Supporting Information 1/3

Stereoselective Synthesis and Absolute Configuration of the C1'–C25' Fragment of Symbiodinolide

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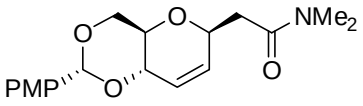
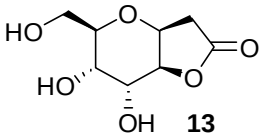
General Method. Reagents were used as received from commercial suppliers unless otherwise indicated. All reactions were carried out under an atmosphere of N_2 or Ar. Reaction solvents were purchased as dehydrated solvents and stored with active molecular sieves 4A under Ar prior to use for reactions. All solvents for work-up procedure were used as received. All inorganic salt solutions are aqueous unless otherwise stated. “Brine” refers to saturated aqueous NaCl solution. “Concentration” refers to removal of solvent under reduced pressure (10-100 mmHg) with a rotary evaporator, followed by a period under high vacuum (< 0.1 mmHg) unless otherwise indicated. Column chromatography was performed with Fuji Silysia silica gel BW-820MH. Preparative TLC separations were performed with TLC plates (Merck 0.5 mm coated silica gel $60F_{254}$ plates). Analytical thin-layer chromatography (TLC) was performed with glass TLC plates (Merck 0.25 mm coated silica gel $60F_{254}$ plates). Data for ^{1}H NMR spectra are reported in the following format: chemical shift (multiplicity, coupling constant, number of atoms). Chemical shifts are indicated in parts per million (ppm) downfield from tetramethylsilane (TMS, δ = 0.00) with residual undeuterated solvent peaks as internal reference, for ^{1}H NMR $CHCl_3$ (7.26), CHD_2OD (3.31) or C_6HD_5 (7.16) and deuterated solvent peaks shifts for ^{13}C NMR $CDCl_3$ (77.2), CD_3OD (49.0), C_6D_6 (128.1). Multiplicities are reported as s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), br (broad) or combinations of those. Coupling constants (*J*) are in hertz.



10

Amide 10. To a suspension of alcohol **9** (4.63 g, 17.5 mmol) in xylene (90 mL) was added *N*,*N*-dimethylacetamide dimethylacetal (90~95% in MeOH, 4.5 mL, 27.7 mmol) at room temperature. The mixture was allowed to warm to 140 °C and stirred at the same temperature for 8 h. The mixture was concentrated to half volume and purified by column chromatography (hexane/EtOAc, 2:1, 1:1, hexane/acetone, 1:1) to give amide **10** (5.40 g, 93%): pale yellow solid; R_f = 0.48 (hexane/acetone, 1:1); $[\alpha]^{25}_{D}$ +93.8 (*c* 0.20, $CHCl_3$); IR (KBr) 1633 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.42 (d, *J* = 8.5 Hz, 2 H), 6.88 (d, *J* = 8.5 Hz, 2 H), 5.96 (brd, *J* = 10.3 Hz, 1 H), 5.85 (dt, *J* = 10.3, 1.7 Hz, 1 H), 5.54 (s, 1 H), 4.86–4.81 (m, 1 H), 4.30 (dd, *J* = 10.2, 4.4 Hz, 1 H), 4.17–4.13 (m, 1 H), 3.80 (s, 1 H), 3.72 (t, *J* = 10.2 Hz, 1 H), 3.62 (ddd, *J* = 10.3, 8.2, 4.4 Hz, 1 H), 3.01 (s, 3 H), 2.96 (s, 3 H), 2.70 (dd, *J* = 15.4, 6.8 Hz, 1 H), 2.44 (dd, *J* = 15.4, 6.8 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.7, 160.1, 131.0, 130.0, 127.5, 126.7, 113.7, 101.1, 75.2, 73.4, 70.9, 69.4, 55.3, 38.8, 37.4, 35.4; HRMS (FAB) calcd for $C_{18}H_{24}O_5N$ $(M + H)^+$ 334.1654, found: 334.1639.

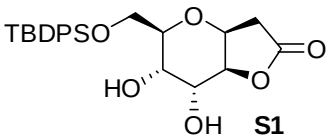


13

Triol 13. To a solution of amide **10** (15.5 g, 46.5 mmol) in THF–H_2O (3:1, 450 mL) was added I_2 (35.0 g, 139 mmol) in three portions at 0 °C and the mixture was stirred at the same temperature for 5 h. The reaction was quenched with saturated aqueous $Na_2S_2O_3$, and the mixture was extracted with $CHCl_3$. The combined organic layer was washed with saturated aqueous $NaHCO_3$, H_2O and brine, and dried over Na_2SO_4. Concentration and short column chromatography (hexane/EtOAc, 4:1, 2:1) gave iodolactone **11** (19.5 g) as a pale yellow oil, which was used for the next reaction without further purification.

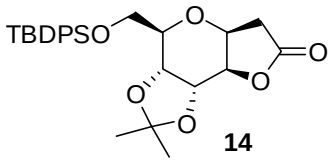
To a solution of iodolactone **11** obtained above in MeOH–THF (2:1, 300 mL) was added NaOMe (4.80 g, 90.2 mmol) at 0 °C and the mixture was stirred at the same temperature. To the mixture was added additional NaOMe (5 h, 2.40 g, 45.1 mmol; 19 h, 2.40 g, 45.1 mmol). The reaction mixture was stirred for 6 h and quenched with saturated aqueous NH_4Cl, and the mixture was extracted with $CHCl_3$. The combined organic layer was washed with H_2O, brine, and dried over Na_2SO_4. Concentration and short column chromatography (hexane/EtOAc, 3:1) gave epoxyester **12** (11.0 g) as a pale yellow oil, which was used for the next reaction without further purification.

A solution of epoxyester **12** obtained above in 50% aqueous TFA (160 mL) was heated to 60 °C and stirred for 2 h. The resulting solution was concentrated, and the azeotropic removal of remaining acid and water was performed with toluene several times. The residue was dissolved small amount of MeOH, then precipitated with Et_2O, and filtered to give triol **13** (5.90 g, 62% in three steps): colorless solid; R_f = 0.38 ($CHCl_3$/MeOH, 4:1); $[\alpha]^{28}_{D}$ –13.5 (*c* 0.24, CH_3OH); IR (KBr) 3382, 3296, 2944, 1793 cm^{-1}; ^1H NMR (400 MHz, CD_3OD) δ 4.49–4.45 (m, 2 H), 4.13 (brt, *J* = 3.2 Hz, 1 H), 3.80 (dd, 11.8, 2.5 Hz, 1 H), 3.73–3.68 (m, 1 H), 3.62–3.57(m, 2 H), 2.85 (dd, *J* = 17.3, 4.4 Hz, 1 H), 2.46 (d, *J* = 17.3 Hz, 1 H); ^{13}C NMR (400 MHz, CD_3OD) δ 177.9, 83.9, 75.9, 72.2, 67.8, 66.8, 63.3, 38.3; HRMS (FAB) calcd for $C_8H_{13}O_6$ $(M + H)^+$ 205.0712, found: 205.0718.



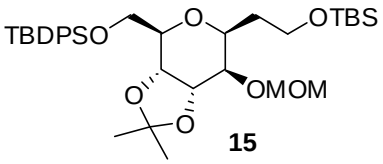
S1

TBDPS Ether S1. To a solution of triol **13** (2.53 g, 12.4 mmol) in DMF (50 mL) were added imidazole (1.26 g, 18.6 mmol) and TBDPSCl (3.4 mL, 14.9 mmol) at room temperature. The mixture was stirred for 2 h at the same temperature. The reaction was quenched with MeOH, and the mixture was poured into H_2O, and extracted with $CHCl_3$. The combined organic layer was washed with H_2O, brine and dried over Na_2SO_4. Concentration and column chromatography (hexane/EtOAc, 4:1, 2:1, 1:1) gave TBDPS ether **S1** (4.54 g, 82%): colorless oil; R_f = 0.19 (hexane/EtOAc, 2:1); $[\alpha]^{26}_D$ –16.6 (*c* 0.55, $CHCl_3$); IR (neat) 3439, 2930, 1792 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.67–7.64 (m, 4 H), 7.48–7.39 (m, 6 H), 4.44–4.42 (m, 2 H), 4.33 (brt, *J* = 2.4 Hz, 1 H), 3.97 (dd, *J* = 9.0, 3.4 Hz, 1 H), 3.89 (dd, *J* = 10.0, 4.0 Hz, 1 H), 3.80–3.70 (m, 2 H), 2.62 (dd, *J* = 17.2, 4.0 Hz, 1 H), 2.45 (d, *J* = 17.2 Hz, 1 H), 1.06 (s, 9 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.7, 135.5, 135.5, 132.4, 132.2, 130.1, 130.1, 127.9, 127.9, 80.3, 70.8, 70.6, 68.3, 65.9, 65.8, 37.3, 26.8, 19.1; HRMS (FAB) calcd for $C_{24}H_{30}O_6SiNa$ $(M + Na)^+$ 465.1709, found: 465.1712.



14

Acetonide 14. To a solution of diol **S1** (4.54 g, 10.2 mmol) in acetone (50 mL) were added 2,2-dimethoxypropane (5.0 mL, 40.9 mmol) and CSA (236 mg, 1.02 mmol) at 0 °C. The mixture was stirred at room temperature for 3 h. The reaction was quenched with Et_3N, and the mixture was concentrated. The residue was purified by column chromatography (hexane/EtOAc, 20:1, 9:1, 4:1) to give acetonide **14** (4.74 g, 96%): colorless oil; R_f = 0.54 (hexane/EtOAc, 1:1); $[\alpha]^{27}_D$ +7.2 (*c* 0.57, $CHCl_3$); IR (neat) 2932, 1798 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.72–7.65 (m, 4 H), 7.45–7.35 (m, 6 H), 4.58 (brd, *J* = 2.9 Hz, 1 H), 4.54 (d, *J* = 5.5 Hz, 1 H), 4.29 (dd, *J* = 4.8, 2.9 Hz, 1 H), 4.08 (dd, *J* = 9.7, 5.5 Hz, 1 H), 3.93 (dd, *J* = 11.5, 2.2 Hz, 1 H), 3.76 (dd, *J* = 11.5, 6.1 Hz, 1 H), 3.29 (ddd, *J* = 9.7, 6.1, 2.2 Hz, 1 H), 2.71 (dd, *J* = 17.6, 4.8 Hz, 1 H), 2.56 (d, *J* = 17.6 Hz, 1 H), 1.42 (s, 3 H), 1.37 (s, 3 H), 1.05 (s, 9 H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 174.0, 135.7, 135.6, 133.7, 133.5, 129.6, 129.6, 127.6, 127.5, 109.0, 77.9, 76.7, 71.9, 71.9, 69.1, 63.7, 36.9, 28.0, 26.8, 25.9, 19.3; HRMS (FAB) calcd for $C_{27}H_{34}O_6SiNa$ $(M + Na)^+$ 505.2022, found: 505.2028.



15

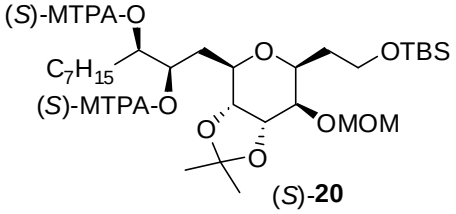
Tetrahydropyran 15. To a solution of lactone **14** (4.74 g, 9.81 mmol) in CH_2Cl_2 (50 mL) was added DIBAL-H (0.94 M in hexane, 11.4 mL, 10.8 mmol) dropwise over 10 min at –78 °C. The mixture was stirred at the same temperature for 1 h. The reaction was quenched with MeOH, and the mixture was allowed to warm up to room temperature. To the mixture was added saturated aqueous Rochelle salt (50 mL). The mixture was stirred for 1 h at room temperature. The organic layer was separated, and the aqueous layer was extracted with EtOAc. The combined organic layer was washed

with brine, dried over Na_2SO_4, and concentrated to give the corresponding lactol (4.58 g) as a colorless oil, which was used for the next reaction without further purification.

To a solution of lactol obtained above in MeOH (50 mL) was added $NaBH_4$ (400 mg, 10.5 mmol) at 0 °C. The mixture was stirred for 15 min at the same temperature. The reaction was quenched with saturated aqueous NH_4Cl, and the mixture was extracted with $CHCl_3$. The combined organic layer was washed with brine, dried over Na_2SO_4, and concentrated to give the corresponding diol (4.87 g) as a colorless oil, which was used for the next reaction without further purification.

To a solution of diol obtained above in DMF (50 mL) were added imidazole (964 mg, 14.2 mmol) and TBSCl (1.71 g, 11.4 mmol) at room temperature. The mixture was stirred for 30 min at the same temperature. The reaction was quenched with MeOH, and the mixture was poured into Et_2O. The mixture was washed with H_2O and brine, dried over Na_2SO_4, and concentrated to give the corresponding TBS ether (6.30 g) as a colorless oil, which was used for the next reaction without further purification.

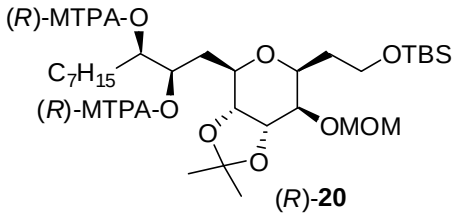
To a solution of alcohol obtained above in CH_2Cl_2 (50 mL) were added (i-Pr)$_2$NEt (6.6 mL, 37.8 mmol) and MOMCl (2.2 mL, 28.4 mmol) at room temperature. The mixture was stirred at 40 °C for 16 h. The reaction mixture was cooled to 0 °C, and quenched with saturated aqueous $NaHCO_3$. The resultant mixture was poured into Et_2O, and the organic layer was washed with H_2O and brine, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography (hexane/EtOAc, 20:1, 10:1, 4:1) to give tetrahydropyran **15** (5.46 g, 86% in four steps): colorless oil; R_f = 0.42 (hexane/EtOAc, 1:1); $[\alpha]^{27}_D$ +20.2 (*c* 1.04, $CHCl_3$); IR (neat) 2930 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73–7.70 (m, 4 H), 7.42–7.32 (m, 6 H), 4.80 (d, J = 7.0 Hz, 1 H), 4.67 (d, J = 7.0 Hz, 1 H), 4.30 (dd, J = 5.1, 2.2 Hz, 1 H), 3.99 (dd, J = 9.3, 5.1 Hz, 1 H), 3.87–3.76 (m, 6 H), 3.46 (ddd, J = 9.3, 6.5, 2.5 Hz, 1 H), 3.42 (s, 3 H), 2.05–1.97 (m, 1 H), 1.75–1.67 (m, 1 H), 1.45 (s, 3 H), 1.36 (s, 3 H), 1.06 (s, 9 H), 0.89 (s, 9 H), 0.04 (s, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 135.7, 135.7, 133.9, 133.8, 129.4, 129.4, 127.5, 127.5, 109.1, 96.8, 79.2, 74.4, 74.3, 71.9, 70.6, 64.7, 59.8, 56.0, 34.4, 28.2, 26.8, 26.4, 25.9, 19.3, 18.3, –5.3, –5.3; HRMS (FAB) calcd for $C_{35}H_{56}O_7Si_2Na$ $(M + Na)^+$ 667.3462, found: 667.3442.



(*S*)-**20**

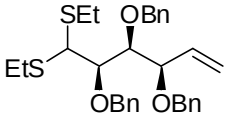
Bis-(*S*)-MTPA Ester (*S*)-20. To a stirred solution of diol **19** (3.8 mg, 69.2 μmol) in CH_2Cl_2 (0.3 mL) were added Et_3N (50 μL, 359 μmol), DMAP (1.0 mg, 8.2 μmol), and (*R*)-MTPACl (3.2 μL, 173 μmol) at room temperature. After the mixture was stirred at the same temperature for 1 h, to this mixture was added (*R*)-MTPACl (3.0 μL, 160 μmol), and the mixture was stirred further 1 h at room temperature. The reaction was quenched with MeOH. Concentration and chromatography (Hexane/EtOAc = 9/1) gave bis-(*S*)-MTPA ester (*S*)-**20** (6.1 mg, 90%): pale yellow oil; R_f = 0.38 (hexane/EtOAc, 4:1); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.54–7.51 (m, 4 H), 7.40–7.37 (m, 6 H), 5.49 (ddd, J = 7.9, 4.6, 1.8 Hz, 1 H), 5.16 (td, J = 7.1, 1.8 Hz, 1 H), 4.80 (d, J = 7.0 Hz, 1 H), 4.69 (d, J = 7.0 Hz, 1 H), 4.27 (dd, J = 5.0, 2.2 Hz, 1 H), 3.85 (ddd, J = 10.3, 7.7, 5.5 Hz, 1 H), 3.77 (brt, J = 1.8 Hz, 1 H), 3.76–3.69 (m, 3 H), 3.49 (s, 3 H), 3.44 (s, 3 H), 3.43 (s, 3 H), 3.25 (td, J = 9.3, 3.3 Hz, 1 H), 2.02-1.97 (m, 2 H), 1.90 (ddd, J = 14.5, 8.2, 3.7 Hz, 1 H), 1.74–1.69 (m, 1 H), 1.60–1.56 (m, 1 H), 1.50–1.45 (m, 1 H), 1.35 (s, 3 H), 1.34 (s, 3

H), 1.29–1.12 (m, 10 H), 0.89 (s, 9 H), 0.88 (t, *J* = 7.3 Hz, 3 H), 0.07 (s, 3 H), 0.06 (s, 3 H).



(*R*)-**20**

Bis-(*R*)-MTPA Ester (*R*)-20. To a stirred solution of diol **19** (4.2 mg, 76.5 μmol) in CH_2Cl_2 (0.3 mL) were added Et_3N (50 μL, 359 μmol), DMAP (1.0 mg, 8.2 μmol), and (*S*)-MTPACl (3.6 μL, 191 μmol) at room temperature. After the mixture was stirred at the same temperature for 1 h, to this mixture was added (*S*)-MTPACl (3.0 μL, 160 μmol), and the mixture was stirred further 1 h at room temperature. The reaction was quenched with MeOH. Concentration and chromatography (Hexane/EtOAc = 9/1) gave the corresponding bis-(*R*)-MTPA ester (6.9 mg, 92%): pale yellow oil; R_f = 0.35 (hexane/EtOAc, 4:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56–7.54 (m, 4 H), 7.40–7.34 (m, 6 H), 5.61 (ddd, *J* = 9.5, 3.3, 1.8 Hz, 1 H), 5.21 (ddd, *J* = 7.9, 6.2, 1.8 Hz, 1 H), 4.79 (d, *J* = 7.0 Hz, 1 H), 4.65 (d, *J* = 7.0 Hz, 1 H), 4.24 (dd, *J* = 5.0, 2.2 Hz, 1 H), 3.84 (ddd, *J* = 10.3, 7.7, 5.5 Hz, 1 H), 3.75–3.70 (m, 3 H), 3.66 (ddd, *J* = 8.9, 4.0, 1.1 Hz, 1 H), 3.50 (s, 3 H), 3.46 (s, 3 H), 3.42 (s, 3 H), 3.11 (td, *J* = 9.7, 3.3 Hz, 1 H), 2.12–1.95 (m, 2 H), 1.74–1.69 (m, 1 H), 1.65 (ddd, *J* = 14.4, 10.4, 3.3 Hz, 1 H), 1.51–1.44 (m, 2 H), 1.30 (s, 3 H), 1.27–1.14 (m, 10 H), 1.19 (s, 3 H), 0.89 (s, 9 H), 0.86 (t, *J* = 7.3 Hz, 3 H), 0.07 (s, 3 H), 0.06 (s, 3 H).

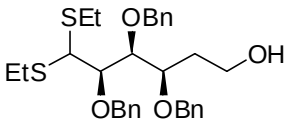


24

Alkene 24. To a solution of alcohol **23** (4.70 g, 8.92 mmol) in CH_2Cl_2 (45 mL) and DMSO (45 mL) at 0 °C were added Et_3N (6.2 mL, 44.6 mmol) and SO_3·pyr (7.10 g, 44.6 mmol). The mixture was stirred for 3 h at the same temperature and diluted with Et_2O. The mixture was washed with saturated aqueous NH_4Cl, saturated aqueous $NaHCO_3$, and brine, and then dried over Na_2SO_4. Concentration and column chromatography (hexane/EtOAc, 5:1) gave the corresponding aldehyde (4.60 g) as a colorless oil.

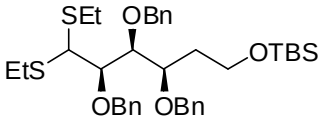
To a suspension of $Ph_3P^+CH_3Br^-$ (6.26 g, 17.5 mmol) in THF (50 mL) was added NaHMDS (1.0 M in THF, 17.5 mL, 17.5 mmol) at 0 °C. After the mixture was stirred for 30 min at the same temperature, to the mixture was added aldehyde obtained above in THF (33 mL) at –20 °C. After the mixture was allowed to warm up to room temperature gradually for 2 h, the reaction was quenched with MeOH. The mixture was diluted with Et_2O, washed with saturated aqueous NH_4Cl and brine, and then dried over Na_2SO_4. Concentration and column chromatography (hexane/EtOAc, 40:1, 10:1) gave alkene **24** (3.99 g, 86% in two steps): pale yellow oil; R_f = 0.23 (hexane/EtOAc, 10:1); $[\alpha]^{18}_D$ –15.2 (*c* 1.74, $CHCl_3$); IR (neat) 2966, 1641 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34–7.22 (m, 15 H), 6.00–5.92 (m, 1 H), 5.34 (d, *J* = 17.3 Hz, 1 H), 5.33 (d, *J* = 10.5 Hz, 1 H), 4.89 (d, *J* = 11.2 Hz, 1 H), 4.79 (d, *J* = 11.5 Hz, 1 H), 4.76 (d, *J* = 11.2 Hz, 1 H), 4.70 (d, *J* = 11.2 Hz, 1 H), 4.64 (d, *J* = 12.0 Hz, 1 H), 4.37 (d, *J* = 12.0 Hz, 1 H), 4.01 (m, 3 H), 3.84 (d, *J* = 3.4 Hz, 1 H), 2.66–2.50 (m, 4 H), 1.21–1.13 (m, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.0, 138.8, 138.1, 135.6, 128.5, 128.4, 128.3, 128.3, 127.9,

127.8, 127.6, 127.4, 119.0, 83.0, 83.0, 80.0, 75.6, 75.3, 70.4, 53.6, 25.4, 25.1, 14.7, 14.5; HRMS (FAB) calcd for $C_{31}H_{38}O_3S_2Na$ $(M + Na)^+$ 545.2160, found: 545.2161.



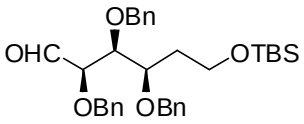
S2

Alcohol S2. To a solution of alkene **24** (3.80 g, 7.36 mmol) in THF (120 mL) was added $BH_3{\cdot}SMe_2$ (1.8 mL, 19.0 mmol) at 0 °C. After the mixture was stirred for 1 h at room temperature, aqueous NaOH (3.0 M, 30.6 mL) and aqueous H_2O_2 (30%, 30.6 mL) were added at 0 °C. The mixture was stirred for 30 min at the same temperature, then diluted with Et_2O, and washed with saturated aqueous Na_2SO_3 and brine. The organic layer was dried over Na_2SO_4, and concentrated. Purification by chromatography (hexane/EtOAc, 20:1, 10:1, 4:1) gave alcohol **S2** (3.42 g, 86%): colorless oil; R_f = 0.47 (hexane/EtOAc, 2:1); $[\alpha]^{19}_D$ +7.8 (*c* 1.74, $CHCl_3$); IR (neat) 3392, 2962 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.32–7.20 (m, 15 H), 4.84 (d, *J* = 11.2 Hz, 1 H), 4.75 (d, *J* = 11.6 Hz, 1 H), 4.75 (d, *J* = 11.6 Hz, 1 H), 4.64 (d, *J* = 11.6 Hz, 1 H), 4.60 (d, *J* = 11.6 Hz, 1 H), 4.45 (d, *J* = 12.6 Hz, 1 H), 4.10–4.02 (m, 2 H), 3.93 (dd, *J* = 6.4, 3.6 Hz, 1 H), 3.70–3.65 (m, 1 H), 3.57–3.53 (m, 2 H), 2.70–2.47 (m, 4 H), 1.94 (brs, 1 H), 1.88–1.78 (m, 1 H), 1.77–1.67 (m, 1 H), 1.18–1.12 (m, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.0, 138.7, 138.5, 138.0, 128.7, 128.6, 128.5, 128.4, 128.4, 128.3, 128.0, 128.0, 127.9, 127.8, 127.6, 127.1, 82.8, 79.8, 77.6, 75.2, 74.9, 72.3, 65.4, 60.5, 53.7, 32.8, 25.6, 25.3, 14.6, 14.5; HRMS (FAB) calcd for $C_{31}H_{40}O_4S_2Na$ $(M + Na)^+$ 563.2266, found: 563.2277.



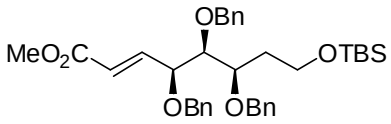
25

Silyl Ether 25. To a solution of alcohol **S2** (469 mg, 0.867 mmol) in DMF (8.7 mL) were added TBSCl (170 mg, 1.13 mmol) and imidazole (88.6 mg, 1.30 mmol). After the mixture was stirred at room temperature for 1 h, the reaction mixture was diluted with EtOAc. The organic layer was washed with H_2O and brine, and then dried over $MgSO_4$. Concentration and column chromatography (hexane/EtOAc, 40:1, 20:1, 10:1) gave silyl ether **25** (548 mg, 96%): colorless oil; R_f = 0.73 (hexane/EtOAc, 4:1); $[\alpha]^{17}_D$ +6.0 (*c* 0.91, $CHCl_3$); IR (neat) 2954 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.40–7.24 (m, 15 H), 4.88 (d, *J* = 11.2 Hz, 1 H), 4.84 (d, *J* = 11.2 Hz, 1 H), 4.79 (d, *J* = 11.6 Hz, 1 H), 4.67 (d, *J* = 11.2 Hz, 1 H), 4.60 (d, *J* = 11.6 Hz, 1 H), 4.54 (d, *J* = 11.2 Hz, 1 H), 4.06–3.97 (m, 3 H), 3.81–3.76 (m, 1 H), 3.65–3.57 (m, 2 H), 2.73–2.62 (m, 2 H), 2.61–2.50 (m, 2 H), 1.99–1.91 (m, 1 H), 1.83–1.73 (m, 1 H), 1.18 (t, *J* = 7.6 Hz, 6 H), 0.89 (s, 9 H), 0.04 (s, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.6, 139.0, 138.8, 138.6, 128.5, 128.4, 128.4, 128.3, 128.3, 128.2, 127.9, 127.8, 127.6, 127.4, 127.0, 126.2, 83.4, 80.4, 75.6, 75.5, 74.8, 72.0, 65.1, 59.7, 54.0, 33.3, 26.1, 26.1, 25.6, 25.3, 18.6, 18.4, 14.6, 14.5, –5.1, –5.2, –5.2; HRMS (FAB) calcd for $C_{37}H_{54}O_4S_2SiNa$ $(M + Na)^+$ 677.3130, found: 677.3127.



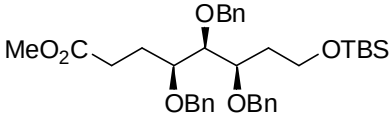
S3

Aldehyde S3. To a solution of dithioacetal **25** (100 mg, 0.153 mmol) in CH_3CN (1.6 mL) and H_2O (0.4 mL) were added $AgNO_3$ (104 mg, 0.611 mmol) and Ag_2O (142 mg, 0.611 mmol). After the mixture was stirred at 40 °C for 18 h, the reaction was quenched with Et_3N. The insoluble material was filtered off through a Celite pad. Concentration and column chromatography (hexane/EtOAc, 20:1, 4:1) gave aldehyde **S3** (66.6 mg, 79%): colorless oil; R_f = 0.57 (hexane/EtOAc, 4:1); $[\alpha]^{20}_D$ +1.0 (*c* 0.37, $CHCl_3$); IR (neat) 2929, 1726 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 9.67 (d, *J* = 1.1 Hz, 1 H), 7.37–7.24 (m, 15 H), 4.78 (d, *J* = 12.0 Hz, 1 H), 4.62 (s, 2 H), 4.54 (d, *J* = 12.0 Hz, 1 H), 4.51 (d, *J* = 11.4 Hz, 1 H), 4.46 (d, *J* = 11.4 Hz, 1 H), 3.97 (d, *J* = 5.1 Hz, 1 H), 3.94–3.90 (m, 1 H), 3.83 (t, *J* = 4.4 Hz, 1 H), 3.61–3.57 (m, 1 H), 3.54–3.50 (m, 1 H), 1.84–1.79 (m, 1 H), 1.75–1.70 (m, 1 H), 0.88 (s, 9 H), 0.01 (s, 6 H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 201.0, 138.3, 137.8, 137.5, 128.6, 128.6, 128.4, 128.4, 128.3, 128.2, 128.1, 127.8, 81.9, 80.7, 75.3, 74.0, 73.2, 72.8, 59.4, 33.5, 26.1, 18.4, –5.2, –5.2; HRMS (FAB) calcd for $C_{33}H_{44}O_5SiNa$ $(M + Na)^+$ 571.2856, found: 571.2868.



26

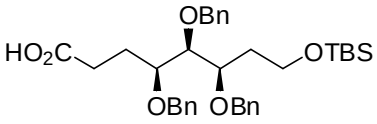
α,β-Unsaturated Ester 26. To a solution of aldehyde **S3** (2.09 g, 3.81 mmol) in benzene (60 mL) was added $Ph_3P{=}CHCO_2Me$ (2.57 g, 7.62 mmol). After the mixture was stirred at 40 °C for 2 h, purification by column chromatography (hexane/EtOAc, 20:1) gave α,β-unsaturated ester **26** (2.26 g, 98%): colorless oil; R_f = 0.46 (hexane/EtOAc, 4:1); $[\alpha]^{25}_D$ +17.9 (*c* 0.60, $CHCl_3$); IR ($CHCl_3$) 2954, 1717 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.35–7.25 (m, 15 H), 6.91 (dd, *J* = 15.8, 6.0 Hz, 1 H), 6.03 (dd, *J* = 15.8, 1.2 Hz, 1 H), 4.74 (d, *J* = 11.6 Hz, 1 H), 4.69 (d, *J* = 11.2 Hz, 1 H), 4.60 (d, *J* = 11.6 Hz, 1 H), 4.56 (d, *J* = 11.6 Hz, 1 H), 4.53 (d, *J* = 11.6 Hz, 1 H), 4.42 (d, *J* = 11.6 Hz, 1 H), 4.26 (td, *J* = 5.6, 1.2 Hz, 1 H), 3.81–3.75 (m, 1 H), 3.72 (s, 3 H), 3.64–3.57 (m, 1 H), 3.55–3.48 (m, 2 H), 1.86–1.77 (m, 1 H), 1.74–1.65 (m, 1 H), 0.87 (s, 9 H), 0.01 (s, 3 H), 0.01 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.6, 145.7, 138.7, 138.3, 137.9, 128.6, 128.5, 128.4, 128.1, 127.9, 127.8, 127.6, 122.4, 82.2, 79.0, 76.0, 74.8, 72.6, 71.9, 59.3, 51.7, 33.4, 26.1, 18.3, –5.3, –5.3; HRMS (FAB) calcd for $C_{36}H_{48}O_6SiNa$ $(M + Na)^+$ 627.3118, found: 627.3110.



S4

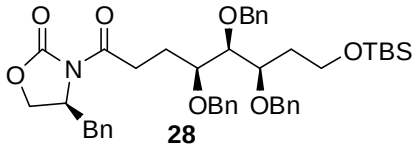
Alkane S4. The mixture of α,β-unsaturated ester **26** (239 mg, 0.395 mmol) and 10% Pd-C (80.0 mg) in EtOAc (22 mL) was stirred under H_2 atmosphere at room temperature for 13 h. The catalyst was filtered off, and the filtrate was concentrated to give alkane **S4** (220 mg, 92%): colorless oil; R_f = 0.46 (hexane/EtOAc, 4:1); $[\alpha]^{19}_D$ –5.4 (*c* 0.51, $CHCl_3$); IR (neat) 2951, 1739 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.32–7.26 (m, 15 H), 4.72 (d, *J* = 11.3 Hz, 1 H), 4.68 (d, *J* = 11.3 Hz, 1 H), 4.67 (d, *J* = 11.3 Hz, 1 H), 4.60 (d, *J* = 10.3 Hz, 1 H), 4.57 (d, *J* = 11.3 Hz, 1 H), 4.50 (d, *J* = 11.3 Hz, 1 H),

3.83–3.80 (m, 1 H), 3.66–3.62 (m, 2 H), 3.60–3.56 (m, 1 H), 3.59 (s, 3 H), 3.50–3.48 (m, 1 H), 2.36–2.31 (m, 1 H), 2.26–2.22 (m, 1 H), 1.97–1.88 (m, 2 H), 1.81–1.70 (m, 2 H), 0.88 (s, 9 H), 0.03 (s, 3 H), 0.02 (s, 3 H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 174.1, 138.8, 138.7, 138,7, 128.5, 128.4, 128.3, 128.2, 127.8, 127.7, 127.7, 81.8, 78.7, 75.9, 74.4, 73.2, 73.0, 59.5, 51.6, 33.7, 30.3, 26.3, 26.1, 18.4, –5.2, –5.2; HRMS (FAB) calcd for $C_{36}H_{50}O_6SiNa$ $(M + Na)^+$ 629.3274, found: 629.3257.



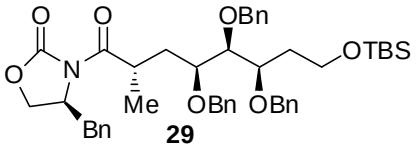
27

Carboxylic Acid 27. To a mixture of ester **S4** (51.0 mg, 84.0 μmol) in THF (1.0 mL) and H_2O (0.5 mL) was added $LiOH{\cdot}H_2O$ (7.1 mg, 0.168 mmol). The mixture was stirred at 40 °C for 7 h. The mixture was neutralized with 1 M aqueous HCl. The mixture was diluted with EtOAc, and washed with saturated aqueous $NaHCO_3$, H_2O, and brine. The organic layer was dried over $MgSO_4$ and concentrated. The residue was purified by column chromatography (hexane/EtOAc, 10:1, 3:1) gave carboxylic acid **27** (47.8 mg, 96%): colorless oil; R_f = 0.46 (hexane/EtOAc, 2:1); $[\alpha]^{19}_D$ +2.4 (*c* 0.04, $CHCl_3$); IR (neat) 2954, 1645 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.33–7.25 (m, 15 H), 4.73–4.67 (m, 3 H), 4.58 (s, 2 H), 4.52 (d, *J* = 11.3 Hz, 1 H), 3.82–3.80 (m, 1 H), 3.67–3.62 (m, 2 H), 3.58–3.54 (m, 1 H), 3.50 (dd, *J* = 6.2, 5.1 Hz, 1 H), 2.37–2.31 (m, 1 H), 2.29–2.24 (m, 1 H), 1.93–1.87 (m, 2 H), 1.78–1.70 (m, 2 H), 1.57 (brs, 1 H), 0.88 (s, 9 H), 0.02 (s, 3 H), 0.02 (s, 3 H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 138.7, 138.6, 138.4, 128.5, 128.5, 128.5, 128.4, 128.2, 127.8, 127.8, 127.8, 81.7, 78.7, 75.7, 74.4, 73.4, 72.9, 59.5, 33.7, 30.0, 26.1, 26.0, 18.4, –5.2, –5.2; HRMS (FAB) calcd for $C_{35}H_{48}O_6SiNa$ $(M + Na)^+$ 615.3118, found: 615.3121.



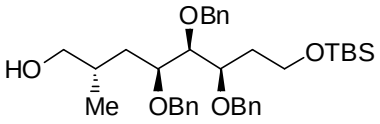
28

Imide 28. To a solution of carboxylic acid **27** (149 mg, 0.251 mmol) in THF (2.5 mL) were added Et_3N (70 μL, 0.503 mmol) and PivCl (46 μL, 0.377 mmol) at 0 °C. After the mixture was stirred for 40 min at the same temperature, to the mixture were added (*S*)-(-)-4-benzyl-2-oxazolidinone (53.5 mg, 0.302 mmol) and LiCl (38.4 mg, 0.905 mmol) at 0 °C. After the mixture was stirred at room temperature for 1 h, the mixture was diluted with Et_2O. The organic layer was washed with H_2O and brine, then dried over $MgSO_4$. Concentration and column chromatography (hexane/EtOAc, 10:1, 3:1) gave imide **28** (159 mg, 84%): colorless oil; R_f = 0.27 (hexane/EtOAc, 4:1); $[\alpha]^{25}_D$ +18.6 (*c* 0.80, $CHCl_3$); IR ($CHCl_3$) 2929, 1780, 1670 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37–7.17 (m, 20 H), 4.77–4.42 (m, 7 H), 4.05 (dd, *J* = 9.2, 2.8 Hz, 1 H), 3.93 (t, *J* = 8.4 Hz, 1 H), 3.85 (dt, *J* = 8.8, 4.4 Hz, 1 H), 3.76–3.54 (m, 4 H), 3.24 (dd, *J* = 13.6, 3.2 Hz, 1 H), 3.10–3.01 (m, 1 H), 2.91–2.82 (m, 1 H), 2.64 (dd, *J* = 13.2, 10.0 Hz, 1 H), 2.06–1.84 (m, 3 H), 1.80–1.70 (m, 1 H), 0.89 (s, 9 H), 0.04 (s, 6 H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 173.1, 153.5, 138.9, 138.8, 138.7, 135.6, 129.5, 129.1, 128.5, 128.4, 128.4, 128.2, 128.0, 127.7, 127.6, 127.6, 127.4, 81.9, 78.9, 75.9, 74.4, 73.2, 72.9, 66.1, 59.6, 55.3, 38.0, 33.8, 31.8, 26.1, 25.6, 18.4, –5.2, –5.2; HRMS (FAB) calcd for $C_{45}H_{57}NO_7SiNa$ $(M + Na)^+$ 774.3802, found: 774.3802.



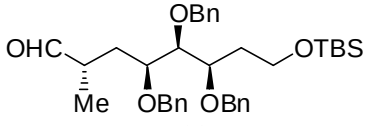
29

Methylated Imide 29. To a solution of imide **28** (8.6 mg, 11.4 μmol) in THF (0.6 mL) was added NaHMDS (1.0 M in THF, 46 μL, 46 μmol) at –78 °C. After the mixture was stirred at the same temperature for 1 h, to the mixture was added MeI (14 μL, 0.228 mmol). The mixture was warmed up to –40 °C for 1 h. The reaction was quenched with MeOH, and the mixture was filtered through a short silica gel column with Et_2O. Concentration and column chromatography (hexane/EtOAc, 20:1, 10:1) gave methylated imide **29** (7.0 mg, 80%): colorless oil; R_f = 0.34 (hexane/EtOAc, 4:1); $[\alpha]^{24}_D$ +36.6 (*c* 0.50, $CHCl_3$); IR ($CHCl_3$) 2929, 1773, 1698 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.36–7.11 (m, 20 H), 4.84 (d, *J* = 12.1 Hz, 1 H), 4.69–4.58 (m, 4 H), 4.45 (d, *J* = 12.1 Hz, 1 H), 4.23–4.20 (m, 1 H), 3.90–3.86 (m, 1 H), 3.83–3.76 (m, 2 H), 3.72–3.68 (m, 1 H), 3.66–3.62 (m, 1 H), 3.58–3.53 (m, 2 H), 3.13–3.07 (m, 2 H), 2.62 (dd, *J* = 13.2, 9.5 Hz, 1 H), 2.20 (dt, *J* = 13.9, 9.5 Hz, 1 H), 1.95–1.90 (m, 1 H), 1.75–1.70 (m, 1 H) 1.57–1.54 (m, 1 H), 1.09 (d, *J* = 7.0 Hz, 3 H), 0.89 (s, 9 H), 0.04 (s, 6 H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 177.3, 153.3, 139.2, 138.8, 138.5, 135.6, 129.5, 129.0, 128.5, 128.5, 128.4, 128.4, 128.3, 127.8, 127.8, 127.3, 126.9, 82.3, 78.9, 75.6, 74.6, 72.7, 65.6, 59.5, 55.2, 37.9, 35.0, 34.9, 33.7, 29.9, 26.1, 19.0, 18.4, –5.2, –5.2; HRMS (FAB) calcd for $C_{46}H_{59}NO_7SiNa$ $(M + Na)^+$ 788.3958, found: 788.3969.



S5

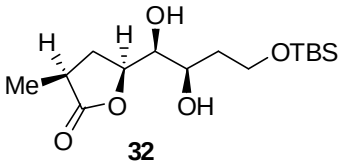
Alcohol S5. To a solution of imide **29** (362 mg, 0.473 mmol) in THF (5.0 mL) was added $LiAlH_4$ (71.8 mg, 1.89 mmol) at 0 °C. After the mixture was stirred at the same temperature for 2 h, the mixture was diluted with EtOAc. The mixture was washed with saturated aqueous NH_4Cl and brine, then dried over Na_2SO_4. Concentration and column chromatography (hexane/EtOAc, 9:1, 4:1) gave alcohol **S5** (213 mg, 76%): colorless oil; R_f = 0.13 (hexane/EtOAc, 4:1); $[\alpha]^{21}_D$ –7.2 (*c* 0.27, $CHCl_3$); IR (neat) 3450, 2952 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.34–7.26 (m, 15 H), 4.72 (d, *J* = 11.6 Hz, 1 H), 4.71 (s, 2 H), 4.65 (d, *J* = 11.2 Hz, 1 H), 4.58 (d, *J* = 11.2 Hz, 1 H), 4.46 (d, *J* = 11.2 Hz, 1 H), 3.85–3.81 (m, 1 H), 3.70–3.65 (m, 2 H), 3.61–3.54 (m, 2 H), 3.41–3.37 (m, 2 H), 2.03–1.92 (m, 1 H), 1.79–1.65 (m, 3 H), 1.62–1.54 (m, 1 H), 1.46–1.38 (m, 1 H), 0.89 (s, 9 H), 0.82 (d, *J* = 6.8 Hz, 3 H), 0.03 (s, 3 H), 0.03 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.9, 138.6, 138.4, 128.5, 128.5, 128.5, 128.4, 128.3, 128.3, 127.8, 127.7, 82.2, 77.9, 76.1, 74.4, 73.3, 73.0, 68.7, 59.4, 35.1, 34.0, 33.3, 26.1, 18.4, 17.2, –5.2, –5.2; HRMS (FAB) calcd for $C_{36}H_{52}O_5SiNa$ $(M + Na)^+$ 615.3482, found: 615.3484.



30

Aldehyde 30. To a solution of alcohol **S5** (54.7 mg, 92.3 μmol) in CH_2Cl_2 (1.0 mL) and DMSO (1.0 mL) were added Et_3N (64 μL, 0.461 mmol) and SO_3·pyr (73.4 mg, 0.461 mmol) at 0 °C. After the mixture was stirred at the same temperature for 1 h, the mixture was diluted with Et_2O. The mixture was washed with saturated aqueous NH_4Cl,

saturated aqueous $NaHCO_3$, H_2O, and brine, then dried over $MgSO_4$. Concentration and column chromatography (hexane/EtOAc, 5:1) gave aldehyde **30** (53.8 mg, 99%): colorless oil; R_f = 0.55 (hexane/EtOAc, 4:1); $[\alpha]^{21}_D$ –1.4 (*c* 0.98, $CHCl_3$); IR (neat) 2954, 1723 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 9.46 (d, *J* = 2.6 Hz, 1 H), 7.33–7.25 (m, 15 H), 4.68–4.56 (m, 5 H), 4.41 (d, *J* = 11.4 Hz, 1 H), 3.83–3.80 (m, 1 H), 3.68–3.51 (m, 4 H), 2.33 (ddd, *J* = 13.9, 7.0, 2.6 Hz, 1 H), 1.98–1.88 (m, 2 H), 1.72–1.67 (m, 1 H), 1.51 (ddd, *J* = 14.3, 7.0, 2.9 Hz, 1 H), 0.91 (d, *J* = 7.0 Hz, 3 H), 0.89 (s, 9 H), 0.03 (s, 3 H), 0.03 (s, 3 H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 204.7, 138.7, 138.5, 138.3, 128.5, 128.4, 128.4, 127.9, 127.8, 127.8, 81.9, 77.5, 75.8, 74.4, 73.1, 73.1, 59.4, 44.1, 33.8, 33.0, 26.1, 18.4, 13.8, –5.2, –5.2; HRMS (FAB) calcd for $C_{36}H_{50}O_5SiNa$ $(M + Na)^+$ 613.3325, found: 613.3329.



32

Lactone 32. To a stirred solution of aldehyde **30** (27.0 mg, 45.7 μmol) in *t*-BuOH (0.80 mL) and H_2O (0.20 mL) were added 2-methyl-2-butene (70 μL, 0.674 mmol), NaH_2PO_4 (71.2 mg, 457 μmol), and $NaClO_2$ (20.6 mg, 228 μmol) at room temperature. After the mixture was stirred at the same temperature for 1.5 h, the mixture was diluted with H_2O, and extracted with EtOAc. The organic layer was washed with brine and dried over Na_2SO_4. Concentration and column chromatography (Hexane/EtOAc = 9/1, 4/1) gave carboxylic acid **31** (22.4 mg, 88%).

To a stirred solution of carboxylic acid **31** (9.1 mg, 15.0 μmol) and 10% Pd-C (22.0 mg) in THF (1.5 mL) was stirred under H_2 atmosphere at room temperature for 6 h. The catalyst was filtered off, and the filtrate was concentrated to give the corresponding triol (5.3 mg).

The solution of triol obtained above in toluene (2.0 mL) was stirred at reflux conditions for 2 h. After the mixture was concentrated, the residue was purified by column chromatography ($CHCl_3$/MeOH = 9/1) to give lactone **32** (4.6 mg, 96% in two steps): colorless solid; R_f = 0.45 ($CHCl_3$/MeOH, 9:1); ^1H NMR (600 MHz, $CDCl_3$) δ 4.51 (quint, *J* = 5.1 Hz, 1 H), 3.98 (dt, *J* = 8.8, 3.3 Hz, 1 H), 3.91–3.83 (m, 2 H), 3.49 (dd, *J* = 5.0, 3.3 Hz, 1 H), 2.73–2.66 (m, 1 H), 2.47–2.42 (m, 1 H), 1.93–1.85 (m, 2 H), 1.74–1.70 (m, 1 H), 1.30 (d, *J* = 7.3 Hz, 3 H), 0.90 (s, 9 H), 0.08 (s, 6 H).