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The Asymmetric Total Synthesis of Cinbotolide: A Revision of the Original Structure

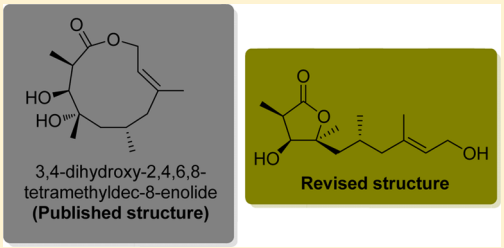
José Manuel Botubol,[†] María Jesús Durán-Peña,[†] Antonio J. Macías-Sánchez,[†] James R . Hanson,[‡] Isidro G. Collado,[†] and Rosario Hernández-Galán*[,†]

[†]Departamento de Química Orgánica, Facultad de Ciencias, Instituto de Biomoléculas, Campus Universitario Rio San Pedro s/n, Universidad de Cádiz, 11510 Puerto Real, Cádiz, Spain

[‡]Department of Chemistry, University of Sussex, Brighton, Sussex, BN1 9QJ, United Kingdom

Supporting Information

ABSTRACT: The structure 3,4-dihydroxy-2,4,6,8-tetramethyldec-8-enolide (**1**) was assigned to a metabolite of *Botrytis cinerea*, but the spectra of several synthetic analogues had significant differences from that of **1**. Examination of the constituents of a *B. cinerea* mutant that overproduces polyketides gave sufficient quantities of **1**, now named cinbotolide, for chemical transformations. These led to a revised γ-butyrolactone structure for the metabolite. This structure has been confirmed by an asymmetric total synthesis, which also established its absolute configuration.



INTRODUCTION

Botrytis cinerea is a well-known phytopathogen that forms a damaging gray mold on a large number of commercial crops.[1] Numerous metabolites have been isolated from this fungus.[2−4]Among these **1** was a polyketide for which the structure 3,4-dihydroxy-2,4,6,8-tetramethyldec-8-enolide was proposed.[5] However, 11-membered lactones are rare, and there are only a few examples that have been found in nature.[6]

In the context of our interest in the metabolites of *B. cinerea*, we have recently attempted to verify the structure of **1** by means of a total synthesis. We obtained several analogues of this structure, among them the (*Z*)-isomer **2** containing a MOM protecting group (Figure 1). However, the spectroscopic

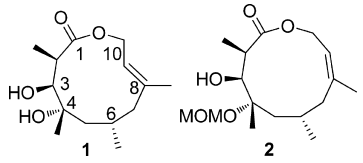


Figure 1. Structures of compounds **1** and **2**.

data of these analogues had significant differences from those reported for the natural product, which suggested that its structure should be revised.[7,8] In the literature there are a number of precedents for corrections[9−15] to the structures of medium-sized lactones.

The study of a mutant of *B. cinerea*, bcbot4, which overproduces polyketides including this metabolite, which we have now named cinbotolide, gave sufficient material for us to carry out simple chemical transformations to clarify its structure. The carbon framework of cinbotolide had been unequivocally established[5] on the basis of the HSQC and HMBC heteronuclear correlations. However, in the light of our synthetic work with the analogues, a significant observation was the absence of a three-bond through-oxygen HMBC correlation for the O═C—O—C—H system in the natural product. This led us to consider an alternative γ-butyrolactone structure **3** for cinbotolide.[8] This lactone might arise by a biosynthetic ring closure of a putative hydroxy-acid precursor involving the nucleophilic attack of a hydroxyl group at C-4 on the terminal carboxylic acid. The γ-butyrolactone would be thermodynamically more stable than the 11-membered lactone.

RESULTS AND DISCUSSION

Acetylation of cinbotolide **1** under standard conditions quantitatively afforded a diacetate **4** (Scheme 1). The chemical shifted observed for signals assigned to H-10 and the HMBC correlation between the signals assigned to H-10 and H-3 and those assigned to the carbonyl groups of the acetates indicated that the free hydroxyl groups were located at C-3 and C-10 (Figure 2) and are incompatible with the original structure. The IR spectrum of the diacetate had carbonyl absorption at 1775 and 1740 cm^{-1} corresponding to the presence of a γ-butyrolactone and acetate esters. Although cinbotolide itself had IR absorption at 1748 cm^{-1} which is rather low for a γ-butyrolactone, this might be affected by hydrogen bonding from the hydroxyl group at C-3.[16] Treatment of cinbotolide with *p*-bromobenzoyl chloride gave a mono-*p*-bromobenzoate **5** and di-*p*-bromobenzoate **6** (Scheme 1) for which similar IR and results were obtained (Scheme 1).

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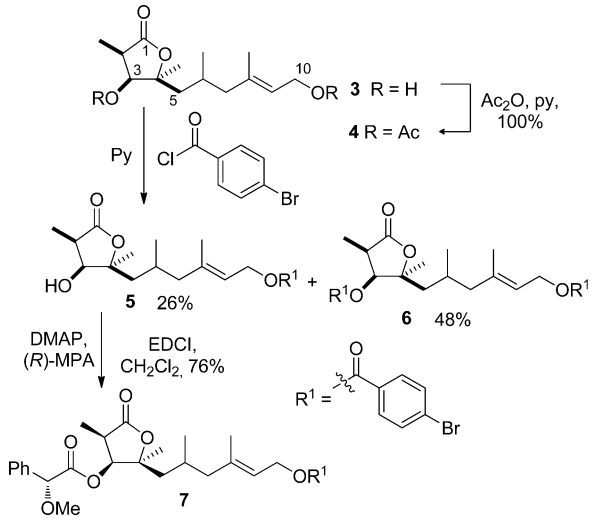
Scheme 1. Synthesis of Compounds 4−7



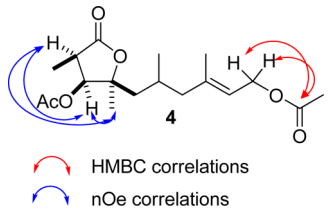


Figure 2. Key HMBC and NOE correlations for **4**.

In the NMR spectra of compound **4**, there were NOE interactions between H-2, H-3 and C4-Me (Figure 2) that supported the relative configuration of the ring as 2*R**,3*S**,4*S**.

Riguera's variable-temperature NMR method[17] was used to determine the absolute configuration at C-3. Esterification of compound **5** with (*R*)-MPA ((*R*)-methoxyphenylacetic acid) afforded compound **7** in 76% yield. The variable-temperature ^{1}H NMR analysis of **7** revealed a negative $\Delta\delta^{T_1T_2}$ value for H-5′ and a positive value for the C2-Me (Figure 3), which indicated

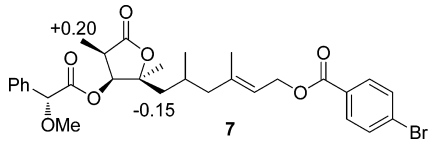
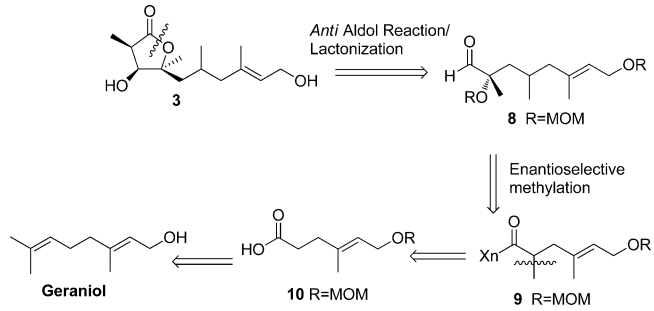


Figure 3. Chemical shifts differences, $\Delta\delta^{T_1T_2}$ (T_1 = 25 °C, T_2 = −60 °C), for H-**5a**′ and C2-Me protons.

a *S*-configuration for C-3. Together with the NOE effects observed for compound **4**, this supports the absolute configuration for the ring as 2*R*,3*S*,4*S*, but leaves the configuration at C-6 undetermined.

In order to confirm the new γ-butyrolactone structure for cinbotolide and establish the absolute configuration of the methyl group in the side chain we have carried out an asymmetric total synthesis of both epimers at C-6. A retrosynthetic analysis of both C-6 epimers of cinbotolide is shown in Scheme 2. In this approach the stereochemistry of the methyl group at C-6 can be effectively controlled through an amidation of the carboxylic acid **10** using a suitable chiral auxiliary and subsequent methylation. Conversion of this compound **9** into the aldehyde **8**, followed by an *anti*

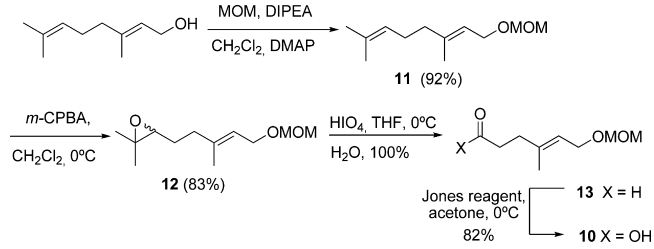
Scheme 2. Retrosynthetic Route for the Synthesis of 3



asymmetric aldol reaction and lactonization, would then provide, separately, both C-6 epimers of cinbotolide.

First the carboxylic acid **10** was prepared following the synthetic route shown in Scheme 3 using the inexpensive

Scheme 3. Synthesis of Carboxylic Acid 10



geraniol as a starting material. The hydroxyl group of geraniol was protected using MOMCl to afford compound **11** which was then subjected to a chemoselective epoxidation with *m*-CPBA at low temperature to give the epoxide **12** in 83% yield. This compound was transformed into the intermediate carboxylic acid **10** by HIO_4 hydrolysis of the epoxide followed by the subsequent cleavage of the diol, to generate the aldehyde **13**. Further oxidation with Jones's reagent gave **10** in an overall yield of 82% from **12**.

The enantioselective methylation of the carboxylic acid **10** in which the primary alcohol was protected as its benzyl ether, has been previously described by Zhou et al. in the synthesis of (−)-kazusamycin A.[18] Following this procedure, compound **10** was converted to the amide **14** using the oxazolidinone (*S*)-**15** in 78% yield (Scheme 4). Enantioselective methylation with MeI afforded[18−20] compound **9** in 74% yield and 92% *de*.[21] This produced the "*S*" stereochemistry for the methyl group at C-6 according to the empirical rule generally accepted.[19]

Reductive cleavage of the oxazolidinone with $NaBH_4$ gave the alcohol **16** in 93% yield. This was subjected to a one-pot oxidation/olefination using the TEMPO-BAIB system and (carbethoxyethylidene)triphenyl phosphorane[22] to stereoselectively produce the ester **17** in good yield. Reduction of the ester group with DIBAL and subsequent Sharpless asymmetric epoxidation with (−)-DIT[23−25] afforded the epoxide **19a** in 78% yield and 80% *de*.[21] Reductive cleavage of the latter with $LiAlH_4$ gave rise to the diol **20a** with the correct stereochemistry at the C-4 position of the natural product. Sequential protection of the primary and tertiary hydroxyl groups with TBS and MOM respectively followed by desilylation and oxidation with PCC, afforded the aldehyde **8a** in good overall yield (Scheme 4).

Condensation of the aldehyde **8a** with the appropriate oxazolidinone (Scheme 5) by the procedure reported by

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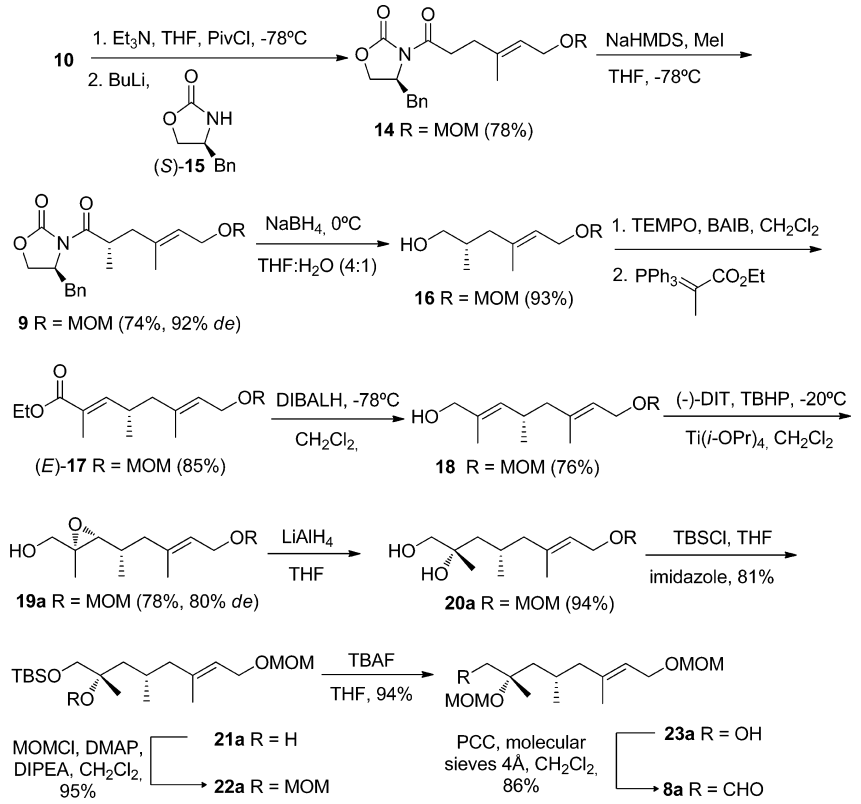
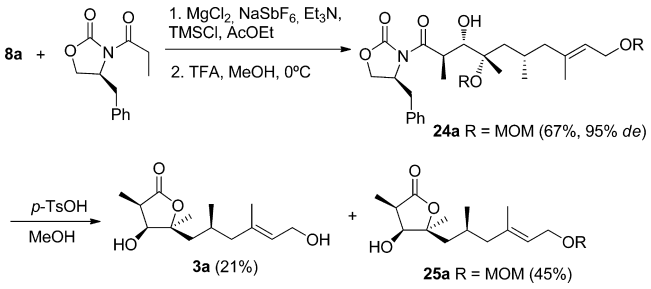
Scheme 4. Preparation of Aldehyde 8a



Scheme 5. Synthesis of 3a



Evans,[26,27] afforded via methanolysis of the silyloxy derivative, the *anti*-aldol product **24a** in 67% yield and 95% *de*.[21] Finally, although several sets of conditions were examined for the removal of the MOM protecting groups, the γ-butyrolactone **3a** was only obtained in low yield when the deprotection was carried out using *p*-TsOH in methanol.[28]

Efforts to improve the yield in the deprotection/lactonization reaction were not continued because this lactone showed slight differences in its NMR data when compared to those reported for cinbotolide. This applied especially to the H-5 and H-7 protons resonances while the H-10 protons appeared as a two-proton doublet while in cinbotolide they were resolved into two separate doublet of doublets (Table 1).

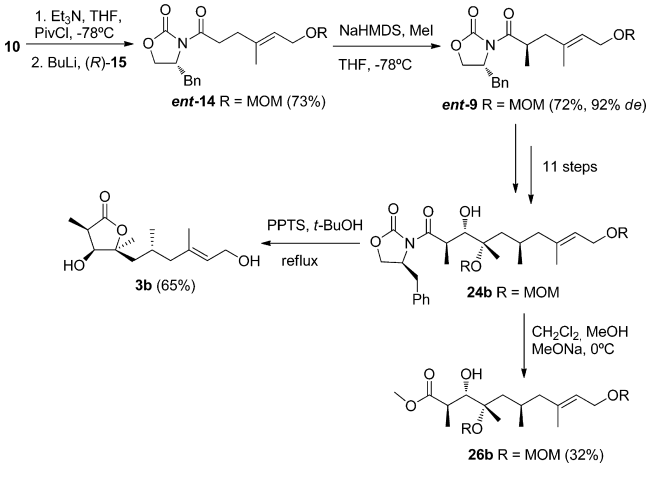
At this point, we carried out the synthesis of the corresponding epimer at C-6 following a similar synthetic strategy to that described in Schemes 4 and 5. The adduct *ent*-**9** was prepared in good yield and *de* from the carboxylic acid **10** by amidation with (*R*)-**15** and enantioselective methylation with MeI.[19] Compound *ent*-**9** was converted to compound **24b** in good overall yield following the route outlined in Scheme 6. In order to confirm the absolute stereochemistry of the alcohol

Table 1. ^{1}H NMR Spectroscopic Differences between 3a and 3[a]

entry	protons	3a	3
1	H-5a	1.70 (dd, *J* 14.5, 3.5)	1.93−1.85 (m)
2	H-5b	1.64 (dd, *J* 14.5, 8.5)	1.55 (dd, *J* 15.8, 8.0)
3	6-Me	1.00 (d, *J* 6.5)	0.96 (d, *J* 6.2)
4	H-7a	2.01 (dd, *J* 13.5, 7.0)	2.15 (dd, *J* 12.2, 5.2)
5	H-7b	1.96 (dd, *J* 13.5, 7.0)	1.93−1.85 (m)
6	H-10a	4.16 (d, *J* 7.0)	4.17 (dd, *J* 12.0, 7.0)
7	H-10b		4.12 (dd, *J* 12.0, 7.0)

[a] δ_H in ppm, *J* in Hz.

Scheme 6. Synthesis of Compound 3b



group at C-3, we carried out different attempts to obtain the MPA or MPTA ester in the hydroxyl group at C-3 for the

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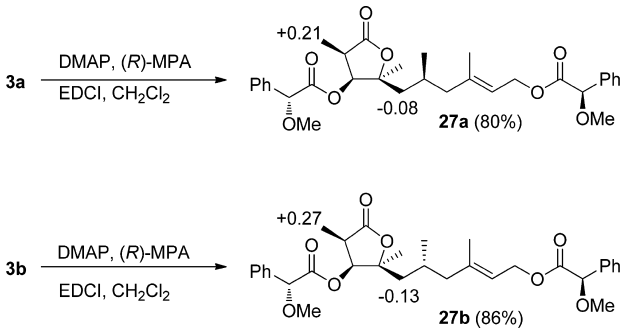
synthesized compounds **24a,b**. All of them were unsuccessful indicating an important steric congestion around C3. At this point, methanolysis of the oxazolidinone group by treatment with sodium methoxide, yielded the methyl ester **26b** (Scheme 6). Although, the MPA ester could not be obtained again, the relative *anti* stereochemistry of the aldol adduct **24b** was determined according to the method of Heathcock on the ester **26b**.[29] Different reaction conditions were then evaluated in order to increase the yield in the deprotection of the MOM ethers and subsequent lactonization. When PPTS[30] in refluxing *t*-BuOH was used, the γ-butyrolactone **3b** was obtained in 65% yield. The spectroscopic data for compound **3b** were identical with those reported for cinbotolide.[5] Since the optical rotation of the natural product had not been reported previously, the synthetic lactone was converted to its diacetate whose optical rotation showed the same sign and magnitude as **4** (−10.3°, *c* = 0.30, $CHCl_3$).

Additionally the absolute configuration of alcohol group at C-3, was confirmed by esterification of **3a** and **3b** with (*R*)-MPA afforded compounds **27a** and **27b** respectively. The Riguera variable-temperature ^1H NMR analysis of both compounds[17] indicated a negative $\Delta\delta^{T_1T_2}$ value for H-5′ and a positive value for the C2-Me (Scheme 7), which confirmed an *S*-configuration for C-3. NOE experiments supported the absolute configuration for the carbons C2−C4 as 2*R*,3*S*,4*S*.

Scheme 7. Synthesis of Compounds 27a,b and Chemical Shifts Differences, $\Delta\delta^{T_1T_2}$ (T_1 = 25 °C, T_2 = −80 °C), for H-5a′ and C2-Me Protons



CONCLUSIONS

The synthesis of the derivatives **4**−**7** of cinbotolide have led us to correct the previously published structure to that of the γ-butyrolactone **3b**. This structure has been confirmed by an asymmetric total synthesis of the two possible epimers at C-6 involving a 16-step synthetic sequence from geraniol. This has established the absolute stereochemistry of cinbotolide as 2*R*,3*S*,4*S*,6*R*.

EXPERIMENTAL SECTION

General Experimental Methods. Unless otherwise noted, materials and reagents were obtained from commercial suppliers and were used without further purification. Dichloromethane, ethyl acetate and triethylamine were freshly distilled from CaH_2 and tetrahydrofuran was dried over sodium and benzophenone and freshly distilled before use. Air- and moisture-sensitive reactions were performed under an argon atmosphere. Purification by semipreparative and analytical HPLC was performed, respectively, with 250 mm × 10 mm (10 μm particles) and 250 mm × 4 mm (5 μm particles) columns using a differential refractometer detector. Silica gel was used for column chromatography. TLC analyses were performed on aluminum plates coated with silica gel with fluorescent indicator (254 nm), 0.25 mm thick. Specific rotations were determined with a digital polarimeter. Infrared spectra were recorded on a FT-IR spectrophotometer and peak position reported in wavenumbers (cm^{-1}). ^1H and ^{13}C NMR measurements were recorded on 400, 500, and 600 MHz spectrometers with $SiMe_4$ as the internal reference. Chemical shifts are reported in parts per million (ppm) and were referenced to $CDCl_3$ (δ_H 7.25, δ_C 77.0), CD_2Cl_2 (δ_H 5.32, δ_C 54.0), C_6D_6 (δ_H 7.16, δ_C 128.4) and acetone-d_6 (δ_H 2.09, δ_C 29.0). NMR assignments were made using a combination of 1D and 2D techniques. Multiplicities are described using the following abbreviations: s = singlet, d = doublet, t = triplet, q = quarter; quint = quintuplet; sext = sextuplet; m = multiplet, br = broad. High-resolution mass spectroscopy (HRMS) was recorded with a double-focusing magnetic sector mass spectrometer in positive ion mode, or in a QTOF mass spectrometer in positive ion electrospray mode at 20 V cone voltage or in positive ion APCI mode.

Acetylation of Natural Product 1. Pyridine (2 drops) was added to a solution of natural product **1** (3.0 mg, 0.01 mmol) in acetic anhydride (0.5 mL) at 0 °C and stirred at room temperature for 18 h. Then, cyclohexane was added (2 mL), and the solvent was evaporated under reduced pressure. This procedure was repeated three times to give quantitatively (3*R*,4*S*,5*S*,2′*R*,4′*E*)-4-acetoxy-5-(6-acetoxy-2,4-dimethylhex-4-enyl)-3,5-dimethyl-4,5-dihydrofuran-2(3*H*)-one (**4**) (3.4 mg, 100%). Yellow oil: $[\alpha]_D^{20}$ −10.3° (*c* 0.30, $CHCl_3$); IR (film) ν_{max} 2945, 1775, 1740, 1455, 1374, 1223, 1087, 1022, 990, 939 cm^{-1}; ^1H NMR (400 MHz, C_6D_6) δ 5.36 (t, *J* = 6.8 Hz, 1H), 4.97 (d, *J* = 5.8 Hz, 1H), 4.58 (d, *J* = 6.8 Hz, 2H), 2.32 (dq, *J* = 6.8, 5.8 Hz, 1H), 2.14 (m, 1H), 1.71 (s, 3H), 1.68−1.61 (m, 3H), 1.59 (s, 3H), 1.48 (s, 3H), 1.26 (dd, *J* = 14.0, 5.2 Hz, 1H), 0.99 (d, *J* = 6.8 Hz, 3H), 0.82 (s, 3H), 0.69 (d, *J* = 6.0 Hz, 3H); ^{13}C NMR (100 MHz, C_6D_6) δ 175.2, 170.1, 169.2, 140.2, 121.5, 85.0, 77.0, 61.0, 48.1, 41.0, 38.5, 26.5, 22.6, 21.1, 20.5, 19.8, 16.0, 8.8; HRMS (ESI^+) calcd for $C_{18}H_{28}O_6Na$ $[M + Na]^+$ 363.1784, found 363.1795.

***p*-Bromobenzoylation of 3.** To a stirred solution of **3** (4.0 mg, 0.016 mmol) in dry pyridine (0.8 mL) were added *p*-bromobenzoyl chloride (14.0 mg, 0.064 mmol) and DMAP (20.0 mg, 0.031 mmol). The reaction mixture was stirred at room temperature for 12 h and was then neutralized by addition of 1 N HCl. The mixture was extracted with CH_2Cl_2 (3 × 5 mL), washed with H_2O (10 mL), dried over anhydrous Na_2SO_4, filtered, and evaporated under reduced pressure to give a crude product that was purified by silica gel column chromatography. Elution with petroleum ether:ethyl acetate (80:20) yielded the compound **5** (1.8 mg, 26%) and **6** (4.6 mg, 48%).

(3*R*,4*S*,5*S*,2′*R*,4′*E*)-5-[6-(*p*-Bromobenzoyloxy)-2,4-dimethylhex-4-enoyl]-4-hydroxy-3,5-dimehtyldihydrofuran-2(3*H*)-one (5). Amorphous solid: $[\alpha]_D^{20}$ +4.3° (*c* 0.1, CH_3OH); IR (film) υ_{max} 3542, 2925, 1772, 1718, 1589, 1456, 1100, 1011, 757 cm^{-1}; ^1H NMR (500 MHz, CD_3COCD_3) δ 7.94 (d, *J* = 8.8 Hz, 2H), 7.71 (d, *J* = 8.8 Hz, 2H), 5.50 (tq, *J* = 6.8, 1.2 Hz, 1H), 4.85 (d, *J* = 6.8, 2H), 4.44 (d, *J* = 5.6 Hz, OH), 4.13 (t, *J* = 5.6 Hz, 1H), 3.04 (dq, *J* = 7.2, 5.6 Hz, 1H), 2.35 (dd, *J* = 13.2, 5.2 Hz, 1H), 1.99 (m, 1H), 1.85 (dd, *J* = 13.2, 9.3 Hz, 1H), 1.83 (dd, *J* = 14.4, 6.2 Hz, 1H), 1.79 (d, *J* = 1.2 Hz, 3H), 1.70 (dd, *J* = 14.4, 6.4 Hz, 1H), 1.38 (s, 3H), 1.14 (d, *J* = 7.2 Hz, 3H), 0.94 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 178.1, 166.1, 142.5, 132.8 (2C), 132.1 (2C), 130.7, 128.2, 121.1, 88.1, 76.6, 62.5, 49.0, 42.0, 40.6, 27.5, 23.0, 21.3, 16.4, 9.0; HRMS ($APCI^+$) calcd for $C_{21}H_{27}O_5BrNa$ $[M + Na]^+$ 461.0940, found 461.0933.

(3*R*,4*S*,5*S*,2′*R*,4′*E*)-4-(*p*-Bromobenzoyloxy)-5-[6-(*p*-bromobenzoyloxy)-2,4-dimethylhex-4-enoyl]-3,5-dimehtyldihydrofuran-2(3*H*)-one (6). Amorphous solid: $[\alpha]_D^{20}$ −12.5° (*c* 0.24, $CHCl_3$); IR (film) υ_{max} 2925, 1771, 1718, 1590, 1458, 1268, 1172, 1099, 1011, 757; ^1H NMR (500 MHz, CD_3COCD_3) δ 8.00 (d, *J* = 8.8 Hz, 2Harom), 7.92 (d, *J* = 8.8 Hz, 2Harom), 7.75 (d, *J* = 8.8 Hz, 2Harom), 7.70 (d, *J* = 8.8 Hz, 2Harom), 5.67 (d, *J* = 5.8, 1H), 5.44 (tq, *J* = 6.8, 1.2 Hz, 1H), 4.85 (dd, *J* = 12.1, 6.8 Hz, 1H), 4.81 (dd, *J* = 12.1, 6.8 Hz, 1H), 3.48 (dq, *J* = 7.2, 5.8 Hz, 1H), 2.24 (dd, *J* = 12.5, 5.5 Hz, 1H), 2.01 (m, 1H), 1.90−1.84 (m, 2H), 1.77 (d, *J* = 1.2 Hz, 3H), 1.64 (dd, *J* = 14.5, 6.7 Hz, 1H), 1.29 (s, 3H), 1.08 (d, *J* = 7.2 Hz, 3H), 0.82 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR (125 MHz, CD_3COCD_3) δ 176.6,

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166.1, 165.3, 142.1, 133.1 (2C), 132.8 (2C), 132.3 (2C), 132.1 (2C), 130.7, 129.3, 129.2, 128.2, 121.4, 86.9, 79.0, 62.4, 48.9, 41.7, 39.6, 27.4, 23.3, 21.5, 16.4, 9.2; HRMS (ESI$^+$) calcd for $C_{28}H_{30}O_6NaBr_2$ [M + Na]$^+$ 643.0307, found 643.0306.

Preparation of (3*R*,4*S*,5*S*,2′*R*,4′*E*)-5-[6-(*p*-Bromobenzoyloxy)-2,4-dimethylhex-4-enoyl]-4-((*R*)-methoxyphenylacetoxy)-3,5-dimehtyldihydrofuran-2(3*H*)-one (7). A mixture of *N*-(3-(dimethylamino)propyl)-*N*′-ethylcarbodiimide (EDCI) (2.2 mg, 10.2 μmol), *N*,*N*′-DMAP (0.18 mg, 1.36 μmol) and (−)-(*R*)-α-methoxy-α-phenylacetic acid (MPA) (1.5 mg, 8.16 mmol) in dry CH_2Cl_2 (0.3 mL) was stirred for 10 min. To the resulting mixture was added the compound **5** (3.0 mg, 6.8 μmol) in CH_2Cl_2 (0.2 mL). After stirring for 18 h, the reaction mixture was evaporated and then added Et_2O (5 mL). The crude was sequentially washed with H_2O (2 mL), twice with saturated sodium bicarbonate solution (20 mL), H_2O (2 mL), dried over anhydrous sodium sulfate, filtered and evaporated under reduced pressure to give ester **7** (3.03 mg, 76% yield). Amorphous solid: $[\alpha]_D^{20}$ −12.5° (*c* 0.24, $CHCl_3$); IR (film) υ_{max} 2925, 1771, 1718, 1590, 1458, 1268, 1172, 1099, 1011, 757; ^{1}H NMR (500 MHz, CD_2Cl_2) δ 7.89 (d, *J* = 8.8 Hz, 2Harom), 7.58 (d, *J* = 8.8 Hz, 2Harom), 7.41−7.33 (m, 5H), 5.44 (tq, *J* = 7.0, 1.2 Hz, 1H), 5.27 (d, *J* = 5.8, 1H), 4.85 (d, *J* = 7.0 Hz, 1H), 4.76 (s, 1H), 3.40 (s, 3H), 2.91 (dq, *J* = 7.3, 5.8 Hz, 1H), 2.26 (dd, *J* = 13.3, 5.3 Hz, 1H), 1.89 (m, 1H), 1.79 (d, *J* = 1.2 Hz, 3H), 1.78 (dd, *J* = 13.2, 8.8 Hz, 1H), 1.63 (dd, *J* = 14.6, 6.2 Hz, 1H), 1.44 (s, 3H), 1.33 (dd, *J* = 14.6, 6.0 Hz, 1H), 0.81 (d, *J* = 6.6 Hz, 3H), 0.71 (d, *J* = 7.2 Hz, 3H); ^{13}C NMR (125 MHz, CD_2Cl_2) δ 176.0, 169.8, 165.7, 141.2, 136.0, 131.7 (2C), 131.1 (2C), 129.7, 129.1, 128.7 (2C), 127.8, 127.3 (2C), 120.4, 86.0, 82.6, 77.6, 62.0, 57.4, 47.7, 40.9, 38.6, 26.4, 22.7, 20.6, 16.1, 7.8; HRMS (ESI$^+$) calcd for $C_{30}H_{35}O_7NaBr$ [M + Na]$^+$ 609.1464, found 609.1473.

Preparation of (*E*)-1-(Methoxymethoxy)-3,7-dimethylocta-2,6-diene (11). Chloromethyl methyl ether (MOMCl) (8.2 mL, 109.1 mmol) was added slowly to a mixture stirred of geraniol (8 g, 51.9 mmol), *N*,*N*′-diisopropylethylamine (20 mL, 114.3 mmol), *N*,*N*′-dimethylaminepyridine (1269 mg, 10.4 mmol) in dry CH_2Cl_2 (250 mL) at 0 °C under an argon atmosphere, and the mixture was allowed to warm to room temperature stirring for 2 h. Then, saturated ammonium chloride solution (100 mL) and CH_2Cl_2 (30 mL) were added, the layers were separated, and the aqueous layer was extracted twice with CH_2Cl_2 (30 mL). The combined organic solution was washed with 1 N HCl (300 mL), saturated sodium bicarbonate (300 mL), twice with brine (300 mL), dried over anhydrous sodium sulfate and filtered. The solvent was evaporated under reduced pressure to give a crude product which was purified by silica gel column chromatography. Elution with petroleum ether:ethyl acetate (95:5) yielded the compound **11** (9430.5 mg, 91.7%) as a yellow oil. Spectroscopic data of compound **11** were identical to those described in the literature.[31]

Preparation of (±)-(*E*)-6,7-Epoxy-1-(methoxymethoxy)-3,7-dimethylocta-2,6-diene (12). A solution of *m*-CPBA (7010.4 mg, 31.3 mmol) in CH_2Cl_2 (59.6 mL) was added at −20 °C to a solution of (*E*)-1-(methoxymethoxy)-3,7-dimethylocta-2,6-diene (**11**) (6194.7 mg, 31.3 mmol) in CH_2Cl_2 (128 mL). Once the reaction was completed (30 min.), a solution of 1 M NaOH was added (120 mL), and the mixture was allowed to warm to room temperature. Then, the layers were separated, and the aqueous layer was extracted twice with CH_2Cl_2 (180 mL). The combined organic solution was washed with brine (300 mL), dried over anhydrous sodium sulfate and filtered. The solvent was evaporated under reduced pressure to give a crude product which was purified by silica gel column chromatography. Elution with petroleum ether:ethyl acetate (90:10) yielded the epoxide **12** (5562.3 mg, 83.1%). Colorless oil: IR (film) ν_{max} 2929, 1451, 1379, 1250, 1149, 1102, 1040, 922 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.39 (tq, *J* = 6.8, 1.2 Hz, 1H), 4.62 (s, 2H), 4.06 (d, *J* = 6.8 Hz, 2H), 3.36 (s, 3H), 2.70 (t, *J* = 6.2 Hz, 1H), 2.21 (dt, *J* = 14.4, 7.6 Hz, 1H), 2.13 (dt, *J* = 14.4, 7.6 Hz, 1H), 1.69 (s, 3H), 1.68−1.63 (m, 2H), 1.29 (s, 3H), 1.24 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 139.9, 120.8, 95.6, 64.0, 63.6, 58.4, 55.2, 36.2, 27.2, 24.8, 18.7, 16.4; HRMS (ESI$^+$) calcd for $C_{12}H_{22}O_3$ [M + H]$^+$ 215.1647, found 215.1634.

Preparation of (*E*)-6-(Methoxymethoxy)-4-methylhex-4-enal (13). A solution of HIO_4 (7260.2 mg, 31.5 mmol) in water (28 mL) was added to (±)-(*E*)-6,7-epoxy-1-(methoxymethoxy)-3,7-dimethylocta-2,6-diene (**12**) (6134.7 mg, 28.7 mmol) dissolved in THF (48 mL) at 0 °C and stirred for 20 min. Then, brine was added (35 mL), and the layers were separated, and the aqueous layer was extracted with ethyl acetate (3 × 80 mL). The combined organic solution was washed with saturated sodium bicarbonate (100 mL) and brine (100 mL), dried over anhydrous sodium sulfate and filtered. The solvent was evaporated under reduced pressure to give quantitatively the aldehyde **13** (4930.7 mg, 100%), which was used without chromatographic purification. Colorless oil: IR (film) ν_{max} 3433, 2936, 2727, 1724, 1442, 1387, 1150, 1101, 1040, 920 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.77 (t, *J* = 1.4 Hz, 1H), 5.37 (tq, *J* = 6.8, 1.2 Hz, 1H), 4.61 (s, 2H), 4.06 (d, *J* = 6.8 Hz, 2H), 3.36 (s, 3H), 2.56 (dt, *J* = 7.6, 1.4 Hz, 2H), 2.36 (t, *J* = 7.6 Hz, 2H), 1.69 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 201.9, 138.6, 121.3, 95.6, 63.5, 55.2, 41.8, 31.5, 16.5; HRMS (ESI$^+$) calcd for $C_9H_{16}O_3Na$ [M + Na]$^+$ 195.0997, found 195.0990.

Preparation of (*E*)-6-(Methoxymethoxy)-4-methylhex-4-enoic acid (10). The above aldehyde **13** (5333.0 mg, 31.0 mmol) was dissolved in acetone (92 mL) and Jones reagent (2.7 M) was added dropwise at 0 °C until the solution remained orange. The organic phase was diluted with ethyl acetate (400 mL) and washed with water (200 mL) until pH = 3. A final washed with brine, dried over $NaSO_4$ and evaporation of the solvent under reduced pressure gave the acid **10** (4411.1 mg, 81.9%), which was used without chromatographic purification for the next step. Colorless oil: IR (film) ν_{max} 3385, 2945, 1734, 1442, 1387, 1206, 1151, 1102, 1036, 946 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.34 (tq, *J* = 6.8, 1.4 Hz, 1H), 4.58 (s, 2H), 4.03 (d, *J* = 6.8 Hz, 2H), 3.33 (s, 3H), 2.44 (m, 2H), 2.32 (t, *J* = 7.6 Hz, 2H), 1.66 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 178.4, 138.7, 120.9, 95.3, 63.4, 55.1, 33.9, 32.3, 16.2; HRMS (ESI$^+$) calcd for $C_9H_{17}O_4$ [M + H]$^+$ 189.1127, found 189.1118.

Preparation of (4*S*,4′*E*)-4-Benzyl-3-[6-(methoxymethoxy)-4-methylhex-4-enoyl]oxazolidin-2-one (14). A round-bottom flask was flame-dried and charged with (*E*)-6-(methoxymethoxy)-4-methylhex-4-enoic acid (**10**) (2477.4 mg, 13.2 mmol) and Et_3N (2.0 mL, 14.5 mmol) in dry THF (17.4 mL), and cooled at −78 °C. Then, pivaloyl chloride (1.6 mL, 13.2 mmol) was added dropwise, and the mixture was stirred at −78 °C for 10 min, and 0 °C for 30 min. In a separated flame-dried round-bottom flask charged with argon, a solution of (4*S*)-benzyloxazolidin-2-one ((*S*)-**15**) (2354.1 mg, 13.3 mmol) in dry THF at −78 °C was added *n*-BuLi (2.5 M solution in Hexane, 5.3 mL, 13.3 mmol). The chelated oxazolidinone was transferred via cannula to the solution of acid/Et_3N/PivCl at −78 °C, and the reaction mixture was allowed to warm to 0 °C. The reaction was stirred for 1 h, and was quenched with aqueous solution of ammonium chloride (50 mL). Then, the layers were separated, and the aqueous layer was extracted with ethyl acetate (3 × 80 mL). The combined organic solution was dried over anhydrous sodium sulfate and filtered. The solvent was evaporated under reduced pressure to give a crude product which was purified by silica gel column chromatography. Elution with petroleum ether:ethyl acetate (75:25) yielded the compound **14** (3580.4 mg, 78.3%). Colorless oil: $[\alpha]_D^{20}$ +45.1° (*c* 0.61, $CHCl_3$); IR (film) ν_{max} 2926, 1782, 1702, 1453, 1353, 1213, 1148, 1104, 1047, 921 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32−7.24 (m, 3H), 7.20−7.18 (m, 2H), 5.42 (tq, *J* = 6.8, 1.2 Hz, 1H), 4.65 (ddt, *J* = 9.6, 7.4, 3.4 Hz, 1H), 4.60 (s, 2H), 4.19 (dd, *J* = 9.2, 7.4 Hz, 1H), 4.15 (dd, *J* = 9.2, 3.4 Hz, 1H), 4.07 (d, *J* = 6.8 Hz, 2H), 3.35 (s, 3H), 3.28 (dd, *J* = 13.4, 3.4 Hz, 1H), 3.11 (ddd, *J* = 16.0, 8.2, 6.8 Hz, 1H), 3.03 (ddd, *J* = 16.0, 8.2, 6.8 Hz, 1H), 2.76 (dd, *J* = 13.4, 9.6 Hz, 1H), 2.42 (dd, *J* = 8.2, 6.8 Hz, 2H), 1.73 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.6, 153.4, 138.8, 135.2, 129.4 (2C), 128.9 (2C), 127.3 (d, Carom), 121.3, 95.6, 66.2, 63.5, 55.2, 55.1, 37.9, 33.9, 33.7, 16.5; HRMS (ESI$^+$) calcd for $C_{19}H_{25}NO_5Na$ [M + Na]$^+$ 370.1630, found 370.1620.

Preparation of (4*S*,2′*S*,4′*E*)-4-Benzyl-3-[6-(methoxymethoxy)-2,4-dimethylhex-4-enoyl]oxazolidin-2-one (9). A solution of $NaN(SiMe_3)_2$ (1.0 M solution in THF, 5.6 mL, 5.6 mmol) was added dropwise at −78° to a solution of (*S*,*E*)-4-benzyl-3-[6-

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(methoxymethoxy)-4-methylhex-4-enoyl]oxazolidin-2-one (**14**) (1762.9 mg, 5.1 mmol) in dry THF (12.7 mL) and stirred for 1 h at the same temperature. Iodomethane (1.7 mL, 25.4 mmol) was added, and the reaction was monitored by TLC at −78 °C (5 h). Then, an aqueous solution of ammonioum chloride (50 mL) was added (25 mL), and the mixture was allowed to warm to room temperature. The layers were separated, and the aqueous layer was extracted with ethyl acetate (3 × 40 mL). The combined organic solution was washed with brine (80 mL), dried over anhydrous sodium sulfate and filtered. The solvent was evaporated under reduced pressure to give a crude product which was purified by silica gel column chromatography. Elution with petroleum ether:ethyl acetate (75:25) yielded the compound **9** (1394.8 mg, 74%, 92% *de*). Colorless oil: $[\alpha]_D^{20}$ +52.1° (*c* 0.92, $CHCl_3$); IR (film) ν_{max} 2932, 1779, 1699, 1456, 1382, 1349, 1209, 1148, 1102, 1041, 969 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.31−7.24 (m, 3H), 7.20−7.18 (m, 2H), 5.36 (tq, *J* = 6.4, 1.2 Hz, 1H), 4.61 (ddt, *J* = 9.6, 7.4, 3.2 Hz, 1H), 4.57 (s, 2H), 4.15 (dd, *J* = 9.0, 7.4 Hz, 1H), 4.11 (dd, *J* = 9.0, 3.2 Hz, 1H), 4.04 (dd, *J* = 11.6, 6.4 Hz, 1H), 4.00 (dd, *J* = 11.6, 6.4 Hz, 1H), 3.95 (sext, *J* = 7.0 Hz, 1H), 3.32 (s, 3H), 3.22 (dd, *J* = 13.4, 3.2 Hz, 1H), 2.74 (dd, *J* = 13.4, 9.6 Hz, 1H), 2.46 (dd, *J* = 13.3, 7.0 Hz, 1H), 2.08 (dd, *J* = 13.5, 7.0 Hz, 1H), 1.67 (s, 3H), 1.17 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.7, 153.0, 137.6, 135.2, 129.3 (2C), 128.8 (2C), 127.2, 122.9, 95.4, 66.0, 63.4, 55.3, 55.1, 43.2, 37.8, 35.5, 16.8, 16.2; HRMS (ESI^+) calcd for $C_{20}H_{27}NO_5Na$ $[M + Na]^+$ 384.1787, found 384.1786.

Preparation of (*S*,*E*)-6-(Methoxymethoxy)-2,4-dimethylhex-4-en-1-ol (16). $NaBH_4$ (1044.9 mg, 28.2 mmol) was added at 0 °C to a stirred solution of (4*S*,2′*S*,4′*E*)-4-benzyl-3-[6-(methoxymethoxy)-2,4-dimethylhex-4-enoyl]oxazolidin-2-one (**9**) (2549.7 mg, 7.1 mmol) in a mixture 4:1 THF:H_2O (35.2 mL). When TLC monitoring indicated the completion of the reaction (12 h), 1 N HCl was added until pH = 7. Layers were separated, and the aqueous layer was extracted with two portions of ethyl acetate (15 mL). The combined organic solution was washed with brine (30 mL), dried over anhydrous sodium sulfate and filtered. Solvent was evaporated under reduced pressure at 0 °C to give a crude product which was purified by silica gel column chromatography. Elution with petroleum ether:ethyl acetate (70:30) yielded the alcohol **16** (1239.3 mg, 93.4%). Colorless oil: $[\alpha]_D^{20}$ −5.1° (*c* 0.23, $CHCl_3$); IR (film) ν_{max} 3420, 2927, 1667, 1453, 1383, 1215, 1149, 1100, 1042, 921 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.30 (t, *J* = 6.8 Hz, 1H), 4.56 (s, 2H), 4.03 (dd, *J* = 12.0, 6.8 Hz, 1H), 4.00 (dd, *J* = 12.0, 6.8 Hz, 1H), 3.40 (dd, *J* = 10.6, 5.4 Hz, 1H), 3.34 (dd, *J* = 10.6, 5.4 Hz, 1H), 3.31 (s, 3H), 2.26 (s, OH), 2.10 (m, 1H), 1.78 (m, 2H), 1.62 (s, 3H), 0.81 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 139.3, 121.9, 95.3, 67.8, 63.5, 55.0, 43.8, 33.4, 16.4, 16.1; HRMS (ESI^+) calcd for $C_{10}H_{20}O_3Na$ $[M + Na]^+$ 211.1310, found 211.1301.

Preparation of (*S*,2*E*,6*E*)-Ethyl 8-(methoxymethoxy)-2,4,6-trimethylocta-2,6-dienoate ((*E*)-17). TEMPO (207.3 mg, 1.3 mmol) and BAIB (4.6 g, 14.3 mmol) were added at 0 °C to a solution of (*S*,*E*)-6-(methoxymethoxy)-2,4-dimethylhex-4-en-1-ol (**16**) (1224.1 mg, 6.5 mmol) in dry CH_2Cl_2 (19.4 mL), and the mixture was stirred for 4 h. Then, (carbethoxyethylidene)triphenylphosphorane (5.0 g, 13.0 mmol) was added, and the solution was stirred for a further 12 h at 40 °C. The solvent was removed under reduced pressure, and the residue was purified by silica gel column chromatography. Elution with petroleum ether:ethyl acetate (94:6) yielded the ester (*E*)-**17** (1495.6 mg, 85.2%). Colorless oil: $[\alpha]_D^{20}$ +5.4° (*c* 0.94, $CHCl_3$); IR (film) ν_{max} 2932, 1711, 1649, 1452, 1367, 1254, 1207, 1149, 1102, 1039, 921, 750 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 6.52 (dq, *J* = 9.8, 1.4 Hz, 1H), 5.32 (tq, *J* = 6.8, 1.2 Hz, 1H), 4.59 (s, 2H), 4.16 (q, *J* = 7.1 Hz, 2H), 4.04 (d, *J* = 6.8 Hz, 2H), 3.34 (s, 3H), 2.68 (dsext, *J* = 9.8, 6.8 Hz, 1H), 2.07 (dd, *J* = 13.6, 6.8 Hz, 1H), 2.03 (dd, *J* = 13.6, 6.8 Hz, 1H), 1.81 (d, *J* = 1.4 Hz, 3H), 1.64 (s, 3H), 1.27 (t, *J* = 7.1 Hz, 3H), 0.96 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.3, 147.2, 138.3, 126.4, 122.5, 95.3, 63.4, 60.4, 55.1, 46.5, 31.4, 19.5, 16.4, 14.2, 12.4; HRMS (ESI^+) calcd for $C_{15}H_{26}O_4Na$ $[M + Na]^+$ 293.1729, found 293.1723.

Preparation of (*S*,2*E*,6*E*)-8-(Methoxymethoxy)-2,4,6-trimethylocta-2,6-dien-1-ol (18). Diisobutylaluminum hydride (DIBALH) (7.8 mL of a solution 1.0 M in CH_2Cl_2, 7.8 mmol) was slowly added to a solution of (*S*,2*E*,6*E*)-ethyl 8-(methoxymethoxy)-2,4,6-trimethylocta-2,6-dienoate ((*E*)-**17**) (958.7 mg, 3.55 mmol) in dry CH_2Cl_2 (11.1 mL) and cooled at −78 °C. The reaction was stirred for 1 h at the same temperature and quenched with ethyl acetate (20 mL). Then, a saturated solution of Rochelle's salt (20 mL) was added, and the mixture was allowed to warm to room temperature while maintaining vigorous stirring for a further hour. The aqueous phase was extracted with ethyl acetate (3 × 50 mL), and the combined organic solutions were washed with brine (80 mL), dried over anhydrous sodium sulfate and filtered. Evaporation of the solvent under reduced pressure rendered a crude product that was purified by silica gel column chromatography. Elution with petroleum ether:ethyl acetate (70:30) yielded (*S*,2*E*,6*E*)-8-(methoxymethoxy)-2,4,6-trimethylocta-2,6-dien-1-ol (**18**) (616.0 mg, 76.1%). Colorless oil: $[\alpha]_D^{20}$ −14.0° (*c* 0.36, $CHCl_3$); IR (film) ν_{max} 3427, 2927, 1645, 1451, 1383, 1214, 1149, 1098, 1038, 921 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.26 (t, *J* = 6.8 Hz, 1H), 5.12 (d, *J* = 8.8 Hz, 1H), 4.59 (d, *J* = 6.8 Hz, 1H), 4.57 (d, *J* = 6.8 Hz, 1H), 4.07 (dd, *J* = 11.4, 6.8 Hz, 1H), 3.99 (dd, *J* = 11.7, 6.8 Hz, 1H), 3.93 (s, 2H), 3.34 (s, 3H), 2.70 (s, OH), 2.57 (dsext, *J* = 8.8, 7.2 Hz, 1H), 1.99 (dd, *J* = 13.4, 7.2 Hz, 1H), 1.93 (dd, *J* = 13.4, 7.2 Hz, 1H), 1.63 (s, 6H), 0.91 (d, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.3, 133.6, 132.3, 121.9, 95.2, 69.1, 63.5, 55.1, 47.5, 30.1, 20.5, 16.3, 13.7; HRMS (ESI^+) calcd for $C_{13}H_{24}O_3Na$ $[M + Na]^+$ 251.1623, found 251.1614.

Preparation of (2*R*,3*R*,4*S*,6*E*)-2,3-Epoxy-8-(methoxymethoxy)-2,4,6-trimethyloct-6-en-1-ol (19a). Ti(*i*-OPr)$_4$ (titanium(IV) isopropoxide, 0.57 mL, 1.94 mmol) was added at −25 °C to a solution of (−)-DIT ((−)-diisopropyl D-tartrate, 538 mg, 2.3 mmol) in dry CH_2Cl_2 (13.9 mL) under an argon atmosphere. The mixture was stirred for 20 min and then, a solution of (*S*,2*E*,6*E*)-8-(methoxymethoxy)-2,4,6-trimethylocta-2,6-dien-1-ol (**18**) (551.8 mg, 2.4 mmol) in dry CH_2Cl_2 (5.7 mL) was added slowly stirring for 20 min. Finally, TBHP (5.0−6.0 M solution in nonane, 0.9 mL, 4.84 mmol) was added slowly. When TLC monitoring indicated the completion of the reaction (2 h), diethyl ether (2 mL) and a saturated Na_2SO_4 solution (2 mL) were added, and the mixture was allowed to warm to room temperature, stirred for an additional hour, filtered with Et_2O (250 mL) through Celite, and the solvent evaporated. The crude was redissolved in diethyl ether (5 mL) and a solution of NaOH (153 mg) in brine (5 mL) was added at 0 °C. The mixture was stirred vigorously for 2 h, and the aqueous layer was separated and extracted with three portions of ethyl acetate (15 mL). The combined organic solution was washed with brine (20 mL), dried over anhydrous sodium sulfate and filtered. Evaporation of the solvent gave a crude product that was purified by silica gel column chromatography. Elution with petroleum ether:ethyl acetate (70:30) yielded the alcohol **19a** (432.6 mg, 77.8%, 80% *de*). Colorless oil: $[\alpha]_D^{20}$ −7.8° (*c* 0.14, $CHCl_3$); IR (film) ν_{max} 3450, 2936, 1639, 1447, 1382, 1147, 1096, 1038, 922 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.37 (tq, *J* = 7.0, 1.2 Hz, 1H), 4.62 (s, 2H), 4.09 (dd, *J* = 11.5, 7.0 Hz, 1H), 4.00 (dd, *J* = 11.5, 7.0 Hz, 1H), 3.58 (d, *J* = 12.0 Hz, 1H), 3.53 (d, *J* = 12.0 Hz, 1H), 3.36 (s, 3H), 2.67 (d, *J* = 9.5 Hz, 1H), 2.05 (dd, *J* = 13.4, 8.3 Hz, 1H), 2.00 (dd, *J* = 13.4, 6.9 Hz, 1H), 1.66 (s, 3H), 1.68−1.59 (m, 1H), 1.25 (s, 3H), 1.06 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.2, 122.6, 95.8, 66.3, 66.1, 63.6, 61.9, 55.3, 44.4, 30.5, 18.0, 16.5, 14.8; HRMS (ESI^+) calcd for $C_{13}H_{25}O_4$ $[M + H]^+$ 245.1753, found 245.1741.

Preparation of (2*S*,4*S*,6*E*)-8-(Methoxymethoxy)-2,4,6-trimethyloct-6-ene-1,2-diol (20a). $LiAlH_4$ (4.0 M solution in THF, 1.0 mL, 3.9 mmol) was added slowly at 0 °C to a solution of (2*R*,3*R*,4*S*,6*E*)-2,3-epoxy-8-(methoxymethoxy)-2,4,6-trimethyloct-6-en-1-ol (**19a**) (432.6 mg, 1.8 mmol) in THF (11.2 mL) under inert atmosphere. The mixture was allowed to warm to room temperature and when TLC monitoring indicated the completion of the reaction (12 h), the mixture was recooled at 0 °C and water (5 mL) and HCl 1N (2 mL) were added slowly until pH = 3. The layers were separated, and the aqueous layer was extracted with two portions of ethyl acetate (15 mL). The combined organic solution was washed with brine (30

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mL), dried over anhydrous sodium sulfate, filtered, and the solvent was evaporated under reduced pressure to give diol **20a** (407.9 mg, 93.5%), which was used in the next step without further purification. Colorless oil: $[\alpha]_D^{20}$ −1.0° (*c* 0.11, $CHCl_3$); IR (film) ν_{max} 3418, 2929, 1644, 1456, 1381, 1149, 1100, 1038, 923 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.33 (tq, *J* = 7.0, 1.2 Hz, 1H), 4.61 (s, 2H), 4.08 (dd, *J* = 11.5, 7.0 Hz, 1H), 4.04 (dd, *J* = 11.5, 7.0 Hz, 1H), 3.41 (d, *J* = 10.8 Hz, 1H), 3.36 (s, 3H), 3.32 (d, *J* = 10.8 Hz, 1H), 1.99 (dd, *J* = 13.2, 7.2 Hz, 1H), 1.87 (dd, *J* = 13.2, 6.8 Hz, 1H), 1.85−1.75 (m, 1H), 1.65 (s, 3H), 1.47 (dd, *J* = 14.4, 3.3 Hz, 1H), 1.26 (dd, *J* = 14.4, 7.8 Hz, 1H), 1.15 (s, 3H), 0.95 (d, *J* = 6.5 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.7, 122.2, 95.5, 73.2, 70.1, 63.5, 55.2, 49.3, 44.6, 26.6, 23.4, 22.0, 16.2; HRMS (ESI^+) calcd for $C_{13}H_{26}O_4Na$ $[M + Na]^+$ 269.1729, found 269.1740.

Preparation of (2*S*,4*S*,6*E*)-1-(*tert*-Butyldimethylsilyloxy)-8-(methoxymethoxy)-2,4,6-trimethyloct-6-en-2-ol (21a). A solution of *tert*-butylchlorodimethylsilane (501.4 mg, 2.76 mmol) in dry THF (1.7 mL) was added to a solution of imidazole (1257.8 mg, 18.4 mmol) and (2*S*,4*S*,6*E*)-8-(methoxymethoxy)-2,4,6-trimethyloct-6-ene-1,2-diol (**20a**) (566.5 mg, 2.3 mmol) in dry THF (3.2 mL) at 0 °C under an argon atmosphere. The mixture was allowed to warm to room temperature and when TLC monitoring indicated the completion of the reaction (1.5 h), were added brine (5 mL). The organic layer was washed three times with brine (5 mL), dried over anhydrous sodium sulfate, filtered, and the solvent evaporated under reduced pressure. The crude product was purified by silica gel column chromatography. Elution with petroleum ether:ethyl acetate (92:8) yielded the compound **21a** (672 mg, 81.2%). Colorless oil: $[\alpha]_D^{20}$ +1.2° (*c* 1.4, $CHCl_3$); IR (film) ν_{max} 3466, 2929, 1644, 1454, 1385, 1255, 1149, 1098, 1038, 837 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.31 (t, *J* = 7.0 Hz, 1H), 4.62 (s, 2H), 4.07 (d, *J* = 7.0, Hz, 2H), 3.37 (d, *J* = 9.4, Hz, 1H), 3.36 (s, 3H), 3.32 (d, *J* = 9.4, Hz, 1H), 2.28 (s, OH), 2.03 (dd, *J* = 16.2, 9.8 Hz, 1H), 1.88−1.81 (m, 2H), 1.64 (s, 3H), 1.36 (dd, *J* = 14.4, 3.4 Hz, 1H), 1.27 (dd, *J* = 14.3, 7.4 Hz, 1H), 1.12 (s, 3H), 0.94 (d, *J* = 6.2 Hz, 3H), 0.89 (s, 9H), 0.05 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.6, 122.1, 95.4, 72.7, 70.9, 63.6, 55.2, 49.4, 44.7, 26.5, 25.9 (3C), 23.5, 21.6, 18.3, 16.1, −5.5 (2C); HRMS (ESI^+) calcd for $C_{19}H_{40}O_4NaSi$ $[M + Na]^+$ 383.2594, found 383.2599.

Preparation of (2*S*,4*S*,6*E*)-1-(*tert*-Butyldimethylsilyloxy)-2,8-bis(methoxymethoxy)-2,4,6-trimethyloct-6-ene (22a). (2*S*,4*S*,6*E*)-1-(*tert*-Butyldimethylsilyloxy)-8-(methoxymethoxy)-2,4,6-trimethyloct-6-en-2-ol (**21a**) (651.6 mg, 1.81 mmol) was converted to (2*S*,4*S*,6*E*)-1-(*tert*-butyldimethylsilyloxy)-2,8-bis(methoxymethoxy)-2,4,6-trimethyloct-6-ene (**22a**) (694.9 mg, 95%) following the methodology described above for the synthesis of (*E*)-1-(methoxymethoxy)-3,7-dimethylocta-2,6-diene (**11**) but using 5 equiv of DIPEA and 3.5 equiv of MOMCl. Colorless oil: $[\alpha]_D^{20}$ +3.4° (*c* 0.51, $CHCl_3$); IR (film) ν_{max} 2929, 2858, 1463, 1384, 1253, 1148, 1104, 1037, 919, 838, 778 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.31 (t, *J* = 7.0 Hz, 1H), 4.73 (d, *J* = 7.5, Hz, 1H), 4.70 (d, *J* = 7.5, Hz, 1H), 4.62 (s, 2H), 4.06 (d, *J* = 7.0, Hz, 2H), 3.48 (d, *J* = 9.8, Hz, 1H), 3.44 (d, *J* = 9.8, Hz, 1H), 3.36 (s, 3H), 3.34 (s, 3H), 2.11 (dd, *J* = 11.8, 4.2 Hz, 1H), 1.87−1.75 (m, 2H), 1.64 (s, 3H), 1.47 (dd, *J* = 15.0, 3.8 Hz, 1H), 1.35 (dd, *J* = 15.0, 7.0 Hz, 1H), 1.19 (s, 3H), 0.89 (d, *J* = 6.0 Hz, 3H), 0.87 (s, 9H), 0.02 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 139.8, 122.0, 95.4, 91.2, 79.0, 68.9, 63.5, 55.3, 55.1, 49.3, 42.8, 26.0, 25.8 (3C), 21.4, 21.3, 18.2, 16.0, −5.6 (2C); HRMS (ESI^+) calcd for $C_{20}H_{41}O_4Si$ $[M\text{-}OMe]^+$ 373.2774, found 373.2774.

Preparation of (2*S*,4*S*,6*E*)-2,8-Bis(methoxymethoxy)-2,4,6-trimethyloct-6-en-1-ol (23a). Tetrabutylammonium fluoride (TBAF, 1.0 M solution, 2.4 mL, 2.4 mmol) was added slowly to a solution stirred of (2*S*,4*S*,6*E*)-1-(*tert*-butyldimethylsilyloxy)-2,8-bis-(methoxymethoxy)-2,4,6-trimethyloct-6-ene (**22a**) (694.9 mg, 1.72 mmol) in dry tetrahydrofuran (16.8 mL) under an argon atmosphere. When TLC monitoring indicated the completion of the reaction (3 h), the mixture was washed three times with brine (10 mL), dried over anhydrous sodium sulfate and filtered. The solvent was evaporated under reduced pressure to give a crude product which was purified by silica gel column chromatography. Elution with petroleum ether:ethyl acetate (75:25) yielded the alcohol **23a** (470.7 mg; 94.4%). Colorless oil: $[\alpha]_D^{20}$ +6.8° (*c* 0.35, $CHCl_3$); IR (film) ν_{max} 3457, 2930, 1644, 1460, 1382, 1146, 1095, 1031, 919 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.32 (t, *J* = 6.8 Hz, 1H), 4.68 (s, 2H), 4.62 (s, 2H), 4.07 (d, *J* = 6.8, Hz, 2H), 3.44 (dd, *J* = 12.0, 6.2 Hz, 1H), 3.41 (s, 3H), 3.37 (s, 3H), 3.35 (dd, *J* = 12.0, 8.0 Hz, 1H), 3.26 (dd, *J* = 8.0, 6.2 Hz, OH), 2.05 (dd, *J* = 16.2, 9.6 Hz, 1H), 1.88−1.80 (m, 2H), 1.64 (s, 3H), 1.43 (dd, *J* = 14.8, 6.8 Hz, 1H), 1.37 (dd, *J* = 14.8, 3.8 Hz, 1H), 1.19 (s, 3H), 0.90 (d, *J* = 6.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.3, 122.4, 95.5, 90.8, 80.0, 68.9, 63.6, 55.4, 55.2, 49.4, 42.3, 26.2, 21.4, 20.3, 16.1; HRMS (ESI^+) calcd for $C_{15}H_{30}O_5Na$ $[M + Na]^+$ 313.1991, found 313.2006.

Preparation of (2*S*,4*S*,6*E*)-2,8-Bis(methoxymethoxy)-2,4,6-trimethyloct-6-enal (8a). Alcohol **23a** (115.5 mg, 0.40 mmol) was dissolved in CH_2Cl_2 (1 mL) and then added dropwise to a suspension of PCC (87.7 mg, 0.6 mmol) and powdered 4 Å molecular sieves (175.4 mg) in CH_2Cl_2 (2 mL) at 0 °C. The reaction was stirred vigorously at 0 °C for 2 h, diethyl ether (6 mL) was then added, and the mixture was stirred for an additional 1 h. The suspension was filtered over a silica gel pad (petroleum ether:ethyl acetate, 80:20, 300 mL). The solvent was evaporated under reduced pressure at 0 °C to give the aldehyde **8a** (98.6 mg, 86%) that was used immediately in the next step. Colorless oil: $[\alpha]_D^{20}$ −9.7° (*c* 0.32, $CHCl_3$); IR (film) ν_{max} 2928, 1732, 1455, 1378, 1148, 1104, 1036, 918 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 9.56 (s, 1H), 5.32 (t, *J* = 6.8 Hz, 1H), 4.68 (s, 1H), 4.65 (d, *J* = 7.4 Hz, 1H), 4.62 (s, 2H), 4.06 (d, *J* = 6.8, Hz, 2H), 3.40 (s, 3H), 3.36 (s, 3H), 2.01 (dd, *J* = 16.4, 10.0 Hz, 1H), 1.92−1.82 (m, 2H), 1.64 (s, 3H), 1.62 (dd, *J* = 14.6, 3.6 Hz, 1H), 1.49 (dd, *J* = 14.6, 8.0 Hz, 1H), 1.29 (s, 3H), 0.86 (d, *J* = 6.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 203.9, 138.9, 122.7, 95.5, 92.0, 82.8, 63.5, 55.8, 55.2, 48.8, 42.6, 26.0, 21.4, 18.6, 16.1; HRMS (ESI^+) calcd for $C_{15}H_{28}O_5Na$ $[M + Na]^+$ 311.1834, found 311.1840.

Preparation of (4*S*,2′*R*,3′*S*,4′*S*,6′*S*,8′*E*)-4-Benzyl-3-[3-hydroxy-4,8-bis(methoxymethoxy)-2,4,6,8-tetramethyldec-8-eneyl]oxazolidin-2-one (24a). (+)-(4*S*)-4-Benzyl-3-propionyloxazolidin-2-one (114.6 mg, 0.49 mmol) was treated with $MgCl_2$ (23.8 mg, 0.24 mmol), $NaSbF_6$ (50.7 mg, 0.20 mmol) and triethylamine (0.15 mL, 1.1 mmol) in ethyl acetate (1 mL) and stirred for 10 min at room temperature. Then, aldehyde **8a** (170.0 mg, 0.59 mmol) dissolved in ethyl acetate (0.5 mL) and chlorotrimethylsilane (0.1 mL, 0.79 mmol) were added sequentially and stirred for 36 h. The orange slurry was pushed through a pad of silica with Et_2O (200 mL), and the solvent removed under reduced pressure. The residue was dissolved in dry methanol (40 mL) and trifluoroacetic acid (0.05 mL, 0.65 mmol) was added at 0 °C. The mixture was stirred for 15 min and solvent was evaporated under reduced pressure to obtain a crude product which was purified by silica gel column chromatography. Elution with petroleum ether:ethyl acetate (80:20) yielded the compound **24a** (205.4 mg, 66.7%, 95% *de*). Colorless oil: $[\alpha]_D^{20}$ +9.2° (*c* 0.12, $CHCl_3$); IR (film) ν_{max} 3457, 2930, 1782, 1673, 1453, 1384, 1209, 1147, 1106, 1030, 920 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.34−7−30 (m, 2H), 7.27−7.22 (m, 3H), 5.29 (t, *J* = 7.0 Hz, 1H), 4.68 (d, *J* = 7.4 Hz, 1H), 4.65 (d, *J* = 7.4 Hz, 1H), 4.60 (s, 2H), 4.68−4.58 (m, 1H), 4.37 (d, *J* = 9.4, Hz, OH), 4.34 (dq, *J* = 7.2, 2.8 Hz, 1H), 4.12 (m, 2H), 4.05 (d, *J* = 7.0, Hz, 2H), 3.58 (dd, *J* = 9.4, 2.8 Hz, 1H), 3.44 (dd, *J* = 13.4, 3.4 Hz, 1H), 3.34 (s, 3H), 3.29 (s, 3H), 2.57 (dd, *J* = 13.4, 10.8 Hz, 1H), 2.14 (m, 1H), 1.90 (dd, *J* = 13.4, 3.0 Hz, 1H), 1.86−1.76 (m, 2H), 1.64 (s, 3H), 1.38−1.35 (m, 1H), 1.37 (d, *J* = 7.2 Hz, 3H),1.33 (s, 3H), 0.88 (d, *J* = 6.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.3, 152.9, 139.6, 135.5, 129.3 (2C), 129.0 (2C), 127.3, 122.1, 95.4, 90.9, 81.8, 80.9, 65.8, 63.5, 55.6, 55.3, 55.1, 49.5, 43.2, 38.0, 34.6, 26.7, 21.5, 21.3, 17.9, 16.1; HRMS (ESI^+) calcd for $C_{28}H_{43}NO_8Na$ $[M + Na]^+$ 544.2886, found 544.2898.

Deprotection of Compound 24a. To a solution of compound **24a** (41.3 mg, 0.079 mmol) in MeOH (1 mL) was added *p*-TsOH (3 mg, 0.016 mmol), and the resulting solution was stirred overnight. The MeOH was evaporated, and the resulting crude was redissolved in EtOAc (5 mL), washed with H_2O (2 mL), dried over Na_2SO_4, and filtered. Evaporation of the solvent gave a crude product that was purified by silica gel column chromatography. Elution with petroleum

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ether:ethyl acetate (70:30) yielded the lactones **25a** (10.9 mg, 45.9%) and **3a** (4.3 mg, 21.3%).

(3*R*,4*S*,5*S*,2′*S*,4′*E*)-4-Hydroxy-5-(6-(methoxymethoxy)-2,4-dimethylhex-4-enyl)-3,5-dimethyl-4,5-dihydrofuran-2(3*H*)-one (25a). Colorless oil: $[\alpha]_D^{20}$ +4.2° (*c* 0.13, $CHCl_3$); IR (film) ν_{max} 3430, 2928, 1751, 1456, 1382, 1213, 1149, 1098, 1035, 937 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.35 (t, *J* = 6.8 Hz, 1H), 4.64 (d, *J* = 6.6 Hz, 1H), 4.62 (d, *J* = 6.6 Hz, 1H), 4.09 (d, *J* = 6.8 Hz, 2H), 4.00 (d, *J* = 5.4 Hz, 1H), 3.37 (s, 3H), 2.92 (dq, *J* = 7.2, 5.4 Hz, 1H), 1.99 (m, 1H), 1.92−1.83 (m, 2H), 1.70 (dd, *J* = 14.6, 3.3 Hz, 1H), 1.66 (s, 3H), 1.61 (dd, *J* = 14.6, 9.1 Hz, 1H), 1.32 (s, 3H), 1.24 (d, *J* = 7.2 Hz, 3H), 1.00 (d, *J* = 6.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 177.3, 138.9, 122.9, 95.6, 87.4, 76.6, 63.9, 55.2, 49.0, 40.5, 39.7, 26.6, 22.5, 21.2, 16.3, 8.3; HRMS (ESI^+) calcd for $C_{16}H_{28}O_5Na$ $[M + Na]^+$ 323.1834, found 323.1831.

(3*R*,4*S*,5*S*,2′*S*,4′*E*)-4-Hydroxy-5-(6-hydroxy-2,4-dimethylhex-4-enyl)-3,5-dimethyl-4,5-dihydrofuran-2(3*H*)-one (3a). Colorless oil: $[\alpha]_D^{20}$ −4.8° (*c* 0.10, $CHCl_3$); IR (film) ν_{max} 3430, 2921, 1748, 1455, 1351, 1218, 1092, 1015, 938 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.42 (t, *J* = 7.0 Hz, 1H), 4.16 (d, *J* = 7.0 Hz, 2H), 4.02 (d, *J* = 5.5 Hz, 1H), 2.93 (dq, *J* = 7.2, 5.5 Hz, 1H), 2.01 (dd, *J* = 13.5, 7.0 Hz, 1H), 1.96 (dd, *J* = 13.5, 7.0 Hz, 1H), 1.92−1.86 (m, 1H), 1.70 (dd, *J* = 14.5, 3.5 Hz, 1H), 1.66 (s, 3H), 1.64 (dd, *J* = 14.5, 8.5 Hz, 1H), 1.33 (s, 3H), 1.24 (d, *J* = 6.8 Hz, 3H), 1.00 (d, *J* = 6.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 177.7, 138.1, 125.7, 87.4, 76.6, 59.3, 48.9, 40.6, 39.7, 26.6, 22.4, 21.1, 16.2, 8.3; HRMS (ESI^+) calcd for $C_{14}H_{23}O_3$ $[M\text{-}H_2O]^+$ 239.1647, found 239.1640.

Preparation of (3*R*,4*S*,5*S*,2′*S*,4′*E*)-5-[6-((*R*)-Methoxyphenylacetoxy)-2,4-dimethylhex-4-enoyl]-4-((*R*)-methoxyphenylacetoxy)-3,5-dimethyldihydrofuran-2(3*H*)-one (27a). (3*R*,4*S*,5*S*,2′*S*,4′*E*)-4-Hydroxy-5-(6-hydroxy-2,4-dimethylhex-4-enyl)-3,5-dimethyl-4,5-dihydrofuran-2(3*H*)-one (**3a**) (0.7 mg, 2.7 μmol) was converted to compound **27a** (1.2 mg, 80.0%) following the methodology described above for the synthesis of **7** from **5**. Amorphous solid: $[\alpha]_D^{20}$ −35.7° (*c* 0.1, $CHCl_3$); IR (film) υ_{max} 2927, 1771, 1720, 1453, 1265, 1190, 1105, 1021, 757; ^1H NMR (600 MHz, CD_2Cl_2) δ 7.34−7.23 (m, 10H), 5.15 (d, *J* = 6.0, 1H), 5.06 (t, *J* = 7.0 Hz, 1H), 4.67 (s, 1H), 4.64 (s, 1H), 4.51 (dd, *J* = 12.0, 7.2 Hz, 1H), 4.45 (dd, *J* = 12.0, 7.2 Hz, 1H), 3.33 (s, 3H), 3.31 (s, 3H), 2.80 (dq, *J* = 7.5, 6.5 Hz, 1H), 1.95 (m, 1H), 1.81 (dd, *J* = 13.0, 8.5 Hz, 1H), 1.71 (m, 2H), 1.54 (s, 3H), 1.26 (s, 3H), 1.20 (dd, *J* = 13.0, 7.5 Hz, 1H) 0.82 (d, *J* = 6.1 Hz, 3H), 0.68 (d, *J* = 7.2 Hz, 3H); ^{13}C NMR (125 MHz, CD_2Cl_2) δ 176.2, 170.7, 169.5, 140.3, 136.3, 135.7, 128.83, 128.77, 128.5 (2C), 128.3, 128.2, 127.0 (4C), 120.5, 86.4, 82.5, 82.3, 77.4, 61.0, 56.9, 56.8, 48.6, 40.2, 37.9, 26.4, 23.1, 20.3, 16.0, 7.9; HRMS (ESI^+) calcd for $C_{32}H_{40}O_8Na$ $[M + Na]^+$ 575.2621, found 575.2617.

Preparation of (4*R*,4′*E*)-4-Benzyl-3-[6-(methoxymethoxy)-4-methylhex-4-eneyl]oxazolidin-2-one (*ent*-14). (*E*)-6-(Methoxymethoxy)-4-methylhex-4-enoic acid (**10**) (2385.7 mg, 12.7 mmol) was converted to (4*R*,4′*E*)-4-benzyl-3-[6-(methoxymethoxy)-4-methylhex-4-enoyl]oxazolidin-2-one (*ent*-**14**) (3214.5 mg, 73.1%) following the methodology described above for the synthesis of **14** from **10**. Colorless oil: $[\alpha]_D^{20}$ −45.1° (*c* 0.31, $CHCl_3$).

Preparation of (4*R*,2′*R*,4′*E*)-4-Benzyl-3-[6-(methoxymethoxy)-2,4-dimethylhex-4-enoyl]oxazolidin-2-one (*ent*-9). (4*R*,4′*E*)-4-Benzyl-3-[6-(methoxymethoxy)-4-methylhex-4-enoyl]-oxazolidin-2-one (*ent*-**14**) (3112.2 mg, 8.97 mmol) was converted to (4*R*,2′*R*,4′*E*)-4-benzyl-3-[6-(methoxymethoxy)-2,4-dimethylhex-4-enoyl]oxazolidin-2-one (*ent*-**9**) (2396.07 mg, 72% yield, 92% *de*.) following the methodology described above for the synthesis of **9** from **14**. Colorless oil: $[\alpha]_D^{20}$ −52.3° (*c* 0.22, $CHCl_3$).

Preparation of (*R*,*E*)-6-(Methoxymethoxy)-2,4-dimethylhex-4-en-1-ol (*ent*-16). (4*R*,2′*R*,4′*E*)-4-Benzyl-3-[6-(methoxymethoxy)-2,4-dimethylhex-4-enoyl]oxazolidin-2-one (*ent*-**9**) (2086.4 mg, 5.78 mmol) was converted to (*R*,*E*)-6-(methoxymethoxy)-2,4-dimethylhex-4-en-1-ol (*ent*-**16**) (999.7 mg, 92%) following the methodology described above for the synthesis of alcohol **16** from **9**. Colorless oil: $[\alpha]_D^{20}$ +5.1° (*c* 0.53, $CHCl_3$).

Preparation of (*R*,2*E*,6*E*)-Ethyl 8-(methoxymethoxy)-2,4,6-trimethylocta-2,6-dienoate (*ent*-17). (*R*,*E*)-6-(Methoxymethoxy)-2,4-dimethylhex-4-en-1-ol (*ent*-**16**) (982.4 mg, 5.22 mmol) was converted to (*R*,2*E*,6*E*)-ethyl 8-(methoxymethoxy)-2,4,6-trimethylocta-2,6-dienoate (*ent*-**17**) (1312.2 mg, 93%) following the methodology described above for the synthesis of ester **17** from **16**. Colorless oil: $[\alpha]_D^{20}$ −5.4° (*c* 0.29, $CHCl_3$).

Preparation of (*R*,2*E*,6*E*)-8-(Methoxymethoxy)-2,4,6-trimethylocta-2,6-dien-1-ol (*ent*-18). (*R*,2*E*,6*E*)-Ethyl 8-(methoxymethoxy)-2,4,6-trimethylocta-2,6-dienoate (*ent*-**17**) (1375.3 mg, 5.10 mmol) was converted to (*R*,2*E*,6*E*)-8-(methoxymethoxy)-2,4,6-trimethylocta-2,6-dien-1-ol (*ent*-**18**) (872.2, 75.1%) following the methodology described above for the synthesis of alcohol **18** from **17**. Colorless oil: $[\alpha]_D^{20}$ +14.0° (*c* 0.26, $CHCl_3$).

Preparation of (2*R*,3*R*,4*R*,6*E*)-2,3-Epoxy-8-(methoxymethoxy)-2,4,6-trimethyloct-6-en-1-ol (19b). (*R*,2*E*,6*E*)-8-(Methoxymethoxy)-2,4,6-trimethylocta-2,6-dien-1-ol (*ent*-**18**) (861.6 mg, 3.78 mmol) was converted to (2*R*,3*R*,4*R*,6*E*)-2,3-epoxy-8-(methoxymethoxy)-2,4,6-trimethyloct-6-en-1-ol (**19b**) (718.0 mg, 77.9% yield, 80% *de*) following the methodology described above for the synthesis of epoxy **19a** from **18**. Colorless oil: $[\alpha]_D^{20}$ +14.3° (*c* 0.15, $CHCl_3$); IR (film) ν_{max} 3446, 2936, 1646, 1454, 1385, 1216, 1149, 1042, 923 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.40 (t, *J* = 6.8 Hz, 1H), 4.62 (s, 2H), 4.09 (d, *J* = 6.8 Hz, 2H), 3.66 (dd, *J* = 12.5, 4.5 Hz, 1H), 3.56 (dd, *J* = 12.5, 8.5 Hz, 1H), 3.37 (s, 3H), 2.75 (d, *J* = 9.2 Hz, 1H), 2.38 (dd, *J* = 14.0, 4.8 Hz, 1H), 1.98 (dd, *J* = 14.0, 9.2 Hz, 1H), 1.79 (dd, *J* = 8.5, 4.5 Hz, O<u>H</u>), 1.67 (s, 3H), 1.60 (dtq, *J* = 9.2, 6.8, 4.8 Hz, 1H), 1.29 (s, 3H), 0.87 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.4, 122.6, 95.5, 65.4, 64.7, 63.6, 60.8, 55.2, 45.1, 31.0, 16.3, 15.6, 14.3; HRMS (ESI^+) calcd for $C_{13}H_{24}O_4Na$ $[M + Na]^+$ 267.1572, found 267.1563.

Preparation of (2*S*,4*R*,6*E*)-8-(Methoxymethoxy)-2,4,6-trimethyloct-6-ene-1,2-diol (20b). (2*R*,3*R*,4*R*,6*E*)-2,3-Epoxy-8-(methoxymethoxy)-2,4,6-trimethyloct-6-en-1-ol (**19b**) (718.0 mg, 2.94 mmol) was converted to (2*S*,4*R*,6*E*)-8-(methoxymethoxy)-2,4,6-trimethyloct-6-ene-1,2-diol (**20b**) (712.5 mg, 98.4%) following the methodology described above for the synthesis of diol **20a** from **19a**. Colorless oil: $[\alpha]_D^{20}$ −0.6° (*c* 0.19, $CHCl_3$); IR (film) ν_{max} 3418, 2929, 1647, 1455, 1385, 1214, 1148, 1104, 1037, 922 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.34 (t, *J* = 6.8 Hz, 1H), 4.62 (s, 2H), 4.09 (dd, *J* = 12.0, 7.4 Hz, 1H), 4.05 (dd, *J* = 12.0, 6.8 Hz, 1H), 3.40 (d, *J* = 11.0 Hz, 1H), 3.37 (d, *J* = 11.0 Hz, 1H), 3.36 (s, 3H), 2.18 (s, O<u>H</u>), 2.08 (dd, *J* = 12.0, 5.8 Hz, 1H), 1.96 (s, O<u>H</u>), 1.89−1.81 (m, 2H), 1.66 (s, 3H), 1.55 (dd, *J* = 14.4, 3.6 Hz, 1H), 1.23 (dd, *J* = 14.4, 6.4 Hz, 1H), 1.17 (s, 3H), 0.93 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 140.0, 122.2, 95.5, 73.1, 70.5, 63.6, 55.2, 49.2, 44.7, 26.3, 23.8, 22.3, 16.2; HRMS (ESI^+) calcd for $C_{13}H_{26}O_4Na$ $[M + Na]^+$ 269.1729, found 269.1731.

Preparation of (2*S*,4*R*,6*E*)-1-(*tert*-Butyldimethylsilyloxy)-8-(methoxymethoxy)-2,4,6-trimethyloct-6-en-2-ol (21b). (2*S*,4*R*,6*E*)-8-(Methoxymethoxy)-2,4,6-trimethyloct-6-ene-1,2-diol (**20b**) (712.5 mg, 2.90 mmol) was converted to (2*S*,4*R*,6*E*)-1-(*tert*-butyldimethylsilyloxy)-8-(methoxymethoxy)-2,4,6-trimethyloct-6-en-2-ol (**21b**) (852.0 mg, 81.6%) following the methodology described above for the synthesis of **21a** from **20a**. Colorless oil: $[\alpha]_D^{20}$ −1.9° (*c* 0.17, $CHCl_3$); IR (film) ν_{max} 3466, 2928, 1645, 1454, 1383, 1251, 1147, 1096, 1035, 832 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.32 (t, *J* = 6.8 Hz, 1H), 4.62 (s, 2H), 4.07 (d, *J* = 6.8, Hz, 2H), 3.38 (d, *J* = 9.2, Hz, 1H), 3.36 (s, 3H), 3.33 (d, *J* = 9.2, Hz, 1H), 2.28 (s, O<u>H</u>), 2.16 (dd, *J* = 11.8, 4.6 Hz, 1H), 1.88−1.78 (m, 2H), 1.65 (s, 3H), 1.50 (dd, *J* = 14.4, 4.4 Hz, 1H), 1.21 (dd, *J* = 14.4, 6.6 Hz, 1H), 1.12 (s, 3H), 0.90 (s, 9H), 0.89 (d, *J* = 6.0 Hz, 3H), 0.05 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.9, 122.0, 95.4, 72.6, 70.8, 63.6, 55.2, 49.2, 44.9, 26.4, 25.9 (3C), 23.8, 21.9, 18.3, 16.1, −5.5, −5.5; HRMS (ESI^+) calcd for $C_{19}H_{40}O_4SiNa$ $[M + Na]^+$ 383.2594, found 383.2600.

Preparation of (2*S*,4*R*,6*E*)-1-(*tert*-Butyldimethylsilyloxy)-2,8-bis(methoxymethoxy)-2,4,6-trimethyloct-6-ene (22b). (2*S*,4*R*,6*E*)-1-(*tert*-Butyldimethylsilyloxy)-8-(methoxy−methoxy)-2,4,6-trimethyloct-6-en-2-ol (**21b**) (852.0 mg, 2.37 mmol) was converted to (2*S*,4*R*,6*E*)-1-(*tert*-butyldimethylsilyloxy)-2,8-bis-(methoxymethoxy)-2,4,6-trimethyloct-6-ene (**22b**) (950.0 mg, 99.4%) following the methodology described above for the synthesis

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of **22a** from **21a**. Colorless oil: $[\alpha]_D^{20}$ +3.5° (*c* 0.47, $CHCl_3$); IR (film) ν_{max} 2929, 2857, 1458, 1380, 1256, 1147, 1101, 1037, 919, 836, 775 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.32 (t, *J* = 6.8 Hz, 1H), 4.72 (s, 2H), 4.62 (s, 2H), 4.07 (d, *J* = 6.8, Hz, 2H), 3.51 (d, *J* = 10.0, Hz, 1H), 3.45 (d, *J* = 10.0, Hz, 1H), 3.36 (s, 3H), 3.34 (s, 3H), 2.15 (dd, *J* = 12.8, 5.0 Hz, 1H), 1.89−1.80 (m, 1H), 1.78 (dd, *J* = 12.8, 9.2 Hz, 1H), 1.64 (s, 3H), 1.54 (dd, *J* = 14.6, 4.2 Hz, 1H), 1.31 (dd, *J* = 14.6, 6.6 Hz, 1H), 1.20 (s, 3H), 0.88 (m, 12H), 0.03 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.8, 121.9, 95.4, 91.2, 79.0, 68.7, 63.6, 55.3, 55.2, 49.3, 43.2, 26.0, 25.9 (3C), 21.8, 21.4, 18.2, 16.1, −5.5 (2C); HRMS (ESI^+) calcd for $C_{21}H_{44}O_5NaSi$ $[M + Na]^+$ 427.2856, found 427.2851.

Preparation of (2*S*,4*R*,6*E*)-2,8-Bis(methoxymethoxy)-2,4,6-trimethyloct-6-en-1-ol (23b). (2*S*,4*R*,6*E*)-1-(*tert*-Butyldimethylsilyloxy)-2,8-bis(methoxymethoxy)-2,4,6-trimethyl oct-6-ene (**22b**) (950.0 mg, 2.35 mmol) was converted to (2*S*,4*R*,6*E*)-2,8-bis-(methoxymethoxy)-2,4,6-trimethyloct-6-en-1-ol (**23b**) (626.8 mg, 92%) following the methodology described above for the synthesis of **22a** from **23a**. Colorless oil: $[\alpha]_D^{20}$ +9.8° (*c* 0.75, $CHCl_3$); IR (film) ν_{max} 3473, 2928, 1645, 1449, 1384, 1212, 1147, 1093, 1032, 918 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.32 (t, *J* = 6.8 Hz, 1H), 4.69 (d, *J* = 7.5 Hz, 1H), 4.65 (d, *J* = 7.5 Hz, 1H), 4.62 (s, 2H), 4.07 (d, *J* = 6.8, Hz, 2H), 3.45 (dd, *J* = 12.5, 6.5, Hz, 1H), 3.40 (s, 3H), 3.37 (s, 3H), 3.35 (dd, *J* = 12.5, 8.0 Hz, 1H), 3.26 (dd, *J* = 8.0, 6.5 Hz, OH), 2.12 (dd, *J* = 17.5, 10.0 Hz, 1H), 1.86−1.78 (m, 2H), 1.63 (s, 3H), 1.60 (dd, *J* = 14.6, 4.0 Hz, 1H), 1.23 (dd, *J* = 14.6, 6.0 Hz, 1H), 1.20 (s, 3H), 0.90 (d, *J* = 6.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 139.6, 122.3, 95.5, 90.7, 79.9, 68.7, 63.5, 55.4, 55.2, 49.1, 42.7, 26.0, 21.9, 20.4, 16.1; HRMS (ESI^+) calcd for $C_{15}H_{30}O_5Na$ $[M + Na]^+$ 313.1991, found 313.1990.

Preparation of (2*S*,4*R*,6*E*)-2,8-Bis(methoxymethoxy)-2,4,6-trimethyloct-6-enal (8b). (2*S*,4*R*,6*E*)-2,8-Bis(methoxymethoxy)-2,4,6-trimethyloct-6-en-1-ol (**23b**) (192.3 mg, 0.66 mmol) was converted to (2*S*,4*R*,6*E*)-2,8-bis(methoxymethoxy)-2,4,6-trimethyloct-6-enal (**8b**) (171.0 mg, 89.5%) following the methodology described above for the synthesis of **8a** from **23a**. Colorless oil: $[\alpha]_D^{20}$ −12.0° (*c* 0.42, $CHCl_3$); IR (film) ν_{max} 2928, 2720, 1732, 1455, 1378, 1215, 1148, 1103, 1038, 919 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 9.53 (s, 1H), 5.32 (t, *J* = 7.0 Hz, 1H), 4.76 (d, *J* = 7.0 Hz, 1H), 4.62 (d, *J* = 7.0 Hz, 1H), 4.61 (s, 2H), 4.07 (d, *J* = 7.0, Hz, 2H), 3.39 (s, 3H), 3.36 (s, 3H), 2.07 (dd, *J* = 16.4, 10.0 Hz, 1H), 1.86−1.78 (m, 2H), 1.69 (dd, *J* = 14.8, 4.2 Hz, 1H), 1.62 (s, 3H), 1.44 (dd, *J* = 14.8, 7.0 Hz, 1H), 1.30 (s, 3H), 0.87 (d, *J* = 6.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 203.5, 139.0, 122.6, 95.5, 91.9, 82.6, 63.5, 55.8, 55.2, 48.8, 42.6, 26.1, 21.3, 18.2, 16.0; HRMS (ESI^+) calcd for $C_{15}H_{28}O_5Na$ $[M + Na]^+$ 311.1834, found 311.1837.

Preparation of (4*S*,2′*R*,3′*S*,4′*S*,6′*R*,8′*E*)-4-Benzyl-3-[3-hydroxy-4,8-bis(methoxymethoxy)-2,4,6,8-tetramethyldec-8-enoyl]oxazolidin-2-one (24b). (2*S*,4*R*,6*E*)-2,8-Bis(methoxymethoxy)-2,4,6-trimethyloct-6-enal (**8b**) (170.0 mg, 0.59 mmol) was converted to (4*S*,2′*R*,3′*S*,4′*S*,6′*R*,8′*E*)-4-benzyl-3-[3-hydroxy-4,8-bis-(methoxymethoxy)-2,4,6,8-tetra-methyldec-8-enoyl]oxazolidin-2-one (**24b**) (223.5 mg, 72.5% yield, 95% *de*) following the methodology described above for the synthesis of **24a** from **8a**. Colorless oil: $[\alpha]_D^{20}$ +5.5° (*c* 0.27, $CHCl_3$); IR (film) ν_{max} 3457, 2930, 1781, 1673, 1460, 1384, 1208, 1147, 1105, 1030, 919 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.36−7−32 (m, 2H), 7.29−7.24 (m, 3H), 5.33 (t, *J* = 6.8 Hz, 1H), 4.66−4.59 (m, 5H), 4.36 (dq, *J* = 7.2, 2.6 Hz, 1H), 4.14 (m, 2H), 4.07 (d, *J* = 6.8, Hz, 2H), 3.61 (br s, 1H), 3.45 (dd, *J* = 13.2, 3.0 Hz, 1H), 3.37 (s, 3H), 3.30 (s, 3H), 2.60 (dd, *J* = 13.2, 10.8 Hz, 1H), 2.16 (dd, *J* = 13.0, 5.2 Hz, 1H), 1.83 (dd, *J* = 13.0, 9.0 Hz, 1H), 1.78 (dd, *J* = 13.0, 6.0 Hz, 1H), 1.74−1.69 (m, 1H), 1.65 (s, 3H), 1.54 (dd, *J* = 13.0, 4.0 Hz, 1H), 1.38 (d, *J* = 7.2 Hz, 3H), 1.32 (s, 3H), 0.92 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 178.3, 152.9, 139.5, 135.5, 129.3 (2C), 129.0 (2C), 127.3, 122.3, 95.4, 90.8, 81.8, 81.0, 65.8, 63.5, 55.6, 55.2, 55.1, 49.4, 42.4, 38.0, 34.6, 26.7, 21.6, 20.9, 17.9, 16.1; HRMS (ESI^+) calcd for $C_{28}H_{43}NO_8Na$ $[M + Na]^+$ 544.2886, found 544.2901.

Preparation of (2*R*,3*S*,4*S*,6*R*,8*E*)-Allyl 3-hydroxy-4,10-bis-(methoxymethoxy)-2,4,6,8-tetramethylnon-8-enoate (26b). (4*S*,2′*R*,3′*S*,4′*S*,6′*R*,8′*E*)-4-Benzyl-3-[3-hydroxy-4,8-bis(methoxy methoxy)-2,4,6,8-tetramethyldec-8-enoyl]oxazolidin-2-one (**24b**) (8 mg, 0.015 mmol) was dissolved in dry CH_2Cl_2 under argon atmosphere (0.6 mL). A solution of sodium methoxide (0.5 M solution in MeOH, 0.03 mL, 0.015 mmol) was added, and the reaction was stirred at 0 °C for 5 min. The reaction was quenched with saturated ammonium chloride (0.5 mL) and CH_2Cl_2 was added (3 mL). The organic layer was washed with brine (1 mL), dried over anhydrous sodium sulfate and filtered. The solvent was evaporated under reduced pressure to give the ester **26b** (1.8 mg, 32%). Colorless oil: $[\alpha]_D^{20}$ −51.8° (*c* 0.1, $CHCl_3$); IR (film) ν_{max} 3439, 2921, 1731, 1455, 1380, 1211, 1034, 746 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.32 (t, *J* = 6.5 Hz, 1H), 4.64 (d, *J* = 7.5, Hz, 1H), 4.63 (d, *J* = 7.5, Hz, 1H), 4.61 (s, 2H), 4.07 (d, *J* = 6.5, Hz, 2H), 3.71 (d, *J* = 9.5 Hz, OH), 3.67 (s, 3H), 3.44 (dd, *J* = 9.5, 2.5 Hz, 1H), 3.36 (s, 3H), 3.32 (s, 3H), 2.77 (dq, *J* = 7.5, 2.5 Hz, 1H), 2.10 (dd, *J* = 13.0, 6.0 Hz, 1H), 1.82 (dd, *J* = 13.0, 8.5 Hz, 1H), 1.72−1.64 (m, 2H), 1.63 (s, 3H), 1.49 (dd, *J* = 13.0, 3.5 Hz, 1H), 1.32 (d, *J* = 7.5 Hz, 3H), 1.25 (s, 3H), 0.91 (d, *J* = 6.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 176.9, 139.4, 122.4, 95.4, 91.1, 81.3, 79.2, 63.5, 55.5, 55.2, 51.5, 49.4, 42.5, 38.7, 26.6, 21.6, 20.2, 17.0, 16.1; HRMS (ESI^+) calcd for $C_{19}H_{36}O_7Na$ $[M + Na]^+$ 399.2359, found 399.2351.

Deprotection of Compound 24b with PPTS. A solution of pyridinium *p*-toluenesulfonate (PPTS, 31.1 mg, 0.12 mmol) in *t*-BuOH (2 mL) was added to a solution of (4*S*,2′*R*,3′*S*,4′*S*,6′*R*,8′*E*)-4-benzyl-3-[3-hydroxy-4,8-bis(methoxymethoxy)-2,4,6,8-tetramethyldec-8-enoyl]oxazolidin-2-one (**24b**) (29.4 mg, 0.06 mmol) at 80 °C and stirred for 12 h. Then, saturated sodium bicarbonate (1 mL) was added and stirred for 10 min. Water (3 mL) and ethyl acetate (10 mL) were added, and the aqueous layer was separated and extracted with three portions of ethyl acetate (10 mL). The combined organic solution was washed with brine (10 mL), dried over anhydrous sodium sulfate and filtered. Evaporation of the solvent gave a crude product that was purified by silica gel column chromatography. Elution with petroleum ether:ethyl acetate (60:40) yielded the lactones **25b** (3.7 mg, 23%) and **3b** (8.8 mg, 65%).

(3*R*,4*S*,5*S*,2′*R*,4′*E*)-4-Hydroxy-5-(6-(methoxymethoxy)-2,4-dimethylhex-4-enyl)-3,5-dimethyl-4,5-dihydrofuran-2(3*H*)-one (25b). Colorless oil: $[\alpha]_D^{20}$ −2.8° (*c* 0.16, $CHCl_3$); IR (film) ν_{max} 3443, 2940, 1750, 1456, 1383, 1215, 1147, 1099, 1037, 934 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.33 (t, *J* = 6.8 Hz, 1H), 4.61 (s, 2H), 4.08 (dd, *J* = 11.6, 6.8 Hz, 1H), 4.05 (dd, *J* = 11.6, 6.8 Hz, 1H), 4.01 (d, *J* = 5.4 Hz, 1H), 3.36 (s, 3H), 2.93 (dq, *J* = 7.2, 5.4 Hz, 1H), 2.15 (dd, *J* = 12.1, 4.9 Hz, 1H), 1.92−1.84 (m, 3H), 1.66 (s, 3H), 1.56 (dd, *J* = 14.1, 6.4 Hz, 1H), 1.34 (s, 3H), 1.22 (d, *J* = 7.2 Hz, 3H), 0.95 (d, *J* = 6.2 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 177.6, 139.4, 122.4, 95.4, 87.7, 76.4, 63.7, 55.2, 48.4, 40.4, 40.0, 26.6, 22.9, 21.4, 16.2, 8.3; HRMS (ESI^+) calcd for $C_{16}H_{28}O_5Na$ $[M + Na]^+$ 323.1834, found 323.1834.

(3*R*,4*S*,5*S*,2′*R*,4′*E*)-4-Hydroxy-5-(6-hydroxy-2,4-dimethylhex-4-enyl)-3,5-dimethyl-4,5-dihydrofuran-2(3*H*)-one (3b). Colorless oil: $[\alpha]_D^{20}$ −2.5° (*c* 0.2, $CHCl_3$); IR (film) ν_{max} 3433, 2931, 1742, 1451, 1361, 1210, 1090, 1018, 936 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.41 (t, *J* = 7.0 Hz, 1H), 4.17 (dd, *J* = 12.0, 7.0 Hz, 1H), 4.12 (dd, *J* = 12.0, 7.0 Hz, 1H), 4.03 (d, *J* = 5.5 Hz, 1H), 2.94 (dq, *J* = 7.2, 5.5 Hz, 1H), 2.15 (dd, *J* = 12.2, 5.2 Hz, 1H), 1.93−1.85 (m, 3H), 1.66 (s, 3H), 1.55 (dd, *J* = 15.8, 8.0 Hz, 1H), 1.35 (s, 3H), 1.24 (d, *J* = 7.5 Hz, 3H), 0.96 (d, *J* = 6.2 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 177.6, 138.4, 125.4, 87.6, 76.5, 59.3, 48.3, 40.4, 40.0, 26.6, 22.8, 21.5, 16.2, 8.3; HRMS (ESI^+) calcd for $C_{14}H_{24}O_4Na$ $[M + Na]^+$ 279.1572, found 279.1563.

Preparation of (3*R*,4*S*,5*S*,2′*R*,4′*E*)-5-[6-((*R*)-Methoxyphenylacetoxy)-2,4-dimethylhex-4-enoyl]-4-((*R*)-methoxyphenylacetoxy)-3,5-dimehtyldihydrofuran-2(3*H*)-one (27b). (3*R*,4*S*,5*S*,2′*R*,4′*E*)-4-Hydroxy-5-(6-hydroxy-2,4-dimethylhex-4-enyl)-3,5-dimethyl-4,5-dihydrofuran-2(3*H*)-one (**3b**) (1.2 mg, 4.7 μmol) was converted to compound **27b** (2.2 mg, 86.0%) following the methodology described above for the synthesis of **7** from **5**. Amorphous solid: $[\alpha]_D^{20}$ −47.5° (*c* 0.13, $CHCl_3$); IR (film) υ_{max} 2925, 1770, 1723, 1453, 1253, 1172, 1108, 1023, 759; ^1H NMR (600 MHz, CD_2Cl_2) δ 7.33−7.27 (m, 10H), 5.18 (d, *J* = 6.0, 1H), 5.16 (t, *J* = 7.0 Hz, 1H), 4.69 (s, 1H), 4.61 (s, 1H), 4.51 (d, *J* = 6.6 Hz, 1H), 3.33 (s, 3H), 3.31 (s, 3H), 2.81 (dq, *J* = 7.2, 5.9 Hz, 1H), 2.11 (dd, *J* =

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13.2, 4.8 Hz, 1H), 1.73 (m, 1H), 1.59 (s, 3H), 1.58 (m, 1H), 1.48 (dd, J = 14.4, 6.6 Hz, 1H), 1.33 (s, 3H), 1.28 (m, 1H), 0.65 (d, J = 7.2 Hz, 3H), 0.62 (d, J = 6.6 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 176.2, 170.6, 169.8, 141.3, 136.3, 135.6, 129.2, 128.8 (2C), 128.7, 128.6 (2C), 127.23 (2C), 127.21 (2C), 119.9, 86.0, 82.6, 82.5, 77.6, 61.9, 57.4, 57.3, 47.5 40.9, 38.5, 26.3, 22.7, 20.6, 16.1, 7.8; HRMS (ESI$^+$) calcd for $C_{32}H_{40}O_8Na$ $[M + Na]^+$ 575.2621, found 575.2619.

■ ASSOCIATED CONTENT

Supporting Information

Copies of ^{1}H and ^{13}C NMR spectra for all new compounds appearing in the schemes, 2D NMR of **3a**, **3b** and **4**−**7** as well as NOE spectra of **3a**, **3b** and **4**. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: rosario.hernandez@uca.es.

Notes

The authors declare no competing financial interest.

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