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THE FIRST SYNTHESIS OF (-)-PLAKOLIDE A

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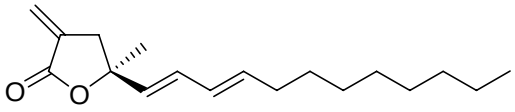
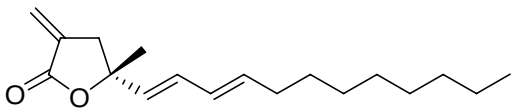
Abstract- (-)-Plakolide A, an α-exomethylene-γ-butyrolactone isolated from the marine sponge *Plakortis* sp., was synthesized starting from (*R*)-lactic acid by applying the chiral self-reproduction procedure.

(-)-Plakolide A is an α-exomethylene-γ-disubstituted γ-butyrolactone isolated recently from a shallow-water marine sponge of the genus *Plakortos* collected from La Palma, Canary Islands and shows significant inhibitory activity in a cell-based assay designed to detect inhibitors of inducible nitric oxide synthase (iNOS).[1] The absolute stereochemistry of (-)-plakolide A was originally assigned to *S* according to its CD spectrum,[1] but our synthetic study of (*S*)-plakolide A (**1**) revealed that the sign of its optical rotation was (+) and as the results, the absolute stereochemistry of the natural (-)-plakolide A should be revised to (*R*)-**2**[2] (Figure 1).



1: (*S*)-(+)-plakolide A



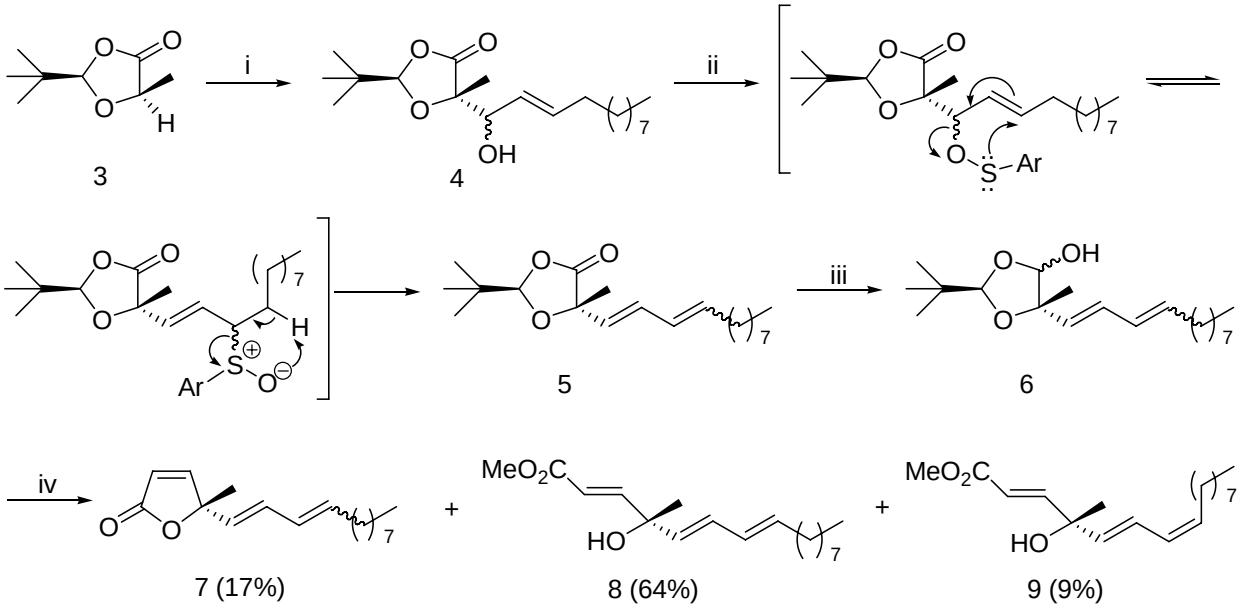
2: (*R*)-(-)-plakolide A (natural)

Figure 1

In the course of our synthetic studies on biologically active natural products, which possess chiral quaternary carbon center accompanying with one oxygen function, we have synthesized (+)-ipomeamarone,[3] (-)-vertinolide[4] and (*S*)-gregatin B[5] by adapting the chiral self-reproduction method developed originally by Seebach *et al*.[6] In continuation of that line, we planned to synthesize natural (*R*)-(-)-plakolide A (**2**).

For the synthesis of natural (*R*)-(-)-plakolide A (**2**), (2*R*,5*R*)-2-*tert*-butyl-5-methyl-1,3-dioxolan-4-one (**3**)[4, 6] was selected as the starting material, which was readily derived from (*R*)-lactic acid and 2,2-dimethylpropanal. The addition of *trans*-2-dodecenal to the enolate derived from **3** occurred stereoselectively from α-side to give the allyl alcohol (**4**) as a 1:1 mixture of diastereoisomers concerning with the orientation of the hydroxyl group.[5] Transformation of the allyl alcohol (**4**) to 1,3-diene (**5**) was examined. [2,3]Sigmatropic rearrangement of the sulfenate of **4** to the sulfoxide and its thermal syn elimination[5, 7] were performed. Thus, the treatment of **4** with 2,4-dinitrophenylsulfenyl chloride (ArSCl) in the presence of triethylamine (Et_3N) at reflux temperature gave the sulfenate, which rearranged to form

the sulfoxide, and the successive thermal *syn* elimination of the sulfoxide occurred to afford an inseparable mixture of *E*,*E*-diene-(**5**) and *E*,*Z*-diene-(**5**) (88:12)[8] in 82% yield. Successive diisobutylaluminum hydride (DIBAL-H) reduction[3] of **5** gave **6** in 98% yield which was treated with trimethyl phosphonoacetate (2.2 eq.) in the presence of NaH (2.2 eq.)[3, 9] at room temperature to afford lactone (**7**), *E*,*E*-ester (**8**) and *E*,*Z*-ester (**9**) in 17, 64 and 9% yields, respectively, after purification of the products by silica gel column chromatography (Scheme 1).

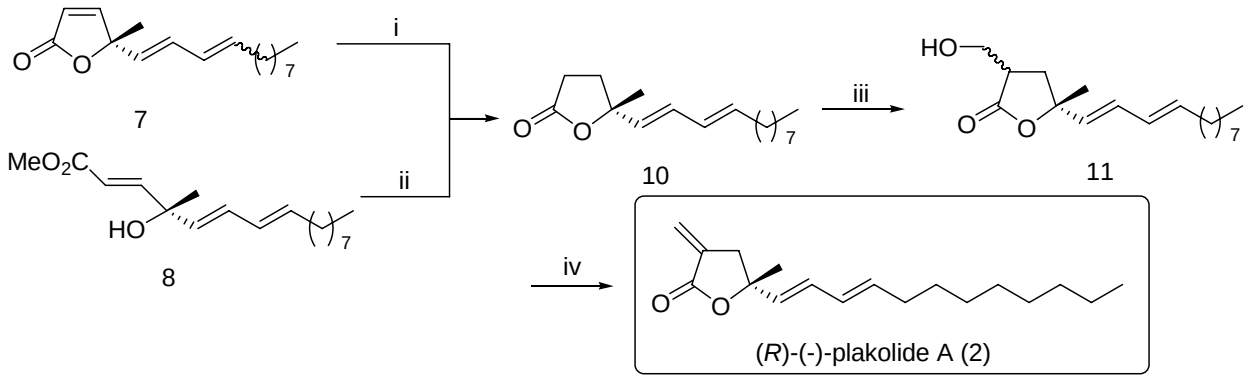


Scheme 1. Reagents and conditions: (i) LDA, *trans*-2-dodecenal, -78 °C, 3 h (74%), (ii) Et_3N, 2,4-dinitrobenzenesulfenyl chloride (ArSCl), heat, 4 h (82%), (iii) DIBAL-H, -78 °C→rt, 40 min (98%), (iv) trimethyl phosphonoacetate, NaH, 1.5 h, rt; dil. HCl

For selective reduction of the unsaturated ester to saturated one in the presence of the conjugated diene in **7** and **8**, reactions with Mg in methanol[10] or with sodium bis(2-methoxyethoxy)aluminum hydride (Red-Al®) in the presence of CuBr and 2-butanol[11] were tried. But the best results were obtained in the case of the reactions of **7** and **8** with DIBAL-H in the presence of CuI in THF-HMPA.[12] Thus, **7** was treated with DIBAL-H (3.0 eq.) in the presence of CuI (3.0 eq.) in THF-HMPA (4:1) to form the *E*,*E*-diene (**10)** in 68% yield[13] and **8** was treated also with DIBAL-H (8.5 eq.) in the presence of CuI (9.0 eq.) in the same solvent system, followed by treatment of the crude products with NaH at -30 °C to give **10** in 70% yield, respectively.

Successively, **10** was converted to α-hydroxymethyllactone (**11**)[14] by action of LDA (2.0 equiv.) and gaseous formaldehyde (-78 to -25 °C) in 84% yield. Finally, treatment of **11** with *p*-toluenesulfonyl chloride (*p*-TsCl) (1.2 equiv.) and Et_3N (2.5 equiv.) in CH_2Cl_2 at 0 °C to room temperature furnished directly (*R*)-(-)-plakolide A (**2**) in 80% yield (Scheme 2). IR, ^{1}H-NMR and MS spectral data are superimposable to those of the natural (-)-plakolide A including the CD spectrum. The specific rotation of the synthesized **2** showed $[\alpha]_D^{24}$ -44.9° (*c*=0.08, MeOH); and that of the natural plakolide A was $[\alpha]_D^{24}$ -41° (*c*=0.1, MeOH).[1]

Thus, the first synthesis of natural (-)-plakolide A was accomplished starting from the known dioxolanone (**3**) in 7 steps and 23% overall yield.



Scheme 2. Reagents and conditions: (i) DIBAL-H, CuI in THF-HMPA, -78 °C, 1.5 h (68%), (ii) DIBAL-H, CuI in THF-HMPA, -78 °C, 30 min; NaH, 0 °C, 1 h (70%), (iii) LDA, HCHO (gas), -30 °C, 15 min (84%), (iv) Et_3N, *p*-TsCl, 0 °C→rt, 39 h (80%)

EXPERIMENTAL

IR spectra were measured with a JASCO FT/IR-460 plus infrared spectrophotometer. NMR spectra were recorded on a JEOL JNM-GSX270 (^{1}H 270 MHz, ^{13}C 67.5 MHz) spectrometer using tetramethylsilane as an internal standard. MS and high-resolution MS spectra (HRMS) were measured with a JEOL JMS-700TKM instrument at 70 eV. Optical rotation was measured with a JASCO DIP-370 polarimeter and CD spectrum was recorded on a JASCO J-720 spectropolarimeter. Microanalysis was carried out on a Yanagimoto MT-3 elemental analyzer.

(2*R*,5*S*)-2-*tert*-Butyl-5-[(*E*)-1-hydroxydodec-2-enyl]-5-methyl-1,3-dioxolan-4-one (4)

A solution of **3** (2.54 g, 16.0 mmol) in THF (13 mL) was added dropwise under stirring to a THF solution of LDA [prepared from diisopropylamine (2.8 mL, 20.0 mmol), *n*-C_4H_9Li (7.6 mL, 19.6 mmol, 2.55 M in hexane, and THF (100 mL)] at -78 ℃, and the mixture was stirred for 45 min. To the obtained solution was added dropwise under stirring a solution of *trans*-2-dodecenal (5.1 mL, 24.0 mmol) in THF (10 mL) at that temperature, and the mixture was stirred for 3 h at -78 ℃. After the mixture was warmed up to rt, half saturated NH_4Cl solution was added and the mixture was extracted with ether. The combined organic layer was washed with saturated brine and dried over anhydrous Na_2SO_4. Removal of the solvent under reduced pressure gave an oil which was purified by SiO_2 flash column chromatography (hexane:ether=9:1) to give **4** (4.02 g, 74%) as a pale yellow oil. IR (neat): 3480, 1797, 1667 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.88 (3H, t, *J*=6.6 Hz, CH_3), 0.956, 0.961 (total 9H, each s, $C(CH_3)_3$), 1.25-1.35 (14H, m, $(C\underline{H}_2)_7CH_3$), 1.29, 1.37 (total 3H, each s, CH_3), 1.91 (1H, m, OH), 2.08 (2H, br quintet, *J*=6.8 Hz, $=CHC\underline{H}_2$), 4.18-4.25 (1H, m, C<u>H</u>OH), 5.39, 5.41 (total 1H, each s, OCHO), 5.55-5.83 (2H, m, CH=CH). HRMS (*m/z*) Calcd for $C_{20}H_{36}O_4$: 340.2614. Found: 340.2644.

(2*R*,5*S*)-2-*tert*-Butyl-5-[(1*E*)-dodeca-1,3-dienyl]-5-methyl-1,3-dioxolan-4-one (5)

To a solution **4** (4.00 g, 11.7 mmol) in CH_2Cl_2 (134 mL) were added under stirring Et_3N (4.3 mL, 30.5 mmol) and 2,4-dinitrobenzenesulfenyl chloride (ArSCl) (6.64 g, 28.2 mmol) and the mixture was heated under reflux for 4 h. After cooling down to rt, pentane was added to form precipitates, which were

removed by filtration. The filtrate was concentrated under reduced pressure to give an oil which was purified by SiO_2 flash column chromatography (hexane:ether=79:1) to afford **5** (3.10 g, 82%) as a pale yellow oil. IR (neat): 1799, 1656 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.88 (3H, t, *J*=6.6 Hz, $CH_2C\underline{H}_3$), 0.980, 0.981 (total 9H, each s, $C(CH_3)_3$), 1.32-1.46 (12H, m, $CH_2(C\underline{H}_2)_6CH_3$), 1.52, 1.54 (total 3H, each s, CH_3), 2.05-2.22 (2H, m, CH=CHC$\underline{H}_2$), 5.14 (1H, s, OCHO), 5.48-6.67 (4H, m, CH=CH-CH=CH). HRMS (*m/z*) Calcd for $C_{20}H_{34}O_3$:322.2508. Found: 322.2528.

(2*R*,5*S*)-2-*tert*-Butyl-5-[(1*E*)-dodeca-1,3-dienyl]-5-methyl-1,3-dioxolan-4-ol (6)

To a solution of **5** (2.85 g, 8.83 mmol) in CH_2Cl_2 (17 mL) was added under stirring DIBAL-H (1.00 M in toluene, 10.6 mL, 10.6 mmol) at -78 °C and the reaction mixture was stirred for 10 min at the same temperature. After addition of MeOH (15 mL), the mixture was stirred for 30 min under warming up to rt. The mixture was filtered through Celite® pad and the filtrate was concentrated under reduced pressure to give **6** (2.81 g, 98%) as a pale yellow oil, which was used directly for the next reaction. IR (neat): 3442, 1656 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.88 (3H, t, *J*=6.6 Hz, $CH_2C\underline{H}_3$), 0.94, 0.95 (total 9H, each s, $C(CH_3)_3$), 1.16-1.45 (12H, m, $CH_2(C\underline{H}_2)_6CH_3$), 1.34, 1.36 (total 3H, each s, CH_3), 2.04-2.23 (2H, m, CH=CHC$\underline{H}_2$), 2.24, 2.68 (total 1H, each br d, *J*=9.0 Hz and *J*=7.7 Hz, OH), 4.66, 4.93 (total 1H, each s, OCHO), 5.09, 5.17 (each 1H, br d, *J*=7.7 Hz and *J*=9.0 Hz, C$\underline{H}_2$OH), 5.44-6.74 (4H, m, CH=CH-CH=CH).

(*S*)-5-[(1*E*)-Dodeca-1,3-dienyl]-5-methylfuran-2(5*H*)-one (7), (*S*,2*E*,5*E*,7*E*)-Methyl 4-hydroxy-4-methylhexadeca-2,5,7-trienoate (8) and (*S*,2*E*,5*E*,7*Z*)-Methyl 4-hydroxy-4-methylhexadeca-2,5,7-trienoate (9)

To a suspension of NaH (672 mg, 16.8 mmol, 60% oil dispersion) in THF (120 mL) was added under stirring trimethyl phosphonoacetate (2.7 mL, 16.8 mmol) and the whole was stirred for 1 h at rt. A solution of **6** (2.47 g, 7.63 mmol) in THF (50 mL) was added to the above solution and the mixture was stirred for 1.5 h at rt. After addition of 2N HCl (1 mL) under ice-cooling, the whole was extracted with ether. The organic layer was washed with saturated brine, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure to give the mixture, which was separated by SiO_2 column chromatography (benzene:ethyl acetate=49:1) into **7** (346 mg, 17%), **8** (1.44 g, 64%), and **9** (200 mg, 9%) as pale yellow oils, respectively. **7**: IR (neat): 1766, 1656 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ:0.88 (3H, t, *J*=6.7 Hz, $CH_2C\underline{H}_3$), 1.23–1.42 (12H, m, $CH_2(C\underline{H}_2)_6CH_3$), 1.58, 1.60 (total 3H, each s, CH_3), 2.04-2.22 (2H, m, CH=CHC$\underline{H}_2$), 5.53, 5.62 (total 1H, each d, *J*=15.3Hz and *J*=16.0 Hz, C$\underline{H}$=CH-CH=CHCH$_2$), 5.72-6.08 (3H, m, CH=CH-C$\underline{H}$=C$\underline{H}$CH$_2$, COC$\underline{H}$=CH), 6.24, 6.55 (total 1H, each dd, *J*=10.2, 15.3 Hz and *J*=10.5, 16.0 Hz, CH=C$\underline{H}$-CH=CHCH$_2$), 7.35, 7.37 (total 1H, each d, *J*=5.6 Hz and *J*=5.6 Hz, COCH=C$\underline{H}$). HRMS (*m/z*) Calcd for $C_{17}H_{26}O_2$: 262.1933. Found: 262.1933. **8**: IR (neat): 3447, 1726, 1657 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ:0.88 (3H, t, *J*=6.6 Hz, $CH_2C\underline{H}_3$), 1.23–1.41 (12H, m, $CH_2(C\underline{H}_2)_6CH_3$), 1.37 (3H, s, CH_3), 1.68 (1H, br s, OH), 2.07 (2H, br q, *J*=6.8 Hz, CH=CHC$\underline{H}_2$), 3.74 (3H, s, $COOCH_3$), 5.63 (1H, d, *J*=15.3Hz, C$\underline{H}$=CH-CH=CHCH$_2$), 5.74 (1H, dt, *J*=6.9, 15.0 Hz, CH=CH-CH=C$\underline{H}$CH$_2$), 5.95 (1H, dd, *J*=10.3, 15.0 Hz, CH=CH-C$\underline{H}$=CHCH$_2$), 6.06 (1H, d, *J*=15.7 Hz, CH=C$\underline{H}$COOCH$_3$), 6.20 (1H, dd, *J*=10.3, 15.3 Hz, CH=C$\underline{H}$-CH=CHCH$_2$), 6.98 (1H, d, *J*=15.7 Hz, C$\underline{H}$=CHCOOCH$_3$). $[\alpha]_D^{26}$ +5.5° (*c*=0.13, MeOH). HRMS (*m/z*) Calcd for $C_{18}H_{30}O_3$: 294.2195. Found: 294.2191. **9**: IR (neat): 3448, 1725, 1657 cm^{-1}. ^{1}H-NMR

($CDCl_3$) δ:0.88 (3H, t, *J*=6.6 Hz, $CH_2C\underline{H}_3$), 1.22−1.42 (12H, m, $CH_2(C\underline{H}_2)_6CH_3$), 1.46 (3H, s, CH_3), 1.72 (1H, br s, OH), 2.17 (2H, br dq, *J*=1.0, 6.8 Hz, $CH=CHC\underline{H}_2$), 3.75 (3H, s, $COOCH_3$), 5.49 (1H, dt, *J*=10.7, 11.0 Hz, $CH=CH-CH=C\underline{H}CH_2$), 5.71 (1H, d, *J*=15.3 Hz, $C\underline{H}=CH-CH=CHCH_2$), 5.95 (1H, dt, *J*=10.3, 15.0 Hz, $CH=CH-C\underline{H}=CHCH_2$), 6.06 (1H, d, *J*=15.7 Hz, $CH=C\underline{H}COOCH_3$), 6.53 (1H, ddd, *J*=1.0, 11.0, 15.3 Hz, $CH=C\underline{H}-CH=CHCH_2$), 6.99 (1H, d, *J*=15.7 Hz, $C\underline{H}=CHCOOCH_3$). $[\alpha]_D^{26}$ -29.2° (*c*=0.10, MeOH). HRMS (*m/z*) Calcd for $C_{18}H_{30}O_3$: 294.2195. Found: 294.2202.

(*R*)-5-[(1*E*,3*E*)-Dodeca-1,3-dienyl]-5-methyldihydrofuran-2(3*H*)-one (10) from 7

To a suspension of 95% CuI (114 mg, 0.57 mmol) in a mixture of THF (1.2 mL) and HMPA (0.3 mL) was added DIBAL-H (1.00 M in toluene, 0.57 mL, 0.57 mmol) at -78 °C and the whole was stirred for 1 h at that temperature. A solution of **7** (50 mg, 0.19 mmol) in THF (1.0 mL) was added to the above mixture at -78 °C and the whole was stirred for 1.5 h at the same temperature. After the mixture was warmed up to 0 °C, the saturated NH_4Cl solution was added to make the mixture neutral and the whole was filtered through Celite® pad. The filtrate was separated and the organic layer was washed with saturated brine After drying over anhydrous Na_2SO_4, the organic layer was concentrated under reduced pressure to give a residue which was purified by SiO_2 flash column chromatography (benzene:ethyl acetate=49:1) to furnish **10** (35 mg, 68%) as a pale yellow oil. IR (neat): 1778, 1658 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ:0.88 (3H, t, *J*=6.6 Hz, $CH_2C\underline{H}_3$), 1.15−1.45 (12H, m, $CH_2(C\underline{H}_2)_6CH_3$), 1.51 (3H, s, CH_3), 2.02-2.26 (4H, m, $COCH_2C\underline{H}_2$, $CH=CHC\underline{H}_2$), 2.54 (1H, d, *J*=5.8 Hz, $COC\underline{H}_2CH_2$), 2.58 (1H, dd, *J*=3.6, 5.4 Hz, $COC\underline{H}_2CH_2$), 5.59 (1H, d, *J*=15.3 Hz, $C\underline{H}=CH-CH=CHCH_2$), 5.75 (1H, dt, *J*=6.9, 15.0 Hz, $CH=CH-CH=C\underline{H}CH_2$), 6.00 (1H, dd, *J*=10.2, 15.0 Hz, $CH=CH-C\underline{H}=CHCH_2$), 6.22 (1H, dd, *J*=10.2, 15.3 Hz, $CH=C\underline{H}-CH=CHCH_2$). $[\alpha]_D^{24}$ +2.1° (*c*=0.09, $CHCl_3$). HRMS (*m/z*) Calcd for $C_{17}H_{28}O_2$: 264.2089. Found: 264.2093.

(*R*)-5-[(1*E*,3*E*)-Dodeca-1,3-dienyl]-5-methyldihydrofuran-2(3*H*)-one (10) from 8

To a suspension of 95% CuI (1.01 g, 5.34 mmol) in a mixture of THF (6.0 mL) and HMPA (1.5 mL) was added DIBAL-H (1.00 M in toluene, 5.0 mL, 5.0 mmol) at -78 °C and the whole was stirred for 1 h at that temperature. A solution of **8** (175 mg, 0.59 mmol) in THF (4.0 mL) was added to the above mixture at -78 °C and the whole was stirred for 30 min at the same temperature. After the mixture was warmed up to 0 °C, the saturated NH_4Cl solution was added to make the mixture neutral and the whole was filtered through Celite® pad. The filtrate was separated and the organic layer was washed with saturated brine After drying over anhydrous Na_2SO_4, the organic layer was concentrated under reduced pressure to give an oil. To a solution of the oil in THF (6.0 ml) was added NaH (47 mg, 1.19 mmol, 60% oil dispersion) at -30 °C, and the whole was stirred for 1 h at the same temperature. After addition of the saturated NH_4Cl solution to make the mixture neutral, the whole was extracted with ether. The organic layer was washed with saturated brine and dried over anhydrous Na_2SO_4. Removal of the solvent under reduced pressure gave a residue which was purified by SiO_2 flash column chromatography (benzene:ethyl acetate=49:1) to furnish **10** (110 mg, 70%) as a pale yellow oil.

(5*R*)-5-[(1*E*,3*E*)-Dodeca-1,3-dienyl]-3-(hydroxymethyl)-5-methyldihydrofuran-2(3*H*)-one (11)

A solution of **10** (163 mg, 1.14 mmol) in THF (6.5 mL) was added dropwise under stirring to a THF

solution of LDA [prepared from diisopropylamine (0.17 mL, 1.23 mmol), *n*-C_4H_9Li (0.48 mL, 1.23 mmol, 2.55 M in hexane, and THF (6.5 mL)] at -78 °C, and the mixture was stirred for 1 h. Gaseous formaldehyde (heating paraformaldehyde (495 mg) to 150-160 °C) was introduced into the above solution for 15 min at -25 °C. After the mixture was warmed up to rt, the saturated NH_4Cl solution was added, and the whole was extracted with ethyl acetate. The organic layer was separated and dried over anhydrous Na_2SO_4. Removal of the solvent under reduced pressure gave a residue which was purified by SiO_2 flash column chromatography (benzene) to afford **11** (125 mg, 84%) and the starting **10** (30 mg). IR (neat) cm^{-1}: 3445, 1761, 1658. ^{1}H-NMR ($CDCl_3$) δ:0.88 (3H, t, *J*=6.7 Hz, $CH_2C\underline{H}_3$), 1.17–1.45 (12H, m, $CH_2(C\underline{H}_2)_6CH_3$), 1.51, 1.55 (total 3H, each s, CH_3), 2.0-2.35 (4H, m, $COC(CH_2OH)C\underline{H}_2$, $CH=CHC\underline{H}_2$), 2.37 (1H, br s, OH), 2.86-3.04 (1H, m, $COC\underline{H}(CH_2OH)CH_2$), 3.72-3.97 (1H, m, $COCH(C\underline{H}_2OH)CH_2$), 5.56, 5.68 (total 1H, each d, *J*=15.3 Hz and *J*=15.5 Hz, $C\underline{H}$=CH-CH=$CHCH_2$), 5.69-5.82 (1H, m, CH=CH-CH=$C\underline{H}CH_2$), 5.96, 6.01 (each 1H, dd, *J*=10.4, 15.0 Hz, *J*=10.2, 15.2 Hz, CH=CH-$C\underline{H}$=$CHCH_2$), 6.20, 6.25 (total 1H, each dd, *J*=10.4, 15.3 Hz and J=10.2, 15.5 Hz, CH=$C\underline{H}$-CH=$CHCH_2$). HRMS (*m/z*) Calcd for $C_{18}H_{30}O_3$: 294.2195. Found: 294.2168.

(*R*)-(-)-Plakolide A (2)

To a solution of **11** (120 mg, 0.41 mmol) in CH_2Cl_2 (2.0 mL) were added Et_3N (0.15 mL, 1.44 mmol) and *p*-toluenesulfonyl chloride (93 mg, 0.49 mmol) at 0 °C. The reaction mixture was stirred for 39 h at rt. To the mixture were added successively CH_2Cl_2 (3.0 mL), the saturated NH_4Cl solution (2.0 mL), and H_2O (2.0 mL) and the whole was stirred. The water layer was separated and extracted with CH_2Cl_2. The combined organic layer was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The residue was purified by SiO_2 flash column chromatography (hexane:ethyl acetate=9:1) to give **11** (11 mg) and **2** (92 mg, 80%) as a colorless oil. IR (neat): 1765, 1663 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ:0.88 (3H, t, *J*=6.6 Hz, $CH_2C\underline{H}_3$), 1.27 (10H, m, $CH_2(C\underline{H}_2)_5CH_3$), 1.37 (2H, m, $CH_2C\underline{H}_2(CH_2)_5CH_3$), 1.52 (3H, s, CH_3), 2.07 (2H, br q, *J*=6.8 Hz, $CH=CHC\underline{H}_2$), 2.79 (1H, dt, *J*=2.6, 16.6 Hz, $C(CH_2)C\underline{H}_2$), 2.92 (1H, dt, *J*=2.6, 16.6 Hz, $C(CH_2)C\underline{H}_2$), 5.60 (1H, t, *J*=2.6 Hz, $C=CH_2$), 5.62 (1H, d, *J*=15.3 Hz, $C\underline{H}$=CH-CH=$CHCH_2$), 5.76 (1H, dt, *J*=7.0, 15.0 Hz, CH=CH-CH=$C\underline{H}CH_2$), 5.99 (1H, dd, *J*=10.4, 15.0 Hz, CH=CH-$C\underline{H}$=$CHCH_2$), 6.22 (1H, dd, *J*=10.4, 15.3 Hz, CH=$C\underline{H}$-CH=$CHCH_2$), 6.23 (1H, t, *J*=2.6 Hz, $C=CH_2$). ^{13}C-NMR ($CDCl_3$) δ: 169.8, 137.4, 135.3, 132.2, 129.7, 128.7, 122.2, 82.4, 40.8, 32.7, 31.9, 29.4, 29.22, 29.18, 29.1, 27.1, 22.6, 14.1. $[\alpha]_D^{24}$ -44.9° (*c*=0.08, MeOH). HRMS (*m/z*) Calcd for $C_{18}H_{28}O_2$: 276.2089. Found: 276.2087. *Anal*. Calcd for $C_{18}H_{28}O_2$: C, 78.21; H, 10.21. Found: C, 78.31; H, 10.08.

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