Supporting Information for

Synthesis of Chiral Tertiary Homoallylic Alcohols via Chelation Controlled Diastereoselective Nucleophilic Addition on α -Alkoxyketones: Application for the Synthesis of C₁-C₁₁ Subunit of 8-*epi* Fostriecin

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Experimental Section:

General Methods: All operations were carried out under an inert nitrogen atmosphere. The ^1H , ^{11}B and ^{13}C NMR were recorded using a Varian Gemini-300 or a Varian Inova-300 spectrometers. Enantiomeric excess (% ee) was measured using Dynamax HPLC fitted with HPXL Solvent Delivery System and Dynamax UV (λ 254 nm) detector. Chiral column used was CHIRALCEL OD-H. Mass spectra were recorded using a Hewlett-Packard 5989B mass spectrometer/5890 series II gas chromatograph or a Finnigan mass spectrometer model 4000. CI gas used was isobutane.

3-(2-Methoxy-ethoxymethoxy)-propene (1): MEM-Cl (25 g, 0.2 mol) and Diisopropylethylamine (35.4 g, 0.27 mol) were added sequentially to a solution of allylic alcohol (12.25 g, 0.21 mol) in CH_2Cl_2 at 0 °C and was then stirred at room temperature for 12 hours. The reaction mixture was quenched with water, diluted with CH_2Cl_2 , and the aqueous layer was extracted with CH_2Cl_2 . The combined organic solutions were washed with brine and dried over MgSO_4 , filtered and concentrated in vacuo. Flash chromatography, using a gradient of ethyl acetate-hexanes as eluant, afforded 23.4 g (80% yield) of **1** as a colorless oil. ^1H NMR (300 MHz, CDCl_3) δ (ppm): 5.92 (ddd, J = 16.05, 10.47, 4.98 Hz, 1H), 5.17 - 5.32 (m, 2H), 4.75 (s, 2H), 4.09 (d, J = 5.6 Hz, 2H), 3.72 (t, J = 4.1 Hz, 2H), 3.56 (t, J = 4.1 Hz, 2H), 3.40 (s, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ (ppm): 134.3, 117.0, 94.7, 71.8, 68.2, 66.8, 59.0.

(1S, 2S)-2-(2-Methoxy-ethoxymethoxy)-1-phenyl-but-3-en-1-ol (4b): A suspension of **1** (0.73 g, 5 mmol) in THF (10 mL) was cooled to -78 °C and *sec*-BuLi (1.3 M in Hexanes, 3.66 mL, 4.76 mmol) was added dropwise. The resultant bright yellow mixture was stirred at -78 °C for 30 minutes. A solution of (+)-B-methoxydiisopinocampheylborane (1.90 g, 6 mmol) in THF (5 mL) was then introduced dropwise via cannula. After stirring 60 min at -78 °C, boron trifluoride etherate (0.95 mL, 7.5 mmol) was added, followed by a pre-cooled (-78 °C) solution of Benzaldehyde (530 mg, 5 mmol) in THF (5 mL) via cannula. Stirring was continued at -78 °C for 3 h, the reaction mixture was oxidized via addition of 3 M NaOH (2.34 mL) and 30% H_2O_2 (2.38 mL). The biphasic solution was stirred for 8 h at ambient temperature. The layers were separated, and the aqueous solution was washed with Et_2O (2x10 mL). The combined organic solutions were washed with brine, dried over MgSO_4 , filtered and concentrated in vacuo. Flash chromatography, using a gradient of ethyl acetate-hexanes as eluant gave 0.84 g (70%) of the homoallylic alcohol **4b**. ^1H NMR (300 MHz, CDCl_3) δ (ppm): 7.25 - 7.40 (m, 5H), 5.54 - 5.66 (m, 1H), 5.12 - 5.18 (m, 2H), 4.82 (d, J = 7.0 Hz, 1H), 4.75 (d, J = 7.0 Hz, 1H), 4.59 (d, J = 7.2 Hz, 1H), 4.19 (t, J = 7.2 Hz, 1H), 3.58 - 3.70 (m, 2H), 3.49 (t, J = 4.5 Hz, 2H), 3.40 (s, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ (ppm): 140.4, 134.3, 128.1, 127.7, 127.1, 119.2, 93.3, 82.2, 76.6, 71.8, 67.4, 59.0; EI-MS: m/z 195, 146, 120, 107, 89 [$(\text{CH}_2\text{OCH}_2\text{CH}_2\text{OCH}_3)^+$, 100%], 77, 59; CI-MS: m/z 253 ($M + H$), 235 ($(M + H) - \text{H}_2\text{O}$), 205, 147, 129, 89 [$(\text{C}_7\text{H}_5)^+$, 100%]; HRMS-CI: ($M + H$) 253.1430 (actual), 253.1440 (calcd.); 95% ee based on HPLC (The alcohol was derivatized as its *p*-nitrobenzoyl ester and analyzed on the HPLC and the ee was determined to be 95%).

(2S, 3S)-3-(2-Methoxy-ethoxymethoxy)-pent-4-en-2-ol (4a): Procedure same as that of **4b**. Yield: 68%; ^1H NMR (300 MHz, CDCl_3) δ (ppm): 5.64 (ddd, J = 17.76, 10.62, 7.83 Hz, 1H), 5.27-5.32 (m, 2H), 4.78 (d, J = 7.0 Hz, 1H), 4.69 (d, J = 7.0 Hz, 1H), 3.78 - 3.86 (m, 2H), 3.63 - 3.73 (m, 2H), 3.53-3.56 (m, 2H), 3.38 (s, 3H), 2.85 (bs, 1H), 1.13 (d, J = 6.3 Hz, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ (ppm): 134.7, 119.6, 92.9, 82.9, 71.7, 69.3, 67.3, 58.8, 18.5; EI-MS: m/z 89 [$(\text{CH}_2\text{OCH}_2\text{CH}_2\text{OCH}_3)^+$, 100%], 77, 70, 59, 45, 43; CI-MS: m/z 191 ($M + H$), 115; 93% ee based on HPLC (The alcohol was derivatized as its *p*-nitrobenzoyl ester and analyzed on the HPLC and the ee was determined to be 93%).

(2S)-2-(2-Methoxy-ethoxymethoxy)-1-phenyl-but-3-en-1-one (5b): A solution of **4b** (5.54 g, 22 mmol) in anhydrous CH_2Cl_2 (50 mL) was treated with 11.48 g (26 mmol) of Dess-Martin periodinane. After stirring at 25 °C for 30 minutes, 20 mL of 10% aqueous $\text{Na}_2\text{S}_2\text{O}_3$ and 20 mL saturated aqueous NaHCO_3 were added and the mixture was stirred for 1 hour. The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 (3x20 mL). The organic layers were combined, dried (Na_2SO_4) and concentrated in vacuo. Chromatography afforded **5b** (4.96 g, 90%) as a colorless oil: ^1H

NMR (300 MHz, CDCl₃) δ (ppm): 8.00 - 8.03 (m, 2H), 7.54 - 7.60 (m, 1H), 7.43 - 7.48 (m, 2H), 5.97 (ddd, J = 17.04, 10.44, 6.54 Hz, 1H), 5.46 - 5.56 (m, 2H), 5.37 (d, J = 10.4 Hz, 1H), 4.90 (d, J = 7.1 Hz, 1H), 4.81 (d, J = 7.1 Hz, 1H), 3.68 (t, J = 4.8 Hz, 2H), 3.45-3.48 (m, 2H), 3.33 (s, 3H); ¹³C NMR (75 MHz, CDCl₃) δ (ppm): 196.7, 135.0, 133.3, 133.0, 129.0, 128.5, 120.0, 94.0, 79.9, 71.5, 67.4, 59.8; EI-MS: m/z 175, 145, 105, 89 [(CH₂OCH₂CH₂OCH₃)⁺, 100%], 77, 59; CI-MS: m/z 251 (M + H), 175 [(M + H - HOCH₂CH₂OCH₃), 100%].

(3S)-3-(2-Methoxy-ethoxymethoxy)-pent-4-en-2-one (5a): Procedure same as that of **5b**. Yield: 92%. ¹H NMR (300 MHz, CDCl₃) δ (ppm): 5.77 (ddd, J = 17.13, 10.32, 6.60 Hz, 1H), 5.36 - 5.51 (m, 2H), 4.80 (d, J = 6.9 Hz, 1H), 4.76 (d, J = 6.9, 1H), 4.60 (d, J = 6.6 Hz, 1H), 3.65-3.80 (m, 2H), 3.53 (t, J = 4.4 Hz, 2H), 3.37 (s, 3H), 2.19 (s, 3H); ¹³C NMR (75 MHz, CDCl₃) δ (ppm): 206.1, 132.3, 119.8, 93.6, 82.8, 71.6, 67.4, 58.8, 25.7; EI-MS: m/z 145 (M - CH₃CO), 113, 89 [(CH₂OCH₂CH₂OCH₃)⁺, 100%], 77, 59, 43; CI-MS: m/z 189 (M + H), 113, 89 [(CH₂OCH₂CH₂OCH₃)⁺, 100%].

(2R, 3S)-3-(2-Methoxy-ethoxymethoxy)-pent-4-en-2-ol (6a): A solution of **5a** (100 mg, 0.53 mmol) in anhydrous THF (5 mL) at -78 °C was treated dropwise with Zn(BH₄)₂ (ca 0.5 M, 1.2 mL), 2 hours after addition, the mixture was allowed to warm up to -40 °C for 1 h, at which time TLC showed complete disappearance of starting materials. 5 mL of saturated aqueous NH₄Cl solution precooled to 0 °C was added and the aqueous layer was extracted with ether (2x5 mL); the organic layers were combined, dried (Na₂SO₄) and concentrated in vacuo. Chromatography affords **6a** (91 mg, 90%) as a colorless oil. ¹H NMR (300 MHz, CDCl₃) δ (ppm): 5.74 (ddd, J = 17.04, 10.77, 7.56 Hz, 1H), 5.29 - 5.36 (m, 2H), 4.71 - 4.82 (m, 2H), 4.03 (dd, J = 7.5, 3.3 Hz, 1H), 3.80 - 3.93 (m, 2H), 3.63 - 3.73 (m, 2H), 3.58 (t, J = 4.5 Hz, 2H), 3.41 (s, 3H), 2.61 (br, 1H), 1.16 (d, J = 6.3 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃) δ (ppm): 134.7, 134.0, 120.0, 119.7, 93.4, 93.2, 83.3, 82.1, 71.8, 69.5, 69.2, 67.6, 67.3, 59.0, 18.6, 17.7.

(2S, 3S)-4-(2-Methoxy-ethoxymethoxy)-3-methyl-hex-5-en-3-ol (6b): A solution of **5a** (100 mg, 0.53 mmol) in anhydrous THF (5 mL) at -78 °C was treated dropwise with ethyl magnesium bromide (3.0 M in Ether, 0.2 mL, 0.60 mmol), 3 hours after addition, 5 mL of pre-cooled NH₄Cl (0 °C) saturated aqueous solution was added via syringe. The layers were diluted with ether and separated, the aqueous layer was extracted with ether (2x5 mL); the organic layers were combined, dried (Na₂SO₄) and concentrated in vacuo. Chromatography afforded **6b** (98 mg, 85%) as a colorless oil. ¹H NMR (300 MHz, CDCl₃) δ (ppm): 5.71 (d, J = 18.09, 10.56, 8.37 Hz, 1H), 5.25-5.32 (m, 2H), 4.78 (d, J = 6.9 Hz, 1H), 4.69 (d, J = 6.9 Hz, 1H), 3.91 (d, J = 8.2 Hz, 1H), 3.81 - 3.87 (m, 1H), 3.61 - 3.68 (m, 1H), 3.55 (t, J = 4.7 Hz, 2H), 3.39 (s, 3H), 2.49 (bs, 1H), 1.52 (q, J = 7.4 Hz, 2H), 1.09 (s, 3H), 0.93 (t, J = 7.6 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃) δ (ppm): 134.3, 120.1, 93.0, 83.2, 73.7, 71.8, 67.4, 59.0, 31.4, 21.6, 7.5.

(2S, 3S)-4-(2-Methoxy-ethoxymethoxy)-3-methyl-hexa-1,5-dien-3-ol (6c): Procedure same as that of **6b**. Yield: 78%. ¹H NMR (300 MHz, CDCl₃) δ (ppm): 5.95 (dd, J = 17.1, 10.8 Hz, 1H), 5.73 (ddd, J = 18.0, 10.2, 8.1 Hz, 1H), 5.10 - 5.36 (m, 4H), 4.76 (d, J = 6.9 Hz, 1H), 4.68 (d, J = 6.9 Hz, 1H), 3.81 - 3.91 (m, 1H), 3.54 - 3.66 (m, 3H), 3.39 (s, 3H), 2.70 (br, 1H), 1.23 (s, 3H); ¹³C NMR (75 MHz, CDCl₃) δ (ppm): 142.7, 133.9, 120.6, 113.2, 92.9, 83.6, 74.2, 71.7, 67.3, 58.9, 23.3; EI-MS: m/z 111, 89 [(CH₂OCH₂CH₂OCH₃)⁺, 100%], 71, 59, 55, 43; CI-MS: m/z 217 (M + H), 199, 169, 141, 111, 89 [(CH₂OCH₂CH₂OCH₃)⁺, 100%].

(2S, 3S)-3-(2-Methoxy-ethoxymethoxy)-4-methyl-hept-1-en-5-yn-4-ol (6d): Procedure same as that of **6b**. Yield: 75%. ¹H NMR (300 MHz, CDCl₃) δ (ppm): 5.77 (ddd, J = 17.1, 10.5, 7.5 Hz, 1H), 5.26 - 5.33 (m, 2H), 4.72 (d, J = 6.9 Hz, 1H), 4.69 (d, J = 6.9 Hz, 1H), 3.96 (d, J = 7.5 Hz, 1H), 3.81 - 3.88 (m, 1H), 3.57 - 3.64 (m, 1H), 3.50 (t, J = 4.8 Hz, 2H), 3.33 (s, 3H), 2.86 (br, 1H), 1.77 (s, 3H), 1.33 (s, 3H); ¹³C NMR (75 MHz, CDCl₃) δ (ppm): 133.6, 120.8, 93.2, 83.4, 81.7, 80.1, 71.8, 69.4, 67.3, 59.0, 25.3, 3.6; EI-MS: m/z 139, 123, 89 [(CH₂OCH₂CH₂OCH₃)⁺, 100%], 83, 67, 59, 43; CI-MS: m/z 229 (M + H), 211, (M + H - H₂O), 181, 153, 135, 123, 89 [(CH₂OCH₂CH₂OCH₃)⁺, 100%].

(1R, 2S)-2-(2-Methoxy-ethoxymethoxy)-1-phenyl-but-3-en-1-ol (6e): Procedure same as that of **6a**. Yield: 92%. ¹H NMR (300 MHz, CDCl₃) δ (ppm): 7.22 - 7.38 (m, 5H), 5.70 (ddd, *J* = 17.2, 10.6, 5.7 Hz, 1H), 5.20 - 5.28 (m, 2H), 4.77 (d, *J* = 5.1 Hz, 1H), 4.73 (d, *J* = 6.9 Hz, 1H), 4.62 (d, *J* = 6.9 Hz, 1H), 4.26 (dd, *J* = 7.3, 5.2 Hz, 1H), 3.48 (m, 2H), 3.43 (m, 2H), 3.36 (s, 3H), 2.76 (br, 1H); ¹³C NMR (75 MHz, CDCl₃) δ (ppm): 140.5, 133.8, 128.0, 127.6, 127.0, 120.2, 93.0, 81.5, 75.5, 71.7, 67.0, 59.0.

(3R, 4S)-4-(2-Methoxy-ethoxymethoxy)-3-phenyl-hex-5-en-3-ol (6f): Procedure same as that of **6b**. Yield: 88%. ¹H NMR (300 MHz, CDCl₃) δ (ppm): 7.18 - 7.38 (m, 5H), 5.53 (ddd, *J* = 17.1, 10.9, 7.7 Hz, 1H), 5.08 - 5.16 (m, 2H), 4.77 (d, *J* = 6.9 Hz, 1H), 4.68 (d, *J* = 6.9 Hz, 1H), 4.25 (d, *J* = 7.71 Hz, 1H), 3.77 - 3.84 (m, 1H), 3.57 - 3.66 (m, 1H), 3.54 (t, *J* = 4.5 Hz, 2H), 3.41 (s, 3H), 2.70 (br, 1H), 1.88 - 2.11 (m, 2H), 0.74 (t, *J* = 7.41 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃) δ (ppm): 142.3, 133.7, 127.8, 126.5, 126.2, 119.9, 93.0, 83.6, 78.3, 71.8, 67.5, 59.1, 31.3, 7.5; EI-MS: *m/z* 175, 135, 89 [(CH₂OCH₂CH₂OCH₃)⁺], 59 [(CH₃OCH₂CH₂)⁺, 100%], 57; CI-MS: *m/z* 281 (M + H), 263 (M + H - H₂O), 251, 233, 175, 157, 89 [(CH₂OCH₂CH₂OCH₃)⁺, 100%].

(3R, 4S)-4-(2-Methoxy-ethoxymethoxy)-3-phenyl-hexa-1,5-dien-3-ol (6g): Procedure same as that of **6b**. Yield: 81%. ¹H NMR (300 MHz, CDCl₃) δ (ppm): 7.26 - 7.55 (m, 5 H), 6.53 (dd, *J* = 17.1, 11.1 Hz, 1H), 5.67 (ddd, *J* = 17.1, 10.8, 7.8 Hz, 1H), 5.51 (dd, *J* = 17.1, 1.2 Hz, 1H), 5.24 - 5.34 (m, 3H), 4.79 (d, *J* = 6.9, 1H), 4.66 (d, *J* = 6.9, 1H), 4.42 (d, *J* = 7.8 Hz, 1H), 3.48 - 3.60 (m, 4H), 3.43 (s, 3H), 2.86 (br, 1H); ¹³C NMR (75 MHz, CDCl₃) δ (ppm): 143.0, 141.9, 133.3, 128.0, 127.0, 126.1, 121.0, 114.3, 92.8, 82.9, 77.7, 71.7, 67.1, 59.0; EI-MS: *m/z* 146, 133, 89 [(CH₂OCH₂CH₂OCH₃)⁺], 59 [(CH₃OCH₂CH₂)⁺, 100%], 55; CI-MS: *m/z* 261 (M + H - H₂O), 185, 89 [(CH₂OCH₂CH₂OCH₃)⁺, 100%].

(3S, 4S)-3-(2-Methoxy-ethoxymethoxy)-4-phenyl-hept-1-en-5-yn-4-ol (6h): Procedure same as that of **6b**. Yield: 77%. ¹H NMR (300 MHz, CDCl₃) δ (ppm): 7.26 - 7.69 (m, 5 H), 5.85 (d, *J* = 17.4, 10.5, 7.8 Hz, 1H), 5.28 - 5.37 (m, 2H), 4.71 (d, *J* = 6.9 Hz, 1H), 4.57 (d, *J* = 6.9 Hz, 1H), 4.23 (d, *J* = 7.8 Hz, 1H), 3.2 - 3.4 (m 7H), 1.97 (s, 3H); ¹³C NMR (75 MHz, CDCl₃) δ (ppm): 141.9, 133.7, 127.7, 127.6, 126.7, 121.3, 92.7, 83.6, 82.8, 80.3, 74.3, 71.6, 66.7, 58.9, 3.8; EI-MS: *m/z* 197, 145, 89 [(CH₂OCH₂CH₂OCH₃)⁺], 67, 59 [(CH₃OCH₂CH₂)⁺, 100%]; CI-MS: *m/z* 273 (M + H - H₂O), 197, (100%), 89 [(CH₂OCH₂CH₂OCH₃)⁺].

(1R, 2S)-1-Phenyl-but-3-ene-1,2-diol (7e): A solution of **6e** (200 mg, 0.79 mmol) in methanol (1 mL) at room temperature was treated with 20 mL mixture of methanol:water:13M HCl (8:1:1). 1 hour after addition, the mixture was diluted with water (20 mL) and extracted with ether, the organic layers were combined, washed with saturated sodium bicarbonate and dried (MgSO₄). The solvent was removed under vacuum and the crude product was purified by column chromatography to obtain 95 mg (73%) **7e** as a colorless liquid. ¹H NMR (300 MHz, CDCl₃) δ (ppm): 7.26 - 7.35 (m, 5H), 5.80 (ddd, *J* = 16.8, 10.5, 6.3 Hz, 1H), 5.19 - 5.30 (m, 2H), 4.75 (d, *J* = 4.8 Hz, 1H), 4.30 - 4.33 (m, 1H), 2.32 (bs, 2H); ¹³C NMR (75MHz, CDCl₃) δ (ppm): 139.9, 135.6, 128.3, 127.8, 126.8, 117.7, 76.7, 76.5; EI-MS: *m/z* 146 (M - H₂O), 107 (100%), 79, 51; CI-MS: *m/z* 163 (M + H), 147 (100%), 129, 107.

(3S, 4R)-4-Phenyl-hex-1-ene-3,4-diol (7f): Procedure same as that of **7e**. Yield: 70%. ¹H NMR (300 MHz, CDCl₃) δ (ppm): 7.20 - 7.33 (m, 5H), 5.62 (ddd, *J* = 16.5, 10.5, 5.7 Hz, 1H), 5.08 - 5.24 (m, 2H), 4.29 (d, *J* = 5.7 Hz, 1H), 2.29 (br, 2H), 1.89 - 2.10 (m, 2H), 0.73 (t, *J* = 7.5 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃) δ (ppm): 142.1, 136.7, 128.1, 126.8, 126.1, 117.4, 79.1, 78.9, 31.1, 7.6; EI-MS: *m/z* 145, 135 (100%), 117, 105, 77, 57; CI-MS: *m/z* 193 (M + H), 175 (100%), 135, 105.

4-(tert-Butyl-dimethyl-silanyloxy)-but-2-enal (9): A solution of *cis*-2-butene-1,4-diol (75 g, 0.85 mol) in DMF (400 mL) at 0 °C was treated with TBS-Cl (64.8 g, 0.43 mol) and imidazole (58 g, 0.85 mol), the reaction mixture was allowed to warm up to 25 °C and stirred overnight. Workup the reaction by adding 500 mL water, the layers were separated and the aqueous layer was extracted with ether (2x 100

mL). The organic layers were combined and dried (Na₂SO₄). Chromatography afforded the allyl alcohol (62.6 g, 72%) as a colorless oil. ¹H NMR (300 MHz, CDCl₃) δ (ppm): 5.61 – 5.74 (m, 2H), 4.25 (d, *J* = 4.4 Hz, 2H), 4.18 (d, *J* = 4.9 Hz, 2H), 2.26 (bs, 1H), 0.90 (s, 9H), 0.08 (s, 6H); ¹³C NMR (75 MHz, CDCl₃) δ (ppm): 131.3, 130.1, 59.6, 58.8, 25.9, 18.3, -5.2.

Pyridinium Chlorochromate (40 g, 0.184 mol) was suspended in methylene chloride (300 mL), 40 g sodium acetate was added as the buffer, and then the above allyl alcohol (24 g, 0.119 mol) was rapidly added at room temperature. The solution became briefly homogeneous before depositing the black insoluble reduced reagent. After 2 hours the oxidation, the black reaction mixture was diluted with 1000 mL anhydrous ether and the solvent was decanted, the black solid was washed twice with ether. Product **9** (19.3 g, 81%) was isolated simply by filtration of organic extracts through silica gel and evaporation of solvent at reduced pressure. ¹H NMR (300 MHz, CDCl₃) δ (ppm): 9.60 (d, *J* = 8.0 Hz, 1H), 6.88 (dt, *J* = 15.5, 3.2 Hz, 1H), 6.34 – 6.44 (m, 1H), 4.43 – 4.46 (m, 2H), 0.92 (s, 9H), 0.09 (s, 6H); ¹³C NMR (75 MHz, CDCl₃) δ: 193.4, 156.5, 130.6, 62.3, 25.8, 18.3, -5.4.

(3R,4R)-7-(tert-Butyl-dimethyl-silanyloxy)-3-(2-methoxy-ethoxymethoxy)-hepta-1,5-dien-4-ol

(10): A suspension of **1** (0.73 g, 5 mmol) in THF (10 mL) was cooled to -78 °C and *sec*-BuLi (1.3 M in Hexanes, 3.66 mL) was added dropwise. The resultant bright yellow mixture was stirred at -78 °C for 30 minutes. A solution of (-)-B-methoxydiisopinocampheylborane (1.90 g, 6 mmol) in THF (5 mL) was introduced dropwise via cannula. After stirring 60 min at -78 °C, boron trifluoride etherate (0.95 mL, 7.5 mmol) was added, followed by a pre-cooled (-78 °C) solution of aldehyde **9** (1 g, 5 mmol) in THF (5 mL) via cannula. After stirring at -78 °C for 3 h, the reaction mixture was quenched via addition of 3 M NaOH (2.34 mL) and 30% H₂O₂ (2.38 mL). The biphasic solution was stirred for 8 h, and warmed to ambient temperature. The layers were separated, and the aqueous solution was washed with Et₂O (2×5 mL). The combined organic solutions were washed with brine, dried over MgSO₄, filtered and concentrated in vacuo. Flash chromatography, using a gradient of ethyl acetate-hexanes as eluant, afforded 1.17 g (69% yield) of **10** as a colorless oil. ¹H NMR (300 MHz, CDCl₃) δ (ppm): 5.87 (dt, *J* = 15.4, 4.4 Hz, 1H), 5.62 – 5.74 (m, 2H), 5.27 – 5.32 (m, 2H), 4.79 (d, *J* = 6.9 Hz, 1H), 4.72 (d, *J* = 6.9 Hz, 1H), 4.17 (m, 2H), 4.06 – 4.10 (m, 1H), 3.91 – 3.96 (m, 1H), 3.80 – 3.87 (m, 1H), 3.63 – 3.70 (m, 1H), 3.54 – 3.56 (m, 2H), 3.39 (s, 3H), 0.89 (s, 9H), 0.05 (s, 6H); ¹³C NMR (75 MHz, CDCl₃) δ (ppm): 134.4, 132.1, 127.7, 119.8, 93.2, 81.5, 73.9, 71.8, 67.6, 63.1, 59.0, 25.9, 18.4, -5.2; 95% ee based on HPLC (The alcohol was derivatized as its *p*-nitrobenzoyl ester and analyzed on the HPLC and the ee was determined to be 95%); EI-MS: *m/z* 133, 89, 75, 59 [100%]; CI-MS: 345 (M - H)⁺, 329 ((M + H) - H₂O), 223 [100%], 89; HRMS-CI: (M + H) 345.2090 (actual), 345.2097 (calcd.).

(3R,4S)-4,7-Bis-(tert-butyl-dimethyl-silanyloxy)-3-(2-methoxy-ethoxymethoxy)-4-methyl-hepta-1,5-diene (11):

A solution of **10** (7.89 g, 23 mmol) in anhydrous CH₂Cl₂ (150 mL) was treated with 11.7 g (27 mmol) of Dess-Martin periodinane. After stirring at 25 °C for 30 minutes, 50 mL of 10% aqueous Na₂S₂O₃ and 20 mL saturated aqueous NaHCO₃ were added. The layers were separated and the aqueous layer was extracted with CH₂Cl₂ (3×20 mL). The organic layers were combined and dried (Na₂SO₄). Chromatography afforded the ketone (7.15 g, 92%) as a colorless oil: ¹H NMR (300 MHz, CDCl₃) δ (ppm): 7.05 (dt, *J* = 15.5, 3.3 Hz, 1H), 6.68 (dt, *J* = 15.5, 2.2 Hz, 1H), 5.80 (ddd, *J* = 17.1, 10.3, 6.6 Hz, 1H), 5.49 (dt, *J* = 17.2, 1.4 Hz, 1H), 5.37 (dt, *J* = 10.3, 1.3 Hz, 1H), 4.83 (d, *J* = 7.0 Hz, 1H), 4.78 (dt, *J* = 6.6, 1.3 Hz, 1H), 4.77 (d, *J* = 7.0 Hz, 1H), 4.37 (dd, *J* = 3.3, 2.3 Hz, 2H), 3.66 – 3.79 (m, 2H), 3.50 – 3.53 (m, 2H), 3.37 (s, 3H), 0.92 (s, 9H), 0.07 (s, 6H); ¹³C NMR (75 MHz, CDCl₃) δ (ppm): 196.1, 147.3, 132.5, 123.1, 120.1, 93.7, 81.9, 71.7, 67.5, 62.5, 59.0, 25.8, 18.4, -5.4; EI-MS: *m/z* 133, 89, 75, 73, 59 [100%]; CI-MS: 345 (M + H)⁺, 269 ((M + H) - HOCH₂OCH₂CH₂OCH₃), 239, 133, 89 [100%], 77; HRMS-CI: (M + H) 345.2091 (actual), 345.2097 (calcd.).

A solution of the above ketone (200 mg, 0.59 mmol) in anhydrous THF (10 mL) at -78 °C was treated with MeMgBr (3 M in ether, 0.22 mL, 0.66 mmol). After stirring at -78 °C for 2 h, 5 mL of pre-cooled NH₄Cl (0 °C) saturated aqueous solution was added via syringe. The layers were diluted with ether and separated, the aqueous layer was extracted with ether (2× 5 mL); the organic layers were combined and dried (Na₂SO₄). The tertiary alcohol was used directly in the next step. ¹H NMR (300 MHz, CDCl₃) δ (ppm): 5.63 – 5.79 (m, 3H), 5.26 – 5.31 (m, 2H), 4.76 (d, *J* = 6.9 Hz, 1H), 4.69 (d, *J* = 6.93 Hz, 1H),

4.18 – 4.19 (m, 2H), 3.92 (d, $J = 7.7$ Hz, 1H), 3.79 – 3.86 (m, 1H), 3.61 – 3.68 (m, 1H), 3.53 – 3.56 (m, 2H), 3.38 (s, 3H), 1.26 (s, 3H), 0.90 (s, 9H), 0.05 (s, 6H); ^{13}C NMR (75 MHz, CDCl_3) δ (ppm): 134.1, 132.6, 128.9, 120.2, 93.5, 84.9, 73.8, 71.8, 67.7, 63.5, 59.0, 25.9, 24.7, 18.6, -5.1; ESI-MS: 383 (Na adduct)

A solution of the above tertiary alcohol in CH_2Cl_2 at -78°C was added tert-Butyldimethylsilyl trifluoromethanesulfonate (187 mg, 0.71 mmol) and 2,6-lutidine (158 mg, 1.47 mmol), after that, the reaction mixture was allowed to warm up to ambient temperature and stirred overnight and worked up the reaction by adding 10 mL water, and extracted with ether (2x 10 mL). The organic layers were combined and dried (Na_2SO_4). Chromatography afforded **11** (218 mg, 79%, two steps) as a colorless oil. ^1H NMR (300 MHz, CDCl_3) δ (ppm): 5.64 – 5.82 (m, 3H), 5.17 – 5.24 (m, 2H), 4.72 (d, $J = 6.9$ Hz, 1H), 4.66 (d, $J = 6.9$ Hz, 1H), 4.16 (d, $J = 3.96$ Hz, 2H), 3.83 (d, $J = 7.4$ Hz, 1H), 3.74 – 3.80 (m, 1H), 3.55 – 3.64 (m, 1H), 3.44 – 3.54 (m, 2H), 3.38 (s, 3H), 1.29 (s, 3H), 0.90 (s, 9H), 0.86 (s, 9H), 0.06 (s, 6H), 0.05 (s, 6H); ^{13}C NMR (75 MHz, CDCl_3) δ (ppm): 135.4, 134.9, 128.6, 118.6, 93.6, 83.9, 76.5, 71.8, 67.0, 63.4, 59.0, 26.0 (2 carbons), 22.5, 18.3 (2 carbons), -1.9, -2.0, -5.2 (2 carbons).

(4S,5R)-4-(tert-Butyl-dimethyl-silanyloxy)-5-(2-methoxy-ethoxymethoxy)-4-methyl-hepta-2,6-dienal (12): A solution of **11** (200 mg, 0.43 mmol) in 30 mL $\text{AcOH}:\text{H}_2\text{O}:\text{THF}$ (3:1:1) mixture was stirred overnight. The reaction mixture was diluted with ether and separated, the aqueous layer was extracted with ether (2x 5 mL); the organic layers were combined and dried (Na_2SO_4). After removal of the solvent the crude alcohol was treated with 227 mg Dess-Martin Periodinane (0.51 mmol), after stirring at 25°C for 30 minutes, 10 mL of 10% aqueous $\text{Na}_2\text{S}_2\text{O}_3$ and saturated aqueous NaHCO_3 were added. The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 (3x5 mL). The organic layers were combined and dried (Na_2SO_4). Chromatography afforded **12** (136 mg, 88%) as a colorless oil: ^1H NMR (300 MHz, CDCl_3) δ (ppm): 9.57 (d, $J = 7.9$ Hz, 1H), 6.88 (d, $J = 15.7$ Hz, 1H), 6.25 (dd, $J = 15.7, 7.9$ Hz, 1H), 5.67 – 5.79 (m, 1H), 5.23 – 5.33 (m, 2H), 4.74 (d, $J = 7.1$ Hz, 1H), 4.65 (d, $J = 7.0$ Hz, 1H), 3.92 – 3.98 (m, 1H), 3.70 – 3.74 (m, 1H), 3.51 – 3.61 (m, 3H), 3.38 (s, 3H), 1.40 (s, 3H), 0.89 (s, 9H), 0.08 (s, 3H), 0.06 (s, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ (ppm): 193.9, 162.7, 133.5, 130.7, 120.3, 93.4, 83.0, 77.1, 71.7, 67.4, 59.1, 25.9, 22.1, 18.4, -1.9; EI-MS: m/z 302, 213, 89, 73, 59 [100%]; CI-MS: 359 ($\text{M} + \text{H}$) $^+$, 303 ($(\text{M} + \text{H}) - \text{C}_4\text{H}_8$), 253, 227, 89 ($\text{CH}_2\text{OCH}_2\text{CH}_2\text{OCH}_3$, [100%]), 77; HRMS-CI: ($\text{M} + \text{H}$) 359.2252 (actual), 359.2254 (calcd.).

(4R, 7S, 8R)- 7-(tert-Butyl-dimethyl-silanyloxy)-8-(2-methoxy-ethoxymethoxy)-7-methyl-deca-1,5,9-trien-4-ol (13): Allylmagnesium bromide (1 M in ether, 2.15 mL, 2.15 mmol) was added dropwise to a solution of (+)-B-methoxydiisopinocampheylborane (680 mg, 2.16 mmol) in THF (10 mL) at -78°C . After stirring for 30 min at -78°C , the reaction mixture was warmed to room temperature over 1 h, then filtered under an argon atmosphere to remove magnesium salts. The filtrate was cooled to -78°C and aldehyde **12** (516 mg, 1.44 mmol) in THF (5 mL) was added via cannula. After 3 h at -78°C , the reaction mixture was diluted with a mixture of 30% aqueous hydrogen peroxide (2.87 mL) and 3 M sodium hydroxide (2.5 mL). Following 12 h at room temperature, the organic layer was separated and the aqueous layer was extracted with ether (2 x 25 mL). The combined organic phases were dried (Na_2SO_4), concentrated in vacuo, and the residue was chromatographed to furnish **13** (375 mg, 65% yield) as a colorless oil. ^1H NMR (300 MHz, CDCl_3) δ (ppm): 5.64 – 5.88 (m, 4H), 5.07 – 5.26 (m, 4H), 4.57 – 4.72 (m, 2H), 4.17 (m, 1H), 3.83 – 3.90 (m, 2H), 3.51 – 3.56 (m, 3H), 3.40 (s, 3H), 2.50 (bs, 1H), 2.27 – 2.35 (m, 2H), 1.28 (s, 3H), 0.86 (s, 9H), 0.05 (s, 6H); ^{13}C NMR (75 MHz, CDCl_3) δ (ppm): 136.6, 134.6, 134.6, 131.5, 118.6, 117.7, 93.4, 83.7, 76.2, 72.0, 71.2, 67.3, 59.2, 41.8, 25.9, 21.9, 18.3, -1.8; EI-MS: m/z 89, 73, 59 [100%]; CI-MS: 383 ($\text{M} + \text{H} - \text{H}_2\text{O}$) $^+$, 327 ($(\text{M} + \text{H} - \text{H}_2\text{O}) - \text{C}_4\text{H}_8$), 163, 89 ($(\text{CH}_2\text{OCH}_2\text{CH}_2\text{OCH}_3)^+$, [100%]), 77; ESI-MS: m/z 423 (Na adduct); HRMS-CI: (M) 400.2645 (actual), 400.2645 (calcd.).

(3S, 4R, 6R)-6-[3-(tert-Butyl-dimethyl-silanyloxy)-4-(2-methoxy-ethoxymethoxy)-3-methyl-hexa-1,5-dienyl]-5,6-dihydro-pyran-2-one (14): A solution of **13** (440 mg, 1.1 mmol) in anhydrous CH_2Cl_2 (15 mL) at 0°C was treated with acrylic acid (0.16 mL, 2.2 mmol), DCC (500 mg, 2.42 mmol) and DMAP (6.8 mg, 0.055 mmol). After that the mixture was allowed to warm up to ambient

temperature and stirred for 3 h, 15 mL water was added to quench the reaction. The layers were dilute with ether and separated, the aqueous layer was extracted with ether (2x10 mL); the organic layers were combined and dried (Na₂SO₄). Chromatography afforded acrylic ester (420 mg, 84%) as a colorless oil. ¹H NMR (300 MHz, CDCl₃) δ (ppm): 6.39 (dd, *J* = 17.3, 1.8 Hz, 1H), 6.11 (dd, *J* = 17.3, 10.4 Hz, 1H), 5.59 – 5.88 (m, 5H), 5.44 (q, *J* = 6.5 Hz, 1H), 5.06 – 5.24 (m, 4H), 4.72 (d, *J* = 6.8 Hz, 1H), 4.65 (d, *J* = 6.9 Hz, 1H), 3.82 (d, *J* = 7.3 Hz, 1H), 3.70 – 3.76 (m 1H), 3.55 – 3.64 (m 1H), 3.51 (t, *J* = 4.4 Hz, 2H), 3.38 (s, 3H), 2.40 – 2.45 (m, 2H), 1.28 (s, 3H), 0.86 (s, 9H), 0.03 (s, 6H); ¹³C NMR (75 MHz, CDCl₃) δ (ppm): 165.3, 138.9, 134.6, 133.1, 130.6, 128.7, 126.9, 119.0, 118.1, 93.6, 83.8, 76.5, 73.2, 71.8, 67.1, 59.1, 39.1, 25.9, 22.3, 18.3, -2.0, -2.1; ESI-MS: 477 (Na adduct), 455; HRMS-ESI: (M) 454.2739 (actual), 454.2751 (calcd.).

A solution of the above acrylic ester (200 mg, 0.44 mmol) in dichloromethane (25 mL) was added dropwise over 30 minutes to a refluxing solution of tricyclohexylphosphine [1,3-bis-(2,4,6-trimethylphenyl)-4,5-dihydroimidazol-2-ylidene][benzylidene]ruthenium(IV)dichloride (36 mg, 0.042 mmol) in dichloromethane (200 mL). After 12 h, the solvent was removed under vacuum and the residue was purified by silica gel column chromatography (gradient: hexane to 10% ethyl acetate/hexane) to give lactone **14** (146 mg, 78% yield) as a viscous liquid. ¹H NMR (300 MHz, CDCl₃) δ (ppm): 6.84 – 6.90 (m, 1H), 5.91 – 6.06 (m 2H), 5.65 – 5.79 (m, 2H), 5.16 – 5.27 (m, 2H), 4.90 – 4.97 (m, 1H), 4.72 (d, *J* = 6.7 Hz, 1H), 4.64 (d, *J* = 6.7 Hz, 1H), 3.84 (d, *J* = 7.3 Hz, 1H), 3.73 – 3.80 (m, 1H), 3.53 – 3.63 (m, 1H), 3.52 (t, *J* = 5.5 Hz, 2H), 3.37 (s, 3H), 2.40 – 2.44 (m, 2H), 1.30 (s, 3H), 0.86 (s, 9H), 0.06 (s, 6H); ¹³C NMR (75 MHz, CDCl₃) δ (ppm): 163.9, 144.5, 139.6, 134.4, 125.8, 121.7, 119.3, 93.5, 83.7, 77.5, 76.5, 71.8, 67.2, 59.1, 29.8, 25.9, 22.6, 18.4, -1.87, -1.93; EI-MS: *m/z* 321 (M - CH₂OCH₂CH₂OCH₃), 281, 149, 133, 89, 73, 59 [100%]; CI-MS: 427 (M + H), 403 (M + H - H₂O), 321[(M + H - H₂O) - CH₂OCH₂CH₂OCH₃], 295, 189, 89 ((CH₂OCH₂CH₂OCH₃)⁺, [100%]), 77; HRMS-CI: (M) 427.2509 (actual), 427.2516 (calcd.).

300 MHz ¹H NMR of compound **1** in CDCl₃

300 MHz ¹H NMR of compound **4b** in CDCl₃

75 MHz ^{13}C NMR of compound **4b** in CDCl_3

300 MHz ^1H NMR of compound **4a** in CDCl_3

75 MHz ^{13}C NMR of compound 4a in CDCl_3

300 MHz ^1H NMR of compound **5b** in CDCl_3

75 MHz ^{13}C NMR of compound **5b** in CDCl_3

300 MHz ¹H NMR of compound **5a** in CDCl₃

75 MHz ¹³C NMR of compound **5a** in CDCl₃

300 MHz ¹H NMR of compound **6a** in CDCl₃

75 MHz ^{13}C NMR of compound **6a** in CDCl_3

300 MHz ¹H NMR of compound **6b** in CDCl₃

75 MHz ^{13}C NMR of compound **6b** in CDCl_3

300 MHz ¹H NMR of compound **6c** in CDCl₃

75 MHz ^{13}C NMR of compound **6c** in CDCl_3

300 MHz ¹H NMR of compound **6d** in CDCl₃

75 MHz ^{13}C NMR of compound **6d** in CDCl_3

300 MHz ¹H NMR of compound **6e** in CDCl₃

75 MHz ^{13}C NMR of compound **6e** in CDCl_3

300 MHz ¹H NMR of compound **6f** in CDCl₃

75 MHz ^{13}C NMR of compound **6f** in CDCl_3

300 MHz ¹H NMR of compound **6g** in CDCl₃

75 MHz ^{13}C NMR of compound **6g** in CDCl_3

300 MHz ¹H NMR of compound **6h** in CDCl₃

75 MHz ^{13}C NMR of compound **6h** in CDCl_3

300 MHz ¹H NMR of compound **7e** in CDCl₃

75 MHz ^{13}C NMR of compound **7e** in CDCl_3

300 MHz ^1H NMR of compound **7f** in CDCl_3

75 MHz ^{13}C NMR of compound **7f** in CDCl_3

300 MHz ^1H NMR of compound **9** in CDCl_3

75 MHz ¹³C NMR of compound 9 in CDCl₃

300 MHz ¹H NMR of compound **10** in CDCl₃

300 MHz ^1H NMR of compound TBS-11 in CDCl_3

75 MHz ^{13}C NMR of compound TBS-11 in CDCl_3

300 MHz ^1H NMR of compound DMP-12 in CDCl_3

75 MHz ^{13}C NMR of compound DMP-12 in CDCl_3

300 MHz ¹H NMR of compound **13** in CDCl₃

75 MHz ^{13}C NMR of compound **13** in CDCl_3

300 MHz ^1H NMR of compound **14** in CDCl_3

75 MHz ¹³C NMR of compound 14 in CDCl₃