A Synthetic Study on Antiviral and Antioxidative Chromene Derivative

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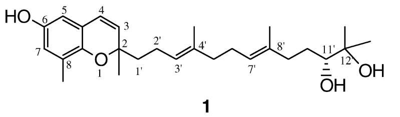
An efficient synthesis of the antiviral and antioxidative chromene (1) was achieved. A small amount of chromene 1 could be derived from plastoquinones 2 and 3, the major constituents of the brown alga, *Sargassum micracanthum*. By the following synthetic scheme involving its application, many kinds of analogs can be synthesized for evaluation of their biological activity and mechanistic study. The total synthesis of 1, started from geranyl acetate and protected 2-bromo-6-methylhydroquinone, was executed with Sharpless asymmetric dihydroxylation for introduction of the terminal diol system and base-catalyzed sigmatropic rearrangement for construction of the chromene skeleton as the crucial steps. The stereochemistry at C-11′ was reconfirmed by this synthesis.

Key words chromene; plastoquinone; antiviral activity; cytotoxic activity; *Sargassum micracanthum*

The chromene derivative **1** was initially found as a mixture of diastereomers at C-2 from the brown alga, *Sargassum micracanthum* (KUETZING) ENDLICHER (Sargassaceae, Fucales) by our group, and was also obtained from plastoquinone **2** by chemical conversion in two steps *via* **3**.[1,2)]

Chromene **1** shows strong antioxidant activity, such as the inhibitory effect of NADPH-dependent lipid peroxidation in rat microsomes at IC_{50} 0.28 μg/ml (in the case of vitamin E as a positive control: IC_{50} 34 μg/ml), as well as remarkable antiviral activity against human cytomegalovirus (HCMV).[1,2)] Focusing on its cytotoxicity, weak and/or no lethal activity was found toward various cells. Therefore, **1** could be a candidate of a new supplement for anti-aging and of a new antiviral agent; however, it is difficult to obtain sufficient amounts of these compounds by isolation from the alga. For the above reasons, we decided to prepare **1** efficiently for further biological investigation and evaluation of the structure–activity relationship. In the first stage for the chemical synthesis, we chose compound **1**, which comprises inseparable diastereomers at C-2, as the target molecule, because the antioxidative activity of the tocopherol/tocotrienol analogs was observed essentially at the same level.[3)] In the next stage for evaluation of their biological activity and mechanistic study, we planned to prepare a number of analogs including each diastereomer at C-2, stereoselectively.



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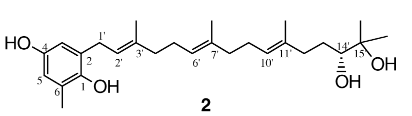

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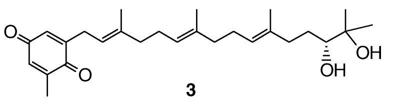

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The synthetic strategy shown in Chart 1, comprised the construction of the chromene skeleton from **D** to **C**, and of the diterpene side chain stereoselectively, that is, the connection formed between **A** and **B**. It also contained Sharpless asymmetric diol formation[3)] on the side chain terminal using geranyl acetate followed by introduction of the sulfone group to prepare **B**. The small segments **E** and **F** can be obtained by modified methods of the known procedures. This paper describes the synthesis of **1** in detail.

Along with the above strategy, the synthetic intermediate **D** possessing a short-length side-chain was prepared. The side-chain segment **F** was obtained from geranyl acetate in seven steps to give the protected allyl bromide **6** (Chart 2). Olefin selective dihydroxylation of geranyl acetate, periodate oxidation, and hydride reduction with $NaBH_4$ provided the primary alcohol **4** in 46% yield for three steps. The obtained alcohol **4** was protected with a *tert*-butyldimethylsilyl (TBS) group followed by hydrolysis of the acetate protection under basic condition to give **5** in 100% yield for two steps. The allyl bromide **6** was obtained by treatment of **5** with methanesulfonyl chloride and triethylamine to give an allyl chloride intermediate, followed by bromination with lithium bromide in 44% yield for two steps. Compound **6** easily de-

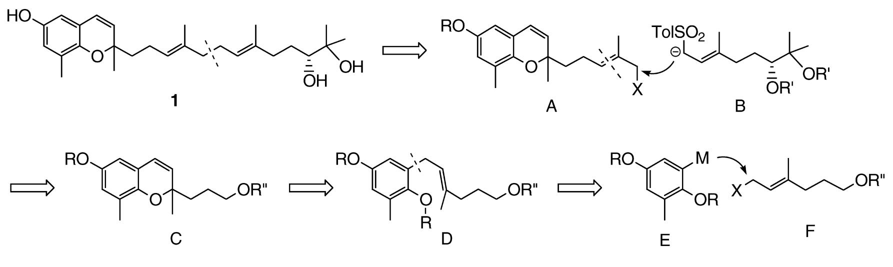

Chart 1

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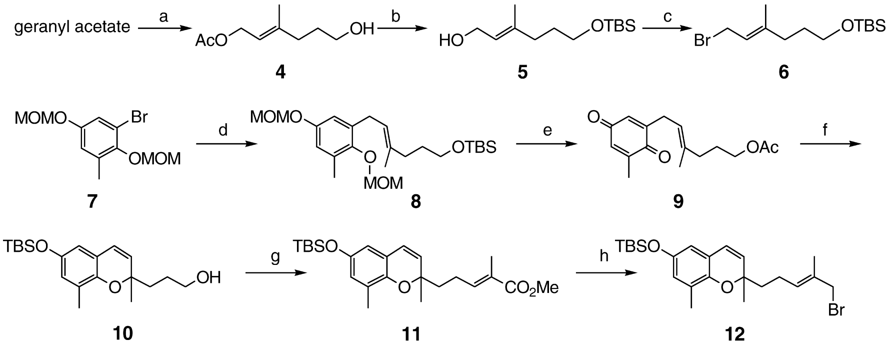
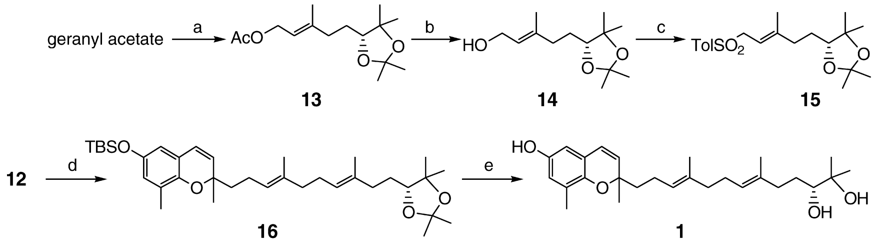


Conditions: (**a**) (1) cat.K$_2$OsO$_4$, K$_3$Fe(CN)$_6$, K$_2$CO$_3$, ^{t}BuOH-H$_2$O, 4°C (47%), (2) NaIO$_4$, acetone-H$_2$O, 20°C (98%), (3) NaBH$_4$, MeOH, 0°C (99%), (**b**) (1) TBSCl, Et$_3$N, DMAP (100%), (2) K$_2$CO$_3$, MeOH, 0°C (100%), (**c**) (1) MsCl, Et$_3$N, 0°C, (2) LiBr, DMF, 20°C (44%, 2 steps), (**d**) (1) BuLi, Et$_2$O, -78°C, (2) CuI-PBu$_3$, -60°C, then **6**, Et$_2$O, -60 to 0°C (75%), (**e**) (1) TBAF, THF (68%), (2) Ac$_2$O, Pyridine (100%), (3) 80% AcOH, 60°C (86%), (4) CAN, CH$_3$CN-H$_2$O, 0°C (85%), (**f**) (1) Pyridine, 20°C (59%), (2) TBSCl, imidazole, DMAP, DMF, (3) K$_2$CO$_3$, MeOH, 0°C (82%, 2 steps), (**g**) (1) DMSO, SO$_3$-pyridine, Et$_3$N, 20°C (quant.), (2) (EtO)$_2$POCH(CH$_3$)CO$_2$Me, ^{t}BuOK, THF, -78°C (59% for *E* form) (*E*/*Z*=5), (**h**) (1) DIBAL, CH$_2$Cl$_2$, -78°C (100%), (2) CBr$_4$, Ph$_3$P, toluene, 20°C (92%).

Chart 2



Conditions: (**a**) (1) AD-mix β, K$_3$Fe(CN)$_6$, K$_2$CO$_3$, CH$_3$SO$_2$NH$_2$ ^{t}BuOH-H$_2$O, 4°C (46%), (2) 2,2-dimethoxypropane, cat. TsOH, MeOH (92%), (**b**) K$_2$CO$_3$, MeOH (96%), (**c**) (1) MsCl, Et$_3$N, 20°C (49%), (2) TolSO$_2$Na, NaI, DMF, 60°C (73%), (**d**) (1) **15**, BuLi, THF, -78°C, then **12**, -78 to 20°C (36%), (2) Pd[Ph$_2$P(CH$_2$)$_3$PPh$_2$]Cl$_2$, LiBEt$_3$H, THF, 0°C (80%), (**e**) 80% AcOH, 40°C (63%).

Chart 3

composed at room temperature or by silica gel separation. For these reasons, the obtained compound **6** was immediately used for the next reaction.

Readily available 2-bromo-6-methyl-1,4-hydroquinone derivative **7** was converted from *o*-cresol by the known procedure.[4,5] Bromide **7** was treated with butyl lithium in ether at −78 °C followed by addition of an ethereal solution of a cuprous iodide–tributylphosphine complex at −60 °C to prepare the phenyl cuprate species. After the mixture was stirred for 1 h at the same temperature, allyl bromide **6** was added, then the reaction mixture was allowed to warm to 0 °C over 2 h to obtain **8** in 75% yield. In this alkylation reaction, the use of a cuprous iodide–tributylphosphine complex, instead of cuprous iodide itself, resulted in better yield due to the homogenous condition.[4,5] The primary protective group of TBS was changed to the corresponding acetate, and subsequent acid treatment to remove two phenolic methoxymethyl (MOM) protections following cerium(IV) ammonium nitrate (CAN) oxidation gave quinone **9** in 50% yield for four steps.

The chromene forming reaction of **9** was carried out by treatment with pyridine for 15 h at rt.[2] In this case, compound **10** was obtained as a racemic mixture at C-2; however, the target molecule was also a mixture. The resulting phenolic hydroxyl was protected by TBS, then hydrolysis of the primary acetate under basic condition afforded **10** (48% yield from **9**). After oxidation to the corresponding aldehyde, three carbons were introduced by Horner–Emmons reaction to give **11** (E:Z=5:1 by ^{1}H-NMR analysis). Chromatographic separation of the mixture of isomers and further transformations with two steps were executed to obtain the *E*-allyl bromide **12** in 53% yield from **10**.

The remaining side chain was prepared from geranyl acetate (Chart 3). The terminal diol involving the chiral secondary hydroxyl group was introduced by Sharpless asymmetric dihydroxylation[3] using AD-mix β (46% yield), and the diol unit was then converted to the acetonide **13** in good yield. After basic hydrolysis of the primary acetate to the corresponding alcohol **14**, sulfone **15** was prepared *via* the unstable allyl chloride by a standard reaction sequence (34% yield, three steps).

The coupling reaction between **12** and the lithium salt of **15** proceeded to give the desired coupling products as a mixture of diastereomers (37% yield from **12**). Pd-catalyzed sulfone removal cleanly occurred to provide **16** in 80% yield. Finally, acid treatment for deprotection of TBS and acetonide afforded chromene **1** in 63% yield. The spectral data including the optical rotation value ($[\alpha]_D$ +12.5°) of the synthetic chromene **1** was identical with those of our reported compound ($[\alpha]_D$ +11.0°). The present synthesis of the chromene **1** has clearly established the absolute configuration at C-11′

as assigned as (*R*).

Synthetic studies toward both optically pure chromene derivatives having C-2 chirality and other analogs for evaluating the structure–bioactivity relationship are currently under preparation. In addition, the biological aspects will be reported near future.

Experimental

Optical rotations were measured with a JASCO DIP-1000 automatic polarimeter. IR spectra were recorded with a Perkin-Elmer FT-IR 1600 spectrophotometer and UV spectra with a JASCO V-530 spectrophotometer. NMR spectra were recorded with a Varian Unity-500 (^{1}H, 500 MHz; ^{13}C, 125 MHz) in $CDCl_3$. ^{1}H–^{1}H correlation spectroscopy (COSY) and nuclear Overhauser effect spectroscopy (NOESY) were measured with a Varian Unity-500 using standard Varian pulse sequences. Chemical shifts are given on a δ (ppm) scale with $CHCl_3$ (^{1}H, 7.26 ppm; ^{13}C, 77.0 ppm) as the internal standard (s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad). Mass spectra were taken with a JEOL JMS-AX505HAD spectrometer. Column chromatography was carried out on Kanto Chemical silica gel 60N (100—210 μm). Normal and reversed phase flash column chromatography was performed on Kanto Chemical silica gel 60N (40—100 μm, normal phase) and Fuji Silysia Chemical ODS DM1021T (100—200 mesh, reversed phase), respectively. Thin layer chromatography (TLC) was carried out on Merck Kieselgel 60F$_{254}$ TLC plate. Diethyl ether (Et_2O) and THF was dried over sodium using benzophenone as indicator. Chloroform, dichloromethane, *N*,*N*-dimethyl formamide (DMF), dimethylsulfoxide (DMSO) and toluene were dried over CaH_2. Methanol, 2-methyl-2-propanol, water, and the eluants for chromatography except for hexane were distilled before use. Hexane was used as purchased. Geranyl acetate was made by acetylation of geraniol, purchased from Kanto chemical, and was distilled before use. 2-Bromo-6-methyl-1,4-hydroquinone dimethoxymethyl ether was also prepared by the known procedure according to the references.

(4*E*)-6-Acetoxy-4-methyl-4-hexen-1-ol (4) To a mixture of potassium hexacyanoferrate(III) (42.3 g, 128 mmol), potassium carbonate (17.8 g, 129 mmol) and potassium osmate(VI) dihydrate (4 mg, 0.01 mmol) in a combined solution of water and 2-methyl-2-propanol (each 250 ml) was added geranyl acetate (12.6 g, 64.2 mmol) at 4 °C. The reaction mixture was stirred for 72 h at 4 °C, $Na_2S_2O_3$ solution (50 ml) was added to quench the active oxidizer, and the mixture was concentrated under reduced pressure. The residue was extracted twice with ethyl acetate (2×300 ml), and the combined extracts were washed with saturated NaCl solution, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The oily residue was purified by silica gel column chromatography [hexane–ethyl acetate (EtOAc, 2 : 1)] to afford diol (6.90 g, 47% yield) as pale yellowish oil. The resulting diol (1.77 g, 7.69 mmol) was dissolved into acetone (70 ml), followed by adding the solution of sodium periodate (2.47 g, 11.5 mmol) in water (70 ml) at 0 °C over 20 min. The reaction mixture was stirred for 2 h at 20 °C, and then extracted thrice with a mixture of hexane–EtOAc (1 : 1, 3×200 ml). The combined extracts were washed with saturated NaCl solution, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was separated by passing over a small plug of silica gel column [hexane–EtOAc (5 : 1), as an eluant] to give aldehyde (1.28 g, 98% yield). The NMR data of this aldehyde are shown as follows; ^{1}H-NMR ($CDCl_3$) δ ppm: 1.69 (3H, br s), 2.02 (3H, s), 2.35 (2H, br, J=7.3 Hz), 2.55 (2H, dt, J=1.7, 7.3 Hz), 4.55 (2H, d, J=6.8 Hz), 5.33 (1H, qt, J=1.2, 6.8 Hz), 9.57 (1H, t, J=1.7 Hz). ^{13}C-NMR ($CDCl_3$) δ ppm: 16.5, 20.9, 31.3, 41.6, 61.0, 119.2, 139.9, 171.0, 201.7.

The aldehyde (1.28 g, 7.52 mmol) obtained above was reduced with sodium borohydride (168 mg, 4.44 mmol) in methanol (35 ml) at 0 °C. After quenched by saturated ammonium chloride solution, the mixture was concentrated, and then extracted thrice with EtOAc (3×100 ml). The combined extracts were washed with saturated NaCl solution, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography [hexane–EtOAc (4 : 1)] to provide alcohol **4** (1.28 g, 99% yield) as colorless oil.

Compound **4**: IR (dry film) cm^{-1}: 3408 (br), 1739, 1668, 1237. ^{1}H-NMR ($CDCl_3$) δ ppm: 1.68 (2H, m), 1.70 (3H, br d, J=1.2 Hz), 2.04 (3H, s), 2.11 (2H, br t, J=7.3 Hz), 3.62 (2H, t, J=6.4 Hz), 4.56 (2H, d, J=6.8 Hz), 5.35 (1H, qt, J=1.2, 6.8 Hz). ^{13}C-NMR ($CDCl_3$) δ ppm: 16.3, 21.0, 30.4, 35.7, 61.3, 62.4, 118.5, 141.8, 171.2. EI-MS *m/z*: 172 (M)$^+$. HR-EI-MS *m/z*: 172.1110 [Calcd for $C_9H_{16}O_3$: 172.1100 (M)$^+$].

(2*E*)-6-*tert*-Butyldimethylsilyloxy-3-methyl-2-hexen-1-ol (5) The obtained alcohol **4** (1.28 g, 7.44 mmol) was converted to the corresponding *tert*-butyldimethylsilyl (TBS) ether by treatment with TBSCl (2.82 g, 18.7 mmol), triethylamine (3.80 ml, 27.3 mmol) and 4-dimethylaminopyridine (DMAP, 5 mg, 0.04 mmol) in dichloromethane (20 ml) at 20 °C for 4 h. The mixture was diluted with a solution of hexane–EtOAc (1 : 1, 300 ml). The organic layer was washed with water and saturated NaCl solution, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography [hexane–EtOAc (10 : 1)]; TBS ether (2.13 g, 100% yield) was obtained as colorless oil. To a mixture of the resulting TBS ether (2.13 g, 7.44 mmol) in methanol (30 ml) was added potassium carbonate (200 mg, 1.45 mol) at 0 °C. The reaction mixture was stirred for 1 h at 0 °C, and then saturated ammonium chloride solution (3 ml) was added to neutralize the mixture. After concentrated under reduced pressure, the residue was extracted twice with EtOAc (2×200 ml). The combined extracts were washed with saturated NaCl solution, dried over Na_2SO_4, filtered, and concentrated. The residue was separated by silica gel column chromatography [hexane–EtOAc (5 : 1)] to give alcohol **5** (1.81 g, 100% yield) as colorless oil.

Compound **5**: IR (dry film) cm^{-1}: 3347 (br), 1668, 1471. ^{1}H-NMR ($CDCl_3$) δ ppm: 0.05 (6H, s), 0.90 (9H, s), 1.64 (2H, m), 1.68 (3H, br s), 2.11 (2H, br t, J=7.3 Hz), 3.62 (2H, t, J=6.4 Hz), 4.56 (2H, d, J=6.8 Hz), 5.35 (1H, qt, J=1.2, 6.8 Hz). ^{13}C-NMR ($CDCl_3$) δ ppm: −5.4, 16.4, 16.6, 25.9 (3C), 30.9, 35.7, 59.4, 62.7, 123.3, 139.7. EI-MS *m/z*: 244 (M)$^+$. HR-EI-MS *m/z*: 244.1842 [Calcd for $C_{13}H_{28}O_2Si$: 244.1859 (M)$^+$].

(2*E*)-1-Bromo-6-*tert*-butyldimethylsilyloxy-3-methyl-2-hexene (6) The obtained alcohol **5** (5.15 g, 21.1 mmol) was treated with methanesulfonyl chloride (3.50 ml, 45.5 mmol), triethylamine (9 ml, 64.7 mmol) in chloroform (50 ml) at 0 °C for 30 min. The reaction mixture was diluted with a solution of hexane–Et_2O (1 : 1, 100 ml). The organic phase was washed with water and saturated NaCl solution, dried over Na_2SO_4, filtered, and concentrated. The crude product containing unstable allyl chloride was separated by passing through a short silica gel column [hexane–Et_2O (9 : 1)] very quickly, then the solvent was removed under reduced pressure. The resulting allyl chloride was immediately converted to the corresponding allyl bromide (**6**) by treatment with lithium bromide (8.60 g, 99.0 mmol) in DMF (50 ml) at 20 °C for 1 h. The same work up described in the formation of allyl chloride was carried out to provide **6** (2.85 g, 44% yield for two steps from **5**) as a pale yellowish oil. Compound **6** was immediately used for the next reaction due to unstableness.

Compound **6**: ^{1}H-NMR ($CDCl_3$) δ ppm: 0.05 (6H, s), 0.89 (9H, s), 1.66 (2H, m), 1.71 (3H, br s), 2.14 (2H, br t, J=7.5 Hz), 3.63 (2H, t, J=6.5 Hz), 4.59 (2H, d, J=6.7 Hz), 5.46 (1H, br t, J=6.7 Hz).

2-[(2′*E*)-6′-*tert*-Butyldimethylsilyloxy-3′-methyl-2′-hexen-1′-yl]-6-methyl-1,4-hydroquinone 1,4-Dimethyl Ether (8) To a mixture of **7** (1.33 g, 4.57 mmol)$^{4,5)}$ in Et_2O (10 ml) was added butyllithium (1.58 M in hexane, 3.80 ml, 6.00 mmol) at −78 °C under N_2. The reaction mixture was stirred for 1 h at −78 °C. The ethereal solution (5 ml) of copper(I) iodide–tributylphosphine complex, prepare from copper(I) iodide (450 mg, 2.36 mmol) and tributylphosphine (2.10 ml, 8.43 mmol), was added to the reaction mixture at −60 °C over 15 min *via* canula, and the mixture was stirred for additional 1 h at this temperature to prepare the aryl cuprate species. Finally, the ethereal solution (10 ml) of ally bromide **6** (1.68 g, 5.47 mmol) was added at −60 °C over 20 min. The reaction mixture was allowed to warm to 0 °C over 2 h, and then a mixture of saturated ammonium chloride solution and 6 N ammonia solution (1 : 1, 40 ml) was added to terminate the reaction. After diluted with Et_2O (200 ml), the mixture was washed with water and saturated NaCl solution, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The oily residue was purified by silica gel column chromatography [hexane–EtOAc (20 : 1)] to give **8** (1.50 g, 75% yield) as colorless oil.

Compound **8**: IR (dry film) cm^{-1}: 2930, 1596, 1471. ^{1}H-NMR ($CDCl_3$) δ ppm: 0.04 (6H, s), 0.89 (9H, s), 1.65 (2H, m), 1.70 (3H, br s), 2.06 (2H, m), 2.28 (3H, s), 3.35 (2H, d, J=7.3 Hz), 3.47 (3H, s), 3.60 (2H, q, J=6.4 Hz), 3.61 (3H, s), 4.91 (2H, s), 5.10 (2H, s), 5.30 (1H, br t, J=0.8, 7.3 Hz), 6.67 (1H, d, J=3.0 Hz), 6.72 (1H, d, J=3.0 Hz). ^{13}C-NMR ($CDCl_3$) −5.3, 16.2, 17.2, 18.3, 25.9 (3C), 28.6, 31.2, 35.8, 55.9, 57.4, 62.9, 94.7, 99.5, 115.3, 116.0, 122.5, 132.1, 135.8, 136.3, 149.0, 153.5. EI-MS *m/z*: 438 (M)$^+$. HR-EI-MS *m/z*: 438.2778 [Calcd for $C_{24}H_{42}O_5Si$: 438.2802 (M)$^+$].

2-[(2′*E*)-6′-Acetoxy-3′-methyl-2′-hexen-1′-yl]-6-methyl-1,4-benzoquinone (9) To a mixture of **8** (1.50 g, 3.42 mmol) in THF (5 ml) was added tetrabutylammonium fluoride (TBAF, 1 M in THF, 4.1 ml, 4.1 mmol) at 20 °C. The reaction mixture was stirred for 1 h at 20 °C to remove TBS group, and then diluted with a mixture of hexane–EtOAc (1 : 1, 100 ml). The mixture was washed with water and saturated NaCl solution, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The oily residue was purified by passed over a small plug of silica gel [hexane–EtOAc (2 : 1)] to give the primary alcohol (750 mg, 68% yield) as pale yellowish oil. The spectral data of this alcohol are shown as follows; ^{1}H-NMR ($CDCl_3$) δ ppm: 1.70 (2H, m), 1.71 (3H, br s), 1.34 (3H, s), 2.12 (2H, br t, J=7.5 Hz), 2.27 (3H, s), 3.36 (2H, d, J=6.8 Hz), 3.46 (3H, s), 3.60 (3H, s), 3.63 (2H, t, J=6.4 Hz), 4.90 (2H, s), 5.10 (2H, s), 5.34 (1H, dt, J=0.8, 6.8 Hz), 6.67 (1H, d, J=3.0 Hz), 6.71 (1H, d, J=3.0 Hz). ^{13}C-NMR ($CDCl_3$) δ ppm: 16.0, 17.2, 28.6, 30.5, 35.8, 55.9, 57.3, 62.4, 94.6, 99.5, 114.8, 116.2, 123.0, 132.1, 125.6, 136.0, 149.0, 153.4. EI-MS *m/z*: 324 $(M)^+$.

The alcohol derivative (1.64 g, 5.06 mmol) was converted to the corresponding acetate by treatment with acetic anhydride (4.0 ml, 42.3 mmol) and pyridine (6.0 ml, 74.2 mmol) at 20 °C for 7 h. After concentration and purification by passing through a short silica gel column [hexane–EtOAc (5 : 1)], the primary acetate was obtained (1.85 g, 100% yield) as colorless oil. The spectral data of this acetate are shown as follows; ^{1}H-NMR ($CDCl_3$) δ ppm: 1.71 (3H, br s), 1.76 (2H, m), 2.04 (3H, s), 2.09 (2H, t, J=7.5 Hz), 2.28 (3H, s), 3.35 (2H, d, J=6.8 Hz), 3.46 (3H, s), 3.60 (3H, s), 4.05 (2H, dt, J=0.8, 7.3 Hz), 4.90 (2H, s), 5.10 (2H, s), 5.31 (1H, dt, J=0.8, 6.8 Hz), 6.66 (1H, d, J=3.0 Hz), 6.72 (1H, d, J=3.0 Hz). ^{13}C-NMR ($CDCl_3$) δ ppm: 16.0, 17.2, 21.0, 26.8, 28.6, 35.8, 55.9, 57.4, 64.2, 94.7, 99.5, 115.2, 116.1, 123.3, 132.1, 135.3, 135.5, 149.0, 153.4, 171.2. EI-MS *m/z*: 366 $(M)^+$.

The above acetate (2.54 g, 6.93 mmol) was treated with 80% acetic acid solution (20 ml) at 60 °C for 12 h to remove MOM group. Concentration and purification by silica gel column chromatography [hexane–EtOAc (4 : 1)] gave the hydroquinone derivative (1.66 g, 86% yield) as pale yellow oil. The NMR spectral data of this hydroquinone are shown as follows; ^{1}H-NMR ($CDCl_3$) δ ppm: 1.72 (3H, br s), 1.81 (2H, m), 2.06 (3H, s), 2.16 (2H, t, J=7.6 Hz), 2.20 (3H, s), 3.29 (2H, d, J=7.3 Hz), 4.10 (2H, t, J=6.8 Hz), 4.52 (1H, s, OH), 5.32 (1H, dt, J=0.8, 7.3 Hz), 6.45 (1H, d, J=3.0 Hz), 6.52 (1H, d, J=3.0 Hz).

To a mixture of hydroquinone (1.66 g, 5.96 mmol) in acetonitrile (50 ml) was added a solution of ammonium cerium(IV) nitrate (CAN, 4.19 g, 7.64 mmol) in water (6.4 ml) at 0 °C. The reaction mixture was stirred for 30 min at 0 °C, and saturated $Na_2S_2O_3$ solution (1 ml) was added to quench active CAN, and the reaction mixture was concentrated under reduced pressure. The residue was extracted twice with EtOAc (2×50 ml), and the combined extracts were washed with saturated NaCl solution, dried over Na_2SO_4, filtered, and concentrated. The oily residue was purified by silica gel column chromatography [hexane–EtOAc (2 : 1)] to provide quinone **9** (1.40 g, 85% yield) as pale yellowish oil.

Compound **9**: IR (dry film) cm^{-1}: 2956, 1738, 1651, 1614, 1242. ^{1}H-NMR ($CDCl_3$) δ ppm: 1.64 (3H, br s), 1.76 (2H, m), 2.05 (3H, s), 2.06 (3H, d, J=1.3 Hz), 2.10 (2H, t, J=7.5 Hz), 3.13 (2H, d, J=7.3 Hz), 4.04 (2H, t, J=6.8 Hz), 5.18 (1H, qt, J=0.8, 7.3 Hz), 6.66 (1H, qd, J=1.3, 3.0 Hz), 6.72 (1H, qd, J=1.3, 3.0 Hz). ^{13}C-NMR ($CDCl_3$) δ ppm: 16.0, 21.0, 26.8, 27.6, 35.8, 64.0, 118.7, 132.3, 133.1, 138.7, 145.9, 148.2, 171.2, 187.9, 188.0. EI-MS *m/z*: 276 $(M)^+$. HR-EI-MS *m/z*: 216.1160 [Calcd for $C_{14}H_{16}O_2$: 216.1150 $(M-CH_3CO_2H)^+$].

3-[6-(*tert*-Butyldimethylsilyloxy)-2,8-dimethyl-2*H*-chromen-2-yl]-propan-1-ol (10) Compound **9** (1.40 g, 5.07 mmol) was treated with pyridine (50 ml) at 20 °C for 15 h under N_2 atmosphere. After concentration and separation by silica gel column [hexane–acetone (3 : 1)], the 2*H*-chromene derivative (820 mg, 59% yield) was obtained as pale yellowish oil. ^{1}H- and ^{13}C-NMR spectral data of chromene are shown as follows; ^{1}H-NMR ($CDCl_3$) δ ppm: 1.34 (3H, s), 1.68 (2H, t, J=6.7 Hz), 1.77 (2H, m), 2.03 (3H, s), 2.10 (3H, s), 4.07 (2H, d, J=6.4 Hz), 5.53 (1H, d, J=9.8 Hz), 6.23 (1H, d, J=9.8 Hz), 6.33 (1H, d, J=3.0 Hz), 6.48 (1H, d, J=3.0 Hz). ^{13}C-NMR ($CDCl_3$) δ ppm: 15.4, 20.9, 23.2, 25.7, 36.9, 64.9, 77.3, 110.3, 117.2, 121.0, 123.3, 124.8, 126.2, 130.0, 144.2, 148.9, 171.8.

The above chromene (600 mg, 2.17 mmol) was converted to the corresponding TBS ether by treatment with TBSCl (981 mg, 6.51 mmol), imidazole (665 mg, 9.77 mmol) and DMAP (5 mg, 0.04 mmol) in DMF (25 ml) at 20 °C for 16 h. The reaction mixture was diluted with a mixture of hexane–EtOAc (1 : 1, 100 ml). The obtaining mixture was washed with water and saturated NaCl solution, dried over Na_2SO_4, filtered, and concentrated. The oily residue was purified by silica gel column chromatography [hexane–EtOAc (10 : 1)] to provide TBS ether (848 mg, quantitative yield) as colorless oil. The NMR spectral data of this TBS ether are shown as follows; ^{1}H-NMR ($CDCl_3$) δ ppm: 0.15 (6H, s), 0.96 (9H, s), 1.35 (3H, s), 1.70 (2H, t, J=6.6 Hz), 1.78 (2H, m), 2.02 (3H, s), 2.11 (3H, s), 4.06 (2H, d, J=6.8 Hz), 5.53 (1H, d, J=9.7 Hz), 6.26 (1H, d, J=9.7 Hz), 6.30 (1H, d, J=3.0 Hz), 6.47 (1H, d, J=3.0 Hz). ^{13}C-NMR ($CDCl_3$) δ ppm: -4.5, 15.5, 18.1, 21.0, 23.4, 25.9, 37.1, 64.7, 77.4, 114.9, 120.9, 121.8, 123.5, 126.0, 129.7, 145.0, 148.4, 171.2.

To a mixture of TBS ether (848 mg, 2.17 mmol) in methanol (50 ml) was added potassium carbonate (300 mg, 2.17 mmol) at 0 °C. The reaction mixture was stirred for 1 h at 0 °C, and then saturated ammonium chloride solution (10 ml) was added to neutralize the mixture. After concentrated under reduced pressure, the residue was extracted twice with EtOAc (2×100 ml). The combined extracts were washed with saturated NaCl solution, dried over Na_2SO_4, filtered, and concentrated. The residue was purified by silica gel column chromatography [hexane–EtOAc (4 : 1)] to give **10** (620 mg, 82% yield).

Compound **10**: IR (dry film) cm^{-1}: 3348 (br), 1588. ^{1}H-NMR ($CDCl_3$) δ ppm: 0.16 (6H, s), 0.97 (9H, s), 1.35 (3H, s), 1.72 (4H, m), 1.92 (1H, br s), 2.11 (3H, s), 3.62 (2H, dd, J=6.4, 6.9 Hz), 5.54 (1H, d, J=9.8 Hz), 6.25 (1H, d, J=9.8 Hz), 6.31 (1H, d, J=3.0 Hz), 6.47 (1H, d, J=3.0 Hz). ^{13}C-NMR ($CDCl_3$) δ ppm: -4.6, 15.4, 18.0, 25.6, 25.8, 27.2, 37.0, 62.9, 77.7, 114.8, 120.9, 121.7, 123.2, 125.9, 129.9, 144.9, 148.4. EI-MS *m/z*: 348 $(M)^+$. HR-EI-MS *m/z*: 348.2094 [Calcd for $C_{20}H_{32}O_3Si$: 348.2121 $(M)^+$].

Methyl (2*E*)-5-[6-(*tert*-Butyldimethylsilyloxy)-2,8-dimethyl-2*H*-chromen-2-yl]-2-methyl-2-pentenoate (11) To a mixture of **10** (620 mg, 1.78 mmol), DMSO (12.7 ml, 179 mmol), and triethylamine (2.0 ml, 14.3 mmol) was portionwisely added sulfur trioxide–pyridine complex (1.70 g, 10.7 mmol) over 10 min at 0 °C under N_2 atmosphere. The mixture was stirred for 1 h at 20 °C. After diluted with a solution of hexane–Et_2O (1 : 1, 100 ml), the mixture was washed with water and saturated NaCl solution, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The oily residue was separated by passed over a small plug of silica gel [hexane–EtOAc (10 : 1)] to give the product mainly containing the aldehyde derivative (616 mg, quantitative yield), which was directly used without further purification. THF solution (10 ml) of the obtained aldehyde (616 mg, 1.78 mmol) was added to a mixture of methyl diethylphosphono-2-propioate (2.40 g, 10.7 mmol) and potassium *tert*-butoxide (850 mg, 7.58 mmol) in THF (20 ml) at -78 °C under N_2. After adding ammonium chloride solution (15 ml) and a solution of hexane–Et_2O (1 : 1, 100 ml), the mixture was washed with water and saturated NaCl solution, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The oily residue was purified by column chromatography [hexane–EtOAc (20 : 1)] to provide **11** (440 mg, 59% yield). The *Z* ester of **11** (164 mg, 22% yield) and the mixture of them (140 mg) were also obtained both as colorless oil. ^{1}H-NMR analysis of the crude product showed the *E*/*Z* ratio to be about 5 : 1.

Compound **11**: IR (dry film) cm^{-1}: 2929, 1715, 1644, 1470. ^{1}H-NMR ($CDCl_3$) δ ppm: 0.16 (6H, s), 0.97 (9H, s), 1.37 (3H, s), 1.76 (2H, m), 1.79 (3H, br d, J=1.7 Hz), 2.12 (3H, s), 2.31 (2H, m), 3.71 (3H, s), 5.53 (1H, d, J=9.8 Hz), 6.28 (1H, d, J=9.8 Hz), 6.31 (1H, d, J=2.6 Hz), 6.47 (1H, d, J=2.6 Hz), 6.77 (1H, qt, J=1.7, 7.2 Hz). ^{13}C-NMR ($CDCl_3$) δ ppm: -4.5, 15.5, 18.1, 23.6, 25.7, 26.1, 39.5, 51.6, 77.5, 114.9, 120.8, 121.9, 123.6, 125.9, 127.5, 129.4, 142.3, 145.0, 148.5, 168.6. EI-MS *m/z*: 416 $(M)^+$. HR-EI-MS *m/z*: 416.2400 [Calcd for $C_{24}H_{36}O_4Si$: 416.2383 $(M)^+$].

cis-Isomer of **11**: IR (dry film) cm^{-1}: 2929, 1718, 1649, 1471. ^{1}H-NMR ($CDCl_3$) δ ppm: 0.16 (6H, s), 0.97 (9H, s), 1.37 (3H, s), 1.77 (2H, m), 1.86 (3H, br d, J=1.3 Hz), 2.11 (3H, s), 2.59 (2H, m), 3.71 (3H, s), 5.56 (1H, d, J=9.8 Hz), 5.95 (1H, qt, J=1.3, 7.5 Hz), 6.26 (1H, d, J=9.8 Hz), 6.30 (1H, d, J=3.0 Hz), 6.46 (1H, d, J=3.0 Hz). ^{13}C-NMR ($CDCl_3$) δ ppm: -4.5, 15.5, 18.1, 20.6, 24.6, 25.7, 25.8, 40.2, 51.2, 77.7, 114.9, 121.0, 121.7, 123.3, 126.0, 126.8, 129.9, 143.2, 145.1, 148.4, 168.4. EI-MS *m/z*: 416 $(M)^+$.

(2*E*)-1-Bromo-5-[6-(*tert*-butyldimethylsilyloxy)-2,8-dimethyl-2*H*-chromen-2-yl]-2-methyl-2-pentene (12) Diisobutylaluminum hydride (0.95 M in hexane, 4.0 ml, 3.80 mmol) was added to a mixture of **11** (440 mg, 1.06 mmol) in dichloromethane (20 ml) at -78 °C under N_2. The reaction mixture was stirred for 1 h, quenched with Rochelle salt solution (8 ml), diluted with Et_2O (200 ml) and stirred additional 1 h at 20 °C. The ethereal solution was dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The oily residue was purified by passed over a small plug of silica gel [hexane–EtOAc (4 : 1)] to afford the primary alcohol (410 mg, 100% yield) as colorless oil. The spectral data of this acetate are shown as follows; IR (dry film) cm^{-1}: 3347 (br), 1588, 1470. ^{1}H-NMR ($CDCl_3$) δ ppm: 0.16 (6H, s), 0.97 (9H, s), 1.35 (3H, s), 1.69 (2H, m), 1.76 (3H, br d, J=1.3 Hz), 2.12 (3H, s), 2.18 (2H, m), 4.01 (2H, br s), 5.29 (1H, dt, J=1.3, 7.7 Hz), 5.52 (1H, d, J=9.8 Hz), 6.25 (1H, d, J=9.8 Hz), 6.30 (1H, d, J=3.0 Hz), 6.47 (1H, d, J=3.0 Hz). ^{13}C-NMR ($CDCl_3$) δ ppm: -4.5, 15.5, 18.1, 21.2, 22.4, 25.7, 26.1, 41.2, 61.5, 77.7, 114.9, 121.3, 121.8, 123.3, 125.9, 128.3, 129.9, 134.3, 145.1, 148.4.

The obtained alcohol (42 mg, 0.11 mmol) was treated with triphenylphosphine (143 mg, 0.55 mmol) and carbon tetrabromide (289 mg, 0.87 mmol) in toluene (3 ml) at 20 °C under N_2 atmosphere for 1 h. The reaction mixture was diluted with a solution of hexane–EtOAc (5 : 1, 50 ml), which was then filtered though a small plug of silica gel [hexane–EtOAc (5 : 1)]. The filtrate was concentrated under reduced pressure to give unstable allyl bromide **12** (45 mg, 92% yield) as pale yellowish oil. It was immediately used for the next reaction. The NMR spectral data of this bromide are shown as follows; ^{1}H-NMR ($CDCl_3$) δ ppm: 0.16 (6H, s), 0.97 (9H, s), 1.35 (3H, s), 1.70 (2H, m), 1.80 (3H, br d, J=1.3 Hz), 2.12 (3H, s), 2.17 (2H, m), 3.94 (2H, br s), 5.52 (1H, d, J=9.8 Hz), 5.59 (1H, br t, J=7.3 Hz), 6.26 (1H, d, J=9.8 Hz), 6.30 (1H, d, J=3.0 Hz), 6.47 (1H, d, J=3.0 Hz).

(2*E*)-3-Methyl-5-{(4*R*)-2,2,5,5-tetramethyl-[1,3]dioxolan-4-yl}-2-pentenyl Acetate (13) To a mixture of potassium hexacyanoferrate(III) (29.8 g, 90.5 mmol), potassium carbonate (12.5 g, 90.4 mmol), methanesulfonamide (4.30 g, 45.2 mmol) and AD-mix β (4.0 g) in a combined solution of water and 2-methyl-2-propanol (each 250 ml) was added geranyl acetate (9.0 g, 45.9 mmol) at 4 °C. The reaction mixture was stirred for 6 d at 4 °C, $Na_2S_2O_3$ solution (50 ml) was added to quench the active oxidizer, and the mixture was concentrated under reduced pressure. The residue was extracted twice with ethyl acetate (2×300 ml), and the combined extracts were washed with saturated NaCl solution, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The oily residue was purified by silica gel column chromatography [hexane–EtOAc (2 : 1)] to afford diol (4.82 g, 46% yield) as colorless oil. The resulting diol (4.0 g, 17.4 mmol) was dissolved into 2,2-dimethoxypropane (30 ml) and methanol (10 ml), followed by addition of *p*-toluenesulfonic acid hydrate (TsOH, 20 mg, 0.11 mmol) at 20 °C. After standing for 2 h at 20 °C, pyridine (0.1 ml) was added and the mixture was concentrated under reduced pressure. The residue was purified by silica gel column chromatography [hexane–EtOAc (6 : 1)] to give acetonide **13** (4.34 g, 92% yield) as colorless oil.

Compound **13**: $[\alpha]_D^{25}$ −16.0° (c=3.77, $CHCl_3$). IR (dry film) cm^{-1}: 1732, 1243. ^{1}H-NMR ($CDCl_3$) δ ppm: 0.99 (3H, s), 1.13 (3H, s), 1.21 (3H, s), 1.30 (3H, s), 1.40 (1H, m), 1.53 (1H, m), 1.63 (3H, s), 1.94 (3H, s), 2.00 (1H, m), 2.18 (1H, m), 3.54 (1H, dd, J=3.0, 9.8 Hz), 4.49 (2H, d, J=6.8 Hz), 5.29 (1H, br t, J=6.8 Hz). ^{13}C-NMR ($CDCl_3$) δ ppm: 16.3, 20.8, 22.7, 25.8, 26.6, 27.1, 28.3, 36.4, 61.0, 79.8, 82.4, 106.3, 118.5, 141.2, 170.7. EI-MS *m/z*: 270 $(M)^+$.

(2*E*)-3-Methyl-5-{(4*R*)-2,2,5,5-tetramethyl-[1,3]dioxolan-4-yl}-2-pentene-1-ol (14) The obtained acetonide (4.0 g, 14.8 mmol) was dissolved into methanol (50 ml) and potassium carbonate (415 mg, 3.0 mmol) was added to the mixture at 20 °C. The reaction mixture was stirred for 3 h, and then neutralized with saturated ammonium chloride solution (2 ml). After concentration under reduced pressure, the residue was diluted with EtOAc (200 ml). The organic layer was washed with water and saturated NaCl solution, dried over Na_2SO_4, filtered, and concentrated. The crude product was purified by silica gel column chromatography [hexane–EtOAc (5 : 1)] to give **14** (3.24 g, 96% yield) as colorless oil.

Compound **14**: $[\alpha]_D^{25}$ +4.3° (c=0.285, $CHCl_3$). IR (dry film) cm^{-1}: 3407 (br), 2980, 1671, 1370. ^{1}H-NMR ($CDCl_3$) δ ppm: 1.01 (3H, s), 1.16 (3H, s), 1.25 (3H, s), 1.33 (3H, s), 1.42 (1H, m), 1.56 (1H, m), 1.61 (3H, br s), 1.99 (1H, m), 2.17 (1H, m), 2.42 (1H, br s, OH), 3.58 (1H, dd, J=3.0, 9.4 Hz), 4.07 (2H, d, J=6.8 Hz), 5.35 (1H, dt, J=1.3, 6.8 Hz). ^{13}C-NMR ($CDCl_3$) δ ppm: 16.2, 22.7, 25.8, 26.7, 27.3, 28.3, 36.4, 58.8, 80.0, 82.7, 106.4, 123.7, 138.2. EI-MS *m/z*: 228 $(M)^+$. HR-EI-MS *m/z*: 228.1700 [Calcd for $C_{13}H_{24}O_3$: 228.1726 $(M)^+$].

(2*E*)-1-(*p*-Toluenesulfonyl)-3-methyl-5-{(4*R*)-2,2,5,5-tetramethyl-[1,3]dioxolan-4-yl}-2-pentene (15) The resulting alcohol **14** (1.27 g, 5.56 mmol) was converted to the corresponding allyl chloride by treatment with methanesulfonyl chloride (1.30 ml, 16.8 mmol) and triethylamine (4.0 ml, 28.7 mmol) in chloroform (20 ml) at 0 °C. The reaction mixture was stirred for 1 h at 20 °C. After dilution with a mixture of hexane–Et_2O (1 : 1, 200 ml), the organic phase was washed with water and saturated NaCl solution, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The oily residue was purified by passed over a small plug of silica gel [hexane–EtOAc (10 : 1)] to provide an unstable allyl chloride (670 mg, 49% yield) as pale yellowish oil. This compound is directly used for the next reaction without further purification. To a mixture of allyl chloride (670 mg, 2.71 mmol) and sodium iodide (2.03 g, 13.5 mmol) in DMF (25 ml) was added sodium *p*-toluenesulfinate (1.21 g, 6.79 mmol) at 20 °C. The reaction mixture was stirred for 3 h at 60 °C. After cooled to 20 °C, 1 : 1 mixture of hexane–EtOAc (100 ml) was added and the organic layer was washed with water and saturated NaCl solution, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The oily residue was purified by silica gel column chromatography [hexane–EtOAc (5 : 1)] to give **15** (727 mg, 73% yield) as colorless viscous oil.

Compound **15**: $[\alpha]_D^{25}$ −5.4° (c=5.35, $CHCl_3$). IR (dry film) cm^{-1}: 2364, 1597, 1370. ^{1}H-NMR ($CDCl_3$) δ ppm: 1.07 (3H, s), 1.23 (3H, s), 1.31 (3H, s), 1.40 (3H, s), 1.38 (1H, m), 1.54 (1H, m), 1.37 (3H, s), 2.04 (1H, m), 2.23 (1H, m), 2.43 (3H, s), 3.60 (1H, dd, J=3.0, 9.9 Hz), 3.79 (2H, d, J=8.1 Hz), 5.29 (1H, dt, J=1.3, 8.1 Hz), 7.30 (2H, d, J=6.8 Hz), 7.73 (2H, d, J=6.8 Hz). ^{13}C-NMR ($CDCl_3$) δ ppm: 16.3, 21.6, 22.9, 26.0, 26.8, 27.4, 28.5, 36.8, 56.0, 80.0, 82.7, 106.6, 110.7, 128.4, 129.6, 144.5, 145.7. EI-MS *m/z*: 366 $(M)^+$. HR-EI-MS *m/z*: 366.1829 [Calcd for $C_{20}H_{30}O_4S$: 366.1865 $(M)^+$].

(3*E*,7*E*)-10-[6-(*tert*-Butyldimethylsilyloxy)-2,8-dimethyl-2*H*-chromen-2-yl]-3,7-dimethyl-1-{(4*R*)-2,2,5,5-tetramethyl-[1,3]dioxolan-4-yl}-deca-3,7-diene (16) To a mixture of **15** (69 mg, 0.188 mmol) in THF (1 ml) at −78 °C under N_2 atmosphere was added butyllithium (1.58 M in hexane, 0.20 ml, 0.316 mmol) dropwisely over 10 min. The mixture was stirred at −78 °C for 1 h. To a reaction mixture was added THF solution (0.2 ml) of allyl bromide **12** (45 mg, 0.100 mmol) over 10 min, and the reaction temperature was gradually warmed to 20 °C over 1 h. After stirred for 1 h at 20 °C, ammonium chloride solution (0.5 ml) to quench the reaction, and a mixture of hexane–Et_2O (1 : 1, 100 ml) was added to the reaction mixture. The organic phase was washed with water and saturated NaCl solution, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The oily residue was purified by silica gel column chromatography [hexane–EtOAc (8 : 1)] to give a diastereomeric mixture of the coupling products (27 mg, 37% yield) as colorless oil. The physical data of the products are shown as follows; IR (dry film) cm^{-1}: 1597, 1470. ^{1}H-NMR ($CDCl_3$) δ ppm: (major signals) 0.16 (6H, s), 0.97 (9H, s), 1.07 (3H, s), 1.21 (3H, s), 1.25 (3H, s), 1.31 (3H, s), 1.41 (3H, s), 1.42 (2H, m), 1.52 (3H, s), 2.10 (3H, s), 2.21 (2H, m), 2.43 (3H, s), 2.80 (2H, m), 3.60 (1H, m), 3.68 (1H, m), 4.92 (1H, t, J=6.8 Hz), 5.12 (1H, t, J=6.8 Hz), 5.49 (1H, d, J=9.8 Hz), 6.23 (1H, d, J=9.8 Hz), 6.28 (1H, d, J=3.0 Hz), 6.45 (1H, d, J=3.0 Hz), 7.29 (2H, d, J=7.7 Hz), 7.70 (2H, d, J=7.7 Hz). EI-MS *m/z*: 583 $[M+H-C_7H_7SO_2]^+$.

To a solution of compounds obtained above (12 mg, 0.016 mmol) and [1,3-bis(diphenylphosphino)propane]palladium(II) dichloride (5.0 mg, 0.0085 mmol) in THF (0.1 ml) was added lithium triethylborohydride (1.05 M in THF, 1.0 ml, 1.05 mmol) at 0 °C under N_2 atmosphere. After stirred for 1 h at 0 °C, ammonium chloride solution (0.2 ml) to terminate the reaction, and a mixture of hexane–Et_2O (1 : 1, 50 ml) was added to the reaction mixture. The organic layer was washed with water and saturated NaCl solution, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography [hexane–EtOAc (10 : 1)] to give **16** (7.6 mg, 80% yield) as colorless oil.

Compound **16**: $[\alpha]_D^{25}$ +2.2° (c=0.495, $CHCl_3$). IR (dry film) cm^{-1}: 2929, 1603, 1470. ^{1}H-NMR ($CDCl_3$) δ ppm: 0.16 (6H, s), 0.97 (9H, s), 1.01 (3H, s), 1.24 (3H, s), 1.32 (3H, s), 1.36 (3H, s), 1.42 (3H, s), 1.47 (1H, m), 1.57 (3H, br s), 1.60 (3H, s), 1.63 (1H, m), 1.68 (2H, m), 1.96 (2H, m), 2.00 (1H, m), 2.06 (3H, m), 2.10 (1H, m), 2.12 (3H, s), 2.17 (1H, m), 3.65 (1H, dd, J=3.4, 9.4 Hz), 5.11 (1H, dt, J=1.3, 6.9 Hz), 5.15 (1H, dt, J=1.3, 6.9 Hz), 5.55 (1H, d, J=9.8 Hz), 6.24 (1H, d, J=9.8 Hz), 6.30 (1H, d, J=3.0 Hz), 6.46 (1H, d, J=3.0 Hz). ^{13}C-NMR ($CDCl_3$) δ ppm: −4.5, 15.5, 15.9, 16.0, 18.1, 22.6, 22.9, 25.7, 25.9, 26.0, 26.5, 26.8, 27.7, 28.5, 39.6, 40.8, 77.7, 80.1, 82.8, 106.4, 114.8, 121.1, 121.7, 123.1, 124.2, 124.7, 126.0, 130.2, 134.2, 135.1, 145.3, 148.3. EI-MS *m/z*: 582 $(M)^+$. HR-EI-MS *m/z*: 582.4094 [Calcd for $C_{36}H_{58}O_4Si$: 582.4104 $(M)^+$].

(3*R*,6*E*,10*E*)-13-(2,8-Dimethyl-6-hydroxy-2*H*-chromen-2-yl)-2,6,10-trimethyltrideca-6,10-diene-2,3-diol (1) Compound **16** (7.6 mg, 0.013 mmol) was treated with 80% acetic acid solution at 40 °C under N_2 atmosphere for 20 h. After the solvent was removed under reduced pressure, the residue was purified by silica gel column chromatography [hexane–EtOAc (2 : 1)] to afford **1** (3.5 mg, 63% yield) as pale yellowish oil: The spectral data obtained for the product were identical to those of both isolated **1** and chemically converted **1** from **2**.[1)]

Compound **1**[1)]: $[\alpha]_D^{25}$ +12.5° (c=0.385, $CHCl_3$). IR (dry film) cm^{-1}: 3400 (br), 1592, 1250. ^{1}H-NMR (500 MHz, $CDCl_3$) δ ppm: 1.16 (3H, s), 1.20 (3H, s), 1.36 (3H, s), 1.41 (1H, m), 1.56 (1H, m), 1.57 (3H, s), 1.59 (3H, s), 1.66 (2H, m), 1.96 (2H, m), 2.02 (1H, m), 2.07 (2H, m), 2.11 (2H, m), 2.14 (3H, s), 2.22 (1H, m), 3.36 (1H, dd, J=2.1, 10.5 Hz), 5.10 (1H, br t, J=6.1 Hz), 5.15 (1H, br t, J=6.3 Hz), 5.58 (1H, d, J=9.9 Hz), 6.24 (1H, d, J=9.9 Hz), 6.33 (1H, d, J=2.7 Hz), 6.49 (1H, d, J=2.7 Hz). ^{13}C-NMR (125 MHz, $CDCl_3$) δ ppm: 15.4, 15.5, 15.9, 22.5, 23.3, 25.8, 26.4, 26.4, 29.6, 36.8, 39.5, 40.7, 73.2, 77.8, 78.3, 110.3, 117.1, 121.3, 122.9, 124.2, 125.0, 126.3, 130.7, 134.8, 135.0, 144.7, 148.7. EI-MS *m/z*: 428 $(M)^+$, 410 $[(M-H_2O)^+]$. HR-EI-MS *m/z*: 428.2945 [Calcd for $C_{27}H_{40}O_4$: 428.2927 $(M)^+$].

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