Supporting Information

Enantioselective Total Synthesis of (+)-Obtusenyne

Michael T. Crimmins* and Mark T. Powell

*Venable and Kenan Laboratories of Chemistry
The University of North Carolina at Chapel Hill
Chapel Hill, North Carolina 27599-3290*

crimmins@email.unc.edu

Experimental Section

Materials and Methods: General. Infrared (IR) spectra were obtained using a Nicolet Magna 560 infrared spectrometer. Proton and carbon nuclear magnetic resonance (^1H NMR and ^{13}C NMR) spectra were recorded on the following instruments: Bruker model DRX 400 (^1H at 400 MHz; ^{13}C at 100 MHz), and Bruker model DRX 500 (^1H at 500 MHz; ^{13}C at 125 MHz). Optical rotations were determined using a Jasco P1010 polarimeter. Thin layer chromatography was conducted on silica gel F₂₅₄ plates purchased from Scientific Adsorbents, Inc. Flash chromatography was performed using silica gel (32 to 63 μm) purchased from Scientific Adsorbents, Inc. Diethyl ether, tetrahydrofuran (THF), and dichloromethane were dried by being passed through a column of neutral alumina immediately prior to use. Alkyl amines and toluene were distilled from calcium hydride immediately prior to use. Hexamethylphosphorous triamide (HMPA) and dimethyl sulfoxide (DMSO) were distilled under reduced pressure from calcium hydride and stored over 4Å molecular sieves.

(1R)-1-[(1S)-Oxiranyl]-but-3-en-1-ol (5). Into a 1 L flask were added 4 Å molecular sieves (16 g), 1,5 hexadiene-3-ol (**6**) (35.0 g, 357 mmol), (-)-dicyclohexyl tartrate (16.7 g, 53 mmol), and dichloromethane (400 mL). The solution was cooled to $-20\text{ }^{\circ}\text{C}$, and $\text{Ti}(\text{O}i\text{-Pr})_4$ (13.3 mL, 36 mmol) was added. After 30 min, $t\text{-BuOOH}$ (5.7 M in dichloromethane, 37.0 mL, 214 mmol) was added dropwise via syringe. The reaction was allowed to stir at $-20\text{ }^{\circ}\text{C}$ for 19 hours. The reaction was poured into a solution of iron III sulfate heptahydrate (132g), citric acid (44 g), and H_2O (400mL) at $0\text{ }^{\circ}\text{C}$ and stirred 30 min. The reaction was filtered through a pad of celite. The layers were separated and the aqueous layer was extracted with dichloromethane (3 x 100 mL). The combined organic layers were dried over Na_2SO_4 , filtered, and concentrated. The residue was purified via flash chromatography to yield 17.1 g (42 %) of (1R)-1-[(1S)-oxiranyl]-but-3-en-1-ol (**5**): ^1H NMR (400 MHz, CDCl_3) δ 5.86 (ddt, $J = 12.2, 10.1, 7.1$ Hz, 1H), 5.16 (dd, $J = 17.1, 1.5$ Hz, 1 H), 5.14 (dd, $J = 9.7, 1.5$ Hz, 1H), 3.83 (brd, $J = 3.1$ Hz, 1H), 3.02 (q, $J = 5.1, 3.6$ Hz, 1H), 2.82-2.71 (m, 2H), 2.44-2.26 (m, 2H), 1.87 (brs, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 38.2, 43.8, 53.9, 68.6, 117.3, 133.7; IR (film) 3420, 3078, 2975, 2872, 1559, 1435, 1366, 1292, 1251, 1068 cm^{-1} ; $[\alpha]_{\text{D}}^{25} = -59.0^{\circ}$ ($c = 1.00$, CDCl_3)

(2S)-2-[(1R)-1-Benzyloxy-but-3-enyl]-oxirane (7). Into a 1 L flask were added (1R)-1-[(1S)-oxiranyl]-but-3-en-1-ol (**6**) (17.1 g, 150 mmol), *tetra-N*-butyl-ammonium iodide (5.5 g, 15.0 mmol), benzyl bromide (26.8 mL, 225 mmol), and THF (450 mL). The solution was cooled to $-78\text{ }^{\circ}\text{C}$ and sodium hydride (60 % in mineral oil, 15.0 g, 375 mmol) was added. The reaction was allowed to warm to $25\text{ }^{\circ}\text{C}$ and stirred 1 h. The reaction was cooled to $0\text{ }^{\circ}\text{C}$ and 150 mL saturated aqueous ammonium chloride was added. The reaction was diluted with H_2O (100 mL) and 50 % ethyl acetate/hexanes (200 mL). The layers were separated and the aqueous layer was extracted with 50 % ethyl acetate/hexanes (2 x 200 mL). The combined organic layers were dried with Na_2SO_4 , filtered, concentrated and purified via flash chromatography using 0 to 10 % ethyl acetate/hexanes as the eluent to provide 25.8 g (87 %) (2S)-2-[(1R)-1-benzyloxy-but-3-enyl]-oxirane (**7**): ^1H NMR (400 MHz, CDCl_3) δ 7.40–7.22 (m, 5H), 5.89 (ddt, $J = 12.2, 10.1, 7.1$ Hz, 1H), 5.14 (dd, $J = 17.2, 1.6$ Hz, 1H), 5.10 (dd, $J = 10.2, 1.6$ Hz, 1H), 4.63 (AB, $J_{\text{AB}} = 11.7$, $\Delta\nu_{\text{AB}} = 43.0$ Hz, 2H), 3.33 (dt, $J = 6.8, 5.3$ Hz, 1H), 2.96 (ddd, $J = 6.3, 3.3, 2.7$ Hz, 1H), 2.78–2.69 (m, 2H), 2.49–2.35 (m, 2H); ^{13}C NMR (100 MHz, CDCl_3) δ 29.7, 37.2, 45.7, 53.1, 72.2, 77.7, 117.4, 127.5, 127.6, 128.3, 134.0, 138.3; IR (film) 2984, 2941, 2909, 1750, 1465, 1447, 1372, 1300, 1246, 1097, 1048 cm^{-1} ; $[\alpha]_{\text{D}}^{24} = +65.0^{\circ}$ ($c = 1.00$, CH_2Cl_2); Anal. Calcd for $\text{C}_{13}\text{H}_{16}\text{O}_2$: C, 76.44; H, 7.90. Found: C, 76.39; H, 7.90.

(3S, 4R)-4-Benzyloxy-hept-6-en-3-ol (8). A 1 L 3-neck flask equipped with an addition funnel and a thermometer was charged with cuprous iodide (2.4 g, 12.6 mmol), and THF

(420 mL). The reaction was cooled to $-30\text{ }^{\circ}\text{C}$ and methyl magnesium chloride (3.0 M in THF, 210 mL, 630 mmol) was added and stirred 10 min. A solution of (2*S*)-2-[(1*R*)-1-benzyloxy-but-3-enyl]-oxirane (**7**) (25.8 g, 128 mmol) in diethyl ether (50 mL) was added. The reaction was stirred 1 h at $-20\text{ }^{\circ}\text{C}$. The reaction was quenched via slow addition of saturated NH_4Cl (100 mL). The reaction was diluted with EtOAc (400 mL) and H_2O (400 mL) and the layers were separated. The organic layer was washed with saturated NH_4Cl (200 mL), H_2O (200 mL), and brine (200 mL). The reaction was dried over Na_2SO_4 , filtered, and concentrated. The residue was purified via flash chromatography using 10 % EtOAc/hexanes as the eluent to provide 24.9 g (90 %) of (3*S*, 4*R*)-4-benzyloxy-hept-6-en-3-ol (**8**): ^1H NMR (400 MHz, CDCl_3) δ 7.38-7.24 (m, 5H), 5.88 (ddt, $J = 12.2, 10.1, 7.1\text{ Hz}$, 1H), 5.15-5.02 (m, 2H), 4.56 (AB, $J_{\text{AB}} = 11.5\text{ Hz}$, $\Delta\nu = 20.6\text{ Hz}$, 2H), 3.67 (dtd, $J = 8.5, 4.5, 4.2\text{ Hz}$, 1H), 3.43 (td, $J = 7.4, 4.2\text{ Hz}$, 1H), 2.46-2.25 (m, 2H), 1.97 (d, $J = 4.5$, 1H), 1.58-1.42 (m, 1H), 0.97 (t, $J = 7.4\text{ Hz}$, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 10.4, 25.0, 33.6, 71.9, 73.5, 81.6, 116.8, 126.7, 127.7, 128.3, 135.3, 138.3; IR (film) 3473, 2985, 2875, 1740, 1465, 1447, 1372, 1280, 1235, 1097, 1046 cm^{-1} ; Anal. Calcd for $\text{C}_{14}\text{H}_{20}\text{O}_2$: C, 76.33; H, 9.15. Found: C, 76.63; H, 9.07.

[(1*S*, 2*R*)-2-Benzyloxy-1-ethyl-pent-4-enyloxy]-acetic acid (9**).** A 500 mL 3-neck flask equipped with an addition funnel and a mechanical stirrer was charged with sodium hydride (60 % dispersion in mineral oil) and THF (30 mL) and the suspension was stirred and cooled to $0\text{ }^{\circ}\text{C}$. The suspension was treated with a solution of the (3*S*, 4*R*)-4-benzyloxy-hept-6-en-3-ol (**8**) (24.9 g, 113 mmol) in THF (30 mL) via dropwise addition

over 20 minutes. The reaction was warmed to 25 °C and stirred 10 min. The reaction was cooled to 0 °C and a solution of bromoacetic acid (23.6 g, 170 mmol) in THF (20 mL) was added dropwise over 30 min. The reaction was warmed to 25 °C and stirred 10 h. The reaction was quenched via addition of H₂O (50 mL). The reaction was diluted with H₂O (300 mL) and Et₂O (200 mL) and separated. The aqueous layer was washed with Et₂O (2 x 200 mL). The aqueous layer was acidified to pH 2 with concentrated H₂SO₄ (~ 15 mL) and extracted with ethyl acetate (4 x 100 mL). The combined ethyl acetate layers were washed with brine (1 x 200 mL), dried over Na₂SO₄, filtered, and concentrated. The residue was purified via flash chromatography to provide 28.2 g, (90 %) of [(1*S*, 2*R*)-2-benzyloxy-1-ethyl-pent-4-enyloxy]-acetic acid (**9**): ¹H NMR (400 MHz, CDCl₃) δ 7.38-7.27 (m, 5H), 5.87 (ddt, *J* = 12.2, 10.1, 7.1 Hz, 1H), 5.18-5.05 (m, 2H), 4.62 (AB, *J*_{AB} = 11.7 Hz, Δ*ν* = 32 Hz, 2H), 4.16 (AB, *J*_{AB} = 17.0 Hz, Δ*ν* = 108 Hz, 2H), 3.55-3.49 (m, 1H), 3.36 (td, *J* = 6.9, 2.7 Hz, 1H), 2.49-2.29 (m, 2H), 1.63 (qd, *J* = 7.5, 6.9 Hz, 1H), 1.46 (qd, *J* = 7.5, 6.8 Hz, 1H), 0.91 (t, *J* = 7.5 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 10.1, 23.9, 33.4, 68.4, 72.4, 79.5, 85.0, 117.3, 128.0, 128.2, 134.9, 137.1, 173.0; IR (film) 3066, 3032, 2968, 2938, 1734, 1455, 1433, 1373, 1244, 1118, 1070, 1028 cm⁻¹; [α]_D²⁸ = +19.9° (*c* = 1.00, CH₂Cl₂); Anal. Calcd for C₁₆H₂₂O₄: C, 69.04; H, 7.97. Found: C, 69.10; H, 7.97.

3-[2-((1*S*, 2*R*)-2-Benzyloxy-1-ethyl-pent-4-enyloxy)-acetyl]-4-isopropyl-oxazolidin-2-one (4**).** To a solution of [(1*S*, 2*R*)-2-benzyloxy-1-ethyl-pent-4-enyloxy]-acetic acid (**9**)

(28.2 g, 101.2 mmol) in diethyl ether (500 mL) was added triethylamine (15.5 mL, 111.4 mmol). The reaction was cooled to $-78\text{ }^{\circ}\text{C}$ and treated with pivaloyl chloride (12.5 mL, 101.2 mmol). The reaction was warmed to $0\text{ }^{\circ}\text{C}$, stirred 1 h and then was recooled to $-78\text{ }^{\circ}\text{C}$. In a separate flask, a solution of (4*R*)-4-isopropyl-oxazolidin-2-one (13.1 g, 101.2 mmol) in THF (650 mL) was cooled to $-78\text{ }^{\circ}\text{C}$ and treated with nBuLi (1.6 M in hexanes, 63.3 mL, 101.2 mmol). The solution of lithiated oxazolidinone was added to the mixed anhydride via cannula and was warmed to $0\text{ }^{\circ}\text{C}$ and stirred 2 h. The reaction was quenched via addition of H_2O (100 mL), and was extracted with EtOAc (2 x 200 mL). The combined organic layers were washed with brine (100 mL), dried over Na_2SO_4 , filtered, and concentrated. The residue was purified via flash chromatography to provide 28.6 g (75 %) of 3-[2-((1*S*, 2*R*)-2-benzyloxy-1-ethyl-pent-4-enyloxy)-acetyl]-4-isopropyl-oxazolidin-2-one (**4**): ^1H NMR (400 MHz, CDCl_3) δ 7.39-7.22 (m, 5H), 5.92 (ddt, $J = 12.7, 10.1, 7.6\text{ Hz}$, 1H), 5.14–5.03 (m, 2H), 4.81 (AB, $J_{\text{AB}} = 17.9\text{ Hz}$, $\Delta\nu = 28\text{ Hz}$, 2H), 4.60 (s, 2H), 4.37 (dt, $J = 7.9, 3.7\text{ Hz}$, 1H), 4.28-4.20 (m, 2H), 3.58 (dt, $J = 7.1, 4.2\text{ Hz}$, 1 H), 3.49 (dt, $J = 7.4, 4.2\text{ Hz}$, 1H), 2.52–2.32 (m, 2H), 1.77-1.65 (m, 1H), 1.64-1.54 (m, 2H), 0.99 (t, $J = 7.4\text{ Hz}$, 3H), 0.90 (d, $J = 7.0\text{ Hz}$, 3H), 0.85 (d, $J = 7.0\text{ Hz}$, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 10.0, 14.4, 17.7, 23.3, 28.1, 34.7, 58.1, 64.2, 70.0, 72.0, 80.2, 83.0, 116.7, 127.3, 127.6, 128.1, 135.4, 138.5, 153.8, 170.2; IR (film) 3066, 2967, 2937, 2878, 1781, 1720, 1389, 1374, 1302, 1259, 1211, 1122, 1057, 1018 cm^{-1} ; $[\alpha]_{\text{D}}^{28} = -51.3^{\circ}$ ($c = 1.00$, CH_2Cl_2); Anal. Calcd for $\text{C}_{22}\text{H}_{31}\text{NO}_5$: C, 67.84; H, 8.02; N, 3.60. Found: C, 68.03; H, 7.85; N, 3.26.

3-[2-((1*S*, 2*R*)-2-Benzyloxy-1-ethyl-pent-4-enyloxy)-(2*S*)-5-methyl-hex-4-enoyl]-(4*R*)-4-isopropyl-oxazolidin-2-one (15). Into a 2L 3 neck flask fitted with a low temperature thermometer, an addition funnel, and a mechanical stirrer was added sodium bis(trimethylsilyl)amide (0.75 M in 3:1 toluene:THF, 167.9 mL, 125.9 mmol). THF (175 mL) was added and the reaction cooled to -78 °C. A solution of 3-[2-((1*S*, 2*R*)-2-benzyloxy-1-ethyl-pent-4-enyloxy)-acetyl]-4-isopropyl-oxazolidin-2-one (**4**) (27.8 g, 71.9 mmol) in THF (100 mL) was added dropwise over 40 minutes. After stirring 30 minutes a solution of 1-iodo-3-methyl-but-2-ene in THF (50 mL) was added dropwise over 30 minutes. The reaction was warmed to -40 °C and stirred 1.5 h. The reaction was quenched via addition of saturated NH₄Cl (100 mL) and concentrated in vacuo to remove THF. The resulting solution was extracted with 50 % ethyl acetate /hexanes (3 x 150 mL). The combined organic layers were dried over Na₂SO₄, filtered, concentrated and purified via flash chromatography using 5 % EtOAc/hexanes as the eluent to yield 27.6 g (82 %) of 3-[2-((1*S*, 2*R*)-2-benzyloxy-1-ethyl-pent-4-enyloxy)-(2*S*)-5-methyl-hex-4-enoyl]-(4*R*)-4-isopropyl-oxazolidin-2-one (**15**): ¹H NMR (400 MHz, CDCl₃) δ 7.33-7.20 (m, 5H), 5.85 (ddt, *J* = 17.1, 10.1, 7.1 Hz, 1H), 5.30-5.20 (m, 1H), 5.10-5.00 (m, 2H), 4.53 (AB, *J*_{AB} = 11.7, Δ*ν* = 6.1 Hz, 2H), 4.42-4.35 (m, 1H), 4.15-4.00 (m, 1H), 3.55-3.35 (m, 2H), 2.55-2.21 (m, 5H), 1.68-1.60 (m, 1H), 1.62 (s, 3H), 1.56 (s, 3H), 1.50-1.40 (m, 1H), 0.95 (t, 7.4Hz, 3H), 0.86 (d, 7.0 Hz, 3H), 0.80 (d, 7.0, 3H); ¹³C NMR (100 MHz,

CDCl₃) δ 10.3, 14.5, 17.8, 18.0, 23.7, 25.8, 28.3, 32.7, 34.9, 58.2, 63.6, 72.1, 76.0, 80.5, 81.6, 116.7, 118.8, 127.3, 127.4, 128.2, 134.7, 135.7, 138.8, 153.5, 173.4; IR (film) 3076, 3029, 2965, 2930, 2875, 1782, 1712, 1454, 1387, 1363, 1301, 1244, 1205, 1158, 1105, 1028 cm⁻¹; $[\alpha]_D^{24} = -53.5^\circ$ ($c = 0.46$, CH₂Cl₂); Anal. Calcd for C₂₇H₃₉NO₅: C, 70.87; H, 8.59; N, 3.06. Found: C, 71.03; H, 8.75; N, 3.16.

2-((1*S*, 2*R*)-2-Benzyloxy-1-ethyl-pent-4-enyloxy)-(2*S*)-5-methyl-hex-4-en-1-ol (16**).**

A 500 mL 3-neck flask equipped with an addition funnel was charged with 3-[2-((1*S*, 2*R*)-2-benzyloxy-1-ethyl-pent-4-enyloxy)-(2*S*)-5-methyl-hex-4-enoyl]-(4*R*)-4-isopropyl-oxazolidin-2-one (**15**) (27.6 g, 60.4 mmol) and THF (500 mL). The reaction was cooled to 0 °C and a solution of NaBH₄ (11.19 g, 295.8 mmol) in H₂O (125 mL) was added dropwise over 5 minutes. The reaction was allowed to warm to 25 °C and stirred 14 h. The reaction was cooled to 0 °C and 10 % HCl (100 mL) was added dropwise. The reaction was diluted with H₂O (100 mL), EtOAc (200 mL) and separated. The aqueous layer was extracted with EtOAc (2 x 100 mL). The combined organic layers were washed with saturated NaHCO₃ (100 mL) and brine (100 mL), dried over Na₂SO₄, filtered, concentrated, and purified via flash chromatography using 10 % EtOAc/hexanes as the eluent to provide 16.5 g, (82 %) of 2-((1*S*, 2*R*)-2-benzyloxy-1-ethyl-pent-4-enyloxy)-(2*S*)-5-methyl-hex-4-en-1-ol (**16**): ¹H NMR (400 MHz, CDCl₃) δ 7.40-7.25 (m, 5H), 5.90 (ddt, 12.2, 10.1, 7.1 Hz, 1H), 5.20-5.00 (m, 3H), 4.61 (s, 2H), 3.68-3.45 (m, 5H), 2.50-2.15 (m, 4H), 1.97 (dd, 6.7, 5.8 Hz, 1H), 1.70-1.50 (m, 2H), 1.67 (s, 3H), 1.60 (s, 3H),

1.59 (s, 1H), 0.95 (t, 7.4 Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 9.9, 17.8, 23.1, 25.7, 29.9, 35.1, 63.9, 72.1, 78.7, 79.7, 80.2, 116.7, 119.7, 127.4, 127.6, 128.2, 133.8, 135.5, 138.6; IR (film) 3468, 2985, 1740, 1374, 1242, 1046 cm^{-1} ; $[\alpha]_D^{28} = +16.5^\circ$ ($c = 1.00$, CH_2Cl_2); Anal. Calcd for $\text{C}_{21}\text{H}_{32}\text{O}_3$: C, 75.86; H, 9.70. Found: C, 75.68; H, 9.61.

2-((1S, 2R)-2-Benzyloxy-1-ethyl-pent-4-enyloxy)-(2S)-5-methyl-hex-4-enal. A 2 L 3-neck flask fitted with a mechanical stirrer was charged with oxalyl chloride (2.0 M in CH_2Cl_2 , 600 mL, 79.4 mmol) and CH_2Cl_2 (600 mL). The reaction was cooled to -78°C and a solution of DMSO (11.3 mL, 158.8 mmol) in CH_2Cl_2 (20 mL) was added dropwise. After stirring 20 min a solution of 2-((1S, 2R)-2-benzyloxy-1-ethyl-pent-4-enyloxy)-(2S)-5-methyl-hex-4-en-1-ol (**15**) in CH_2Cl_2 was added dropwise. After stirring 20 min Et_3N (36.0 mL, 258.1 mmol) was added dropwise and the reaction was allowed to warm to -15°C and stirred 2 h. The reaction was poured into 1 L EtOAc and 200 mL saturated NH_4Cl was added. The layers were separated and the organic layer was washed with saturated NaHCO_3 (100 mL), brine (100 mL), dried over Na_2SO_4 , filtered, concentrated, filtered through silica gel using 25 % ethyl acetate/hexanes as the eluent, and concentrated to provide 2-((1S, 2R)-2-benzyloxy-1-ethyl-pent-4-enyloxy)-(2S)-5-methyl-hex-4-enal which was used immediately in the next step.

5-[(1*S*, 2*R*)-2-Benzyloxy-1-ethyl-pent-4-enyloxy]-(4*R*, 5*S*)-8-methyl-nona-1,7-dien-4-ol (17). Into a 2 L 3-neck flask equipped with a thermometer, a mechanical stirrer, and an addition funnel was placed the methoxyborane derived from 2-carene (22.4 g, 70.8 mmol) and Et₂O (500 mL). The reaction was cooled to 0 °C and allyl magnesium bromide was added dropwise. The reaction was stirred 1 h and cooled to –78 °C. A solution of 2-((1*S*, 2*R*)-2-benzyloxy-1-ethyl-pent-4-enyloxy)-(2*S*)-5-methyl-hex-4-enal (11.7 g, 35.4 mmol) was added dropwise. The reaction was stirred 2 h and was then quenched via addition of CH₃OH (70 mL). The reaction was warmed to 25 °C and the ether was removed in vacuo. The residue was dissolved in THF (500 mL), 3N NaOH (50 mL), and 30 % H₂O₂ (100 mL) and heated to reflux for 3 h. The reaction was cooled to 25 °C and extracted with EtOAc (3 x 200 mL). The combined organic layers were washed with brine (200 mL), dried over Na₂SO₄, filtered, concentrated, and purified via flash chromatography using 5 % EtOAc/hexanes as the eluent to provide 5-[(1*S*, 2*R*)-2-benzyloxy-1-ethyl-pent-4-enyloxy]-(4*R*,5*S*)-8-methyl-nona-1,7-dien-4-ol (**17**): ¹H NMR (400 MHz, CDCl₃) δ 7.35-7.25 (m, 5H), 5.93-5.80 (m, 2H), 5.20 (bt, 7.2 Hz, 1H), 5.18-5.07 (m, 4H), 4.61 (AB, *J*_{AB} = 11.6 Hz, Δ*ν* = 21 Hz, 2H), 3.80-3.70 (m, 1H), 3.55-3.48 (m, 3H), 2.50-2.15 (m, 6H), 2.07 (d, 4.5 Hz, 1H), 1.68 (s, 3H), 1.68-1.55 (m, 3H), 1.60 (s, 3H), 0.95 (t, 7.4 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 10.0, 17.8, 23.0, 25.7, 28.2, 35.1, 36.5, 71.6, 72.0, 79.7, 80.3, 80.4, 116.6, 117.2, 120.7, 127.3, 127.5, 127.7, 128.2, 128.4, 133.1, 135.6, 138.7; IR (film) 3361, 2924, 1460, 1413, 1374, 1336, 1136, 1084,

1038 cm⁻¹; [α]_D²⁸ = +17.1° (*c* = 1.00, CH₂Cl₂); Anal. Calcd for C₂₄H₃₆O₃: C, 77.38; H, 9.74. Found: C, 77.10; H, 9.70.

[(1*R*, 2*S*)-1-Allyl-2-((1*S*, 2*R*)-2-benzyloxy-1-ethyl-pent-4-enyloxy)-5-methyl-hex-4-enyloxy]-*tert*-butyl-dimethyl-silane (3**).** To a solution of 5-[(1*S*, 2*R*)-2-benzyloxy-1-ethyl-pent-4-enyloxy]-(4*R*,5*S*)-8-methyl-nona-1,7-dien-4-ol (**17**) (2.0 g, 5.4 mmol) in CH₂Cl₂ (100 mL) at 0 °C was added 2,6-lutidine (0.94 mL, 8.1 mmol). After stirring 5 min *tert*-butyl-dimethyl-silyl triflate (1.54 mL, 6.7 mmol) was added and the reaction was stirred 1.5 h. The reaction was poured into saturated NH₄Cl (100 mL) and extracted with 50 % ethyl acetate/hexanes (3 x 125 mL). The combined organic layers were dried over Na₂SO₄, filtered, concentrated, and purified via flash chromatography to provide 2.7 g (99 %) of [(1*R*, 2*S*)-1-allyl-2-((1*S*, 2*R*)-2-benzyloxy-1-ethyl-pent-4-enyloxy)-5-methyl-hex-4-enyloxy]-*tert*-butyl-dimethyl-silane (**3**): ¹H NMR (400 MHz, CDCl₃) δ 7.38-7.24 (m, 5H), 5.95-5.75 (m, 2H), 5.20-5.00 (m, 5H), 4.60 (AB, *J*_{AB} = 11.6, Δ*ν* = 14.3 Hz, 2H), 3.75-3.65 (m, 1H), 3.60-3.45 (m, 2H), 2.45-2.15 (m, 6H), 1.75-1.55 (m, 2H), 1.68 (s, 3H), 1.60 (s, 3H), 0.97 (t, 7.4 Hz, 3H), 0.91 (s, 9H), 0.04 (s, 6H); ¹³C NMR (100 MHz, CDCl₃) δ -4.5, -4.3, 1.0, 9.9, 17.9, 18.1, 23.0, 25.7, 25.8, 25.9, 30.1, 35.3, 37.2, 72.0, 74.6, 80.3, 80.8, 81.8, 116.4, 121.3, 127.3, 127.6, 128.2, 132.8, 136.0, 136.4, 139.0; IR (film) 3071, 3028, 2957, 2925, 2860, 1643, 1377, 1356, 1263, 1084 cm⁻¹; [α]_D²⁴ =

+105.3° ($c = 1.00$, CH_2Cl_2); Anal. Calcd for $\text{C}_{30}\text{H}_{50}\text{O}_3\text{Si}$: C, 74.02; H, 10.35. Found: C, 73.88; H, 10.14.

{(1*R*)-1-[(1*S*)-1-((1*S*, 2*R*)-2-Benzoyloxy-1-ethyl-pent-4-enyloxy)-2-(3,3-dimethyl-oxiranyl)-ethyl]-but-3-enyloxy}-*tert*-butyl-dimethyl-silane (19**).** A solution of [(1*R*, 2*S*)-1-allyl-2-((1*S*, 2*R*)-2-benzyloxy-1-ethyl-pent-4-enyloxy)-5-methyl-hex-4-enyloxy]-*tert*-butyl-dimethyl-silane (**3**) (2.7 g, 5.5 mmol) in CH_2Cl_2 (100 mL) at -40°C was treated with *meta*-chloroperoxybenzoic acid (1.3 g, 5.5 mmol) and the reaction was allowed to warm to 25°C . After stirring 4 h the reaction was poured into saturated NaHCO_3 (100 mL) and extracted with EtOAc (3 x 100 mL). The organic layers were washed with brine (100 mL), dried over Na_2SO_4 , filtered, concentrated, and purified via flash chromatography to provide 2.2 g (80 %) of {(1*R*)-1-[(1*S*)-1-((1*S*, 2*R*)-2-benzyloxy-1-ethyl-pent-4-enyloxy)-2-(3,3-dimethyl-oxiranyl)-ethyl]-but-3-enyloxy}-*tert*-butyl-dimethyl-silane (**19**) as a mixture of diastereomers: ^1H NMR (400 MHz, CDCl_3) δ 7.41-7.26 (m, 5H), 5.91-5.71 (m, 2H), 5.10-4.95 (m, 4H), 4.60-4.49 (m, 2H), 3.82-3.41 (m, 4H), 2.91-2.87 (m, 1H), 2.46-2.14 (m, 4H), 1.91-1.67 (m, 2H), 1.60-1.48 (m, 1H), 1.32-1.18 (m, 8H), 0.96-0.82 (m, 12), 0.05-0.03 (m, 6H); ^{13}C NMR (100 MHz, CDCl_3) δ -4.4, -4.3, -4.2, 10.1, 18.1 (2), 18.8, 19.0, 23.4, 24.7, 25.9 (2), 30.6 (2), 31.4, 34.7, 34.8, 36.6, 37.9, 58.4, 58.6, 61.7, 61.9, 71.6, 71.9, 74.9, 75.1, 79.4, 79.6, 80.1, 80.3, 80.4, 81.1, 116.5, 116.6, 116.9 (2), 127.3, 127.4 (2), 127.6, 127.7, 127.8, 127.9, 128.2 (4), 128.4, 135.6, 135.7, 135.9 (2), 138.7, 138.9; IR (film) 3071, 3028, 2957, 2925, 2860, 1643,

1426, 1377, 1356, 1328, 1263, 1084 cm^{-1} ; $[\alpha]_{\text{D}}^{24} = +40.9^\circ$ ($c = 1.00$, CH_2Cl_2). Anal.

Calcd for $\text{C}_{30}\text{H}_{50}\text{O}_4\text{Si}$: C, 71.66; H, 10.02. Found: C, 71.61; H, 10.00.

[(2*S*, 3*R*, 8*R*, 9*S*)-8-Benzyloxy-2-(3,3-dimethyl-oxiranylmethyl)-9-ethyl-2,3,4,7,8,9-hexahydro-oxonin-3-yloxy]-*tert*-butyl-dimethyl-silane (20). Into a flask equipped with a reflux condenser was added {(1*R*)-1-[(1*S*)-1-((1*S*, 2*R*)-2-benzyloxy-1-ethyl-pent-4-enyloxy)-2-(3,3-dimethyl-oxiranyl)-ethyl]-but-3-enyloxy}-*tert*-butyl-dimethyl-silane (**19**) (0.22 g, 0.44 mmol) and CH_2Cl_2 (150 mL). The solution was degassed by bubbling argon through the stirring solution for 30 min. The solution was heated to reflux and $[(\text{Cy}_3\text{P})_2\text{Cl}_2\text{Ru}=\text{CHPh}]$ (36 mg, 0.04 mmol) was added. After stirring for 12 h the reaction was cooled to 25 $^\circ\text{C}$ and opened to the air for 2 h. The reaction was concentrated in vacuo and the residue purified via flash chromatography using 2.5 % EtOAc/hexanes as the eluent to provide 0.16 g (80 %) of [(2*R*, 3*S*, 8*R*, 9*S*)-8-benzyloxy-2-(3,3-dimethyl-oxiranylmethyl)-9-ethyl-2,3,4,7,8,9-hexahydro-oxonin-3-yloxy]-*tert*-butyl-dimethyl-silane (**20**) as a mixture of diastereomers: first diastereomer ^1H NMR (400 MHz, CDCl_3) δ 7.35-7.21 (m, 5H), 5.75-5.60 (m, 2H), 4.58 (AB, $J_{\text{AB}} = 11.2$, $\Delta\nu = 84.0$ Hz, 2H), 3.72-3.68 (m, 1H), 3.50-3.36 (m, 3H), 3.03 (t, 5.4 Hz, 1H), 2.70-2.37 (m, 3H), 1.96-1.70 (m, 4H), 1.30 (s, 3H), 1.19 (s, 3H), 0.94 (t, 7.3 Hz, 3H), 0.86 (s, 9H), 0.12 (s, 3H), 0.06 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ -4.7, -4.3, 9.4, 17.9, 18.9, 23.7, 24.8, 25.8, 28.0, 29.7, 31.9, 32.1, 57.6, 61.3, 73.2, 78.7, 127.2, 127.7, 128.0, 128.4, 138.1; IR (film) 3056, 2987, 2828, 1548, 1419, 1270, 1256, 1156, 1064 cm^{-1} ; $[\alpha]_{\text{D}}^{23} = -$

61.7° ($c = 1.00$, CH_2Cl_2): second diastereomer ^1H NMR (400 MHz, CDCl_3) δ 7.35-7.24 (m, 5H), 5.76 (td, 9.9, 9.2 Hz, 1H), 5.61 (dt, 9.2, 8.4, 1H), 4.54, (AB, $J_{\text{AB}} = 11.3$, $\Delta\nu = 90.0$ Hz, 2H), 3.61 (d, $J = 2.0$ Hz, 2H), 3.53-3.43 (m, 2H), 2.96 (dd, $J = 3.5$, 3.1 Hz, 1H), 2.73-2.40 (m, 3H), 2.27 (dd, $J = 8.0$, 6.5 Hz, 1H), 1.95-1.60 (m, 3H), 1.29 (s, 1H), 1.22 (s, 3H), 0.91 (t, $J = 7.4$ Hz, 3H), 0.86 (s, 9H), 0.09 (s, 3H), 0.02 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ -4.5, -4.2, 8.3, 17.8, 19.1, 24.2, 24.7, 25.7, 29.7, 31.7, 33.6, 58.0, 61.0, 71.2, 72.9, 77.4, 78.7, 126.8, 127.7, 127.9, 128.1, 128.3, 138.2; IR (film) 3056, 2987, 2828, 1548, 1419, 1270, 1256, 1156, 1064 cm^{-1} ; $[\alpha]_{\text{D}}^{23} = -90.8^\circ$ ($c = 1.00$, CH_2Cl_2).
 Anal. Calcd for $\text{C}_{26}\text{H}_{46}\text{O}_4\text{Si}$: C, 70.84; H, 9.77. Found: C, 70.82; H, 9.74

[(2*S*, 3*R*, 8*R*, 9*S*)-8-Benzyloxy-3-(*tert*-butyl-dimethyl-silanyloxy)-9-ethyl-2,3,4,7,8,9-hexahydro-oxonin-2-yl]-acetaldehyde. Into a 25 mL flask was added [(2*R*, 3*S*, 8*R*, 9*S*)-8-benzyloxy-2-(3,3-dimethyl-oxiranylmethyl)-9-ethyl-2,3,4,7,8,9-hexahydro-oxonin-3-yloxy]-*tert*-butyl-dimethyl-silane (**20**) (0.25 g, 0.53 mmol) THF (7 mL), and 0.1 N HClO_4 (2 mL). The reaction was stirred 8 h and poured into a separatory funnel containing saturated NaHCO_3 (5 mL) and H_2O (5 mL). The reaction was extracted with ethyl acetate (3 x 5 mL), dried over Na_2SO_4 , filtered, and concentrated. The resulting 1,2-diol was dissolved in THF (5 mL) and H_2O (5 mL) and treated with Bu_4NHSO_4 (0.18 g, 0.53 mmol) and NaIO_4 (0.340 g, 1.59 mmol) and stirred for 2 h. The reaction was poured into saturated NaHCO_3 (5 mL) and H_2O (5 mL). The reaction was extracted with EtOAc (3 x 10 mL), dried over Na_2SO_4 , filtered, concentrated, and filtered through silica gel using 25 % EtOAc/hexanes as the eluent to provide [(2*R*, 3*S*, 8*R*, 9*S*)-8-benzyloxy-3-

(*tert*-butyl-dimethyl-silanyloxy)-9-ethyl-2,3,4,7,8,9-hexahydro-oxonin-2-yl]-acetaldehyde which was used directly in the next step.

2-[(2*S*, 3*R*, 8*R*, 9*S*)-8-Benzoyloxy-3-(*tert*-butyl-dimethyl-silanyloxy)-9-ethyl-2,3,4,7,8,9-hexahydro-oxonin-2-yl]-ethanol (21**).** Into a 25 mL flask was placed [(2*R*, 3*S*, 8*R*, 9*S*)-8-benzyloxy-3-(*tert*-butyl-dimethyl-silanyloxy)-9-ethyl-2,3,4,7,8,9-hexahydro-oxonin-2-yl]-acetaldehyde, (150 mg, 0.36 mmol) and CH₃OH, (10 mL). The solution was cooled to 0 °C and NaBH₄ (15.1 mg, 0.40 mmol), was added. The reaction was stirred 30 min and poured into saturated NH₄Cl (25 mL). The mixture was extracted with EtOAc (3 x 10 mL) and the combined organic layers were dried over Na₂SO₄, filtered, concentrated, and purified via flash chromatography to provide 147 mg (65 % over 3 steps) of 2-[(2*R*, 3*S*, 8*R*, 9*S*)-8-benzyloxy-3-(*tert*-butyl-dimethyl-silanyloxy)-9-ethyl-2,3,4,7,8,9-hexahydro-oxonin-2-yl]-ethanol (**21**): ¹H NMR (400 MHz, CDCl₃) δ 7.40-7.25 (m, 5H), 5.75-5.62 (m, 2H), 4.55 (AB, *J*_{AB} = 11.4, Δ*ν* = 83.7 Hz, 2H) 3.90-3.67 (m, 3H), 3.53-3.38 (m, 3H), 2.68-2.39 (m, 4H), 2.10-1.70 (m, 5H), 0.99 (t, *J* = 7.3 Hz, 3H), 0.90 (s, 9H), 0.14 (s, 3H), 0.08 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ -4.8, -4.2, 1.0, 17.9, 24.3, 25.8, 28.0, 29.6, 32.5, 34.6, 60.0, 71.3, 72.5, 76.2, 78.6, 78.9, 127.2, 127.7, 127.8, 127.9, 128.3, 138.1; IR (film) 3623-3155, 3054, 2987, 2956, 2931, 1551, 1422, 1410, 1356, 1274, 1152, 1078 cm⁻¹; [α]_D²² = 75.3° (*c* = 1.00, CH₂Cl₂); Anal. Calcd for C₂₅H₄₂O₄Si: C, 74.02; H, 10.35. Found: C, 73.88; H, 10.14.

(2*S*, 3*R*, 8*R*, 9*S*)-8-Benzyloxy-9-ethyl-2-(2-hydroxy-ethyl)-2,3,4,7,8,9-hexahydro-oxonin-3-ol (22). A 50 mL flask was charged with 2-[(2*R*, 3*S*, 8*R*, 9*S*)-8-benzyloxy-3-(*tert*-butyl-dimethyl-silanyloxy)-9-ethyl-2,3,4,7,8,9-hexahydro-oxonin-2-yl]-ethanol (**21**) (0.45 g, 1.0 mmol) and THF (15 mL). The solution was cooled to 0 °C and TBAF (1.0 M in THF, 1.0 mL, 1.0 mmol) was added and the reaction was stirred 2 h. The reaction was poured into EtOAc (200 mL) and washed with saturated NH₄Cl (50 mL), H₂O (50 mL), brine (50 mL) dried over Na₂SO₄, filtered, concentrated, and purified via flash chromatography to provide 297 mg (90 %) of (2*R*, 3*S*, 8*R*, 9*S*)-8-benzyloxy-9-ethyl-2-(2-hydroxy-ethyl)-2,3,4,7,8,9-hexahydro-oxonin-3-ol (**22**): ¹H NMR (400 MHz, CDCl₃) δ 7.40-7.25 (m, 5H), 5.80-5.68 (m, 2H), 4.60 (AB, *J*_{AB} = 11.4, Δ*ν* = 85.0 Hz, 2H), 4.00-3.76 (m, 3H), 3.55-3.45 (m, 2H) 3.40-3.32 (m, 1H), 2.83-2.70 (m, 3H), 2.50-1.72 (m, 7H), 0.99 (t, 7.3 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 9.6, 24.1, 28.7, 31.5, 36.4, 59.5, 71.3, 72.1, 75.8, 78.8, 80.2, 126.7, 127.7, 128.0, 128.4, 128.5, 137.9; IR (film) 3723-3055, 3017, 2957, 2909, 2878, 1448, 1356, 1274, 1152, 1100, 1073, 1019 cm⁻¹; [α]_D²³ = 62.1° (*c* = 1.00, CH₂Cl₂).

(2*S*, 3*R*, 8*R*, 9*S*)-8-Benzyloxy-2-[2-(*tert*-butyl-diphenyl-silanyloxy)-ethyl]-9-ethyl-2,3,4,7,8,9-hexahydro-oxonin-3-ol (23). A 25 mL flask was charged with (2*R*, 3*S*, 8*R*, 9*S*)-8-benzyloxy-9-ethyl-2-(2-hydroxy-ethyl)-2,3,4,7,8,9-hexahydro-oxonin-3-ol (**22**)

(297 mg, 0.89 mmol), imidazole (91 mg, 1.34 mmol), and DMF (2mL). *tert*-Butyl-dimethyl-silyl-chloride (0.232 mL, 0.89 mmol) was added and the reaction was stirred for 14 h. The reaction was quenched via addition of CH₃OH (0.3 mL) and poured into EtOAc (200 mL). The reaction was washed with H₂O (50 mL) and brine (50 mL), dried over Na₂SO₄, filtered, concentrated, and purified via flash chromatography using 5-25 % EtOAc/hexanes to provide 458 mg (91 %) of (2*R*, 3*S*, 8*R*, 9*S*)-8-benzyloxy-2-[2-(*tert*-butyl-diphenyl-silanyloxy)-ethyl]-9-ethyl-2,3,4,7,8,9-hexahydro-oxonin-3-ol (**23**): ¹H NMR (400 MHz, CDCl₃) δ 7.71-7.61 (m, 4H), 7.45-7.20 (m, 11H), 5.80-5.65 (m, 2H), 4.52 (AB, *J*_{AB} = 11.4, Δ*ν* = 94.3 Hz, 2H), 3.95-3.87 (m, 1H), 3.82-3.70 (m, 2H), 3.51-3.40 (m, 2H), 3.30 (dd, *J* = 6.5, 5.4 Hz, 1H), 3.07 (s, 1H), 2.72-2.62 (m, 2H), 2.45-2.30 (m, 2H), 2.10-1.90 (m, 2H), 1.80-1.68 (m, 1H), 1.55-1.45 (m, 2H), 1.05 (s, 9H), 0.84 (t, *J* = 7.3 Hz, 3H) ; ¹³C NMR (100 MHz, CDCl₃) δ 9.8, 19.1, 24.4, 26.9, 29.2, 29.7, 31.1, 36.6, 61.5, 71.4, 72.4, 75.4, 77.2, 79.4, 80.6, 127.1, 127.7, 127.8, 128.0, 128.4, 128.6, 129.8, 129.9, 133.2 (2), 135.6, 135.7, 138.3; IR (film) 3761-3109, 3071, 2957, 2859, 1458, 1426, 1388, 1268, 1111, 1067 cm⁻¹; [α]_D²² = 35.7° (*c* = 0.87, CH₂Cl₂); Anal. Calcd for C₃₅H₄₆O₄Si: C, 75.23; H, 8.30. Found: C, 75.06; H, 8.53.

[2-((2*S*, 3*S*, 8*R*, 9*S*)-8-Benzyloxy-3-chloro-9-ethyl-2,3,4,7,8,9-hexahydro-oxonin-2-yl)-ethoxy]-*tert*-butyl-diphenyl-silane (24**).** A 25 mL flask was charged with (2*R*, 3*S*, 8*R*, 9*S*)-8-benzyloxy-2-[2-(*tert*-butyl-diphenyl-silanyloxy)-ethyl]-9-ethyl-2,3,4,7,8,9-hexahydro-oxonin-3-ol (**23**) (225 mg, 0.42 mmol), 1-methyl-cyclohexene (1.0 mL 8.4 mmol), carbon tetrachloride (1.93 mL, 20.0 mmol), and toluene (4.0 mL). The reaction

was heated to 80 °C and a solution of trioctylphosphine (0.73 mL, 1.6 mmol) in toluene (3.2 mL) was added dropwise over 140 min. The reaction was cooled to 25 °C and concentrated in vacuo. The reaction was purified via flash chromatography using 2.5 % EtOAc/hexanes as the eluent to provide 155 mg (64 %) of [2-((2*S*, 3*S*, 8*R*, 9*S*)-8-benzyloxy-3-chloro-9-ethyl-2,3,4,7,8,9-hexahydro-oxonin-2-yl)-ethoxy]-*tert*-butyl-diphenyl-silane (**24**): ¹H NMR (400 MHz, C₆D₆) δ 7.57-7.68, (m, 4H), 7.25-7.05 (m, 11H), 5.64 (dt, *J* = 10.4, 6.5 Hz, 1H), 5.31 (dt, *J* = 10.4, 6.5, 1H), 4.34 (AB, *J*_{AB} = 11.7, Δ*ν* = 90.7 Hz, 2H), 4.02 (ddd, *J* = 7.9, 2.7, 1.9 Hz, 1H), 3.98 (ddd, *J* = 9.5, 3.2, 1.9 Hz, 1H), 3.74-3.61 (m, 3H), 3.38-3.23 (m, 2H), 3.03-2.92 (m, 1H), 2.35-2.20 (m, 2H), 2.19-2.08 (m, 2H), 2.05-1.94 (m, 1H), 1.67-1.52 (m, 1H), 1.13 (s, 9H), 1.02 (t, *J* = 7.3 Hz, 3H) ¹³C NMR (100 MHz, C₆D₆) δ 11.0, 19.4, 25.2, 27.2, 30.6, 33.1, 36.8, 61.3, 62.2, 69.5, 71.5, 80.4, 83.8, 126.5, 127.9, 127.8, 128.1 (2), 128.6, 130.1 (2), 131.4, 134.1 (2), 135.9, 138.8; IR (film) 3025, 2963, 2930, 2854, 1459, 1426, 1377, 1269, 1106, 1073 cm⁻¹; [α]_D²² = 33.7° (*c* = 0.39, CH₂Cl₂); Anal. Calcd for C₃₅H₄₅ClO₃Si: C, 72.82; H, 7.86. Found: C, 72.78; H, 7.90.

(2*S*, 3*R*, 8*S*, 9*S*)-9-[2-(*tert*-Butyl-diphenyl-silanyloxy)-ethyl]-8-chloro-2-ethyl-2,3,4,7,8,9-hexahydro-oxonin-3-ol (25**).** A solution of [2-((2*S*, 3*S*, 8*R*, 9*S*)-8-benzyloxy-3-chloro-9-ethyl-2,3,4,7,8,9-hexahydro-oxonin-2-yl)-ethoxy]-*tert*-butyl-diphenyl-silane (**24**) (146 mg, 0.25 mmol) in CH₂Cl₂ (2.5 mL) was treated with BCl₃-Me₂S (2.0 M in CH₂Cl₂, 1.25 mL, 2.50 mmol) and stirred for 16 h. The reaction was quenched via addition of saturated NaHCO₃ (1.0 mL). The reaction was diluted with saturated

NaHCO₃ (20 mL), H₂O (20 mL) and was extracted with Et₂O (4 x 25 mL). The combined organic layers were washed with brine (25 mL) dried over Na₂SO₄, filtered, concentrated, and purified via flash chromatography to provide 106 mg (87 %) of (2*R*, 3*S*, 8*S*, 9*S*)-9-[2-(*tert*-butyl-diphenyl-silanyloxy)-ethyl]-8-chloro-2-ethyl-2,3,4,7,8,9-hexahydro-oxonin-3-ol (**25**): ¹H NMR (400 MHz, C₆D₆) δ 7.78-7.69 (m, 4H), 7.31-7.20 (m, 6H), 5.68 (td, *J* = 10.5, 7.5 Hz, 1H), 5.29 (td, *J* = 10.5, 6.3 Hz, 1H), 3.98 (ddd, *J* = 9.6, 3.8, 2.0 Hz, 1H), 3.86 (ddd, *J* = 11.5, 3.8, 2.0 Hz, 1H), 3.72-3.60 (m, 2H), 3.40-3.31 (m, 2H), 3.22 (td, *J* = 11.5, 10.5 Hz, 1H), 2.91-2.80 (m, 1H), 2.35-2.20 (m, 2H), 2.18-2.08 (m, 1H), 1.88-1.75 (m, 2H), 1.60-1.50 (m, 1H), 1.16 (s, 9H), 1.04 (t, *J* = 7.3 Hz, 3H); ¹³C NMR (100 MHz, C₆D₆) δ 1.3, 10.9, 19.4, 25.1, 27.2, 30.1, 33.0, 34.8, 36.8, 61.3, 62.3, 72.5, 85.0, 126.6, 130.1, 130.6, 134.1, 136.0; IR (film) 3632-3143, 3068, 3021, 2986, 2951, 2876, 1458, 1378, 1355, 1310, 1254, 1110, 1037 cm⁻¹; [α]_D²² = 22.3° (*c* = 0.39, CH₂Cl₂); Anal. Calcd for C₂₈H₃₉ClO₃Si: C, 69.03; H, 8.07. Found: C, 68.91; H, 8.12.

[(2*S*, 3*S*, 8*S*, 9*S*)-2-(8-Bromo-3-chloro-9-ethyl-2,3,4,7,8,9-hexahydro-oxonin-2-yl)-ethoxy]-*tert*-butyl-diphenyl-silane (**26**). To a solution of (2*R*, 3*S*, 8*S*, 9*S*)-9-[2-(*tert*-butyl-diphenyl-silanyloxy)-ethyl]-8-chloro-2-ethyl-2,3,4,7,8,9-hexahydro-oxonin-3-ol (**25**) (106 mg, 0.22 mmol), carbon tetrabromide (246 mg, 0.741 mmol) in toluene (15 mL) was added trioctylphosphine (0.99 mL, 2.22 mmol). The solution was heated to 75 °C and stirred 14 h. The reaction was cooled to 25 °C and treated with saturated Na₂SO₃

(5 mL). The reaction was extracted with Et₂O (3 x 15 mL). The combined organic layers were washed with brine (25 mL) dried over Na₂SO₄, filtered, concentrated, and purified via flash chromatography to provide 104 g (86 %) of [(2*S*, 3*S*, 8*S*, 9*S*)-2-(8-bromo-3-chloro-9-ethyl-2,3,4,7,8,9-hexahydro-oxonin-2-yl)-ethoxy]-*tert*-butyl-diphenyl-silane (**26**): ¹H NMR (400 MHz, CDCl₃) δ 7.68-7.60, (m, 4H), 7.45-7.34 (m, 6H), 5.70-5.61 (m, 2H), 4.46(ddd, *J* = 7.7, 6.0, 2.6 Hz, 1H), 4.30-4.12 (m, 2H), 3.90-3.86 (m, 1H), 3.80 (dt, *J* = 10.5, 6.0 Hz, 1H), 3.72 (ddd, *J* = 10.5, 7.6, 6.0 Hz, 1H), 3.02-2.62 (m, 4H), 2.12 (ddt, *J* = 13.7, 7.6, 6.0 Hz, 1H), 2.00 (ddt, *J* = 13.7, 7.6, 6.0 Hz, 1H), 1.82-1.65 (m, 2H), 1.05 (s, 9H), 0.86, (t, *J* = 7.3 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 10.3, 19.2, 27.0, 28.7, 29.7, 29.6, 30.1, 36.7, 56.6, 60.9, 63.6, 127.7, 127.9, 128.8, 129.6, 129.7, 129.9, 130.4, 133.7, 133.9, 134.3, 135.6, 135.7; IR (film) 3054, 2969, 2924, 2868, 1588, 1456, 1406, 1366, 1261, 116, 1061 cm⁻¹; [α]_D²² = 45.7° (*c* = 0.57, CH₂Cl₂); Anal. Calcd for C₂₈H₃₈BrClO₂Si: C, 61.14; H, 6.96. Found: C, 61.00; H, 7.03.

(2*S*, 3*S*, 8*S*, 9*S*)-2-(8-Bromo-3-chloro-9-ethyl-2,3,4,7,8,9-hexahydro-oxonin-2-yl)-ethanol (27). Into a 25 mL plastic bottle was placed [(2*S*, 3*S*, 8*S*, 9*S*)-2-(8-bromo-3-chloro-9-ethyl-2,3,4,7,8,9-hexahydro-oxonin-2-yl)-ethoxy]-*tert*-butyl-diphenyl-silane (**26**) (104 mg, 0.19 mmol), and acetonitrile (12.3 mL). The reaction was cooled to 0 °C and 47 % aqueous HF was added. The reaction was warmed to 25 °C and stirred 14 h. The reaction was quenched by addition of saturated NaHCO₃ (25 mL) and extracted with Et₂O (4 x 25 mL). The combined organic layers were washed with brine (50 mL), dried over Na₂SO₄, filtered, concentrated, and purified via flash chromatography to provide

57.2 mg (98 %) of (2*S*, 3*S*, 8*S*, 9*S*)-2-(8-bromo-3-chloro-9-ethyl-2,3,4,7,8,9-hexahydro-oxonin-2-yl)-ethanol (**27**): ¹H NMR (500 MHz, C₆D₆, 50 °C) δ 5.49 (dt, *J* = 9.8, 8.7 Hz, 1H), 5.38 (td, *J* = 9.4, 7.2 Hz, 1H), 4.14 (bs, 1H), 3.82-3.68 (m, 3H), 3.58 (ddd, *J* = 12.4, 5.3, 1.6 Hz, 1H), 3.50 (dt, *J* = 10.7, 5.3 Hz, 1H), 2.79 (bs, 1H), 2.50-2.34 (m, 3H), 2.01 (dddd, *J* = 15.4, 6.6, 6.5, 5.3 Hz, 1H), 1.78-1.55 (m, 3H), 0.75 (t, 7.4 Hz, 3H); ¹³C NMR (125 MHz, C₆D₆, 50 °C) δ 10.4, 29.4, 32.0, 33.8, 37.8, 57.2, 59.8, 64.9, 75.0, 76.4, 129.8, 130.3; IR (film) 3675-3184, 3054, 2969, 2924, 2868, 1456, 1406, 1366, 1261, 1116, 1061 cm⁻¹; [α]_D²³ = 64.9° (*c* = 1.00, CH₂Cl₂); Anal. Calcd for C₁₂H₂₀BrClO₂: C, 46.25; H, 6.07. Found: C, 46.07; H, 6.05.

[(2*S*, 3*S*, 8*S*, 9*S*)-8-Bromo-3-chloro-9-ethyl-2,3,4,7,8,9-hexahydro-oxonin-2-yl]-acetaldehyde. To a solution of (2*S*, 3*S*, 8*S*, 9*S*)-2-(8-bromo-3-chloro-9-ethyl-2,3,4,7,8,9-hexahydro-oxonin-2-yl)-ethanol (**27**) (28.6 mg, 0.092 mmol) in CH₂Cl₂ (15 mL) was added Dess-Martin periodinane (58.6 mg, 0.138 mmol) and the reaction stirred 10 h and was quenched via addition of 10 % aqueous Na₂S₂O₃. The reaction was diluted with saturated NH₄Cl and extracted with EtOAc (3 x 20 mL). The combined organic layers were washed with brine (50 mL) dried over Na₂SO₄, filtered, concentrated, and purified via flash chromatography using 5 % EtOAc/hexanes to provide 25 mg (90 %) of [(2*S*, 3*S*, 8*S*, 9*S*)-8-bromo-3-chloro-9-ethyl-2,3,4,7,8,9-hexahydro-oxonin-2-yl]-acetaldehyde which was used directly in the next step.

(2*S*, 3*S*, 8*S*, 9*S*)-3-Bromo-8-chloro-2-ethyl-9-(3-iodo-allyl)-2,3,4,7,8,9-hexahydro-oxonine (28). A 25 mL flask was charged with iodomethyl-triphenyl-phosphonium iodide (429 mg, 0.81 mmol) and THF (2 mL). A solution of $\text{NaN}(\text{SiMe}_3)_2$ (0.75 M in 3:1 toluene:THF, 0.86 mL, 0.648 mmol) was added and the reaction stirred 1 minute before cooling to $-60\text{ }^\circ\text{C}$ where upon HMPA (0.225 mL, 1.30 mmol) was added. The reaction was cooled to $-78\text{ }^\circ\text{C}$ and a solution of [(2*S*, 3*S*, 8*S*, 9*S*)-8-bromo-3-chloro-9-ethyl-2,3,4,7,8,9-hexahydro-oxonin-2-yl]-acetaldehyde (25 mg, 0.081 mmol) in THF (1 mL) was added dropwise. The reaction was stirred 1 h and quenched via addition of saturated NH_4Cl (2 mL). The reaction was warmed to $25\text{ }^\circ\text{C}$ and filtered through silica gel and celite using EtOAc as the eluent. The solution was washed with brine (50 mL) dried over Na_2SO_4 , filtered, concentrated, and purified via flash chromatography to provide 25.3 mg (72 % 9:1, Z:E) of (2*S*, 3*S*, 8*S*, 9*S*)-3-bromo-8-chloro-2-ethyl-9-(3-iodo-allyl)-2,3,4,7,8,9-hexahydro-oxonine (**28**): ^1H NMR (400 MHz, CDCl_3) δ 6.45-6.16 (m, 2H), 5.75-5.56 (m, 2H), 4.40-3.90 (m, 4H), 3.10-2.52 (m, 6H), 2.00-1.74 (m, 2H), 0.87 (t, 7.4 Hz, 3H); ^{13}C NMR (100 MHz, C_6D_6) δ 10.5, 29.2, 32.1, 40.3, 41.0, 57.0, 63.6, 74.5, 78.3, 84.6, 131.0, 137.6, 141.9; IR (film) 3078, 3025, 2970, 2875, 1735, 1455, 1376, 1304, 1274, 1238, 1188, 1170, 1141 cm^{-1} ; $[\alpha]_D^{23} = 73.4^\circ$ ($c = 0.86$, CH_2Cl_2).

[5-((2*S*, 3*S*, 8*S*, 9*S*)-8-Bromo-3-chloro-9-ethyl-2,3,4,7,8,9-hexahydro-oxonin-2-yl)-pent-3-en-1-ynyl]-triethyl-silane. A solution of CuI (3.8 mg, 0.020 mmol), Pd(PPh₃)₄ (5.8 mg, 0.005 mmol) in THF (2 mL) was treated with Et₂NH (0.104 mL, 1.00 mmol) and cooled to 0 °C. Triethylsilylacetylene (0.071 mL, 0.500 mmol) was added followed by a solution of (2*S*, 3*S*, 8*S*, 9*S*)-3-bromo-8-chloro-2-ethyl-9-(3-iodo-allyl)-2,3,4,7,8,9-hexahydro-oxonine (**28**) (22.2 mg, 0.005 mmol) in THF (4 mL). The reaction was stirred 2 h, poured into saturated NH₄Cl (5 mL), and extracted with EtOAc (3 x 5 mL). The organic layers were washed with brine (5 mL), dried over Na₂SO₄, filtered, concentrated, and purified via flash chromatography to provide 21.8 mg (95 %) of [5-((2*S*, 3*S*, 8*S*, 9*S*)-8-bromo-3-chloro-9-ethyl-2,3,4,7,8,9-hexahydro-oxonin-2-yl)-pent-3-en-1-ynyl]-triethyl-silane: ¹H NMR (500 MHz, C₆D₆) δ 5.75 (dt, *J* = 4.0, 3.9 Hz, 1H), 5.51 (d, *J* = 10.9 Hz, 1H) 5.41 (m, 1H), 4.06 (m, 1H), 3.81 (d, *J* = 11.7 Hz, 1H), 3.73 (d, *J* = 10.3 Hz, 1H), 3.64 (m, 1H), 3.03-2.82 (m, 2H) 2.80-2.50 (m, 2H), 1.92-1.80 (m, 1H), 1.72-1.64 (m, 1H), 1.10 (t, *J* = 7.9 Hz, 9H), 0.79 (t, 7.3 Hz, 3H), 0.68 (q, *J* = 7.9 Hz, 6H); ¹³C NMR (125 MHz, C₆D₆) δ 1.6, 5.1, 8.0, 10.5, 29.1, 30.4, 31.7, 36.0, 57.0, 63.8, 91.9, 97.8, 103.7, 112.3, 121.1, 130.6, 140.5; IR (film) 3030, 2964, 2878, 2150, 1735, 1456, 1305, 1250, 1200, 1144, 1090, 1075 cm⁻¹; [α]_D²⁶ = 110.1° (*c* = 0.31, CH₂Cl₂); Anal. Calcd for C₂₁H₃₄BrClOSi: C, 56.56; H, 7.68. Found: C, 56.49; H, 7.73.

(+)-Obtusenyne (1). To a solution of [5-((2*S*, 3*S*, 8*S*, 9*S*)-8-bromo-3-chloro-9-ethyl-2,3,4,7,8,9-hexahydro-oxonin-2-yl)-pent-3-en-1-ynyl]-triethyl-silane (10.9 mg, 0.024 mmol) in THF (5 mL) was added TBAF (1.0 M in THF, 0.122 mL, 0.122 mmol) at -78°C . The reaction was allowed to warm to 0°C and stirred 30 minutes. Saturated NH_4Cl (15 mL) was added and the reaction was extracted with Et_2O (3 x 25 mL). The combined organics were washed with brine (25 mL) dried over Na_2SO_4 , filtered, concentrated, and purified via flash chromatography to provide 7.8 mg (97 %) of (+)-obtusenyne (**1**): ^1H NMR (500 MHz, CDCl_3) δ 6.02 (dt, $J = 10.8, 7.2$ Hz, 1H), 5.75-5.60 (m, 2H), 5.58-5.54 (m, 1H), 4.40-4.24 (m, 2H), 4.16-4.00 (m, 1H), 3.98-3.92 (m, 1H), 3.15 (d, $J = 2.2$ Hz, 1H) 3.05-2.72 (m, 4H), 2.92 (dddd, $J = 14.5, 7.2, 7.0, 1.3$ Hz, 1H), 2.79 (dddd, 14.5, 7.2, 7.2, 1.2, 1H), 1.93 (dq, $J = 14.2, 7.2, 6.3$ Hz, 1H), 1.79 (ddq, $J = 14.2, 7.6, 7.2$ Hz, 1H), 0.92 (t, $J = 7.2$ Hz, 3H); ^{13}C NMR (125 MHz, CDCl_3 , 50°C) δ 10.3, 28.7, 31.6, 35.1, 56.5, 63.2, 80.1, 82.6, 110.9, 128.9, 130.6, 140.6; IR (film) 3300, 3149, 3056, 2964, 2880, 2858, 2148, 1754, 1665, 1620, 1456, 1305, 1250, 1200, 1156, 1087, 1044; $[\alpha]_D^{26} = 153.2^{\circ}$ ($c = 0.25$, CH_2Cl_2); Anal. Calcd for $\text{C}_{15}\text{H}_{20}\text{BrCl}$: C, 54.32; H, 6.08. Found: C, 54.17; H, 6.11.

1-[(2*S*, 3*R*, 8*R*, 9*S*)-3-(tert-Butyl-dimethyl-silanyloxy)-9-ethyl-8-hydroxy-2,3,4,7,8,9-hexahydro-oxonin-2-yl]-3-methyl-butane-2,3-diol (30). Sodium (460 mg, 20 mmol) and naphthalene (3.34 g, 26 mmol) were placed in a 250 mL flask and purged with nitrogen. THF (80 mL) was added and the reaction sonicated for 3 h producing a dark green solution. A 100 mL flask was charged with 1-[(2*S*, 3*R*, 8*R*, 9*S*)-3-(tert-Butyl-

dimethyl-silanyloxy)-9-ethyl-8-benzyloxy-2,3,4,7,8,9-hexahydro-oxonin-2-yl]-3-methyl-butane-2,3-diol (**20**) (629 mg, 1.28 mmol) and THF (30 mL). The solution was cooled to 0 °C and 20 mL of the sodium naphthalenide solution was added dropwise by syringe. The reaction was sonicated 2 h at 0 °C and then quenched via addition of saturated NH₄Cl. The reaction was extracted with EtOAc (3 x 25 mL), washed with brine, dried over Na₂SO₄, filtered, concentrated and purified via flash chromatography using 50 % EtOAc/hexanes as the eluent to provide 454 mg, (88 %) of 1-[(2*S*, 3*R*, 8*R*, 9*S*)-3-(tert-butyl-dimethyl-silanyloxy)-9-ethyl-8-hydroxy-2,3,4,7,8,9-hexahydro-oxonin-2-yl]-3-methyl-butane-2,3-diol (**30**): ¹H NMR (500 MHz, CDCl₃) δ 5.72-5.59 (m, 2H), 4.05 (dt, *J* = 7.2, 6.9 Hz, 1H), 3.72-3.58 (m, 4H), 3.42-3.29 (m, 2H), 2.85-2.55 (m, 2H), 2.42 (s, 2H), 2.26-2.17 (m, 1H) 1.98 (s, 1H), 1.90-1.61 (m, 4H), 1.20 (t, 7.1 Hz, 1H), 1.13 (s, 1H), 1.07 (d, *J* = 7.2 Hz, 1H), 0.98-0.90 (m, 2H), 0.88 (s, 9H), 0.08 (d, 7.3 Hz, 3H), 0.03 (d, 7.3 Hz, 3H); ¹³C NMR (125 MHz, CDCl₃) δ -4.7, -4.6, -4.3, 8.9, 9.6, 14.1, 17.7, 17.8, 20.9, 23.3, 23.5, 24.0, 24.1, 25.7, 25.9, 26.3, 29.5, 30.7, 32.1, 32.7, 33.3, 33.5, 34.2, 60.3, 70.1, 70.4, 72.5, 72.7, 72.8, 73.3, 75.2, 76.4, 77.3, 77.8, 80.1, 126.3, 127.3, 127.5, 128.7; IR (film) 3712-3055, 3017, 2952, 2930, 2892, 2859, 1649, 1464, 1377, 1350, 1247, 1062, 1002, 937, 823, 769 cm⁻¹; [α]_D²² = -37.2° (*c* = 0.96, CH₂Cl₂); Anal. Calcd for C₂₁H₄₂O₅Si: C, 62.64; H, 10.51. Found: C, 62.68; H, 10.49.

[(2*R*, 3*S*, 8*R*, 9*S*)-8-hydroxy-3-(*tert*-butyl-dimethyl-silanyloxy)-9-ethyl-2,3,4,7,8,9-hexahydro-oxonin-2-yl]-acetaldehyde (**31**). 1-[(2*S*, 3*R*, 8*R*, 9*S*)-3-(*tert*-Butyl-dimethyl-

silanyloxy)-9-ethyl-8-hydroxy-2,3,4,7,8,9-hexahydro-oxonin-2-yl]-3-methyl-butane-2,3-diol (**30**) (314 mg, 0.78 mmol) was dissolved in THF (5 mL) and H₂O (5 mL) and treated with Bu₄NHSO₄ (265 mg, 0.78 mmol) and NaIO₄ (667 mg, 3.12 mmol) and stirred for 2 h. The reaction was poured into saturated NaHCO₃ (5 mL) and H₂O (5 mL). The reaction was extracted with EtOAc (3 x 15 mL), dried over Na₂SO₄, filtered, concentrated, and filtered through silica gel using 25 % EtOAc/hexanes as the eluent to provide 267 mg (90 %) (2*R*, 3*S*, 8*R*, 9*S*)-8-hydroxy-3-(*tert*-butyl-dimethyl-silanyloxy)-9-ethyl-2,3,4,7,8,9-hexahydro-oxonin-2-yl-acetaldehyde (**31**) which was used directly in the next step.

(2*S*, 3*R*, 8*R*, 9*S*)-8-(*tert*-Butyl-dimethyl-silanyloxy)-2-ethyl-9-(3-iodo-allyl)-2,3,4,7,8,9-hexahydro-oxonin-3-ol (**32**). A 500 mL flask was charged with iodomethyl-triphenyl-phosphonium iodide (3.7 g, 7.0 mmol) and THF (210 mL). A solution of NaN(SiMe₃)₂ (0.75 M in 3:1 toluene:THF, 7.5 mL, 5.6 mmol) was added and the reaction stirred 1 minute before cooling to –60 °C where upon HMPA (2.0 mL, 11.2 mmol) was added. The reaction was cooled to –78 °C and a solution of (2*R*, 3*S*, 8*R*, 9*S*)-8-hydroxy-3-(*tert*-butyl-dimethyl-silanyloxy)-9-ethyl-2,3,4,7,8,9-hexahydro-oxonin-2-yl-acetaldehyde (**31**) (267 mg, 0.70 mmol) in THF (20 mL) was added dropwise. The reaction was stirred 1 h and quenched via addition of saturated NH₄Cl (20 mL). The reaction was warmed to 25 °C and filtered through a silica gel and celite pad using EtOAc as the eluent. The solution was washed with brine (50 mL) dried over Na₂SO₄,

filtered, concentrated, and purified via flash chromatography to provide 235 mg (72 %) of (2*S*, 3*R*, 8*R*, 9*S*)-8-(*tert*-butyl-dimethyl-silanyloxy)-2-ethyl-9-(3-iodo-allyl)-2,3,4,7,8,9-hexahydro-oxonin-3-ol (**32**): ¹H NMR (400 MHz, CDCl₃) δ 6.47 (ddd, *J* = 7.0, 6.4, 5.9 Hz, 1H), 6.31 (d, *J* = 7.1 Hz, 1H), 5.75-5.66 (m, 2H), 3.65-3.51 (m, 3H), 3.36 (ddd, *J* = 4.8, 4.5, 4.2 Hz, 1H), 2.50-2.28 (m, 6H), 1.75-1.65 (m, 3H), 0.92 (t, *J* = 7.3 Hz, 3H), 0.89 (s, 9H), 0.11 (s, 3H), 0.08 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ -4.5, -4.3, 8.9, 17.9, 24.2, 26.0, 31.8, 33.0, 37.9, 70.8, 72.5, 77.5, 79.0, 83.9, 126.6, 128.4, 138.4; IR (film) 3706-3060, 3017, 2957, 2924, 2848, 1643, 1454, 1372, 1258, 1080, 921, 834, 739; [α]_D²³ = -20.2° (*c* = 1.02, CH₂Cl₂); Anal. Calcd for C₁₉H₃₅IO₃Si: C, 48.92; H, 7.56. Found: C, 48.50; H, 7.67.

(2*S*, 3*R*, 8*R*, 9*S*)-8-(*tert*-Butyl-dimethyl-silanyloxy)-2-ethyl-9-(5-triethylsilyl-pent-2-en-4-ynyl)-2,3,4,7,8,9-hexahydro-oxonin-3-ol (33). A solution of CuI (38 mg, 0.20 mmol), Pd(PPh₃)₄ (58 mg, 0.05 mmol) in THF (20 mL) was treated with Et₂NH (1.04 mL, 10.0 mmol) and cooled to 0 °C. Triethylsilylacetylene (0.71 mL, 5.0 mmol) was added followed by a solution of (2*S*, 3*R*, 8*R*, 9*S*)-8-(*tert*-Butyl-dimethyl-silanyloxy)-2-ethyl-9-(3-iodo-allyl)-2,3,4,7,8,9-hexahydro-oxonin-3-ol (**32**) (235 mg, 0.49 mmol) in THF (20 mL). The reaction was stirred 2 h, poured into saturated NH₄Cl (30 mL), and extracted with EtOAc (3 x 25 mL). The organic layers were washed with brine (25 mL), dried over Na₂SO₄, filtered, concentrated, and purified via flash chromatography to

provide 222 mg (95 %) of (2*S*, 3*R*, 8*R*, 9*S*)-8-(*tert*-butyl-dimethyl-silanyloxy)-2-ethyl-9-(5-triethylsilanyl-pent-2-en-4-ynyl)-2,3,4,7,8,9-hexahydro-oxonin-3-ol (**33**): ¹H NMR (400 MHz, CDCl₃) δ 6.11 (ddd, *J* = 11.0, 6.2, 5.1 Hz, 1H), 5.78 (ddd, *J* = 17.9, 10.3 Hz, 1H), 5.70 (ddd, *J* = 10.3, 10.3, 6.5 Hz, 1H), 5.60 (d, 11.0, 1H), 3.68-3.51 (m, 3H), 3.35 (ddd, *J* = 4.8, 4.5, 4.2 Hz, 1H), 2.70-2.65 (m, 2H), 2.60-2.50 (m, 2H), 2.47-2.31 (m, 2H), 1.81-1.64 (m, 2H), 1.25 (s, 1H), 0.97 (t, *J* = 7.9 Hz, 9H), 0.91 (t, *J* = 7.4 Hz, 3H) 0.89 (s, 9H), 0.61 (q, *J* = 7.9 Hz, 6H), 0.11 (s, 3H), 0.06 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ -4.7, -4.3, 4.4, 7.5, 8.8, 17.9, 23.9, 25.9, 29.7, 31.8, 33.2, 70.7, 72.5, 96.9, 103.3, 110.5, 126.5, 128.6, 142.1; IR (film) 3658-3033, 3006, 2957, 2914, 2871, 2849, 1458, 1257, 1090, 1002, 943, 835, 775; [α]_D²³ = 35.9° (*c* = 0.53, CH₂Cl₂); Anal. Calcd for C₂₇H₅₀O₃Si₂: C, 67.72; H, 10.52. Found: C, 67.43; H, 10.45.

(2*S*, 3*S*, 8*R*, 9*S*)-3-Bromo-8-(*tert*-butyl-dimethyl-silanyloxy)-2-ethyl-9-(5-triethylsilanyl-pent-2-en-4-ynyl)-2,3,4,7,8,9-hexahydro-oxonine (34). A 25 mL flask was charged with (2*S*, 3*R*, 8*R*, 9*S*)-8-(*tert*-Butyl-dimethyl-silanyloxy)-2-ethyl-9-(5-triethylsilanyl-pent-2-en-4-ynyl)-2,3,4,7,8,9-hexahydro-oxonin-3-ol (**33**) (190 mg, 0.39 mmol), 1-methyl-cyclohexene (0.46 mL 3.9 mmol), carbon tetrabromide (2.56 g, 7.72 mmol), and toluene (27.0 mL). The reaction was heated to 80 °C and a solution of trioctylphosphine (1.72 mL, 3.9 mmol) in toluene (3.5 mL) was added dropwise over 2.5

h. The reaction was cooled to 25 °C and concentrated in vacuo. The reaction was purified via flash chromatography using 2.5 % EtOAc/hexanes as the eluent to provide 288 mg (86 %) of (2*S*, 3*S*, 8*R*, 9*S*)-3-bromo-8-(*tert*-butyl-dimethyl-silanyloxy)-2-ethyl-9-(5-triethylsilanyl-pent-2-en-4-ynyl)-2,3,4,7,8,9-hexahydro-oxonine (**34**): ¹H NMR (400 MHz, CDCl₃) δ 6.15 (ddd, *J* = 11.0, 6.2, 5.1 Hz, 1H), 5.84 (ddd, *J* = 17.9, 10.3 Hz, 1H), 5.59 (d, 11.0, 1H), 5.42 (ddd, *J* = 10.3, 10.3, 6.5 Hz, 1H), 4.02 (d, *J* = 9.7 Hz, 1H), 3.77 (ddd, *J* = 11.0, 11.0, 3.5 Hz, 1H), 3.54 (dd, *J* = 7.2, 7.2 Hz, 1H), 3.34-3.27 (m, 2H), 3.02 (s, 1H), 2.81-2.76 (m, 1H), 2.60-2.48 (m, 2H), 2.03-2.00 (m, 1H), 1.85-1.70 (m, 2H), 1.00 (t, *J* = 7.9 Hz, 9H), 0.89 (s, 9H), 0.76 (t, *J* = 7.4 Hz, 3H), 0.61 (q, *J* = 7.9 Hz, 6H), 0.13 (s, 3H), 0.08 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ -4.7, -4.3, 4.4, 7.5, 9.8, 17.8, 25.8, 28.7, 33.6, 33.9, 34.4, 55.7, 73.0, 96.8, 103.3, 110.2, 126.9, 130.4, 142.9; IR (film) 3006, 2952, 2919, 2864, 2854, 2142, 1643, 1464, 1415, 1388, 1361, 1257, 1078, 1041, 904, 834, 739; [α]_D²³ = 111.8° (*c* = 1.00, CH₂Cl₂); Anal. Calcd for C₂₇H₄₉BrO₂Si₂: C, 59.86; H, 9.12. Found: C, 59.79; H, 9.11.

(2*S*, 3*S*, 8*R*, 9*S*)-8-Bromo-9-ethyl-2-pent-2-en-4-ynyl-2,3,4,7,8,9-hexahydro-oxonin-3-ol. A solution of (2*S*, 3*S*, 8*R*, 9*S*)-3-Bromo-8-(*tert*-butyl-dimethyl-silanyloxy)-2-ethyl-9-(5-triethylsilanyl-pent-2-en-4-ynyl)-2,3,4,7,8,9-hexahydro-oxonine (**34**) (112 mg, 0.21 mmol) in THF (50 mL) was cooled to -78 °C and treated with *n*-Bu₄NF (1.0 M in THF,

1.0 mL mL, 1.03 mmol). The reaction was allowed to warm to -20 °C and stirred 30 minutes. Saturated NH₄Cl (15 mL) was added and the reaction was extracted with Et₂O (3 x 25 mL). The combined organics were washed with brine (25 mL) dried over Na₂SO₄, filtered, concentrated, and purified via flash chromatography to provide 60 mg (91 %) of (2*S*, 3*S*, 8*R*, 9*S*)-8-bromo-9-ethyl-2-pent-2-en-4-ynyl-2,3,4,7,8,9-hexahydro-oxonin-3-ol: ¹H NMR (400 MHz, CDCl₃) δ 6.23 (ddd, *J* = 10.9, 10.9, 6.7 Hz, 1H), 5.84 (ddd, *J* = 18.1, 10.1, 10.1 Hz, 1H), 5.57 (d, *J* = 10.9, 1.9 Hz, 1H), 4.08 (d, *J* = 11.0 Hz, 1H), 3.80-3.76 (m, 1H), 3.63 (dd, *J* = 7.9, 7.7 Hz, 1H), 3.33 (s, 1H), 3.24-3.18 (m, 1H), 3.14 (s, 1H), 2.98-2.92 (m, 2H), 2.66 (ddd, *J* = 15.5, 15.5, 7.4 Hz, 2H), 2.55 (ddd, 11.1, 11.1, 6.1 Hz, 1H), 2.20-2.10 (m, 1H), 1.98-1.75 (m, 3H), 1.24 (s, 3H), 0.80 (t, *J* = 7.4 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 9.8, 28.4, 33.2, 33.5, 34.1, 55.7, 72.8, 74.2, 80.4, 81.5, 82.4, 109.6, 127.4, 129.8, 142.7; IR (film) 3516-3186, 3289, 2957, 2919, 2876, 1458, 1361, 1198, 1172, 1062, 1055, 1019, 883, 726; [α]_D²³ = 105.8° (*c* = 1.00, CH₂Cl₂); Anal. Calcd for C₁₅H₂₁BrO₂: C, 57.52; H, 6.76. Found: C, 57.46; H, 6.96.

(+)-Obtusenyne (1). A 25 mL flask was charged with (2*S*, 3*S*, 8*R*, 9*S*)-8-bromo-9-ethyl-2-pent-2-en-4-ynyl-2,3,4,7,8,9-hexahydro-oxonin-3-ol (25 mg, 0.08 mmol), 1-methylcyclohexene (0.237 mL 2.0 mmol), carbon tetrachloride (0.385 mL, 3.94 mmol), and toluene (5.0 mL). The reaction was heated to 80 °C and a solution of trioctylphosphine (0.214 mL, 0.48 mmol) in toluene (0.5 mL) was added dropwise over 4 h. The solution

was cooled to 25 °C and concentrated in vacuo. The reaction was purified via flash chromatography using 1.0 % EtOAc/hexanes as the eluent to provide 19 mg (70 %) of (+)-obtusenyne (**1**) that was identical to the material prepared previously.