Supporting Information

Catalytic Enantioselective Total Synthesis of (−)-Platyphyllide and Its Structural Revision

Shiharu Hiraoka, Shinji Harada, and Atsushi Nishida*

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General Experimental Details

Infrared (IR) spectra were recorded using a FT/IR spectrophotometer. NMR spectra were recorded at 400 MHz or 600 MHz for $^1$H NMR and 100 MHz for $^{13}$C NMR. Chemical shifts in CDCl$_3$ were reported in the scale relative to (CH$_3$)$_4$Si (0.00 ppm) for $^1$H NMR. For $^{13}$C NMR, chemical shifts were reported in the scale relative to CHCl$_3$ (77.0 ppm) as an internal reference. Column chromatography was performed with silica gel Fuji Silysia Chemical Ltd. PSQ 60. Optical rotations were measured at 589 nm. Mass spectra were recorded using FAB or ESI mode. The enantiomeric excess (ee) was determined by HPLC analysis measured at 254 nm. Reactions were carried out in dry solvents under argon atmosphere, unless otherwise stated. Anhydrous Yb(OTf)$_3$ was purchased from Aldrich. Dry CH$_2$Cl$_2$ was purchased from Kanto Chemical Co., Inc. Other solvents and reagents were purified by usual methods.
(S)-3-(2-Methoxy-4-oxocyclohex-2-enecarbonyl)oxazolidin-2-one (13). A solution of 12 (29 mg, 0.083 mmol, 65% ee) in MeCN (71 μL) was added Pd(OAc)$_2$ (18 mg, 0.083 mmol) and stirred for 3 h. The mixture was diluted with CH$_2$Cl$_2$ (3 mL) and filtered through a cotton plug (Cerite also applicable). After volatile material was removed under reduced pressure, resulting residue was purified by column chromatography (SiO$_2$, hexane/ AcOEt = 1/1) to give 13 (15.3 mg, yield 77%) as a colorless solid. The enantiomeric excess was determined to be 65% ee (no racemization) by HPLC analysis (Daicel Chiralpak AD-H, hexane/iPrOH = 60/40, f: 0.75 mL/min, 254 nm, 21.1 min (major), 22.6 min (minor).)

$^1$H NMR (CDCl$_3$, 400 MHz) δ: 2.20 - 2.35 (2H, m), 2.36 - 2.50 (2H, m), 3.71 (3H, s), 4.03 - 4.16 (2H, m), 4.48 (2H, t, $J = 7.6$ Hz), 4.92 (1H, t, $J = 6.0$ Hz), 5.53 (1H, s), $^{13}$C NMR (CDCl$_3$, 100 MHz) δ: 24.7, 34.0, 42.7, 43.1, 56.1, 62.0, 104.4, 153.1, 170.4, 173.7, 198.1, IR(neat) 1759, 1685, 1646, 1607 cm$^{-1}$, HRMS(ESI) calcd for C$_{11}$H$_{13}$O$_5$NNa 262.0686, found 262.0675, $[^\alpha]_{D}^{16}$ –37.0 (c 0.5, CHCl$_3$, 65% ee)


(E)-Triethyl(4-methoxybuta-1,3-dien-2-yloxy)silane (1a). A solution of (E)-4-methoxybut-3-en-2-one (SI-1, 1.58 g, 15.8 mmol) and Et$_3$N (6 mL, 43.0 mmol) in anhydrous Et$_2$O (30 mL) was added TESOTf (4 mL, 17.7 mmol) dropwise at –20 ºC. The mixture was then warmed to 0 ºC and stirred for 2 h at the same temperature. The mixture was then diluted with n-hexane (20 mL) and washed with ice-cold saturated aqueous NaHCO$_3$, and brine. After volatile material was removed under reduced pressure, bulb-to-bulb distillation of resulting residue (0.1 mmHg, heating at 90 ºC) gave 1a (2.5 g, yield 74%) as a colorless liquid. $^1$H NMR (CDCl$_3$, 400 MHz) δ: 0.72 (6H, q, $J = 8.0$ Hz), 0.99 (9H, t, $J = 8.0$ Hz), 3.59 (3H, s), 4.08 (1H, s), 4.09 (1H, s), 5.35 (1H, d, $J = 12.0$ Hz), 6.89 (1H, d, $J = 12.0$ Hz), $^{13}$C NMR (CDCl$_3$, 100 MHz) δ: 4.8, 6.6, 56.3, 90.4, 103.1, 150.2, 154.1, IR(neat) 1651 cm$^{-1}$, LRMS(FAB) m/z 215 [M+H]$^+$, HRMS(FAB) calcd for C$_{11}$H$_{23}$O$_2$Si 215.1467, found 215.1467
Dimethylation of 12. A 1.09 M solution of methylithium in diethyl ether (13.2 mL, 14.4 mmol) was added dropwise to a solution of 12 (2.0 g, 5.70 mmol) in THF (58 mL) at –78 ºC. The mixture was stirred for 15 min at the same temperature. Saturated aqueous ammonium chloride (20 mL) was added to quench the reaction. The separated water layer was extracted three times with AcOEt, and combined organic layers were washed with brine and dried over Na₂SO₄. After volatile material was removed under reduced pressure, resulting residue was purified by column chromatography (SiO₂, hexane/AcOEt = 9/1) to give 14 (838 mg, yield 48%) as a colorless oil, 15 (735 mg, yield 38%) as a colorless oil, and 16 (270 mg, yield 13%) as a colorless oil.

2-((1S,2S)-2-Methoxy-4-(triethylsilyloxy)cyclohex-3-enyl)propan-2-ol (14). ¹H NMR (CDCl₃, 400 MHz) δ 0.69 (6H, q, J = 8.0 Hz), 0.98 (9H, t, J = 8.0 Hz), 1.17 (3H, s), 1.23 (3H, s), 1.25-1.35 (1H, m), 1.65-1.71 (1H, m), 1.72-1.78 (1H, m), 1.96-2.02 (1H, m), 2.13-2.25 (1H, m), 3.33 (3H, s), 4.21 (1H, d, J = 11.2 Hz), 4.74 (1H, s), 4.95 (1H, s); ¹³C NMR (CDCl₃, 100 MHz) δ 5.0, 6.6, 23.7, 24.8, 29.5, 30.3, 48.0, 53.8, 72.9, 78.6, 102.5, 154.0; IR(neat) 3464, 1666 cm⁻¹; LRMS(FAB) m/z 323 [M+Na]⁺; HRMS(FAB) calcd for C₁₆H₃₂O₃SiNa 323.2018, found 323.2006; [α]D²⁵ +4.47 (c 1.0, CHCl₃, 60% ee).

For the enantiomer, [α]D²₃ –8.28 (c 0.28, CHCl₃, 60% ee).

(1S,2S)-N-(2-hydroxyethyl)-2-methoxy-4-((triethyl-silyloxy)cyclohex-3-enecarboxamide (15). ¹H NMR (CDCl₃, 400 MHz) δ 0.69 (6H, q, J = 8.0 Hz), 0.98 (9H, t, J = 8.0 Hz), 1.17-1.83 (1H, m), 2.00-2.08 (2H, m), 2.13-2.20 (1H, m), 2.25 (1H, ddd, J = 3.2, 9.2, 12.4 Hz), 2.89 (1H, brs), 3.34 (3H, s), 3.34-3.52 (2H, m), 3.72 (2H, brs), 4.15 (2H, d, J = 4.4 Hz), 4.97 (1H, s), 6.69 (1H, brs); ¹³C NMR (CDCl₃, 100 MHz) δ 5.0, 6.6, 23.4, 29.1, 42.5, 46.0, 55.1, 62.3, 77.7, 102.5, 153.8, 175.2; IR(neat) 3300, 1658 cm⁻¹; LRMS(FAB) m/z 352 [M+Na]⁺; HRMS(FAB) calcd for C₁₆H₃₁NO₄SiNa 352.1920, found 352.1922; [α]D²³ –6.35 (c 1.0, CHCl₃, 60% ee).

2-((1S,2S)-2-Methoxy-4-((triethylsilyloxy)cyclohex-3-enecarboxamido)ethyl acetate (16). ¹H NMR (CDCl₃, 400 MHz) δ 0.68 (6H, q, J = 7.6 Hz), 0.98 (9H, t, J = 7.6 Hz), 1.70-1.81 (1H, m), 2.00-2.09
(2H, m), 2.08 (3H, s), 2.13-2.18 (1H, m), 2.22 (1H, ddd, \( J = 3.2, 9.0, 12.2 \) Hz), 3.33 (3H, s), 3.49-3.61 (2H, m), 4.11 (1H, d, \( J = 8.8 \) Hz), 4.16 (2H, t, \( J = 1.4 \) Hz), 4.97 (1H, s), 6.56 (1H, brs); \(^{13}\)C NMR (CDCl\(_3\), 100 MHz) \( \delta \) 4.9, 6.5, 20.8, 23.3, 29.0, 38.3, 45.7, 55.0, 63.3, 77.6, 102.4, 153.9, 170.9, 173.9; IR(neat) 3306, 1741, 1659 cm\(^{-1}\); LRMS(FAB) m/z 394 [M+Na]\(^+\); HRMS(FAB) calcd for C\(_{18}\)H\(_{33}\)NO\(_5\)SiNa 394.2026, found 394.2028; \([\alpha]\)\(_D\)\(^{22}\) –3.23 (c 1.0, CHCl\(_3\), 60% ee).

Stoichiometric Ito-Saegusa oxidation of 14. A solution of 14 (8.0 mg, 0.027 mmol) in MeCN (70 \( \mu \)L) was added Pd(OAc)\(_2\) (5.9 mg, 0.027 mmol) and stirred for 3 h. The mixture was diluted with CH\(_2\)Cl\(_2\) (3 mL) and filtered through a cotton plug (Cerite also applicable). After volatile material was removed under reduced pressure, resulting residue was purified by column chromatography (SiO\(_2\), hexane/ AcOEt = 1/1) to give 17 (4.5 mg, yield 90%) as a colorless solid.

\((4S,5S)-4-(2-Hydroxypropan-2-yl)-5-methoxycyclohex-2-enone (18)\). \(^1\)H NMR (CDCl\(_3\), 400 MHz) \( \delta \) 1.24 (3H, s), 1.38 (3H, s), 2.44 (1H, dd, \( J = 10.4, 16.0 \) Hz), 2.68 (1H, dt, \( J = 2.8, 8.4 \) Hz), 3.00 (1H, dd, \( J = 4.0, 16.0 \) Hz), 3.41 (3H, s), 3.89 (1H, ddd, \( J = 4.0, 8.4, 10.4 \) Hz), 3.99 (1H, s), 6.09 (1H, ddd, \( J = 0.6, 2.8, 10.4 \) Hz), 6.83 (1H, dd, \( J = 2.8, 10.4 \) Hz); \(^{13}\)C NMR (CDCl\(_3\), 100 MHz) \( \delta \) 26.7, 28.6, 42.2, 52.5, 55.6, 72.5, 78.1, 130.4, 148.3, 197.4; IR(neat) 3420, 1670 cm\(^{-1}\); LRMS(FAB) m/z 185 [M+H]\(^+\); HRMS(FAB) calcd for C\(_{10}\)H\(_{17}\)O\(_3\) 185.1178, found 185.1178; \([\alpha]\)\(_D\)\(^{24}\) +74.0 (c 0.2, CHCl\(_3\), 60% ee).

\((R)-6-(2-Hydroxypropan-2-yl)-3-vinylcyclohex-2-enone (5)\). Vinylation of 17 in Scheme 4. CeCl\(_3\)•7H\(_2\)O (6.6 mg, 0.018 mmol) in a flask was dried at 150 °C under reduced pressure (<0.1 mmHg) for 3 h with stirring. After cooling to room temperature, the flask was charged with dry argon, and a solution of 17 (11.2 mg, 0.061 mmol) in THF (2.6 mL) was added. To this mixture, was added a 1.0 M solution of vinylmagnesium bromide in THF (597 \( \mu \)L, 0.61 mmol) dropwise at –78 °C. The mixture was then warmed to room temperature and stirred for 30 min. The reaction was quenched by addition of 1N HCl (2 mL) slowly at 0 °C, and then neutralized with saturated aqueous NaHCO\(_3\) (3 mL). The separated
water layer was extracted three times with AcOEt, and combined organic layers were washed with brine and dried over Na₂SO₄. After volatile material was removed under reduced pressure, resulting residue was purified by column chromatography (SiO₂, hexane/AcOEt = 3/1) to give 5 (9.0 mg, yield 82%) as a colorless oil, and starting material 17 (1.1 mg, yield 10%). ¹H NMR (CDCl₃, 400 MHz) δ 1.22 (3H, s), 1.25 (3H, s), 1.73 (1H, ddd, J = 4.8, 13.0, 26.4 Hz), 2.16-2.21 (1H, m), 2.35-2.45 (2H, m), 2.70 (1H, ddd, J = 2.6, 4.6, 17.8 Hz), 5.14 (1H, s), 5.52 (1H, d, J = 10.8 Hz), 5.73 (1H, d, J = 14.8 Hz), 5.95 (1H, s), 6.50 (1H, dd, J = 10.8, 14.8 Hz); ¹³C NMR (CDCl₃, 100 MHz) δ 24.1, 26.1, 28.8, 35.4, 48.7, 55.8, 73.2, 104.6, 178.3, 199.2; IR(neat) 3438, 1637 cm⁻¹; LRMS(FAB) m/z 181 [M+H]⁺; HRMS(FAB) calcd for C₁₁H₁₇O₂ 181.1229, found 181.1232; [α]D²² –163.6 (c 1.0, CHCl₃, 54% ee). For the enantiomer ent-5 in Scheme 7, [α]D¹⁸ +202.5 (c 1.0, CHCl₃, 90% ee). Ee value for ent-5 can be measured as follows: Daicel Chiralpak AD-H, hexane/iPrOH = 95/5, f: 1.0mL/min, 254 nm, tR: 12.6 min (minor) and 21.1 min (major).

**Vinylation of ent-17 in Scheme 7.** A solution of ent-17 (70 mg, 0.39 mmol) in THF (19 mL) was added a 1.0 M solution of vinylmagnesium bromide in THF (3.8 mL, 3.5 mmol) in one portion at –78 ºC. The mixture was then warmed to room temperature, and stirred for 15 min. The reaction was quenched by addition of 1N HCl (5 mL) slowly at 0 ºC and then neutralized with saturated aqueous NaHCO₃ (7 mL). The separated water layer was extracted three times with AcOEt, and combined organic layers were washed with brine and dried over Na₂SO₄. After volatile material was removed under reduced pressure, resulting residue was purified by column chromatography (SiO₂, hexane/AcOEt = 3/1) to give ent-5 (50 mg, yield 63%) as a colorless oil, and starting material ent-17 (9.4 mg, yield 13%).

**Trans-Selective reduction of 5 using sodium triacetoxyborohydride.** A solution of 5 (53 mg, 0.29 mmol) in acetonitrile (2.7 mL) was added NaBH(OAc)₃ (623 mg, 2.9 mmol) and the mixture was stirred for 1 h. Saturated aqueous NaHCO₃ (1 mL) was added to quench the reaction. The separated water layer was extracted three times with AcOEt and combined organic layers were washed with brine and dried.
over Na₂SO₄. After volatile material was removed under reduced pressure, resulting residue was purified by column chromatography (SiO₂, hexane/AcOEt = 3/1) to give a mixture of trans-alcohol 6 and cis-alcohol ent-7 (42 mg, yield 79%, 6/ent-7 = 3/1) as a colorless oil. Diastereomeric ratio was determined by ¹H NMR spectra of the mixture.

**Trans-Selective reduction of ent-5 using borane.** A solution of ent-5 (11.9 mg, 0.067 mmol) in THF (1.3 mL) was added BH₃•THF (526 μL, 0.533 mmol) at –78 ºC and stirred for 39 h. The reaction was quenched by addition of 1N NaOH (1 mL). The separated water layer was extracted three times with AcOEt, and combined organic layers were washed with brine and dried over Na₂SO₄. After volatile material was removed under reduced pressure, resulting residue was purified by column chromatography (SiO₂, hexane/AcOEt = 3/1) to give the mixture of trans-alcohol ent-6 and cis-alcohol 7 (10.9 mg, yield 92%, ent-6/7 = 7/1) as a colorless oil. Diastereomeric ratio was determined by ¹H NMR spectra of the mixture. The enantiomeric purity of ent-6 can be enriched by recrystallization. A mixture of ent-6 and 7 (84.4 mg) was recrystallized from hexane/AcOEt to give racemic 6 (5.2 mg, yield 6%) as a colorless crystal, and mixture of chiral ent-6 and 7 (77.9 mg, yield 92%) from mother liquid as a colorless oil.

(1S,6S)-6-(2-Hydroxypropan-2-yl)-3-vinylcyclohex-2-enol (6). Spectral data of major diastereomer in the mixture were as follows; ¹H NMR (CDCl₃, 400 MHz) δ 1.23 (3H, s), 1.25-1.30 (1H, m), 1.33 (3H, s), 1.64 (1H, ddd, J = 2.6, 9.4, 12.8 Hz), 1.74-1.79 (2H, m), 2.10-2.18 (1H, m), 2.28 (1H, dd, J = 5.6, 17.2 Hz), 3.07 (1H, s), 4.01 (1H, s), 4.52 (1H, d, J = 8.8 Hz), 5.03 (1H, d, J = 10.8 Hz), 5.15 (1H, d, J = 17.6 Hz), 5.64 (1H, s), 6.38 (1H, dd, J = 10.8, 17.6 Hz); ¹³C NMR (CDCl₃, 100 MHz) δ 23.8, 24.0, 24.4, 30.3, 51.4, 69.8, 74.9, 112.6, 131.6, 136.8, 138.6; IR(neat) 3193 cm⁻¹; HRMS(ESI) calcd for C₁₁H₁₈O₂Na 205.1199, found 205.1199; mp 97.5-98.0 ºC.

(1R,6S)-6-(2-Hydroxypropan-2-yl)-3-vinylcyclohex-2-enol (ent-7). Cis-selective Luche reduction of 5. A solution of 5 (3.6 mg, 0.020 mmol) in EtOH/CH₂Cl₂ (1/1, 474 μL) was added CeCl₃•7H₂O (8.1
mg, 0.022 mmol) at –20 ºC. After stirring for 5 min, NaBH₄ (1.8 mg, 0.049 mmol) was added and resulting mixture was warmed to 0 ºC for 30 min with stirring. Water (1 mL) was added to quench the reaction, and the separated water layer was extracted three times with CH₂Cl₂ and combined organic layers were washed with brine and dried over Na₂SO₄. After volatile material was removed under reduced pressure, resulting residue was purified by column chromatography (SiO₂, hexane/ AcOEt = 3/1) to give a mixture of cis-alcohol ent-7 and trans-alcohol 6 (3.0 mg, yield 84%, ent-7/6 = 14/1) as a colorless oil. Diastereomeric ratio was determined by ¹H NMR of the mixture. Spectral data of major diastereomer in the mixture were as follows; ¹H NMR (CDCl₃, 400 MHz) δ: 1.28 (3H, s), 1.31-1.39 (1H, m), 1.42 (3H, s), 1.64 (1H, ddd, J = 2.6, 9.4, 12.8 Hz), 1.64 (1H, ddd, J = 5.2, 13.2, 20.0 Hz), 1.88-1.96 (2H, m), 2.07 (1H, ddd, J = 5.2, 12.4, 17.4 Hz), 2.48 (1H, dd, J = 4.6, 17.4 Hz), 3.15 (1H, brs), 4.59 (1H, s), 5.10 (1H, d, J = 10.8 Hz), 5.28 (1H, d, J = 17.6 Hz), 5.85 (1H, d, J = 5.6 Hz), 6.37 (1H, dd, J = 10.8, 17.6 Hz), 13C NMR (CDCl₃, 100 MHz) δ: 17.0, 25.1, 28.2, 29.0, 47.2, 66.1, 72.3, 114.0, 128.3, 138.7, 140.3, IR(neat) 3334, 1725 cm⁻¹, HRMS(ESI) calcd for C₁₁H₁₈O₂Na 205.1199, found 205.1192.

Propargylation of ent-6 and 7. A mixture of ent-6 and 7 (77.9 mg, 0.43 mmol, ent-6/7 = 7/1) was successively added 60% aqueous NaOH (2.2 mL), tetrabutylammonium iodide (15.3 mg, 0.04 mmol), and propargyl bromide (45.9 µL, 0.60 mmol). The mixture was stirred for 30 min and the reaction was then quenched with saturated aqueous NH₄Cl (5 mL). The separated water layer was extracted three times with AcOEt and combined organic layers were washed with brine and dried over Na₂SO₄. After volatile materials was removed under reduced pressure, resulting residue was purified by column chromatography (SiO₂, hexane/AcOEt = 10/1) to give ent-8 (70.4 mg, yield 71%) as colorless oil, cis isomer ent-19 (9.0 mg, yield 9%) as colorless oil, and starting material ent-6 (6.7 mg, yield 9%).

2-((1S,2S)-2-(Prop-2-ynyloxy)-4-vinylcyclohex-3-enyl)propan-2-ol (8). ¹H NMR (CDCl₃, 400 MHz) δ 1.24 (3H, s), 1.25 (3H, s), 1.26-1.36 (1H, m), 1.79 (1H, ddd, J = 2.8, 9.6, 12.8 Hz), 1.88-1.92 (1H, m), 2.13-2.20 (1H, m), 2.26-2.31 (1H, m), 2.49 (1H, t, J = 2.4 Hz), 4.08 (1H, s), 4.21 (1H, dd, J = 2.4, 12.0 Hz), 4.30 (1H, dd, J = 2.4, 12.0 Hz), 4.51 (1H, d, J = 9.2 Hz), 5.07 (1H, d, J = 10.8 Hz), 5.20
(1H, d, $J = 17.6$ Hz), 5.77 (1H, s), 6.36 (1H, dd, $J = 10.8$, 17.6 Hz); $^{13}$C NMR (CDCl$_3$, 100 MHz) $\delta$ 23.7, 24.4, 24.8, 29.2, 49.1, 54.3, 73.0, 75.2, 76.9, 79.1, 113.3, 126.3, 138.2, 138.9; IR(neat) 3487, 1732 cm$^{-1}$; HRMS(ESI) calcd for C$_{14}$H$_{20}$O$_2$Na 243.1356, found 243.1352; $[\alpha]_D^{24} +76.3$ (c 1.3, CHCl$_3$, 54% ee). For the enantiomer **ent-8** in Scheme 7, $[\alpha]_D^{24} –132.0$ (c 0.94, CHCl$_3$, 94% ee).

2-((1$S$,2$R$)-2-(Prop-2-ynyloxy)-4-vinylcyclohex-3-enyl)propan-2-ol (19). $^1$H NMR (CDCl$_3$, 400 MHz) $\delta$ 1.24 (3H, s), 1.39 (3H, s), 1.43 (1H, dt, $J = 3.2$, 12.4 Hz), 1.83 (1H, ddd, $J = 5.2$, 12.4, 25.4 Hz), 1.87-1.92 (1H, m), 2.05-2.14 (1H, m), 2.44-2.51 (1H, m), 2.46 (1H, t, $J = 2.4$ Hz), 3.27 (1H, s), 4.21 (1H, dd, $J = 2.4$, 12.0 Hz), 4.30 (1H, dd, $J = 2.4$, 12.0 Hz), 4.50 (1H, t, $J = 4.4$ Hz), 5.11 (1H, d, $J = 10.8$ Hz), 5.29 (1H, d, $J = 17.6$ Hz), 5.97 (1H, d, $J = 5.2$ Hz), 6.39 (1H, dd, $J = 10.8$, 17.6 Hz); $^{13}$C NMR (CDCl$_3$, 100 MHz) $\delta$ 17.6, 25.2, 28.0, 28.8, 47.2, 54.4, 71.0, 71.7, 74.9, 77.3, 114.0, 124.5, 138.8, 142.3; IR(neat) 3510, 1725 cm$^{-1}$; HRMS(ESI) calcd for C$_{14}$H$_{20}$O$_2$Na 243.1356, found 243.1353; $[\alpha]_D^{24} +76.3$ (c 0.94, CHCl$_3$, 54% ee).

2-((8$S$,8a$R$)-6,7,8,8a-Tetrahydro-2$H$-naphtho[1,8-bc]furan-8-yl)propan-2-ol (20). A solution of 8 (10.8 mg, 0.049 mmol) in toluene (1 mL) was stirred for 24 h at 100 °C under O$_2$. After toluene was removed under reduced pressure, resulting residue was purified by column chromatography (SiO$_2$, hexane/ AcOEt = 10/1) to give a mixture of 20 and 21 (10.8 mg, quant., 20/21 = 92/8) as a colorless oil. This mixture was utilized in next step without further purification. After careful SiO$_2$ column chromatography (SiO$_2$, hexane/AcOEt = 10/1), 20 can be isolated as a pure form. $^1$H NMR (CDCl$_3$, 400 MHz) $\delta$ 1.27 (3H, s), 1.32 (3H, s), 1.42-1.56 (1H, m), 1.74 (1H, ddd, $J = 2.8$, 10.4, 12.8 Hz), 1.96-2.02 (1H, m), 2.75 (1H, ddd, $J = 6.8$, 10.8, 17.6 Hz), 2.96 (1H, dd, $J = 6.8$, 17.6 Hz), 4.95 (2H, dd, $J = 8.0$, 10.8 Hz), 5.08 (1H, ddd, $J = 2.4$, 12.4 Hz), 7.02 (1H, d, $J = 7.6$ Hz), 7.07 (1H, d, $J = 7.6$ Hz), 7.20 (1H, t, $J = 7.6$ Hz); $^{13}$C NMR (CDCl$_3$, 100 MHz) $\delta$ 23.8, 24.8, 26.8, 28.1, 51.1, 72.9, 73.0, 81.4, 118.3, 125.6, 127.9, 128.5, 132.8, 138.4; IR(neat) 3404 cm$^{-1}$; LRMS(FAB) m/z 241 [M+Na]$^+$; HRMS(FAB) calcd for
C_{14}H_{18}O_2Na 241.1204, found 241.1199; [\alpha]_D^{23} -11.1 (c 0.55, CHCl_3, 54% ee). For the enantiomer, [\alpha]_D^{19} +30.2 (c 0.55, CHCl_3, 95% ee).

(8S,8aR)-8-(2-Hydroxypropan-2-yl)-6,7,8,8a-tetrahydro-2H-naphtho[1,8-bc]furan-2-one (9). To a mixture of 20 and 21 (4.7 mg, 20/21 = 10/1, 0.022 mmol as 20) in CCl_4/MeCN/H_2O (2.2 mL, 2/2/1 ratio), RuO_2\cdot xH_2O (0.1 mg) and NaIO_4 (16.7 mg, 0.080 mmol) was added successively at 0 ºC. After being stirred for 3.5 h, saturated aqueous sodium thiosulfate (2 mL) was added to quench the reaction. The separated water layer was extracted three times with CH_2Cl_2, and combined organic layers were washed with brine and dried over Na_2SO_4. After volatile material was removed under reduced pressure, resulting residue was purified by column chromatography (SiO_2, CH_2Cl_2/ AcOEt = 5/1) to give 9 (2.6 mg, yield 58%) as a colorless solid. ^1H NMR (CDCl_3, 400 MHz) δ 1.36 (3H, s), 1.42 (3H, s), 1.72-1.83 (1H, m), 2.16 (1H, s), 2.23 (1H, ddd, J = 2.4, 7.2, 9.6 Hz), 2.79-2.88 (1H, m), 3.13 (1H, dd, J = 3.6, 20.4 Hz), 5.28 (1H, d, J = 12.4 Hz), 7.40 (1H, d, J = 7.6 Hz), 7.46 (1H, t, J = 7.6 Hz), 7.69 (1H, d, J = 7.6 Hz); ^13C NMR (CDCl_3, 100 MHz) δ 22.8, 26.0, 27.4, 27.4, 49.6, 72.1, 79.7, 122.9, 124.0, 129.8, 132.1, 133.9, 148.9, 170.0; IR(neat) 3422, 1742 cm^{-1}; LRMS(FAB) m/z 255 [M+H]^+; HRMS(FAB) calcd for C_{14}H_{16}O_3Na 255.0997, found 255.0987; [\alpha]_D^{24} -2.8 (c 0.31, CHCl_3, 54% ee). For the enantiomer ent-9 in Scheme 7, [\alpha]_D^{20} +6.2 (c 0.25, CHCl_3, 95% ee).

(8R,8aR)-8-(Prop-1-en-2-yl)-6,7,8,8a-tetrahydro-2H-naphtho[1,8-bc]furan-2-one (4, platyphyllide). A solution of 9 (2.7 mg, 0.012 mmol) in pyridine (483 μL) was added thionyl chloride (6 μL, 0.082 mmol) at 0 ºC. After being stirred for 10 min, saturated aqueous NaHCO_3 (1 mL) was added to quench the reaction. The separated water layer was extracted three times with AcOEt, and combined organic layers were washed with brine and dried over Na_2SO_4. After volatile material was removed under reduced pressure, resulting residue was purified by column chromatography (SiO_2, hexane/AcOEt = 8/1) to give 4 (2.0 mg, yield 80%) as a colorless solid. ^1H NMR (CDCl_3, 400 MHz) δ 1.89 (3H, s), 1.94
(1H, ddt, $J = 2.0, 4.0, 10.0$ Hz), 2.16 (1H, ddt, $J = 1.6, 3.6, 8.0$ Hz), 2.21-2.27 (1H, m), 2.81-2.89 (1H, m), 3.16 (1H, dd, $J = 8.0, 18.0$ Hz), 4.98-4.99 (2H, m), 5.23 (1H, d, $J = 10.8$ Hz), 7.39 (1H, d, $J = 7.6$ Hz), 7.45 (1H, t, $J = 7.6$ Hz), 7.68 (1H, d, $J = 7.6$ Hz); $^{13}$C NMR (CDCl$_3$, 100 MHz) δ 20.6, 25.9, 26.7, 46.3, 80.4, 112.4, 122.9, 124.7, 129.8, 132.1, 133.7, 144.1, 148.7, 170.4; IR(neat) 1760 cm$^{-1}$; HRMS(ESI) calcd for C$_{14}$H$_{14}$O$_2$Na 237.0886, found 237.0876; $[\alpha]_D^{22} +25.0$ (c 0.14, CHCl$_3$, 54% ee).

For the enantiomer ent-4 (natural platyphyllide) in Scheme 7, $[\alpha]_D^{20} –54.8$ (c 0.16, CHCl$_3$, 95% ee). mp 96.0-97.0 ºC.

**Scheme SI-2.** Details of Scheme 6.

((1S,2S)-2-Methoxy-4-(triethylsilyloxy)cyclohex-3-enyl)methanol (SI-2). To a solution of ent-12 (385 mg, 1.1 mmol, 60% ee) in THF (10 mL), were added MeOH (65 μL, 1.6 mmol) and LiBH$_4$ in THF (2.0 M in THF, 0.81 mL, 1.6 mmol) at 0 ºC and then warmed to rt. After being stirred for 45 min at rt, water (5 mL) was added at 0 ºC and stirred for additional 5 min. The mixture was extracted three times with AcOEt and combined organic layers were washed with brine and dried over Na$_2$SO$_4$. After volatile material was removed under reduced pressure, resulting residue was purified by column chromatography (SiO$_2$, hexane/ AcOEt = 2/1) to give SI-2 (258 mg, yield 88%) as a colorless oil. $^1$H NMR (CDCl$_3$, 400 MHz) δ: 0.68 (6H, q, $J = 8.0$ Hz), 0.98 (9H, t, $J = 8.0$ Hz), 1.35-1.45 (1H, m), 1.71-
1.76 (1H, m), 1.79-1.86 (1H, m), 1.99 (1H, dt, \( J = 4.0, 15.2 \) Hz), 2.13-2.21 (1H, m), 2.64 (1H, dd, \( J = 3.2, 6.8 \) Hz), 3.33 (3H, s), 3.58-3.70 (2H, m), 3.91-3.93 (1H, m), 4.98 (1H, s), \(^{13}\)C NMR (CDCl\(_3\), 100 MHz) \( \delta \): 5.0, 6.6, 22.7, 28.8, 40.1, 54.4, 66.3, 79.6, 102.6, 154.1, IR(neat) 3413, 1660 cm\(^{-1}\), HRMS(ESI) calcd for C\(_{14}\)H\(_{28}\)O\(_3\)NaSi 295.1700, found 295.1689, \([\alpha]_D^{17} –12.6 \) (c 1.0, CHCl\(_3\), 60% ee)

\((1S,2S)-2\text{-Methoxy}-4\text{-(triethylsilyloxy)}\text{-cyclohex-3-enyl})\text{methyl 4-bromobenzoate (22).}\) To a solution of SI-2 (233 mg, 0.85 mmol) in CH\(_2\)Cl\(_2\) (8.2 mL), were added pyridine (4.1 mL) and \( p \)-bromobenzoyl chloride (750 mg, 3.4 mmol) at 0 °C. After being stirred for 10 min, saturated aqueous NaHCO\(_3\) (5 mL) was added to quench the reaction. The mixture was extracted three times with CH\(_2\)Cl\(_2\), and combined organic layers were washed with brine and dried over Na\(_2\)SO\(_4\). After volatile material was removed under reduced pressure, resulting residue was purified by column chromatography (SiO\(_2\), hexane/ AcOEt = 10/1) to give 22 (358 mg, yield 91%) as a colorless oil. \(^1\)H NMR (CDCl\(_3\), 400 MHz) \( \delta \): 0.69 (6H, q, \( J = 8.0 \) Hz), 0.99 (9H, t, \( J = 8.0 \) Hz), 1.59-1.65 (1H, m), 1.90-2.21 (4H, m), 3.33 (3H, s), 3.83 (1H, brs), 4.29 (1H, dd, \( J = 6.8, 11.2 \) Hz), 4.41 (1H, dd, \( J = 5.2, 11.2 \) Hz), 5.01 (1H, s), 7.58 (2H, d, \( J = 8.4 \) Hz), 7.90 (2H, d, \( J = 8.4 \) Hz), \(^{13}\)C NMR (CDCl\(_3\), 100 MHz) \( \delta \): 4.9, 6.6, 22.7, 28.2, 37.5, 55.0, 65.9, 76.1, 102.4, 127.9, 129.1, 131.0, 131.6, 154.2, 165.8, IR(neat) 1718, 1590 cm\(^{-1}\), HRMS(ESI) calcd for C\(_{21}\)H\(_{31}\)O\(_4\)NaSiBr 477.1073, found 477.1057, \([\alpha]_D^{16} –13.3 \) (c 1.0, CHCl\(_3\), 60% ee)

\((1S,2S,3R)-3\text{-Hydroxy}-2\text{-methoxy}-4\text{-{oxocyclohexyl})methyl 4-bromobenzoate (SI-3).}\) To a solution of 22 (103 mg, 0.22 mmol) in acetone (1 mL), was added DMDO in acetone (9 mL, estimated to be 0.07-0.09 M, 0.63-0.81 mmol)\(^1\) and stirred at rt for 1 h. After volatile material was removed under reduced pressure, resulting residue was used in the next step without purification.

To a solution of the crude product in THF (2.2 mL), was added TBAF (1.0 M in THF, 290 \( \mu \)L, 290 mmol) at 0 °C. After being stirred for 15 min, saturated aqueous NH\(_4\)Cl (1 mL) was added to quench the reaction. The mixture was extracted three times with CH\(_2\)Cl\(_2\), and combined organic layers were washed with brine and dried over Na\(_2\)SO\(_4\). After volatile material was removed under reduced pressure,
resulting residue was purified by column chromatography (SiO2, hexane/ AcOEt = 2/1) to give SI-3 (54 mg, yield 68%, 2 steps) as a colorless oil. 1H NMR (CDCl3, 400 MHz) δ: 1.54 (1H, dddd, J = 4.0, 14.0, 14.0, 14.0 Hz), 2.12-2.19 (1H, m), 2.23-2.31 (1H, m), 2.47 (1H, ddd, J = 6.4, 14.0, 14.0 Hz), 2.62 (1H, ddd, J = 2.4, 4.0, 14.0 Hz), 3.14 (1H, dd, J = 9.2, 10.4 Hz), 3.62 (3H, s), 3.74 (1H, brs), 4.24 (1H, d, J = 9.2 Hz), 4.46 (1H, dd, J = 5.6, 10.8 Hz), 4.57 (1H, dd, J = 3.2, 10.8 Hz), 7.60 (2H, d, J = 8.8 Hz), 7.87 (2H, d, J = 8.8 Hz), 13C NMR (CDCl3, 100 MHz) δ: 24.6, 37.4, 40.7, 60.5, 64.8, 81.2, 85.2, 128.3, 128.7, 131.0, 131.8, 165.6, 207.6, IR(neat) 3460, 1713, 1589 cm⁻¹, HRMS(ESI) calcd for C15H17O5NaBr 379.0157, found 379.0147, [α]D16 –29.2 (c 0.25, CHCl3, 60% ee)

((1S,2S,3R)-3-(((1R,4S)-7,7-Dimethyl-2-oxobicyclo[2.2.1]heptan-1-yl)methylsulfonyloxy)-2-methoxy-4-oxycyclohexyl)methyl 4-bromobenzoate (23). To a solution of SI-3 (53 mg, 0.15 mmol) in CH2Cl2 (1.5 mL), were successively added Et3N (250 μL), DMAP (7.5 mg, 0.061 mmol), and (−)-canphorsulfonyl chloride (74 mg, 0.30 mmol) in CH2Cl2 (1.5 mL) at 0 ºC. After being stirred for 10 min, saturated aqueous NaHCO3 (1 mL) was added to quench the reaction. The mixture was extracted three times with AcOEt. Combined organic layers were washed with brine and dried over Na2SO4. After volatile material was removed under reduced pressure, diastereomeric ratio was determined to be ca. 4/1 (corresponding to the ee of 12') by 1H NMR of the crude product (See a chart of 1H NMR). The crude product was purified by column chromatography (SiO2, hexane/ AcOEt = 3.5/1) to give 23 (11.5 mg, yield 13%) as a colorless amorphous and diastereomixture of 23 (47 mg, dr: 3/1, yield 55%). Recrystallization of 23 from ether/hexane gave colorless crystal. 1H NMR (CDCl3, 400 MHz) δ: 0.92 (3H, s), 1.13 (3H, s), 1.45 (1H, ddd, J = 4.0, 9.2, 12.8 Hz), 1.52-1.63 (1H, m), 1.75 (1H, ddd, J = 4.8, 9.2, 14.0 Hz), 1.98 (1H, d, J = 18.4 Hz), 2.03-2.14 (3H, m), 2.28-2.35 (1H, m), 2.36-2.52 (3H, m), 2.59 (1H, ddd, J = 2.4, 4.0, 14.0 Hz), 5.16 (1H, d, J = 15.2 Hz), 4.50 (1H, dd, J = 4.8, 11.2 Hz), 4.57 (1H, dd, J = 3.2, 11.2 Hz), 5.16 (1H, d, J = 9.6 Hz), 7.61 (2H, d, J = 8.8 Hz), 7.88 (2H, d, J = 8.8 Hz), 13C NMR (CDCl3, 100 MHz) δ: 19.7, 19.8, 23.8, 25.1, 26.8, 38.5, 41.8, 42.5, 42.8, 47.8, 49.2, 58.0, 61.1, 64.3, 81.9, 87.1, 128.5, 128.5, 131.0, 131.9, 165.5, 200.6, 214.0, IR(neat)
1719, 1660, 1590 cm$^{-1}$, HRMS(ESI) calcd for C$_{25}$H$_{31}$O$_8$NaBr 593.0821, found 593.0775, $[\alpha]_D^{20}$ –41.9 (c 0.58, CHCl$_3$), mp 171.5-172.0 °C.
Scheme SI-3. Determination of Absolute Configuration of Diels-Alder Adduct ent-12 by Conversion to Known Chiral Compound.

To confirm the stereochemistry, the Diels-Alder adduct ent-12 was converted to SI-4 and SI-5, and compare the optical rotation with reported data. Our synthetic SI-4 represents plus sign of optical rotation, which corresponds to (+)-(R)-SI-4, synthesized by Rawal. Rawal et al. determined their absolute configuration by conversion to known benzylated compound (+)-(R)-SI-5.1 (–)-(S)-ent-SI-5 was synthesized and used as an intermediate of asymmetric total synthesis of natural (–)-reserpine by Stork et al.3 Synthesis of (+)-(R)-SI-5 was also reported by Smith, III et al., and its stereochemistry was unambiguously determined by X-ray crystallographic analysis of Johnson sulfoximine derivative.4

(R)-4-(hydroxymethyl)cyclohex-2-enone (SI-4). To a solution of SI-2 (21.6 mg, 0.079 mmol) in CH₂Cl₂ (762 μL), was added TFA (15 μL) and stirred for 5 min. Saturated aqueous NaHCO₃ (3 mL) was added to quench the reaction. The mixture was extracted three times with CH₂Cl₂, and combined organic layers were washed with brine and dried over Na₂SO₄. After volatile material was removed under reduced pressure, resulting residue was purified by column chromatography (SiO₂, hexane/ AcOEt = 1/1) to give SI-4 (3.8 mg, yield 38%) as a colorless solid. Spectral data were completely accord with those reported.² [α]D²⁰ +65.6 (c 0.19, CHCl₃, 51% ee)
(R)-4-(benzyloxymethyl)cyclohex-2-enone (SI-5).

SI-5 was obtained by reported procedure. Spectral data were completely accord with those reported.2

\[ \alpha_d^{17} +67.4 \ (c \ 0.15, \ \text{MeOH}, \ 51\% \ \text{ee}) \]
The absolute configuration of our synthetic (+)-platyphyllide was also estimated by using Mosher's method. As shown in Scheme SI-4, (+)-platyphyllide (54% ee) was converted into a diastereomixture (dr: 3.4/1 by $^1$H NMR, corresponding to the ee of (+)-platyphyllide) of (−)-(S)-MTPA ester SI-8. The $^1$H NMR peaks of olefin and methyl groups of the major diastereomer were shifted to a lower magnetic field, while those of benzylic methylene were shifted to a higher magnetic field (Magnified chart is shown in Figure SI-1.). These observations showed that the major diastereomer of SI-8 had an (R) configuration at a secondary alcohol, which is consistent with a previous assignment of the Diels-Alder adducts.
(S)-((1R,2R)-8-((tert-Butyldiphenylsilyloxy)methyl)-2-(prop-1-en-2-yl)-1,2,3,4-tetrahydronaphthalen-1-yl) 3,3,3-trifluoro-2-methoxy-2-phenylpropanoate (SI-8). Synthesis of Mosher’s ester derivative SI-8. A solution of (+)-platyphyllide (2.0 mg, 9.3 μmol, 54 % ee) in CH₂Cl₂ (186 μL) was added lithium aluminum hydride (excess) at 0 ºC. The mixture was stirred at the same temperature for 5 min and then warmed to rt. After being stirred for 5 min, water (1 mL) was added to quench the reaction. The separated water layer was extracted three times with CH₂Cl₂ and combined organic layers were washed with brine and dried over Na₂SO₄. After volatile material was removed under reduced pressure, resulting residue was roughly chromatographed (SiO₂, hexane/AcOEt = 3/1) to give SI-6 (1.0 mg).

A solution of SI-6 in CH₂Cl₂ (450 μL) was added Et₃N (1.3 μL, 9.1 μmol), DMAP (catalytic amount) and TBDPSCl (1.8 μL, 9.1 μmol). The mixture was stirred for 3 h. MeOH (200 μL) was added to quench the reaction. After volatile material was removed under reduced pressure, resulting residue was roughly chromatographed (SiO₂, hexane/AcOEt = 10/1) to give SI-7 and starting material SI-6. SI-6 was converted to SI-7 again under the same condition, to give SI-7 (total 5.5 mg).

A solution of SI-7 in CH₂Cl₂/pyridine (126 μL) was added DMAP (1 mg, 7.2 μmol) and (−)-MTPACl (8.6 mg, 37 μmol). The mixture was stirred for 12 h. Water (1 mL) was added to quench the reaction. The separated water layer was extracted three times with CH₂Cl₂ and combined organic layers were washed with brine and dried over Na₂SO₄. After volatile material was removed under reduced pressure, resulting residue was purified by preparative TLC (SiO₂, hexane/AcOEt = 5/1) to give diastereomixture of SI-8 (3.1 mg, 50 % for 3 steps) as a colorless oil. HRMS(ESI) calcd for C₄₀H₄₃O₄F₃SiNa 695.2775, found 695.2778.
The image contains two NMR spectra and a chemical structure. The chemical structure is labeled as 22. The spectra show peaks at various ppm values, indicating the presence of different chemical shifts for the compound. The chemical structure includes TESO, OMe, O, and a bromine (Br) group.
SI-3
diastereomixture (crude)
SI-8
(diasstereomixture)
ONO

60% ee

from

OMe

12

ONO

ONONO

ONONO

60% ee

from

OMe

ent-12

ONONO

ONONO

ONONO

60% ee

from

OMe

ent-12
racemic

>99.5% ee
racemic 17

ent-17

94% ee
racemic

ent-5
90% ee
References


