCO_2H (8.0 mL, 0.20 mol), and NEt_3 (11 mL, 80 mmol) in dry 1,4-dioxane (60 mL) successively at room temperature, and the resulting mixture was stirred at the same temperature for 5 min. Then, a solution of ethyl (4*R*,5*R*,7*R*,*E*)-10-(*tert*-butyldiphenylsilanyloxy)-4,5-epoxy-7-(4-methoxybenzyloxy)-4-methyldec-2-enoate (**21**) (26.0 g, 42.1 mmol) in dry 1,4-dioxane (70 mL) was added to the mixture at room temperature. After being stirred at the same temperature for 5.5 h, the mixture was concentrated *in vacuo* and the residue was purified by column chromatography (EtOAc:hexane = 1:4) to afford an alcohol, which was used for the next reaction without further purification. To a stirred solution of the above alcohol in dry CH_2Cl_2 (126 mL) were added imidazole (8.6 g, 0.13 mol), DMAP (1.0 g, 8.4 mmol), and TESCl (11 mL, 63 mmol) successively at 0 °C. The resulting mixture was stirred at the same temperature for 8 h. To the mixture was added saturated aqueous NH_4Cl solution to quench the reaction. The resulting mixture was extracted with CH_2Cl_2 twice. The combined organic phases were washed with brine, dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The residue was purified by column chromatography (EtOAc:hexane = 1:19) to yield ethyl (4*R*,5*R*,7*R*,*E*)-10-(*tert*-butyldiphenylsilanyloxy)-7-(4-methoxybenzyloxy)-4-methyl-5-triethylsilanyloxydec-2-enoate (**22**) (24.8 g, 33.8 mmol, 80% from ethyl (4*R*,5*R*,7*R*,*E*)-10-(*tert*-butyldiphenylsilanyloxy)-4,5-epoxy-7-(4-methoxybenzyloxy)-4-methyldec-2-enoate (**21**)) as a pale yellow oil. The *Z* isomer of ethyl (4*R*,5*R*,7*R*,*E*)-10-(*tert*-butyldiphenylsilanyloxy)-4,5-epoxy-7-(4-methoxybenzyloxy)-4-methyldec-2-enoate (**21**) was converted into the C4 diastereomer of ethyl (4*R*,5*R*,7*R*,*E*)-10-(*tert*-butyldiphenylsilanyloxy)-7-(4-methoxybenzyloxy)-4-methyl-5-triethylsilanyloxydec-2-enoate (**22**). This diastereomer was not separated because the stereocenter of C4 will be lost by oxidation of (2*S*,5*S*,6*R*,8*R*,11*E*,13*E*,15*R*,16*R*,17*E*)- and (2*R*,5*S*,6*R*,8*R*,11*E*,13*E*,15*R*,16*R*,17*E*)-5,15,17-trimethyl-2,8,16-tris(triethylsilanyloxy)henicosa-11,13,17-trien-3,4,6-triol (**31a**−**b**). ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.57 (6H, q, J = 7.8 Hz), 0.91−0.98 (12H, m), 1.06 (9H, s), 1.29 (3H, t, J = 7.1 Hz), 1.51−1.74 (6H, m), 2.34−2.42 (1H, m), 3.39−3.45 (1H, m), 3.64−3.70 (2H, m), 3.74−3.79 (1H, m), 3.80 (3H, s), 4.19 (2H, m), 4.35 (1H, d, J = 11.2 Hz), 4.40 (1H, d, J = 11.2 Hz), 5.75 (1H, dd, J = 1.0, 15.9 Hz), 6.85 (2H, d, J = 8.5 Hz), 7.01 (1H, dd, J = 7.1, 15.9 Hz), 7.21 (2H, d, J = 8.5 Hz), 7.36−7.44 (6H, m), 7.67 (4H, dd, J = 1.2, 7.8 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ 5.1, 6.9, 13.2, 14.3, 19.2, 26.8, 28.1, 29.8, 38.6, 41.4, 55.2, 60.1, 64.0, 70.1, 72.2, 75.2, 113.7, 120.9, 127.6, 129.3, 129.5, 130.8, 134.0, 135.5, 151.8, 159.0, 166.6. IR (neat): 2955, 2875, 1719, 1513, 1248, 1091 cm^{-1}. LRMS (ESI) m/z: 755 ([M + Na]$^+$). HRMS (ESI, [M + Na]$^+$): calcd for $C_{43}H_{64}O_6NaSi_2$, 755.4134: found, 755.4118. $[\alpha]_D^{24}$: +6.8 (c 1.08, $CHCl_3$).

*(5R,6R,8R,E)-11-(tert-Butyldiphenylsilanyloxy)-8-(4-methoxybenzyloxy)-5-methyl-6-triethylsilanyloxyundec-3-en-2-one (**23**).* To a stirred solution of ethyl (4*R*,5*R*,7*R*,*E*)-10-(*tert*-butyldiphenylsilanyloxy)-7-(4-methoxybenzyloxy)-4-methyl-5-triethylsilanyloxydec-2-enoate (**22**) (13.4 g, 18.3 mmol) in dry toluene (37 mL) was added DIBAL (40 mL, 40 mmol, 1.0 M in toluene) at −78 °C, and the resulting mixture was stirred at the same temperature for 40 min. Then, MeOH (4.0 mL) was added to the mixture. After being stirred at −78 °C for 15 min, the reaction mixture was poured into saturated aqueous Rochell salt solution (80 mL), and the mixture was stirred at room temperature until the mixture turned into a clear solution. The resulting mixture was extracted with EtOAc twice. The combined organic phases were washed with brine, dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The residue was purified by column chromatography (EtOAc:hexane = 1:4) to yield (4*R*,5*R*,7*R*,*E*)-10-(*tert*-butyldiphenylsilanyloxy)-7-(4-methoxybenzyloxy)-4-methyl-5-triethylsilanyloxydec-2-en-1-ol (**S14**) (12.4 g, 17.9 mmol, 98%) as a pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.57 (6H, q, J = 7.8 Hz), 0.92−0.96 (12H, m), 1.06 (9H, s), 1.28 (1H, brs), 1.49−1.75 (6H, m), 2.24−2.34 (1H, m), 3.42−3.48 (1H, m), 3.64−3.70 (3H, m), 3.79 (3H, s), 4.10 (2H, d, J = 5.6 Hz), 4.38 (2H, d, J = 2.7 Hz), 5.57 (1H, dt, J = 15.6, 5.6 Hz), 5.72 (1H, dd, J = 6.8, 15.6 Hz), 6.85 (2H, d, J = 8.5 Hz), 7.22 (2H, d, J = 8.5 Hz), 7.35−7.44 (6H, m), 7.67 (4H, dd, J = 1.5, 7.8 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ 5.2, 7.0, 14.5, 19.2, 26.9, 28.1, 29.9, 38.4, 41.5, 55.3, 64.0, 64.1, 70.2, 73.1, 75.7, 113.7, 127.6, 128.8, 129.3, 129.5, 131.1, 134.0, 135.4, 135.5, 159.0. IR (neat): 3428, 2954, 2874, 1612, 1513, 1428, 1248, 1111 cm^{-1}. LRMS (ESI) m/z: 713 ([M + Na]$^+$). HRMS (ESI, [M + Na]$^+$): calcd for $C_{41}H_{62}O_5NaSi_2$, 713.4028: found, 713.4019. $[\alpha]_D^{21}$: +9.3 (c 1.08, $CHCl_3$). To a stirred solution of (4*R*,5*R*,7*R*,*E*)-10-(*tert*-butyldiphenylsilanyloxy)-7-(4-methoxybenzyloxy)-4-methyl-5-triethylsilanyloxydec-2-en-1-ol (**S14**) (2.24 g, 3.24 mmol) in dry CH_2Cl_2 (32 mL) were added $NaHCO_3$ (2.0 g, 24 mmol) and DMP (2.1 g, 4.9 mmol) successively at 0 °C. The resulting mixture was stirred at room temperature

dx.doi.org/10.1021/jo502198y | J. Org. Chem. 2015, 80, 114−132

for 40 min. To the mixture was added saturated aqueous $Na_2S_2O_3$ solution to quench the reaction at 0 °C. The resulting mixture was extracted with CH_2Cl_2 twice. The combined organic phases were washed with brine, dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The residue was purified by column chromatography (EtOAc:hexane = 1:9) to yield (4*R*,5*R*,7*R*,*E*)-10-(*tert*-butyldiphenylsilanyloxy)-7-(4-methoxybenzyloxy)-4-methyl-5-triethylsilanyloxydec-2-en-1-al (**S15**) (2.21 g, 3.21 mmol, 99%) as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.57 (6H, q, J = 7.8 Hz), 0.94 (9H, t, J = 7.8 Hz), 1.01 (3H, d, J = 6.8 Hz), 1.06 (9H, s), 1.53−1.73 (6H, m), 2.47−2.57 (1H, m), 3.41−3.46 (1H, m), 3.65−3.71 (2H, m), 3.78−3.81 (1H, m), 3.79 (3H, s), 4.33 (1H, d, J = 11.2 Hz), 4.42 (1H, d, J = 11.2 Hz), 6.04 (1H, ddd, J = 1.2, 7.8, 15.9 Hz), 6.84−6.90 (3H, m), 7.20 (2H, d, J = 8.5 Hz), 7.36−7.44 (6H, m), 7.67 (4H, dd, J = 1.2, 7.8 Hz), 9.50 (1H, d, J = 7.8 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ 5.1, 6.9, 13.0, 19.2, 26.9, 28.0, 29.8, 38.5, 41.8, 55.3, 63.9, 70.1, 72.0, 75.1, 113.7, 127.6, 129.3, 129.6, 130.7, 132.4, 133.9, 135.5, 159.1, 161.4, 194.1. IR (neat): 2954, 2875, 1693, 1513, 1248, 1111 cm^{-1}. LRMS (EI) m/z: 688 ([M]$^+$). HRMS (EI, [M]$^+$): calcd for $C_{41}H_{60}O_5Si_2$, 688.3979: found, 688.3965. $[\alpha]_D^{23}$: +11.3 (*c* 1.00, $CHCl_3$). To a stirred solution of (4*R*,5*R*,7*R*,*E*)-10-(*tert*-butyldiphenylsilanyloxy)-7-(4-methoxybenzyloxy)-4-methyl-5-triethylsilanyloxydec-2-en-1-al (**S15**) (16.6 mg, 0.0241 mmol) in dry THF (0.24 mL) was added MeLi (93 μL, 0.048 mmol, 0.52 M in Et_2O) at −78 °C, and the resulting mixture was stirred at the same temperature for 30 min. To the mixture was added saturated aqueous NH_4Cl solution to quench the reaction. The resulting mixture was extracted with EtOAc twice. The combined organic phases were washed with brine, dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The residue was purified by column chromatography (EtOAc:hexane = 1:9) to yield (5*R*,6*R*,8*R*,*E*)-11-(*tert*-butyldiphenylsilanyloxy)-8-(4-methoxybenzyloxy)-5-methyl-6-triethylsilanyloxyundec-3-en-2-ol (**S16**) (14.2 mg, 0.0201 mmol, 84%) as a pale yellow oil and a mixture of diastereomers. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.57 (6H, q, J = 7.8 Hz), 0.91−0.96 (12H, m), 1.05 (9H, s), 1.25 (3H, d, J = 6.3 Hz), 1.42 (1H, brs), 1.49−1.72 (6H, m), 2.20−2.28 (1H, m), 3.42−3.48 (1H, m), 3.65−3.70 (3H, m), 3.79 (3H, s), 4.26 (1H, dq, J = 6.3, 6.3 Hz), 4.36 (1H, d, J = 11.2 Hz), 4.40 (1H, d, J = 11.2 Hz), 5.45 (1H, dd, J = 6.6, 15.6 Hz), 5.62−5.70 (1H, m), 6.85 (2H, d, J = 8.5 Hz), 7.22 (2H, d, J = 8.5 Hz), 7.35−7.44 (6H, m), 7.67 (4H, dd, J = 1.2, 7.6 Hz). IR (neat): 3422, 2955, 2875, 1513, 1428, 1248, 1111 cm^{-1}. LRMS (EI) m/z: 704 ([M]$^+$). HRMS (EI, [M]$^+$): calcd for $C_{42}H_{64}O_5Si_2$, 704.4292: found, 704.4297. To a stirred solution of (5*R*,6*R*,8*R*,*E*)-11-(*tert*-butyldiphenylsilanyloxy)-8-(4-methoxybenzyloxy)-5-methyl-6-triethylsilanyloxyundec-3-en-2-ol (**S16**) (11.5 g, 16.3 mmol) in dry CH_2Cl_2 (50 mL) were added $NaHCO_3$ (7.5 g, 90 mmol) and DMP (8.3 g, 20 mmol) successively at 0 °C. The resulting mixture was stirred at room temperature for 1.5 h. To the mixture was added saturated aqueous $Na_2S_2O_3$ solution to quench the reaction at 0 °C. The resulting mixture was extracted with CH_2Cl_2 twice. The combined organic phases were washed with brine, dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The residue was purified by column chromatography (EtOAc:hexane = 1:9) to yield (5*R*,6*R*,8*R*,*E*)-11-(*tert*-butyldiphenylsilanyloxy)-8-(4-methoxybenzyloxy)-5-methyl-6-triethylsilanyloxyundec-3-en-2-one (**23**) (10.6 g, 15.1 mmol, 92%) as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.57 (6H, q, J = 8.0 Hz), 0.92−0.99 (12H, m), 1.06 (9H, s), 1.53−1.71 (6H, m), 2.23 (3H, s), 2.35−2.43 (1H, m), 3.40−3.45 (1H, m), 3.67−3.69 (2H, m), 3.77−3.81 (1H, m), 3.79 (3H, s), 4.33 (1H, d, J = 11.4 Hz), 4.42 (1H, d, J = 11.4 Hz), 5.98 (1H, dd, J = 1.2, 16.2 Hz), 6.79−6.87 (3H, m), 7.21 (2H, d, J = 8.7 Hz), 7.35−7.44 (6H, m), 7.64−7.68 (4H, m). ^{13}C NMR (100 MHz, $CDCl_3$): δ 5.1, 6.9, 13.2, 19.2, 26.7, 26.9, 28.0, 29.8, 38.7, 41.5, 55.3, 64.0, 70.1, 72.2, 75.2, 113.7, 127.6, 129.1, 129.3, 129.6, 130.8, 134.0, 135.5, 151.0, 159.1, 198.7. IR (neat): 2954, 2875, 1677, 1513, 1249, 1090 cm^{-1}. LRMS (ESI) m/z: 725 ([M + Na]$^+$). HRMS (ESI, [M + Na]$^+$): calcd for $C_{42}H_{62}O_5NaSi_2$, 725.4028: found, 725.4015. $[\alpha]_D^{28}$: +7.5 (*c* 0.80, $CHCl_3$).

*(2S,5R,6R,8R,E)-11-(tert-Butyldiphenylsilanyloxy)-8-(4-methoxybenzyloxy)-5-methyl-6-triethylsilanyloxyundec-3-en-2-ol (**24a**).* To a stirred solution of (*R*)-Me-CBS (3.2 g, 12 mmol) in dry toluene (48 mL) was added BH_3·THF (11 mL, 11 mmol, 1.0 M in THF) at 0 °C, and the resulting mixture was stirred at the same temperature for 10 min. Then, a solution of (5*R*,6*R*,8*R*,*E*)-11-(*tert*-butyldiphenylsilanyloxy)-8-(4-methoxybenzyloxy)-5-methyl-6-triethylsilanyloxyundec-3-en-2-one (**23**) (4.80 g, 6.83 mmol) in dry toluene (20 mL) was added to the mixture at −78 °C. After being stirred at the same temperature for 5 h, the mixture was treated with MeOH to quench the reaction. The mixture was concentrated *in vacuo*, and the residue was purified by column chromatography (EtOAc:hexane = 1:4) to give a quantitative yield of (2*S*,5*R*,6*R*,8*R*,*E*)-11-(*tert*-butyldiphenylsilanyloxy)-8-(4-methoxybenzyloxy)-5-methyl-6-triethylsilanyloxyundec-3-en-2-ol (**24a**) (*dr* > 95:5) as a pale yellow oil. The absolute configuration was determined by Mosher's method (Figure S4, Supporting Information[20]). ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.57 (6H, q, J = 8.0 Hz), 0.92−0.96 (12H, m), 1.05 (9H, s), 1.25 (3H, d, J = 6.3 Hz), 1.50−1.73 (7H, m), 2.17−2.31 (1H, m), 3.40−3.57 (1H, m), 3.65−3.69 (3H, m), 3.79 (3H, s), 4.23−4.31 (1H, m), 4.36 (1H, d, J = 11.2 Hz), 4.40 (1H, d, J = 11.2 Hz), 5.45 (1H, ddd, J = 1.0, 6.6, 15.6 Hz), 5.65 (1H, dd, J = 7.3, 15.6 Hz), 6.84 (2H, d, J = 8.5 Hz), 7.22 (2H, d, J = 8.5 Hz), 7.35−7.44 (6H, m), 7.67 (dd, J = 1.5, 7.8 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ 5.2, 7.0, 14.5, 19.2, 23.3, 26.9, 28.1, 30.0, 38.6, 41.4, 55.3, 64.1, 69.1, 70.2, 73.1, 75.7, 113.7, 127.6, 129.3, 129.5, 131.1, 133.5, 133.9, 134.0, 135.6, 159.0. IR (neat): 3420, 2955, 2875, 1513, 1248, 1111 cm^{-1}. LRMS (FAB) m/z: 727 ([M + Na]$^+$). HRMS (FAB, [M + Na]$^+$): calcd for $C_{42}H_{64}O_5NaSi_2$, 727.4184: found, 727.4203. $[\alpha]_D^{27}$: +1.3 (*c* 0.87, $CHCl_3$).

*(2R,5R,6R,8R,E)-11-(tert-Butyldiphenylsilanyloxy)-8-(4-methoxybenzyloxy)-5-methyl-6-triethylsilanyloxyundec-3-en-2-ol (**24b**).* Using the same procedure as above, a quantitative yield of (2*R*,5*R*,6*R*,8*R*,*E*)-11-(*tert*-butyldiphenylsilanyloxy)-8-(4-methoxybenzyloxy)-5-methyl-6-triethylsilanyloxyundec-3-en-2-ol (**24b**) (pale yellow oil, *dr* > 95:5) was obtained from (5*R*,6*R*,8*R*,*E*)-11-(*tert*-butyldiphenylsilanyloxy)-8-(4-methoxybenzyloxy)-5-methyl-6-triethylsilanyloxyundec-3-en-2-one (**23**) (4.20 g, 5.97 mmol), (*S*)-Me-CBS (2.8 g, 10 mmol), and BH_3·THF (9.6 mL, 9.6 mmol, 1.0 M in THF). The absolute configuration was determined by Mosher's method (Figure S5, Supporting Information[20]). ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.57 (6H, q, J = 8.0 Hz), 0.91−0.96 (12H, m), 1.06 (9H, s), 1.25 (3H, d, J = 6.3 Hz), 1.49−1.72 (7H, m), 2.20−2.28 (1H, m), 3.42−3.47 (1H, m), 3.65−3.70 (3H, m), 3.79 (3H, s), 4.23−4.30 (1H, m), 4.36 (1H, d, J = 11.2 Hz), 4.40 (1H, d, J = 11.2 Hz), 5.45 (1H, ddd, J = 1.0, 6.6, 15.6 Hz), 5.67 (1H, dd, J = 6.8, 15.6 Hz), 6.85 (2H, d, J = 8.5 Hz), 7.22 (2H, d, J = 8.5 Hz), 7.35−7.44 (6H, m), 7.67 (dd, J = 1.5, 7.8 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ 5.2, 7.0, 14.4, 19.2, 23.4, 26.9, 28.1, 30.0, 38.5, 41.2, 55.3, 64.1, 69.1, 70.2, 73.1, 75.7, 113.7, 127.6, 129.3, 129.5, 131.1, 133.3, 133.8, 134.0, 135.6, 159.0. IR (neat): 3436, 2955, 2875, 1513, 1248, 1112 cm^{-1}. LRMS (ESI) m/z: 727 ([M + Na]$^+$). HRMS (ESI, [M + Na]$^+$): calcd for $C_{42}H_{64}O_5NaSi_2$, 727.4184: found, 727.4171. $[\alpha]_D^{25}$: +9.2 (*c* 0.99, $CHCl_3$).

*(2S,5R,6R,8R,E)-11-(tert-Butyldiphenylsilanyloxy)-2,8-bis(4-methoxybenzyloxy)-5-methylundec-3-en-6-ol (**25a**).* To a stirred solution of (2*S*,5*R*,6*R*,8*R*,*E*)-11-(*tert*-butyldiphenylsilanyloxy)-8-(4-methoxybenzyloxy)-5-methyl-6-triethylsilanyloxyundec-3-en-2-ol (**24a**) (956 mg, 1.36 mmol) in dry toluene (14 mL) were added PMBOC(=NH)CCl_3 (0.85 mL, 4.1 mmol) and La(OTf)$_3$ (80 mg, 0.14 mmol) successively at 0 °C. After being stirred at room temperature for 2 h, the mixture was treated with saturated aqueous $NaHCO_3$ solution to quench the reaction at 0 °C. The resulting mixture was extracted with EtOAc twice. The combined organic phases were washed with brine, dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by column chromatography (EtOAc:hexane = 1:19) to afford PMB ether, which was used for the next reaction without further purification. To a stirred solution of PMB ether in CH_2Cl_2 (7.0 mL) and EtOH (7.0 mL) was added CSA (32 mg, 0.14 mmol) at 0 °C. After being stirred at room temperature for 50 min, the mixture was treated with saturated aqueous $NaHCO_3$ solution to quench the reaction. The resulting mixture was extracted with EtOAc twice. The combined organic phases were washed with brine, dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The residue was purified by column chromatography (EtOAc:hexane = 1:4) to yield (2*S*,5*R*,6*R*,8*R*,*E*)-11-(*tert*-butyldiphenylsilanyloxy)-2,8-bis(4-methoxybenzyloxy)-5-methylundec-3-en-6-ol (**25a**) (691 mg,

dx.doi.org/10.1021/jo502198y | *J. Org. Chem.* 2015, 80, 114−132

0.972 mmol, 71% from (2*S*,5*R*,6*R*,8*R*,*E*)-11-(*tert*-butyldiphenylsilanyloxy)-8-(4-methoxybenzyloxy)-5-methyl-6-triethylsilanyloxyundec-3-en-2-ol (**24a**)) as a pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.03−1.09 (12H, m), 1.24 (3H, d, J = 6.3 Hz), 1.52−1.74 (6H, m), 2.21−2.26 (1H, m), 3.59−3.68 (5H, m), 3.77 (3H, s), 3.79 (3H, s), 3.83−3.89 (1H, m), 4.28 (1H, d, J = 11.2 Hz), 4.34 (1H, d, J = 11.2 Hz), 4.47 (1H, d, J = 11.2 Hz), 4.55 (1H, d, J = 11.2 Hz), 5.40 (1H, dd, J = 7.6, 15.6 Hz), 5.59 (1H, dd, J = 7.8, 15.6 Hz), 6.84 (2H, d, J = 8.8 Hz), 6.85 (2H, d, J = 8.8 Hz), 7.22 (2H, d, J = 8.8 Hz), 7.23 (2H, d, J = 8.8 Hz), 7.35−7.42 (6H, m), 7.66 (4H, dd, J = 1.5, 8.0 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ 15.6, 19.2, 21.8, 26.9, 27.4, 29.4, 37.8, 42.7, 55.2, 55.3, 63.8, 69.3, 70.1, 75.3, 75.4, 79.7, 113.7, 113.9, 127.6, 129.2, 129.5, 129.6, 130.0, 131.0, 132.3, 133.9, 135.3, 135.5, 159.0, 159.3. IR (neat): 3482, 2931, 2858, 1513, 1248 cm^{-1}. LRMS (ESI) m/z: 733 ([M + Na]$^+$). HRMS (ESI, [M + Na]$^+$): calcd for $C_{44}H_{58}O_6NaSi$, 733.3895: found, 733.3888. $[\alpha]_D^{28}$: −30.0 (c 0.92, $CHCl_3$).

*(2R,5R,6R,8R,E)-11-(tert-Butyldiphenylsilanyloxy)-2,8-bis(4-methoxybenzyloxy)-5-methylundec-3-en-6-ol (**25b**).* Using the same procedure as above, PMB ether was obtained from (2*R*,5*R*,6*R*,8*R*,*E*)-11-(*tert*-butyldiphenylsilanyloxy)-8-(4-methoxybenzyloxy)-5-methyl-6-triethylsilanyloxyundec-3-en-2-ol (**24b**) (4.30g, 6.10 mmol), PMBOC(=NH)CCl_3 (3.8 mL, 18 mmol), and La(OTf)$_3$ (358 mg, 0.610 mmol). (2*R*,5*R*,6*R*,8*R*,*E*)-11-(*tert*-Butyldiphenylsilanyloxy)-2,8-bis(4-methoxybenzyloxy)-5-methylundec-3-en-6-ol (**25b**) (3.95 g, 5.56 mmol, 91% from (2*R*,5*R*,6*R*,8*R*,*E*)-11-(*tert*-butyldiphenylsilanyloxy)-8-(4-methoxybenzyloxy)-5-methyl-6-triethylsilanyloxyundec-3-en-2-ol (**24b**), colorless oil) was obtained from the PMB ether and CSA (142 mg, 0.610 mmol). ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.02 (3H, d, J = 6.6 Hz), 1.05 (9H, s), 1.24 (3H, d, J = 6.3 Hz), 1.51−1.72 (6H, m), 2.20−2.29 (1H, m), 3.58−3.70 (5H, m), 3.76 (3H, s), 3.78 (3H, s), 3.85−3.90 (1H, m), 4.28 (1H, d, J = 11.0 Hz), 4.34 (1H, d, J = 11.0 Hz), 4.46 (1H, d, J = 11.2 Hz), 4.54 (1H, d, J = 11.2 Hz), 5.41 (1H, dd, J = 7.8, 15.6 Hz), 5.61 (1H, dd, J = 7.8, 15.6 Hz), 6.83 (2H, d, J = 8.5 Hz), 6.84 (2H, d, J = 8.5 Hz), 7.22 (4H, 2d, J = 8.5 Hz), 7.35−7.43 (6H, m), 7.64 (4H, dd, J = 1.5, 8.0 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ 15.3, 19.2, 21.8, 26.9, 27.5, 29.5, 37.9, 42.6, 55.2, 55.3, 63.8, 69.4, 70.1, 75.3, 75.5, 79.6, 113.8, 114.0, 127.6, 129.2, 129.5, 129.6, 130.0, 131.0, 132.3, 133.9, 135.2, 135.5, 159.0, 159.3. IR (neat): 3487, 2931, 2858, 1513, 1248, 1111 cm^{-1}. LRMS (ESI) m/z: 733 ([M + Na]$^+$). HRMS (ESI, [M + Na]$^+$): calcd for $C_{44}H_{58}O_6NaSi$, 733.3895: found, 733.3880. $[\alpha]_D^{27}$: +3.8 (c 0.86, $CHCl_3$).

*(2S,5S,6R,8R)-11-(tert-Butyldiphenylsilanyloxy)-2,8-bis(4-methoxybenzyloxy)-5-methylundecane-3,4,6-triol (**26a**).* To a stirred solution of (2*S*,5*R*,6*R*,8*R*,*E*)-11-(*tert*-butyldiphenylsilanyloxy)-2,8-bis(4-methoxybenzyloxy)-5-methylundec-3-en-6-ol (**25a**) (3.37 g, 4.73 mmol) in *t*-BuOH (23 mL) and H_2O (23 mL) were added NMO (1.8 g, 15 mmol) and OsO_4 (9.5 mL, 0.47 mmol, 0.05 M in THF) successively at room temperature. After being stirred at the same temperature for 17 h, the mixture was treated with saturated aqueous $Na_2S_2O_3$ solution to quench the reaction at 0 °C. The resulting mixture was extracted with EtOAc twice. The combined organic phases were washed with brine, dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by column chromatography (EtOAc:hexane = 1:1) to yield (2*S*,5*S*,6*R*,8*R*)-11-(*tert*-butyldiphenylsilanyloxy)-2,8-bis(4-methoxybenzyloxy)-5-methylundecane-3,4,6-triol (**26a**) (3.02 g, 4.05 mmol, 86%) as a yellow oil and a mixture of diastereomers. The diastereomeric ratio (2:1) was determined by ^{1}H NMR. The diastereomer was not separated because stereocenters of C2 and C3 will be lost by oxidation of (2*S*,5*S*,6*R*,8*R*,11*E*,13*E*,15*R*,16*R*,17*E*)-5,15,17-trimethyl-2,8,16-tris(triethylsilanyloxy)henicosa-11,13,17-trien-3,4,6-triol (**31a**). ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.84 (2.0H, d, J = 7.1 Hz), 0.91 (1.0H, d, J = 7.1 Hz), 1.06 (9H, s), 1.26 and 1.29 (3H, d, J = 6.3, 6.3 Hz), 1.41−1.96 (7H, m), 2.69−2.74 (0.7H, m), 3.33−3.89 (13.3H, m), 4.05−4.83 (6H, m), 6.84−6.89 (4H, m), 7.19−7.23 (4H, m), 7.36−7.44 (6H, m), 7.66 (4H, d, J = 7.6 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ 8.4, 11.9, 15.6, 16.4, 19.2, 26.9, 27.4, 29.3, 36.5, 39.0, 55.2, 55.2, 55.2, 63.8, 70.2, 70.3, 70.5, 71.2, 71.3, 72.1, 72.2, 73.6, 74.3, 74.7, 79.9, 80.1, 113.7, 113.8, 113.9, 114.0, 127.6, 129.3, 129.4, 129.5, 129.5, 129.5, 129.6, 129.8, 129.9, 130.2, 130.5, 133.9, 133.9, 135.5, 159.2, 159.3, 159.3, 159.3. IR (neat): 3441, 2933, 2858, 1514, 1249, 1111 cm^{-1}. LRMS (FAB) m/z: 745 ([M + H]$^+$). HRMS (FAB, [M + H]$^+$): calcd for $C_{44}H_{61}O_8Si$, 745.4130: found, 745.4120.

*(2R,5S,6R,8R)-11-(tert-Butyldiphenylsilanyloxy)-2,8-bis(4-methoxybenzyloxy)-5-methylundecane-3,4,6-triol (**26b**).* Using the same procedure as above, (2*R*,5*S*,6*R*,8*R*)-11-(*tert*-butyldiphenylsilanyloxy)-2,8-bis(4-methoxybenzyloxy)-5-methylundecane-3,4,6-triol (**26b**) (955 mg, 1.28 mmol, 70%, colorless oil, mixture of diastereomers) was obtained from (2*R*,5*R*,6*R*,8*R*,*E*)-11-(*tert*-butyldiphenylsilanyloxy)-2,8-bis(4-methoxybenzyloxy)-5-methylundec-3-en-6-ol (**25b**) (1.30 g, 1.83 mmol), NMO (686 mg, 5.86 mmol), and OsO_4 (3.6 mL, 0.18 mmol, 0.05 M in THF). The diastereomeric ratio (1.7:1.3) was determined by ^{1}H NMR. The diastereomer was not separated because stereocenters of C2 and C3 will be lost by oxidation of (2*R*,5*S*,6*R*,8*R*,11*E*,13*E*,15*R*,16*R*,17*E*)-5,15,17-trimethyl-2,8,16-tris(triethylsilanyloxy)henicosa-11,13,17-trien-3,4,6-triol (**31b**). ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.85 (1.7H, d, J = 7.1 Hz), 0.91 (1.3H, d, J = 7.3 Hz), 1.06 (9H, s), 1.23 and 1.25 (3H, d, J = 6.8, 6.3 Hz), 1.39−1.89 (7H, m), 2.77−2.78 (0.4H, m), 3.30−3.88 (13.6H, m), 4.09−4.82 (6H, m), 6.83−6.88 (4H, m), 7.18−7.27 (4H, m), 7.36−7.44 (6H, m), 7.66 (4H, dd, J = 1.5, 7.8 Hz). ^{13}C NMR (150 MHz, $CDCl_3$): δ 8.6, 11.2, 15.4, 16.3, 19.2, 26.9, 27.4, 27.5, 29.3, 29.4, 37.1, 38.0, 38.6, 39.6, 42.3, 55.3, 63.7, 63.8, 70.2, 70.2, 70.7, 70.9, 71.1, 71.7, 72.2, 73.0, 73.7, 74.1, 76.6, 79.8, 80.2, 113.8, 113.9, 113.9, 114.0, 127.6, 129.2, 129.4, 129.5, 129.5, 129.6, 129.6, 129.7, 129.8, 130.0, 130.2, 130.6, 133.9, 133.9, 135.5, 159.1, 159.3, 159.3, 159.4. IR (neat): 3445, 2932, 2858, 1513, 1249, 1111, 1035 cm^{-1}. LRMS (ESI) m/z: 767 ([M + Na]$^+$). HRMS (ESI, [M + Na]$^+$): calcd for $C_{44}H_{60}O_8NaSi$, 767.3950: found, 767.3936.

*(4R,6R,7S,10S)-4,10-Bis(4-methoxybenzyloxy)-7-methyl-6,8,9-triacetyloxyundecan-1-ol (**27a**).* To a stirred solution of (2*S*,5*S*,6*R*,8*R*)-11-(*tert*-butyldiphenylsilanyloxy)-2,8-bis(4-methoxybenzyloxy)-5-methylundecane-3,4,6-triol (**26a**) (3.00 g, 4.03 mmol) in dry CH_2Cl_2 (40 mL) were added DIPEA (10 mL, 61 mmol), DMAP (49 mg, 0.40 mmol), and Ac_2O (3.8 mL, 40 mmol) successively at 0 °C. After being stirred at room temperature for 22 h, the mixture was treated with saturated aqueous NH_4Cl solution to quench the reaction. The resulting mixture was extracted with CH_2Cl_2 twice. The combined organic phases were washed with brine, dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The residue was purified by column chromatography (EtOAc:hexane = 1:2) to yield (4*R*,6*R*,7*S*,10*S*)-1-(*tert*-butyldiphenylsilanyloxy)-4,10-bis(4-methoxybenzyloxy)-7-methyl-6,8,9-triacetyloxyundecane (**S22a**) (3.38 g, 3.88 mmol, 96%) as a pale yellow oil as a mixture of diastereomers. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.91 (1.0H, d, J = 7.1 Hz), 0.97 (2.0H, d, J = 6.8 Hz), 1.04 and 1.05 (9H, s), 1.15 (3H, d, J = 6.1 Hz), 1.55−1.63 (6H, m), 1.81−2.11 (10H, m), 3.36−3.88 (10H, m), 4.21−4.78 (4H, m), 4.93−5.31 (3H, m), 6.80−6.88 (4H, m), 7.17−7.27 (4H, m), 7.32−7.44 (6H, m), 7.67 (4H, dd, J = 1.7, 7.8 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ 9.8, 15.9, 19.2, 20.8, 20.8, 20.9, 20.9, 21.0, 21.2, 21.2, 26.9, 28.0, 28.0, 29.5, 30.0, 35.9, 36.0, 36.2, 37.9, 55.2, 55.2, 63.9, 64.0, 69.5, 69.7, 70.0, 70.4, 71.0, 71.4, 71.5, 72.3, 73.2, 73.5, 73.6, 74.8, 76.0, 76.3, 113.6, 113.7, 113.7, 113.7, 127.6, 127.6, 128.9, 129.1, 129.2, 129.4, 129.4, 129.5, 129.5, 129.7, 129.7, 130.5, 130.8, 134.0, 134.1, 135.5, 159.0, 159.2, 170.3, 170.4, 170.8. IR (neat): 2953, 2859, 1749, 1514, 1249 cm^{-1}. LRMS (ESI) m/z: 893 ([M + Na]$^+$). HRMS (ESI, [M + Na]$^+$): calcd for $C_{50}H_{66}O_{11}NaSi$, 893.4267: found, 893.4248. To a stirred solution of (4*R*,6*R*,7*S*,10*S*)-1-(*tert*-butyldiphenylsilanyloxy)-4,10-bis(4-methoxybenzyloxy)-7-methyl-6,8,9-triacetyloxyundecane (**S22a**) (3.38 g, 3.88 mmol) in dry THF (39 mL) were added AcOH (0.33 mL, 5.8 mmol) and TBAF (5.8 mL, 5.8 mmol, 1.0 M in THF) successively at 0 °C. After being stirred at room temperature for 28 h, the mixture was treated with saturated aqueous $NaHCO_3$ solution to quench the reaction. The resulting mixture was extracted with EtOAc twice. The combined organic phases were washed with brine, dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The residue was purified by column chromatography (EtOAc:hexane = 1:0) to yield (4*R*,6*R*,7*S*,10*S*)-4,10-bis(4-methoxybenzyloxy)-7-methyl-6,8,9-triacetyloxyundecan-1-ol (**27a**) (2.13 g, 3.37 mmol, 87%) as a yellow oil and a mixture of diastereomers. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.92 (1.0H, d, J = 6.8 Hz),

dx.doi.org/10.1021/jo502198y | J. Org. Chem. 2015, 80, 114−132

1.00 (2.0H, d, J = 6.8 Hz), 1.11−1.25 (3H, m), 1.49−1.80 (6H, m), 1.85−2.14 (10H, m), 3.54−3.58 (4H, m), 3.69−3.89 (7H, m), 4.29−4.62 (4H, m), 4.68−5.32 (3H, m), 6.79−6.87 (4H, m), 7.10−7.33 (4H, m). ^{13}C NMR (100 MHz, $CDCl_3$): δ 9.6, 9.8, 15.4, 15.8, 20.8, 20.8, 20.8, 20.9, 21.1, 27.8, 28.1, 29.4, 29.7, 36.0, 36.2, 36.9, 38.2, 55.2, 55.2, 62.2, 62.5, 69.4, 70.0, 70.1, 70.4, 71.0, 71.3, 71.6, 71.7, 73.2, 73.4, 73.5, 74.8, 75.3, 75.5, 113.6, 113.7, 129.1, 129.4, 129.5, 129.6, 129.8, 130.2, 130.4, 130.4, 159.2, 170.3, 170.4, 170.6, 170.8, 171.2. IR (neat): 3460, 2939, 2871, 1739, 1514, 1248, 1031 cm^{-1}. LRMS (ESI) m/z: 655 ([M + Na]$^+$). HRMS (ESI, [M + Na]$^+$): calcd for $C_{34}H_{48}O_{11}Na$, 655.3089: found, 655.3077.

*(4R,6R,7S,10R)-4,10-Bis(4-methoxybenzyloxy)-7-methyl-6,8,9-triacetyloxyundecan-1-ol (**27b**).* Using the same procedure as above, (4*R*,6*R*,7*S*,10*R*)-1-(*tert*-butyldiphenylsilanyloxy)-4,10-bis(4-methoxybenzyloxy)-7-methyl-6,8,9-triacetyloxyundecane (**S22b**) (991 mg, 1.14 mmol, 89%, pale yellow oil, mixture of diastereomers) was obtained from (2*R*,5*S*,6*R*,8*R*)-11-(*tert*-butyldiphenylsilanyloxy)-2,8-bis-(4-methoxybenzyloxy)-5-methylundecane-3,4,6-triol (**26b**) (955 mg, 1.28 mmol), Ac_2O (1.2 mL, 13 mmol), DIPEA (3.3 mL, 19 mmol), and DMAP (16 mg, 0.13 mmol). ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.92 (1.3H, d, J = 7.0 Hz), 1.00 (1.7H, d, J = 7.0 Hz), 1.04 and 1.05 (9H, s), 1.13 (1.3H, d, J = 6.3 Hz), 1.22 (1.7H, d, J = 6.0 Hz), 1.50−1.69 (6H, m), 1.86−2.08 (10H, m), 3.36−3.88 (10H, m), 4.24−4.77 (4H, m), 4.95−5.30 (3H, m), 6.75−6.86 (4H, m), 7.18−7.29 (4H, m), 7.34−7.43 (6H, m), 7.65−7.67 (4H, m). ^{13}C NMR (150 MHz, $CDCl_3$): δ 9.9, 10.0, 15.3, 16.1, 19.2, 20.8, 20.8, 20.8, 20.9, 20.9, 21.2, 26.9, 28.0, 28.0, 29.4, 29.7, 35.4, 36.0, 36.1, 37.9, 55.2, 55.2, 63.9, 63.9, 69.3, 69.7, 69.9, 70.5, 70.8, 71.1, 72.2, 72.2, 73.1, 73.5, 73.8, 74.7, 75.9, 76.0, 113.6, 113.7, 113.7, 127.6, 127.6, 128.9, 129.2, 129.4, 129.5, 129.5, 129.5, 130.2, 130.5, 130.8, 130.8, 134.0, 134.0, 135.5, 159.0, 159.0, 159.1, 159.2, 170.2, 170.2, 170.4, 170.4, 170.5, 170.6. IR (neat): 2934, 2858, 1740, 1514, 1248 cm^{-1}. LRMS (ESI) m/z: 893 ([M + Na]$^+$). HRMS (ESI, [M + Na]$^+$): calcd for $C_{50}H_{66}O_{11}NaSi$, 893.4267: found, 893.4247. Using the same procedure as above, (4*R*,6*R*,7*S*,10*R*)-4,10-bis(4-methoxybenzyloxy)-7-methyl-6,8,9-triacetyloxyundecan-1-ol (**27b**) (668 mg, 1.06 mmol, 93%, colorless oil, mixture of diastereomers) was obtained from (4*R*,6*R*,7*S*,10*R*)-1-(*tert*-butyldiphenylsilanyloxy)-4,10-bis(4-methoxybenzyloxy)-7-methyl-6,8,9-triacetyloxyundecane (**S22b**) (991 mg, 1.14 mmol), AcOH (0.98 mL, 1.7 mmol), and TBAF (1.7 mL, 1.7 mmol, 1.0 M in THF). ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.93 (1.3H, d, J = 7.0 Hz), 1.02 (1.7H, d, J = 6.8 Hz), 1.15 (1.3H, d, J = 6.3 Hz), 1.22 (1.7H, d, J = 6.3 Hz), 1.49−1.75 (6H, m), 1.85−2.10 (10H, m), 3.37−3.63 (4H, m), 3.76−3.89 (7H, m), 4.30−4.78 (4H, m), 4.96−5.30 (3H, m), 6.79−6.87 (4H, m), 7.10−7.35 (4H, m). ^{13}C NMR (150 MHz, $CDCl_3$): δ 9.9, 10.0, 15.5, 16.0, 20.8, 20.9, 21.2, 27.9, 28.1, 29.4, 29.7, 35.7, 36.2, 36.8, 38.4, 55.2, 62.3, 62.5, 69.2, 70.0, 70.1, 70.6, 70.7, 71.2, 71.2, 71.5, 72.2, 73.1, 73.5, 73.7, 74.6, 74.7, 75.3, 75.3, 113.7, 113.7, 113.7, 129.0, 129.4, 129.5, 129.5, 129.7, 129.7, 130.4, 130.4, 159.1, 159.2, 159.2, 170.3, 170.4, 170.5, 170.5, 170.7, 171.0. IR (neat): 3461, 2939, 2871, 1739, 1514, 1247, 1031 cm^{-1}. LRMS (ESI) m/z: 655 ([M + Na]$^+$). HRMS (ESI, [M + Na]$^+$): calcd for $C_{34}H_{48}O_{11}Na$, 655.3089: found, 655.3074.

*(5R,7R,8S,11S,E)-5,11-Bis(4-methoxybenzyloxy)-1-iodo-8-methyl-7,9,10-triacetyloxydodec-1-ene (**28a**).* To a stirred solution of (4*R*,6*R*,7*S*,10*S*)-4,10-bis(4-methoxybenzyloxy)-7-methyl-6,8,9-triacetyloxyundecan-1-ol (**27a**) (450 mg, 0.711 mmol) in dry CH_2Cl_2 (7.1 mL) were added $NaHCO_3$ (448 mg, 5.33 mmol) and DMP (454 mg, 1.07 mmol) successively at 0 °C. After being stirred at room temperature for 3.5 h, the mixture was treated with saturated aqueous $Na_2S_2O_3$ solution to quench the reaction at 0 °C. The resulting mixture was extracted with EtOAc twice. The combined organic phases were washed with brine, dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The residue was purified by column chromatography (EtOAc:hexane = 1:1) to yield (4*R*,6*R*,7*S*,10*S*)-4,10-bis(4-methoxybenzyloxy)-7-methyl-6,8,9-triacetyloxyundecan-1-al (**S23a**) (444 mg, 0.704 mmol, 99%) as a yellow oil and a mixture of diastereomers. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.92 (1.0H, d, J = 6.8 Hz), 1.00 (2.0H, d, J = 7.1 Hz), 1.15−1.25 (3H, m), 1.50−2.15 (14H, m), 2.41−2.52 (2H, m), 3.28−3.73 (2H, m), 3.77−3.80 (6H, m), 4.26−4.77 (4H, m), 4.95−5.30 (3H, m), 6.79−6.88 (4H, m), 7.11−7.34 (4H, m), 9.68−9.77 (1H, m). ^{13}C NMR (150 MHz, $CDCl_3$): δ 9.7, 9.9, 15.4, 15.8, 20.8, 20.8, 20.9, 21.1, 25.9, 26.1, 35.9, 36.2, 36.9, 38.2, 39.6, 39.8, 55.2, 55.2, 69.2, 70.2, 70.4, 71.0, 71.3, 71.5, 71.6, 73.2, 73.4, 73.5, 74.8, 75.0, 75.0, 113.7, 113.7, 113.7, 113.8, 129.0, 129.1, 129.4, 129.5, 129.6, 129.8, 130.2, 130.4, 159.1, 159.2, 159.2, 170.2, 170.3, 170.4, 170.5, 170.7, 171.0, 202.1, 202.4. IR (neat): 2937, 2837, 2726, 1739, 1514, 1248, 1031 cm^{-1}. LRMS (ESI) m/z: 653 ([M + Na]$^+$). HRMS (ESI, [M + Na]$^+$): calcd for $C_{34}H_{46}O_{11}Na$, 653.2932: found, 653.2917. To a stirred solution of $CrCl_2$ (865 mg, 7.04 mmol) in dry THF (0.60 mL) and dry 1,4-dioxane (3.6 mL) was added a solution of (4*R*,6*R*,7*S*,10*S*)-4,10-bis(4-methoxybenzyloxy)-7-methyl-6,8,9-triacetyloxyundecan-1-al (**S23a**) (444 mg, 0.704 mmol) and CHI_3 (1.66 g, 4.22 mmol) in dry THF (0.40 mL) and dry 1,4-dioxane (2.4 mL) at 0 °C. After being stirred at 0 °C for 13 h, the mixture was treated with H_2O to quench the reaction at 0 °C. The resulting mixture was extracted with EtOAc twice. The combined organic phases were washed with brine, dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by column chromatography (EtOAc:hexane = 1:1) to yield (5*R*,7*R*,8*S*,11*S*,*E*)-5,11-bis(4-methoxybenzyloxy)-1-iodo-8-methyl-7,9,10-triacetyloxydodec-1-ene (**28a**) (249 mg, 0.330 mmol, 47%) as a pale yellow oil and a mixture of diastereomers. The *E*:*Z* ratio was revealed in the next reaction. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.92 (1.0H, d, J = 7.1 Hz), 0.99 (2.0H, d, J = 6.8 Hz), 1.11−1.25 (3H, m), 1.41−1.74 (4H, m), 1.88−2.21 (12H, m), 3.24−3.71 (2H, m), 3.77−3.80 (6H, m), 4.26−4.77 (4H, m), 4.94−5.30 (3H, m), 5.83 and 5.94 (1H, d, J = 14.6, 14.4 Hz), 6.15−6.51 (1H, m), 6.79−6.88 (4H, m), 7.10−7.33 (4H, m). ^{13}C NMR (100 MHz, $CDCl_3$): δ 9.8, 9.9, 15.4, 15.8, 20.8, 20.8, 21.0, 21.0, 21.1, 31.5, 31.7, 31.9, 32.2, 35.8, 36.6, 38.1, 55.3, 55.3, 69.2, 70.0, 70.4, 71.0, 71.3, 71.5, 71.7, 73.2, 73.4, 73.6, 74.5, 74.8, 74.9, 74.9, 113.7, 113.7, 113.8, 129.1, 129.4, 129.6, 129.7, 130.2, 130.4, 130.4, 146.0, 146.1, 159.2, 170.3, 170.4, 170.8. IR (neat): 2935, 2836, 1740, 1514, 1248, 1032 cm^{-1}. LRMS (ESI) m/z: 777 ([M + Na]$^+$). HRMS (ESI, [M + Na]$^+$): calcd for $C_{35}H_{47}O_{10}INa$, 777.2106: found, 777.2085.

*(5R,7R,8S,11R,E)-5,11-Bis(4-methoxybenzyloxy)-1-iodo-8-methyl-7,9,10-triacetyloxydodec-1-ene (**28b**).* Using the same procedure as above, (4*R*,6*R*,7*S*,10*R*)-4,10-bis(4-methoxybenzyloxy)-7-methyl-6,8,9-triacetyloxyundecan-1-al (**S23b**) (510 mg, 0.809 mmol, 76%, pale yellow oil, mixture of diastereomers) was obtained from (4*R*,6*R*,7*S*,-10*R*)-4,10-bis(4-methoxybenzyloxy)-7-methyl-6,8,9-triacetyloxyundecan-1-ol (**27b**) (668 mg, 1.06 mmol), $NaHCO_3$ (668 mg, 7.95 mmol), and DMP (674 mg, 1.59 mmol). ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.92 (1.3H, d, J = 7.1 Hz), 1.01 (1.7H, d, J = 6.8 Hz), 1.15 (1.3H, d, J = 6.3 Hz), 1.22 (1.7H, d, J = 6.3 Hz), 1.46−2.10 (14H, m), 2.42−2.54 (2H, m), 3.30−3.61 (2H, m), 3.76−3.80 (6H, m), 4.26−4.81 (4H, m), 4.96−5.30 (3H, m), 6.79−6.87 (4H, m), 7.10−7.33 (4H, m), 9.65−9.77 (1H, m). ^{13}C NMR (150 MHz, $CDCl_3$): δ 10.0, 10.1, 15.5, 16.0, 20.8, 20.8, 20.9, 21.1, 26.0, 26.0, 35.6, 36.2, 36.8, 38.3, 39.7, 39.8, 55.2, 69.0, 70.2, 70.2, 70.6, 70.8, 71.1, 71.4, 72.2, 73.1, 73.6, 73.7, 74.6, 74.8, 74.9, 113.7, 113.7, 113.7, 113.8, 129.0, 129.4, 129.5, 129.5, 130.2, 130.4, 159.1, 159.2, 159.2, 170.3, 170.4, 170.5, 170.6, 170.8, 202.0, 202.4. IR (neat): 2937, 2837, 1737, 1514, 1247, 1029 cm^{-1}. LRMS (ESI) m/z: 653 ([M + Na]$^+$). HRMS (ESI, [M + Na]$^+$): calcd for $C_{34}H_{46}O_{11}Na$, 653.2932: found, 653.2914. Using the same procedure as above, (5*R*,7*R*,8*S*,11*R*,*E*)-5,11-bis(4-methoxybenzyloxy)-1-iodo-8-methyl-7,9,10-triacetyloxydodec-1-ene (**28b**) (256 mg, 0.339 mmol, 42%, pale yellow oil, mixture of diastereomers) was obtained from (4*R*,6*R*,7*S*,10*R*)-4,10-bis(4-methoxybenzyloxy)-7-methyl-6,8,9-triacetyloxyundecan-1-al (**S23b**) (510 mg, 0.809 mmol), $CrCl_2$ (994 mg, 8.09 mmol), and CHI_3 (1.91 g, 4.85 mmol). The *E*:*Z* ratio was revealed in the next reaction. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.92 (1.3H, d, J = 6.8 Hz), 1.01 (1.7H, d, J = 6.8 Hz), 1.15 (1.3H, d, J = 6.3 Hz), 1.22 (1.7H, d, J = 6.3 Hz), 1.48−1.72 (4H, m), 1.86−2.10 (12H, m), 3.27−3.61 (2H, m), 3.77−3.80 (6H, m), 4.26−4.75 (4H, m), 4.97−5.31 (3H, m), 5.85 and 5.93 (1H, d, J = 14.1, 14.4 Hz), 6.16−6.53 (1H, m), 6.79−6.88 (4H, m), 7.18−7.24 (4H, m). ^{13}C NMR (100 MHz, $CDCl_3$): δ 10.1, 10.1, 15.5, 16.1, 20.9, 20.9, 21.2, 29.7, 31.2, 31.6, 31.7, 31.9, 32.2, 35.0, 35.4, 35.9, 36.6, 38.3, 55.3, 55.3, 69.0, 70.0, 70.6, 70.8, 71.1, 71.5, 72.3, 73.1, 73.7, 74.3, 74.7, 74.9, 74.9, 74.9, 113.7, 113.7, 113.8, 113.8, 129.0, 129.4, 129.5, 129.6, 129.7, 129.8, 130.4, 145.9, 146.1, 159.1, 159.2, 170.3, 170.4, 170.5, 170.7.

dx.doi.org/10.1021/jo502198y | J. Org. Chem. 2015, 80, 114−132

IR (neat): 2935, 2837, 1740, 1513, 1247, 1031 cm^{-1}. LRMS (ESI) *m/z*: 777 ($[M + Na]^+$). HRMS (ESI, $[M + Na]^+$): calcd for $C_{35}H_{47}O_{10}INa$, 777.2106: found, 777.2089.

*(5R,7R,8S,11S,E)-5,11-Bis(triethylsilanyloxy)-1-iodo-8-methyl-7,9,10-triacetyloxydodec-1-ene (**29a**).* To a stirred solution of (5*R*,7*R*,8*S*,11*S*,*E*)-5,11-bis(4-methoxybenzyloxy)-1-iodo-8-methyl-7,9,10-triacetyloxydodec-1-ene (**28a**) (249 mg, 0.330 mmol) in CH_2Cl_2 (15 mL) and pH 7 phosphate buffer (1 mL) was added DDQ (225 mg, 0.990 mmol) at 0 °C. After being stirred at the same temperature for 4 h, the mixture was treated with saturated aqueous $NaHCO_3$ solution to quench the reaction. The resulting mixture was extracted with CH_2Cl_2 twice. The combined organic phases were washed with brine, dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by column chromatography (EtOAc:hexane = 1:4) to afford an alcohol, which was used for the next reaction without further purification. To a stirred solution of the above alcohol in dry CH_2Cl_2 (3.3 mL) were added 2,6-lutidine (0.18 mL, 1.6 mmol) and TESOTf (0.18 mL, 0.79 mmol) successively at 0 °C. After being stirred at the same temperature for 40 min, the mixture was treated with saturated aqueous NH_4Cl solution to quench the reaction. The resulting mixture was extracted with EtOAc twice. The combined organic phases were washed with brine, dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by column chromatography (EtOAc:hexane = 1:4) to yield (5*R*,7*R*,8*S*,11*S*,*E*)-5,11-bis(triethylsilanyloxy)-1-iodo-8-methyl-7,9,10-triacetyloxydodec-1-ene (**29a**) (205 mg, 0.276 mmol, 84% from (5*R*,7*R*,8*S*,11*S*,*E*)-5,11-bis(4-methoxybenzyloxy)-1-iodo-8-methyl-7,9,10-triacetyloxydodec-1-ene (**28a**)) as a pale yellow oil and a mixture of diastereomers. The *E*:*Z* ratio was found to be ca. 85:15 determined by ^1H NMR analysis. The *Z* isomer was separated in the final stage of the synthesis. ^1H NMR (400 MHz, $CDCl_3$): δ 0.55−0.62 (12H, m), 0.90−1.00 (21H, m), 1.12−1.25 (3H, m), 1.39−1.88 (5H, m), 1.98−2.12 (11H, m), 3.59−3.72 (1H, m), 3.81−3.85 (1H, m), 4.89−5.29 (3H, m), 6.02 (0.85H, d, *J* = 14.4 Hz), 6.19−6.20 (0.15H, m), 6.46−6.55 (0.85H, m), 6.85−6.92 (0.15H, m). ^{13}C NMR (100 MHz, $CDCl_3$): δ 5.0, 5.0, 5.0, 6.8, 6.8, 6.9, 6.9, 7.0, 9.8, 9.9, 19.3, 20.1, 20.8, 20.9, 21.0, 21.0, 29.7, 30.6, 31.5, 31.9, 34.2, 35.4, 37.0, 38.4, 39.8, 40.1, 67.3, 67.5, 68.4, 68.5, 69.0, 71.0, 71.1, 71.4, 74.7, 75.2, 75.8, 146.2, 146.4, 170.1, 170.5, 170.5, 170.8. IR (neat): 2954, 2912, 2877, 1741, 1371, 1233 cm^{-1}. LRMS (FAB) *m/z*: 743 ($[M + H]^+$). HRMS (FAB, $[M + H]^+$): calcd for $C_{31}H_{60}O_8Si_2I$, 743.2866: found, 743.2889.

*(5R,7R,8S,11R,E)-5,11-Bis(triethylsilanyloxy)-1-iodo-8-methyl-7,9,10-triacetyloxydodec-1-ene (**29b**).* Using the same procedure as above, (5*R*,7*R*,8*S*,11*R*,*E*)-5,11-bis(4-methoxybenzyloxy)-1-iodo-8-methyl-7,9,10-triacetyloxydodec-1-ene (**28b**) (256 mg, 0.339 mmol), DDQ (229 mg, 1.01 mmol), and pH 7 phosphate buffer (1 mL) were used in the first step. (5*R*,7*R*,8*S*,11*R*,*E*)-5,11-Bis(triethylsilanyloxy)-1-iodo-8-methyl-7,9,10-triacetyloxydodec-1-ene (**29b**) (189 mg, 0.254 mmol, 75% from (5*R*,7*R*,8*S*,11*R*,*E*)-5,11-bis(4-methoxybenzyloxy)-1-iodo-8-methyl-7,9,10-triacetyloxydodec-1-ene (**28b**), pale yellow oil, mixture of diastereomers) was obtained using 2,6-lutidine (0.12 mL, 1.4 mmol), and TESOTf (0.16 mL, 0.71 mmol). The *E*:*Z* ratio was found to be ca. 85:15 determined by ^1H NMR analysis. The *Z* isomer was separated in the final stage of the synthesis. ^1H NMR (400 MHz, $CDCl_3$): δ 0.55−0.63 (12H, m), 0.93−1.01 (21H, m), 1.15 (1.7H, d, *J* = 6.3 Hz), 1.23 (1.3H, d, *J* = 6.3 Hz), 1.43−1.91 (5H, m), 1.98−2.12 (11H, m), 3.55−3.90 (2H, m), 4.90−5.24 (3H, m), 5.99−6.04 (0.85H, m), 6.17−6.21 (0.15H, m), 6.47−6.55 (0.85H, m), 6.84−6.90 (0.15H, m). ^{13}C NMR (100 MHz, $CDCl_3$): δ 4.9, 5.0, 5.0, 5.1, 6.7, 6.8, 6.9, 6.9, 9.9, 10.1, 19.3, 20.3, 20.8, 20.9, 20.9, 20.9, 21.1, 21.1, 31.6, 31.9, 34.3, 35.3, 36.9, 38.6, 39.7, 39.8, 67.3, 67.4, 68.4, 68.5, 68.8, 70.7, 71.7, 71.9, 74.7, 74.7, 75.8, 76.0, 146.2, 146.4, 170.0, 170.3, 170.3, 170.4, 170.5, 170.8. IR (neat): 2954, 2913, 2877, 1741, 1371, 1232 cm^{-1}. LRMS (FAB) *m/z*: 743 ($[M + H]^+$). HRMS (FAB, $[M + H]^+$): calcd for $C_{31}H_{60}O_8Si_2I$, 743.2866: found, 743.2889.

*(4E,5R,6R,8E,10E,14R,16R,17S,20S)-16,18,19-Triacetyloxy-5,7,17-trimethyl-6,14,20-tris(triethylsilanyloxy)henicosa-4,8,10-triene (**30a**).* To a stirred solution of (1*E*,3*R*,4*R*,5*E*)-3,5-dimethyl-1-tributylstannyl-4-triethylsilanyloxynona-1,5-diene (**15**) (23.0 mg, 0.0402 mmol) and (5*R*,7*R*,8*S*,11*S*,*E*)-5,11-bis(triethylsilanyloxy)-1-iodo-8-methyl-7,9,10-triacetyloxydodec-1-ene (**29a**) (20.0 mg, 0.0269 mmol) in dry NMP (0.27 mL) were added $[Bu_4N^+][Ph_2POO^-]$ (18.4 mg, 0.0402 mmol) and $PdCl_2(MeCN)_2$ (0.7 mg, 2.7 μmol) at room temperature in a glovebox. After being stirred at the same temperature for 12 h, the mixture was treated with saturated aqueous $NaHCO_3$ solution to quench the reaction. The resulting mixture was extracted with EtOAc twice. The combined organic phases were washed with brine, dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by column chromatography (EtOAc:hexane = 1:9) to yield (4*E*,5*R*,6*R*,8*E*,10*E*,14*R*,16*R*,17*S*,20*S*)-16,18,19-triacetyloxy-5,7,17-trimethyl-6,14,20-tris(triethylsilanyloxy)henicosa-4,8,10-triene (**30a**) (17.5 mg, 0.0195 mmol, 72%) as a yellow oil and a mixture of diastereomers. ^1H NMR (400 MHz, $CDCl_3$): δ 0.50−0.62 (18H, m), 0.79−1.00 (38H, m), 1.11−1.41 (7H, m), 1.50−1.65 (5H, m), 1.97−2.13 (12H, m), 2.23−2.32 (1H, m), 3.61−3.67 (2H, m), 3.81−3.87 (1H, m), 4.85−5.05 (2H, m), 5.17−5.29 (2H, m), 5.50−5.62 (1.7H, m), 5.67−5.73 (0.3H, m), 5.91−6.06 (1.7H, m), 6.25−6.32 (0.3H, m). ^{13}C NMR (150 MHz, $CDCl_3$): δ 4.9, 4.9, 5.0, 5.0, 5.1, 6.8, 6.8, 6.9, 6.9, 6.9, 9.8, 11.1, 13.7, 13.9, 16.8, 19.2, 20.1, 20.8, 20.9, 20.9, 21.0, 22.6, 28.3, 29.6, 36.6, 36.9, 39.4, 40.9, 67.4, 67.5, 68.9, 69.2, 71.1, 75.2, 83.4, 127.3, 129.5, 130.9, 131.4, 136.1, 136.4, 170.1, 170.5, 170.7. IR (neat): 2956, 2876, 1744, 1458, 1371, 1233, 1119, 1068, 1019 cm^{-1}. LRMS (ESI) *m/z*: 919 ($[M + Na]^+$). HRMS (ESI, $[M + Na]^+$): calcd for $C_{48}H_{92}O_9NaSi_3$, 919.5941: found, 919.5925.

*(4E,5R,6R,8E,10E,14R,16R,17S,20R)-16,18,19-Triacetyloxy-5,7,17-trimethyl-6,14,20-tris(triethylsilanyloxy)henicosa-4,8,10-triene (**30b**).* Using the same procedure as above, (4*E*,5*R*,6*R*,8*E*,10*E*,14*R*,16*R*,17*S*,20*R*)-16,18,19-triacetyloxy-5,7,17-trimethyl-6,14,20-tris(triethylsilanyloxy)henicosa-4,8,10-triene (**30b**) (43.2 mg, 0.0481 mmol, 83%, yellow oil, mixture of diastereomers) was obtained from (1*E*,3*R*,4*R*,5*E*)-3,5-dimethyl-1-tributylstannyl-4-triethylsilanyloxynona-1,5-diene (**15**) (50.0 mg, 0.0875 mmol), (5*R*,7*R*,8*S*,11*R*,*E*)-5,11-bis(triethylsilanyloxy)-1-iodo-8-methyl-7,9,10-triacetyloxydodec-1-ene (**29b**) (43.0 mg, 0.0579 mmol), $[Bu_4N^+][Ph_2POO^-]$ (40.2 mg, 0.0875 mmol), and $PdCl_2(MeCN)_2$ (1.5 mg, 5.8 μmol). ^1H NMR (400 MHz, $CDCl_3$): δ 0.50−0.65 (18H, m), 0.81−1.00 (38H, m), 1.02−1.41 (7H, m), 1.47−1.83 (5H, m), 1.93−2.15 (12H, m), 2.23−2.32 (1H, m), 3.62−3.89 (3H, m), 4.85−5.18 (3H, m), 5.24−5.26 (1H, m), 5.49−5.71 (2H, m), 5.90−6.06 (1.7H, m), 6.25−6.32 (0.3H, m). ^{13}C NMR (150 MHz, $CDCl_3$): δ 4.9, 4.9, 5.0, 5.0, 5.1, 6.7, 6.8, 6.9, 6.9, 6.9, 9.8, 10.1, 11.0, 11.1, 11.1, 13.9, 16.8, 19.1, 20.3, 20.7, 20.8, 20.9, 20.9, 21.0, 21.1, 22.6, 28.2, 28.3, 29.6, 35.7, 36.5, 36.8, 38.2, 39.1, 39.3, 40.9, 67.3, 68.9, 68.9, 69.0, 69.0, 70.6, 71.9, 72.1, 75.9, 76.1, 83.4, 127.3, 127.3, 129.5, 129.6, 130.9, 131.0, 131.3, 131.7, 135.8, 136.1, 136.4, 136.4, 169.9, 170.2, 170.3, 170.4, 170.7. IR (neat): 2956, 2877, 1744, 1458, 1370, 1233, 1117, 1070, 1018 cm^{-1}. LRMS (ESI) *m/z*: 919 ($[M + Na]^+$). HRMS (ESI, $[M + Na]^+$): calcd for $C_{48}H_{92}O_9NaSi_3$, 919.5941: found, 919.5927.

*(2S,5S,6R,8R,11E,13E,15R,16R,17E)-5,15,17-Trimethyl-2,8,16-tris(triethylsilanyloxy)henicosa-11,13,17-trien-3,4,6-triol (**31a**).* To a stirred solution of (4*E*,5*R*,6*R*,8*E*,10*E*,14*R*,16*R*,17*S*,20*S*)-16,18,19-triacetyloxy-5,7,17-trimethyl-6,14,20-tris(triethylsilanyloxy)henicosa-4,8,10-triene (**30a**) (15.5 mg, 0.0173 mmol) in dry CH_2Cl_2 (1.0 mL) was added DIBAL (0.17 mL, 0.17 mmol, 1.0 M in toluene) at −78 °C, and the resulting mixture was stirred at the same temperature for 1 h. Then, to the mixture was added saturated aqueous Rochell salt solution to quench the reaction. After being stirred at room temperature until the mixture turned into a clear solution, the resulting mixture was extracted with CH_2Cl_2 twice. The combined organic phases were washed with brine, dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by column chromatography ($CHCl_3$: MeOH = 9:1) to yield (2*S*,5*S*,6*R*,8*R*,11*E*,13*E*,15*R*,16*R*,17*E*)-5,15,17-trimethyl-2,8,16-tris(triethylsilanyloxy)henicosa-11,13,17-trien-3,4,6-triol (**31a**) (7.1 mg, 9.2 μmol, 53%) as a pale yellow oil and a mixture of diastereomers. ^1H NMR (400 MHz, $CDCl_3$): δ 0.47−0.69 (18H, m), 0.81−1.00 (36H, m), 1.18−1.42 (6H, m), 1.46−1.75 (7H, m), 1.91−2.33 (5H, m), 2.64−4.89 (9H, m), 5.24−5.27 (1H, m), 5.48−5.63 (1.7H, m), 5.67−5.72 (0.3H, m), 5.91−6.07 (1.7H, m), 6.22−6.30 (0.3H, m). ^{13}C NMR (150 MHz, $CDCl_3$): δ 4.9, 4.9, 5.0, 5.1, 6.8, 6.8, 6.9, 8.1, 9.4, 11.0, 12.2, 13.7, 13.9, 16.7, 16.8, 20.1, 20.5, 22.6, 27.8, 29.1, 29.6, 29.7, 37.8, 38.0, 38.8, 40.8, 40.9, 70.4, 70.8, 71.8,

dx.doi.org/10.1021/jo502198y | J. Org. Chem. 2015, 80, 114−132

73.5, 74.0, 74.2, 74.3, 83.4, 127.4, 129.4, 130.8, 131.2, 136.4, 136.4. IR (neat): 3419, 2956, 2876, 1457, 1415, 1378, 1239, 1072, 1005, 742, 726 cm^{-1}. LRMS (ESI) *m/z*: 793 ([M + Na]$^+$). HRMS (ESI, [M + Na]$^+$): calcd for $C_{42}H_{86}O_6NaSi_3$, 793.5624: found, 793.5599.

*(2R,5S,6R,8R,11E,13E,15R,16R,17E)-5,15,17-Trimethyl-2,8,16-tris-(triethylsilanyloxy)henicosa-11,13,17-trien-3,4,6-triol (**31b**).* Using the same procedure as above, (2*R*,5*S*,6*R*,8*R*,11*E*,13*E*,15*R*,16*R*,17*E*)-5,15,17-trimethyl-2,8,16-tris(triethylsilanyloxy)henicosa-11,13,17-trien-3,4,6-triol (**31b**) (7.1 mg, 9.2 μmol, 51%, yellow oil, mixture of diastereomers) was obtained from (4*E*,5*R*,6*R*,8*E*,10*E*,14*R*,16*R*,-17*S*,20*R*)-16,18,19-triacetyloxy-5,7,17-trimethyl-6,14,20-tris(triethylsilanyloxy)henicosa-4,8,10-triene (**30b**) (16.1 mg, 0.0179 mmol), and DIBAL (0.18 mL, 0.18 mmol, 1.0 M toluene). ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.50−0.67 (18H, m), 0.81−0.99 (36H, m), 1.21−1.40 (6H, m), 1.47−1.74 (7H, m), 1.92−2.31 (5H, m), 2.78−4.90 (9H, m), 5.24−5.27 (1H, m), 5.47−5.63 (1.7H, m), 5.67−5.73 (0.3H, m), 5.91−6.07 (1.7H, m), 6.22−6.29 (0.3H, m). ^{13}C NMR (150 MHz, $CDCl_3$): δ 4.9, 4.9, 5.1, 5.1, 5.1, 6.8, 6.8, 6.9, 8.6, 11.1, 11.6, 13.9, 16.8, 16.8, 19.9, 20.2, 22.6, 27.8, 28.0, 29.6, 29.7, 37.6, 37.9, 39.1, 39.8, 40.3, 40.9, 40.9, 42.3, 70.6, 70.7, 72.1, 72.8, 72.9, 73.1, 73.7, 73.7, 74.7, 83.4, 83.4, 127.4, 127.4, 129.4, 129.5, 130.8, 131.0, 131.1, 131.2, 136.4, 136.5. IR (neat): 3448, 2956, 2876, 1741, 1458, 1414, 1377, 1239, 1071, 1006, 743, 727 cm^{-1}. LRMS (ESI) *m/z*: 793 ([M + Na]$^+$). HRMS (ESI, [M + Na]$^+$): calcd for $C_{42}H_{86}O_6NaSi_3$, 793.5624: found, 793.5592.

*2-Hydroxy-3(2H)-furanone **33a**.* To a stirred solution of DMSO (8.8 μL, 0.17 mmol) in dry CH_2Cl_2 (0.50 mL) was added trifluoroacetic anhydride (12 μL, 0.083 mmol) at −78 °C, and the resulting mixture was stirred at the same temperature for 15 min. Then, a solution of (2*S*,5*S*,6*R*,8*R*,11*E*,13*E*,15*R*,16*R*,17*E*)-5,15,17-trimethyl-2,8,16-tris(triethylsilanyloxy)henicosa-11,13,17-trien-3,4,6-triol (**31a**) (12.8 mg, 0.0166 mmol) in dry CH_2Cl_2 (0.50 mL) was added to the mixture. After being stirred at −78 °C for 30 min, the reaction mixture was treated with triethylamine (35 μL, 0.25 mmol) and then warmed to room temperature. The mixture was stirred for another 20 min, before saturated aqueous NH_4Cl solution was added to the solution at 0 °C. The resulting mixture was extracted with EtOAc twice. The combined organic phases were washed with brine, dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by flash column chromatography (EtOAc:hexane = 1:9) to yield the 2-hydroxy-3(2*H*)-furanone **33a** (8.7 mg, 0.0114 mmol, 69%) as a pale yellow oil. ^{1}H NMR (400 MHz, CD_3OD): δ 0.49−0.72 (18H, m), 0.81−1.04 (32.5H, m), 1.15 (0.5H, d, *J* = 6.3 Hz), 1.27−1.34 (3H, m), 1.35−1.44 (2H, m), 1.50−1.65 (7H, m), 1.73−1.81 (1H, m), 1.98−2.04 (2H, m), 2.15−2.32 (3H, m), 2.61−2.69 (1H, m), 2.82−2.90 (1H, m), 3.69 (1H, d, *J* = 8.0 Hz), 4.05 (1H, d, *J* = 6.3 Hz), 4.18−4.24 (1H, m), 5.31 (1H, t, *J* = 7.0 Hz), 5.52−5.59 (2H, m), 5.92−6.03 (2H, m). ^{13}C NMR (100 MHz, CD_3OD): δ 5.8, 5.9, 5.9, 7.2, 7.2, 7.3, 7.3, 11.5, 14.3, 17.5, 17.6, 23.7, 29.2, 30.6, 37.4, 38.5, 42.4, 71.0, 71.4, 84.8, 105.1, 111.7, 128.6, 131.2, 132.3, 132.4, 136.9, 137.8, 187.5, 206.0. IR (neat): 3310, 2956, 2913, 2876, 1690, 1613, 1457, 1413, 1375, 1239, 1117, 1005, 742, 727 cm^{-1}. LRMS (ESI) *m/z*: 787 ([M + Na]$^+$). HRMS (ESI, [M + Na]$^+$): calcd for $C_{42}H_{80}O_6NaSi_3$, 787.5155: found, 787.5137. $[\alpha]_D^{28}$: +24.3 (*c* 0.17, $CHCl_3$).

*2-Hydroxy-3(2H)-furanone **33b**.* Using the same procedure as above, 2-hydroxy-3(2*H*)-furanone **33b** (10.8 mg, 0.0141 mmol, 69%, pale yellow oil) was obtained from (2*R*,5*S*,6*R*,8*R*,11*E*,13*E*,15*R*,16*R*,-17*E*)-5,15,17-trimethyl-2,8,16-tris(triethylsilanyloxy)henicosa-11,13,17-trien-3,4,6-triol (**31b**) (15.7 mg, 0.0204 mmol), TFAA (14 μL, 0.10 mmol), DMSO (11 μL, 0.20 mmol), and NEt_3 (43 μL, 0.31 mmol). ^{1}H NMR (600 MHz, CD_3OD): δ 0.49−0.71 (18H, m), 0.82−1.05 (32H, m), 1.20−1.32 (3H, m), 1.36−1.42 (2H, m), 1.52−1.77 (8H, m), 1.97−2.04 (2H, m), 2.12−2.33 (3H, m), 2.62−2.83 (2H, m), 3.68 (1H, d, *J* = 7.9 Hz), 4.05 (1H, q, *J* = 6.2 Hz), 4.09−4.13 (1H, m), 5.31 (1H, t, *J* = 6.8 Hz), 5.52−5.58 (2H, m), 5.90−6.07 (2H, m). ^{13}C NMR (150 MHz, CD_3OD): δ 5.8, 5.9, 5.9, 7.2, 7.2, 7.3, 7.3, 11.5, 14.3, 17.5, 17.6, 23.7, 28.7, 30.6, 37.4, 38.5, 42.4, 70.8, 71.4, 84.9, 105.5, 111.4, 128.6, 131.3, 132.3, 132.5, 136.8, 137.8, 187.5, 205.8. IR (neat): 3311, 2956, 2876, 1696, 1617, 1458, 1413, 1375, 1239, 1115, 1005, 742 cm^{-1}. LRMS (ESI) *m/z*: 787 ([M + Na]$^+$). HRMS (ESI, [M + Na]$^+$): calcd for $C_{42}H_{80}O_6NaSi_3$, 787.5155: found, 787.5122. $[\alpha]_D^{25}$: −8.1 (*c* 0.54, $CHCl_3$).

*(1S)-JBIR-108 (**1**).* To a stirred solution of 2-hydroxy-3(2*H*)-furaone **33a** (8.5 mg, 0.011 mmol) in dry THF (0.20 mL) was added HF·Py (14 μL, 0.11 mmol) at 0 °C. After being stirred at the same temperature for 30 min, the mixture was treated with saturated aqueous $NaHCO_3$ solution to quench the reaction. The resulting mixture was extracted with CH_2Cl_2 twice. The combined organic phases were concentrated *in vacuo*. The residue was purified by reversed-phase column chromatography (MeOH:H_2O = 4:1), followed by reversed-phase HPLC (C18 column: 10 × 150 mm, MeCN:H_2O = 40:60 to 60:40, 5 mL/min, monitoring at 231 and 254 nm) to yield (1*S*)-JBIR-108 (**1**) (2.0 mg, 4.7 mmol, 43%) as a colorless oil. ^{1}H NMR (600 MHz, CD_3OD): δ 0.86 (3H, d, *J* = 6.9 Hz), 0.92 (3H, t, *J* = 7.4 Hz), 1.18 (1H, d, *J* = 6.2 Hz), 1.30 (2H, d, *J* = 6.4 Hz), 1.37−1.42 (2H, m), 1.58−1.66 (8H, m), 2.03 (2H, dt, *J* = 7.0, 7.0 Hz), 2.15−2.20 (1H, m), 2.23−2.33 (2H, m), 2.67−2.78 (2H, m), 3.64 (1H, d, *J* = 8.2 Hz), 3.88−3.91 (1H, m), 3.96−4.07 (1H, m), 5.36 (1H, t, *J* = 7.0 Hz), 5.56−5.62 (2H, m), 6.02−6.12 (2H, m). ^{13}C NMR (150 MHz, CD_3OD): δ 5.7, 11.4, 14.2, 16.3, 16.7, 17.9, 23.8, 29.7, 30.6, 38.0, 38.1, 38.3, 41.5, 69.4, 69.6, 70.0, 70.9, 83.4, 105.5, 105.6, 112.1, 112.5, 128.8, 131.7, 132.4, 132.5, 132.6, 136.3, 137.3, 187.9, 188.4, 204.3, 205.7 (some of diastereomer carbons at C2 were observed). IR (neat): 3379, 2959, 2927, 2871, 1697, 1612, 1452, 1376, 1105, 989 cm^{-1}. LRMS (ESI) *m/z*: 445 ([M + Na]$^+$). HRMS (ESI, [M + Na]$^+$): calcd for $C_{24}H_{38}O_6Na$, 445.2561: found, 445.2554. $[\alpha]_D^{27}$: −5.1 (*c* 0.10, $CHCl_3$).

*(1R)-JBIR-108 (**2**).* Using the same procedure as above, (1*R*)-JBIR-108 (**2**) (1.7 mg, 4.0 μmol, 57%, colorless oil) was obtained from 2-hydroxy-3-furanoe **33b** (5.4 mg, 7.1 μmol), and HF·Py (8.8 μL, 0.071 mmol). ^{1}H NMR (600 MHz, CD_3OD): δ 0.86 (3H, d, *J* = 6.9 Hz), 0.92 (3H, t, *J* = 7.4 Hz), 1.17 (1H, d, *J* = 6.4 Hz), 1.30 (2H, d, *J* = 6.4 Hz), 1.37−1.43 (2H, m), 1.56−1.70 (8H, m), 2.03 (2H, dt, *J* = 7.2, 7.2 Hz), 2.15−2.21 (1H, m), 2.24−2.37 (2H, m), 2.67−2.78 (2H, m), 3.64 (1H, d, *J* = 8.2 Hz), 3.90 (1H, q, *J* = 6.4 Hz), 3.97−4.08 (1H, m), 5.36 (1H, t, *J* = 7.2 Hz), 5.56−5.62 (2H, m), 6.02−6.09 (2H, m). ^{13}C NMR (150 MHz, CD_3OD): δ 5.7, 5.8, 11.4, 14.2, 16.3, 16.7, 17.9, 23.8, 29.7, 29.8, 30.6, 37.7, 38.2, 38.3, 41.5, 41.8, 69.4, 69.6, 70.1, 70.7, 83.4, 105.4, 105.7, 112.3, 112.4, 128.8, 131.7, 131.7, 132.4, 132.5, 132.5, 132.6, 136.3, 136.4, 137.3, 188.0, 188.2, 204.3, 205.6 (some of diastereomer carbons at C2 were observed). IR (neat): 3361, 2958, 2927, 1700, 1616, 1457, 1102, 989 cm^{-1}. LRMS (ESI) *m/z*: 445 ([M + Na]$^+$). HRMS (ESI, [M + Na]$^+$): calcd for $C_{24}H_{38}O_6Na$, 445.2561: found, 445.2544. $[\alpha]_D^{27}$: −19.8 (*c* 0.08, $CHCl_3$).

*Tri-(R)-MTPA Ester **38**.* To a stirred solution of (1*S*)-JBIR-108 (**1**) (0.9 mg, 2.1 μmol) in dry CH_2Cl_2 (0.40 mL) were added DCC (4.0 mg, 0.019 mmol), DMAP (1.0 mg, 8.0 μmol), and (*R*)-(+)-MTPA-OH (4.4 mg, 0.019 mmol) at room temperature. The resulting mixture was stirred at the same temperature for 30 min (until TLC spots converged in one spot). To the mixture was added Et_2O. The resulting mixture was washed with water and brine, dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The residue was purified by column chromatography (EtOAc:hexane = 1:19). The residue was further purified by GPC to yield tri-(*R*)-(+)-MTPA ester **38** (0.9 mg, 0.86 μmol, 40%) as a colorless oil and a mixture of C2 diastereomers. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.84−1.11 (6H, m), 1.26 (2H, s), 1.37−1.45 (4H, m), 1.60−1.65 (4H, m), 1.73 (1H, s), 1.97−2.73 (7H, m), 3.27−3.58 (11H, m), 5.15−5.62 (4H, m), 5.75−5.99 (1H, m), 6.23−6.32 (1H, m), 6.60−6.69 (1H, m), 7.23−7.56 (15H, m). LRMS (ESI) *m/z*: 1075 ([M + Na]$^+$). HRMS (ESI, [M + Na]$^+$): calcd for $C_{54}H_{57}O_{11}F_9Na$, 1075.3649: found, 1075.3632.

*Tri-(R)-MTPA Ester **39**.* Using the same procedure as above, tri-(*R*)-(+)-MTPA ester **39** (0.8 mg, 0.76 μmol, 40%, colorless oil, mixture of C2 diastereomers) was obtained from (1*R*)-JBIR-108 (**2**) (0.8 mg, 1.9 μmol), DCC (3.5 mg, 0.017 mmol), DMAP (0.7 mg, 5.7 μmol), and (*R*)-(+)-MTPA-OH (4.0 mg, 0.017 mmol). ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.88−0.92 (6H, m), 1.22−1.26 (6H, m), 1.33−1.43 (2H, m), 1.68−1.77 (3H, m), 2.02−2.62 (7H, m), 3.21−3.55 (11H, m), 5.18−5.60 (4H, m), 5.93−5.97 (1H, m), 6.27−6.33 (1H, m), 6.58−6.74 (1H), 7.31−7.57 (15H, m). LRMS (ESI) *m/z*: 1075

dx.doi.org/10.1021/jo502198y | J. Org. Chem. 2015, 80, 114−132

([M + Na]$^+$). HRMS (ESI, [M + Na]$^+$): calcd for $C_{54}H_{57}O_{11}F_9Na$, 1075.3649: found, 1075.3633.

Synthesis of Model Compounds. *3-Hydroxy-2-methylbutyric Acid Ethyl Ester (**S24**).* To a stirred solution of ethyl 2-methylacetoacetate (2.94 mL, 21.0 mmol) in EtOH (104 mL) was added $NaBH_4$ (787 mg, 21.0 mmol) at −78 °C, and the resulting mixture was stirred at −40 °C for 75 min. The reaction mixture was poured into 3 M HCl. Then, saturated aqueous $NaHCO_3$ solution was added to neutralize the mixture, and the resulting mixture was concentrated *in vacuo*. The residue was extracted with EtOAc twice. The combined organic phases were washed with brine, dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The residue was purified by column chromatography (EtOAc:hexane = 1:1) to yield 3-hydroxy-2-methylbutyric acid ethyl ester (**S24**) (2.90 g, 20.0 mmol, 95%) as a colorless oil and a mixture of diastereomers. The diastereomer was not separated because these stereocenters will be lost by oxidation of (6*S*)-6-(*tert*-butyldiphenylsilanyloxy)-3-methylheptane-2,4,5-triol (**34a**) and (6*R*)-6-(*tert*-butyldiphenylsilanyloxy)-3-methylheptane-2,4,5-triol (**34b**). The diastereomeric ratio (1:1) was determined by ^{1}H NMR. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.18−1.23 (6H, m), 1.28 (3H, t, J = 7.1 Hz), 2.41−2.53 (1H, m), 2.65 (0.50H, d, J = 4.9 Hz), 2.75 (0.50H, d, J = 5.6 Hz), 3.84−3.92 (0.50H, m), 4.04−4.11 (0.50H, m), 4.18 (1H, q, J = 7.1 Hz), 4.18 (1H, q, J = 7.1 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ 11.0, 13.9, 14.1, 19.8, 20.6, 45.5, 46.9, 60.5, 67.9, 69.3, 175.8, 175.9. IR (neat): 3446, 2979, 2939, 2908, 1733, 1458, 1376, 1262, 1189, 1096 cm^{-1}. LRMS (EI) m/z: 147 ([M + H]$^+$). HRMS (EI, [M + H]$^+$): calcd for $C_7H_{15}O_3$, 147.1021: found, 147.1017.

*3-Methoxymethoxy-2-methylbutyric Acid Ethyl Ester (**S25**).* To a stirred solution of 3-hydroxy-2-methylbutyric acid ethyl ester (**S24**) (1.00 g, 6.84 mmol) in dry CH_2Cl_2 (34 mL) were added DIPEA (2.4 mL, 14 mmol) and MOMCl (0.78 mL, 10 mmol) successively at 0 °C. The resulting mixiture was stirred at room temperature for 20 h. To the mixture was added saturated aqueous NH_4Cl solution to quench the reaction. The resulting mixture was extracted with CH_2Cl_2 twice. The combined organic phases were washed with saturated aqueous $NaHCO_3$ solution and brine, dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The residue was purified by column chromatography (EtOAc:hexane = 1:4) to yield 3-methoxymethoxy-2-methylbutyric acid ethyl ester (**S25**) (1.30 g, 6.83 mmol, 100%) as a colorless oil and a mixture of diastereomers. The diastereomeric ratio was changed to 3:2 during the reaction. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.12−1.22 (6H, m), 1.27 (3H, t, J = 7.1 Hz), 2.52 (0.40H, dq, J = 6.1, 7.1 Hz), 2.60 (0.60H, dq, J = 7.3, 7.3 Hz), 3.35 (1.8H, s), 3.36 (1.2H, s), 3.89−4.00 (1H, m), 4.15 (2H, q, J = 7.1 Hz), 4.61−4.69 (2H, m). ^{13}C NMR (100 MHz, $CDCl_3$): δ 12.0, 12.5, 14.1, 14.1, 17.0, 18.1, 45.6, 45.8, 55.3, 55.3, 60.1, 60.2, 74.1, 74.7, 95.3, 95.3, 174.4, 174.7. IR (neat): 2981, 2939, 2889, 1735, 1457, 1379, 1189, 1147, 1107, 1072, 1041 cm^{-1}. LRMS (EI) m/z: 159 ([M − OMe]$^+$). HRMS (EI, [M − OMe]$^+$): calcd for $C_8H_{15}O_3$, 159.1016: found, 159.1008.

*3-Methoxymethoxy-2-methylbutan-1-ol (**S26**).* To a stirred solution of $LiAlH_4$ (1.09 g, 28.8 mmol) in dry THF (61 mL) was added 3-methoxymethoxy-2-methylbutyric acid ethyl ester (**S25**) (2.19 g, 11.5 mmol) in dry THF (20 mL) at 0 °C. The resulting mixture was stirred at the same temperature for 45 min and then stirred at room temperature for 50 min. To the mixture was added saturated aqueous Na_2SO_4 solution to quench the reaction. The resulting mixture was filtered and concentrated *in vacuo*. The residue was purified by column chromatography (EtOAc:hexane = 1:1) to yield 3-methoxymethoxy-2-methylbutan-1-ol (**S26**) (1.42 g, 9.58 mmol, 83%) as a colorless oil and a mixture of diastereomers. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.88 (1.2H, d, J = 6.8 Hz), 0.94 (1.8H, d, J = 7.1 Hz), 1.18 (1.2H, d, J = 6.6 Hz), 1.19 (1.8H, d, J = 6.3 Hz), 1.71−1.81 (0.60H, m), 1.83−1.89 (0.40H, m), 2.96 (1H, brs), 3.39 (1.2H, s), 3.40 (1.8H, s), 3.50−3.59 (1H, m), 3.64−3.70 (1.6H, m), 3.86−3.91 (0.40H, m), 4.61 (0.60H, d, J = 6.8 Hz), 4.62 (0.40H, d, J = 6.6 Hz), 4.69 (0.40H, d, J = 6.6 Hz), 4.72 (0.60H, d, J = 6.8 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ 11.3, 13.4, 16.3, 17.5, 40.0, 41.0, 55.4, 55.4, 65.0, 65.6, 74.8, 76.9, 94.9, 95.1. IR (neat): 3429, 2969, 2932, 2886, 1456, 1378, 1148, 1105, 1038, 918 cm^{-1}. LRMS (EI) m/z: 149 ([M + H]$^+$). HRMS (EI, [M + H]$^+$): calcd for $C_7H_{17}O_3$, 149.1178: found, 149.1174.

*(3-Methoxymethoxy-2-methylbutyl)triphenylphosphonium Iodide (**S27**).* To a stirred solution of 3-methoxymethoxy-2-methylbutan-1-ol (**S26**) (1.00 g, 6.70 mmol) in benzene:Et_2O (1:2, 33 mL) were added imidazole (1.10 g, 16.7 mmol), PPh_3 (4.40 g, 16.7 mmol), and iodine (2.10 g, 16.7 mmol) successively at 0 °C, and the resulting mixture was stirred at room temperature for 7 h. To the mixture was added saturated aqueous $NaHCO_3$ solution to quench the reaction. The resulting mixture was extracted with EtOAc twice. The combined organic phases were washed with brine, dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by column chromatography (EtOAc:hexane = 1:4) to afford a mixture of the iodide and PPh_3, which was used for the next reaction without further purification. To a stirred solution of the above mixture in MeCN (34 mL) was added additional PPh_3 (8.80 g, 34.0 mmol) at room temperature, and the resulting mixture was refluxed for 34 h. The mixture was concentrated *in vacuo*, and the residue was purified by column chromatography (EtOAc:hexane = 1:4 to $CHCl_3$:MeOH = 9:1) to yield (3-methoxymethoxy-2-methylbutyl)triphenylphosphonium iodide (**S27**) (3.05 g, 5.86 mmol, 87% from 3-methoxymethoxy-2-methylbutan-1-ol (**S26**)) as a white amorphous mass and a mixture of diastereomers. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.82 (1.2H, d, J = 5.9 Hz), 0.83 (1.8H, d, J = 6.6 Hz), 1.21 (1.8H, d, J = 6.1 Hz), 1.25 (1.2H, d, J = 6.3 Hz), 1.98−2.07 (0.60H, m), 2.19−2.28 (0.40H, m), 3.27 (1.2H, s), 3.33 (1.8H, s), 3.50−3.87 (3H, m), 4.52 (0.40H, d, J = 6.6 Hz), 4.60 (0.40H, d, J = 6.6 Hz), 4.61 (0.60H, d, J = 6.6 Hz), 4.69 (0.60H, d, J = 6.6 Hz), 7.70−7.76 (6H, m), 7.80−7.84 (3H, m), 7.88−7.94 (6H, m). ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.9, 16.4, 16.5, 16.9, 16.9, 17.3, 25.5, 26.0, 33.1, 33.1, 34.5, 34.5, 55.3, 55.5, 77.7, 77.9, 94.5, 95.7, 117.6, 117.8, 118.5, 118.7, 130.2, 130.2, 130.3, 130.3, 133.3, 133.4, 134.8, 134.8, 134.9, 134.9. IR (neat): 3053, 2977, 2898, 1587, 1484, 1438, 1111, 1035 cm^{-1}. LRMS (EI) m/z: 393 ([M − I]$^+$). HRMS (EI, [M − I]$^+$): calcd for $C_{25}H_{30}O_2P$, 393.1978: found, 393.1977.

*(R)-2-(tert-Butyldiphenylsilanyloxy)propionaldehyde (**S28**).* To a stirred solution of (*R*)-2-(*tert*-butyldiphenylsilanyloxy)propionic acid methyl ester[32] (1.00 g, 2.90 mmol) in dry hexane (5.8 mL) was added DIBAL (1.00 M in toluene, 2.9 mL) at −78 °C, and the resulting mixture was stirred at the same temperature for 1.5 h. Then, MeOH (0.29 mL) was added to the mixture. After being stirred at −78 °C for 15 min, the reaction mixture was poured into saturated aqueous Rochell salt solution (5.8 mL), and the mixture was stirred at room temperature until the mixture turned into a clear solution. The resulting mixture was extracted with EtOAc twice. The combined organic phases were washed with brine, dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The residue was purified by column chromatography (EtOAc:hexane = 1:19) to yield (*R*)-2-(*tert*-butyldiphenylsilanyloxy)propionaldehyde (**S28**) (898 mg, 2.87 mmol, 99%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.11 (9H, m), 1.22 (3H, d, J = 6.8 Hz), 4.10 (1H, dq, J = 1.0, 6.8 Hz), 7.36−7.47 (6H, m), 7.64−7.68 (4H, m), 9.65 (1H, d, J = 1.0 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ 18.4, 19.2, 26.8, 74.4, 127.7, 127.8, 129.9, 130.0, 132.9, 133.3, 135.7, 135.7, 203.8. IR (neat): 2960, 2932, 2859, 1739, 1428, 1112, 823, 740, 702 cm^{-1}. LRMS (EI) m/z: 255 ([M − tBu]$^+$). HRMS (EI, [M − tBu]$^+$): calcd for $C_{15}H_{15}O_2Si$, 255.0836: found, 255.0819. $[\alpha]_D^{19}$: +16.1 (*c* 1.00, $CHCl_3$).

*(2S)-2-(tert-Butyldiphenylsilanyloxy)-6-methoxymethoxy-5-methylheptan-2-ene (**S29a**).* To a solution of (3-methoxymethoxy-2-methylbutyl)triphenylphosphonium iodide (**S27**) (1.04 g, 2.00 mmol) in dry THF (7.5 mL) was added BuLi (2.69 M in hexane, 0.74 mL) dropwise at room temperature, and the resulting mixture was stirred for 30 min. Then, a solution of (*S*)-2-(*tert*-butyldiphenylsilanyloxy)-propionaldehyde[33] (611 mg, 2.00 mmol) in dry THF (2.5 mL) was added to the mixture at the same temperature, and the reaction mixture was stirred for 10 min. The mixture was partitioned between saturated aqueous NH_4Cl solution and EtOAc. The resulting mixture was extracted with EtOAc twice. The combined organic phases were washed with saturated aqueous $NaHCO_3$ solution and brine, dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The residue was purified by column chromatography (EtOAc:hexane = 1:9) to yield (2*S*)-2-(*tert*-butyldiphenylsilanyloxy)-6-methoxymethoxy-5-methylheptan-2-ene

dx.doi.org/10.1021/jo502198y | *J. Org. Chem.* 2015, 80, 114−132

(**S29a**) (614 mg, 1.44 mmol, 72%) as a colorless oil and a mixture of isomers. The isomer was not separated because stereocenters coming from *E* and *Z* isomers will be lost by oxidation of (6*S*)-6-(*tert*-butyldiphenylsilanyloxy)-3-methylheptane-2,4,5-triol (**34a**). The ratio of isomers could not be determined due to complex NMR spectra. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.68−1.26 (18H, m), 2.01−2.28 (1H, m), 3.22−3.56 (4H, m), 4.25−4.67 (3H, m), 5.01−5.62 (2H, m), 7.32−7.43 (6H, m), 7.65−7.70 (4H, m). ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.9, 16.0, 16.5, 16.6, 16.6, 16.7, 17.0, 17.1, 17.3, 17.5, 17.5, 18.2, 19.1, 19.2, 24.5, 24.6, 24.6, 24.6, 24.7, 25.1, 26.9, 27.0, 37.4, 37.6, 37.8, 38.4, 41.2, 41.6, 41.8, 55.2, 55.3, 66.0, 66.1, 66.5, 66.5, 70.2, 70.3, 70.4, 70.5, 76.2, 76.3, 76.4, 76.6, 76.6, 76.6, 94.8, 95.0, 95.1, 95.2, 95.2, 95.2, 127.3, 127.3, 127.4, 127.4, 127.4, 127.5, 127.5, 129.4, 129.4, 129.4, 129.5, 129.5, 129.8, 130.2, 130.4, 130.5, 131.1, 131.2, 131.2, 131.3, 135.3, 135.8, 135.8, 135.8, 135.8, 135.8, 135.9, 135.9. IR (neat): 2966, 2931, 2888, 2858, 1473, 1428, 1369, 1111, 1038 cm^{-1}. LRMS (EI) *m*/*z*: 395 ([M − OMe]$^+$). HRMS (EI, [M − OMe]$^+$): calcd for $C_{25}H_{35}O_2Si$, 395.2401: found, 395.2376.

*(2R)-2-(tert-Butyldiphenylsilanyloxy)-6-methoxymethoxy-5-methylheptan-2-ene (**S29b**).* Using the same procedure as above, (2*R*)-2-(*tert*-butyldiphenylsilanyloxy)-6-methoxymethoxy-5-methylheptan-2-ene (**S29b**) (159 mg, 0.370 mol, 75%, colorless oil, mixture of isomers) was obtained from (3-methoxymethoxy-2-methylbutyl)-triphenylphosphonium iodide (**S27**) (261 mg, 0.500 mmol), BuLi (2.69 M in hexane, 0.19 mL), and (*R*)-2-(*tert*-butyldiphenylsilanyloxy)propionaldehyde (**S28**) (156 mg, 0.500 mmol). The isomer was not separated because stereocenters coming from *E* and *Z* isomers will be lost by oxidation of (6*R*)-6-(*tert*-butyldiphenylsilanyloxy)-3-methylheptane-2,4,5-triol (**34b**). The ratio of isomers could not be determined due to complex NMR spectra. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.68−1.19 (18H, m), 2.01−2.29 (1H, m), 3.22−3.56 (4H, m), 4.25−4.67 (3H, m), 5.01−5.62 (2H, m), 7.32−7.44 (6H, m), 7.65−7.71 (4H, m). ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.9, 16.0, 16.5, 16.6, 16.6, 16.7, 17.0, 17.1, 17.3, 18.2, 19.1, 19.2, 19.2, 24.5, 24.5, 24.7, 25.1, 26.9, 27.0, 37.4, 37.6, 37.8, 38.3, 41.2, 55.2, 55.3, 55.3, 66.0, 66.1, 66.5, 70.2, 70.3, 76.2, 76.3, 76.4, 94.8, 94.8, 95.0, 95.1, 95.1, 95.2, 95.2, 127.3, 127.4, 127.4, 127.4, 127.5, 127.5, 129.4, 129.4, 129.4, 129.5, 129.5, 129.8, 130.2, 130.4, 130.5, 131.2, 131.2, 131.3, 134.2, 134.3, 134.6, 134.6, 134.6, 134.6, 134.7, 134.9, 135.3, 135.8, 135.8, 135.8, 135.8, 135.8, 135.9, 135.9. IR (neat): 2966, 2931, 2889, 2858, 1473, 1428, 1369, 1111, 1038 cm^{-1}. LRMS (EI) *m*/*z*: 395 ([M − OMe]$^+$). HRMS (EI, [M − OMe]$^+$): calcd for $C_{25}H_{35}O_2Si$, 395.2401: found, 395.2407.

*(6S)-6-(tert-Butyldiphenylsilanyloxy)-3-methylhept-4-en-2-ol (**S30a**).* To a stirred solution of (2*S*)-2-(*tert*-butyldiphenylsilanyloxy)-6-methoxymethoxy-5-methylheptan-2-ene (**S29a**) (614 mg, 1.44 mmol) in dry CH_2Cl_2 (7.2 mL) were added 2,2′-bipyridyl (675 mg, 4.32 mmol) and TMSOTf (0.530 mL, 2.88 mmol) successively at 0 °C. The resulting mixture was stirred at the same temperature for 25 min. Then, H_2O (2.9 mL) and Et_2O (2.9 mL) were added to the mixture, and the reaction mixture was stirred vigorously at room temperature for 24 h. The reaction mixture was extracted with EtOAc twice. The combined organic phases were washed with 3 M HCl, saturated aqueous $NaHCO_3$ solution, and brine, dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by column chromatography (EtOAc:hexane = 1:9) to yield (6*S*)-6-(*tert*-butyldiphenylsilanyloxy)-3-methylhept-4-en-2-ol (**S30a**) (234 mg, 0.610 mmol, 42%) as a colorless oil and a mixture of isomers. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.64−1.20 (19H, m), 1.85−2.10 (1H, m), 3.25−3.60 (1H, m), 4.26−4.63 (1H, m), 4.99−5.70 (2H, m), 7.34−7.44 (6H, m), 7.65−7.71 (4H, m). ^{13}C NMR (100 MHz, $CDCl_3$): δ 15.1, 15.1, 16.2, 16.2, 16.4, 16.4, 16.9, 19.1, 19.1, 19.1, 19.2, 19.2, 19.7, 19.8, 19.9, 19.9, 20.0, 20.4, 24.6, 24.6, 24.7, 24.8, 25.1, 26.9, 27.0, 39.2, 39.5, 40.0, 40.2, 43.2, 43.4, 44.4, 44.4, 65.9, 65.9, 66.4, 66.6, 70.1, 70.2, 70.3, 70.9, 70.9, 70.9, 71.0, 71.1, 71.2, 71.3, 71.7, 127.4, 127.4, 127.4, 127.5, 127.5, 129.4, 129.5, 129.5, 129.5, 129.7, 129.9, 130.0, 130.2, 130.7, 130.9, 130.9, 134.1, 134.2, 134.2, 134.3, 134.4, 134.5, 134.5, 135.5, 135.7, 135.8, 135.8, 135.8, 135.9, 135.9, 136.6, 136.6, 136.8, 136.9. IR (neat): 3371, 2966, 2931, 2858, 1428, 1112, 1086, 1054 cm^{-1}. LRMS (EI) *m*/*z*: 325 ([M − *t*Bu]$^+$). HRMS (EI, [M − *t*Bu]$^+$): calcd for $C_{20}H_{25}O_2Si$, 325.1618: found, 325.1630.

*(6R)-6-(tert-Butyldiphenylsilanyloxy)-3-methylhept-4-en-2-ol (**S30b**).* Using the same procedure as above, (6*R*)-6-(*tert*-butyldiphenylsilanyloxy)-3-methylhept-4-en-2-ol (**S30b**) (69.7 mg, 0.180 mmol, 52%, colorless oil, mixture of isomers) was obtained from (2*R*)-2-(*tert*-butyldiphenylsilanyloxy)-6-methoxymethoxy-5-methylheptan-2-ene (**S29b**) (150 mg, 0.350 mmol), 2,2′-bipyridyl (156 mg, 1.00 mmol), and TMSOTf (0.126 mL, 0.700 mmol). ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.64−1.25 (19H, m), 1.85−2.10 (1H, m), 3.27−3.89 (1H, m), 4.26−4.63 (1H, m), 4.99−5.70 (2H, m), 7.34−7.44 (6H, m), 7.65−7.71 (4H, m). ^{13}C NMR (100 MHz, $CDCl_3$): δ 15.1, 16.2, 16.4, 16.4, 16.9, 19.1, 19.1, 19.1, 19.1, 19.7, 19.8, 19.9, 20.0, 20.2, 20.4, 24.6, 24.7, 24.8, 25.0, 26.9, 26.9, 39.2, 39.5, 40.0, 40.2, 43.2, 43.4, 44.3, 44.4, 65.9, 65.9, 66.4, 66.5, 70.1, 70.2, 70.9, 70.9, 70.9, 71.1, 71.1, 71.3, 71.7, 127.4, 127.4, 127.4, 127.5, 127.5, 129.4, 129.5, 129.5, 129.7, 129.9, 129.9, 130.2, 130.7, 130.9, 134.1, 134.1, 134.2, 134.2, 134.2, 134.4, 134.4, 134.5, 135.4, 135.7, 135.8, 135.8, 135.8, 135.8, 135.9, 136.6, 136.6, 136.7, 136.9. IR (neat): 3360, 2966, 2930, 2858, 1428, 1112, 1086, 1053 cm^{-1}. LRMS (EI) *m*/*z*: 325 ([M − *t*Bu]$^+$). HRMS (EI, [M − *t*Bu]$^+$): calcd for $C_{20}H_{25}O_2Si$, 325.1618: found, 325.1625.

*(6S)-6-(tert-Butyldiphenylsilanyloxy)-3-methylheptane-2,4,5-triol (**34a**).* To a stirred solution of (6*S*)-6-(*tert*-butyldiphenylsilanyloxy)-3-methylhept-4-en-2-ol (**S30a**) (234 mg, 0.610 mmol) in *t*-BuOH:H_2O (1:1, 3.0 mL) were added NMO (234 mg, 2.00 mmol) and OsO_4 (0.05 M in THF, 2.5 mL) successively at room temperature. The resulting mixture was stirred at 50 °C for 47 h. To the mixture was added saturated aqueous $Na_2S_2O_3$ solution to quench the reaction. The resulting mixture was extracted with EtOAc twice. The combined organic phases were washed with brine, dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by column chromatography (EtOAc:hexane = 1:4 to 1:1) to yield (6*S*)-6-(*tert*-butyldiphenylsilanyloxy)-3-methylheptane-2,4,5-triol (**34a**) (154 mg, 0.370 mmol, 61%) as a brown oil and a mixture of diastereomers. The diastereomer was not separated because these stereocenters will be lost by oxidation of (6*S*)-6-(*tert*-butyldiphenylsilanyloxy)-3-methylheptane-2,4,5-triol (**34a**). The ratio of isomers could not be determined due to complex NMR spectra. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.83−1.28 (18H, m), 1.72−1.98 (1H, m), 2.19−4.25 (7H, m), 7.37−7.46 (6H, m), 7.67−7.74 (6H, m). ^{13}C NMR (100 MHz, $CDCl_3$): δ 4.1, 4.3, 9.5, 9.6, 10.7, 10.9, 11.4, 13.2, 13.6, 13.7, 16.0, 16.2, 16.5, 18.0, 19.2, 19.3, 19.3, 19.6, 19.7, 19.8, 19.9, 20.2, 20.8, 21.0, 21.3, 21.4, 21.6, 21.6, 21.8, 21.9, 22.0, 27.0, 27.0, 27.0, 38.3, 38.5, 38.8, 39.0, 39.1, 39.1, 39.7, 39.8, 42.4, 42.6, 42.9, 67.7, 68.3, 68.7, 69.1, 69.8, 69.9, 70.0, 70.3, 70.7, 70.7, 70.8, 70.8, 71.0, 71.3, 72.1, 72.2, 73.0, 73.1, 73.6, 73.7, 73.8, 73.9, 74.0, 74.2, 74.3, 74.5, 74.8, 75.0, 75.0, 75.2, 75.5, 76.0, 76.1, 76.1, 127.6, 127.6, 127.6, 127.6, 127.7, 127.7, 127.7, 127.8, 127.8, 127.8, 127.9, 129.7, 129.7, 129.8, 129.8, 129.8, 129.9, 129.9, 130.0, 130.1, 130.1, 132.8, 132.9, 132.9, 133.0, 133.1, 133.3, 133.5, 133.6, 133.7. 133.7, 133.9, 133.9, 135.7, 135.7, 135.8, 135.8, 135.8, 135.9, 135.9, 135.9. IR (neat): 3398, 2967, 2932, 2858, 1462, 1428, 1390, 1112, 998, 967 cm^{-1}. LRMS (EI) *m*/*z*: 359 ([M − *t*Bu]$^+$). HRMS (EI, [M − *t*Bu]$^+$): calcd for $C_{20}H_{27}O_4Si$, 359.1673: found, 359.1661.

*(6R)-6-(tert-Butyldiphenylsilanyloxy)-3-methylheptane-2,4,5-triol (**34b**).* Using the same procedure as above, (6*R*)-6-(*tert*-butyldiphenylsilanyloxy)-3-methylheptane-2,4,5-triol (**34b**) (57.3 mg, 0.140 mmol, 81%, brown oil, mixture of diastereomers) was obtained from (6*R*)-6-(*tert*-butyldiphenylsilanyloxy)-3-methylhept-4-en-2-ol (**S30b**) (63.7 mg, 0.170 mmol), NMO (64.0 mg, 0.54 mmol) and OsO_4 (0.05 M in THF, 0.68 mL). The diastereomer was not separated because these stereocenters will be lost by oxidation of (6*R*)-6-(*tert*-butyldiphenylsilanyloxy)-3-methylheptane-2,4,5-triol (**34b**). The ratio of isomers could not be determined due to complex NMR spectra. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.83−1.29 (18H, m), 1.70−1.94 (1H, m), 2.17−4.23 (7H, m), 7.37−7.46 (6H, m), 7.67−7.74 (6H, m). ^{13}C NMR (100 MHz, $CDCl_3$): δ 4.0, 4.3, 9.5, 9.6, 10.7, 10.9, 13.1, 13.7, 16.0, 16.2, 16.2, 16.4, 18.0, 19.2, 19.2, 19.3, 19.3, 19.3, 19.9, 20.2, 20.6, 20.6, 20.6, 20.8, 21.0, 21.4, 21.6, 21.6, 21.8, 21.9, 22.0, 27.0, 27.0, 27.1, 38.3, 38.3, 38.5, 38.6, 38.6, 38.8, 38.9, 38.9, 39.1, 39.7, 42.4, 42.4, 42.6, 42.6, 68.6, 69.7, 69.9, 70.2, 70.2, 70.4, 70.7, 70.8, 70.9, 72.3, 72.3, 73.0, 73.2, 73.5, 73.6, 73.8, 73.8, 73.9, 73.9, 74.0, 74.3, 74.7, 75.1, 75.5, 76.1, 76.1, 127.5, 127.6, 127.6, 127.6, 127.7, 127.7, 127.7, 127.8, 127.8, 127.8, 127.9, 129.7, 129.7, 129.7, 129.8, 129.8, 129.8, 129.8, 129.9,

dx.doi.org/10.1021/jo502198y | *J. Org. Chem.* 2015, 80, 114−132

129.9, 129.9, 130.0, 130.1, 130.1, 133.1, 133.6, 133.6, 133.7, 133.7, 133.9, 133.9, 133.9, 135.7, 135.7, 135.7, 135.8, 135.8, 135.8, 135.9, 135.9, 135.9. IR (neat): 3406, 2966, 2932, 2859, 1462, 1428, 1390, 1112, 1076, 998, 967 cm^{-1}. LRMS (EI) *m/z*: 359 ([M − *t*Bu]$^+$). HRMS (EI, [M − *t*Bu]$^+$): calcd for $C_{20}H_{27}O_4Si$, 359.1673: found, 359.1685.

*2-[(S)-1-(tert-Butyldiphenylsilanyloxy)ethyl]-2-hydroxy-4,5-dimethylfuran-3-one (**35a**).* To a stirred solution of DMSO (47 μL, 0.89 mmol) in dry CH_2Cl_2 (0.50 mL) was added trifluoroacetic anhydride (63 μL, 0.45 mmol) in dry CH_2Cl_2 (0.50 mL) at −78 °C, and the resulting mixture was stirred at the same temperature for 15 min. Then, a solution of (6*S*)-6-(*tert*-butyldiphenylsilanyloxy)-3-methylheptane-2,4,5-triol (**34a**) (37.0 mg, 0.0890 mmol) in dry CH_2Cl_2 (1.0 mL) was added to the mixture, and the resulting mixture was stirred at −78 °C for 30 min. Then, triethylamine (0.19 mL, 1.3 mmol) was added to the mixture, and the resulting mixture was stirred at room temperature for 10 min. To the mixture was added saturated aqueous NH_4Cl solution to quench the reaction at 0 °C. The resulting mixture was extracted with EtOAc twice. The combined organic phases were washed with brine, dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by flash column chromatography (EtOAc:hexane = 1:4) to yield 2-[(*S*)-1-(*tert*-butyldiphenylsilanyloxy)-ethyl]-2-hydroxy-4,5-dimethylfuran-3-one (**35a**) (14.6 mg, 0.0355 mmol, 40%) as a colorless oil and a mixture of diastereomers. The diastereomeric ratio (1:1) was determined by ^{1}H NMR. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.87 (1.5H, d, *J* = 6.3 Hz), 0.98 (4.5H, s), 1.06 (4.5H, s), 1.12 (1.5H, d, *J* = 6.3 Hz), 1.64 (1.5H, s), 1.65 (1.5H, s), 2.19 (1.5H, s), 2.20 (1.5H, s), 4.02 (0.50H, q, *J* = 6.3 Hz), 4.11 (0.50H, brs), 4.17 (0.50H, q, *J* = 6.3 Hz), 4.56 (0.50H, brs), 7.36−7.45 (6H, m), 7.66−7.74 (4H, m). ^{13}C NMR (100 MHz, $CDCl_3$): δ 5.5, 5.6, 15.0, 15.0, 16.4, 16.4, 19.2, 19.2, 26.5, 26.8, 71.6, 72.1, 103.1, 103.6, 110.0, 110.1, 127.4, 127.5, 127.6, 127.8, 129.5, 129.8, 129.9, 132.5, 132.7, 133.5, 134.2, 135.6, 135.7, 135.8, 135.9, 185.8, 186.1, 200.6, 202.5. IR (neat): 3313, 2930, 2857, 1692, 1612, 1428, 1215, 1113 cm^{-1}. LRMS (EI) *m/z*: 353 ([M − *t*Bu]$^+$). HRMS (EI, [M − *t*Bu]$^+$): calcd for $C_{20}H_{21}O_4Si$, 353.1204: found, 353.1217. $[\alpha]_D^{21}$: +32.5 (*c* 0.065, $CHCl_3$).

*2-[(R)-1-(tert-Butyldiphenylsilanyloxy)ethyl]-2-hydroxy-4,5-dimethylfuran-3-one (**35b**).* Using the same procedure as above, 2-[(*R*)-1-(*tert*-butyldiphenylsilanyloxy)ethyl]-2-hydroxy-4,5-dimethylfuran-3-one (**35b**) (14.1 mg, 0.0340 mmol, 42%, colorless oil, mixture of diastereomers) was obtained from (6*R*)-6-(*tert*-butyldiphenylsilanyloxy)-3-methylheptane-2,4,5-triol (**34b**) (34.2 mg, 0.0820 mmol), DMSO (44 μL, 0.82 mmol), trifluoroacetic anhydride (58 μL, 0.41 mmol), and NEt_3 (0.17 mL, 1.2 mmol). The diastereomeric ratio (1:1) was determined by ^{1}H NMR. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.87 (1.5H, d, *J* = 6.3 Hz), 0.98 (4.5H, s), 1.06 (4.5H, s), 1.12 (1.5H, d, *J* = 6.3 Hz), 1.64 (1.5H, s), 1.65 (1.5H, s), 2.18 (1.5H, s), 2.20 (1.5H, s), 4.02 (0.50H, q, *J* = 6.3 Hz), 4.06 (0.50H, brs), 4.17 (0.50H, q, *J* = 6.3 Hz), 4.54 (0.50H, brs), 7.35−7.47 (6H, m), 7.65−7.74 (4H, m). ^{13}C NMR (100 MHz, $CDCl_3$): δ 5.3, 5.4, 14.7, 16.1, 16.2, 19.0, 19.0, 26.4, 26.6, 71.3, 71.8, 102.5, 102.6, 109.7, 109.8, 127.2, 127.3, 127.4, 127.6, 129.4, 129.6, 129.6, 129.8, 132.2, 132.3, 133.2, 133.7, 135.4, 135.5, 135.5, 135.7, 184.9, 185.3, 199.7, 200.1. IR (neat): 3318, 2930, 2857, 1692, 1613, 1428, 1216, 1113 cm^{-1}. LRMS (EI) *m/z*: 353 ([M − *t*Bu]$^+$). HRMS (EI, [M − *t*Bu]$^+$): calcd for $C_{20}H_{21}O_4Si$, 353.1204: found, 353.1212. $[\alpha]_D^{20}$: −27.6 (*c* 0.065, $CHCl_3$).

*Acetic Acid 2-[(S)-1-(tert-Butyldiphenylsilanyloxy)ethyl]-4,5-dimethyl-3-oxo-2,3-dihydrofuran-2-yl Ester (**S31a**).* To a stirred solution of 2-[(*S*)-1-(*tert*-Butyldiphenylsilanyloxy)ethyl]-2-hydroxy-4,5-dimethylfuran-3-one (**35a**) (13.9 mg, 0.0340 mmol) in dry CH_2Cl_2 (0.17 mL) were added DMAP (6.0 mg, 0.051 mmol) and acetic anhydride (3.9 μL, 0.041 mmol) at 0 °C. The resulting mixture was stirred at room temperature for 15 min. To the mixture was added MeOH to quench the reaction. The resulting mixture was diluted with Et_2O and washed with 3 M HCl, saturated aqueous $NaHCO_3$ solution, and brine, dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The residue was purified by flash column chromatography (EtOAc:hexane = 1:9) to yield acetic acid 2-[(*S*)-1-(*tert*-butyldiphenylsilanyloxy)ethyl]-4,5-dimethyl-3-oxo-2,3-dihydrofuran-2-yl ester (**S31a**) (11.5 mg, 0.0250 mmol, 75%) as a colorless oil and a mixture of diastereomers. The diastereomeric ratio (1:1) was determined by ^{1}H NMR. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.91 (4.5H, s), 1.00 (4.5H, s), 1.09 (3H, d, *J* = 6.3 Hz), 1.71 (1.5H, s), 1.74 (1.5H, s), 1.93 (1.5H, s), 2.01 (1.5H, s), 2.08 (1.5H, s), 2.21 (1.5H, s), 4.19 (0.50H, q, *J* = 6.3 Hz), 4.26 (0.50H, q, *J* = 6.3 Hz), 7.36−7.45 (6H, m), 7.65−7.69 (4H, m). ^{13}C NMR (100 MHz, $CDCl_3$): δ 5.6, 5.8, 14.4, 14.4, 16.3, 16.7, 19.3, 19.3, 20.6, 20.6, 26.4, 26.7, 71.1, 71.7, 100.6, 100.8, 111.9, 111.9, 127.4, 127.6, 127.6, 127.7, 129.6, 129.7, 129.8, 129.9, 132.3, 133.3, 133.6, 134.3, 135.7, 135.8, 135.9, 135.9, 167.4, 167.5, 182.1, 199.1, 200.1. IR (neat): 2956, 2931, 2894, 2858, 1766, 1726, 1650, 1428, 1218, 1114 cm^{-1}. LRMS (FAB) *m/z*: 453 ([M + H]$^+$). HRMS (FAB, [M + H]$^+$): calcd for $C_{26}H_{33}O_5Si$, 453.2092: found, 453.2092.

*Acetic Acid 2-[(R)-1-(tert-Butyldiphenylsilanyloxy)ethyl]-4,5-dimethyl-3-oxo-2,3-dihydrofuran-2-yl Ester (**S31b**).* Using the same procedure as above, acetic acid 2-[(*R*)-1-(*tert*-butyldiphenylsilanyloxy)ethyl]-4,5-dimethyl-3-oxo-2,3-dihydrofuran-2-yl ester (**S31b**) (5.2 mg, 0.012 mmol, 62%, colorless oil, mixture of diastereomers) was obtained from 2-[(*R*)-1-(*tert*-butyldiphenylsilanyloxy)ethyl]-2-hydroxy-4,5-dimethylfuran-3-one (**35b**) (7.6 mg, 0.019 mmol), DMAP (3.4 mg, 0.028 mmol), and acetic anhydride (2.1 μL, 0.022 mmol). The diastereomeric ratio (1:1) was determined by ^{1}H NMR. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.91 (4.5H, s), 1.00 (4.5H, s), 1.09 (3H, d, *J* = 6.3 Hz), 1.71 (1.5H, s), 1.74 (1.5H, s), 1.93 (1.5H, s), 2.00 (1.5H, s), 2.08 (1.5H, s), 2.21 (1.5H, s), 4.19 (0.50H, q, *J* = 6.3 Hz), 4.26 (0.50H, q, *J* = 6.3 Hz), 7.35−7.45 (6H, m), 7.65−7.70 (4H, m). ^{13}C NMR (150 MHz, $CDCl_3$): δ 5.6, 5.8, 14.4, 14.4, 16.3, 16.7, 19.3, 19.3, 20.6, 20.6, 26.4, 26.7, 71.1, 71.7, 100.6, 100.9, 111.9, 111.9, 127.4, 127.6, 127.6, 127.7, 129.6, 129.7, 129.8, 129.9, 132.4, 133.4, 133.6, 134.3, 135.8, 135.9, 135.9, 135.9, 167.4, 167.5, 182.0, 182.0, 199.0, 200.1. IR (neat): 2958, 2931, 2895, 2858, 1766, 1726, 1650, 1428, 1218, 1114 cm^{-1}. LRMS (EI) *m/z*: 395 ([M − *t*Bu]$^+$). HRMS (EI, [M − *t*Bu]$^+$): calcd for $C_{22}H_{23}O_5Si$, 395.1309: found, 395.1294.

■ ASSOCIATED CONTENT

Supporting Information

Determination of absolute configurations of **11**, **17**, **24a**, and **24b**, ^{1}H and ^{13}C NMR spectra of **7**, **11**−**15**, **17**−**23**, **24a**−**31a**, **24b**−**31b**, **33a**, **33b**, **1**, **2**, JBIR-108, **34a**−**34b**, and **35a**−**35b**, and ^{1}H NMR spectra of **38**, **39**, and tri-(*R*)-MTPA ester of JBIR-108. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

This work was supported by a grant from the New Energy and Industrial Technology Department Organization (NEDO) of Japan and a Grant-in-Aid for Scientific Research (23380067 to K.S.-y.) from the Japan Society for the Promotion of Science (JSPS).

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(8) This ratio (1:0.5:0.1) was determined by Me intensities of the doublet for the methyl protons H_3-21 (δ_H 1.30: δ_H 1.17: δ_H 1.18 (1:0.5:0.1)). Later, it was revealed that theoretical ratio was 1.2 (=1 (major component) + 0.2 (minor component)):0.5 (C-2 epimer of major component):0.1 (C-2 epimer of minor component). The exact detection of the 0.2 (minor component) was difficult due to the peak overlapped in natural JBIR-108 (δ_H 1.32−1.36); see Figure 5.
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