**Total Synthesis and Absolute Configuration of Otteliones A
and B, Novel and Potent Antitumor Agents from a
Freshwater Plant**

– Supporting Information –

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General Procedure.

All reactions involving air- and moisture-sensitive reagent were carried out using oven dried glassware and standard syringe-septum cap techniques. Routine monitorings of reaction were carried out using glass-supported Merck silica gel 60 F₂₅₄ TLC plates. Flash column chromatography was performed on Kanto Chemical Silica Gel 60N (spherical, neutral 40-50 μ m) with the solvents indicated.

Materials.

All solvents and reagent were used as supplied with the following exceptions. Tetrahydrofuran and diethyl ether were freshly distilled from sodium/benzophenone under argon.

Instrumentation.

Measurements of optical rotations were performed with a JASCO P-1020 automatic digital polarimeter. Melting points were taken on a Yanaco MP-3 micro melting point apparatus and are uncorrected. ¹H and ¹³C NMR spectra were measured with a Bruker DRX-500 (500 MHz) spectrometer. Chemical shifts were expressed in ppm using tetramethylsilane (δ =0) as an internal standard. The following abbreviations are used: singlet (s), doublet (d), triplet (t), multiplet (m), and broad (br). Infrared (IR) spectral measurements were carried out with a JASCO FT/IR-5300 spectrometer. Low-resolution mass (MS) spectra was measured on a Shimadzu GCMS-QP2010. High-resolution mass (HRMS) spectra was measured on a JEOL MStation JMS-700 mass spectrometer.

(1*R*,4*S*,4*aR*,5*R*,6*R*,7*R*,8*S*,8*aS*)-5-*tert*-Butyldimethylsiloxy-8-hydroxy-6,7-*O*-isopropylidenedioxy-1,4,4*a*,5,6,7,8,8*a*-octahydro-*endo*-1,4-methanonaphthalen-8-ol (7).

Sodium borohydride (153 mg, 4.0 mmol) was added to a stirred solution of (1*R*,4*S*,4*aS*,5*R*,6*S*,7*S*,8*aS*)-5-*tert*-butyldimethylsiloxy-6,7-*O*-isopropylidenedioxy-1,4,4*a*,5,6,7,8,8*a*-octahydro-*endo*-1,4-methanonaphthalen-8-one (**6**) (737 mg, 2.0 mmol) in THF-H₂O (22 ml, 10:1) at 0°C. After 30 min, the reaction was quenched with saturated aqueous ammonium chloride (5 ml), and extracted with ether (2 x 100 ml). The organic layer was washed with saturated aqueous sodium hydrogen carbonate (2 x 50 ml) and brine (2 x 50 ml), then dried over Na₂SO₄. Concentration of the solvent *in vacuo* afforded a residue, which was purified by column chromatography (hexane-ethyl acetate, 10:1→4:1) to give **7** (643 mg, 87%) as a white solid. Recrystallization from hexane-ether afforded colorless needles, mp 147.0-147.7°C; [α]_D²⁰ -25.1° (*c* 0.98, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 0.10 (6H, s), 0.90 (9H, s), 1.23-1.34 (4H, m), 1.38-1.49 (4H, m), 2.58-2.79 (2H, m), 2.80-3.05 (2H, m), 3.80-4.30 (4H, m), 6.03 (1H, s), 6.09 (1H, s); ¹³C NMR (125 MHz, CDCl₃) δ -4.95, -4.71, 18.0, 23.8, 25.8, 26.6, 44.9, 51.7, 78.1, 107.7, 134.5; IR (KBr) 3426, 2934, 2858, 2363, 1630, 1381, 1251, 1207, 1167, 1111, 1064, 898, 862, 837, 777 cm⁻¹; CIMS *m/z* 367 (M+H⁺); *Anal* calcd for C₂₀H₃₄O₄Si: C, 65.53; H, 9.35, found C, 65.57; H, 9.35.

(2*S*,2*aS*,4*R*,4*aS*,5*R*,6*R*,7*R*,7*aS*,7*bR*)-5-*tert*-Butyldimethylsiloxy-2-hydroxy-6,7-(*O*-isopropylidenedioxy)decahydroindeno[7,1-*bc*]furan-4-carbaldehyde (5).

Osmium tetroxide in *tert*-butyl alcohol (0.04 M solution, 1.30 ml, 0.06 mmol) and sodium metaperiodate (467 mg, 2.2 mmol) were added successively to a stirred solution of (1*R*,4*S*,4*aR*,5*R*,6*R*,7*R*,8*S*,8*aS*)-5-*tert*-butyldimethylsiloxy-8-hydroxy-6,7-*O*-isopropylidenedioxy-1,4,4*a*,5,6,7,8,8*a*-octahydro-*endo*-1,4-methanonaphthalen-8-ol (**7**) (200 mg, 0.55 mmol) in *tert*-butyl alcohol-THF-H₂O (10 ml, 8:6:3) at 0°C, and the mixture was allowed to warm up to room temperature. After 12 h, the reaction was quenched with 10% aqueous sodium thiosulfate (10 ml), and the resulting mixture was extracted with ether (2 x 50 ml). The combined extracts were washed with saturated aqueous sodium hydrogen carbonate (2 x 20 ml) and brine (2 x 20 ml), then dried over Na₂SO₄. Concentration of the solvent *in vacuo* afforded a residue, which was purified by column chromatography (hexane-ethyl acetate, 5:1) to give **5** (136 mg, 62%) as a

white solid. Recrystallization from hexane-ether afforded colorless needles, mp 120.7-121.5°C; $[\alpha]_D^{20} +19.0^\circ$ (*c* 0.99, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 0.06 (3H, s), 0.12 (3H, s), 0.88 (9H, s), 1.34 (3H, s), 1.44 (3H, s), 2.11 (1H, m), 2.22 (1H, m), 2.26 (1H, d, *J*=2.3 Hz), 2.74-2.91 (3H, m), 2.94 (1H, m), 4.17 (1H, dd, *J*=6.7, 4.5 Hz), 4.23 (1H, s), 4.47 (1H, dd, *J*=12.2, 6.7 Hz), 4.47 (1H, dd, *J*=12.2, 6.7 Hz), 5.27 (1H, d, *J*=2.3 Hz), 9.93 (1H, s); ¹³C NMR (125 MHz, CDCl₃) δ -4.43, -4.37, 18.2, 24.3, 25.9, 27.0, 30.2, 40.6, 41.9, 52.0, 55.8, 69.4, 73.6, 75.7, 76.0, 103.1, 107.7, 202.9; IR (KBr) 3433, 2955, 2928, 2854, 1714, 1469, 1371, 1246, 1221, 1151, 1103, 1057, 1012, 956, 898, 860, 831, 775, 511 cm⁻¹; HREIMS *m/z* calcd for C₂₀H₃₄O₆Si (M⁺), 398.2125, found 398.2124.

(2*S*,2*aS*,4*R*,4*aR*,5*R*,6*R*,7*R*,7*aS*,7*bR*)-5-*tert*-Butyldimethylsiloxy-4-[hydroxy[4-methoxy-3-(methoxymethoxy)phenyl]methyl]-6,7-(*O*-isopropylidenedioxy)decahydroindeno[7,1-*bc*]furan-2-ol (10a,b).

n-Butyllithium in *n*-hexane (1.55 M solution, 4.40 ml, 7.0 mmol) was added dropwise to a stirred solution of 4-bromo-1-methoxy-2-(methoxymethoxy)benzene (**9**)¹ (2.30 g, 7.7 mmol) in dry THF (40 ml) at -78°C under argon. After 1 h, a solution of (2*S*,2*aS*,4*R*,4*aS*,5*R*,6*R*,7*R*,7*aS*,7*bR*)-5-*tert*-butyldimethylsiloxy-2-hydroxy-6,7-(*O*-isopropylidenedioxy)decahydroindeno[7,1-*bc*]furan-4-carbaldehyde (**5**) (930 mg, 2.3 mmol) in dry THF (30 ml) was added to the above mixture at -78°C. After 1 h, the reaction was quenched with saturated aqueous ammonium chloride (10 ml), and the resulting mixture was extracted with ether (2 x 100 ml). The organic layer was washed with saturated aqueous sodium hydrogen carbonate (2 x 30 ml) and brine (30 ml), then dried over Na₂SO₄. Concentration of the solvent *in vacuo* afforded a residue, which was purified by column chromatography (hexane-ethyl acetate, 2:1→1:1) to give **10a** (1.06 g, 80%) (more polar) and **10b** (263 mg, 20%) (less polar).

10a: colorless oil; $[\alpha]_D^{20} +20.1^\circ$ (*c* 0.74, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 0.17 (3H, s), 0.24 (3H, s), 0.95 (9H, s), 1.26 (6H, s), 1.81 (1H, br), 1.88 (1H, br), 1.97-2.10 (1H, m), 2.27 (1H, br), 2.29 (1H, d, *J*=2.4 Hz), 2.47-2.57 (1H, m), 2.76-2.87 (2H, m), 3.51 (3H, s), 3.88 (3H, s), 3.99 (1H, t, *J*=3.4 Hz), 4.18-4.27 (1H, m), 4.41-4.45 (1H, m), 4.47 (1H, dd, *J*=1.6, 7.1 Hz), 4.81-4.91 (1H, m), 5.23 (2H, s), 5.27 (1H, d, *J*=2.5 Hz), 6.88 (1H, d, *J*=8.3 Hz), 7.03 (1H, dd, *J*=8.3, 1.9 Hz), 7.22 (1H, d, *J*=1.9 Hz); ¹³C NMR (125 MHz, CDCl₃) δ -4.07, -3.82, 18.5, 23.7, 26.1, 26.4, 32.7, 36.6, 42.1, 52.1, 52.4, 53.4, 55.9, 56.1, 68.6, 73.9, 74.9, 76.0, 95.6, 103.6, 107.4, 111.7, 114.9, 120.5, 136.6, 146.7, 149.4; IR (neat) 3423, 2932, 2856, 1606, 1510, 1464, 1385, 1259, 1211, 1155, 1132, 1080, 1012, 868, 835, 775 cm⁻¹; HREIMS *m/z* calcd for C₂₉H₄₆O₉Si (M⁺), 566.2911, found 566.2904.

10b: colorless oil; $[\alpha]_D^{20} +12.5^\circ$ (*c* 0.74, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 0.20 (3H, s), 0.24 (3H, s), 0.97 (9H, s), 1.26 (3H, s), 1.38-1.42 (1H, m), 1.44 (3H, s), 1.67-1.76 (1H, m), 1.77 (1H, s), 2.16 (1H, s), 2.33-2.42 (1H, m), 2.50-2.58 (1H, m), 2.63-2.72 (1H, m), 2.84-2.92 (1H, m), 3.51 (3H, s), 3.87 (3H, s),

4.35-4.40 (1H, m), 4.48 (1H, d, $J=7.0$ Hz), 4.54 (1H, d, $J=6.4$ Hz), 4.53-4.59 (1H, m), 4.86 (1H, d, $J=10.7$ Hz), 5.18 (1H, s), 5.21 (2H, s), 6.87 (1H, d, $J=8.3$ Hz), 6.97 (1H, d, $J=7.7$ Hz), 7.19 (1H, s); ^{13}C NMR (125 MHz, CDCl_3) δ -3.81, -3.66, 18.5, 23.7, 25.8, 26.2, 26.5, 32.6, 36.4, 42.0, 52.6, 53.1, 68.3, 72.4, 73.8, 74.5, 75.1, 95.6, 103.8, 107.5, 111.6, 114.8, 120.0, 137.6, 146.4, 149.3; IR (neat) 3435, 2934, 1510, 1464, 1383, 1261, 1157, 1078, 1049, 1006, 868, 835, 775 cm^{-1} ; HRFABMS m/z calcd for $\text{C}_{29}\text{H}_{46}\text{O}_9\text{Si}$ (M^+), 566.2911, found 566.2914.

(1*R*,3*R*,3*aR*,4*R*,5*R*,6*R*,7*S*,7*aS*)-4-*tert*-Butyldimethylsiloxy-7-hydroxy-3-[hydroxy[4-methoxy-3-(methoxymethoxy)phenyl]methyl]-5,6-(*O*-isopropylidenedioxy)octahydroindene-1-carbaldehyde (11).

1,8-Diazabicyclo[5.4.0]undec-7-ene (DBU) (4.70 mL, 32 mmol) was added to a stirred solution of (2*S*,2*aS*,4*R*,4*aR*,5*R*,6*R*,7*R*,7*aS*,7*bR*)-5-*tert*-butyldimethylsiloxy-4-[hydroxy[4-methoxy-3-(methoxymethoxy)phenyl]methyl]-6,7-(*O*-isopropylidenedioxy)decahydroindeno[7,1-*bc*]furan-2-ol (**10a**) (900 mg, 1.6 mmol) in dry toluene (32 mL) at room temperature under argon. The mixture was heated at reflux for 1.5 h. After cooling, the mixture was directly subjected to column chromatography (ethyl acetate) in order to remove DBU. The fractions containing **11** and starting material **10a** were collected and then concentrated *in vacuo*. The residue was purified by column chromatography (hexane-ethyl acetate, 2:1→1:1) to give less polar **11** (270 mg, 30%) (colorless oil) and more polar starting material **10a** (540 mg, 60 %). **11**: $[\alpha]_{\text{D}}^{20}$ -34.3° (c 0.98, CHCl_3); ^1H NMR (500 MHz, CDCl_3) δ 0.23 (3H, s), 0.31 (3H, s), 0.97 (9H, s), 2.00-2.12 (1H, m), 2.22-2.43 (3H, m), 3.01-3.09 (1H, m), 3.35-3.44 (1H, m), 3.50 (3H, s), 3.81-3.86 (1H, m), 3.87 (3H, s), 4.02 (1H, ddd, $J=4.1, 6.6, 10.8$ Hz), 4.14-4.22 (1H, m), 4.45 (1H, dr), 4.73 (1H, dr), 6.87 (1H, d, $J=8.3$ Hz), 6.99 (1H, dd, $J=2.0, 8.3$ Hz), 7.18, (1H, d, $J=2.0$ Hz); ^{13}C NMR (125 MHz, CDCl_3) δ -4.33, -3.84, 14.2, 18.1, 21.0, 23.8, 25.9, 26.1, 50.7, 55.9, 56.2, 60.3, 75.7, 75.9, 77.2, 95.6, 108.5, 111.8, 114.9, 120.1, 135.9, 146.7, 203.0; IR (neat) 3422, 2934, 2860, 1718, 1512, 1383, 1261, 1211, 1155, 1078, 1022, 864, 839, 781 cm^{-1} ; HREIMS m/z calcd for $\text{C}_{29}\text{H}_{46}\text{O}_9\text{Si}$ (M^+), 566.2911, found 566.2916.

(1*R*,3*R*,3*aS*,4*S*,5*R*,6*R*,7*R*,7*aR*)-7-*tert*-Butyldimethylsiloxy-1-[hydroxy[4-methoxy-3-(methoxymethoxy)phenyl]methyl]-3-hydroxymethyl-5,6-(*O*-isopropylidenedioxy)octahydroindene-4-ol (12).

A solution of (1*R*,3*R*,3*aR*,4*R*,5*R*,6*R*,7*S*,7*aS*)-4-*tert*-butyldimethylsiloxy-7-hydroxy-3-[hydroxy[4-methoxy-3-(methoxymethoxy)phenyl]methyl]-5,6-(*O*-isopropylidenedioxy)octahydroindene-1-carbaldehyde (**11**) (306 mg, 0.54 mmol) in dry THF (6 ml) was added dropwise to a stirred suspension of lithium aluminium hydride (41.0 mg, 1.1 mmol) in dry tetrahydrofuran (4 ml) at 0°C under argon. After 1 min, water (41 μ l), 15% aqueous sodium hydroxide (41 μ l), water (123 μ l), and Na₂SO₄ (500 mg) were added successively to the mixture, and the resulting mixture was stirred for 30 min at room temperature. The mixture was filtrated through a pad of Celite[®], and the filtrate was concentrated *in vacuo* to afford a residue, which was purified by column chromatography (hexane-ethyl acetate, 1:1→ethyl acetate) to give **12** (294 mg, 96%) as a colorless oil: $[\alpha]_D^{20}$ -36.6° (*c* 0.83, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 0.22 (3H, s), 0.96 (3H, s), 1.26 (6H, s), 1.63 (1H, br), 1.74 (1H, br), 1.90-2.00 (1H, m), 2.31-2.39 (2H, m), 2.46-2.55 (1H, m), 2.68 (1H, br), 3.39-3.47 (1H, m), 3.51 (3H, s), 3.48-3.56 (1H, m), 3.56-3.63 (1H, m), 3.83-3.90 (1H, m), 3.87 (3H, s), 4.04 (1H, br), 4.17-4.23 (1H, m), 4.42 (1H, dd, *J*=5.2, 7.3 Hz), 4.81-4.86 (1H, m), 5.23 (2H, s), 6.87 (1H, d, *J*=8.3 Hz), 7.01 (1H, dd, *J*=2.0, 8.3 Hz), 7.19 (1H, d, *J*=2.0 Hz); ¹³C NMR (125 MHz, CDCl₃) δ -4.31, -3.99, 18.1, 24.0, 25.9, 26.1, 26.2, 30.2, 40.0, 43.7, 49.0, 55.9, 56.2, 67.3, 67.4, 72.0, 73.0, 76.4, 76.5, 95.5, 108.5, 111.5, 114.5, 120.0, 136.4, 146.5, 149.1; IR (neat) 3435, 2932, 1512, 1383, 1259, 1155, 1078, 1018, 864, 837., 779 cm⁻¹; HREIMS *m/z* calcd for C₂₉H₄₈O₉Si (M⁺), 568.3068, found 568.3085.

(1*R*,3*R*,3*aS*,4*S*,5*R*,6*R*,7*R*,7*aR*)-4-Acetoxy-3-acetoxymethyl-7-*tert*-butyldimethylsiloxy-1-[acetoxyl[4-methoxy-3-(methoxymethoxy)phenyl]methyl]-5,6-(*O*-isopropylidenedioxy)octahydroindene (13).

Acetic anhydride (1.50 ml, 16 mmol) and 4-dimethylaminopyridine (DMAP) (19.0 mg, 0.16 mmol) were added to a stirred solution of (1*R*,3*R*,3*aS*,4*S*,5*R*,6*R*,7*R*,7*aR*)-7-*tert*-butyldimethylsiloxy-1-[hydroxy[4-methoxy-3-(methoxymethoxy)phenyl]methyl]-3-hydroxymethyl-5,6-(*O*-isopropylidenedioxy)octahydro-

indene-4-ol (**12**) (294 mg, 0.52 mmol) in pyridine (5 ml) at room temperature. After 1 h, the mixture was diluted with ether (50 ml). The organic layer was washed with 3% hydrochloric acid (2 x 10 ml), saturated aqueous sodium hydrogen carbonate (2 x 10 ml), and brine (10 ml), then dried over Na₂SO₄. Concentration of the solvent *in vacuo* gave a residue, which was purified by column chromatography (hexane-ethyl acetate, 1:1) to give **13** (324 mg, 95%) as a colorless oil: $[\alpha]_D^{20}$ -38.8° (c 1.16, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 0.20 (3H, s), 0.33 (3H, s), 0.96 (9H, s), 1.13 (3H, s), 1.21 (3H, s), 1.62 (1H, ddd, *J*=3.8, 8.6, 12.6 Hz), 1.99 (3H, s), 2.03 (3H, s), 2.09 (3H, s), 1.96-2.13 (2H, m), 2.31-2.37 (1H, m), 2.66-2.75 (1H, m), 2.76-2.85 (1H, m), 3.51 (3H, s), 3.86 (3H, s), 3.84-3.89 (1H, m), 3.94-4.03 (2H, m), 4.06 (1H, dd, *J*=2.4, 6.3 Hz), 4.21 (1H, dd, *J*=4.9, 6.3 Hz), 5.20-5.26 (2H, m), 5.43 (1H, dd, *J*=4.7, 8.4 Hz), 5.82 (1H, d, *J*=10.6 Hz), 6.86 (1H, d, *J*=8.3 Hz), 7.05 (1H, dd, *J*=1.9, 8.3 Hz), 7.23 (1H, d, *J*=1.9 Hz); ¹³C NMR (125 MHz, CDCl₃) δ -3.96, -3.89, 18.1, 20.9, 21.2, 24.7, 26.0, 26.4, 31.9, 37.3, 39.7, 41.8, 46.0, 55.9, 56.2, 68.2, 68.8, 69.3, 73.5, 76.6, 77.1, 95.6, 108.1, 111.3, 115.4, 121.7, 132.5, 146.5, 149.6, 169.9, 170.4, 171.3; IR (neat) 2935, 2856, 1738, 1608, 1516, 1466, 1371, 1238, 1157, 1371, 1238, 1157, 1132, 1078, 1024, 869, 837, 775, 607, 518, 412 cm⁻¹; HREIMS *m/z* calcd for C₃₅H₅₄O₁₂Si (M⁺), 694.3385, found 694.3380.

(1*S*,3*R*,3*aS*,4*S*,5*R*,6*R*,7*R*,7*aR*)-7-*tert*-Butyldimethylsiloxy-3-hydroxymethyl-5,6-*O*-isopropylidenedioxy-1-[4-methoxy-3-(methoxymethoxy)benzyl]octahydroindene-4-ol (14**).**

A solution of (1*R*,3*R*,3*aS*,4*S*,5*R*,6*R*,7*R*,7*aR*)-4-acetoxy-3-acetoxymethyl-7-*tert*-butyldimethylsiloxy-1-[acetoxy[4-methoxy-3-(methoxymethoxy)phenyl]methyl]-5,6-*O*-isopropylidenedioxyoctahydroindene (**13**) (340 mg, 0.49 mmol) in dry THF (15 ml) was added dropwise to a stirred solution of lithium (100 mg, 9.0 mmol) in liquid ammonia (30 ml) at -78°C under argon. After 5 min, the reaction was quenched with saturated aqueous ammonium chloride (5 ml) at the same temperature. The mixture was then allowed to stand at room temperature for 4 h in order to evaporate off ammonia. The mixture was extracted with ethyl acetate (2 x 100 ml), and the extracts were washed successively with saturated aqueous sodium hydrogen carbonate (2 x 50 ml) and brine (50 ml), then dried over Na₂SO₄. Concentration of the solvent *in vacuo* afforded a residue, which was purified by column chromatography (hexane-ethyl acetate, 1:1) to give **14** (265 mg, 98%) as a colorless oil: $[\alpha]_D^{20}$ -27.7° (c 0.91, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 0.23 (3H, s), 0.26 (3H, s), 0.97 (9H, s), 1.34 (3H, s), 1.44 (3H, s), 1.43-1.49 (1H, m), 1.63-1.72 (1H, m), 1.81 (1H, br), 2.26-2.38 (2H, m), 2.50-2.57 (2H, m), 2.60-2.69 (1H, m), 2.88 (1H, dd, *J*=4.6, 13.3 Hz), 3.43 (1H, dd, *J*=7.3, 10.3 Hz), 3.47-3.55 (1H, m), 3.52 (3H, s), 3.86 (3H, s), 3.90-4.04 (2H, m), 4.06 (1H, t, *J*=3.0 Hz), 4.28 (1H, dd, *J*=2.9, 7.2 Hz), 4.50-4.55 (1H, m), 5.19-5.23 (2H, m), 6.77 (1H, dd, *J*=1.9, 8.2 Hz), 6.82 (1H, d, *J*=8.2 Hz), 6.99 (1H, d, *J*=1.9 Hz); ¹³C NMR (125 MHz,

CDCl₃) δ -4.46, -3.56, 18.1, 24.0, 25.9, 26.4, 33.8, 35.4, 40.1, 40.6, 42.4, 42.8, 55.9, 56.1, 67.1, 67.3, 71.6, 76.1, 76.3, 95.5, 108.4, 111.6, 116.9, 122.1, 134.3, 146.3, 147.8; IR (neat) 3433, 2932, 2858, 1512, 1466, 1383, 1261, 1211, 1155, 1134, 1078, 1016, 923, 868, 837, 808, 779 cm⁻¹; HREIMS m/z calcd for C₂₉H₄₈O₈Si (M⁺), 552.3118, found 552.3129.

(1*R*,3*S*,3*aR*,4*R*,5*R*,6*S*,7*aR*)-4-*tert*-Butyldimethylsiloxy-5,6-*O*-isopropylidenedioxy-3-[4-methoxy-3-(methoxymethoxy)benzyl]-7-oxooctahydroindene-1-carbaldehyde (15**).**

Dess-Martin periodinane (609 mg, 1.4 mmol) was added to a stirred solution of (1*S*,3*R*,3*aS*,4*S*,5*R*,6*R*,7*R*,7*aR*)-7-*tert*-butyldimethylsiloxy-3-hydroxymethyl-5,6-*O*-isopropylidenedioxy-1-[4-methoxy-3-(methoxymethoxy)benzyl]octahydroindene-4-ol (**14**) (265 mg, 0.48 mmol) in dry dichloromethane (10 ml) at room temperature. After 30 min, the reaction was quenched with 10% aqueous sodium thiosulfate (3 ml), and the resulting mixture was extracted with ether (2 x 25 ml). The organic layer was washed with saturated aqueous sodium hydrogen carbonate (2 x 10 ml) and brine (10 ml), then dried over Na₂SO₄. Concentration of the solvent *in vacuo* afforded a residue, which was purified by column chromatography (hexane-ethyl acetate, 6:1) to give **15** (210 mg, 80%) as a colorless oil: $[\alpha]_D^{20}$ +24.5° (*c* 2.50, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 0.16 (3H, s), 0.22 (3H, s), 0.86 (9H, s), 1.34 (3H, s), 1.57 (3H, s), 1.54-1.92 (2H, m), 2.13-2.23 (1H, m), 2.57 (1H, dd, *J*=10.0, 13.5 Hz), 2.81 (1H, dd, *J*=5.3, 13.5 Hz), 3.13-3.19 (1H, m), 3.47-3.51 (3H, s), 3.52 (3H, s), 3.68 (1H, dd, *J*=5.1, 9.6 Hz), 4.09-4.11 (1H, m), 4.33 (1H, d, *J*=7.4 Hz), 4.40 (1H, dd, *J*=3.1, 7.4 Hz), 5.21 (2H, s), 6.75 (1H, dd, *J*=1.9, 8.2 Hz), 6.82 (1H, d, *J*=8.2 Hz), 6.97 (1H, d, *J*=1.9 Hz); ¹³C NMR (125 MHz, CDCl₃) δ -4.07, -3.56, 17.9, 24.0, 25.6, 25.9, 30.5, 35.2, 43.3, 44.1, 44.8, 52.1, 55.9, 56.1, 68.8, 77.2, 80.4, 95.5, 111.7, 112.0, 116.7, 121.9, 133.2, 146.4, 148.0, 201.9, 206.2; IR (neat) 2932, 2858, 1728, 1514, 1466, 1383, 1263, 1209, 1157, 1134, 1060, 1006, 925, 858, 837, 808, 777, 538, 468, 405 cm⁻¹; HREIMS m/z calcd for C₂₉H₄₄O₈Si (M⁺), 548.2805, found 548.2801.

(1*S*,3*S*,3*aS*,5*R*,6*R*,7*R*,7*aR*)-7-*tert*-Butyldimethylsiloxy-5,6-*O*-isopropylidenedioxy-1-[4-methoxy-3-(methoxymethoxy)benzyl]-4-methylene-3-(vinyl)octahydroindene (3**).**

Wittig reagent (methylene triphenylphosphorane) in benzene solution was first prepared as follows: a suspension of methyl triphenylphosphonium bromide (1.22g, 3.4 mmol) and potassium *tert*-butoxide (380 mg, 3.4 mmol) in dry benzene (10 ml) were heated at reflux for 4 h under argon, and the solution was cooled to room temperature. A solution of the Wittig reagent in benzene (1.0 ml, 0.34 mmol) was added very slowly to a stirred solution of (1*R*,3*S*,3*aR*,4*R*,5*R*,6*S*,7*aR*)-4-*tert*-butyldimethylsiloxy-5,6-*O*-isopropylidenedioxy-3-[4-methoxy-3-(methoxymethoxy)benzyl]-7-oxooctahydroindene-1-carbaldehyde (**15**) (187 mg, 0.34 mmol) in dry benzene (8 ml) at room temperature under argon. After the first olefination of the formyl group was completed (monitored by TLC), a solution of the Wittig reagent in benzene (4.0 ml, 1.36 mmol) was added once again and the resulting mixture was refluxed for 30 min to pursue the second olefination of the carbonyl group. After cooling, the reaction was quenched with water (2 ml), and the mixture was extracted with ether (2 x 30 ml). The organic layer was washed with brine (10 ml), then dried over Na₂SO₄. Concentration of the solvent *in vacuo* afforded a residue, which was purified by column chromatography (hexane-ethyl acetate, 20:1→10:1) to give **3** (177 mg, 95%) as a colorless oil: $[\alpha]_D^{20}$ -21.9° (*c* 0.93, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 0.14 (3H, s), 0.18 (3H, s), 0.88 (9H, s), 1.35 (9H, s), 1.41 (1H, ddd, *J*=3.6, 8.4, 12.2 Hz), 1.45 (3H, s), 1.91-2.00 (1H, m), 2.36-2.44 (1H, m), 2.53 (1H, dd, *J*=10.3, 13.3 Hz), 2.57-2.63 (1H, m), 2.72-2.77 (1H, m), 2.83 (1H, dd, *J*=5.2, 13.3 Hz), 2.85-2.92 (1H, m), 3.51 (3H, s), 3.84 (3H, s), 3.95-3.97 (1H, m), 4.15 (1H, dd, *J*=2.4, 7.3 Hz), 4.62 (1H, d, *J*=7.3 Hz), 4.84-4.87 (1H, m), 4.93-4.98 (1H, m), 5.14-5.17 (1H, m), 5.19-5.24 (2H, s), 5.22 (1H, m), 5.88, (1H, ddd, *J*=7.8, 10.2, 17.8 Hz), 6.78-6.8/ (2H, m), 7.00 (1H, d, *J*=1.3 Hz); ¹³C NMR (125 MHz, CDCl₃) δ -4.15, -3.57, 18.0, 24.2, 25.8, 26.4, 36.2, 38.2, 42.0, 43.0, 44.8, 49.2, 55.9, 56.1, 70.0, 78.5, 78.8, 95.6, 108.6, 111.6, 111.7, 114.1, 117.0, 122.2, 134.6, 145.8, 146.1, 146.3, 147.8; IR (neat) 2932, 2858, 1637, 1512, 1464, 1381, 1259, 1209, 1157, 1134, 1078, 1059, 1030, 1005, 908, 864, 835, 810, 775 cm⁻¹; HREIMS *m/z* calcd for C₃₁H₄₈O₆Si (M⁺), 544.3220, found 544.3224.

(1*S*,3*S*,3*aR*,4*R*,5*R*,6*R*,7*aS*)-4-*tert*-Butyldimethylsiloxy-3-(3-hydroxy-4-methoxybenzyl)-7-methylene-1-(vinyl)octahydroindene-5,6-diol (16**).**

A solution of trifluoroacetic acid-water (11 ml, 10:1) was added dropwise to a stirred solution of (1*S*,3*S*,3*aS*,5*R*,6*R*,7*R*,7*aR*)-7-*tert*-butyldimethylsiloxy-5,6-*O*-isopropylidenedioxy-1-[4-methoxy-3-(methoxymethoxy)benzyl]-4-methylene-3-(vinyl)octahydroindene (**3**) (177 mg, 0.33 mmol) in THF (1 ml) at 0°C. After 10 min, the mixture was neutralized with 6M aqueous sodium hydroxide and then extracted with ethyl acetate (2 x 50 ml). The organic layer was washed with saturated aqueous sodium hydrogen carbonate (2 x 10 ml) and brine (10 ml), then dried over Na₂SO₄. Concentration of the solvent *in vacuo* afforded a residue, which was purified by column chromatography (hexane-ethyl acetate, 3:1) to

give **16** (128 mg, 86%) as a colorless oil: $[\alpha]_D^{20} +19.2^\circ$ (*c* 1.97, CHCl_3); ^1H NMR (500 MHz, CDCl_3) δ 0.22 (3H, s), 0.26 (3H, s), 0.98 (9H, s), 1.59 (1H, ddd, *J*=5.7, 10.0, 15.8 Hz), 1.74 (1H, d, *J*=6.1 Hz), 1.93 (1H, d, *J*=7.5 Hz), 1.94-2.02 (1H, m), 2.27-2.32 (1H, m), 2.41-2.51 (2H, m), 2.69 (1H, dd, *J*=8.9, 13.6 Hz), 2.77-2.86 (2H, m), 3.86 (3H, s), 3.95-3.99 (1H, m), 4.26 (1H, t, *J*=4.0 Hz), 4.70-4.74 (1H, m), 4.80-4.86 (1H, m), 4.86-4.90 (1H, m), 4.95 (1H, s), 5.15 (1H, t, *J*=1.8 Hz), 5.54 (1H, s), 5.62 (1H, ddd, *J*=8.3, 10.1, 18.3 Hz), 6.66 (1H, dd, *J*=2.1, 8.2 Hz), 6.76 (1H, d, *J*=8.2 Hz), 6.78 (1H, d, *J*=2.1 Hz); ^{13}C NMR (125 MHz, CDCl_3) δ -4.05, -3.37, 18.1, 26.1, 35.5, 37.1, 43.2, 44.2, 47.5, 54.3, 56.0, 68.2, 72.7, 75.4, 110.6, 110.8, 113.4, 114.6, 119.6, 135.3, 142.8, 144.7, 145.4, 145.8; IR (neat) 3422, 2932, 2858, 1639, 1591, 1512, 1442, 1259, 1130, 1062, 1037, 904, 873, 835, 775, 706 cm^{-1} ; HRFABMS *m/z* calcd for $\text{C}_{26}\text{H}_{41}\text{O}_5\text{Si}$ [(*M*+*H*)⁺], 461.2723, found 461.2697.

(1*S*,3*S*,3*aR*,4*R*,5*R*,6*R*,7*aS*)-3-(3-Acetoxy-4-methoxybenzyl)-4-*tert*-butyldimethylsiloxy-7-methylene-1-(vinyl)octahydroindene-5,6-diol (17**).**

17

2M aqueous sodium hydroxide (0.38 ml) and acetic anhydride (76 μl , 0.81 mmol) were added dropwise to a stirred solution of (1*S*,3*S*,3*aR*,4*R*,5*R*,6*R*,7*aS*)-4-*tert*-butyldimethylsiloxy-3-(3-hydroxy-4-methoxybenzyl)-7-methylene-1-(vinyl)octahydroindene-5,6-diol (**16**) (128 mg, 0.28 mmol) in 2-propanol (1.7 ml) at room temperature. After 30 min, the mixture was diluted with ethyl acetate (30 ml). The organic layer was washed with water (10 ml) and brine (10 ml), then dried over Na_2SO_4 . Concentration of the solvent *in vacuo* gave a residue, which was purified by column chromatography (benzene-ethyl acetate, 10:1) to give **17** (127 mg, 91%) as a colorless oil: $[\alpha]_D^{20} +20.9^\circ$ (*c* 0.80, CHCl_3); ^1H NMR (500 MHz, CDCl_3) δ 0.21 (3H, s), 0.24 (3H, s), 0.97 (9H, s), 1.56-1.63 (1H, m), 1.78 (1H, d, *J*=5.8 Hz), 1.92 (1H, d, *J*=7.6 Hz), 1.94-2.01 (1H, m), 2.27-2.30 (1H, m), 2.31 (3H, s), 2.39-2.49 (2H, m), 2.72 (1H, dd, *J*=8.8, 13.7 Hz), 2.77-2.86 (1H, dd, *J*=6.3, 13.7 Hz), 2.83 (1H, m), 3.80 (3H, s), 3.95-3.99 (1H, m), 4.23-4.26 (1H, m), 4.68-4.72 (1H, m), 4.80-4.85 (1H, m), 4.88 (1H, dd, *J*=1.3, 10.0 Hz), 4.94 (1H, s), 5.14-5.16 (1H, m), 5.62 (1H, ddd, *J*=8.3, 10.0, 17.1 Hz), 6.85 (1H, d, *J*=2.1 Hz), 6.87 (1H, d, *J*=8.3 Hz), 7.00 (1H, dd, *J*=2.1, 8.3 Hz); ^{13}C NMR (125 MHz, CDCl_3) δ -4.06, -3.36, 18.1, 20.7, 26.1, 35.3, 37.1, 43.1, 44.2, 47.5, 54.3, 55.9, 68.2, 72.7, 75.4, 110.9, 112.4, 113.5, 122.6, 126.4, 134.6, 139.5, 142.7, 145.7, 149.1, 168.3; IR (neat) 3449, 2955, 2932, 2858, 1768, 1639, 1512, 1464, 1442, 1369, 1263, 1205, 1122, 1062, 1035, 902, 873, 835, 775, 706 cm^{-1} ; HRFABMS *m/z* calcd for $\text{C}_{28}\text{H}_{43}\text{O}_6\text{Si}$ [(*M*+*H*)⁺], 503.2829, found 503.2832.

(3aR,4R,4aR,5S,7S,7aS)-5-(3-Acetoxy-4-methoxybenzyl)-4-tert-butyldimethylsiloxy-8-methylene-7-(vinyl)octahydroindeno[5,6-d][1,3]dioxole-2-thione (18).

A solution of thiophosgene (18 μ l, 0.24 mmol) in dry dichloromethane (0.5 ml) was added dropwise to a stirred mixture of (1S,3S,3aR,4R,5R,6R,7aS)-3-(3-acetoxy-4-methoxybenzyl)-4-tert-butyldimethylsiloxy-7-methylene-1-(vinyl)octahydroindene-5,6-diol (**17**) (60.0 mg, 0.12 mmol) in dry dichloromethane (2 ml) containing 4-dimethylaminopyridine (72.0 mg, 0.60 mmol) at room temperature. After 30 min, silica gel (1.0 g) was added to the reaction mixture, and the solvent was carefully evaporated off *in vacuo*. The resulting solid was charged on the top of a silica gel column chromatography, and elution using hexane-ethyl acetate (10:1) gave **18** (60 mg, 93%) as a colorless oil: $[\alpha]_D^{20} +25.3^\circ$ (*c* 0.60, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 0.16 (3H, s), 0.22 (3H, s), 0.87 (9H, s), 1.44-1.50 (1H, m), 1.88-1.96 (1H, m), 2.31 (3H, s), 2.31-2.34 (1H, m), 2.40-2.52 (2H, m), 2.79-2.84 (1H, m), 2.86-2.93 (2H, m), 3.80 (3H, s), 4.15-4.18 (1H, m), 4.85 (1H, dd, *J*=2.4, 8.5 Hz), 4.91, (1H, d, *J*=10.1 Hz), 4.94-4.99 (1H, m), 5.28-5.33 (2H, m), 5.47 (1H, d, *J*=2.5 Hz), 5.85 (1H, ddd, *J*=7.8, 10.1, 17.2 Hz), 6.82 (1H, d, *J*=2.1 Hz), 6.89 (1H, d, *J*=8.3 Hz), 6.97 (1H, dd, *J*=2.1, 8.3 Hz); ¹³C NMR (125 MHz, CDCl₃) δ -4.41, -3.49, 17.9, 20.7, 25.6, 35.7, 38.0, 42.5, 43.0, 43.9, 49.6, 55.9, 67.6, 82.1, 85.3, 112.5, 112.6, 118.8, 122.7, 126.5, 133.5, 139.6, 141.1, 144.6, 149.4, 169.0, 190.8; IR (neat) 3076, 2955, 2932, 2858, 1768, 1639, 1583, 1512, 1464, 1442, 1369, 1331, 1267, 1205, 1163, 1124, 1089, 1064, 1032, 995, 958, 904, 866, 837, 777, 758 cm⁻¹; HREIMS *m/z* calcd for C₂₉H₄₀O₆SSi (M⁺), 544.2315, found 544.2316.

(1S,3S,3aR,4S,7aS)-3-(3-Acetoxy-4-methoxybenzyl)-4-tert-butyldimethylsiloxy-7-methylene-1-vinyl-1,2,3,3a,7,7a-hexahydroindene (19).

A solution of (3aR,4R,4aR,5S,7S,7aS)-5-(3-acetoxy-4-methoxybenzyl)-4-tert-butyldimethylsiloxy-8-methylene-7-(vinyl)octahydroindeno[5,6-d][1,3]dioxole-2-thione (**18**) (24.0 mg, 44 μ mol) in triethyl phosphite (4.4 ml) was heated at reflux for 2 h under argon. After cooling, excess triethyl phosphite was removed using a short column chromatography (hexane). The combined fractions were concentrated *in*

vacuo to afford a residue, which was purified by column chromatography (benzene-ethyl acetate, 100:1) to give (**19**) (16 mg, 78%) as a colorless oil: $[\alpha]_D^{20} +98.4^\circ$ (*c* 1.07, CHCl_3); ^1H NMR (500 MHz, CDCl_3) δ 0.11 (3H, s), 0.16 (3H, s), 0.92 (9H, s), 1.50-1.57 (1H, m), 1.93 (1H, ddd, $J=8.3, 10.1, 12.7$ Hz), 2.11-2.16 (1H, m), 2.30 (2H, s), 2.38-2.50 (2H, m), 2.70 (1H, dd, $J=9.3, 13.7$ Hz), 2.78-2.87 (1H, m), 2.96 (1H, dd, $J=6.0, 13.7$ Hz), 3.80 (3H, s), 4.45 (1H, t, $J=4.9$ Hz), 4.84-4.92 (3H, m), 4.95 (1H, s), 5.73 (1H, ddd, $J=8.8, 10.0, 16.9$ Hz), 5.83 (1H, dd, $J=4.9, 9.7$ Hz), 6.13 (1H, d, $J=9.8$ Hz), 6.85-6.89 (2H, m), 7.01 (1H, dd, $J=2.0, 8.3$ Hz); ^{13}C NMR (125 MHz, CDCl_3) δ -4.08, -3.29, 18.1, 20.7, 26.0, 35.7, 43.9, 45.9, 47.9, 49.6, 55.9, 65.5, 112.2, 113.5, 114.3, 122.8, 126.6, 129.9, 131.1, 135.4, 139.5, 143.3, 144.0, 148.9, 169.0; IR (neat) 2928.2, 2856.8, 1770.8, 1512.3, 1464.1, 1367.6, 1261.5, 1203.6, 1124.6, 1030.0, 881.5, 835.2, 773.5 cm^{-1} ; HREIMS *m/z* calcd for $\text{C}_{28}\text{H}_{40}\text{O}_4\text{Si}$ (M^+), 468.2696, found 468.2700.

(1*S*,3*S*,3*aR*,4*S*,7*aS*)-3-(3-Hydroxy-4-methoxybenzyl)-7-methylene-1-vinyl-1,2,3,3*a*,7,7*a*-hexahydroindene-4-ol (20**).**

20

Tetrabutylammonium fluoride (TBAF) in THF (1 M, 0.43 ml, 0.43 mmol) was added in a stirred solution of (1*S*,3*S*,3*aR*,4*S*,7*aS*)-3-(3-acetoxy-4-methoxybenzyl)-4-*tert*-butyldimethylsiloxy-7-methylene-1-vinyl-1,2,3,3*a*,7,7*a*-hexahydroindene (**19**) (20.0 mg, 43 μmol) in THF (1 ml) at room temperature. After 48 h, the reaction was quenched with saturated aqueous ammonium chloride (0.5 ml), and extracted with ethyl acetate (2 x 15 ml). The combined extracts were washed with saturated aqueous sodium hydrogen carbonate (2 x 5 ml) and brine (5 ml), then dried over Na_2SO_4 . Concentration of the solvent *in vacuo* afforded a residue, which was purified by column chromatography (benzene-ethyl acetate, 4:1) to give **20** (11 mg, 83%) as a colorless oil: $[\alpha]_D^{20} +74.6^\circ$ (*c* 0.35, CHCl_3); ^1H NMR (500 MHz, CDCl_3) δ 1.05 (1H, br), 1.65 (1H, ddd, $J=6.0, 10.1, 16.1$ Hz), 1.98-2.03 (1H, m), 2.04-2.10 (1H, m), 2.44 (1H, dd, $J=6.3, 10.8$ Hz), 2.47-2.55 (1H, m), 2.55-2.61 (1H, m), 2.87 (1H, dd, $J=8.3, 13.7$ Hz), 2.98 (1H, dd, $J=7.2, 13.7$ Hz), 3.86 (3H, s), 4.36 (1H, br), 4.82-4.88 (2H, m), 4.90 (1H, dd, $J=1.9, 10.0$ Hz), 5.01 (1H, s), 5.54 (1H, br), 5.70 (1H, ddd, $J=8.8, 10.0, 18.7$ Hz), 5.93 (1H, dd, $J=5.6, 9.7$ Hz), 6.19 (1H, d, $J=9.7$ Hz), 6.73 (1H, dd, $J=1.9, 8.2$ Hz), 6.76 (1H, d, $J=8.2$ Hz), 6.84 (1H, d, $J=1.9$ Hz); ^{13}C NMR (125 MHz, CDCl_3) δ 36.7, 37.9, 44.4, 44.9, 48.6, 49.9, 55.9, 64.3, 110.4, 113.9, 114.7, 115.8, 119.9, 128.1, 131.5, 135.8, 142.0, 143.7, 144.5, 145.3; IR (neat) 3510, 2924, 1591, 1512, 1442, 1273, 1130, 1008, 904, 80, 761 cm^{-1} ; HREIMS *m/z* calcd for $\text{C}_{20}\text{H}_{24}\text{O}_3$ (M^+), 312.1725, found 312.1729.

(1*S*,3*S*,3*aR*,4*S*,7*aS*)-3-(3-Dichloroacetoxy-4-methoxybenzyl)-1,2,3,3*a*,7,7*a*-hexahydro-7-methylene-1-(vinyl)indene-4-ol (21**).**

A solution of dichloroacetic anhydride (10 μ l, 65 μ mol) in dry dichloromethane (0.2 ml) was added very slowly to a stirred solution of (1*S*,3*S*,3*aR*,4*S*,7*aS*)-3-(3-hydroxy-4-methoxybenzyl)-7-methylene-1-vinyl-1,2,3,3*a*,7,7*a*-hexahydroindene-4-ol (**20**) (17.0 mg, 54 μ mol) in dry dichloromethane (1 ml) containing pyridine (9.0 μ l, 0.1 mmol) at room temperature. The reaction mixture was diluted with ethyl acetate (10 ml), and the organic layer was washed with brine (5 ml), and dried over Na_2SO_4 . Concentration of the solvent *in vacuo* afforded a residue, which was purified by column chromatography (benzene-ethyl acetate, 20:1) to give **21** (12 mg, 52%) as a white cloudy oil: $[\alpha]_{\text{D}}^{20} +71.5^\circ$ (*c* 0.37, CHCl_3); ^1H NMR (500 MHz, CDCl_3) δ 1.02 (1H, d, $J=6.3$ Hz), 1.64 (1H, ddd, $J=6.0, 10.1, 19.0$ Hz), 1.97-2.03 (1H, m), 2.05-2.10 (1H, m), 2.43-2.47 (1H, m), 2.47-2.54 (1H, m), 2.54-2.61 (1H, m), 2.93 (1H, dd, $J=8.6, 13.9$ Hz), 3.03 (1H, dd, $J=6.9, 13.9$ Hz), 4.31-4.36 (1H, m), 4.83-4.88 (2H, m), 4.92 (1H, dd, $J=1.8, 9.9$ Hz), 5.02 (1H, s), 5.70 (1H, ddd, $J=8.8, 9.9, 18.7$ Hz), 5.91-5.96 (1H, m), 6.18 (1H, s), 6.20 (1H, d, $J=9.6$ Hz), 6.91 (1H, d, $J=8.4$ Hz), 7.01 (1H, d, $J=2.0$ Hz), 7.14 (1H, dd, $J=2.0, 8.4$ Hz); ^{13}C NMR (125 MHz, CDCl_3) δ 35.9, 37.8, 44.3, 44.9, 48.6, 49.9, 56.1, 64.0, 64.3, 112.6, 114.0, 116.0, 121.9, 127.6, 128.0, 131.6, 135.4, 138.8, 141.9, 143.5, 148.6, 162.5; IR (neat) 3568, 2926, 2345, 1782, 1512, 1269, 1141, 1028, 815, 407 cm^{-1} ; HREIMS m/z calcd for $\text{C}_{22}\text{H}_{24}\text{Cl}_2\text{O}_4$ (M^+), 422.1052, found 422.1050.

(1*S*,3*S*,3*aS*,7*aS*)-3-(3-Dichloroacetyl-4-methoxybenzyl)-1,2,3,3*a*,7,7*a*-hexahydro-7-methylene-1-(vinyl)indene-4-one (22**).**

Dess-Martin periodinane (34.0 mg, 81 μ mol) was added to a stirred solution of (1*S*,3*S*,3*aR*,4*S*,7*aS*)-3-(3-dichloroacetoxy-4-methoxybenzyl)-1,2,3,3*a*,7,7*a*-hexahydro-7-methylene-1-(vinyl)indene-4-ol (**21**) (17.0 mg, 40 μ mol) in dry dichloromethane (1 ml) at room temperature. After 15 min, the reaction was quenched with 20% aqueous sodium thiosulfate (0.4 ml), and the mixture was extracted with ethyl acetate (2 x 10 ml). The combined extracts were washed with brine (5 ml), then dried over Na_2SO_4 . Concentration of the solvent *in vacuo* afforded a residue, which was purified by column chromatography (hexane-ethyl acetate, 4:1) to give **22** (16 mg, 95%) as a white cloudy oil: $[\alpha]_{\text{D}}^{20} +22.4^\circ$ (*c* 0.83, CHCl_3);

^1H NMR (500 MHz, CDCl_3) δ 1.58-1.64 (1H, m), 1.69-1.77 (1H, m), 2.42-2.51 (1H, m), 2.54-2.63 (2H, m), 2.73-2.78 (1H, m), 2.78-2.82 (1H, m), 3.16 (1H, dd, $J=6.9, 13.6$ Hz), 3.80 (3H, s), 4.90-4.95 (1H, m), 4.96-4.99 (1H, m), 5.29 (1H, d, $J=1.1$ Hz), 5.32 (1H, s), 5.75 (1H, ddd, $J=8.2, 10.1, 18.3$ Hz), 5.92 (1H, dd, $J=0.6, 9.9$ Hz), 6.18 (1H, s), 6.89 (1H, d, $J=8.4$ Hz), 6.97 (1H, d, $J=8.4$ Hz), 6.98 (1H, d, $J=2.1$ Hz), 7.11 (1H, dd, $J=2.1, 8.4$ Hz); ^{13}C NMR (125 MHz, CDCl_3) δ 35.5, 35.6, 36.3, 48.7, 49.1, 51.0, 56.1, 64.0, 112.6, 114.5, 120.1, 122.2, 128.0, 128.3, 134.8, 138.7, 141.6, 142.5, 145.8, 148.8, 162.5, 200.2; IR (neat) 2932, 1784, 1660, 1512, 1442, 1267, 1217, 1141, 1028, 912, 814 cm^{-1} ; HREIMS m/z calcd for $\text{C}_{22}\text{H}_{22}\text{Cl}_2\text{O}_4$ (M^+), 420.0895, found 420.0888.

(1*S*,3*S*,3*aR*,7*aS*)-1,2,3,3*a*,7,7*a*-Hexahydro-3-(3-hydroxy-4-methoxybenzyl)-7-methylene-1-(vinyl)indene-4-one (1) (ottelione A).

1 (ottelione A)

(1*S*,3*S*,3*aS*,7*aS*)-3-(3-Dichloroacetyl-4-methoxybenzyl)-1,2,3,3*a*,7,7*a*-hexahydro-7-methylene-1-(vinyl)indene-4-one (**22**) (13.0 mg, 31 μmol) was dissolved in a solution of 50% aqueous sodium hydrogen carbonate-acetonitrile (1.0 ml, 1:1), and the mixture was stirred for 1 h at room temperature. The mixture was diluted with ethyl acetate (10 ml), and the organic layer was washed with brine (5 ml), then dried over Na_2SO_4 . Concentration of the solvent *in vacuo* afforded a residue, which was purified by column chromatography (benzene-ethyl acetate, 20:1) to give **1** (8.5 mg, 90%) as white cloudy oil: $[\alpha]_{\text{D}}^{25} +17.3^\circ$ (c 0.55, CHCl_3); ^1H NMR (500 MHz, CDCl_3) δ 1.52-1.59 (1H, m), 1.69-1.76 (1H, m), 2.46-2.55 (2H, m), 2.58-2.66 (1H, m), 2.78 (1H, t, $J=8.2$ Hz), 2.86 (1H, dd, $J=5.9, 8.2$ Hz), 3.01-3.08 (1H, m), 3.85 (3H, s), 4.91-4.99 (2H, m), 5.30-5.34 (2H, m), 5.53 (1H, br), 5.76 (1H, ddd, $J=8.2, 10.1, 18.2$ Hz), 5.39 (1H, d, $J=10.0$ Hz), 6.68 (1H, dd, $J=2.0, 8.2$ Hz), 6.75 (1H, d, $J=8.2$ Hz), 6.79 (1H, d, $J=2.0$ Hz), 6.99 (1H, d, $J=9.9$ Hz); ^{13}C NMR (125 MHz, CDCl_3) δ 35.6, 35.8, 46.3, 48.5, 49.0, 51.4, 55.9, 110.4, 114.4, 114.9, 119.9, 120.2, 128.3, 135.1, 141.8, 142.9, 144.6, 145.2, 145.9, 200.4; IR (neat) 3439, 2926, 1658, 1589, 1510, 1440, 1275, 1236, 1130, 1030, 958, 800, 760 cm^{-1} ; HREIMS m/z calcd for $\text{C}_{20}\text{H}_{22}\text{O}_3$ (M^+), 310.1569, found 310.1571.

(1*S*,3*S*,3*aS*,7*aS*)-1,2,3,3*a*,7,7*a*-Hexahydro-3-(3-hydroxy-4-methoxybenzyl)-7-methylene-1-(vinyl)indene-4-one (**2**) (ottelione B).

2 (ottelione B)

Potassium *tert*-butoxide (8.0 mg, 0.13 mmol) was added to a stirred solution of ottelione A (**1**) (8.0 mg, 26 μ mol) in *tert*-butyl alcohol (1 ml) at room temperature. After 2 h, the mixture was diluted with ethyl acetate (10 ml). The organic layer was washed with saturated aqueous ammonium chloride (2 x 2 ml), saturated sodium hydrogen carbonate (2 x 2 ml) and brine (2 ml), then dried over Na₂SO₄. Concentration of the solvent *in vacuo* afforded a residue, which was purified by column chromatography (hexane-ethyl acetate, 4:1) to give a mixture of **2** and **1** (6.3 mg, 79%, **2**:**1**=77:23 determined by 500 MHz ¹H NMR) as colorless viscous oil. Isolation of **2** from this mixture was performed by means of HPLC (DAICEL CHIRALPAK® AD-H, i.d. 4.6 x 250 mm, hexane:2-propanol=4:1, 0.5 ml/min; measurement of UV 254 nm absorbance, ¹R-**2**: 34.7 min, ¹R-**1**: 29.6 min) to give **2** (1.8 mg, 23%) as a white solid, mp 142.2–143.0°C; [α]_D²⁵ –330.0° (*c* 0.18, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 1.59 (1H, ddd, *J*=8.2, 10.2, 13.8 Hz), 1.78 (1H, ddd, *J*=6.7, 9.8, 13.8 Hz), 2.27 (1H, dd, *J*=9.8, 13.9 Hz), 2.34 (1H, dd, *J*=10.2, 13.9 Hz), 2.46–2.56 (2H, m), 2.69–2.77 (1H, m), 3.14 (1H, dd, *J*=3.6, 13.4 Hz), 3.86 (3H, s), 4.97–5.01 (1H, m), 5.06–5.11 (1H, m), 5.30 (1H, s), 5.44 (1H, s), 5.52 (1H, br), 5.74 (1H, ddd, *J*=8.0, 10.2, 18.2 Hz), 5.94 (1H, d, *J*=9.7 Hz), 6.69 (1H, dd, *J*=2.0, 8.1 Hz), 6.76 (1H, d, *J*=8.1 Hz), 6.80 (1H, d, *J*=2.0 Hz), 7.00 (1H, d, *J*=9.7 Hz); ¹³C NMR (125 MHz, CDCl₃) δ 36.9, 37.9, 40.6, 44.5, 50.5, 55.9, 58.3, 110.5, 114.6, 115.3, 117.1, 120.5, 128.7, 134.1, 141.5, 144.8, 144.9, 125.2, 147.6, 200.6; IR (KBr) 3395, 2930, 1664, 1589, 1512, 1440, 1275, 1176, 1126, 1035, 916, 808, 761 cm^{–1}; HRFABMS *m/z* calcd for C₂₀H₂₃O₃ [(M+H)⁺], 311.1647, found 311.1633.

Reference

1. 4-Bromo-1-methoxy-2-(methoxymethoxy)benzene (**9**) was prepared starting from the known 5-bromo-2-methoxyphenol [A. Diaz, J. G. Siro, J. L. Garcia-Navio, J. J. Vaquero, J. Alvarez-Builla, *Synthesis* **1997**, 559] as follows.

Diisopropylethylamine (10.6 ml, 62 mmol) and chloromethylmethylether (3.77 ml, 49 mmol) were added successively to a stirred solution of 5-bromo-2-methoxyphenol (8.40 g, 41 mmol) in dichloromethane (40 ml) at 0°C under argon, and the mixture was gradually warmed up to room temperature. After 4 h, the reaction was quenched with saturated ammonium chloride (40 ml), and the resulting mixture was extracted with ether (2 x 400 ml). The combined extracts were washed successively with 3% HCl (2 x 100 ml), saturated aqueous sodium hydrogen carbonate (2 x 100 ml), and brine (2 x 100 ml), then dried over Na₂SO₄. Concentration of the solvent *in vacuo* afforded a residue, which was purified by column chromatography (hexane-ethyl acetate, 4:1) to give **9** (8.90 g, 88%) as a colorless oil: ¹H NMR (250 MHz, CDCl₃) δ 3.51 (3H, s), 3.86 (3H, s), 5.21 (2H, s), 6.76 (1H, d, *J*=8.7 Hz), 7.10 (1H, dd, *J*=2.4, 8.7 Hz), 7.30 (1H, d, *J*=2.4 Hz); IR (neat) 2999, 2957, 2905, 2835, 1587, 1502, 1462, 1388, 1321, 1298, 1253, 1224, 1199, 1178, 1155, 1132, 1082, 1028, 991, 923, 850, 800, 763, 621 cm⁻¹; EIMS *m/z* 248 [(*M*+2)⁺, ⁸¹Br], 246 (*M*⁺, ⁷⁹Br).