-Supporting Information-

**A Highly Stereoselective and Efficient Total Synthesis of (+)-
Laurencin**

Seungyoup Baek, Hyunil Jo, Hansoo Kim, Hyoungsu Kim,

Sanghee Kim, and Deukjoon Kim*

College of Pharmacy, Seoul National University, San 56-1, Shillim-Dong, Kwanak-Ku,

Seoul 151-742, Korea

* To whom correspondence should be addressed.

Tel: +82-2-880-7850. Fax: +82-2-888-0649.

E-mail: deukjoon@snu.ac.kr

Preparation of Allylated Glycolate 2-oxazolidinone **6**

To a cooled ($-78\text{ }^{\circ}\text{C}$) solution of (*S*)-(+)-4-benzyl-3-benzyloxyacetyl-2-oxazolidinone **(5)** (1.94 g, 6.0 mmol) in anhydrous THF (15 mL, 0.4 M) was added dropwise NaHMDS (6.6 mL, 1.0 M in THF, 6.6 mmol). After the mixture was stirred for 30 min, allyliodide (3.4 g, 12.1 mmol) was added. The resulting mixture was warmed to $-45\text{ }^{\circ}\text{C}$ and stirred for 1.5 h. The reaction was quenched with saturated aqueous NH_4Cl and the mixture was diluted with ethyl acetate (100 mL). The layers were separated, and the aqueous layer was extracted twice with ethyl acetate (50 mL). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4 , and concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, hexane/ethyl acetate, 3/1) to afford the allylated acyloxazolidinone **6** as a colorless oil (2.16 g, 76%):

$[\alpha]_{\text{D}}^{25} = +64.6$ (*c* 3.30, CHCl_3); [for two diastereomers] ^1H NMR (500 MHz, CDCl_3) δ 7.21-7.40 (m, 10 H), 5.75-5.77 (m, 2 H), 5.14-5.18 (m, 1 H), 4.62-4.65 (m, 3 H), 4.53 (d, $J = 11.5\text{ Hz}$, 1 H), 4.29-4.34 (m, 1 H), 4.20 (d, $J = 5.4\text{ Hz}$, 2 H), 4.12-4.17 (m, 1 H), 3.86-3.91 (m, 1 H), 3.52 (ddd, $J = 11.2, 4.8, 4.8\text{ Hz}$, 1 H), 3.28 (dd, $J = 13.4, 2.9\text{ Hz}$, 1 H), 2.75 (dd, $J = 13.4, 9.9\text{ Hz}$, 1 H), 2.65-2.68 (m, 2 H), 1.81-1.84 (m, 1 H), 1.69-1.74

(m, 1 H), 1.51-1.61 (m, 4 H); [for two diastereomers] ^{13}C NMR (100 MHz, CDCl_3) δ 171.8, 152.7, 137.2, 134.7, 129.06, 129.00, 128.6, 127.9, 127.79, 127.67, 127.4, 127.0, 126.65, 126.54, 97.66, 97.55, 76.5, 72.2, 66.5, 62.56, 62.50, 61.87, 61.78, 54.6, 37.4, 30.8, 30.3, 25.1, 19.20, 19.14; IR (neat) 2942, 1780, 1709 cm^{-1} ; HRMS (FAB) found 480.2386 $[(\text{M}+\text{H})^+]$; calcd for $\text{C}_{28}\text{H}_{34}\text{NO}_6$; 480.2308]

Preparation of Methyl Ester 7

To a solution of acyloxazolidinone **6** (2.10 g, 4.5 mmol) in anhydrous MeOH (50 mL, 0.09 M), was added *N,N*-dimethylaminopyridine (0.28 g, 2.3 mmol) at room temperature. The resulting mixture was stirred for 12 h at room temperature and concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, hexane/ethyl acetate, 5/1) to give methylester **7** as a colorless oil (1.19 g, 77%): $[\alpha]_{\text{D}}^{25} = +36.9$ (*c* 2.80, CHCl_3); [for two diastereomers] ^1H NMR (500 MHz, CDCl_3) δ 7.28-7.37 (m, 5 H), 5.70-5.75 (m, 1 H), 5.63-5.66 (m, 1 H), 4.62 (brdd, $J = 3.3, 3.3$ Hz, 1 H), 4.59 (AB, $J_{\text{AB}} = 11.7$ Hz, $\Delta\nu_{\text{AB}} = 135.9$ Hz, 2 H), [for one diastereomer: 4.28 (dd, $J = 12.1, 5.9$ Hz) + 4.10 (dd, $J = 12.1, 7.1$ Hz) 1 H], [for the other: 4.25 (dd, $J = 12.1, 5.9$

Hz) + 4.08 (dd, $J = 12.1, 7.1$ Hz) 1 H], 4.01 (dd, $J = 6.3, 6.3$ Hz, 2 H), 3.85-3.89 (m, 1 H), 3.77 (s, 3 H), 3.48-3.52 (m, 1 H), 2.59-2.62 (m, 2 H), 1.80-1.85 (m, 1 H), 1.69-1.74 (m, 1 H), 1.50-1.61 (m, 4 H); [for two diastereomers] ^{13}C NMR (100 MHz, CDCl_3) δ 172.3, 137.2, 129.0, 128.1, 127.7, 127.6, 126.9, 126.8, 97.7, 97.5, 77.38, 77.34, 72.1, 62.45, 62.35, 61.95, 61.90, 51.7, 31.0, 30.41, 30.39, 25.2, 19.26, 19.23; IR (neat) 2945, 1749 cm^{-1} ; HRMS (FAB) found 335.1849 $[(\text{M}+\text{H})^+]$; calcd for $\text{C}_{19}\text{H}_{27}\text{O}_5$: 335.1780].

Preparation of Alcohol 8

To a cooled ($-78\text{ }^{\circ}\text{C}$) solution of methyl ester **7** (212.1 mg, 0.63 mmol) in anhydrous Et_2O (10 mL, 0.063 M) was added dropwise Dibal-H (0.69 mL, 1.0 M in n -hexane, 0.69 mmol). After the reaction mixture was stirred for 30 min at $-30\text{ }^{\circ}\text{C}$, EtMgBr (0.84 mL, 3.0 M in Et_2O , 2.52 mmol) was added. The cloudy reaction mixture was gradually warmed to room temperature over 2 h and stirred for an additional 10 h. The clear reaction mixture was recooled to $-30\text{ }^{\circ}\text{C}$ and quenched with MeOH. To it was added saturated aqueous NH_4Cl and Na,K-tartrate solution were added at $-30\text{ }^{\circ}\text{C}$. After being stirred 1 h at room temperature, the resulting mixture was poured into Et_2O (50 mL).

The layers were separated, and aqueous layer was extracted twice with Et₂O (50 mL). The combined organic layers were dried over anhydrous Na₂SO₄. Concentration *in vacuo*, and purification of the residue by column chromatography (silica gel, hexane/ethyl acetate, 10/1 to 3/1) afforded alcohol **8** as a colorless oil (175.3 mg, 83%): $[\alpha]_D^{25} = -25.3$ (*c* 1.26, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 7.41-7.48 (m, 5 H), 5.88-5.79 (m, 2 H), [for one diastereomer: 4.80 (brdd, *J* = 3.5, 3.5 Hz) + for the other: 4.77 (brdd, *J* = 3.5, 3.5 Hz) 1 H], 4.73 (AB, *J*_{AB} = 11.6 Hz, Δ*v*_{AB} = 89.2 Hz, 2 H), [for one diastereomer: 4.47 (dd, *J* = 11.8, 5.3 Hz) + 4.28 (dd, *J* = 11.8, 5.3 Hz) 1 H], [for the other: 4.41 (dd, *J* = 11.8, 3.7 Hz) + 4.23 (dd, *J* = 11.8, 6.0 Hz) 1 H], 3.98-4.04 (m, 2 H), 3.63-3.67 (m, 1 H), 3.58-3.61 (m, 1 H), 3.49 (ddd, *J* = 5.6, 5.6, 5.6 Hz, 1 H), 2.94 (dd, *J* = 6.4, 6.4 Hz, 1 H), 2.65-2.70 (m, 1 H), 2.52-2.57 (m, 1 H), 1.96-1.99 (m, 1 H), 1.82-1.87 (m, 1 H), 1.63-1.75 (m, 6 H), 1.10 (dd, *J* = 7.5, 7.5 Hz, 3 H); [**for two diastereomers**] ¹³C NMR (100 MHz, CDCl₃) δ 138.3, 129.1, 129.0, 128.3, 128.11, 128.06, 127.8, 127.6, 97.9, 97.5, 81.12, 81.10, 73.6, 72.2, 62.7, 62.5, 62.1, 61.9, 30.57, 30.49, 28.49, 28.46, 26.20, 26.15, 25.4, 19.4, 19.3, 10.2; IR (neat) 3463, 2939 cm⁻¹.

Preparation of Amide 9

To a cooled (0 °C) solution of alcohol **8** (6.4 g, 19.0 mmol) in anhydrous THF (70 mL, 0.27 M) was added NaH (1.1 g, 60 % dispersion with mineral oil, 21.0 mmol). After 10 min at the same temperature, 2-bromo-*N,N*-dimethylacetamide (3.4 g, 21.0 mmol) was added, and stirring was continued for 4 h at room temperature. The reaction was recooled to 0 °C, quenched with H₂O, and warmed to room temperature. The mixture was diluted with ethyl acetate and the layer was separated. The aqueous layer was extracted with ethyl acetate (100 mL). The combined organic layers were washed with saturated aqueous NH₄Cl and brine, dried over anhydrous MgSO₄, and concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, hexane/ethyl acetate, 2/1 to 1/1) to afford amide **9** as a colorless oil (6.90 g, 90%): $[\alpha]_D^{25} = +1.20$ (c 1.44, CHCl₃); [for two diastereomers] ¹H NMR (500 MHz, CDCl₃) δ 7.24-7.34 (m, 5 H), 5.63-5.72 (m, 2 H), 4.55-4.62 (m, 3 H), 4.17-4.30 (m, 3 H), 4.05-4.11 (m, 1 H), 3.86 (brdd, *J* = 9.2, 9.2 Hz, 1 H), 3.53-3.56 (m, 1 H), 3.48-3.50 (m, 1 H), 3.39-3.41 (m, 1 H), 2.96 (s, 3 H), 2.91 (s, 3 H), 2.30-2.44 (m, 2 H), 1.79-1.83 (m, 1 H), 1.64-1.72 (m, 2 H),

1.48-1.58 (m, 5 H), 0.93 (dd, $J = 7.4, 7.4$ Hz, 3 H); [for two diastereomers] ^{13}C NMR (100 MHz, CDCl_3) δ 169.3, 138.6, 129.3, 128.1, 127.8, 127.6, 127.3, 97.9, 97.7, 82.7, 79.84, 79.78, 72.4, 70.02, 70.00, 62.76, 62.67, 62.11, 61.95, 36.4, 35.2, 30.6, 30.5, 28.28, 28.26, 25.4, 22.6, 19.4, 19.3, 10.0; IR (neat) 3464, 2939, 1651 cm^{-1} ; HRMS (EI) found 419.2679 [M^+ ; calcd for $\text{C}_{24}\text{H}_{37}\text{NO}_5$: 419.2672].

Preparation of Allylic Alcohol **10**

To a solution of amide **9** (5.50 g, 13.1 mmol) in absolute EtOH (100 mL, 0.13 M) was added PTSA (0.67 g, 2.6 mmol) at room temperature. After the mixture was stirred for 12 h at room temperature, excess triethylamine was added, and the resulting solution was concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, ethyl acetate/MeOH, 10/1) to give allylic alcohol **10** as a colorless oil (4.29 g, 95%): $[\alpha]_{\text{D}}^{25} = -9.34$ (c 2.00, CHCl_3); ^1H NMR (500 MHz, CDCl_3) δ 7.25-7.33 (m, 5 H), 5.73-5.79 (m, 1 H), 5.52-5.58 (m, 1 H), 4.58 (AB, $J_{\text{AB}} = 11.6$ Hz, $\Delta\nu_{\text{AB}} = 32.3$ Hz, 2 H), 4.19 (AB, $J_{\text{AB}} = 13.2$ Hz, $\Delta\nu_{\text{AB}} = 54.2$ Hz, 2 H), 4.19 (dd, $J = 12.6, 7.5$ Hz, 1 H), 4.07 (dd, $J = 12.6, 6.1$ Hz, 1 H), 3.56 (ddd, $J = 7.5, 4.7, 4.7$ Hz, 1 H), 3.39 (ddd, $J = 7.5, 4.7, 4.7$ Hz,

1 H), 3.20 (brs, 1 H), 2.96 (s, 3 H), 2.91 (s, 3 H), 2.52 (ddd, $J = 14.4, 7.2, 7.2$ Hz, 1 H), 2.31 (ddd, $J = 14.4, 7.2, 7.2$ Hz, 1 H), 1.65-1.73 (m, 1 H), 1.50-1.59 (m, 1 H), 0.91 (dd, $J = 7.4, 7.4$ Hz, 3 H); ^{13}C NMR (100 MHz, CDCl_3) δ 169.4, 138.3, 131.2, 128.1, 127.8, 127.5, 82.4, 79.4, 72.4, 69.4, 57.7, 36.4, 35.2, 27.9, 22.4, 10.1 (one sp^2 carbon is not observed); IR (neat) 3419, 2930, 1651 cm^{-1} ; HRMS (EI) found 335.2091 [M^+ ; calcd for $\text{C}_{19}\text{H}_{29}\text{NO}_4$: 335.2097].

Preparation of Allylic Chloride 4

To a solution of allylic alcohol **10** (2.1 g, 6.3 mmol) in CCl_4 (70 mL, 0.09 M) was added triphenylphosphine (8.3 g, 31.5 mmol) at room temperature. The mixture was heated to reflux for 2 h, cooled to room temperature, and concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, hexane/acetone, 10/1 to 5/1) to afford allylic chloride **4** as a colorless oil (2.0 g, 91%): $[\alpha]_{\text{D}}^{25} = -15.04$ (c 0.55, CHCl_3); ^1H NMR (500 MHz, CDCl_3) δ 7.24-7.33 (m, 5 H), 5.67-5.76 (m, 2 H), 4.58 (AB, $J_{\text{AB}} = 11.6$ Hz, $\Delta\nu_{\text{AB}} = 13.1$ Hz, 2 H), 4.21 (s, 2 H), 4.13 (dd, $J = 11.7, 7.2$ Hz, 1 H), 4.05 (dd, $J = 11.7, 6.7$ Hz, 1 H), 3.58 (ddd, $J = 8.8, 4.6, 4.6$ Hz, 1 H), 3.40 (ddd, $J = 9.0, 4.6, 4.6$

Hz, 1 H), 2.96 (s, 3 H), 2.92 (s, 3 H), 2.45 (ddd, $J = 14.9, 4.4, 4.4$ Hz, 1 H), 2.34 (ddd, $J = 14.9, 7.1, 7.1$ Hz, 1 H), 1.65-1.73 (m, 1 H), 1.47-1.57 (m, 1 H), 0.94 (dd, $J = 7.4, 7.4$ Hz, 3 H); ^{13}C NMR (100 MHz, CDCl_3) δ 169.3, 138.4, 131.4, 128.2, 127.7, 127.5, 127.0, 82.6, 79.4, 72.6, 69.8, 39.5, 36.4, 35.2, 27.8, 22.5, 10.2; IR (neat) 2930, 1652, 1105 cm^{-1} ; HRMS (EI) found 353.1761 [M^+ ; calcd for $\text{C}_{19}\text{H}_{28}\text{NO}_3^{35}\text{Cl}$: 353.1758].

Preparation of Oxocene 3

To a solution of allylic chloride **4** (121.4 mg, 0.34 mmol) in anhydrous toluene (45 mL, 0.008 M) was added dropwise KHMDS (1.4 mL, 0.5 M solution in toluene, 0.68 mmol) over 30 min at room temperature. After being stirred for an additional 30 min at the same temperature, reaction mixture was quenched with saturated aqueous NH_4Cl . The mixture was diluted with ethyl acetate (100 mL) and washed with water. The aqueous layer was extracted twice with ethyl acetate (50 mL). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4 , and concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, *n*-hexane/ethyl acetate, 2/1 to 1/1) to afford oxocene **3** as a colorless oil (102.4 mg, 94.0%): $[\alpha]_{\text{D}}^{25} = -12.71$ (c 1.49,

CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 7.24-7.35 (m, 5 H), 5.84-5.89 (m, 1 H), 5.71-5.77 (m, 1 H), 4.58 (AB, *J*_{AB} = 12.0 Hz, Δ*v*_{AB} = 116.5 Hz, 2 H), 4.09 (d, *J* = 9.5 Hz, 1 H), 3.47-3.52 (m, 2 H), 3.19 (s, 3 H), 2.93 (s, 3 H), 2.77-2.83 (m, 1 H), 2.72 (ddd, *J* = 11.0, 11.0, 9.5 Hz, 1 H), 2.43 (ddd, *J* = 11.0, 5.8, 5.8 Hz, 1 H), 2.24 (ddd, *J* = 14.1, 5.2, 1.0 Hz, 1 H), 1.69-1.78 (m, 1 H), 1.49-1.58 (m, 1 H), 0.83 (dd, *J* = 7.4, 7.4 Hz, 3 H); ¹³C NMR (100 MHz, CDCl₃) δ 170.8, 138.7, 129.7, 129.3, 128.2, 127.6, 127.4, 84.3, 83.2, 80.6, 70.9, 37.4, 36.2, 31.7, 29.2, 25.3, 10.5; IR (neat) 2922, 1646 cm⁻¹; HRMS (EI) found 317.1982 [*M*⁺; calcd for C₁₉H₂₇NO₃: 317.1991].

Preparation of Ketone 2

To a cooled (−78 °C) solution of acetonitrile (4.0 mL, 76.6 mmol) in anhydrous THF (100 mL, 0.77 M) was added dropwise *n*-BuLi (30.6 mL, 2.5 M in *n*-hexane, 76.6 mmol). After the mixture was stirred for 30 min at −40 °C, amide **3** (530.0 mg, 1.7 mmol) in anhydrous THF (10 mL, 0.17 M) was added. The resulting mixture was gradually warmed to room temperature over 1 h and stirred for an additional 1 h. The reaction was quenched with saturated aqueous NH₄Cl and poured into ethyl acetate (100

mL). The layers were separated, and the aqueous layer was extracted twice with ethyl acetate (100 mL). The combined organic layers were dried over with brine and anhydrous Na₂SO₄, and concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, hexane/ethyl acetate, 10/1 to 5/1) to afford ketone **2** as a colorless oil (378.0 mg, 71%): $[\alpha]_D^{25} = +31.93$ (*c* 1.28, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 7.30-7.40 (m, 5 H), 5.79-5.89 (m, 2 H), 4.61 (AB, *J*_{AB} = 11.8 Hz, Δ*v*_{AB} = 123.4 Hz, 2 H), 3.92 (AB, *J*_{AB} = 20.3 Hz, Δ*v*_{AB} = 36.2 Hz, 2 H), 3.86 (dd, *J* = 7.3, 4.7 Hz, 1 H), 3.53-3.57 (m, 2 H), 2.64 (ddd, *J* = 11.2, 10.5, 10.5 Hz, 1 H), 2.52-2.56 (m, 2 H), 2.46-2.51 (m, 1 H), 1.80-1.84 (m, 1 H), 1.57-1.64 (m, 1 H), 0.88 (dd, *J* = 7.4, 7.4 Hz, 3 H); ¹³C NMR (100 MHz, CDCl₃) δ 199.2, 138.0, 130.5, 128.3, 127.83, 127.75, 127.71, 113.9, 86.0, 84.9, 80.3, 71.5, 31.0, 29.6, 29.0, 25.4, 10.7; IR (neat) 1735, 1635 cm⁻¹; HRMS (EI) found 313.1669 [*M*⁺; calcd for C₁₉H₂₃NO₃: 313.1678].

Preparation of Alcohol **11**

To a cooled (−78 °C) solution of ketone **2** (254.2 mg, 0.81 mmol) in anhydrous THF (20 mL, 0.04 M) was added dropwise L-Selectride (2.43 mL, 1.0 M in THF, 2.43 mmol).

After being stirred for 1 h at -78°C , the reaction was quenched with saturated aqueous NH_4Cl and diluted with Et_2O (100 mL). The layers were separated, and the aqueous layer was extracted twice with Et_2O (50 mL). The combined organic layers were dried over with brine and anhydrous Na_2SO_4 , and concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, hexane/ethyl acetate, 5/1) to afford alcohol **11** as a colorless oil (210.0 mg, 82%, 99% BRSM) and starting material **2** (43.2 mg, 17%): $[\alpha]_{\text{D}}^{25} = -81.7$ (c 0.92, CHCl_3); ^1H NMR (500 MHz, CDCl_3) δ 7.28-7.38 (m, 5 H), 5.88 (ddd, $J = 9.7, 7.8, 7.8$ Hz, 1 H), 5.77 (ddd, $J = 9.1, 7.9, 7.9$ Hz, 1 H), 4.60 (AB, $J_{\text{AB}} = 11.8$ Hz, $\Delta\nu_{\text{AB}} = 124.6$, Hz, 2 H), 3.81 (dddd, $J = 5.7, 5.7, 5.7, 5.7$ Hz, 1 H), 3.61 (ddd, $J = 7.0, 7.0, 2.3$ Hz, 1 H), 3.54 (ddd, $J = 10.5, 4.8, 2.4$ Hz, 1 H), 3.41 (dd, $J = 9.6, 4.9$ Hz, 1 H), 3.00 (d, $J = 6.0$ Hz, 1 H), 2.74 (dd, $J = 16.8, 6.0$ Hz, 1 H), 2.67 (ddd, $J = 11.3, 11.3, 11.3$ Hz, 1 H), 2.60 (dd, $J = 16.8, 5.7$ Hz, 1 H), 2.57-2.63 (m, 1 H), 2.49 (ddd, $J = 11.7, 5.8, 5.8$ Hz, 1 H), 2.11 (dd, $J = 13.6, 8.4$ Hz, 1 H), 1.63-1.76 (m, 2 H), 0.87 (dd, $J = 7.4, 7.4$ Hz, 3 H); ^{13}C NMR (100 MHz, CDCl_3) δ 138.0, 129.4, 128.9, 128.3, 127.9, 127.7, 117.4, 83.2, 81.9, 80.0, 71.5, 70.3, 30.7, 28.8, 25.2, 22.4, 10.4.

Preparation of TIPS-Enyne 13

[Dibal-H reduction] To a cooled ($-78\text{ }^{\circ}\text{C}$) solution of β -hydroxy nitrile **11** (31.5 mg, 0.1 mmol) in anhydrous toluene (5 mL, 0.02 M) was added dropwise Dibal-H (0.4 mL, 1.0 M in *n*-hexane, 0.4 mmol). After being stirred for 1 h at $-78\text{ }^{\circ}\text{C}$, the reaction was quenched with MeOH. The solution was acidified to pH 2 with 1 N HCl aqueous solution at room temperature. After being stirred for 16 h at room temperature, the reaction mixture was poured into saturated $\text{NaHCO}_3/\text{Et}_2\text{O}$ (1/2, 30 mL). The layers were separated, and the aqueous layer was extracted twice with Et_2O (10 mL). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4 , and concentrated *in vacuo* to give the crude aldehyde **12** (30.0 mg, 82%). Without further purification, crude aldehyde **12** was carried on to the next step. **[Wittig Olefination]** A cooled suspension ($-78\text{ }^{\circ}\text{C}$) of triphenyl-(3-triisopropylsilyl-prop-2-ynyl)-phosphonium bromide (538.0 mg, 1.0 mmol) in dry THF (10 mL, 0.1 M) was added dropwise *n*-BuLi (0.63 mL, 1.6 M solution in *n*-hexane, 1.0 mmol). The resulting solution was stirred for 30 min at $-40\text{ }^{\circ}\text{C}$, then recooled to $-78\text{ }^{\circ}\text{C}$, and stirring was stopped. The salts were allowed to settle over 30 min, leaving a pale red supernatant solution of the ‘salt-free’

ylide over a white precipitate. The supernatant solution (4 mL) was added rapidly via syringe to a solution of the above crude aldehyde **12** (30.0 mg, 0.1 mmol) in dry THF (4 mL) at 0 °C and the resulting mixture was stirred for 1 h at 0 °C. The reaction was quenched with H₂O, and the mixture was allowed to warm to room temperature. Saturated aqueous NH₄Cl and Et₂O were added, the layers were separated, and the aqueous layer was extracted with Et₂O. The combined organic layers were washed with brine, dried over anhydrous Na₂SO₄, and concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, *n*-hexane/ethyl acetate, 20/1) to afford (*E*)-enyne **13** as a colorless oil with (*Z*)-enyne (*E*:*Z* = 10:1, total 28.9 mg, 59%): [**For (*E*)-enyne**] [α]_D²⁵ = -39.2 (*c* 0.88, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 7.28-7.35 (m, 5 H), 6.27 (ddd, *J* = 15.9, 7.1, 7.1 Hz, 1 H), 5.82 (ddd, *J* = 9.6, 8.3, 8.3 Hz, 1 H), 5.70 (ddd, *J* = 10.0, 8.5, 8.5 Hz, 1 H), 5.61 (d, *J* = 15.9 Hz, 1 H), 4.60 (AB, *J*_{AB} = 11.9 Hz, $\Delta\nu_{AB}$ = 126.4 Hz, 2 H), 3.47-3.55 (m, 3 H), 3.13 (dd, *J* = 9.6, 6.9 Hz, 1 H), 2.84 (d, *J* = 3.0 Hz, 1 H), 2.67 (ddd, *J* = 11.0, 11.0, 11.0 Hz, 1 H), 2.40-2.48 (m, 3 H), 2.27 (ddd, *J* = 15.0, 7.5, 7.5 Hz, 1 H), 2.07 (dd, *J* = 14.0, 8.4 Hz, 1 H), 1.58-1.71 (m, 2 H), 1.07 (s, 21 H), 0.84 (dd, *J* = 7.3, 7.3 Hz, 3 H); ¹³C NMR (100 MHz, CDCl₃) δ 141.3, 138.3, 129.4, 129.2, 128.3, 128.0, 127.7, 112.2, 105.5, 89.4, 84.3, 83.3, 80.1, 73.0, 71.4, 37.1, 30.8, 28.8, 25.3, 18.6, 11.2, 10.5; HRMS (FAB) found 497.3444 [(M+H)⁺; calcd for

C₃₁H₄₉O₃Si: 497.3451].

Preparation of Acetate **14**

To a solution of ca.10:1 mixture of enynes **13** (29.8 mg, 0.060 mmol) in CH₂Cl₂ (2 mL, 0.03 M) was added pyridine (0.05 mL, ca. 0.63 mmol), acetic anhydride (0.3 mL, ca. 0.29 mmol), and catalytic amount of *N,N*-dimethylaminopyridine at room temperature. After being stirred for 1 h, the reaction mixture was diluted with Et₂O. Saturated aqueous NH₄Cl was added, 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, and concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, *n*-hexane/ethyl acetate, 100/0 to 100/1) to afford (*E*)-enyne acetate **14** as a colorless oil (28.5 mg, 88%): $[\alpha]_D^{25} = -23.0$ (*c* 0.77, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 7.27-7.36 (m, 5 H), 6.08 (ddd, *J* = 15.9, 7.1, 7.1 Hz, 1 H), 5.78 (ddd, *J* = 10.0, 8.0, 8.0 Hz, 1 H), 5.68 (ddd, *J* = 10.0, 9.0, 9.0 Hz, 1 H), 5.59 (d, *J* = 15.9 Hz, 1 H), 4.97 (ddd, *J* = 8.3, 3.9, 3.9 Hz, 1 H), 4.60 (AB, *J*_{AB} = 12.0 Hz, Δ*v*_{AB} = 117.4 Hz, 2 H), 3.41-3.47 (m, 2 H), 3.45 (dd, *J* = 10.4, 3.7 Hz, 1 H), 2.69 (ddd, *J* = 10.9, 10.9, 10.9 Hz, 1 H), 2.59 (ddd, *J* = 14.9, 4.9, 4.9 Hz, 1 H), 2.37-2.47 (m, 3 H), 2.07 (s, 3 H),

2.03 (dd, $J = 13.9, 7.8$ Hz, 1 H), 1.67 (dddd, $J = 14.3, 7.4, 7.4, 7.4, 6.8$ Hz, 1 H), 1.53 (dddd, $J = 14.3, 7.4, 7.4, 7.4, 6.9$ Hz, 1 H), 1.07 (s, 21 H), 0.86 (dd, $J = 7.4, 7.4$ Hz, 3 H); ^{13}C NMR (100 MHz, CDCl_3) δ 170.6, 140.3, 138.6, 129.39, 129.32, 128.2, 128.0, 127.5, 112.8, 105.4, 89.7, 84.2, 81.4, 80.3, 74.8, 71.1, 33.5, 29.9, 28.8, 25.4, 21.1, 18.6, 11.3, 10.6; IR (neat) $1740, \text{cm}^{-1}$; HRMS (EI) found 538.3481 [M^+ ; calcd for $\text{C}_{33}\text{H}_{50}\text{O}_4\text{Si}$: 538.3478].

Preparation of Alcohol 15

To a solution of benzyl-ether **14** (25.2mg, 0.047 mmol) in 1,2-dichloroethane (3.6 mL) and pH 7.0 buffer solution (0.4mL) was added DDQ (42.8 mg, 0.188 mmol) at room temperature. After being stirred for 4 h at 40°C , the reaction was cooled to room temperature. Saturated aqueous NaHCO_3 (3 mL) was added and the resulting dark red solution was stirred vigorously for 2 h. The layers were separated and the aqueous layer was extracted twice with dichloromethane (10 mL). The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, *n*-hexane/ethyl acetate, 5/1 to 3/1) to give alcohol

15 as a colorless oil (18.9 mg, 90%): $[\alpha]_D^{25} = -30.0$ (*c* 0.21, CHCl_3); ^1H NMR (500 MHz, CDCl_3) δ 6.12 (ddd, $J = 15.8, 7.6, 7.6$ Hz, 1 H), 5.74-5.83 (m, 2 H), 5.59 (ddd, $J = 15.8, 1.4, 1.4$ Hz, 1 H), 5.00 (ddd, $J = 8.1, 4.6, 4.6$ Hz, 1 H), 3.71 (dddd, $J = 8.4, 8.4, 4.6, 1.8$ Hz, 1 H), 3.49 (ddd, $J = 8.6, 4.6, 2.2$ Hz, 1 H), 3.43 (ddd, $J = 7.8, 6.2, 1.6$ Hz, 1 H), 2.52-2.58 (m, 2 H), 2.34-2.46 (m, 3 H), 2.17 (ddd, $J = 14.3, 8.2, 2.3$ Hz, 1 H), 2.10 (s, 3 H), 1.52-1.70 (m, 2 H), 1.10 (s, 21 H), 0.96 (dd, $J = 7.4, 7.4$ Hz, 3 H); ^{13}C NMR (100 MHz, CDCl_3) δ 170.4, 139.8, 129.4, 128.9, 112.9, 105.2, 90.0, 83.1, 80.4, 74.3, 73.6, 34.1, 33.5, 29.7, 25.5, 21.0, 18.6, 11.2, 10.4; IR (neat) 3433, 1741, cm^{-1} ; HRMS (EI) found 448.2996 [M^+ ; calcd for $\text{C}_{26}\text{H}_{44}\text{O}_4\text{Si}$: 448.3009].

Preparation of Enyne 16

To a cooled (0 °C) solution of enyne **15** (17.4 mg, 0.039 mmol) in THF (2 mL) was added dropwise TBAF (0.1 mL, 1.0 M solution in THF, 0.1 mmol). After being stirred for 30 min, the reaction 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*. The residue was purified by column chromatography (silica gel, *n*-hexane/ethylacetate, 5/1 to 3/1) to afford enyne **16** as a colorless oil (10.7 mg, 95%): $[\alpha]_D^{25} = -27.0$ (*c* 0.16, CHCl_3); ^1H NMR (500 MHz, CDCl_3) δ 6.19 (ddd, $J = 15.9, 7.3, 7.3$ Hz, 1 H), 5.74-5.83 (m, 2 H), 5.57 (dd, $J = 15.9, 1.5$ Hz, 1 H), 5.01 (ddd, $J = 8.3, 4.5, 4.5$ Hz, 1 H), 3.71 (ddd, $J = 8.2, 8.2, 4.5$ Hz, 1 H), 3.48 (ddd, $J = 8.4, 4.4, 2.2$ Hz, 1 H), 3.42 (ddd, $J = 6.4, 6.4, 1.2$ Hz, 1 H), 2.82 (d, $J = 1.9$ Hz, 1 H), 2.34-2.57 (m, 5 H), 2.17 (ddd, $J = 14.3, 8.1, 2.3$ Hz, 1 H), 2.10 (s, 3 H), 1.53-1.68 (m, 2 H), 0.96 (dd, $J = 7.4, 7.4$ Hz, 3 H); ^{13}C NMR (100 MHz, CDCl_3) δ 170.4, 141.2, 129.5, 128.8, 111.5, 83.1, 81.9, 80.5, 76.7, 74.3, 73.6, 34.2, 33.5, 29.8, 25.5, 21.1, 10.5.

Preparation of (+)-Laurencin (**1**)

To a solution of alcohol **16** (7.4 mg, 0.025 mmol) in dry toluene (2 mL) were added carbon tetrabromide (33.1 mg, 0.1 mmol) and *n*-trioctylphosphine (0.1 mL, tech. 90%, 0.25 mmol) at room temperature. After the resulting mixture was stirred for 20 min at room temperature, it was stirred at 70 °C for an additional 12 h. The reaction mixture was cooled to room temperature and concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, *n*-hexane/ethyl acetate, 20/1) to afford (+)-laurencin

(1) as a pale oil (4.5 mg, 50%): $[\alpha]_{\text{D}}^{25} = +72.5$ (c 0.17, CHCl_3); ^1H NMR (500 MHz, CDCl_3) δ 6.18 (ddd, $J = 15.9, 6.9, 6.9$ Hz, 1 H), 5.88-5.98 (m, 2 H), 5.56 (ddd, $J = 15.9, 1.4, 1.4$ Hz, 1 H), 5.02 (ddd, $J = 8.5, 4.1, 4.1$ Hz, 1 H), 4.10 (ddd, $J = 9.9, 3.3, 3.3$ Hz, 1 H), 3.46 (ddd, $J = 9.9, 7.3, 2.5$ Hz, 1 H), 3.42 (dd, $J = 10.5, 4.5$ Hz, 1 H), 3.18 (ddd, $J = 13.5, 8.7, 3.6$ Hz, 1 H), 2.85 (d, $J = 2.0$ Hz, 1 H), 2.35-2.56 (m, 4 H), 2.08-2.13 (m, 1 H), 2.10 (s, 3 H), 1.98 (dddd, $J = 14.4, 7.4, 7.4, 7.4, 2.5$ Hz, 1 H), 1.59 (dddd, $J = 14.4, 7.4, 7.4, 7.4$ Hz, 1 H), 1.01 (dd, $J = 7.4, 7.4$ Hz, 3 H); ^{13}C NMR (100 MHz, CDCl_3) δ 170.3, 141.1, 129.2, 128.9, 111.6, 84.6, 81.8, 81.4, 76.7, 74.0, 56.0, 33.8, 32.3, 29.7, 25.8, 21.0, 9.3; IR (neat) 3290, 2925, 1739, 1451, 1372, 1234, 1072 cm^{-1} ; HRMS (FAB) found 355.0917 $[(\text{M}+1)^+]$; calcd for $\text{C}_{17}\text{H}_{24}^{79}\text{BrO}_3$: 355.0909.

Glycolate Oxazolidinone **6**
100 MHz ^{13}C NMR, CDCl_3

Methyl ester 7

100 MHz ^{13}C NMR, CDCl_3

Alcohol **8**
500 MHz ^1H NMR, CDCl_3

Alcohol 8

100 MHz ^{13}C NMR, CDCl_3

Allylic Alcohol **10**
500 MHz ^1H NMR, CDCl_3

Allylic Alcohol **10**
 100 MHz ^{13}C NMR, CDCl_3

Allylic Alcohol **4**
500 MHz ^1H NMR, CDCl_3

Allylic Alcohol **4**
500 MHz ^1H NMR, CDCl_3

Oxocene **3**

100 MHz ^{13}C NMR, CDCl_3

Ketone **2**
500 MHz ^1H NMR, CDCl_3

Ketone 2

100 MHz ^{13}C NMR, CDCl_3

Alcohol 11
500 MHz ^1H NMR, CDCl_3

Alcohol 11

100 MHz ^{13}C NMR, CDCl_3

Acetate 14
100 MHz ^{13}C NMR, CDCl_3

Enyne 16
400 MHz ^1H NMR, CDCl_3

Enyne 16
100 MHz ^{13}C NMR, CDCl_3

Synthetic (+)-Laurencin (1)
100 MHz ^{13}C NMR, CDCl_3

Synthetic (+)-Laurencin (1)
500 MHz ^1H NMR, CDCl_3

Kim's Synthetic (+)-Laurencin (500 MHz ^1H NMR)

Holmes' Synthetic (500 MHz ^1H NMR)

Kim's Synthetic (+)-Laurencin (125 MHz ^{13}C NMR)

Holmes' Synthetic (62.5 MHz ^{13}C NMR)