Supporting Information

Construction of 8-Membered Rings by Olefin Geometry-Dependent Internal Alkylation: First Asymmetric Total Syntheses of (+)-3-(*E*)- and (+)-3-(*Z*)- Pinnatifidenyne

Hyongsu Kim, Won Jun Choi, Jaeyoon Jung, Sanghee Kim, and Deukjoon Kim*

[*] Prof. Deukjoon Kim, Hyongsu Kim, Won Jun Choi and Jaeyoon Jung

College of Pharmacy, Seoul National University

Fax: +82-2-888-0649. E-mail: deukjoon@plaza.snu.ac.kr

Prof. Sanghee Kim

Natural Products Research Institute

College of Pharmacy, Seoul National University

Experimentals

(E)-Allylic Chloride 1a. ^1H NMR (500 MHz, CDCl_3) δ 5.79 (ddd, $J = 15.1, 6.9, 6.9$ Hz, 1 H), 5.63 (ddd, $J = 15.1, 7.2, 7.2$ Hz, 1 H), 4.13 (s, 2 H), 4.03 (d, $J = 6.9$ Hz, 1 H), 3.51 (dd, $J = 6.3, 6.3$ Hz, 1 H), 3.02 (s, 3 H), 2.96 (s, 3 H), 2.16 (ddd, $J = 7.2, 7.2, 7.2$ Hz, 2 H), 1.72 (dddd, $J = 7.2, 7.2, 6.3, 6.3$ Hz, 2 H); ^{13}C NMR (100 MHz, CDCl_3) δ 169.2, 135.1, 126.4, 70.5, 70.2, 45.3, 36.3, 35.4, 28.7, 28.5; IR (neat) 3419, 2919, 1651, 1558, 1116, 668, 468 cm^{-1}

(Z)-Allylic Chloride 1b. ^1H NMR (500 MHz, CDCl_3) δ 5.61-5.67 (m, 2 H), 4.14 (s, 2 H), 4.11 (d, $J = 7.1$ Hz, 1 H), 3.52 (dd, $J = 6.2, 6.2$ Hz, 1 H), 3.01 (s, 3 H), 2.96 (s, 3 H), 2.23 (ddd, $J = 7.1, 7.1, 7.1$ Hz, 2 H), 1.72 (dddd, $J = 7.1, 7.1, 6.2, 6.2$ Hz, 2 H); ^{13}C NMR (100 MHz, CDCl_3) δ 169.2, 134.3, 125.9, 70.4, 70.1, 39.4, 36.3, 35.4, 29.1, 23.6; IR (neat) 3478, 2936, 1651 cm^{-1}

Preparation of Tetrahydropyran 2. To a solution of (*E*)-allylic chloride **1a** (25.8 mg,

0.117 mmol) in THF (24 mL, 0.007 M) was added KHMDS (0.7 mL, 0.5 M solution in toluene, 0.35 mmol) dropwise at 80 $^{\circ}\text{C}$. After being stirred for 5

min, the reaction mixture was cooled to rt, quenched with saturated aqueous NH_4Cl , and poured into EtOAc (100 mL). The layers were separated, and aqueous layer was extracted twice with EtOAc (50 mL). The combined organic layers were washed with brine and dried over anhydrous Na_2SO_4 . Concentration of the solution *in vacuo*, and purification of the residue by column chromatography (silica gel, hexane/ethyl acetate, 2/1) afford tetrahydropyran **2** as a colorless oil (17.5 mg, 82%): ^1H NMR (500 MHz, CDCl_3) δ 5.71 (ddd, $J = 17.5, 10.5, 7.1$ Hz, 1 H), 5.10 (d, $J = 17.5$ Hz, 1 H), 5.04 (d, $J = 10.5$ Hz, 1 H),

4.04 (dddd, $J = 11.0, 4.4, 2.2, 2.2$ Hz, 1 H), 3.90 (d, $J = 9.8$ Hz, 1 H), 3.42 (ddd, $J = 11.0, 11.0, 2.7$ Hz, 1 H), 3.07 (s, 3 H), 2.95 (s, 3 H), 2.61-2.72 (m, 1 H), 1.93-2.00 (m, 1 H), 1.70-1.83 (m, 1 H), 1.54-1.69 (m, 1 H), 1.47 (dddd, $J = 12.3, 12.3, 12.3, 4.0$ Hz, 1H); ^{13}C NMR (75 MHz, CDCl_3) δ 169.1, 138.2, 115.9, 78.9, 68.2, 41.0, 37.1, 35.7, 28.4, 25.1.

Preparation of Oxocene 3. To a solution of (Z)-allylic chloride **1b** (16.3 mg, 0.074

mmol) in THF (15 mL, 0.005 M) were added KHMDS (0.45 mL, 0.5 M solution in THF, 0.225 mmol) dropwise at 50 °C. After being stirred for 5

min, the reaction mixture was cooled to rt, and quenched with saturated aqueous NH_4Cl , poured into EtOAc (100 mL). The layers were separated, and aqueous layer was extracted twice with EtOAc (50 mL), the combined organic layers were washed with brine dried over anhydrous Na_2SO_4 . Concentration *in vacuo*, and Purification of the residue by column chromatography (silica gel, hexane/ethyl acetate, 2/1) afford oxocene **3** (11.7 mg, 86%) and tetrahydropyran **2** (1.9 mg, 14%): ^1H NMR (500 MHz, CDCl_3) δ 5.79-5.86 (m, 2 H), 4.16 (dd, $J = 9.8, 2.2$ Hz, 1 H), 3.89 (ddd, $J = 11.9, 5.4, 4.0$ Hz, 1 H), 3.56 (ddd, $J = 11.9, 8.6, 3.6$ Hz, 1 H), 3.10 (s, 3 H), 2.96 (s, 3 H), 2.77 (ddd, $J = 14.5, 9.9, 6.6$ Hz, 1 H), 2.36-2.42 (m, 1 H), 2.25 (ddd, $J = 14.5, 7.2, 2.8$ Hz, 1 H), 2.10-2.14 (m, 1 H), 1.81-1.86 (m, 1 H), 1.51-1.56 (m, 1 H); ^{13}C NMR (100 MHz, CDCl_3) δ 170.5, 132.0, 127.4, 77.9, 68.2, 36.9, 35.8, 30.5, 29.3, 24.0; IR (neat) 3501, 2930, 1651, 1108 cm^{-1} ;

Preparation of SEM Ether 8. To a cooled (0 °C) solution of epoxyl alcohol **7** (2.5 g, 25 mmol) in THF (50 mL), was added NaH (1.21 g, 60% dispersion in mineral oil, 30 mmol).

The reaction mixture was stirred for 30 min at 0 °C, and SEMCl (6.3 g, 37.5 mmol) was added dropwise. After being stirred for 2.5 h at rt, the reaction mixture was quenched with saturated aqueous NH₄Cl, poured into diethyl ether (200 mL) and the layers were separated. The aqueous layer was extracted twice with diethyl ether, the combined organic layers were washed with brine, dried over anhydrous Na₂SO₄, and concentrated *in vacuo*. Purification of the residue by column chromatography (silica gel, *n*-hexane/ethyl acetate, 20/1) afforded SEM ether **8** as a colorless oil (4.3 g, 90%): $[\alpha]_D^{25} = +56.5$ (*c* 1.69, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 5.79 (ddd, *J* = 17.4, 10.4, 17.4 Hz, 1 H), 5.36 (ddd, *J* = 17.4, 1.4, 1.4 Hz, 1 H), 5.32 (ddd, *J* = 10.4, 1.2, 1.2 Hz, 1 H), 4.71 (s, 3 H), 4.08 (dd, *J* = 7.1, 4.3 Hz, 1 H), 3.71 (ddd, *J* = 9.8, 9.8, 6.8 Hz, 1 H), 3.59 (ddd, *J* = 9.8, 9.8, 6.8 Hz, 1 H), 3.07 (ddd, *J* = 4.1, 4.1, 2.7 Hz, 1 H), 2.80 (dd, *J* = 5.2, 4.0 Hz, 1 H), 2.71 (dd, *J* = 5.2, 2.6 Hz, 1 H), 0.92-0.96 (m, 2 H), 0.03 (s, 9 H); ¹³C NMR (100 MHz, CDCl₃) δ 134.0, 118.8, 92.4, 75.9, 64.9, 52.7, 44.4, 17.8, -1.6.

Preparation of Homopropargylic Alcohol 9. To a cooled (-78 °C) solution of 2-prop-2-ynyloxy-tetrahydropyran (8.0 g, 57 mmol) in THF (100 mL), was added *n*-BuLi (35 mL, 1.6 M in *n*-hexane, 56 mmol) and the reaction mixture was stirred for 30 min at the same temperature. Epoxide **8** (5.2 g, 22.6 mmol) and BF₃·Et₂O (8 mL, 56 mmol) were added immediately. The reaction mixture was stirred for 30 min at -78 °C, quenched with

saturated aqueous NH_4Cl , poured into diethyl ether (300 mL), and stirred for 1 h at rt. The layers were separated, and the aqueous layer was extracted twice with diethyl ether. The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4 , and concentrated *in vacuo*. Purification of the residue by column chromatography (silica gel, *n*-hexane/ethyl acetate, 5/1) afforded homopropargylic alcohol **9** as a colorless oil (7.5 g, 90%): $[\alpha]_D^{25} = +61.7$ (*c* 1.70, CHCl_3); [for two diastereomers] ^1H NMR (500 MHz, CDCl_3) δ 5.75-5.72 (m, 1 H), 5.37 (d, $J = 11.0$ Hz, 1 H), 5.36 (d, $J = 17.0$ Hz, 1 H), 4.82 (dd, $J = 3.3, 3.3$ Hz, 1 H), 4.72 (d, $J = 6.9$ Hz, 1 H), 4.70 (d, $J = 6.9$ Hz, 1 H), 4.20-4.32 (m, 2 H), 4.13 (dd, $J = 7.6, 4.5$ Hz, 1 H), 3.82-3.87 (m, 2 H), 3.80 (ddd, $J = 9.8, 9.8, 6.9$ Hz, 1 H), 3.52-3.58 (m, 2 H), 2.60 (dd, $J = 3.7, 3.7$ Hz, 1 H), 2.46-2.48 (m, 2 H), 1.5-1.87 (m, 6 H), 0.93-0.93 (m, 2 H), 0.04 (s, 9 H); [for two diastereomers] ^{13}C NMR (100 MHz, CDCl_3) δ 133.6, 119.9, 96.4, 92.2, 82.4, 79.3, 77.8, 71.5, 65.2, 61.6, 54.3, 30.0, 25.1, 22.9, 18.8, 17.8, -1.6; IR (neat) 3450 (br), 2950 cm^{-1} ; HRMS (CI) found 371.2251 $[(\text{M}+\text{H})^+]$; calcd for $\text{C}_{19}\text{H}_{35}\text{O}_5\text{Si}$, 371.2254]

Preparation of DMB Ether 10. To a cooled (0 °C) solution of alcohol **9** (5.2 g, 14 mmol) in THF/DMF (3/1, 100 mL) was added NaH (1.7 g, 60% dispersion in mineral oil, 42 mmol). The reaction mixture was stirred for 30 min at 0 °C, and 3,4-dimethoxybenzyl bromide (DMBBr) (4.9 g, 21 mmol) was added. After being stirred for 1.5 h at rt, the

reaction mixture was quenched with saturated aqueous NH_4Cl , poured into diethyl ether (200 mL) and the layers were separated. The aqueous layer was extracted twice with diethyl ether. The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4 , and concentrated *in vacuo*. Purification of the residue by column chromatography (silica gel, hexane/ethyl acetate, 5/1) afforded DMB ether **10** as a colorless oil (6.7 g, 92%): $[\alpha]_D^{25} = +13.3$ (c 0.23, CHCl_3); [for two diastereomers] ^1H NMR (500 MHz, CDCl_3) δ 6.96 (s, 1 H), 6.90 (d, $J = 8.1$ Hz, 1 H), 6.83 (d, $J = 8.1$ Hz, 1 H), 5.82 (ddd, $J = 17.6, 10.3, 7.7$ Hz, 1 H), 5.34 (d, $J = 17.6$ Hz, 1 H), 5.37 (d, $J = 10.3$ Hz, 1 H), 4.82 (dd, $J = 3.3, 3.3$ Hz, 1 H), 4.72 (d, $J = 6.9$ Hz, 2 H), 4.69 (d, $J = 6.9$ Hz, 2 H), 4.66 (s, 2 H), 4.20-4.32 (m, 3 H), 3.90 (s, 3 H), 3.88 (s, 3H), 3.81-3.86 (m, 1 H), 3.69-3.75 (m, 1 H), 3.66 (ddd, $J = 5.9, 5.9, 4.8$ Hz, 1 H), 3.51-3.60 (m, 2 H), 2.53 (m, 2 H), 1.52-1.84 (m, 6 H), 0.94 (dd, $J = 8.1, 8.1$ Hz, 2 H), 0.03 (s, 9 H); [for two diastereomers] ^{13}C NMR (100 MHz, CDCl_3) δ 148.8, 148.4, 134.6, 130.8, 120.1, 119.2, 111.1, 110.7, 96.4, 92.2, 83.2, 79.21, 79.17, 78.0, 77.26, 77.25, 72.47, 72.43, 65.1, 61.8, 55.7, 55.6, 54.3, 30.1, 25.2, 21.3, 19.0, 17.9, -1.6; IR (neat) 2948, 1515, 1463, 1264, 1114, 1026, 937, 860, 837 cm^{-1} ; EIMS m/z (relative intensity) 520 (M^+ , 30); Anal. Calcd for $\text{C}_{28}\text{H}_{44}\text{O}_7\text{Si}$: C, 64.58; H, 8.52; found C, 64.00; H, 8.66.

Preparation of *cis*-Alkene 11. To a solution of propargylic ether **10** (3.2 g, 6.1 mmol) in

stirred for 2.5 h. The reaction mixture was cooled to $-20\text{ }^{\circ}\text{C}$, and water was added to quench the excess 9-BBN. The reaction mixture was stirred vigorously for 10 min, then 3 N NaOH (30 mL) and H_2O_2 (20 mL) were added cautiously at $-20\text{ }^{\circ}\text{C}$. The reaction mixture was stirred for 10 h at rt and diethyl ether (100 mL) was added. The layers were separated, and the aqueous layer was extracted twice with diethyl ether (100 mL). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4 , and concentrated *in vacuo*. Purification of the residue by column chromatography (silica gel, *n*-hexane/ethyl acetate, 2/1) afforded alcohol **12** as colorless oils (2.14 g, 83%): $[\alpha]_{\text{D}}^{25} = -32.3$ (*c* 1.22, CHCl_3); **[for two diastereomers]** ^1H NMR (500 MHz, CDCl_3) δ 6.88 (s, 1 H), 6.84 (d, $J = 8.2$ Hz, 1 H), 6.80 (d, $J = 8.2$ Hz, 1 H), 5.60-5.70 (m, 2 H), 4.76 (d, $J = 5.8$ Hz, 1 H), 4.70 (d, $J = 5.8$ Hz, 1 H), 4.57-4.61 (m, 1 H), 4.60 (d, $J = 11.4$ Hz, 1 H), 4.50 (d, $J = 11.4$ Hz, 1 H), for one diastereomer [4.28 (dd, $J = 11.8, 4.5$ Hz) + 4.10 (dd, $J = 11.8, 4.9$ Hz), 1 H], for the other [4.21 (dd, $J = 12.6, 3.9$ Hz) + 4.02 (dd, $J = 12.6, 5.1$ Hz), 1 H], 3.81-3.89 (m, 2 H), 3.86 (s, 3 H), 3.85 (s, 3 H), 3.68-3.74 (m, 3 H), 3.52-3.59 (m, 2 H), 3.45-3.49 (m, 1 H), 2.82-2.84 (m, 1 H), 2.27-2.40 (m, 2 H), 1.48-1.82 (m, 8 H), 0.93 (dd, $J = 8.5, 8.5$ Hz, 2 H), 0.00 (s, 9 H); **[for two diastereomers]** ^{13}C NMR (100 MHz, CDCl_3) δ 144.65, 148.26, 130.76, 130.75, 129.32, 129.13, 127.61, 119.95, 119.93, 110.90, 110.53, 97.95, 97.19, 94.70, 80.38, 80.32, 76.51, 76.44, 72.01, 71.98, 65.48, 62.66, 62.33, 62.14, 61.73, 58.79, 55.61, 55.52, 32.69, 32.65, 30.40, 30.30, 28.79, 28.75, 25.18, 25.16, 19.35, 19.05, 17.81, -1.70; IR (neat) 3470 (br), 2947, 1595, 1516, 1463, 1264, 1028, 860, 836 cm^{-1} ; Anal. Calcd for $\text{C}_{28}\text{H}_{48}\text{O}_8\text{Si}$: C, 62.19; H, 8.95; found 61.97; H, 9.14

Preparation of PMB Ether 13. To a cooled (0 °C) solution of alcohol **12** (1.4 g, 2.6 mmol) in THF/DMF (1/1, 30 mL) was added NaH (0.32 g, 60% dispersion in mineral oil, 7.8 mmol). The reaction mixture was stirred for 30 min at 0 °C, and PMBBr (0.9 g, 3.9 mol) was added. After being stirred for 13 h at rt, the reaction mixture was quenched with H₂O at 0 °C, poured into saturated aqueous NH₄Cl/diethyl ether (1/4, 250 mL) and the layers were separated. The aqueous layer was extracted twice with diethyl ether. The combined organic layers were washed with brine, dried over anhydrous Na₂SO₄, filtered, and concentrated *in vacuo*. Purification of the residue by column chromatography (silica gel, *n*-hexane/ethyl acetate, 10/1 to 5/1) afforded PMB ether **13** as colorless oils (1.6 g, 94%): $[\alpha]_D^{25} = -12.0$ (*c* 1.34, CHCl₃); **[for two diastereomers]** ¹H NMR (500 MHz, CDCl₃) δ 7.26 (d, *J* = 8.6 Hz, 2 H), 6.91 (s, 1 H), 6.88 (d, *J* = 8.6 Hz, 2 H), 6.85 (d, *J* = 8.1 Hz, 1 H), 6.81 (d, *J* = 8.1 Hz, 1 H), 5.63-5.71 (m, 2 H), 4.78 (d, *J* = 6.8 Hz, 1 H), 4.70 (d, *J* = 6.8 Hz, 1 H), 4.60-4.63 (m, 2 H), 4.48 (d, *J* = 11.4 Hz, 1 H), 4.44 (s, 2 H), 4.23-4.30 (m, 2 H), 4.05-4.12 (m, 2 H), 3.88 (s, 3 H), 3.87 (s, 3 H), 3.81 (s, 3 H), 3.84-3.91 (m, 2 H), 3.67 (dd, *J* = 9.5, 8.5 Hz, 1 H), 3.63 (dd, *J* = 9.5, 8.5 Hz, 1 H), 3.48-3.60 (m, 4 H), 2.25-2.41 (m, 2 H), 1.50-1.88 (m, 8 H) 0.93 (dd, *J* = 8.5, 8.5 Hz, 2 H), 0.02 (s, 9 H); **[for two diastereomers]** ¹³C NMR (100 MHz, CDCl₃) δ 158.85, 148.62, 148.15, 131.05, 131.03, 130.25, 129.48, 129.44, 128.94, 127.53, 119.83, 119.81, 113.44, 110.85, 110.49, 97.71, 97.46, 94.45, 80.58, 80.47, 75.54, 75.51, 72.33, 71.76, 71.73, 66.47, 65.10, 62.66,

62.55, 61.93, 61.78, 55.58, 55.47, 54.90, 30.76, 30.39, 30.52, 28.70, 28.66, 25.19, 19.27, 19.17, 17.77, -1.66; IR (neat) 2948, 1612, 1515, 1463, 1247, 1095, 1030, 836, 764 cm^{-1} ; Anal. calcd for $\text{C}_{28}\text{H}_{44}\text{O}_7\text{Si}$: C, 64.58; H, 8.52; found 64.00; H, 8.66.

Preparation of Amide 14. [SEM Deprotection] To a mixture of SEM ether **13** (310 mg, 0.47 mmol) and 4 Å molecular sieves (2.5 g) was added TBAF (4.7 mL, 1 M solution in THF, 4.7 mmol) at 0 °C. The reaction mixture was concentrated *in vacuo*, DMPU (10 mL) was added, and the mixture was stirred for 5 h at 80 °C. The reaction mixture was then cooled, diluted with Et_2O (50 mL), and saturated aqueous NH_4Cl , and the layers were separated. The aqueous layer was extracted twice with diethyl ether. The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4 , and concentrated *in vacuo*. Purification of the residue by column chromatography (silica gel, *n*-hexane/ethyl acetate, 5/1 to 2/1) afforded the secondary alcohol as a colorless oil (189 mg, 76%): $[\alpha]_D^{25} = -22.6$ (*c* 1.00, CHCl_3); [for two diastereomers] ^1H NMR (500 MHz, CDCl_3) δ 7.26 (d, $J = 8.5$ Hz, 2 H), 6.90 (s, 1 H), 6.89 (d, $J = 8.5$ Hz, 2 H), 6.87 (d, $J = 8.1$ Hz, 1 H), 6.83 (d, $J = 8.1$ Hz, 1 H), 5.71-5.75 (m, 2 H), [for one diastereomer 4.66 (dd, $J = 3.4, 3.4$ Hz) + for the other 4.63 (dd, $J = 3.6, 3.6$ Hz) 1 H], 4.57 (d, $J = 11.3$ Hz, 1 H), 4.50 (d, $J = 11.3$ Hz, 1 H), 4.46 (s, 2 H), [for one diastereomer: 4.31 (dd, $J = 12.5, 5.8$ Hz) + 4.14 (dd, $J = 12.5, 7.1$ Hz) 1 H], [for the other: 4.28 (dd, $J = 12.5, 5.1$ Hz) + 4.11 (dd, $J = 12.5, 6.6$ Hz) 1 H], 3.83-3.89 (m, 2 H), 3.89 (s, 6 H), 3.81 (s, 3 H), 3.62-3.71 (m, 2 H), 3.50-3.53 (m, 1 H),

3.41 (ddd, $J = 5.5, 4.6, 4.6$ Hz 1 H), [for one diastereomer 3.23 (d, $J = 3.1$ Hz) + for the other 3.20 (d, $J = 3.3$ Hz) 1 H], 2.38-2.54 (m, 2 H), 1.91-1.94 (m, 1 H), 1.71-1.84 (m, 3 H), 1.51-1.61 (m, 4 H) ; [for two diastereomers] ^{13}C NMR (100 MHz, CDCl_3) δ 159.2, 148.9, 148.5, 131.02, 130.15, 130.13, 129.67, 129.65, 129.22, 127.7, 120.3, 113.7, 111.2, 110.8, 97.9, 97.7, 81.4, 72.8, 71.23, 71.17, 68.43, 68.39, 62.8, 62.6, 62.19, 62.09, 55.9, 55.8, 55.2, 32.24, 32.21, 30.56, 30.50, 27.8, 27.7, 25.4, 19.42, 19.34; IR (neat) 3469 (br), 2939, 1611, 1515, 1467, 1247, 1080, 1031, 814, 763 cm^{-1} ; HRMS (CI) found 531.2961 $[(\text{M}+\text{H})^+]$; calcd for $\text{C}_{30}\text{H}_{43}\text{O}_8$: 531.2958; Anal. calcd for $\text{C}_{30}\text{H}_{43}\text{O}_8$: C, 67.77; H, 8.15; found 67.12; H, 8.09. **[O-Alkylation]** To a cooled (0 °C) solution of the above alcohol (0.99 g, 1.9 mmol) in THF (30 mL) was added NaH (0.1 g, 60% dispersion in mineral oil, 3.4 mmol). The reaction mixture was stirred for 10 min at 0 °C, and 2-bromo-*N,N*-dimethylacetamide (0.34 g, 2.1 mmol) was added. After being stirred for 8 h at rt, the reaction mixture was quenched with H_2O at 0 °C, and poured into saturated aqueous NH_4Cl /dichloromethane (1/4, 200 mL). The layers were separated, and the aqueous layer was extracted twice with dichloromethane, and the combined organic layers were washed with brine, dried over anhydrous Na_2SO_4 , and concentrated *in vacuo*. Purification of the residue by column chromatography (silica gel, *n*-hexane/ethyl acetate, 2/1 to 1/1) afforded amide **14** as a colorless oil (1.15 g, 99%): $[\alpha]^{25}_{\text{D}} = -16.1$ (c 1.11, CHCl_3); [for two diastereomers] ^1H NMR (500 MHz, CDCl_3) δ 7.26 (d, $J = 8.6$ Hz, 2 H), 6.79-6.90 (m, 5 H), 5.62-5.70 (m, 2 H), 4.60 (brs, 1 H), 4.57 (d, $J = 11.4$ Hz, 1 H), 4.49 (d, $J = 11.4$ Hz, 1 H), 4.31 (s, 2 H), 4.26 (d, $J = 13.3$ Hz, 1 H), 4.22-4.29 (m, 1 H), 4.18 (d, $J = 13.3$ Hz, 1 H), 4.05-4.12 (m, 1 H), 3.87 (s, 6 H), 3.80-3.87 (m, 2 H), 3.78 (s, 3 H), 3.73 (ddd, $J = 7.9,$

3.5, 3.5 Hz, 1 H), 3.55-3.65 (m, 3 H), 3.47-3.50 (m, 2 H), 2.920 (s, 3 H), 2.917 (s, 3 H), 2.40-2.45 (m, 1 H), 2.30-2.34 (m, 1 H), 1.80-1.89 (m, 3 H), 1.65-1.75 (m, 1 H), 1.49-1.58 (m, 4 H); [for two diastereomers] ^{13}C NMR (100 MHz, CDCl_3) δ 168.52, 158.48, 148.25, 147.82, 130.66, 130.64, 129.95, 129.02, 128.66, 127.25, 127.24, 119.61, 119.59, 113.03, 110.66, 110.20, 97.26, 97.04, 79.72, 79.64, 78.05, 71.89, 71.35, 69.02, 66.00, 62.23, 61.50, 61.40, 55.20, 55.13, 54.50, 35.69, 34.59, 30.42, 30.03, 30.015, 28.05, 24.84, 18.90, 18.84; IR (neat) 2938, 1651, 1515, 1463, 1247, 1093, 1030, 813 cm^{-1} ; EIMS m/z (relative intensity) [530 ($\text{M}-\text{CH}_2\text{CONMe}_2$) $^+$, 20]; Anal. calcd for $\text{C}_{34}\text{H}_{49}\text{NO}_9$: C, 66.32; H, 8.02; N, 2.27; found C, 65.53; H, 7.99, N, 2.36.

Preparation of Chloro Amide 15. To a cooled (0 $^{\circ}\text{C}$) solution of amide **14** (1.1 g, 1.8 mmol) in dichloromethane (36 mL) and pH 7.4 phosphate buffer solution (4 mL) was added DDQ (0.4 g, 1.8 mmol). The reaction mixture was stirred for 1 h and saturated aqueous NaHCO_3 (5 mL) was added. The resulting dark red mixture was stirred vigorously for 2 h and the layers were separated. The aqueous layer was extracted twice with dichloromethane. The combined organic layers were dried over anhydrous Na_2SO_4 , concentration *in vacuo* and purification of the residue by column chromatography (silica gel, *n*-hexane/ethyl acetate, 1/1 to ethyl acetate/methanol, 10/1) gave the secondary

alcohol as a colorless oil (0.71 g, 85%); $[\alpha]_D^{25} = +2.3$ (c 1.22, MeOH); [for two diastereomers] ^1H NMR (500 MHz, CDCl_3) δ 7.23 (d, $J = 8.5$ Hz, 2 H), 6.85 (d, $J = 8.5$ Hz, 2 H), 5.71-5.78 (m, 1H), 5.62-5.67 (m, 1 H), 4.93 (br d, $J = 6.2$ Hz, 1 H), 4.62 (d, $J = 3.8$ Hz, 1 H), 4.45 (d, $J = 11.5$ Hz, 1 H), 4.38 (d, $J = 11.5$ Hz, 1 H), 4.31 (d, $J = 15.5$ Hz, 1 H), 4.25 (ddd, $J = 12.2, 7.0, 7.0$ Hz, 1 H), 4.04-4.11 (m, 1 H), 4.03 (d, $J = 15.5$ Hz, 1 H), 3.84 (dd, $J = 8.9, 8.9$ Hz, 1 H), 3.78 (s, 3 H), 3.53-3.63 (m, 4H), 3.48 (dd, $J = 9.7, 4.8$ Hz, 1 H), 2.92 (s, 3 H), 2.83 (s, 3 H), 2.23-2.33 (m, 2 H), 1.76-1.87 (m, 3 H), 1.66-1.69 (m, 1 H), 1.49-1.56 (m, 4 H); [for two diastereomers] ^{13}C NMR (100 MHz, CDCl_3) δ 170.74, 170.69, 159.0, 130.5, 130.4, 130.3, 129.2, 127.31, 127.26, 113.6, 97.8, 97.6, 82.70, 82.66, 72.4, 71.6, 68.2, 66.1, 62.71, 62.69, 62.2, 62.0, 55.12, 35.52, 35.48, 35.46, 30.51, 30.49, 30.3, 29.8, 29.7, 25.3, 19.4, 19.3; IR (neat) 3332 (br), 2940, 1650, 1513, 1457, 1344, 1249, 1177, 1113, 1030, 816 cm^{-1} ; HRMS (CI) found 466.2804 $[(\text{M}+\text{H})^+]$; calcd for $\text{C}_{25}\text{H}_{40}\text{O}_7$: 466.2805]. **[Chlorination]** To a stirred solution of the above hydroxy amide (352 mg, 0.76 mmol) in dry CCl_4 (20 mL) were added pyridine (2 mL) and trioctylphosphine (1.56 g, 3.8 mmol) at rt. After stirring the mixture for 20 min, the reaction mixture was stirred for 4 h in an 80 $^\circ\text{C}$ oil bath. After being cooled to rt, the reaction mixture was concentrated *in vacuo*. Purification of the residue by column chromatography (silica gel, *n*-hexane/ethyl acetate, 2/1 to 1/1) gave chloro amide **15** as a colorless oil (318 mg, 87%); $[\alpha]_D^{25} = -21.0$ (c 1.61, MeOH); [for two diastereomers] ^1H NMR (500 MHz, CDCl_3) δ 7.26 (d, $J = 8.6$ Hz, 2 H), 6.88 (d, $J = 8.6$ Hz, 2 H), 5.71-5.76 (m, 1H), 5.62-5.69 (m, 1 H), 4.63 (ddd, $J = 3.9, 3.0, 3.0$ Hz, 1 H), 4.441 (s, 1 H), 4.436 (s, 1 H), 4.25-4.30 (m, 1 H), 4.24 (d, $J = 13.7$ Hz, 1 H), 4.19 (d, $J = 13.7$ Hz, 1 H), 4.05-4.11 (m, 2 H), 3.87 (ddd, $J =$

11.1, 7.9, 2.9 Hz, 1 H), 3.81 (s, 3 H), 3.78 (ddd, $J=8.2, 4.2, 4.2$ Hz, 1 H), 3.55-3.65 (m, 2H), 3.49-3.53 (m, 1 H), 2.97 (s, 3 H), 2.94 (s, 3 H), 2.70 (br dd, $J = 15.0, 2.6$ Hz, 1 H), 2.53 (dddd, $J = 15.0, 9.8, 9.8, 2.6$ Hz, 1 H), 2.05-2.10 (m, 1H), 1.82 -1.88 (m, 2H), 1.66-1.75 (m, 1 H), 1.51-1.61 (m, 4 H); [for two diastereomers] ^{13}C NMR (100 MHz, CDCl_3) δ 168.6, 158.9, 130.1, 129.1, 128.7, 128.5, 113.5, 97.9, 97.6, 79.7, 72.3, 69.6, 69.5, 65.9, 62.82, 62.76, 62.64, 62.5, 62.1, 61.9, 55.0, 36.2, 35.2, 31.2, 30.43, 30.36, 30.2, 25.2, 19.4, 19.2; IR (neat) 2940, 1656, 1513, 1458, 1249, 1177, 1112, 1031, 817 cm^{-1} ; HRMS (CI) found 484.2467 $[(\text{M}+\text{H})^+]$; calcd for $\text{C}_{25}\text{H}_{37}\text{NO}_6^{35}\text{Cl}$: 484.2466].

Preparation of Cyclization Substrate 6. [THP Deprotection] To a solution of crude THP-ether **15** (314 mg, 0.79 mmol) in ethanol (20 mL, 98%) was added *p*-toluenesulfonic acid monohydrate (30 mg, 0.15 mmol) at rt. The reaction mixture was stirred for 1 h, triethylamine (1 mL) was added, and the mixture was concentrated *in vacuo*. Purification of the residue by column chromatography (silica gel, ethyl acetate/methanol, 20/1 to 5/1) gave the allylic alcohol as a colorless oil (257 mg, 99%); $[\alpha]_{\text{D}}^{25} = -24.5$ (c 1.19, MeOH); ^1H NMR (500 MHz, CDCl_3) δ 7.27 (d, $J = 8.6$ Hz, 2 H), 6.90 (d, $J = 8.6$ Hz, 2 H), 5.78-5.83 (m, 1H), 5.56-5.61 (m, 1 H), 4.47 (d, $J=11.5$ Hz, 2 H), 4.43 (d, $J=11.5$ Hz, 2 H), 4.30 (d, $J=12.6$ Hz, 1 H), 4.28 (d, $J = 13.6$ Hz, 1 H), 4.12 (d, $J = 13.6$ Hz, 1 H), 4.04-4.11

(m, 2 H), 3.82 (s, 3 H), 3.78 (ddd, $J = 8.2, 4.2, 4.2$ Hz, 1 H), 3.54-3.64 (m, 2H), 2.94-3.00 (m, 1 H), 2.95 (s, 3 H), 2.94 (s, 3 H), 2.41 (ddd, $J = 14.5, 7.2, 7.2$ Hz, 1 H), 2.09 (dddd, $J = 15.0, 7.8, 7.8, 5.3$ Hz, 1 H), 1.87 (dddd, $J = 15.0, 8.0, 8.0, 5.3$ Hz, 1 H); ^{13}C NMR (100 MHz, CDCl_3) δ 168.9, 158.9, 131.6, 130.0, 129.2, 127.1, 113.5, 79.4, 72.2, 69.1, 65.8, 62.6, 57.7, 55.0, 36.1, 35.2, 31.0, 29.9 ; IR (neat) cm^{-1} ; **[Bromination]** To a cooled (-20°C) solution of the above allylic alcohol (234 mg, 0.59 mmol) in dry dichloromethane (10 mL) were added pyridine (1 mL), carbon tetrabromide (390 mg, 1.17 mmol) and triphenylphosphine (384 mg, 1.46 mmol). After being stirred for 30 min, the reaction mixture was concentrated *in vacuo*. Rapid purification of the residue by column chromatography (silica gel, *n*-hexane/acetone, 5/1 to 3/1) gave allylic bromide **6** as a colorless oil (241 mg, 89%); ^1H NMR (300 MHz, CDCl_3); ^1H NMR (500 MHz, CDCl_3) δ 7.26 (d, $J = 8.8$ Hz, 2 H), 6.88 (d, $J = 8.8$ Hz, 2 H), 5.88 (ddd, $J = 10.3, 10.3, 8.5$ Hz, 1 H), 5.68 (ddd, $J = 10.3, 7.6, 7.6$ Hz, 1 H), 4.44 (s, 1 H), 4.43 (s, 1 H), 4.21 (s, 2 H), 4.10 (ddd, $J = 9.8, 3.7, 3.7$ Hz, 1 H), 4.01 (d, $J = 10.2$ Hz, 1 H), 3.97 (d, $J = 10.2$ Hz, 1 H), 3.81 (s, 3 H), 3.77-3.81 (m, 1 H), 3.56-3.63 (m, 2 H), 2.95 (s, 3 H), 2.94 (s, 3 H), 2.74-2.81 (m, 1 H), 2.51-2.59 (m, 1 H), 2.06-2.13 (m, 1 H), 1.82-1.90 (m, 1 H).

Preparation of Oxocene 5. To a solution of allylic bromide **6** (102 mg, 0.22 mmol) in

THF (35 mL) was added LiHMDS (1.2 mL, 0.2 M solution in THF, 0.24 mmol) dropwise over 30 min at rt. After being stirred for 10 min, the reaction mixture was quenched with saturated aqueous NH_4Cl , poured into EtOAc (100 mL) and washed with brine. The layers were separated, the aqueous layer was extracted twice with EtOAc (50 mL), and the combined organic layers were dried over anhydrous Na_2SO_4 . Concentration of extract *in vacuo* and Purification of the residue by column chromatography (silica gel, *n*-hexane/ethyl acetate, 2/1) afforded oxocene **5** as a colorless oil (72 mg, 86%); $[\alpha]_{\text{D}}^{25} = -12.2$ (c 0.22, MeOH); ^1H NMR (500 MHz, CDCl_3) δ 7.28 (d, $J = 7.6$ Hz, 2 H), 6.91 (d, $J = 8.6$ Hz, 2 H), 5.97 (ddd, $J = 10.2, 7.7, 7.7$ Hz, 1H), 5.76 (dddd, $J = 10.2, 10.2, 6.5, 1.6$ Hz, 1H), 4.49 (d, $J = 11.4$ Hz, 1 H), 4.38 (d, $J = 11.4$ Hz, 1 H), 4.20 (dd, $J = 10.5, 1.2$ Hz, 1 H), 4.10 (ddd, $J = 9.1, 4.0, 2.5$ Hz, 1 H), 4.00 (ddd, $J = 11.5, 5.0, 2.5$ Hz, 1 H), 3.83 (s, 3 H), 3.48-3.54 (m, 2H), 3.215 (s, 3 H), 2.92-2.99 (m, 1 H), 2.98 (s, 3 H), 2.76-2.82 (m, 1 H), 2.60 (ddd, $J = 12.5, 5.8, 5.8$ Hz, 1 H), 2.32 (ddd, $J = 14.4, 8.5, 1.2$ Hz, 1 H), 2.03 (dddd, $J = 14.1, 9.1, 4.3, 4.3$ Hz, 1 H), 1.76 (dddd, $J = 14.1, 9.5, 5.4, 5.4$ Hz, 1 H); ^{13}C NMR (100 MHz, CDCl_3) δ 170.6, 159.1, 130.32, 130.27, 129.4, 129.2, 113.7, 82.5, 76.8, 72.7, 65.9, 65.5, 55.2, 37.2, 36.3, 34.9, 34.1, 31.6; IR (neat) 2932, 1643, 1512, 1455, 1248, 1177, 1090, 1034, 820, 752, 690 cm^{-1} ; HRMS (CI) found 382.1784 $[(\text{M}+\text{H})^+]$; calcd for $\text{C}_{20}\text{H}_{29}\text{NO}_4^{37}\text{Cl}$: 382.1785].

Preparation of Ketone 16. To a cooled (0 °C) solution of amide **5** (52 mg, 0.136 mmol) in THF (5 mL) was added EtMgBr (0.4 mL, 1.0 M solution in THF, 0.4 mmol) dropwise over 10 min. After being stirred for 1 h at the same temperature, the reaction mixture was quenched with saturated aqueous NH₄Cl and poured into Et₂O. The layers were separated, and the aqueous layer was extracted twice with Et₂O. The combined organic layers were washed with brine, dried over anhydrous Na₂SO₄, concentrated *in vacuo*. Purification of the residue by column chromatography (silica gel, *n*-hexane/ethyl acetate, 20/1 to 10/1) gave ketone **16** as a colorless oil (46 mg, 92%); $[\alpha]_D^{25} = -43.6$ (*c* 0.28, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 7.21 (d, *J* = 8.6 Hz, 2 H), 6.86 (d, *J* = 8.6 Hz, 2 H), 5.88 (ddd, *J* = 10.3, 8.2, 8.2 Hz, 1H), 5.76 (dddd, *J* = 10.1, 10.1, 6.6, 1.1 Hz, 1H), 4.41 (d, *J* = 11.6 Hz, 1 H), 4.34 (d, *J* = 11.6 Hz, 1 H), 4.05 (ddd, *J* = 9.4, 3.3, 2.5 Hz, 1 H), 3.97 (ddd, *J* = 11.1, 4.7, 2.5 Hz, 1 H), 3.81 (s, 3 H), 3.64 (dd, *J* = 8.3, 3.7 Hz, 1 H), 3.43-3.50 (m, 2 H), 2.88 (ddd, *J* = 11.1, 10.3, 10.3 Hz, 1 H), 2.69 (dddd *J* = 19.1, 7.2, 7.2, 7.2 Hz, 1 H), 2.48-2.56 (m, 2 H), 2.39-2.47 (m, 2 H), 2.04 (dddd, *J* = 14.1, 8.8, 4.1, 4.1 Hz, 1 H), 1.75 (dddd, *J* = 14.1, 9.0, 5.7, 3.6 Hz, 1 H), 0.99 (dd, *J* = 7.2, 7.2 Hz 3 H); ¹³C NMR (125 MHz, CDCl₃) δ 211.7, 159.3, 129.9, 129.2, 113.8, 85.9, 76.5, 72.7, 65.9, 65.5, 55.2, 34.6, 34.5, 31.8, 31.4, 7.0; IR (neat) 2935, 1715, 1608, 1512, 1456, 1252, 1171, 1099, 1033, 821 cm⁻¹; HRMS (CI) found 367.1672 [(M+H)⁺; calcd for C₂₀H₂₈O₄³⁷Cl:367.1676].

Preparation of (S)-Alcohol 17. To a cooled (-78 °C) solution of ketone **16** (103.0 mg, 0.281 mmol) in THF (10 mL) was added lithium tri-*sec*-butylborohydride (L-Selectride®) (0.4 mL, 1.0 M solution in THF, 0.4 mmol) dropwise over 10 min. After being stirred for 1 h at the same temperature, the reaction mixture was quenched with MeOH, and 3N NaOH (2 mL) and H₂O₂ (1 mL) were added. The reaction mixture was allowed to warm to rt, then stirred overnight, and the layers were separated. The aqueous layer was extracted twice with Et₂O, and the combined organic layers were washed with brine, dried over anhydrous Na₂SO₄, and concentrated *in vacuo*. Purification of the residue by column chromatography (silica gel, *n*-hexane/ethyl acetate, 10/1 to 5/1) gave (S)-alcohol **17** as a colorless oil (104.0 mg, 100%); $[\alpha]_D^{25} = +8.7$ (*c* 0.82, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 7.26 (d, *J* = 8.6 Hz, 2 H), 6.90 (d, *J* = 8.6 Hz, 2 H), 5.92 (ddd, *J* = 10.3, 8.0, 8.0 Hz, 1H), 5.71 (dddd, *J* = 10.2, 10.2, 3.5, 1.7 Hz, 1H), 4.44 (s, 2 H), 4.11 (ddd, *J* = 8.1, 4.4, 2.3 Hz, 1 H), 3.96 (ddd, *J* = 11.3, 4.9, 2.3 Hz, 1 H), 3.83 (s, 3 H), 3.62 (ddd, *J* = 9.3, 9.3, 3.7 Hz, 1 H), 3.51 (ddd, *J* = 9.6, 5.2, 5.2 Hz, 1 H), 3.36-3.41 (m, 1 H), 3.17 (ddd, *J* = 9.5, 7.8, 1.2 Hz, 1 H), 2.94 (dddd, *J* = 12.0, 11.3, 11.3, 1.1 Hz, 1 H), 2.64 (d, *J* = 4.1 Hz, 1 H), 2.53 (ddd, *J* = 12.0, 5.8, 5.8 Hz, 1 H), 2.47 (ddd, *J* = 14.1, 7.0, 7.0 Hz, 1 H), 2.14 (ddd, *J* = 14.1, 8.5, 1.4 Hz, 1 H), 2.03 (dddd, *J* = 14.3, 9.3, 4.4, 4.4 Hz, 1 H), 1.80 (dddd, *J* = 14.3, 9.3, 4.7, 4.7 Hz, 1 H), 1.56 (dddd, *J* = 14.0, 7.4, 7.4, 7.4, 3.4 Hz, 1 H), 1.42 (dddd, *J* = 14.0, 12.0, 7.4, 7.4, 7.4 Hz, 1 H), 1.00 (dd, *J* = 7.4, 7.4 Hz, 3 H); ¹³C NMR (100 MHz, CDCl₃) δ 159.1, 130.6, 130.2, 129.4, 128.5, 113.7, 83.3, 75.8, 75.0, 72.5, 65.71, 65.66, 55.2, 34.6, 34.3, 30.8, 26.2, 9.9; IR (neat) 3450, 2933, 1612, 1512, 1457, 1303, 1248, 1176, 1086, 1037, 822, 749 cm⁻¹; HRMS (CI) found 369.1826 [(M+H)⁺]; calcd for

C₂₀H₃₀O₄Cl: 369.1832].

Preparation of (R)-Alcohol 18. [Mitsunobu Reaction] To a cooled (0 °C) solution of (S)-alcohol **17** (104 mg, 0.28 mmol) in dry THF (5 mL), were sequentially added diisopropyl azodicarboxylate (286 mg, 1.4 mmol), triphenylphosphine (440 mg, 1.68 mmol) and *p*-nitrobenzoic acid (280 mg, 1.68 mmol). After being stirred for 3 h at 0 °C, the reaction mixture was concentrated *in vacuo*. Direct Purification of the residue by column chromatography (silica gel, *n*-hexane/ethyl acetate, 40/1 to 20/1) gave the *p*-nitrobenzoate as a colorless oil (120 mg, 82%); $[\alpha]_D^{25} = +19.4$ (*c* 0.96, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 8.32 (d, *J* = 8.8 Hz, 2 H), 8.25 (d, *J* = 8.8 Hz, 2 H), 7.14 (d, *J* = 8.6 Hz, 2 H), 6.87 (d, *J* = 8.6 Hz, 2 H), 5.92 (ddd, *J* = 9.8, 8.2, 8.2 Hz, 1H), 5.74 (dddd, *J* = 9.7, 9.7, 6.8, 1.7 Hz, 1H), 5.08 (ddd, *J* = 8.7, 4.5, 4.5 Hz, 1 H), 4.27 (s, 1 H), 4.26 (s, 1 H), 4.06 (m, 1 H), 3.94 (ddd, *J* = 11.3, 4.8, 2.2 Hz, 1 H), 3.82 (s, 3 H), 3.54 (ddd, *J* = 9.2, 9.2, 4.1 Hz, 1 H), 3.42 (ddd, *J* = 9.8, 5.0, 5.0 Hz, 1 H), 2.94 (ddd, *J* = 11.7, 11.7, 11.1 Hz, 1 H), 2.42-2.56 (m, 2 H), 2.20 (dd, *J* = 13.1, 8.6 Hz, 1 H), 1.96 (dddd, *J* = 13.7, 8.9, 4.5, 4.5 Hz, 1 H), 1.80-1.88 (m, 2 H), 1.76 (dddd, *J* = 13.7, 8.9, 4.6, 4.6 Hz, 1 H), 0.96 (dd, *J* = 7.4, 7.4 Hz, 3 H); ¹³C NMR (125 MHz, CDCl₃) δ 164.3, 159.2, 150.5, 135.8, 130.7, 130.19, 130.15, 129.2, 129.1, 123.5, 113.7, 80.9, 79.3, 75.9, 72.4, 65.8, 65.6, 55.2, 34.6, 34.4,

30.4, 223.0, 10.1; HRMS (EI) found 517.1872 [M^+ ; calcd for $C_{27}H_{32}O_7 N_7^{35}Cl$: 517.1867].

[Reductive Debenzoylation] A solution of the above 4-nitrobenzoate (130 mg, 0.25 mmol) in THF (8.0 mL) was added to a mixture of $LiAlH_4$ (53 mg, 1.40 mmol) and THF (4.0 mL) at 0 °C. After stirring the mixture for 1 h at the same temperature, water (0.05 mL), 3 N NaOH (0.05 mL) and water (0.15 mL) were added to the mixture in order. The mixture was stirred for 3 h at rt and then filtered through a pad of Celite®. The filtrate was concentrated *in vacuo* and the resulting residue was purified by column chromatography (silica gel, *n*-hexane/ethyl acetate, 5 / 1) to afford (*R*)-alcohol **18** as a colorless oil (89 mg, 96%); $[\alpha]_D^{25} = +30.4$ (c 0.32, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 7.26 (d, $J = 8.6$ Hz, 2 H), 6.90 (d, $J = 8.6$ Hz, 2 H), 5.92 (ddd, $J = 10.2, 8.1, 8.1$ Hz, 1H), 5.71 (dddd, $J = 10.2, 10.2, 6.5, 1.7$ Hz, 1H), 4.46 (d, $J = 11.7$ Hz, 1 H), 4.41 (d, $J = 11.7$ Hz, 1 H), 4.09 (ddd, $J = 9.0, 3.5, 2.4$ Hz, 1 H), 3.95 (ddd, $J = 11.5, 5.0, 2.4$ Hz, 1 H), 3.83 (s, 3 H), 3.49-3.60 (m, 3 H), 3.23 (ddd, $J = 10.0, 3.4, 1.0$ Hz, 1 H), 2.94 (dddd, $J = 11.2, 11.2, 11.2, 0.9$ Hz, 1 H), 2.47-2.55 (m, 2 H), 2.28 (d, $J = 5.1$ Hz, 1 H), 2.11 (ddd, $J = 14.2, 8.5, 1.3$ Hz, 1 H), 2.00 (dddd, $J = 14.0, 9.3, 5.2, 0.8$ Hz, 1 H), 1.74 (ddd, $J = 14.0, 8.8, 4.7$ Hz, 1 H), 1.42-1.50 (m, 2 H), 1.00 (dd, $J = 7.4, 7.4$ Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.2, 131.2, 130.2, 129.5, 128.3, 113.8, 83.3, 76.2, 76.0, 72.6, 66.18, 66.0, 55.2, 34.7, 34.4, 28.5, 25.4, 10.5; HRMS (CI) found 369.1822 [$(M+H)^+$; calcd for $C_{20}H_{30}O_4^{37}Cl$: 369.1832].

Preparation of (S)-Bromide 19. To a solution of (*R*)-alcohol **18** (88.4 mg, 0.24 mmol) in dry toluene (5 mL) were added carbon tetrabromide (760 mg, 2.4 mmol), 1-methyl cyclohexene (0.4 mL, 3.3 mmol) and trioctylphosphine (1.2 mL, tech. 90%, 3.8 mmol) at rt. After stirring the mixture for 20 min at rt, the mixture was stirred for 4 h in an 80 °C oil bath. After cooling to rt, the reaction mixture was concentrated *in vacuo*. Purification of the residue by column chromatography (silica gel, *n*-hexane/ethyl acetate, 20/1) gave (*S*)-bromide **19** as a colorless oil (86.4 mg, 83%) along with its $\Delta^{13,14}$ elimination product (~3%); $[\alpha]_D^{25} = +5.0$ (*c* 0.90, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 7.28 (d, *J* = 8.8 Hz, 2 H), 6.91 (d, *J* = 8.8 Hz, 2 H), 5.93 (ddd, *J* = 10.3, 7.6, 7.6 Hz, 1H), 5.71 (dddd, *J* = 10.3, 10.3, 6.6, 1.7 Hz, 1H), 4.44 (s, 2 H), 4.09 (ddd, *J* = 8.9, 4.0, 2.5 Hz, 1 H), 3.97 (ddd, *J* = 10.6, 3.0, 3.0 Hz, 1 H), 3.94 (ddd, *J* = 11.7, 5.0, 2.5 Hz, 1 H), 3.84 (s, 3 H), 3.50 -3.56 (m, 3 H), 2.94 (dddd, *J* = 11.7, 11.7, 11.7, 0.6 Hz, 1 H), 2.50-2.59 (m, 2 H), 2.43 (ddd, *J* = 13.9, 8.4, 1.0 Hz, 1 H), 1.98-2.05 (m, 2 H), 1.72-1.79 (m, 2 H), 1.08 (dd, *J* = 7.2, 7.2 Hz, 3 H); ¹³C NMR (125 MHz, CDCl₃) δ 159.3, 130.8, 130.2, 129.5, 128.8, 113.8, 83.2, 76.4, 72.8, 66.1, 65.8, 61.2, 55.2, 34.5, 34.4, 29.6, 26.7, 12.9; HRMS (EI) found 430.0917 [*M*⁺; calcd for C₂₀H₂₈O₃⁷⁹Br³⁵Cl: 430.0910], 432.0905 [C₂₀H₂₈O₃⁸¹Br³⁵Cl or C₂₀H₂₈O₃⁷⁹Br³⁷Cl].

Preparation of Alcohol 20. To a cooled (0 °C) solution of PMB-ether **19** (86.4 mg, 0.20 mmol) in dichloromethane (9 mL) and pH 7.4 phosphate buffer solution (0.5 mL) was added DDQ (90 mg, 0.40 mmol). The reaction mixture was stirred for 1 h at rt, saturated aqueous NaHCO₃ (3 mL) was added, and the resulting dark red solution was stirred vigorously for 2 h at rt. The layers were separated, and the aqueous layer was extracted twice with dichloromethane. The combined organic layers were dried over anhydrous Na₂SO₄, and concentrated *in vacuo*. Purification of the residue by column chromatography (silica gel, *n*-hexane/ethyl acetate, 5/1 to 3/1) gave alcohol **20** as a colorless oil (60.3 mg, 97%); $[\alpha]_D^{25} = +25.8$ (*c* 1.27, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 5.93 (ddd, *J* = 10.2, 7.8, 7.8 Hz, 1H), 5.73 (dddd, *J* = 10.2, 10.2, 6.5, 1.5 Hz, 1H), 4.10 (ddd, *J* = 8.3, 4.3, 2.5 Hz, 1 H), 3.99-4.03 (m, 2 H), 3.73 -3.76 (m, 2 H), 3.60 (dd, *J* = 9.8, 3.2 Hz, 1 H), 2.97 (ddd, *J* = 12.0, 12.0, 10.5 Hz, 1 H), 2.53-2.63 (m, 2 H), 2.44 (ddd, *J* = 13.8, 8.5, 0.7 Hz, 1 H), 2.00-2.09 (m, 2 H), 1.73-1.82 (m, 2 H), 1.65 (br s, 1 H), 1.09 (dd, *J* = 7.2, 7.2 Hz, 3 H); ¹³C NMR (125 MHz, CDCl₃) δ 130.8, 128.8, 83.2, 76.4, 65.8, 61.2, 59.2, 36.8, 34.4, 29.7, 26.8, 12.8; HRMS (EI) found 310.0347 [*M*⁺; calcd for C₁₂H₂₀O₂⁷⁹Br³⁵Cl: 310.0335], 312.0363 [C₁₂H₂₀O₂⁸¹Br³⁵Cl or C₁₂H₂₀O₂⁷⁹Br³⁷Cl].

Preparation of 3-(*E*)-Vinyl iodide 22a. [Dess-Martin Oxidation]: To a solution of alcohol **20** (59.4 mg, 0.19 mmol) in dry CH₂Cl₂ (4 mL) was added Dess-Martin

periodinane (161 mg, 0.38 mmol) at rt. The reaction mixture was stirred for 1 h, diluted with *n*-hexane (10 mL), filtered through a short plug of silica gel, and concentrated *in vacuo* to give the crude aldehyde **21** (60.4 mg, 103%). Without further purification, crude aldehyde **21** was carried on to the next step. **[Takai-Olefination]**: Anhydrous CrCl₂ (140.1 mg, flame-dried under argon, 1.14 mmol) and freshly distilled THF (4 mL) were stirred for 30 min at rt, generating a creamy gray-green suspension. After cooling the mixture to 0 °C, a solution of crude aldehyde **21** (104 mg, 0.19 mmol) and iodoform (150 mg, 0.38 mmol) in dry THF (3 mL) was injected via a syringe. The resulting dark red reaction mixture was stirred at 0 °C for 3.5 h. The reaction mixture was transferred into separatory funnel, washed with H₂O, saturated aqueous Na₂S₂O₃ and brine, dried over anhydrous Na₂SO₄ and concentrated *in vacuo*. Purification of the residue by column chromatography (silica gel, *n*-hexane/dichloromethane, 100/0 to 100/5) afforded an inseparable 8:1 mixture of (*E*)-vinyl iodide **22a** and (*Z*)-vinyl iodide **22b** (56.2 mg, total 68% for 2 steps); **For (*E*)-vinyl iodide 22a**: ¹H NMR (500 MHz, CDCl₃) δ 6.47 (ddd, *J* = 14.4, 7.7, 7.7 Hz, 1H), 6.23 (ddd, *J* = 14.4, 1.1, 1.1 Hz, 1H), 5.94 (dddd, *J* = 10.2, 7.8, 7.8, 0.8 Hz, 1H), 5.73 (dddd, *J* = 10.2, 10.2, 6.6, 1.8 Hz, 1H), 3.93-3.99 (m, 2 H), 3.85 (ddd, *J* = 7.7, 5.2, 2.5 Hz, 1H), 3.48 (dd, *J* = 10.0, 3.1 Hz, 1 H), 2.98 (dddd, *J* = 11.4, 11.4, 11.4, 0.9 Hz, 1 H), 2.62-2.68 (m, 1 H), 2.48-2.58 (m, 2 H), 2.31-2.40 (m, 2 H), 2.04 (dddd, *J* = 14.5, 7.3, 7.3, 7.3, 3.4 Hz, 1H), 1.81 (dddd, *J* = 14.5, 7.3, 7.3, 7.3, 2.9 Hz, 1H), 1.06 (dd, *J* = 7.3, 7.3 Hz, 3 H); ¹³C NMR (125 MHz, CDCl₃) δ 141.7, 130.9, 128.7, 83.4, 78.9, 64.3, 61.0, 40.4, 34.3, 30.4, 27.3, 12.8.

Preparation of TMS-3-(*E*)-enyne **23a.** To a solution of an 8:1 mixture of vinyl iodides {**22a** and **22b**} (24.1 mg, 0.056 mmol) in Et₂NH (1 mL) was added Pd(Ph₃)₄ (6.5 mg, 0.0056 mmol). The mixture was stirred at rt for 10 min in the dark (flask wrapped with foil). To a solution of CuI (2.1 mg, 0.0112 mmol) in Et₂NH (1 mL) was added trimethylsilylacetylene (11.0 μl, 0.112 mmol). The mixture was stirred at rt for 10 min and then added via syringe to the solution of vinyl iodides {**22a** and **22b**}. The reaction mixture was stirred for 1 h, and concentrated *in vacuo*. Purification of the residue by column chromatography (silica gel, *n*-hexane/dichloromethane, 100/0 to 100/1) afforded (*E*)-enyne **23a** (16.4 mg, 73%), the (*Z*)-enyne **23b** (1.9 mg, 9%) and a mixture of (*E*)- and (*Z*)-enynes (2.0 mg, 9%); **For (*E*)-enyne **23a**** [α]_D²⁵ = -10.1 (*c* 0.31, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 6.10 (ddd, *J* = 15.9, 7.6, 7.6 Hz, 1H), 5.93 (dddd, *J* = 10.3, 7.6, 7.6, 1.0 Hz, 1H), 5.69 (dddd, *J* = 10.3, 10.3, 6.6, 1.9 Hz, 1H), 5.65 (ddd, *J* = 15.9, 1.2, 1.2 Hz, 1H), 3.95-4.00 (m, 2 H), 3.83 (ddd, *J* = 7.0, 7.0, 2.4 Hz, 1H), 3.50 (dd, *J* = 10.0, 3.3 Hz, 1 H), 2.98 (dddd, *J* = 11.6, 11.6, 11.6, 0.7 Hz, 1 H), 2.62-2.68 (m, 1 H), 2.51-2.57 (m, 2 H), 2.44 (dddd, *J* = 14.0, 7.2, 7.2, 1.2 Hz, 1H), 2.36 (ddd, *J* = 14.0, 8.4, 0.8 Hz, 1H), 2.04 (dddd, *J* = 14.6, 7.2, 7.2, 7.2, 3.5 Hz, 1H), 2.04 (dddd, *J* = 14.6, 7.2, 7.2, 7.2, 2.7 Hz, 1H), 1.06 (dd, *J* = 7.3, 7.2 Hz, 3 H), 0.2 (s, 9 H); ¹³C NMR (125 MHz, CDCl₃) δ 140.4, 130.8, 128.8, 113.1, 103.4, 93.9, 83.1, 79.5, 64.4, 61.1, 37.7, 34.3, 30.5, 27.4, 12.8, -0.1; HRMS (EI) found 402.0788 [*M*⁺; calcd for C₁₈H₂₈O⁷⁹Br³⁵Cl: 402.0781]

Preparation of 3-(*E*)-Pinnatifidenyne (4a). To a cooled (0 °C) solution of (*E*)-enyne **23a** (7.5 mg, 0.019 mmol) in THF (1 mL) was added dropwise tetrabutylammonium fluoride (0.04 mL, 1.0 M solution in THF, 0.04 mmol). After being stirred for 1 h at the same temperature, the reaction mixture was quenched with saturated aqueous NH₄Cl and poured into Et₂O (10 mL). The layers were separated, and the aqueous layer was extracted twice with Et₂O. The combined organic layers were dried over anhydrous Na₂SO₄, concentrated *in vacuo*. Purification of the residue by column chromatography (silica gel, *n*-hexane/ethyl acetate, 100/1 to 20/1) gave 3-(*E*)-pinnatifidenyne (**4a**) as a white solid (6.0 mg, 97%); $[\alpha]_{\text{D}}^{25} = +7.6$ (c 0.30, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 6.13 (ddd, *J* = 15.9, 7.6, 7.6 Hz, 1H), 5.91 (dddd, *J* = 10.2, 8.1, 8.1 Hz, 1H), 5.69 (dddd, *J* = 10.2, 10.2, 6.6, 1.7 Hz, 1H), 5.59 (dd, *J* = 15.9, 2.0 Hz, 1H), 3.92-3.97 (m, 2 H), 3.82 (ddd, *J* = 7.0, 7.0, 2.4 Hz, 1H), 3.47 (dd, *J* = 10.1, 3.3 Hz, 1 H), 2.89 (ddd, *J* = 11.4, 11.4, 11.4, 1 H), 2.84 (d, *J* = 2.1 Hz, 1 H), 2.60-2.66 (m, 1 H), 2.49-2.58 (m, 2 H), 2.40 (dddd, *J* = 14.1, 7.1, 7.1, 1.2 Hz, 1H), 2.35 (ddd, *J* = 14.1, 8.5, 1.0 Hz, 1H), 2.03 (dddd, *J* = 14.4, 7.2, 7.2, 7.2, 3.4 Hz, 1H), 1.80 (dddd, *J* = 14.4, 10.2, 7.2, 7.2, 7.2, Hz, 1H), 1.08 (dd, *J* = 7.2, 7.2 Hz, 3 H); ¹³C NMR (125 MHz, CDCl₃) δ 141.3, 130.9, 128.8, 112.0, 83.2, 81.9, 79.4, 76.8, 64.4, 61.1, 37.7, 34.3, 30.4, 27.3, 12.7; IR (neat) 3740, 3293, 2926, 1455, 1099, 961, 748 cm⁻¹; HRMS (EI) found 330.0400 [*M*⁺; calcd for C₁₅H₂₀O ⁷⁹Br³⁵Cl: 330.0386], 332.0345

[C₁₂H₂₀O₂⁸¹Br³⁵Cl or C₁₂H₂₀O₂⁷⁹Br³⁷Cl].

Preparation of 3-(Z)-Vinyl iodide 22b. A suspension of iodomethyltriphenylphosphonium iodide (90 mg, 0.17 mmol) in dry THF (2 mL, 0.085 M) was cooled to -78°C with stirring, and KHMDS (0.34 mL, 0.5 M solution in toluene, 0.17 mmol) was added dropwise. The resulting yellow solution was stirred for 30 min at -30°C , then cooled to -78°C and stirring was stopped. The salts were allowed to settle over 30 min, leaving a pale yellow supernatant solution of the ‘salt-free’ ylide over a white precipitate. The supernatant solution (1 mL) was added rapidly via syringe to a solution of crude aldehyde **21** (3.5 mg, 0.011 mmol) in dry THF (1 mL) at -78°C and the reaction mixture was stirred for 30 min. The reaction mixture was quenched with H₂O and allowed to warm to rt. Saturated aqueous NH₄Cl and Et₂O were added. The layers were separated, and the aqueous layer was extracted twice with Et₂O. The combined organic layers were dried over anhydrous Na₂SO₄, and concentrated *in vacuo*. Purification of the residue by column chromatography (silica gel, *n*-hexane/ethyl acetate, 100/1 to 20/1) gave pure (Z)-vinyl iodide **22b** (4.5 mg, 92%); ¹H NMR (500 MHz, CDCl₃) δ 6.37 (d, $J = 7.2$ Hz, 1H), 6.23 (ddd, $J = 7.2, 7.2, 7.2$ Hz, 1H), 5.92 (ddd, $J = 10.2, 7.4, 7.4$ Hz, 1H), 5.70 (dddd, $J = 10.2, 10.2, 6.7, 1.9$ Hz, 1H), 3.94-3.98 (m, 2 H), 3.90 (ddd, $J = 8.1, 5.9, 2.5$ Hz, 1H), 3.48 (dd, $J = 10.1, 3.4$ Hz, 1 H), 2.96 (dddd, $J = 11.8, 11.8, 11.8, 0.9$ Hz, 1 H), 2.66 (ddd, $J = 14.2, 7.3, 7.3$ Hz, 1H), 2.58-2.65 (m, 1 H), 2.53 (ddd, 2.04 $J = 12.4, 5.8, 5.8$ Hz),

2.34-2.39 (m, 2 H), 2.07 (dddd, $J = 14.4, 7.2, 7.2, 7.2, 3.2$ Hz, 1H), 1.80 (dddd, $J = 14.4, 10.2, 7.2, 7.2, 7.2$ Hz, 1H), 1.09 (dd, $J = 7.2, 7.2$ Hz, 3 H).

Preparation of TMS-3-(Z)-enyne 23b. To a solution of vinyl iodide **22b** (4.5 mg, 0.01 mmol) in Et₂NH (1 mL) was added Pd(Ph₃)₄ (2.5 mg, 0.002 mmol). The mixture was stirred at rt for 10 min in the dark (flask wrapped with foil). To a solution of CuI (1.0 mg, 0.004 mmol) in Et₂NH (1 mL) was added trimethylsilylacetylene (9.8 μ L, 0.1 mmol). The mixture was stirred at rt for 5 min and then added via syringe to the solution of (Z)-vinyl iodide **22b** and Pd(Ph₃)₄ in THF. The reaction mixture was stirred for 4 h, and concentrated *in vacuo*. Purification of the residue by column chromatography (silica gel, *n*-hexane/dichloromethane, 100/0 to 100/1) afforded TMS-(Z)-enyne **23b** (3.3 mg, 73%); ¹H NMR (400 MHz, CDCl₃) δ 6.00 (ddd, $J = 10.9, 7.4, 7.4$ Hz, 1H), 5.94 (ddd, $J = 10.2, 8.0, 8.0$ Hz, 1H), 5.72 (dddd, $J = 10.2, 10.2, 6.6, 1.8$ Hz, 1H), 5.62 (d, $J = 10.9$ Hz, 1H), 3.93-4.01 (m, 3 H), 3.49 (dd, $J = 10.0, 3.2$ Hz, 1 H), 3.00 (dddd, $J = 11.4, 11.4, 11.4, 0.8$, 1 H), 2.86 (dddd, $J = 14.4, 7.9, 7.9, 0.7$ Hz, 1 H), 2.62-2.65 (m, 1 H), 2.50-2.56 (m, 2 H), 2.39 (ddd, $J = 13.9, 8.4, 0.8$ Hz, 1H), 2.08 (dddd, $J = 14.5, 7.2, 7.2, 7.2, 3.4$ Hz, 1H), 1.80 (dddd, $J = 14.5, 10.1, 7.2, 7.2, 7.2$ Hz, 1H), 1.11 (dd, $J = 7.2, 7.2$ Hz, 3 H), 0.22 (s, 9 H); ¹³C NMR (125 MHz, CDCl₃) δ 140.0, 130.8, 128.8, 112.2, 101.4, 83.4, 79.6, 64.8,

61.1, 34.8, 34.4, 30.3, 27.2, 12.8. (one carbon is not observed)

Preparation of 3-(Z)-Pinnatifidenyne (4b). To a cooled (0 °C) solution of TMS-(Z)-enynone **23b** (3.3 mg, 0.008 mmol) in THF (1 mL) was added dropwise tetrabutylammonium fluoride (16 μ L, 1.0 M solution in THF, 0.016 mmol). After being stirred for 1 h at 0 °C, the reaction mixture was quenched with saturated aqueous NH_4Cl and poured into Et_2O (10 mL). The layers were separated, and the aqueous layer was extracted twice with Et_2O . The combined organic layers were dried over anhydrous Na_2SO_4 , and concentrated *in vacuo*. Purification of the residue by column chromatography (silica gel, *n*-hexane/ethyl acetate, 100/1 to 20/1) gave 3-(Z)-pinnatifidenyne (**4b**) (2.7 mg, 96%); $[\alpha]_D^{25} = +40.0$ (*c* 0.14, CHCl_3); ^1H NMR (500 MHz, CDCl_3) δ 6.02 (dddd, $J = 10.8, 7.6, 7.6, 0.7$ Hz, 1H), 5.91 (dddd, $J = 10.3, 8.5, 8.5, 0.8$ Hz, 1H), 5.69 (dddd, $J = 10.3, 10.3, 6.6, 1.9$ Hz, 1H), 5.57 (dddd, $J = 10.8, 2.1, 1.1, 1.1$ Hz, 1H), 3.99 (ddd, $J = 7.0, 7.0, 2.9$ Hz, 1H), 3.96 (ddd, $J = 9.2, 5.1, 2.6$ Hz, 1H), 3.88 (ddd, $J = 8.3, 5.7, 2.6$ Hz, 1H), 3.47 (dd, $J = 10.1, 3.2$ Hz, 1H), 3.14 (d, $J = 1.9$ Hz, 1H), 2.96 (dddd, $J = 11.6, 11.6, 11.2, 0.9$ Hz, 1H), 2.82 (dddd, $J = 14.0, 8.0, 8.0, 1.1$ Hz, 1H), 2.61 (dddd, $J = 14.0, 10.1, 8.0, 2.1$ Hz, 1H), 2.49-2.55 (m, 2H), 2.37 (ddd, $J = 14.0, 8.4, 1.1$ Hz, 1H), 2.07 (dddddd, $J = 14.64, 7.2, 7.2, 7.2, 3.7$ Hz, 1H), 1.80 (dddddd, $J = 14.6, 10.3, 7.2, 7.2, 7.2$,

Hz, 1H), 1.08 (dd, $J = 7.2, 7.2$ Hz, 3 H); ^{13}C NMR (100 MHz, CDCl_3) δ 140.9, 130.9, 128.8, 111.0, 83.4, 82.5, 79.9, 79.7, 64.9, 61.0, 34.9, 34.4, 30.1, 27.1, 12.8; HRMS (EI) found 330.0400 [M^+ ; calcd for $\text{C}_{15}\text{H}_{20}\text{O}^{79}\text{Br}^{35}\text{Cl}$: 330.0386], 332.0345 [$\text{C}_{12}\text{H}_{20}\text{O}_2^{81}\text{Br}^{35}\text{Cl}$ or $\text{C}_{12}\text{H}_{20}\text{O}_2^{79}\text{Br}^{37}\text{Cl}$].

Scheme 4^a : Synthesis of oxocene **5** via a cyclization-chlorination sequence

^a Reagents and Conditions : (a) PTSA, EtOH, rt, 1 h, 95%; (b) Ph_3P , CCl_4 , reflux, 4 h, 91%; (c) KHMDS, toluene, rt, 1 h, 71%; (d) DDQ, CH_2Cl_2 , pH 7.4 buffer, 0 °C, 1 h, 75%; (e) CCl_4 , Oct₃P, $\text{BnEt}_3\text{N}^+\text{Cl}^-$, toluene, 0 to 70 °C, 5 h, 80%.

Preparation of Allylic Alcohol 24. To a solution of THP-ether **15** (250.1 mg, 0.41 mmol) in ethanol (20 mL) was added *p*-toluenesulfonic acid monohydrate (20 mg, 0.10 mmol). The reaction mixture was stirred for 1 h, triethylamine (1 mL) was added, and the

mixture was concentrated *in vacuo*. Purification of the residue by column chromatography (silica gel, ethyl acetate/methanol, 20/1 to 5/1) gave allylic alcohol **24** as a colorless oil (205.1 mg, 95%); $[\alpha]_D^{25} = -19.4$ (c 0.96, MeOH); ^1H NMR (500 MHz, CDCl_3) δ 7.27 (d, $J = 8.6$ Hz, 2 H), 6.81-6.90 (m, 2 H), 5.78-5.84 (m, 1 H), 5.60 (ddd, $J = 10.1, 8.1, 8.1$ Hz, 1 H), 4.58 (d, $J = 11.4$ Hz, 1 H), 4.51 (d, $J = 11.4$ Hz, 1 H), 4.46 (d, $J = 11.5$ Hz, 1 H), 4.43 (d, $J = 11.5$ Hz, 1 H), 4.20 (s, 2 H), 4.14-4.20 (m, 1 H), 4.06 (ddd, $J = 12.6, 6.2, 6.2$ Hz, 1 H), 3.892 (s, 3 H), 3.889 (s, 3 H), 3.74 (ddd, $J = 13.7, 7.7, 3.7$, 1 H), 3.56-3.64 (m, 3H), 2.93 (s, 3 H), 2.92 (s, 3 H), 2.80 (dd, $J = 5.5, 5.5$ Hz, 1 H), 2.54 (ddd, $J = 14.6, 7.4, 7.4$, 1 H), 2.31 (ddd, $J = 14.6, 7.4, 7.4$, 1 H), 1.87-1.95 (m, 2 H); ^{13}C NMR (100 MHz, CDCl_3) δ 169.1, 158.9, 148.6, 148.3, 130.9, 130.6, 130.1, 129.2, 128.1, 120.2, 113.5, 111.1, 110.5, 79.3, 78.4, 72.4, 71.8, 69.3, 66.2, 57.6, 55.7, 55.6, 55.0, 36.1, 35.1, 30.7, 28.0; HRMS (CI) found 532.2923 $[(\text{M}+\text{H})^+]$; calcd for $\text{C}_{29}\text{H}_{42}\text{NO}_8$: 532.2910].

Preparation of Allylic Chloride 25. To a solution of allylic alcohol **24** (205.1 mg, 0.39 mmol) in dry CCl_4 (20 mL) were added triphenylphosphine (1.6 g, 3.8 mmol) at rt and the reaction mixture was stirred for 4 h under reflux. After being cooled to rt, the reaction mixture was concentrated *in vacuo*. Purification of the residue by column chromatography (silica gel, *n*-hexane/ethyl acetate, 2/1 to 1/1) gave allylic chloride **25** as a colorless oil (193.0 mg, 91%); $[\alpha]_D^{25} = -24.1$ (c 1.0, MeOH); ^1H NMR (500 MHz, CDCl_3) δ 7.27 (d, $J = 8.6$ Hz, 2 H), 6.82-6.90 (m, 2 H), 5.71-5.74 (m, 2 H), 4.58 (d, $J = 11.4$ Hz, 1 H), 4.491 (d, $J = 11.4$ Hz, 1 H), 4.50 (s, 2 H), 4.27 (d, $J = 13.4$ Hz, 1 H), 4.21 (d, $J = 13.4$ Hz, 1 H), 4.11 (d, $J = 6.5$ Hz, 1 H), 4.10 (d, $J = 6.5$ Hz, 1 H), 3.894 (s, 3 H), 3.891 (s, 3 H), 3.82 (s, 3 H), 3.74 (ddd, $J = 7.7, 3.9, 3.9$ Hz, 1 H), 3.59-3.64 (m, 3H), 2.94 (s, 3 H), 2.93 (s, 3 H),

2.46-2.51 (m, 1 H) 2.34-2.37 (m, 1 H), 1.85-1.92 (m, 2 H); ^{13}C NMR (100 MHz, CDCl_3) δ 169.0, 159.0, 148.7, 148.4, 131.4, 130.9, 130.4, 129.2, 126.9, 120.2, 113.6, 111.1, 110.7, 80.0, 78.5, 72.5, 72.0, 69.5, 66.5, 55.8, 55.7, 55.1, 39.5, 36.2, 35.1, 31.0, 28.0; HRMS (EI) found 549.2498 $[(\text{M}+\text{H})^+]$; calcd for $\text{C}_{29}\text{H}_{40}\text{ClNO}_7$: 549.2493].

Preparation of Oxocene 26. To a solution of allylic chloride **25** (19.0 mg, 0.035 mmol) in dry toluene (5.8 mL) was added KHMDS (0.8 mL, 0.05 M solution in toluene, 0.040 mmol) dropwise over 30 min at rt. After being stirred for 30 min, the reaction mixture was quenched with saturated aqueous NH_4Cl , poured into EtOAc (100 mL) and washed with brine. The layers were separated, and the aqueous layer was extracted twice with EtOAc (50 mL). The combined organic layers were dried over anhydrous Na_2SO_4 , concentrated *in vacuo*. Purification of the residue by column chromatography (silica gel, hexane/ethyl acetate, 2/1) afforded cyclization product **26** as a colorless oil (12.8 mg, 71%); $[\alpha]_D^{25} = -141.3$ (c 0.72, MeOH); ^1H NMR (500 MHz, CDCl_3) δ 7.24 (d, $J = 8.6$ Hz, 2 H), 6.83-6.90 (m, 5 H), 5.94 (ddd, $J = 10.2, 7.8, 7.8$ Hz, 1 H), 5.87 (ddd, $J = 10.2, 10.2, 7.3$ Hz, 1 H), 4.62 (d, $J = 11.3$ Hz, 1 H), 4.42 (d, $J = 11.3$ Hz, 1 H), 4.39 (s, 1 H), 4.38 (s, 1 H), 4.24 (d, $J = 9.8$ Hz, 1 H), 3.892 (s, 3 H), 3.887 (s, 3 H), 3.82 (s, 3 H), 3.60-3.61 (m, 2 H), 3.46-3.56 (m, 2H), 2.96 (s, 3 H), 2.94 (s, 3 H), 2.77 (dd, $J = 12.2, 12.2$ Hz, 1 H), 2.67-2.73 (m, 1 H), 2.47 (ddd, $J = 13.5, 6.3, 1.6$ Hz, 1 H), 2.09-2.17 (m, 2 H), 1.62-1.66 (m, 2 H); ^{13}C NMR (100 MHz, CDCl_3) δ 171.1, 159.0, 148.9, 148.6, 130.9, 130.7, 130.1, 129.0, 128.1, 120.4, 113.6, 111.2, 110.8, 83.3, 81.2, 78.8, 72.2, 71.5, 66.4, 55.9, 55.8, 55.2, 36.9, 35.8, 33.3, 31.7, 27.5; HRMS (EI) found 513.2732 $[(\text{M}+\text{H})^+]$; calcd for $\text{C}_{29}\text{H}_{39}\text{NO}_7$: 513.2727].

Preparation of Alcohol 27. To a cooled (0 $^\circ\text{C}$) solution of oxocene **26** (20.3 mg, 0.040

mmol) in dichloromethane (4 mL) and pH 7.4 phosphate buffer solution (0.4 mL) was added DDQ (10.0 mg, 0.045 mmol). The reaction mixture was stirred for 1 h and saturated aqueous NaHCO₃ (1 mL) was added. The resulting dark red solution was stirred vigorously for 1 h. The layers were separated, and the aqueous layer was extracted twice with dichloromethane. The combined organic layers were dried over anhydrous Na₂SO₄, and concentration *in vacuo*. Purification of the residue by column chromatography (silica gel, *n*-hexane/ethyl acetate, 1/1 to ethyl acetate/methanol, 10/1) gave alcohol **27** as a viscous oil (15.4 mg, 75%); [α]_D²⁵ = -112.8 (*c* 0.97, MeOH); ¹H NMR (500 MHz, CDCl₃) δ 7.25 (d, *J* = 8.6 Hz, 2 H), 6.89 (d, *J* = 8.6 Hz, 2 H), 5.90-5.98 (m, 2 H), 4.43 (s, 2 H), 4.25 (dd, *J* = 9.5, 1.7 Hz, 1 H), 3.82 (s, 3 H), 3.61 (ddd, *J* = 9.5, 5.0, 5.0 Hz, 1 H), 3.55 (ddd, *J* = 9.1, 9.1, 3.7 Hz, 1 H), 3.49 (ddd, *J* = 11.4, 7.1, 4.4 Hz, 1 H), 3.02 (s, 3 H), 2.95 (s, 3 H), 2.867 (ddd, *J* = 12.4, 8.9, 3.2 Hz, 1 H), 2.66-2.72 (m, 2 H), 2.32 (ddd, *J* = 13.5, 5.7, 5.7 Hz, 1 H), 2.23 (ddd, *J* = 14.3, 8.0, 8.0 Hz, 1 H), 2.06 (dddd, *J* = 14.6, 9.1, 9.1, 4.5 Hz, 1 H), 1.79-1.85 (m, 1 H); ¹³C NMR (125 MHz, CDCl₃) δ 170.9, 159.2, 130.0, 129.7, 129.3, 128.4, 113.8, 81.1, 80.6, 75.3, 72.6, 66.4, 55.2, 37.1, 35.9, 34.0, 32.3, 31.3; IR (neat) 3401, 2929, 1643, 1512, 1247, 1091, 821, 759 cm⁻¹; HRMS (EI) found 363.2047 [(M+H)⁺; calcd for C₂₀H₂₉NO₅: 363.2046].

Preparation of Oxocene 5. To a cooled (0 °C) solution of alcohol **27** (17.2 mg, 0.047 mmol) in dry toluene (4 mL) were added benzyltriethylammonium chloride (220 mg, 0.94 mmol), CCl₄ (90 μ L, 0.94 mmol) and trioctylphosphine (0.4 mL, tech. 90%, 0.94 mmol) at rt. After being stirred for 20 min, the reaction mixture was stirred for 5 h in a 70 °C oil

bath. After cooling to rt, the reaction mixture was concentrated *in vacuo*. Purification of the residue by column chromatography (silica gel, *n*-hexane/ethyl acetate, 2/1 to 1/1) gave diene **28** (7.6 mg, 47%), and oxocene **5** (5.9 mg, 33%) which was identical to that obtained *via* Scheme 3.

Scheme 5^a : Synthesis of 3-(*E*)- and 3-(*Z*)-13-*epi*-pinnatifidenyne

^a Reagents and Conditions: (a) CBr₄, Oct₃P, toluene, rt to 80 °C, 4 h, 77%; (b) DDQ, CH₂Cl₂, pH 7.4, 0 °C to rt, 1 h, 97%; (c) Dess-Martin periodinane, CH₂Cl₂, rt, 1 h; (d) CHI₃, CrCl₂, THF, 0 °C to rt, 4 h, 91% (for 2 steps); (e) TMS-acetylene, (Ph₃P)₄Pd, CuI, Et₂NH, rt, 1 h, >81%; (f) TBAF, THF, 0 °C to rt, 1 h, 96%; (g) [Ph₃P⁺CHI]⁻, KHMDS, THF, -30 to -78 °C, 1 h, 87%; (h) TMS-acetylene, (Ph₃P)₄Pd, CuI, Et₂NH, rt, 1 h, 98%; (i). TBAF, THF, 0 °C, 1 h, 95%.

Preparation of (R)-Bromide 29. To a solution of (S)-alcohol **18** (96.0 mg, 0.24 mmol) in dry toluene (7 mL) were added carbon tetrabromide (863 mg, 2.6 mmol), 1-methylcyclohexene (0.5 mL, 4.1 mmol) and trioctylphosphine (1.6 mL, tech. 90%, 3.9 mmol) at rt. After stirring mixture for 20 min at rt, the reaction mixture was stirred for 4 h in an 80 °C oil bath. After cooling to rt, the reaction mixture was concentrated *in vacuo*. Purification of the residue by column chromatography (silica gel, *n*-hexane/ethyl acetate, 20/1) gave (R)-bromide **29** as a colorless oil (86.0 mg, 77%); $[\alpha]_D^{25} = +31.0$ (*c* 0.82, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 7.24 (d, *J* = 8.6 Hz, 2 H), 6.86 (d, *J* = 8.8 Hz, 2 H), 5.88 (ddd, *J* = 10.1, 8.0, 8.0 Hz, 1H), 5.71 (dddd, *J* = 10.1, 10.1, 6.5, 1.2 Hz, 1H), 4.43 (d, *J* = 11.7 Hz, 1 H), 4.39 (d, *J* = 11.7 Hz, 1 H), 4.05 (ddd, *J* = 7.6, 4.8, 2.2 Hz, 1 H), 3.93 (ddd, *J* = 11.1, 4.8, 2.2 Hz, 1 H), 3.85 (ddd, *J* = 10.0, 5.9, 3.1 Hz, 1 H), 3.81 (s, 3 H), 3.57 (ddd, *J* = 9.3, 9.3, 4.3 Hz, 1 H), 3.46 (ddd, *J* = 5.3, 5.3, 4.9 Hz, 1 H), 3.37 (ddd, *J* = 8.8, 6.1, 1.4 Hz, 1 H), 2.91 (dddd, *J* = 11.3, 11.3, 11.3, 1.1 Hz, 1 H), 2.49-2.58 (m, 2 H), 2.44 (ddd, *J* = 14.0, 8.5, 1.5 Hz, 1 H), 1.98-2.05 (m, 2 H), 1.76-1.81 (m, 1 H), 1.57-1.66 (m, 1 H), 1.08 (dd, *J* = 7.2, 7.2 3 H); ¹³C NMR (125 MHz, CDCl₃) δ 159.2, 130.2, 129.4, 129.0, 113.8, 83.1, 76.2, 65.8, 65.6, 62.0, 55.2, 34.4, 34.3, 31.9, 27.9, 12.7; HRMS (EI) found 430.0911 [M⁺; calcd for C₂₀H₂₈O₃ ⁷⁹Br³⁵Cl: 430.0910]

Preparation of Alcohol 30. To a cooled (0 °C) solution of PMB-ether **29** (86.0 mg, 0.20 mmol) in dichloromethane (9 mL) and pH 7.4 buffer solution (0.5 mL) was added DDQ (90 mg, 0.40 mmol). The reaction mixture was stirred for 1 h at rt and saturated aqueous NaHCO₃ (3 mL) was added. The resulting dark red solution was stirred vigorously for 2 h. The layers were separated, the aqueous layer was extracted twice with dichloromethane,

and the combined organic layers were dried over anhydrous Na₂SO₄. Concentration *in vacuo* and purification of the residue by column chromatography (silica gel, *n*-hexane/ethyl acetate, 5/1 to 3/1) gave alcohol **30** as a colorless oil (60.2 mg, 97%); $[\alpha]_D^{25} = +83.7$ (c 1.20, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 5.93 (ddd, *J* = 10.0, 8.0, 8.0, 1.6 Hz, 1H), 5.76 (dddd, *J* = 10.0, 10.0, 6.5, 1.5 Hz, 1H), 4.12 (ddd, *J* = 8.0, 5.4, 2.6 Hz, 1 H), 4.08 (ddd, *J* = 11.2, 4.9, 2.4 Hz, 1 H), 3.96 (ddd, *J* = 10.2, 5.4, 3.4 Hz, 1 H), 3.81-3.86 (m, 1 H), 3.74-3.80 (m, 1 H), 3.58 (ddd, *J* = 8.0, 5.4, 1.1 Hz, 1 H), 2.98 (dddd, *J* = 11.3, 11.3, 11.3, 1.2 Hz, 1 H), 2.55-2.65 (m, 2 H), 2.46 (ddd, *J* = 14.0, 8.5, 1.5 Hz, 1 H), 2.07-2.13 (m, 2 H), 1.77-1.85 (m, 2 H), 1.30 (br s, 1 H), 1.10 (dd, *J* = 7.2, 7.2 Hz, 3 H); ¹³C NMR (125 MHz, CDCl₃) δ 130.3, 129.0, 83.4, 76.2, 65.6, 62.2, 59.1, 36.7, 34.3, 31.9, 27.7, 12.7; IR (neat) 3391, 2933, 1650, 1455, 1095, 748, 686 cm⁻¹; HRMS (EI) found 310.0325 [*M*⁺; calcd for C₁₂H₂₀O₂ ⁷⁹Br³⁵Cl: 310.0335], 312.0329 [C₁₂H₂₀O₂ ⁸¹Br³⁵Cl or C₁₂H₂₀O₂ ⁷⁹Br³⁷Cl].

Preparation of 3-(*E*)-Vinyl iodide 32a. [Dess-Martin Oxidation] To a solution of alcohol **30** (27.8 mg, 0.089 mmol) in dry CH₂Cl₂ (4 mL) was added Dess-Martin periodinane (57.0 mg, 0.13 mmol) at rt. The reaction mixture was stirred for 1 h, diluted with *n*-hexane (10 mL), filtered through a short plug of silica gel, and concentrated *in vacuo* to give crude aldehyde **31** (27.5 mg, 100%). Without further purification, crude aldehyde **31** was carried on to the next step. **[Takai-Olefination]** Anhydrous CrCl₂ (70.1 mg, flame-dried under argon, 0.53 mmol) and freshly distilled THF (4 mL) were stirred for 30 min at rt, generating a creamy gray-green suspension. After cooling to 0 °C, a solution of the above crude aldehyde **31** (27.5 mg, 0.089 mmol) and iodoform (70 mg,

0.18 mmol) in dry THF was injected via syringe. The resulting dark red reaction mixture was stirred at rt for 3.5 h. The reaction mixture was washed with H₂O, saturated aqueous Na₂S₂O₃ and brine, dried over anhydrous Na₂SO₄ and concentrated *in vacuo*. Purification of the residue by column chromatography (silica gel, *n*-hexane/dichloromethane, 100/0 to 100/5) afforded an inseparable 8:1 mixture of (*E*)-vinyl iodide **32a** and (*Z*)-vinyl iodide **32b** (32.0 mg, 91% for 2 steps); [for (*E*)-vinyl iodide **32a**] ¹H NMR (500 MHz, CDCl₃) δ 6.49 (ddd, *J* = 14.4, 7.7, 7.7 Hz, 1H), 6.23 (d, *J* = 14.4 Hz, 1H), 5.93 (ddd, *J* = 10.3, 7.9, 7.9, Hz, 1H), 5.73 (dddd, *J* = 10.3, 10.3, 6.7, 1.6 Hz, 1H), 3.98 (ddd, *J* = 11.4, 4.9, 2.4 Hz, 1H), 3.93 (ddd, *J* = 8.8, 5.4, 3.4 Hz, 1H), 3.85 (ddd, *J* = 7.0, 7.0, 2.4 Hz, 1H), 3.46 (dd, *J* = 7.1, 5.5 Hz, 1 H), 2.97 (dddd, *J* = 11.2, 11.2, 11.2, 0.9 Hz, 1 H), 2.53-2.64 (m, 3 H), 2.46 (ddd, *J* = 14.0, 8.5, 1.2 Hz, 1H), 2.39 (ddd, *J* = 14.0, 6.8, 6.8, 0.8 Hz, 1H), 2.07 (dddd, *J* = 14.7, 7.2, 7.2, 7.2, 3.4 Hz, 1H), 1.80 (dddd, *J* = 14.7, 7.2, 7.2, 7.2, 9.9 Hz, 1H), 1.00 (dd, *J* = 7.2, 7.2 Hz, 3 H); ¹³C NMR (125 MHz, CDCl₃) δ 141.6, 130.5, 128.9, 83.8, 78.9, 78.6, 64.2, 61.6, 40.2, 34.2, 31.8, 27.7, 12.7.

Preparation of 3-(*E*)-13-*Epi*-Pinnatifienyne (33a). [Sonogashira Coupling] To a solution of 8:1 mixture of vinyl iodides {**32a** and **32b**} (32.0 mg, 0.074 mmol) in Et₂NH (1 mL) was added Pd(Ph₃)₄ (8.5 mg, 0.00746 mmol). The mixture was stirred at rt for 10 min in the dark (flask wrapped with foil). To a solution of CuI (2.8 mg, 0.015 mmol) in Et₂NH (1 mL) was added trimethylsilylacetylene (10.0 μL, 0.22 mmol). The mixture was stirred at rt for 10 min and then added via syringe to the solution of the mixture of vinyl iodides. The reaction mixture was stirred for 1 h at rt, concentrated *in vacuo*, and the residue was purified by column chromatography (silica gel, *n*-hexane/dichloromethane,

100/0 to 100/1) to afford (*E*)-enyne **32a** (24.0 mg, 81%), (*Z*)-enyne **32b** (3.0 mg, 10%) and a 1:1 mixture of (*E*)- and (*Z*)-enynes (2.0 mg, 7%). **[Desilylation]** To a cooled (0 °C) solution of the above (*E*)-enyne **32a** (24.0 mg, 0.059 mmol) in THF (2 mL) was added dropwise tetrabutylammonium fluoride (0.12 mL, 1.0 M solution in THF, 0.12 mmol). After being stirred for 1 h at rt, the reaction mixture was quenched with saturated aqueous NH₄Cl and poured into Et₂O (10 mL). The layers were separated, the aqueous layer was extracted twice with Et₂O, and the combined organic layers were dried over anhydrous Na₂SO₄. Concentration *in vacuo* and purification of the residue by column chromatography (silica gel, *n*-hexane/ethyl acetate, 100/1 to 20/1) gave 3-(*E*)-13-*epi*-pinnatifidenyne (**33a**) as a viscous oil (18.9 mg, 96%); [α]_D²⁵ = +55.3 (*c* 0.75, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 6.14 (ddd, *J* = 15.9, 7.6, 7.6 Hz, 1H), 5.90 (ddd, *J* = 10.1, 8.1, 8.1 Hz, 1H), 5.70 (dddd, *J* = 10.1, 10.1, 6.6, 1.3 Hz, 1H), 5.60 (dd, *J* = 15.9, 1.4 Hz, 1H), 3.97 (ddd, *J* = 11.4, 5.0, 2.4 Hz, 1H), 3.91 (ddd, *J* = 9.5, 5.8, 3.6 Hz, 1H), 3.82 (ddd, *J* = 7.0, 7.0, 2.4 Hz, 1H), 3.45 (ddd, *J* = 9.3, 6.0, 1.1 Hz, 1H), 2.94 (dddd, *J* = 11.3, 11.3, 11.3, 0.7 Hz, 1H), 2.83 (d, *J* = 2.1 Hz, 1H), 2.52-2.62 (m, 3H), 2.44-2.50 (m, 2H), 2.06 (dddd, *J* = 14.6, 7.2, 7.2, 7.2, 3.4 Hz, 1H), 1.78 (dddd, *J* = 14.6, 9.9, 7.2, 7.2, 7.2, Hz, 1H), 1.08 (dd, *J* = 7.2, 7.2 Hz, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 141.3, 130.5, 129.0, 112.1, 83.8, 81.9, 79.6, 76.8, 64.3, 61.6, 37.4, 34.2, 32.0, 27.7, 12.6; IR (neat) 3740, 3293, 2926, 1455, 1099, 961, 748 cm⁻¹; HRMS (EI) found 330.0400 [*M*⁺; calcd for C₁₅H₂₀O ⁷⁹Br³⁵Cl: 330.0386], 332.0345 [C₁₂H₂₀O₂⁸¹Br³⁵Cl or C₁₂H₂₀O₂⁷⁹Br³⁷Cl].

Preparation of 3-(*Z*)-13-*Epi*-Vinyl iodide 32b. A suspension of iodomethyltriphenylphosphonium iodide (110 mg, 0.21 mmol) in dry THF (2 mL, 0.105

M) was cooled to $-78\text{ }^{\circ}\text{C}$ with stirring and KHMDs (0.4 mL, 0.5 M solution in toluene, 0.210 mmol) was added dropwise. The resulting yellow solution was stirred for 30 min at $-30\text{ }^{\circ}\text{C}$ then cooled to $-78\text{ }^{\circ}\text{C}$ and stirring was stopped. The salts were allowed to settle over 30 min, leaving a pale yellow supernatant solution of the 'salt-free' ylide over white precipitate. The supernatant solution (1 mL, 0.1 mmol) was added rapidly via syringe to a solution of aldehyde **31** (4.5 mg, 0.015 mmol) in dry THF (1 mL) at $-78\text{ }^{\circ}\text{C}$ and the reaction mixture was stirred for 30 min. The reaction mixture was quenched with H_2O , allowed to warm to rt, and poured into saturated aqueous NH_4Cl and Et_2O (1/4, 20 mL). The layers were separated, and the aqueous layer was extracted twice with Et_2O . The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4 , and concentrated *in vacuo*. Purification of the residue by column chromatography (silica gel, hexane/ethyl acetate, 100/1 to 20/1) gave pure (Z)-vinyl iodide **32b** (5.5 mg, 87%); ^1H NMR (300 MHz, CDCl_3) δ 6.23-6.36 (m, 2 H), 5.91 (ddd, $J = 10.2, 8.3, 8.3\text{ Hz}$, 1 H), 5.72 (ddd, $J = 10.2, 10.2, 6.6\text{ Hz}$, 1H), 3.96 (ddd, $J = 11.2, 4.9, 2.4\text{ Hz}$, 1 H), 3.87-3.94 (m, 2 H), 3.51 (ddd, $J = 9.5, 6.3, 3.4\text{ Hz}$, 1H), 2.96 (dddd, $J = 11.0, 11.0, 11.0, 1.2\text{ Hz}$, 1 H), 2.67 (ddd, $J = 14.4, 7.1, 7.1\text{ Hz}$, 1H), 2.49-2.58 (m, 3 H), 2.45 (ddd, $J = 14.4, 6.6, 6.6\text{ Hz}$, 1 H), 2.07 (dddd, $J = 14.6, 7.3, 7.3, 7.3, 3.2\text{ Hz}$, 1H), 1.80 (dddd, $J = 14.6, 9.8, 7.3, 7.3, 7.3\text{ Hz}$, 1H), 1.09 (dd, $J = 7.3, 7.3\text{ Hz}$, 3 H).

Preparation of 3-(Z)-13-Epi-Pinnatifidenyne (33b). [Sonogashira Coupling] To a solution of vinyl iodide **32b** (5.5 mg, 0.013 mmol) in Et_2NH (1 mL) was added $\text{Pd}(\text{Ph}_3)_4$ (3.5 mg, 0.003 mmol). The mixture was stirred at rt for 10 min in the dark (flask wrapped with foil). To a solution of CuI (2.0 mg, 0.008 mmol) in Et_2NH (1 mL) was

trimethylsilylacetylene (9.8 μ L, 0.1 mmol). The mixture was stirred at rt for 5 min and then added via syringe to the solution of 3-(Z)-13-*epi*-vinyl iodide. The reaction mixture was stirred for 1 h, and concentrated *in vacuo*. Purification of the residue by column chromatography (silica gel, *n*-hexane/dichloromethane, 100/0 to 100/5) afforded TMS-3-(Z)-13-*epi*-enyne (5.0 mg, 98%). **[Desilylation]** To a cooled (0 $^{\circ}$ C) solution of the above 3-(Z)-13-*epi*-enyne (5.0 mg, 0.012 mmol) in THF (1 mL) was added dropwise tetrabutylammonium fluoride (24 μ L, 1.0 M solution in THF, 0.024 mmol). After being stirred for 1 h at 0 $^{\circ}$ C, the reaction mixture was quenched with saturated aqueous NH_4Cl and poured into Et_2O (10 mL). The layers were separated, and the aqueous layer was extracted twice with Et_2O . The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4 , and concentrated *in vacuo*. Purification of the residue by column chromatography (silica gel, *n*-hexane/ethyl acetate, 100/1 to 20/1) gave 3-(Z)-13-*epi*-pinnatifidenyne (**33b**) (4.0 mg, 95%); $[\alpha]_D^{25} = +101.8$ (c 0.22, CHCl_3); ^1H NMR (500 MHz, CDCl_3) δ 6.06 (ddd, $J = 10.8, 7.6, 7.6$ Hz, 1H), 5.90 (ddd, $J = 10.3, 7.9, 7.9$ Hz, 1H), 5.71 (ddd, $J = 10.3, 10.3, 6.6$ Hz, 1H), 5.57 (ddd, $J = 10.8, 1.1, 1.1$ Hz, 1H), 3.98 (ddd, $J = 11.3, 4.9, 2.5$ Hz, 1H), 3.89-3.92 (m, 2 H), 3.48 (ddd, $J = 6.7, 6.7, 3.8$ Hz, 1 H), 3.15 (d, $J = 1.8$ Hz, 1H), 2.96 (dddd, $J = 11.2, 11.2, 11.2, 1.3$, 1 H), 2.85 (ddd, $J = 14.8, 7.4, 7.4$ Hz, 1 H), 2.59 (ddd, $J = 14.8, 7.0, 7.0$ Hz, 1H), 2.45-2.56 (m, 3 H), 2.12 (dddd, $J = 14.6, 7.2, 7.2, 7.2, 3.5$ Hz, 1H), 1.79 (dddd, $J = 14.6, 9.9, 7.2, 7.2, 7.2$, Hz, 1H), 1.08 (dd, $J = 7.2, 7.2$ Hz, 3 H); ^{13}C NMR (100 MHz, CDCl_3) δ 140.7, 130.5, 129.0, 111.0, 83.9, 82.7, 79.9, 79.6, 64.7, 61.5, 34.7, 34.3, 32.1, 27.6, 12.5

Table 1. ¹H NMR comparison of natural and synthetic 3-(*E*)-pinnatifidenyne

Proton at Carbon No.	¹ H NMR	
	Natural 3-(<i>E</i>)-pinnatifidenyne (260 MHz, CDCl ₃)	Synthetic 3-(<i>E</i>)-pinnatifidenyne (400 MHz, CDCl ₃)
1	2.83 (d, <i>J</i> = 1.6)	2.84 (d, <i>J</i> = 2.1 Hz)
3	5.59 (dd, <i>J</i> = 15.7, 1.6)	5.59 (dd, <i>J</i> = 15.9, 2.0 Hz)
4	6.14 (dt, <i>J</i> = 15.7, 7.7)	6.13 (ddd, <i>J</i> = 15.9, 7.6, 7.6)
5	2.40 (dt, <i>J</i> = 14.1, 7.7) 2.35 (ddd, <i>J</i> = 14.1, 7.8, 7.7)	2.40 (dddd, <i>J</i> = 14.1, 7.1, 7.1, 1.2) 2.51-2.57 (m)
6	3.82 (ddd, <i>J</i> = 7.8, 7.7, 2.3)	3.82 (ddd, <i>J</i> = 7.0, 7.0, 2.4),
7	3.93 (ddd, <i>J</i> = 10.6, 3.0, 2.3)	3.92-3.94 (m)
8	2.95 (ddd, <i>J</i> = 12.3, 10.6, 7.0) 2.53 (ddd, <i>J</i> = 12.3, 3.0, 1.2)	2.96 (dddd, <i>J</i> = 11.7, 11.7, 10.3, 0.7) 2.51-2.57 (m)
9	5.69 (ddd, <i>J</i> = 10.5, 7.0, 1.2)	5.69 (dddd, <i>J</i> = 10.2, 10.2, 6.6, 1.7)
10	5.91 (ddd, <i>J</i> = 10.5, 7.9, 0.1)	5.91 (dddd, <i>J</i> = 10.2, 8.1, 8.1)
11	2.63 (ddd, <i>J</i> = 14.2, 10.5, 0.1) 2.35 (ddd, <i>J</i> = 14.2, 7.9, 3.1)	2.58-2.66 (m) 2.35 (ddd, <i>J</i> = 14.1, 8.5, 1.0)
12	3.46 (ddd, <i>J</i> = 10.5, 4.3, 3.1)	3.47 (dd, <i>J</i> = 10.1, 3.2)
13	3.96 (ddd, <i>J</i> = 11.5, 4.3, 3.6)	3.94-3.97 (m)
14	2.01 (dq, <i>J</i> = 14.5, 7.2, 3.6) 1.80 (ddq, <i>J</i> = 14.5, 11.5, 7.2)	2.03 (dddd, <i>J</i> = 14.4, 7.2, 7.2, 7.2, 3.4) 1.80 (dddd, <i>J</i> = 14.4, 10.2, 7.2, 7.2, 7.2)
15	1.07 (t, <i>J</i> = 7.2)	1.08 (dd, <i>J</i> = 7.2, 7.2)

Table 2. ¹H NMR comparison of natural and synthetic 3-(Z)-pinnatifidenyne

Proton at Carbon No.	¹ H NMR	
	Natural 3-(Z)-pinnatifidenyne (260 MHz, CDCl ₃)	Synthetic 3-(Z)-pinnatifidenyne (500 MHz, CDCl ₃)
1	3.13 (d, <i>J</i> = 2.0)	3.14 (d, <i>J</i> = 1.9)
3	5.57 (dd, <i>J</i> = 10.8, 2.0)	5.57 (dddd, <i>J</i> = 10.8, 2.1, 1.1, 1.1)
4	6.03 (dt, <i>J</i> = 10.8, 7.6)	6.03 (dddd, <i>J</i> = 10.8, 7.6, 7.6, 0.7)
5	2.82 (dt, <i>J</i> = 14.2, 7.6) 2.55 (ddd, <i>J</i> = 10.8, 7.6, 6.2)	2.82 (dddd, <i>J</i> = 14.0, 8.0, 8.0, 1.1) 2.54 (m)
6	3.88 (ddd, <i>J</i> = 7.6, 6.2, 2.6)	3.88 (ddd, <i>J</i> = 8.3, 5.7, 2.6),
7	3.95 (ddd, <i>J</i> = 10.5, 4.2, 2.6)	3.96 (ddd, <i>J</i> = 9.2, 5.1, 2.6)
8	2.96 (ddd, <i>J</i> = 12.1, 10.5, 7.0) 2.51 (ddd, <i>J</i> = 12.1, 4.2, 1.1)	2.96 (dddd, <i>J</i> = 11.6, 11.6, 11.2, 0.9) 2.52 (m)
9	5.69 (ddd, <i>J</i> = 10.2, 7.0, 1.1)	5.69 (dddd, <i>J</i> = 10.3, 10.3, 6.6, 1.9)
10	5.91 (ddd, <i>J</i> = 10.2, 7.6, 0.2)	5.91 (dddd, <i>J</i> = 10.3, 8.5, 8.5, 0.8)
11	2.63 (ddd, <i>J</i> = 14.0, 10.2, 0.2) 2.37 (ddd, <i>J</i> = 14.0, 7.6, 3.0)	2.61 (dddd, <i>J</i> = 14.0, 10.1, 8.0, 2.1) 2.37 (ddd, <i>J</i> = 14.0, 8.4, 1.1)
12	3.47 (ddd, <i>J</i> = 10.2, 4.1, 3.0)	3.47 (dd, <i>J</i> = 10.1, 3.2)
13	3.98 (ddd, <i>J</i> = 11.5, 4.1, 3.4)	3.99 (ddd, <i>J</i> = 7.0, 2.9, 2.9)
14	2.06 (dtd, <i>J</i> = 14.7, 7.2, 3.4) 1.79 (ddt, <i>J</i> = 14.6, 11.6, 7.2)	2.07 (dddd, <i>J</i> = 14.6, 7.2, 3.7) 1.80 (dddd, <i>J</i> = 14.6, 10.3, 7.2)
15	1.08 (t, <i>J</i> = 7.2)	1.08 (dd, <i>J</i> = 7.2, 7.2)

Table 3. ^{13}C NMR comparison of 3-(*Z*)-pinnatifidenyne and 3-(*E*)-pinnatifidenyne

Carbon Number	3-(<i>Z</i>)-pinnatifidenyne		Δ (nat.-syn.)	3-(<i>E</i>)-pinnatifidenyne		Δ (nat.-syn.)
	Natural (20 MHz) ref. peak (0, TMS)	Synthetic (100 MHz) ref. peak (77.0, CDCl_3)		Natural ^a (20 MHz) ref. peak (0, TMS)	Synthetic (125 MHz) ref. peak (77.0, CDCl_3)	
1	82.6	82.5	+0.1	76.8	76.8	0
2	80	80	0	not observed	81.9	
3	111.1	111	+0.1	112.1	112.1	0
4	140.6	140.9	-0.3	141.3	141.3	0
5	35	35	0	37.7	37.7	0
6	79.9	79.7	+0.2	79.5	79.5	0
7	64.8	64.9	-0.1	64.5	64.5	0
8	34.4	34.4	0	34.3	34.3	0
9	128.8	128.8	0	128.8	128.8	0
10	130.9	130.9	0	130.9	130.9	0
11	30.2	30.1	+0.1	30.5	30.4	+0.1
12	83.4	83.4	0	83.3	83.3	0
13	61	61	0	61	61.1	-0.1
14	27.1	27.1	0	27.4	27.3	+0.1
15	12.8	12.8	0	12.8	12.8	0
- Carbon (1) of synthetic 3-(<i>E</i>)-pinnatifidenyne was assigned by DEPT- ^{13}C NMR which overlapped with the peak of CDCl_3 .						

S68

S89