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Highly Efficient Stereocontrolled Total Synthesis of Polyfunctional Carotenoid, Peridinin**

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General Procedure

All commercially available reagents were used without further purification. All solvents were used after distillation. Tetrahydrofuran (THF) and diethyl ether were refluxed over and distilled from sodium-benzophenone ketyl. Dichloromethane was refluxed over and distilled from P_2O_5. Dimethylformamide (DMF) and dimethyl sulfoxide (DMSO) were distilled from CaH_2 under reduced pressure. Methanol was refluxed over and distilled from $Mg(OMe)_2$. Triethylamine and diisopropylamine were refluxed over and distilled from KOH.

Preparative separation was performed by column chromatography on silica gel (FUJI Silysia Ltd., BW-200) or alumina (Sigma-Aldrich Co. Ltd., activated, neutral, Brockmann I, standard grade, ~150 mesh, 58Å). Analytical and preparative HPLC was carried out on a JASCO PU-1580 and UV-1570 instrument with UV-VIS detector. IR spectra were recorded on a JASCO FT/IR-8000 MCT-5E spectrometer. ^{1}H NMR and ^{13}C NMR spectra were recorded on a JEOL α-400 spectrometer and chemical shifts were represented as δ-values relative to the internal standard TMS. Melting points were uncorrected.

Methyl (4*R*)-4-*tert*-butyldimethylsiloxy-2,2,6-trimethylcyclohexene-1-carboxylate. To a solution of **5**[4] (23.0 g, 57.1 mmol) in DMF (170 mL) was added tetrakis(triphenylphosphine) palladium (1.95 g, 1.69 mmol), triethylamine (24.3 mL, 171 mmol) and methanol (70 mL). After being stirred for 3 h at 70 °C under CO atmosphere, the reaction mixture was poured into a saturated aqueous NH_4Cl solution, and then extracted with ethyl acetate. The organic layers were combined, washed with brine, dried over $MgSO_4$, filtered and concentrated *in vacuo*. Purification by silica gel column chromatography (from 5% to 10% ethyl acetate in hexane) afforded the corresponding methyl ester (17.4 g, 97%) as a colorless oil: $[\alpha]_D^{24}$ –50.45 (*c* 0.79, $CHCl_3$); IR (NaCl, cm^{-1}) 2975, 2930, 2359, 1724, 1462, 1433, 1383, 1252, 1227, 1086, 1040; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.99 (m, 1H), 3.74 (s, 3H), 2.22 (ddd, 1H, *J* = 17.3, 5.6, 1.5 Hz), 2.02 (ddd, 1H, *J* = 17.3, 9.3, 1.0 Hz), 1.67 (s, 3H), 1.63 (ddd, 1H, *J* = 12.4, 3.7, 1.7 Hz), 1.47 (dd, 1H, *J* = 12.0, 12.0 Hz), 1.20 (s, 3H), 1.04 (s, 3H), 0.89 (s, 9H), 0.053 (s, 3H), 0.047 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.90, 134.52, 132.29, 65.20, 51.14, 47.74, 41.48, 35.77, 29.16, 28.53, 25.85, 21.11, 18.14, -4.65, -4.66; EI$^+$ HRMS Found *m/z* 312.2122, Calcd. for $C_{17}H_{32}O_3Si$ M$^+$ 312.2119.

(4*R*)-*tert*-Butyldimethylsiloxy-2,2,6-trimethylcyclohexene-1-methanol (6). To a suspension of lithium aluminum hydride (4.20 g, 73.6 mmol) in THF (200 mL) was added dropwise a solution of the methyl ester (17.4 g, 36.8 mmol) obtained previously in THF (50 mL) at 0 °C. The reaction mixture was stirred at 45 °C for 20 h, and water-saturated ether and then water were added successively. The precipitate was removed by filtration through a pad of Celite, and the filtrate was concentrated *in vacuo*. Purification of the obtained oil by silica gel column chromatography (from 10% to 30% ethyl acetate in hexane) afforded allyl alcohol **6** (9.18 g, 87%) as colorless crystals, whose spectral and physical date were in good agreement with those reported[6]: m.p. 62.0-63.0 °C; $[\alpha]_D^{23}$ –59.52 (*c* 0.84, $CHCl_3$); IR (KBr, cm^{-1}) 3287, 2957, 2928, 2857, 1462, 1383, 1364, 1254, 1088; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.15 (d, 1H, *J* = 11.5 Hz), 4.07 (d, 1H, *J* = 11.5 Hz), 3.92 (m, 1H), 2.18 (ddd, 1H, *J* = 16.8, 5.6, 1.7 Hz), 2.05 (dd, 1H, *J* = 16.8, 9.5 Hz), 1.76 (s, 3H), 1.64 (ddd, 1H, *J* = 12.5, 3.7, 2.2 Hz), 1.48 (dd, 1H, *J* = 12.0, 12.0 Hz), 1.10 (s, 3H), 1.05 (s, 3H), 0.88 (s, 9H), 0.05 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.26, 131.35, 65.61, 58.37, 48.53, 42.73, 36.76, 29.41, 28.54, 25.92, 19.53, 18.23, -4.60.

(1*R*,2*R*,4*S*)-4-*tert*-Butyldimethylsiloxy-1,2-epoxy-2,6,6-trimethylcyclohexane-1-methanol (7). To a mixture of (-)-diethyl-D-tartrate (1.80 mL, 10.5 mmol, dehydrated by azeotropic distillation) and powdered molecular sieves 4Å (5.0 g) in dichloromethane (120 mL) was added freshly distilled tetraisopropyl orthotitanate (2.10 mL, 7.03 mmol) at –20 °C. After the mixture was stirred for 10 min at the same temperature, *tert*-butylhydroperoxide (1.5M in toluene, 46.5 mL, 69.8 mmol, dehydrated by azeotropic distillation) was added dropwise, and the reaction mixture was stirred for 10 min. To this mixture was added a solution of **6** (10.0 g, 35.2 mmol) in dichloromethane (50 mL) at the same temperature, and the mixture was stirred for 30 min at –20 °C. The resulting mixture was poured into an aqueous solution of $FeSO_4$-citric acid at 0 °C. After being stirred for further 20 min at room temperature, the mixture was extracted with chloroform. The organic layers were combined, dried over $MgSO_4$, filtered and concentrated *in vacuo*. Purification by silica gel column chromatography (from 10% to 30% ethyl acetate in hexane) afforded a mixture of α-epoxy alcohol **7** and its diastereomer (10.4 g, 99%) as a colorless oil, the ratio of which was determined as 96 to 4 based on ^{1}H NMR analysis. The obtained diastereomeric mixture was used in the next reaction without further purification.

Data for **7**: IR (NaCl, cm^{-1}) 3449, 2957, 2859, 1639, 1469, 1387, 1253, 1088; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.83 (d, 1H, *J* = 12.0 Hz), 3.77 (m, 1H), 3.71 (d, 1H, *J* = 12.0 Hz), 2.22 (ddd, 1H, *J* = 14.4, 4.9, 2.0 Hz), 1.63 (dd, 1H, *J* = 14.2, 8.5 Hz), 1.44 (ddd, 1H, *J* = 12.9, 3.2, 2.0 Hz), 1.40 (s, 3H), 1.23 (dd, 1H, *J* = 10.5, 10.3 Hz), 1.14 (s, 3H), 1.06 (s, 3H), 0.87 (s, 9H), 0.05 (s, 3H), 0.04 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 68.21, 65.76, 64.32, 59.92, 48.01, 42.27, 34.11, 27.02, 25.82, 24.84, 19.69, 18.08, -4.65, -4.70; FAB$^+$ HRMS Found *m/z* 301.2191, Calcd. for $C_{16}H_{32}O_3Si$ [M+H]$^+$ 300.2199.

(1*S*,2*R*,4*S*)-4-*tert*-Butyldimethylsiloxy-1,2-epoxy-2,6,6-trimethylcyclohexane-1-carbaldehyde (4). To a solution of oxalyl chloride (3.60 mL, 41.6 mmol) in dichloromethane (70 mL) was added dropwise DMSO (3.50 mL, 49.9 mmol) at –78 °C, and the mixture was stirred for 10 min at the same temperature. To this mixture was added a solution of **7** (5.00 g, 16.6 mmol) in dichloromethane (10 mL), and the resulting mixture was stirred for 40 min at –78 °C, and then triethylamine (11.5 mL, 83.2 mmol) was added. After the mixture was stirred for 20 min at room temperature, water was added, and the mixture was extracted with diethyl ether. The organic layers were combined, dried over $MgSO_4$, filtered and concentrated *in vacuo*. Purification by short silica gel column chromatography (5% ethyl acetate in hexane containing 3% triethylamine) afforded aldehyde **4** (4.92 g, 100%) as a colorless oil. The analytical sample was further purified by silica gel column chromatography (3% triethylamine in hexane) to separate the (5*S*,6*R*)-stereoisomer (carotenoid numbering).

Data for **4**: $[\alpha]_D^{22}$ –76.84 (*c* 0.84, $CHCl_3$); IR (NaCl, cm^{-1}) 2957, 2932, 2858, 1728, 1470, 1385, 1254, 1088; ^1H NMR (400 MHz, $CDCl_3$) δ 9.80 (s, 1H), 3.85 (m, 1H), 2.24 (ddd, 1H, *J* = 14.6, 5.4, 1.2 Hz), 1.71 (dd, 1H, *J* = 14.9, 7.6 Hz), 1.49 (ddd, 1H, *J* = 13.2, 3.4, 1.2 Hz), 1.38 (s, 3H), 1.28 (dd, 1H, *J* = 13.2, 9.0 Hz), 1.28 (s, 3H), 1.07 (s, 3H), 0.88 (s, 9H), 0.05 (s, 3H), 0.04 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 200.40, 72.25, 66.13, 64.19, 46.28, 40.78, 33.55, 27.99, 26.21, 25.78, 20.59, 18.01, -4.79, -4.84; EI^+ HRMS Found *m/z* 298.1973, Calcd. for $C_{16}H_{30}O_3Si$ M^+ 298.1963.

(1*S*,3*R*,4*R*)-3,4-Epoxy-4-ethynyl-3,5,5-trimethylcyclohexanol (8). To a suspension of chloromethyltriphenylphosphonium chloride (6.05 g, 17.4 mmol) in THF (45 mL) was added dropwise *n*BuLi (1.6 M in hexane, 10.0 mL, 16.1 mmol) at -78 °C. After the mixture was stirred for 30 min at -78 °C, a solution of **4** (4.00 g, 13.4 mmol) in THF (20 mL) was added. After being stirred for 3 h at –30 °C, the reaction mixture was filtered through a pad of Celite. Water was added to the filtrate, and the resulting mixture was extracted with diethyl ether. The organic layers were combined, washed with brine, dried over $MgSO_4$, filtered and concentrated *in vacuo* to afford crude vinyl chloride as a mixture of *E* and *Z* isomer, which was used in the next reaction without further purification.

To a solution of the crude vinyl chloride thus obtained in DMSO (40 mL) was added potassium *tert*-butoxide (3.31 g, 29.5 mmol) at room temperature. After being stirred for 30 min at the same temperature, the reaction mixture was poured into a saturated aqueous NH_4Cl solution, and then extracted with diethyl ether. The organic layers were combined, washed with brine, dried over $MgSO_4$, filtered and concentrated *in vacuo*. Purification by silica gel column chromatography (from 20% to 50% ethyl acetate in hexane) and crystallization from diethyl ether-hexane afforded acetylene **8** (1.27 g, 53% for 2 steps) as colorless crystals, whose spectral and physical date were in good agreement with those reported[9]: m.p. 71.5-72.5 °C; $[\alpha]_D^{21}$ –45.63 (*c* 0.58, $CHCl_3$); IR (KBr, cm^{-1}) 3480, 3449, 3258, 3233, 2978, 2934, 2870, 2108; ^1H NMR (400 MHz, $CDCl_3$) δ 3.82 (m, 1H), 2.42 (s, 1H), 2.35 (ddd, 1H, *J* = 14.4, 5.2, 1.7 Hz), 1.64 (dd, 1H, *J* = 14.4, 8.4 Hz), 1.60 (ddd, 1H, *J* = 13.2, 3.4, 1.7 Hz), 1.52 (s, 3H), 1.28 (s, 3H), 1.22 (dd, 1H, *J* = 13.0, 10.3 Hz), 1.12 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 80.52, 74.13, 66.53, 63.77, 45.72, 39.74, 34.01, 29.69, 25.39, 21.40.

Methyl (2*E*,4*E*)-7-[(1'*R*,2'*R*,4'*S*)-1',2'-epoxy-4'-hydroxy-2',6',6'-trimethylcyclohexyl]-5-methylhepta-2,4-diene-6-ynate (9). To a solution of **8** (2.15 g 11.9 mmol) and **12** (3.00 g 11.9 mmol) in diisopropylamine (60 mL) was added tetrakis(triphenylphosphine)palladium (138 mg, 0.12 mmol) and cuprous iodide (22.5 mg, 0.12 mmol) at room temperature. After being stirred for 1 h at the same temperature, the reaction mixture was poured into a saturated aqueous NH_4Cl solution, and then extracted with diethyl ether. The organic layers were combined, washed with brine, dried over $MgSO_4$, filtered and concentrated *in vacuo*. Purification by silica gel column chromatography (from 20% to 50% ethyl acetate in hexane) afforded coupling product **9** (3.04 g, 84%) as a pale yellow oil: $[\alpha]_D^{22}$ 5.28 (*c* 0.63, $CHCl_3$); IR (NaCl, cm^{-1}) 3439, 2963, 2930, 2872, 2211, 1719, 1618; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54 (dd, 1H, *J* = 15.1, 12.0 Hz), 6.47 (ddd, 1H, *J* = 12.0, 1.5, 0.98 Hz), 5.91 (d, 1H, *J* = 15.1 Hz), 3.84 (m, 1H), 3.76 (s, 3H), 2.37 (ddd, 1H, *J* = 14.4, 5.1, 1.7 Hz), 2.03 (d, 3H, *J* = 0.98 Hz), 1.66 (dd, 1H, *J* = 14.4, 8.8 Hz), 1.62 (ddd, 1H, *J* = 13.0, 3.4, 1.7 Hz), 1.51 (s, 3H), 1.27 (s, 3H), 1.24 (dd, 1H, *J* = 13.0, 10.5 Hz), 1.13 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.28, 138.88, 133.22, 127.10, 121.65, 89.82, 88.53, 67.33, 63.59, 51.60, 45.74, 39.81, 34.42, 29.77, 25.58, 21.62, 18.12; EI$^+$ HRMS Found *m/z* 304.1679, Calcd. for $C_{18}H_{24}O_4$ M$^+$ 304.1675.

(2*E*,4*E*)-7-[(1'*R*,2'*R*,4'*S*)-2',4'-Dihydroxy-2',6',6'-trimethylcyclohexylidene]-5-methyl-hepta-2,4,6-trien-1-ol (10). To a solution of **9** (2.80 g, 9.44 mmol) in dichloromethane (95 mL) was added dropwise diisobutylaluminum hydride (1.0M in dichloromethane, 94.5 mL, 94.5 mmol) at 0 °C. After the reaction mixture was stirred for 10 min at the same temperature, water and 2N aqueous HCl solution were added, and then the resulting mixture was extracted with ethyl acetate. The organic layers were combined, washed with brine, dried over $MgSO_4$, filtered and concentrated *in vacuo*. Purification by silica gel column chromatography (from 50% to 70% ethyl acetate in hexane) afforded allene triol **10** (2.10 g, 80%) as a pale yellow solid: $[\alpha]_D^{22}$ –37.19 (*c* 0.46, MeOH); IR (KBr, cm^{-1}) 3356, 2965, 2928, 2870, 2209, 1935, 1725, 1663, 1603, 1456, 1375, 1258, 1157, 1071; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.56 (dd, 1H, *J* = 15.1, 11.2 Hz), 6.02 (d, 1H, *J* = 11.2 Hz), 5.98 (s, 1H), 5.85 (dt, 1H, *J* = 15.1, 5.9 Hz), 4.32 (m, 1H), 4.23 (d, 2H, *J* = 5.9 Hz), 2.26 (ddd, 1H, *J* = 12.9, 3.9, 2.2 Hz), 1.95 (ddd, 1H, *J* = 12.2, 3.6, 2.2 Hz), 1.76 (s, 3H), 1.20-1.50 (m, 4H), 1.34 (s, 3H), 1.33 (s, 3H), 1.06 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.01, 132.50, 131.70. 127.84, 126.45, 117.66, 102.62, 72.90, 64.25, 63.59, 49.40, 48.89, 35.70, 32.11, 31.32, 29.31, 13.75; EI$^+$ HRMS Found *m/z* 278.1817, Calcd. for $C_{17}H_{26}O_3$ M$^+$ 278.1882.

(2*E*,4*E*)-7-[(1'*R*,2'*R*,4'*S*)-4'-Acetoxy-2'-hydroxy-2',6',6'-trimethylcyclohexylidene]-5-methylhepta-2,4,6-trien-1-al. A mixture of **10** (2.00 g, 7.18 mmol) and manganese dioxide (25 g) in ethyl acetate (75 mL) was stirred at room temperature for 3 h. The reaction mixture was filtered through a pad of Celite, and the solvents were removed *in vacuo* to afford crude aldehyde, which was used in the next reaction without further purification.

To a solution of crude aldehyde in pyridine (30 mL) was added acetic anhydride (1.08 mL, 11.5 mmol) at room temperature, and the reaction mixture was stirred for 15 h at the same temperature. A saturated aqueous $CuSO_4$ solution was added, and then the resulting mixture was extracted with ethyl acetate. The organic layers were combined, washed with brine, dried over $MgSO_4$, filtered and concentrated *in vacuo*. Purification by silica gel column chromatography (from 30% to 50% ethyl acetate in hexane) afforded the corresponding acetate (1.96 g, 86% for 2 steps) as a pale yellow solid, whose spectral and physical date were in good agreement with those reported[12]: $[\alpha]_D^{21}$ –17.37 (*c* 0.51, $CHCl_3$); IR (KBr, cm^{-1}) 3447, 2965, 2928, 1931, 1728, 1672, 1605, 1370, 1245; ^1H NMR (400 MHz, $CDCl_3$) δ 9.55 (d, 1H, *J* = 8.1 Hz), 7.41 (dd, 1H, *J* = 14.9, 11.7 Hz), 6.24 (d, 1H, *J* = 11.7 Hz), 6.11 (dd, 1H, *J* = 15.1, 8.1 Hz), 6.07 (s, 1H), 5.34 (m, 1H), 2.27 (ddd, 1H, *J* = 12.7, 4.2, 2.0 Hz), 2.00 (s, 3H), 1.97 (m, 1H), 1.90 (s, 3H), 1.47 (dd, 1H, *J* = 12.5, 12.0 Hz), 1.37 (s, 3H), 1.37 (m, 1H), 1.32 (s, 3H), 1.05 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 204.03, 193.65, 170.32, 147.75, 143.85, 130.63, 125.28, 118.08, 102.51, 67.74, 45.23, 45.20, 35.76, 31.84, 30.90, 28.88, 21.25, 14.29.

(2*E*,4*E*)-7-[(1’*R*,2’*R*,4’*S*)-4’-Acetoxy-2’-hydroxy-2’,6’,6’-trimethylcyclohexylidene]-5-methylhepta-2,4,6-trien-1-ol (2). To a solution of the acetate (1.96 mg, 6.21 mmol) obtained above in methanol (60 mL) was added sodium borohydride (707 mg, 18.7 mmol) at 0 °C. The reaction mixture was stirred for 15 min at room temperature, and water was added dropwise, and then the resulting mixture was extracted with ethyl acetate. The organic layers were combined, washed with brine, dried over $MgSO_4$, filtered and concentrated *in vacuo* to afford allene **2** (1.95 g, 98%) as a pale yellow solid: $[\alpha]_D^{21}$ –6.91 (*c* 0.45, $CHCl_3$); IR (KBr, cm^{-1}) 3397, 2969, 2926, 2861, 1935, 1734, 1657, 1640, 1456, 1368; ^1H NMR (400 MHz, $CDCl_3$) δ 6.55 (ddt, 1H, *J* = 15.1, 11.2, 1.5 Hz), 6.02 (d, 1H, *J* = 11.2 Hz), 6.00 (s, 1H), 5.85 (dt, 1H, *J* = 15.1, 6.0 Hz), 5.37 (tt, 1H, *J* = 11.5, 4.2 Hz), 4.24 (brm, 2H), 2.28 (ddd, 1H, *J* = 12.9, 4.1, 2.2 Hz), 2.04 (s, 3H), 1.99 (ddd, 1H, *J* = 12.44, 4.2, 2.2 Hz), 1.76 (s, 3H), 1.38 (s, 3H), 1.35 (s, 3H), 1.30-1.50 (m, 2H), 1.07 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 201.96, 170.43, 132.35, 131.79, 127.79, 126.61, 117.44, 102.78, 72.58, 67.99, 63.60, 45.40, 45.20, 35.64, 32.03, 31.22, 29.15, 21.39, 13.76; EI^+ HRMS Found *m/z* 320.1997, Calcd. for $C_{19}H_{28}O_4$ M^+ 320.1987.

Methyl (2*E*,4*E*)-5-iodohexa-2,4-dienate (12). A mixture of **11**[11] (5.00 g, 25.3 mmol) and manganese dioxide (25.0 g) in diethyl ether (150 mL) was stirred at room temperature for 2 h. The precipiate was filtered through a pad of Celite, and the filtrate was concentrated *in vacuo* to afford crude aldehyde, which was used in the next reaction without further purification.

To a solution of trimethyl phosphonoacetate (5.98 g, 32.8 mmol) in THF (120 mL) was added sodium hydride (730 mg, 30.4 mmol) at 0 °C, and the mixture was stirred for 10 min. To this mixture was added a solution of the crude aldehyde in THF (30 mL) at 0 °C. After being stirred for

5 min at room temperature, the reaction mixture was poured into water, and then extracted with ethyl acetate. The organic layers were combined, dried over $MgSO_4$, filtered and concentrated *in vacuo*. Purification by silica gel column chromatography (5% ethyl acetate in hexane) afforded methyl ester **12** (4.70 g, 74% for 2 steps) as an oil: IR (NaCl, cm^{-1}) 2992, 2949, 2917, 2841, 1717, 1622, 1433, 1379, 1345, 1310, 1267, 1234; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 (dd, 1H, *J* = 15.1, 11.5 Hz), 6.93 (dd, 1H, *J* = 11.5, 0.73 Hz), 5.85 (d, 1H, *J* = 15.4 Hz), 3.76 (s, 3H), 2.66 (d, 3H, *J* = 1.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.18, 138.49, 137.94, 120.79, 108.08, 51.67, 28.86; EI^{+} HRMS Found *m/z* 251.9630, Calcd. for $C_7H_9O_2I$ M^{+} 251.9647.

3-[(1”*E*)-(1’’*S*,2”*R*,4”*S*)-*tert*-Butyldimethylsiloxy-1”,2’’-epoxy-2”,6”,6”-trimethylcyclohex-1”-ylethene-1’-yl]-2-*tert*-butyldimethylsilylfuran (13). To a suspension of **14**[15] (2.16 g, 4.02 mmol) in diethyl ether (20 mL) was added dropwise *n*BuLi (1.6M in hexane, 2.52 mL, 4.02 mmol) at 0 °C. After the mixture was stirred for 10 min at 0 °C, a solution of **4** (1.0 g, 3.35 mmol) in diethyl ether (5 mL) was added, and the reaction mixture was stirred for 3 h at room temperature. It was filtered through a pad of Celite. Water was added to the filtrate, and the resulting mixture was extracted with ether. The organic layers were combined, washed with brine, dried over $MgSO_4$, filtered and concentrated *in vacuo* to afford crude silylfuran **13**, which was used in the next reaction without further purification.

(5*RS*)-Hydroxy-3-[(1’*E*)-2’-(1”*S*,2’’*R*,4”*S*)-4”-*tert*-butyldimethylsiloxy-1”,2”-epoxy-2”,6”,6”-trimethylcyclohex-1”-ylethen-1’-yl]-2(5*H*)-furanone (15). A solution of crude **13** and tetraphenyl porphine (5 mg) in dichloromethane (50 mL) was irradiated with halogen-tungsten lamp under oxygen atmosphere for 30 min at –78 °C. After the mixture was allowed to warm to room temperature, the solvents were removed *in vacuo*. Purification by silica gel column chromatography (from 2% to 50% ethyl acetate in hexane) afforded γ-hydroxybutenolide **15** (2.01 g, 77% for 2 steps) as a yellow oil: $[\alpha]_D^{21}$ –47.49 (*c* 0.34, $CHCl_3$); IR (NaCl, cm^{-1}) 3376, 2957, 2932, 2859, 1769, 1659; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.22 (d, 1H, *J* = 15.6 Hz), 6.93 (s, 1H), 6.27 (d, 1H, *J* = 15.6 Hz), 5.95 (s, 1H), 4.97 (brs, 1H), 3.83 (m, 1H), 2.23 (ddd, 1H, *J* = 14.6, 5.1, 1.5 Hz), 1.65 (dd, 1H, *J* = 14.6, 8.3 Hz), 1.49 (ddd, 1H, *J* = 12.9, 3.4, 1.7 Hz), 1.26 (dd, 1H, *J* = 12.9, 10.0 Hz), 1.16 (s, 6H), 0.92 (s, 3H), 0.86 (s, 9H), 0.04 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.79, 142.96, 135.56, 131.33, 120.66, 96.20, 70.55, 67.46, 64.57, 46.76, 41.13, 34.96, 29.25, 25.82, 24.89, 19.94, 18.09, -4.78, -4.81; EI^{+} HRMS Found *m/z* 394.2175, Calcd. for $C_{21}H_{34}O_5Si$ M^{+} 394.2173.

(2*E*,4*E*)-5-[(1’*S*,2’*R*,4’*S*)-4’-*tert*-Butyldimethylsiloxy-1’,2’-epoxy-2’,6’,6’-trimethylcyclo hex-1’-yl]-3-allyloxycarbonylpenta-2,4-dienal (16). To a solution of **15** (2.20 g, 5.58 mmol) obtained previously in DMSO (34 mL) was added diisopropylethylamine (2.89 mL, 16.7 mmol) at room temperature. After the reaction mixture was stirred for 3 h at the same temperature, allyl bromide (2.41 mL, 27.8 mmol) was added. After being stirred for an additional 1 h, the reaction mixture was poured into a saturated aqueous NH_4Cl solution, and then extracted with ethyl acetate. The organic layers were combined, washed with brine, dried over $MgSO_4$, filtered and concentrated *in vacuo*. Purification by silica gel column chromatography (from 3% to 10% ethyl acetate in hexane) afforded (*Z*)-β-alkoxycarbonyldienal **16** (1.69 g, 70%) as a pale yellow oil: $[\alpha]_D^{22}$ –77.47 (*c* 0.97, $CHCl_3$); IR (NaCl, cm^{-1}) 2959, 2930, 2857, 1734, 1680, 1626, 1589, 1472, 1381, 1345; ^1H NMR (400 MHz, $CDCl_3$) δ 9.83 (d, 1H, *J* = 7.6 Hz), 6.50 (d, 1H, *J* = 15.6 Hz), 6.36 (d, 1H, *J* = 15.6 Hz), 6.10 (d, 1H, *J* = 7.6 Hz), 5.98 (ddt, 1H, *J* = 17.1, 10.5, 6.1 Hz), 5.42 (dd, 1H, *J* = 17.1, 1.2 Hz), 5.34 (dd, 1H, *J* = 10.3, 1.2 Hz), 4.83 (m, 2H), 3.84 (m, 1H), 2.24 (ddd, 1H, *J* = 14.6, 4.9, 1.5 Hz), 1.65 (dd, 1H, *J* = 14.4, 8.1 Hz), 1.50 (ddd, 1H, *J* = 13.2, 3.4, 1.5 Hz), 1.25 (dd, 1H, *J* = 13.2, 9.8 Hz), 1.17 (s, 3H), 1.13 (s, 3H), 0.95 (s, 3H), 0.87 (s, 9H), 0.05 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 190.82, 165.49, 147.92, 138.53, 129.82, 128.85, 120.28, 70.19, 67.57, 66.55, 64.45, 46.64, 41.14, 35.12, 29.16, 25.84, 25.10, 20.00, 15.26, -4.75, -4.79; EI^+ HRMS Found *m/z* 434.2487, Calcd. for $C_{24}H_{38}O_5Si$ M^+ 434.2488.

(3*Z*,5*E*)-1,1-Dibromo-6-[(1'*S*,2'*R*,4'*S*)-4'-*tert*-butyldimethylsiloxy-1',2'-epoxy-2',6',6'-trimethylcyclohex-1'-yl]-4-allyloxycarbonylhexa-1,3,5-trien (17). To a solution of carbon tetrabromide (2.91 g, 8.79 mmol) in dichloromethane (15 mL) was added dropwise a solution of triphenylphosphine (4.61 g, 17.6 mmol) in dichloromethane (20 mL) at –20 °C. After the reaction mixture was stirred for 20 min, a solution of **16** (1.91 g, 4.39 mmol) and triethylamine (1.22 mL, 8.79 mmol) in dichloromethane (15 mL) was added at -60 °C, and then the mixture was stirred for 1 h at the same temperature. Precipitates which appeared by addition of hexane, were removed by filtration through a pad of Celite, and then the solvents were removed *in vacuo*. Purification by silica gel column chromatography (from 2% to 5% ethyl acetate in hexane) afforded dibromide **17** (2.31 g, 89%) as a yellow oil: $[\alpha]_D^{21}$ –45.81 (*c* 1.19, $CHCl_3$); IR (NaCl, cm^{-1}) 2957, 2930, 2858, 1721, 1462, 1383, 1364; ^1H NMR (400 MHz, $CDCl_3$) δ 7.56 (d, 1H, *J* = 11.2 Hz), 6.44 (d, 1H, *J* = 11.2 Hz), 6.30 (d, 1H, *J* = 15.6 Hz), 6.26 (d, 1H, *J* = 15.6 Hz), 5.98 (ddt, 1H, *J* = 17.1, 10.2, 5.9 Hz), 5.39 (dd, 1H, *J* = 17.1, 1.2 Hz), 5.30 (dd, 1H, *J* = 10.5, 1.2 Hz), 4.75 (m, 2H), 3.85 (m, 1H), 2.24 (ddd, 1H, *J* = 14.4, 5.1, 1.5 Hz), 1.64 (dd, 1H, *J* = 14.4, 8.3 Hz), 1.50 (ddd, 1H, *J* = 13.2, 3.4, 1.5 Hz), 1.24 (dd, 1H, *J* = 13.2, 10.0 Hz), 1.18 (s, 3H), 1.12 (s, 3H), 0.96 (s, 3H), 0.87 (s, 9H), 0.05 (s, 3H), 0.04 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.18, 133.41, 131.45, 131.37, 129.97, 98.19, 70.33, 67.21, 65.78, 64.62, 46.96, 41.31, 35.11, 29.30, 25.87, 24.98, 20.02 -4.73, -4.76; EI^+ HRMS Found *m/z* 588.0916, Calcd. for $C_{25}H_{38}O_4{}^{79}Br_2Si$ M^+ 588.0907.

((3*Z*,5*E*)-6-[(1'*S*,2'*R*,4'*S*)-4'-Hydroxy-1',2'-epoxy-2',6',6'-trimethylcyclohex-1'-yl]-4-allyloxycarbonylhexa-3,5-dien-1-yne (18). To a solution of **17** (1.50 g, 2.54 mmol) in THF (25 mL) was added tetra-*n*-butylammonium fluoride (4.00 g, 15.2 mmol) at room temperature. After being stirred for 20 hat 45 °C, the reaction mixture was poured into a saturated aqueous NH_4Cl solution, and then extracted with diethyl ether. The organic layers were combined, washed with brine, dried over $MgSO_4$, filtered and concentrated *in vacuo*. Purification by short silica gel column chromatography (from 10% to 30% ethyl acetate in hexane) afforded terminal acetylene **18** (652 mg, 81%) as an orange oil, which was immediately used in next reaction.

Data for **18**: IR (NaCl, cm^{-1}) 3412, 3293, 3086, 2963, 2930, 2874, 2097, 1725, 1649, 1582, 1453, 1383, 1366, 1223, 1163, 1049; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.25 (s, 2H), 5.99 (ddt, 1H, *J* = 17.1, 10.5, 5.9 Hz), 5.84 (d, 1H, *J* = 2.7 Hz), 5.42 (dd, 1H, *J* = 17.1, 1.2 Hz), 5.29 (dd, 1H, *J* = 10.5, 1.2 Hz), 4.80 (m, 2H), 3.88 (m, 1H), 3.42 (d, 1H, *J* = 2.7 Hz), 2.37 (ddd, 1H, *J* = 14.2, 5.1, 1.7 Hz), 1.50-1.70 (m, 2H), 1.23 (dd, 1H, *J* = 13.2, 10.5 Hz), 1.19 (s, 3H), 1.12 (s, 3H), 0.97 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.64, 142.92, 131.84, 131.50, 128.77, 118.96, 113.05, 87.07, 80.03, 69.93, 67.33, 65.81, 63.99, 46.91, 40.75, 35.21, 29.30, 24.77, 19.77; EI$^+$ HRMS Found *m/z* 316.1684, Calcd. for $C_{19}H_{24}O_4$ M$^+$ 316.1673.

(5*Z*)-[(2’*E*)-4’-Hydroxy-2’-methyl-1’-butenylidene]-3-[(1”*E*)-2”-(1”’*S*,2”’*R*,4”’*S*)-4”’-hydroxy-1”’,2”’-epoxy-2”’,6”’,6”’-trimethylcyclohex-1”’-ylethen-1”-yl]-2-furanone (3). To a solution of **18** (650 mg, 2.04 mmol) and **11** (450 mg, 2.28 mmol) in triethylamine (20 mL) was added tetrakis(triphenylphosphine)palladium (236 mg, 0.20 mmol) and cuprous iodide (40 mg, 0.20 mmol) at room temperature. The reaction mixture was stirred at room temperature until **18** was completely consumed by monitoring with TLC (*ca*. 1 h), and formic acid (0.30 mL, 6.52 mmol) was added dropwise. After being stirred for the additional 20 h, the resulting mixture was poured into a saturated aqueous NH_4Cl solution, and extracted with diethyl ether. The organic layers were combined, washed with brine, dried over $MgSO_4$, filtered and concentrated *in vacuo*. Purification by short silica gel column chromatography (from 70% ethyl acetate in hexane) afforded ylidenebutenolide **3** (345 mg, 49%) as an orange solid: IR (KBr, cm^{-1}) 3420, 2965, 2928, 1755, 1640, 1440, 1381, 1248, 1154, 1121, 1047; $[\alpha]^D$ –38.52 (*c* 0.83, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.19 (d, 1H, *J* = 15.6 Hz), 7.04 (s, 1H), 6.37 (d, 1H, *J* = 15.6 Hz), 5.97 (t, 1H, *J* = 6.6 Hz), 5.65 (s, 1H), 4.36 (d, 2H, *J* = 6.6 Hz), 3.90 (m, 1H), 2.40 (ddd, 1H, *J* = 14.4, 5.1, 1.7 Hz), 1.50-1.70 (m, 2H), 1,25 (m, 1H), 1.21 (s, 6H), 0.97 (s, 3H); ^{13}C MNR (100 MHz, $CDCl_3$) δ 168.63, 146.63, 136.89, 134.28, 133.93, 125.92, 121.46, 117.61, 70.37, 67.49, 64.13, 59.49, 47.04, 40.87, 35.26, 29.446, 24.86, 19.82, 15.48; EI$^+$ HRMS Found *m/z* 346.1788, Calcd. for $C_{20}H_{26}O_5$ M$^+$ 346.1779.

2-[(((2’*E*,4’*E*)-7’-(1”*R*,2”*R*,4”*S*)-4”-Acetoxy-2”-hydroxy-2”,6”,6”-trimethylcyclohexylidene)-5’-methylhepta-2’,4’,6’-trienyl)thio] benzothiazole. To a solution of **2** (465 mg, 1.45 mmol), 2-mercaptobenzothiazole (291 mg, 1.74 mmol) and triphenylphosphine (456 mg, 1.74 mmol) in THF (15 mL) was added dropwise diisopropyl azodicarboxylate (0.27 mL, 1.88 mmol) at 0 °C. The reaction mixture was stirred for 1.5 h at room temperature, and the all solvents were removed *in vacuo*. To a residue was added diethyl ether, and the precipitate was removed by filtration through a pad of Celite to give the crude products as a solution, which was concentrated *in vacuo*. Purification by short silica gel column chromatography (from 20% to 50% ethyl acetate in hexane) afforded the thioether (529 mg, 78%) as a pale yellow solid: $[\alpha]_D^{21}$ –7.02 (*c* 0.89, $CDCl_3$); IR (KBr, cm^{-1}) 3426, 3061, 3029, 2965, 2926, 1933, 1719, 1632, 1458, 1427, 1372, 1250, 1182, 1163, 1109, 1073, 1030; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 (dd, 1H, *J* = 7.8, 1.2 Hz), 7.76 (dd, 1H, *J* = 7.8, 1.2 Hz), 7.42 (ddd, 1H, *J* = 7.8, 7.8, 1.2 Hz), 7.30 (ddd, 1H, *J* = 7.8, 7.8, 1.2 Hz), 6.65 (dd, 1H, *J* = 14.6, 11.0 Hz), 5.98 (d, 1H, *J* = 11.0 Hz), 5.96 (s, 1H), 5.86 (dt, 1H, *J* = 14.6, 7.6 Hz), 5.37 (tt, 1H, *J* = 11.5, 4.2 Hz), 4.10 (d, 2H, *J* = 7.8 Hz), 2.27 (ddd, 1H, *J* = 12.7, 3.9, 2.2 Hz), 2.03 (s, 3H), 1.98 (ddd, 1H, *J* = 12.4, 4.4, 2.2 Hz), 1.74 (s, 3H), 1.37 (s, 3H), 1.33 (s, 3H), 1.30-1.50 (m, 2H), 1.05 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.09, 170.36, 166.17, 153.18, 135.31, 132.83, 131.04, 126.4445, 126.33, 126.00, 124.22, 121.48, 120.95, 117.45, 102.72, 72.52, 67.95, 45.36, 45.18, 36.18, 35.62, 32.01, 31.19, 29.10, 21.37, 13.78; EI$^+$ HRMS Found *m/z* 469.1748, Calcd. for $C_{26}H_{31}O_3NS_2$ M$^+$ 469.1743.

2-[(((2’*E*,4’*E*)-7’-(1”*R*,2”*R*,4”*S*)-4”-Acetoxy-2”-hydroxy-2”,6”,6”-trimethylcyclohexylidene)-5’-methylhepta-2’,4’,6’-trienyl)sulfonyl] benzothiazole (21). To a solution of the thioether (500 mg, 1.07 mmol) in ethanol (10 mL) was added dropwise a solution of ammonium heptamolybdate tetrahydrate (132 mg, 0.11 mmol) in hydrogen peroxide (30 wt.% in water, 2.0 mL) at 0 ^{o}C. After being stirred for 1 h at the same temperature, the reaction mixture was poured into brine, and then extracted with diethyl ether. The organic layers were combined, dried over $MgSO_4$, filtered and concentrated *in vacuo*. Purification by short alumina column chromatography (from 30% to 50% ethyl acetate in hexane) afforded the sulfone **21** (474 mg, 89%) as a pale yellow solid: $[\alpha]_D^{21}$ –6.15 (*c* 0.77, $CDCl_3$); IR (KBr, cm-1) 3356, 2976, 2928, 1935, 1725, 1630, 1472, 1426, 1375, 1331, 1248, 1148, 1109, 1073; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.24 (dd, 1H, *J* = 7.8, 1.2 Hz), 8.01 (dd, 1H, *J* = 7.8, 1.2 Hz), 7.65 (ddd, 1H, *J* = 7.8, 7.8, 1.2 Hz), 7.59 (ddd, 1H, *J* = 7.8, 7.8, 1.2 Hz), 6.53 (dd, 1H, *J* = 15.1, 11.7 Hz), 5.95 (d, 1H, *J* = 11.7 Hz), 5.93 (s, 1H), 5.61 (dt, 1H, *J* = 15.1, 7.8 Hz), 5.36 (tt, 1H, *J* = 11.7, 4.4 Hz), 4.32 (d, 2H, *J* = 7.8 Hz), 2.27 (ddd, 1H, *J* = 12.7, 4.4, 2.0 Hz), 2.03 (s, 3H), 1.97 (ddd, 1H, *J* = 12.7, 4.4, 2.0 Hz), 1.57 (s, 3H), 1.36 (s, 3H), 1.30 (s, 3H), 1.30-1.50 (m, 2H), 1.02 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.46, 170.38, 165.61, 152.56, 137.04, 136.83, 135.26, 127.93, 127.58, 125.54, 125.36, 122.27, 117.56, 115.08, 102.41, 72.41, 67.87, 59.00, 45.29, 45.15, 35.62, 31.92, 31.04, 29.02, 21.32, 13.62; EI$^+$ HRMS Found *m/z* 501.1637, Calcd. for $C_{26}H_{31}O_5NS_2$ M$^+$ 501.1642.

(5*Z*)-[(2’*E*)-2’-Methyl-4’-oxo-2’-butenylidene]-3-[(1”*E*)-2”-(1’”*S*,2’”*R*,4’”*S*)-4’”-hydroxy-1’”,2’”-epoxy-2’”,6’”,6’”-trimethylcyclohex-1’”-ylethen-1”-yl]-2-furanone (22). To a solution of **3** (180 mg, 0.51 mmol) in diethyl ether (6.0 mL) was added manganese dioxide (3.0 g) at room temperature. After being stirred at the same temperature for 5 min, the reaction mixture was filtered through a pad of Celite. The solvents were removed *in vacuo* to afford crude aldehyde **22**, which was used to the next reaction without further purification.

Peridinin (1). To a solution of **21** (261 mg, 0.51 mmol) and crude **22** in THF (10 mL) was added dropwise sodium bis(trimethylsilyl)amide (1.0M in THF, 1.00 mL, 1.00 mmol) at –78 ^{o}C in the dark. After being stirred for 5 min at the same temperature, the reaction mixture was poured into brine, and then extracted with diethyl ether. The organic layers were combined, washed with brine, dried over $MgSO_4$, filtered and concentrated *in vacuo*. Purification by short silica gel column chromatography (from 50 % ethyl acetate in hexane) in the dark afforded a mixture of all-*trans*-peridinin (**1**) and its 15-*cis*-isomer (**23**) (168 mg, 50%, *ca*. 1 : 3 based on ^{1}H NMR analysis) as a red film.

A solution of a mixture of all-*trans*-peridinin (**1**) and its 15-*cis*-isomer (**23**) in benzene (2.0 mL) was left at room temperature in the dark. After 3 days, the thermodynamical equilibrium was reached *E* : *Z* = >5 : 1, and then purification and partial separation by preparative HPLC [column: Develosil CN-UG (0.6 x 25 cm); mobile phase: acetone / *n*-hexane = 1 / 10; flow rate: 1.54 mL / min.; UV-detect: 450 nm; retention time: (all-*trans*-isomer) 50 min., (15-*cis*-isomer) 53 min.] in the dark, was afforded the desired optically active peridinin (**1**) as a red powder.

Data for peridinin (**1**): IR (KBr, cm^{-1}) 3418, 2963, 2926, 2857, 1929, 1738, 1657, 1524, 1456, 1439, 1365, 1250, 1161, 1121, 1030; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.17 (d, 1H, *J* = 15.6 Hz), 7.02 (s, 1H), 6.61 (dd, 1H, *J* = 14.2, 11.7 Hz), 6.51 (dd, 1H, *J* = 14.2, 10.5 Hz), 6.45 (d, 1H, *J* = 11.5 Hz), 6.384 (dd, 1H, *J* = 14.4, 10.5 Hz), 6.377 (d, 1H, *J* = 15.6 Hz), 6.11 (d, 1H, *J* = 11.2 Hz), 6.06 (s, 1H), 5.73 (s, 1H), 5.38 (tt, 1H, *J* = 11.7, 4.4 Hz), 3.90 (m, 1H), 2.40 (ddd, 1H, *J* = 14.2, 5.0, 1.5 Hz), 2.28 (ddd, 1H, *J* = 13.0, 4.2, 2.0 Hz), 2.23 (s, 3H), 2.04 (s, 3H), 1.99 (ddd, 1H, *J* = 12.4, 4.0, 2.0 Hz), 1.80 (s, 3H), 1.38 (s, 3H), 1.35 (s, 3H), 1.21 (s, 3H), 1.20 (s, 3H), 1.07 (s, 3H), 0.98 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.64, 170.36, 168.75, 146.77, 138.00, 137.20, 136.30, 133.97, 133.89, 133.63, 133.02, 131.47, 128.93, 128.14, 124.78, 121.79, 119.21, 117.62, 103.31, 72.66, 70.44, 67.92, 67.51, 64.22, 47.12, 45.40, 45.21, 40.93, 35.79, 35.31, 32.05, 31.27, 29.51, 29.16, 24.89, 21.39, 19.87, 15.40, 14.00; EI$^+$ HRMS Found *m/z* 630.3544, Calcd. for $C_{39}H_{50}O_7$ M$^+$ 630.3554.