Development and Elucidation of a Pd-based Cyclization/Oxygenation Sequence for Natural Product Synthesis

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Experimental Data for Compounds

General Procedures. All reactions were carried out under an argon atmosphere with dry solvents under anhydrous conditions, unless otherwise noted. Dry tetrahydrofuran (THF), toluene, dimethylformamide (DMF), diethyl ether (Et₂O) and dichloromethane (CH₂Cl₂) were obtained by passing commercially available pre-dried, oxygen-free formulations through activated alumina columns. Yields refer to chromatographically and spectroscopically (¹H and ¹³C NMR) homogeneous materials, unless otherwise stated. Reagents were purchased at the highest commercial quality and used without further purification, unless otherwise stated. Reactions were magnetically stirred and monitored by thin-layer chromatography (TLC) carried out on 0.25 mm E. SiliCycle silica gel plates silica gel plates (60F-254) using UV light as visualizing agent, and an ethanolic solution of phosphomolybdic acid and cerium sulfate, and heat as developing agents. SiliCycle silica gel (60, academic grade, particle size 0.040–0.063 mm) was used for flash column chromatography. Preparative thin-layer chromatography separations were carried out on 0.50 mm E. Merck silica gel plates (60F-254). NMR spectra were recorded on Bruker 500 MHz and 400 MHz instruments and calibrated using residual undeuterated solvent as an internal reference. The following abbreviations were used to explain the multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, sx = sextet, m = multiplet. IR spectra were recorded on a Perkin-Elmer 1000 series FT-IR spectrometer. High-resolution mass spectra (HRMS) were recorded on an Agilent 6244 Tof-MS using ESI (Electrospray Ionization) or CI (Chemical Ionization) at the University of Chicago Mass Spectroscopy Core Facility.

Abbreviations. EtOAc = ethyl acetate, THF = tetrahydrofuran, DBU = 1,8-diazabicyclo[5.4.0]undec-7-ene, MVK = methyl vinyl ketone, EtOH = ethanol, MeOH = methanol, KHMDS = potassium bis(trimethylsilyl)amide, Bn = benzyl, Ac = acetyl, *t*-BuOH = *t*-butanol, *t*-BuOK = potassium *t*-butoxide, LiHMDS = lithium bis(trimethylsilyl)amide, Ad = adamantyl, Phth = phthalimide, Piv = pivaloyl, MPO = 4-methoxypyridine *N*-oxide, LDA = lithium diisopropylamide, TBAF = tetra-*n*-butylammonium fluoride, DIBAL-H = diisobutylaluminum hydride, DMSO = dimethyl sulfoxide, IBX = 2-iodoxybenzoic acid, *n*-BuLi = *n*-butyllithium, *t*-AmylOH = 2-methylbutan-2-ol.

Preparation of triflates

Triflate 17. To a solution of methyl 4,4-dimethyl-2-oxocyclohexane-1-carboxylate (S1) (1.84 g, 10.0 mmol, 1.0 equiv) in EtOH (50 mL) at 23 °C was added DBU (7.60 g, 50.0 mmol, 5.0 equiv) and methyl vinyl ketone (2.10 g, 30.0 mmol, 3.0 equiv). The resultant solution was then stirred at 23 °C for 3 h. Upon completion, the reaction contents were diluted with EtOAc (30 mL) and guenched by the addition of saturated aqueous NH₄Cl (30 mL). The resultant mixture was poured into a separatory funnel and the layers were separated. The aqueous layer was then extracted with EtOAc (2 × 30 mL). The combined organic layers were washed with H₂O (30 mL) and brine (30 mL) before being dried (Na₂SO₄), filtered, and concentrated. The resultant residue was purified by flash column chromatography (silica gel, hexanes:EtOAc, 5:1) to provide the desired Michael adduct S2 (2.41 g, 95% yield) as a pale yellow oil. S2: $R_f = 0.23$ (silica gel, hexanes:EtOAc = 5:1); IR (film) v_{max} 3628, 3414, 2956, 1713, 1435, 1369, 1102, 1075, 940, 853 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 3.72 (s, 3 H), 2.56–2.49 (m, 1 H); 2.43–2.39 (m, 1 H), 2.34 (d, J = 13.3 Hz, 1 H), 2.18-2.13 (m, 1 H), 2.12 (s, 3 H), 2.11-2.07 (m, 1 H),1.89–1.83 (m, 1 H), 1.65–1.49 (m, 2 H), 1.51–1.49 (m, 1 H), 1.02 (s, 3 H), 0.87 (s, 3 H); ¹³C NMR (125 MHz, CDCl₃) δ 207.7, 207.4, 172.4, 58.8, 53.8, 52.5, 38.8, 36.7, 35.6, 31.9, 31.1, 30.0, 28.1, 25.7; HRMS (ESI) calcd for $C_{14}H_{23}O_4^+$ [M + H $^+$] 255.1591, found 255.1593. Next, to a suspension of Ph₃PCH₂Br (2.68 g, 7.50 mmol, 1.5 equiv) in THF (30 mL) at 0 °C was added n-BuLi (2.40 mL, 2.5 M in THF, 6.00 mmol, 1.2 equiv). The resultant mixture was stirred at 0 °C for 15 min and then a solution of S2 (1.27 g, 5.00 mmol, 1.0 equiv) in THF (20 mL) was added. The resultant mixture was stirred at 0 °C for 2 h. Upon completion, the reaction contents were diluted with EtOAc (30 mL) and quenched by the addition of saturated aqueous NH₄Cl (30 mL). The mixture was warmed to 23 °C, poured into a separatory funnel, and the resultant layers were separated. The aqueous layer was then extracted with EtOAc (2 × 30 mL). The combined organic layers were washed with brine (30 mL) before being dried (Na₂SO₄), filtered, and concentrated. The resultant residue was purified by flash column chromatography (silica gel, hexanes:EtOAc,

50:1) to provide ketone S3 (0.756 g, 60% yield) as a pale yellow oil. S3: $R_f = 0.68$ (silica gel, hexanes: EtOAc, 5:1); IR (film) v_{max} 2956, 2857, 1714, 1650, 1454, 1369, 1252, 1199, 1100, 887 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 4.70 (s, 1 H), 4.68 (s, 1 H), 3.72 (s, 3 H), 2.46 (dt, J = 13.6, 3.7 Hz, 1 H), 2.31 (d, J = 13.1 Hz, 1 H), 2.15 (dd, J = 13.1, 2.4 Hz, 1 H), 2.06-2.00 (m, 1 H), 1.92–1.86 (m, 2 H), 1.72 (s, 3 H), 1.70–1.57 (m, 3 H), 1.51–1.47 (m, 1 H), 1.02 (s, 3 H), 0.87 (s, 3 H); ¹³C NMR (125 MHz, CDCl₃) δ 207.3, 172.3, 145.3, 110.0, 59.4, 53.9, 52.3, 36.7, 35.7, 32.7, 32.2, 31.4, 31.3, 25.5, 22.6; HRMS (ESI) calcd for $C_{15}H_{25}O_3^+$ [M + H⁺] 253.1798, found 253.1805. Finally, to a solution of ketone S3 (1.26 g, 5.00 mmol) in THF (40 mL) at -78 °C was added KHMDS (7.50 mL, 1.0 M in THF, 7.50 mmol, 1.5 equiv). The resultant yellow solution was then stirred at 0 °C for 90 min before being cooled to -78 °C. A solution of Comin's reagent (2.35 g, 6.00 mmol, 1.2 equiv) in THF (10 mL) was then added. The resultant solution was stirred at -78 °C for 1 h before being diluted with EtOAc (30 mL) and quenched by the addition of saturated aqueous NH₄Cl (30 mL). The mixture was warmed to 0 °C, poured into a separatory funnel, and the resultant layers were separated. The aqueous layer was then extracted with EtOAc (2 × 30 mL). The combined organic layers were washed with brine (30 mL) before being dried (Na₂SO₄), filtered, and concentrated. The resultant residue was purified by flash column chromatography (Et₃N-buffered silica gel, hexanes) to provide triflate 17 (1.29 g, 67% yield) as a colorless oil. 17: $R_f = 0.69$ (silica gel, hexanes: EtOAc, 10:1); IR (film) v_{max} 2962, 2869, 1739, 1669, 1651, 1417, 1214, 1144, 1004, 950, 899, 816 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 5.63 (s, 1 H), 4.73 (s, 1 H), 4.67 (s, 1 H), 3.74 (s, 3 H), 2.23–2.18 (m, 1 H), 2.05–1.92 (m, 3 H), 1.87–1.76 (m, 2 H), 1.73 (s, 3 H), 1.50–1.48 (m, 2 H), 1.10 (s, 3 H), 1.06 (s, 3 H); ¹³C NMR (125 MHz, CDCl₃) δ 173.1, 146.8, 144.7, 129.9, 119.3, 117.0, 110.6, 52.3, 50.2, 33.48, 33.46, 33.3, 32.2, 29.9, 29.1, 27.8, 22.3; HRMS (ESI) calcd for $C_{16}H_{24}O_5F_3S^+$ [M + H⁺] 385.1291, found 385.1298.

Triflate S6. Prepared as described above starting from 4,4-dimethyl-2-oxocyclohexane-1-carboxylate (0.552 g, 3.00 mmol, 1.0 equiv) and 1-(benzyloxy)but-3-en-2-one^[1] (1.58 g, 9.00 mmol, 3.0 equiv) to afford triflate **S6** (0.139 g, 9% overall yield) as a colorless oil. **S4**: $R_f = 0.29$ (silica gel, hexanes:EtOAc, 5:1); IR (film) v_{max} 3510, 2954, 2866, 1712, 1454, 1248, 1201, 1101 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 7.42–7.30 (m, 5 H), 4.57 (s, 2 H), 4.04 (s, 2 H), 3.70 (s, 3 H), 2.59–2.52 (m, 1 H), 2.45–2.37 (m, 2 H), 2.34 (d, J = 13.2 Hz, 1 H), 2.16–2.11 (m, 2 H), 1.92–1.86 (m, 1 H), 1.62–1.49 (m, 3 H), 1.02 (s, 3 H), 0.87 (s, 3 H); ¹³C NMR (125 MHz, CDCl₃) δ 207.6, 207.2, 172.3, 137.2, 128.5, 128.0, 127.9, 74.8, 73.4, 58.8, 53.8, 52.4, 36.7, 35.6, 34.2, 31.8, 31.1, 27.6, 25.6; HRMS (ESI) calcd for $C_{21}H_{29}O_5^+$ [M + H⁺] 361.2010, found 361.2009. **S5**: $R_f = 0.50$ (silica gel, hexanes:EtOAc, 10:1); IR (film) v_{max} 3443, 3030, 2954, 2863, 1713, 1652, 1496, 1368, 1199, 1098, 1028, 904, 698 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 7.37–7.28 (m, 5 H), 5.06 (s, 1 H), 4.96 (s, 1 H), 4.48 (s, 2 H), 3.96 (s, 2 H), 3.70 (s, 3 H), 2.58–2.52 (m, 1 H), 2.45–2.37 (m, 2 H), 2.33 (d, J = 13.2 Hz, 1 H), 2.16–2.09 (m, 2 H), 1.91–1.85 (m, 1 H), 1.64–1.56 (m, 2 H), 1.50–1.48 (m, 1 H), 1.01 (s, 3 H), 0.86 (s, 3 H); ¹³C NMR (125 MHz,

CDCl₃) δ 207.1, 172.2, 145.5, 138.4, 128.3, 128.1, 127.7, 127.5, 73.0, 72.0, 59.4, 53.9, 52.3, 36.7, 35.1, 32.7, 31.31, 31.28; HRMS (ESI) calcd for $C_{22}H_{31}O_4^+$ [M + H⁺] 359.2217, found 359.2231. **S6**: $R_f = 0.62$ (silica gel, hexanes:EtOAc, 10:1); IR (film) v_{max} 3032, 2959, 2866, 1738, 1669, 1454, 1416, 1365, 1213, 1144, 1093, 901, 817 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 7.37–7.28 (m, 5 H), 5.63 (s, 1 H), 5.08 (s, 1H), 4.96 (s, 1 H), 4.51–4.46 (m, 2 H), 3.96 (dd, J = 16.1, 12.5 Hz, 1 H), 3.72 (s, 3 H), 2.22–2.18 (m, 1 H), 2.12–2.02 (m, 3 H), 1.89–1.83 (m, 1 H), 1.80–1.75 (m, 1 H), 1.51–1.48 (m, 2 H), 1.09 (s, 3 H), 1.05 (s, 3 H); ¹³C NMR (125 MHz, CDCl₃) δ 173.1, 146.7, 145.0, 138.2, 130.1, 128.4, 127.7, 127.6, 122.1, 119.6, 117.0, 114.5, 112.6, 73.0, 72.0, 52.4, 50.2, 33.5, 33.4, 33.3, 29.9, 29.0, 27.8, 27.6; HRMS (ESI) calcd for $C_{23}H_{30}O_6F_3S^+$ [M + H⁺] 491.1710, found 491.1694.

$$\begin{array}{c} \text{Me} \\ \text{Me} \\$$

Triflate S9. To t-BuOK (2.4 mL, 1.0 M in t-BuOH, 2.40 mmol, 1.2 equiv) at 23 °C was added methyl 4.4-dimethyl-2-oxocyclohexane-1-carboxylate (0.368 g, 2.00 mmol, 1.0 equiv). The resultant mixture was stirred at 23 °C for 10 min before 5-iodo-2-methylpent-1-ene (\$7)^[2] (0.504 g, 2.40 mmol, 1.2 equiv) was added. The resultant mixture was heated to 85 °C and stirred at that temperature for 18 h.^[3] Upon completion, the reaction contents were cooled to 23 °C, diluted with EtOAc (10 mL), and guenched by the addition of saturated agueous NH₄Cl (10 mL). The mixture was poured into a separatory funnel and the layers were separated. The aqueous layer was then extracted with EtOAc (2 × 10 mL). The combined organic layers were washed with brine (10 mL) before being dried (Na₂SO₄), filtered, and concentrated. The resultant residue was purified by flash column chromatography (silica gel, hexanes:EtOAc, 100:1→50:1) to provide ketone S8 (0.241 g, 45% yield) as a pale yellow oil. S8: $R_f = 0.45$ (silica gel, hexanes: EtOAc, 10:1); IR (film) v_{max} 3073, 2956, 2869, 1712, 1649, 1456, 1255, 1199, 1168, 1101, 888, 749 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 4.70 (s, 1 H), 4.66 (s, 1 H), 3.72 (s, 3 H), 2.44 (dt, J = 13.7, 3.6 Hz, 1 H), 2.30 (d, J = 13.1 Hz, 1 H), 2.14 (dd, J = 13.1, 2.3 Hz, 1 H), 2.00 (d, J = 13.1, 2.3 Hz, 1 H), 2.00 (d, J = 13.1, 2.3 Hz, 1 H), 2.00 (d, J = 13.1, 2.3 Hz, 1 H), 2.00 (d, J = 13.1, 2.3 Hz, 1 H), 2.00 (d, J = 13.1, 2.3 Hz, 1 H), 2.00 (d, J = 13.1, 2.3 Hz, 1 H), 2.00 (d, J = 13.1, 2.3 Hz, 1 H), 2.00 (d, J = 13.1, 2.3 Hz, 1 H), 2.00 (d, J = 13.1, 2.3 Hz, 1 H), 2.00 (d, J = 13.1, 2.3 Hz, 1 H), 2.00 (d, J = 13.1, 2.3 Hz, 1 H), 2.00 (d, J = 13.1, 2.3 Hz, 1 H), 2.00 (d, J = 13.1, 2.3 Hz, 1 H), 2.00 (d, J = 13.1, 2.3 Hz, 1 H), 2.00 (d, J = 13.1, 2.3 Hz, 1 H), 2.00 (d, J = 13.1, 2.3 Hz, 1 H), 2.00 (d, J = 13.1, 2.3 Hz, 1 H), 2.00 (d, J = 13.1, 2.3 Hz, 1 H), 2.00 (d, J = 13.1, 2.3 Hz, 1 H), 2.00 (d, J = 13.1, 2.3 Hz, 1 H), 2.00 (d, J = 13.1, 2.3 Hz, 1 H), 2.00 (d, J = 13.1, 2.3 Hz, 1 H), 2.00 (d, J = 13.1, 2.3 Hz, 1 H), 2.00 (d, J = 13.1, 2.3 Hz, 1 H), 2.00 (d, J = 13.1, 2.3 Hz, 1 H), 2.00 (d, J = 13.1, 2.3 Hz, 1 H), 2.00 (d, J = 13.1, 2.3 Hz, 1 H), 2.00 (d, J = 13.1, 2.3 Hz, 1 H), 2.00 (d, J = 13.1, 2.3 Hz, 1 H), 2.00 (d, J = 13.1, 2.3 Hz, 1 H), 2.00 (d, J = 13.1, 2.3 Hz, 1 H), 2.00 (d, J = 13.1, 2.3 Hz, 1 H), 2.00 (d, J = 13.1, 2.3 Hz, 1 H), 2.00 (d, J = 13.1, 2.3 Hz, 1 H), 2.00 (d, J = 13.1, 2.3 Hz, 1 H), 2.00 (d, J = 13.1, 2.3 Hz, 1 H), 2.00 (d, J = 13.1, 2.3 Hz, 1 H), 2.00 (d, J = 13.1, 2.3 Hz, 1 H), 2.00 (d, J = 13.1, 2.3 Hz, 1 H), 2.00 (d, J = 13.1, 2.3 Hz, 1 H), 2.00 (d, J = 13.1, 2.3 Hz, 1 H), 2.00 (d, J = 13.1,(t, J = 7.4 Hz, 1 H), 1.88-1.82 (m, 1 H), 1.69 (s, 3 H), 1.65-1.46 (m, 4 H), 1.36-1.30 (m, 1 H),1.01 (s, 3 H), 0.86 (s, 3 H); ¹³C NMR (125 MHz, CDCl₃) δ 207.3, 172.5, 145.2, 110.2, 59.6, 53.9, 52.2, 37.9, 36.7, 35.7, 34.0, 31.4, 31.3, 25.5, 22.2, 22.1; HRMS (ESI) calcd for $C_{16}H_{27}O_3^{+}$ [M + H⁺] 267.1955, found 267.1955. Pressing forward, triflate **S9** was prepared as described above starting from S8 (0.084 g, 0.31 mmol, 1.0 equiv) to afford triflate S9 (0.089 g, 71% yield) as a colorless oil. S9: $R_f = 0.58$ (silica gel, hexanes: EtOAc, 10:1); IR (film) v_{max} 2960, 2890, 1739, 1670, 1651, 1417, 1212, 1144, 1005, 900, 816 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 5.60 (s, 1 H), 4.71 (s, 1 H), 4.66 (s, 1 H), 3.72 (s, 3 H), 2.22–2.17 (m, 1 H), 2.06–1.97 (m, 2 H), 1.86– 1.64 (m, 3 H), 1.68 (s, 3 H), 1.49–1.38 (m, 4 H), 1.09 (s, 3 H), 1.05 (s, 3 H); ¹³C NMR (125 MHz, CDCl₃) δ 173.3, 147.0, 144.9, 129.7, 119.6, 117.0, 110.5, 52.3, 50.2, 37.8, 34.6, 33.5, 33.4, 29.9, 29.3, 27.8, 22.1, 22.0; HRMS (ESI) calcd for $C_{17}H_{26}O_5F_3S^+$ [M + H⁺] 399.1448, found 399.1454.

Triflate S10. Prepared as described above starting from **54**^[4] (0.694 g, 3.33 mmol, 1.0 equiv) to afford triflate **S10** (0.985 g, 87% yield) as a colorless oil. **S10**: $R_f = 0.48$ (silica gel, hexanes); $[\alpha]_D^{20} = +57.0^{\circ}$ (c = 0.53 in CHCl₃); IR (film) v_{max} 2963, 2874, 1666, 1643, 1417, 1209, 1144, 969, 893 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 5.73 (s, 1 H), 4.89–4.87 (m, 1 H), 4.68–4.67 (m, 1 H), 2.46–2.42 (m, 1 H), 2.32–2.26 (m, 1 H), 2.12 (d, J = 13.2 Hz, 1 H), 1.97 (d, J = 13.3 Hz, 1 H), 1.98–1.92 (m, 1 H), 1.82–1.77 (m, 1 H), 1.78 (s, 3 H), 1.59–1.52 (m, 1 H), 1.15–1.08 (m, 1 H), 1.05 (s, 3 H), 1.04 (d, J = 7.1 Hz, 3 H), 1.00 (s, 3 H); ¹³C NMR (125 MHz, CDCl₃) δ 151.5, 142.9, 128.2, 121.5, 119.8, 117.2, 114.9, 47.6, 46.6, 37.3, 30.4, 30.1, 26.7, 26.5, 25.6, 25.5, 21.2; HRMS (CI) calcd for $C_{15}H_{24}O_{3}F_{3}S^{+}[M + H^{+}]$ 343.1393, found 343.1391.

S11

Triflate S11. Prepared as described above starting from methyl 4,4-dimethyl-2-oxocyclopentane-1-carboxylate^[5] (0.200 g, 1.17 mmol, 1.0 equiv) and 5-iodo-2-methylpent-1-ene (0.275 g, 1.40 mmol, 1.2 equiv) to afford triflate **S11** (0.298 g, 69% yield) as a pale yellow oil. **S11**: R_f = 0.58 (silica gel, hexanes:EtOAc, 10:1); IR (film) v_{max} 2960, 2870, 1740, 1654, 1424, 1366, 1249, 1215, 1142, 1047, 995, 842, 805, 762, 602 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 5.60 (s, 1 H), 4.73 (s, 1 H), 4.69 (s, 1 H), 3.74 (s, 3 H), 2.44 (d, J = 13.5 Hz, 1H), 2.10–2.04 (m, 1 H), 1.95–1.91 (m, 2 H), 1.78–1.73 (m, 1 H), 1.74 (d, J = 13.5 Hz, 1 H), 1.73 (s, 3 H), 1.17 (s, 3 H), 1.14 (s, 3 H); ¹³C NMR (125 MHz, CDCl₃) δ 173.5, 145.9, 144.5, 127.2, 122.2, 119.7, 117.2, 114.6, 110.5, 57.9, 52.4, 45.9, 40.0, 34.1, 32.6, 29.9, 28.9, 22.4; HRMS (ESI) calcd for $C_{15}H_{22}O_5F_3S^+$ [M + H⁺] 371.1135, found 371.1141.

Triflate S15. To a solution of 2-methanesulfonylbenzothiazole (**S13**, 1.28 g, 6.00 mmol, 2.0 equiv) and 2,5,5-trimethyl-2-(3-oxobutyl)cyclohexane-1,3-dione^[6] (**S12**, 0.672 g, 3.00 mmol,

1.0 equiv) in THF (30 mL) at -78 °C was added LHMDS (3.90 mL, 1.0 M in THF, 3.90 mmol, 1.3 equiv). The resultant mixture was stirred at -78 °C for 3 h, and then the mixture was warmed to 23 °C and stirred for an additional 1 h. Upon completion, the reaction mixture was diluted with EtOAc (20 mL), cooled to 0 °C, quenched by the addition of saturated aqueous NH₄Cl (20 mL), and warmed to 23 °C. The resultant mixture was then poured into a separatory funnel and the layers were separated. The aqueous layer was extracted with EtOAc (2 × 30 mL). The combined organic layers were washed with brine (30 mL) before being dried (Na₂SO₄), filtered, and concentrated. The resultant residue was purified by flash column chromatography (silica gel, hexanes:EtOAc, 20:1→10:1) to provide ketone S14 (0.226 g, 34% yield) as a yellow oil. [Note: S12 was not stable under strongly basic conditions, thus attempts at a Wittig reaction variant gave only trace product]. S14: $R_f = 0.47$ (silica gel, hexanes: EtOAc, 4:1); IR (film) v_{max} 2955, 2871, 1727, 1693, 1650, 1456, 1373, 1331, 1254, 1070, 955, 889 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 4.69 (s, 1 H), 4.63 (s, 1 H), 2.70 (d, J = 14.5 Hz, 2 H), 2.46 (d, J = 14.5 Hz, 2 H), 1.87– 1.80 (m, 4 H), 1.67 (s, 3 H), 1.22 (s, 3 H), 1.06 (s, 3 H), 0.87 (s, 3 H); ¹³C NMR (125 MHz, CDCl₃) δ 209.8, 144.6, 110.4, 64.4, 51.4, 35.9, 32.2, 30.6, 29.4, 27.6, 22.5, 17.9; HRMS (ESI) calcd for $C_{14}H_{23}O_2^+$ [M + H⁺] 233.1693, found 233.1699. Pressing forward, triflate S15 was prepared as described above starting from S14 (0.044 g, 0.20 mmol, 1.0 equiv) and using KHMDS (0.180 mL, 1.0 M in THF, 0.9 equiv) to afford triflate S15 (0.063 g, 87% yield) as a colorless oil. **S15**: $R_f = 0.68$ (silica gel, hexanes: EtOAc, 10:1); IR (film) v_{max} 2966, 2937, 1724, 1673, 1416, 1245, 1214, 1142, 1001, 887, 797 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 5.88 (s, 1 H), 4.70 (s, 1 H), 4.66 (s, 1 H), 2.52 (d, J = 14.0 Hz, 2 H), 2.37 (d, J = 13.9 Hz, 2 H), 2.04-1.98 (m, 1 H), 1.82–1.78 (m, 2 H), 1.69 (s, 3 H), 1.66–1.61 (m, 1 H), 1.30 (s, 3 H), 1.16 (s, 3 H), 1.13 (s, 3 H); ¹³C NMR (125 MHz, CDCl₃) δ 208.2, 149.1, 144.5, 126.7, 119.6, 117.0, 110.5, 51.6, 50.9, 34.0, 33.1, 33.0, 29.8, 29.3, 23.4, 22.3; HRMS (ESI) calcd for $C_{15}H_{22}O_4F_3S^+[M+H^+]$ 355.1185, found 355.1194.

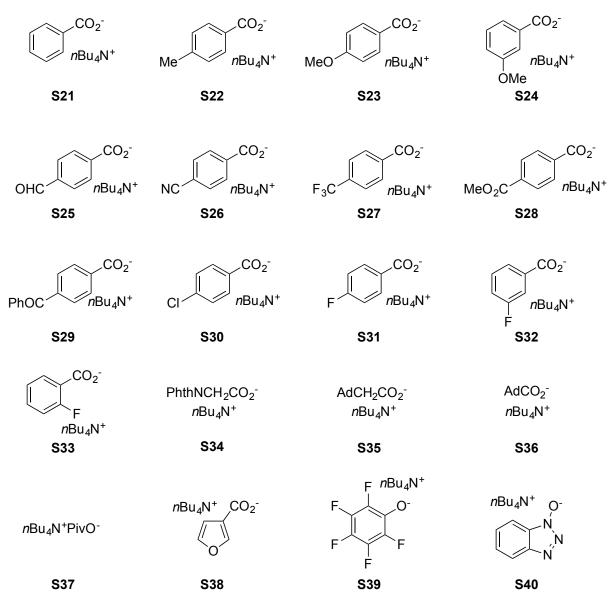
Triflate S20. S16 (0.423 g, 83% yield b.r.s.m.) was prepared as a pale yellow oil following the reported procedure starting from **S1** (0.736 g, 4.00 mmol, 1.0 equiv). [7] **S16**: $R_f = 0.26$ (silica gel, hexanes:EtOAc, 5:1); IR (film) v_{max} 3459, 2958, 2870, 1720, 1456, 1436, 1370,

1289, 1258, 1200, 1164, 1123, 1099, 1039, 1006, 978, 796; ¹H NMR (500 MHz, CDCl₃) δ 4.31 (s, 1 H), 3.79 (s, 3 H), 2.60–2.56 (m, 1 H), 2.48–2.39 (m, 2 H), 1.83–1.79 (m, 1 H), 1.63–1.60 (m, 1H), 1.08 (s, 3 H), 0.93 (s, 3 H); ¹³C NMR (125 MHz, CDCl₃) δ 207.0, 170.5, 79.9, 53.0, 51.4, 36.9, 35.1, 33.4, 30.6, 26.1; HRMS (ESI) calcd for $C_{10}H_{15}O_3^+$ [M + H⁺ – H₂O] 183.1016, found 183.1022. Next, to a solution of S16 (0.200 g, 1.00 mmol, 1.0 equiv) in CH₂Cl₂ (10 ml) at 0 °C was added 1,2-bis(trimethylsiloxyl)ethane (0.618 g, 5.00 mmol, 5.0 equiv) and TMSOTf (44.0 mg, 0.20 mmol, 0.2 equiv). The mixture was then stirred at 23 °C for 20 h. Upon completion, the reaction contents were quenched by the addition of saturated aqueous NaHCO₃ (10 mL). The mixture was poured into a separatory funnel and the layers were separated. The aqueous layer was then extracted with CH₂Cl₂ (2 × 10 mL). The combined organic layers were dried (Na₂SO₄), filtered, and concentrated. The resultant residue was purified by flash column chromatography (hexanes:EtOAc, 10:1→5:1) to provide ketal S17 (0.205 g, 84% yield) as a white solid. S17: $R_f = 0.22$ (silica gel, hexanes: EtOAc, 5:1); IR (film) v_{max} 3505, 2952, 1732, 1449, 1388, 1264, 1217, 1168, 1074, 1043, 988, 826, 614; ¹H NMR (500 MHz, CDCl₃) δ 3.94– 3.89 (m, 3 H), 3.78–3.74 (m, 1 H), 3.77 (s, 3 H), 3.38 (d, J = 1.7 Hz, 1 H), 2.29–2.22 (m, 1 H), 1.78-1.74 (m, 2 H), 1.58-1.52 (m, 1 H), 1.45 (dd, J = 13.8, 1.4 Hz, 1 H), 1.32 (dtd, J = 13.6, 4.8, 1.3 Hz, 1 H), 1.04 (s, 3 H), 0.96 (s, 3 H); ¹³C NMR (125 MHz, CDCl₃) δ 174.3, 110.1, 76.9, 65.8, 64.7, 52.8, 43.7, 32.9, 32.0, 31.2, 28.7, 26.7; HRMS (ESI) calcd for $C_{12}H_{19}O_4^+$ [M + H⁺ – H₂O₁ 227.1278, found 227.1281. Pressing forward, to a suspension of NaH (0.200 g, 60%) dispersion in mineral oil, 5.00 mmol, 5.0 equiv) in DMF (5 ml) at 0 °C was added a solution of ketal S17 (0.244 g, 1.00 mmol, 1.0 equiv) in DMF (5 ml). The resultant mixture was then stirred for 30 min at 0 °C before 3-bromo-2-methylpropene (0.675 g, 5.00 mmol, 5.0 equiv) was added. The reaction contents were then warmed to 23 °C and stirred at that temperature for 2 h. Upon completion, the reaction contents were cooled to 0 °C, diluted with Et₂O (10 ml), and quenched by the slow addition of H₂O. The resultant mixture was poured into a separatory funnel and the layers were separated. The aqueous layer was then extracted with Et₂O (2 × 10 mL). The combined organic layers were washed with H₂O (3 × 10 mL) and brine (10 mL) before being dried (Na₂SO₄), filtered, and concentrated. The resultant residue was purified by flash column chromatography (silica gel, hexanes:EtOAc, 5:1) to provide ketal S18 (0.298 g, 99% yield) as a colorless oil. **S18**: $R_f = 0.28$ (silica gel, hexanes:EtOAc = 5:1); IR (film) v_{max} 2951, 2913, 1735, 1453, 1254, 1214, 1165, 1083, 1057, 900; ¹H NMR (500 MHz, CDCl₃) δ 5.03 (s, 1 H), 4.85 (s, 1 H), 3.96-3.92 (m, 1 H), 3.89-3.85 (m, 2 H), 3.81-3.78 (m, 3 H), 3.75 (s, 3 H), 2.26 (ddd, J =15.1, 13.6, 3.8 Hz, 1 H), 2.01 (dt, J = 15.2, 3.8 Hz, 1 H), 1.85 (d, J = 13.8 Hz, 1 H), 1.75 (s, 3 H), 1.40 (dd, J = 13.8, 1.7 Hz, 1 H), 1.37 (td, J = 13.5, 3.5 Hz, 1 H), 1.23 (ttd, J = 13.5, 5.6, 1.8 Hz, 1 H), 1.04 (s, 3 H), 0.93 (s, 3 H); ¹³C NMR (125 MHz, CDCl₃) δ 172.0, 141.5, 111.4, 110.0, 82.4, 67.5, 65.0, 64.9, 52.2, 43.6, 32.9, 32.6, 31.3, 26.5, 24.7, 19.7; HRMS (ESI) calcd for C₁₆H₂₇O₅⁺ $[M + H^{+}]$ 299.1853, found 299.1870. Next, to a solution of ketal **S18** (0.298 g, 1.00 mmol, 1.0 equiv) in acetone (15 mL) at 23 °C was added HCl (10.0 mL, 1.0 M in H₂O, 10.0 mmol, 10 equiv). The resultant solution was heated to 60 °C for 12 h. Upon completion, the reaction contents were cooled to 23 °C, poured into a separatory funnel, and the resultant layers were separated. The aqueous layer was then extracted with EtOAc (3 × 10 mL). The combined organic layers were washed with brine (10 mL) before being dried (Na₂SO₄), filtered, and concentrated. The resultant residue was purified by flash column chromatography (silica gel, hexanes:EtOAc, 10:1) to provide ketone S19 (0.254 g, 99% yield) as a colorless oil. S19: $R_f =$ 0.30 (silica gel, hexanes:EtOAc = 10:1); IR (film) v_{max} 2957, 2928, 2870, 1751, 1724, 1456, 1370, 1298, 1256, 1160, 1127, 1080, 1054, 899; ¹H NMR (500 MHz, CDCl₃) δ 5.03 (s, 1 H),

4.89 (s, 1 H), 4.15 (d, J = 12.0 Hz, 1 H), 3.79 (s, 3 H), 3.78 (d, J = 12.0 Hz, 1 H), 2.54 (d, J = 13.2 Hz, 1 H), 2.34 (ddd, J = 14.8, 5.6, 4.2 Hz, 1 H), 2.17 (dd, J = 13.2, 1.6 Hz, 1 H), 2.12 (ddd, J = 14.8, 11.3, 4.3 Hz, 1 H), 1.83 (ddd, J = 13.9, 11.2, 4.3 Hz, 1 H), 1.77 (s, 3 H), 1.36 (dddd, J = 13.8, 5.5, 4.3, 1.6 Hz, 1 H), 1.04 (s, 3 H), 0.98 (s, 3 H); ¹³C NMR (125 MHz, CDCl₃) δ 205.8, 170.6, 141.8, 111.9, 85.4, 69.7, 52.3, 52.2, 36.5, 33.8, 31.3, 30.1, 26.7, 19.6; HRMS (ESI) calcd for $C_{14}H_{23}O_4^+$ [M + H⁺] 255.1591, found 255.1599. Pressing forward, triflate **S20** was prepared as described above starting from **S19** (0.079 g, 0.31 mmol, 1.0 equiv) to afford triflate **S20** (0.083 g, 69% yield) as a yellow oil. **S20**: $R_f = 0.32$ (silica gel, hexanes:EtOAc, 10:1); IR (film) $v_{max} = 0.32$ (silica gel, hexanes:EtOAc, 10:1); IR (film) $v_{max} = 0.32$ (silica gel, hexanes:EtOAc, 10:1); IR (film) $v_{max} = 0.32$ (silica gel, hexanes:EtOAc, 10:1); IR (film) $v_{max} = 0.32$ (silica gel, hexanes:EtOAc, 10:1); IR (film) $v_{max} = 0.32$ (silica gel, hexanes:EtOAc, 10:1); IR (film) $v_{max} = 0.32$ (silica gel, hexanes:EtOAc, 10:1); IR (film) $v_{max} = 0.32$ (silica gel, hexanes:EtOAc, 10:1); IR (film) $v_{max} = 0.32$ (silica gel, hexanes:EtOAc, 10:1); IR (film) $v_{max} = 0.32$ (silica gel, hexanes:EtOAc, 10:1); IR (film) $v_{max} = 0.32$ (silica gel, hexanes:EtOAc, 10:1); IR (film) $v_{max} = 0.32$ (silica gel, hexanes:EtOAc, 10:1); IR (film) $v_{max} = 0.32$ (silica gel, hexanes:EtOAc, 10:1); IR (film) $v_{max} = 0.32$ (silica gel, hexanes:EtOAc, 10:1); IR (film) $v_{max} = 0.32$ (silica gel, hexanes:EtOAc, 10:1); IR (film) $v_{max} = 0.32$ (silica gel, hexanes:EtOAc, 10:1); IR (film) $v_{max} = 0.32$ (silica gel, hexanes:EtOAc, 10:1); IR (film) $v_{max} = 0.32$ (silica gel, hexanes:EtOAc, 10:1); IR (film) $v_{max} = 0.32$ (silica gel, hexanes:EtOAc, 10:1); IR (film) $v_{max} = 0.32$ (silica gel, hexanes:EtOAc, 10:1); IR (film) $v_{max} = 0.32$ (silica gel, hexanes:EtOAc, 1

Preparation of nucleophilic salts

To a solution of corresponding acid or phenol (5.00 mmol) in anhydrous MeOH (5 mL) was added n-Bu₄NOH (5.05 mL, 1.0 M in MeOH, 5.05 mmol, 1.01 equiv) at 23 °C, and the resultant solution was stirred at 23 °C for 1 h. Upon completion, the resultant mixture was coevaporated with benzene under an Ar atmosphere and the residue was dried over P_2O_5 on vacuum overnight. If the dried residue was a liquid, it was cooled to 0 °C to form a solid (>95% yield). The solid was then recrystallized from minimal EtOAc under Ar atmosphere to provide the anhydrous salt (~30–60% yield) for use in subsequent reaction. The salts can be kept stable in dry box for months. [Note: the pentafluorophenoate salt (**S39**) was unstable and should be used immediately].



Tetrabutylammonium benzolate (S21). Pale yellow solid; 1 H NMR (500 MHz, CDCl₃) δ 8.10–8.08 (m, 2 H), 7.30–7.28 (m, 3 H), 3.56–2.32 (m, 8 H), 1.66–1.59 (m, 8 H), 1.40 (sx, J = 7.4 Hz, 8 H), 0.96 (t, J = 7.3 Hz, 12 H); 13 C NMR (125 MHz, CDCl₃) δ 170.9, 141.4, 129.4, 128.2, 126.9, 58.5, 23.9, 19.6, 13.5.

Tetrabutylammonium 4-methylbenzoate (S22). Pale yellow solid; ¹H NMR (500 MHz, CDCl₃) δ 7.85 (d, J = 8.0 Hz, 2 H), 6.98 (d, J = 7.8 Hz, 2 H), 3.04–3.00 (m, 8 H), 2.23 (s, 3 H), 1.41–1.35 (m, 8 H), 1.27–1.19 (m, 8 H), 1.07 (sx, J = 7.4 Hz, 8 H), 0.83 (t, J = 7.3 Hz, 12 H); ¹³C NMR (125 MHz, CDCl₃) δ 171.0, 138.3, 137.4, 129.4, 127.8, 58.0, 23.6, 21.1, 19.4, 13.5.

Tetrabutylammonium 4-methoxybenzoate (S23). Pale yellow solid; ¹H NMR (500 MHz, CDCl₃) δ 7.87–7.84 (m, 2 H), 6.61–6.58 (m, 2 H), 3.01–2.97 (m, 8 H), 1.36–1.29 (m, 8 H), 1.16 (sx, J = 7.4 Hz, 8 H), 0.74 (t, J = 7.3 Hz, 12 H); ¹³C NMR (125 MHz, CDCl₃) δ 170.6, 160.0, 133.9, 130.9, 112.0, 58.3, 55.0, 23.8, 19.5, 13.5.

Tetrabutylammonium 3-methoxybenzoate (S24). White solid; ¹H NMR (500 MHz, CDCl₃) δ 7.56–7.55 (m, 2 H), 7.09–7.06 (m, 1 H), 6.75–6.73 (m, 1 H), 3.71 (s, 3 H), 3.09–3.06 (m, 8 H), 1.46–1.39 (m, 8 H), 1.25 (sx, J = 7.3 Hz, 8 H), 0.83 (t, J = 7.2 Hz, 12 H); ¹³C NMR (125 MHz, CDCl₃) δ 170.9, 158.9, 142.3, 128.0, 122.0, 115.3, 113.9, 58.4, 55.2, 23.8, 19.6, 13.6.

Tetrabutylammonium 4-formylbenzoate (S25). White solid; ¹H NMR (500 MHz, CDCl₃) δ 9.94 (s, 1 H); 8.12 (d, J = 8.0 Hz, 2 H), 7.73 (d, J = 8.0 Hz, 2 H), 3.20–3.17 (m, 8 H), 1.55–1.49 (m, 8 H), 1.30 (sx, J = 7.4 Hz, 8 H), 0.86 (t, J = 7.4 Hz, 12 H); ¹³C NMR (125 MHz, CDCl₃) δ 192.7, 170.1, 146.6, 136.3, 129.8, 129.0, 58.6, 23.9, 19.6, 13.6.

Tetrabutylammonium 4-cyanobenzoate (S26). Yellow solid; ¹H NMR (500 MHz, CDCl₃) δ 7.98 (d, J = 8.4 Hz, 2 H), 7.36 (d, J = 8.4 Hz, 2 H), 3.09–3.06 (m, 8 H), 1.44–1.37 (m, 8 H), 1.18 (sx, J = 7.4 Hz, 8 H), 0.74 (t, J = 7.3 Hz, 12 H); ¹³C NMR (125 MHz, CDCl₃) δ 169.0, 145.6, 131.0, 129.8, 119.6, 111.2, 58.5, 23.8, 19.5, 13.5.

Tetrabutylammonium 4-(trifluoromethyl)benzoate (S27). Pale yellow solid; 1 H NMR (500 MHz, CDCl₃) δ 8.17 (d, J = 7.9 Hz, 2 H), 7.52 (d, J = 8.1 Hz, 2 H), 3.32–3.30 (m, 8 H), 1.64–1.58 (m, 8 H), 1.41–1.34 (m, 8 H), 1.26 (sx, J = 7.4 Hz, 8 H), 0.94 (t, J = 7.3 Hz, 12 H); 13 C NMR (125 MHz, CDCl₃) δ 169.5, 144.7, 130.0, 129.8, 129.5, 125.6, 124.0, 123.9, 58.4, 23.8, 19.5, 13.4.

Tetrabutylammonium 4-(methoxycarbonyl)benzoate (S28). White solid; ¹H NMR (500 MHz, CDCl₃) δ 8.08 (d, J = 8.0 Hz, 2 H), 7.92 (d, J = 8.0 Hz, 2 H), 3.85 (s, 3 H), 3.26–3.22 (m, 8 H), 1.58–1.52 (m, 8 H), 1.34 (sx, J = 7.3 Hz, 8 H), 0.90 (t, J = 7.3 Hz, 12 H); ¹³C NMR (125 MHz, CDCl₃) δ 170.4, 167.5, 145.6, 129.7, 129.2, 128.6, 58.7, 51.8, 24.0, 19.7, 13.6.

Tetrabutylammonium 4-benzoylbenzoate (S29). Yellow solid; 1 H NMR (500 MHz, CDCl₃) δ 8.05–8.03 (m, 2 H), 7.63–7.61 (m, 2 H), 7.45–7.42 (m, 1 H), 7.34–7.31 (m, 2 H), 3.14–3.11 (m, 8 H), 1.49–1.42 (m, 8 H), 1.24 (sx, J = 7.4 Hz, 8 H), 0.80 (t, J = 7.3 Hz, 12 H); 13 C NMR (125 MHz, CDCl₃) δ 197.1, 170.2, 145.0, 137.8, 137.2, 132.2, 129.8, 129.2, 129.1, 128.1, 58.5, 23.8, 19.6, 13.6.

Tetrabutylammonium 4-chlorobenzoate (S30). Green solid; ¹H NMR (500 MHz, CDCl₃) δ 7.95–7.93 (m, 2 H), 7.16–7.13 (m, 2 H), 3.15–3.12 (m, 8 H), 1.51–1.45 (m, 8 H), 1.28 (sx, J = 7.4 Hz, 8 H), 0.86 (t, J = 7.3 Hz, 12 H); ¹³C NMR (125 MHz, CDCl₃) δ 170.2, 139.2, 134.4, 130.9, 127.2, 58.5, 23.9, 19.6, 13.6.

Tetrabutylammonium 4-fluorobenzoate (S31). White solid; ¹H NMR (500 MHz, CDCl₃) δ 8.00–7.97 (m, 2 H), 6.86–6.82 (m, 2 H), 3.13–3.10 (m, 8 H), 1.49–1.42 (m, 8 H), 1.27 (sx, J = 7.4 Hz, 8 H), 0.85 (t, J = 7.3 Hz, 12 H); ¹³C NMR (125 MHz, CDCl₃) δ 170.2, 164.3, 162.4, 131.4, 131.3, 125.2, 113.6, 113.5, 58.8, 24.1, 19.7, 13.6.

Tetrabutylammonium 3-fluorobenzoate (S32). White solid; ¹H NMR (500 MHz, CDCl₃) δ 7.75–7.73 (m, 1 H), 7.63–7.61 (m, 1 H), 7.13–7.09 (m, 1 H), 6.86–6.83 (m, 1 H), 3.14–3.10 (m, 8 H), 1.47–1.43 (m, 8 H), 1.26–1.21 (m, 8 H), 0.84–0.80 (m, 12 H); ¹³C NMR (125 MHz, CDCl₃) δ 169.7, 163.4, 161.4, 143.9, 128.3, 125.0, 116.0, 115.8, 115.1, 115.0, 58.5, 23.9, 19.6, 13.6.

Tetrabutylammonium 2-fluorobenzoate (S33). White solid, ¹H NMR (500 MHz, CDCl₃) δ 7.65–7.62 (m, 1 H), 7.06–7.02 (m, 1 H), 6.91–6.88 (m, 1 H), 6.82–6.78 (m, 1 H), 3.17–3.13 (m, 8 H), 1.49–1.45 (m, 8 H), 1.25 (sx, J = 7.4 Hz, 8 H), 0.83 (t, J = 7.4 Hz, 12 H); ¹³C NMR (125 MHz, CDCl₃) δ 169.0, 161.2, 159.2, 131.2, 131.1, 128.5, 123.0, 115.4, 115.2, 58.4, 23.9, 19.6, 13.6.

Tetrabutylammonium *N***-Phthaloylglycinate (S34).** Pale yellow solid; ¹H NMR (500 MHz, CDCl₃) δ 7.77 (dd, J = 5.4, 3.0 Hz, 2 H), 7.62 (dd, J = 5.4, 3.0 Hz, 2 H), 4.21 (s, 2 H), 3.32–3.28 (m, 8 H), 1.66–1.60 (m, 8 H), 1.40 (sx, J = 7.4 Hz, 8 H), 0.97 (t, J = 7.3 Hz, 12 H); ¹³C NMR (125 MHz, CDCl₃) δ 169.7, 168.6, 133.1, 122.7, 58.6, 42.5, 24.0, 19.7, 13.6.

Tetrabutylammonium 2-(adamantan-1-yl)acetate (S35). Pale yellow solid; ¹H NMR (500 MHz, CDCl₃) δ 3.30–3.26 (m, 8 H), 1.87 (s, 2 H), 1.81 (s, 3 H), 1.63 (d, J = 2.2 Hz, 6 H), 1.59–1.53 (m, 14 H), 1.34 (sx, J = 7.4 Hz, 8 H), 0.90 (t, J = 7.3 Hz, 12 H); ¹³C NMR (125 MHz, CDCl₃) δ 176.9, 58.7, 55.0, 43.0, 37.3, 32.1, 29.0, 24.1, 19.7, 13.7.

Tetrabutylammonium adamantane-1-carboxylate (S36). Pale yellow solid; ¹H NMR (500 MHz, CDCl₃) δ 3.28–3.26 (m, 8 H), 1.87–1.84 (m, 9 H), 1.63–1.55 (m, 14 H), 1.37 (sx, J = 7.4 Hz, 8 H), 0.94 (t, J = 7.3 Hz, 12 H); ¹³C NMR (125 MHz, CDCl₃) δ 183.2, 8.7, 49.8, 41.8, 40.7, 37.4, 29.0, 24.1, 19.7, 13.7.

Tetrabutylammonium pivalate (S37). Pale yellow solid; 1 H NMR (500 MHz, CDCl₃) δ 3.24–3.20 (m, 8 H), 1.57–1.51 (m, 8 H), 1.33 (sx, J = 7.4 Hz, 8 H), 1.04 (s, 9 H), 0.89 (t, J = 7.4 Hz, 12 H); 13 C NMR (125 MHz, CDCl₃) δ 183.4, 58.6, 39.5, 28.9, 24.0, 19.7, 13.7.

Tetrabutylammonium furan-3-carboxylate (S38). Brown solid; 1 H NMR (500 MHz, CDCl₃) δ 7.63–7.62 (m, 1 H), 7.10 (t, J = 1.6 Hz, 1 H), 6.53–6.52 (m, 1 H), 3.09–3.06 (m, 8 H), 1.45–1.38 (m, 8 H), 1.22 (sx, J = 7.4 Hz, 8 H), 0.79 (t, J = 7.4 Hz, 12 H); 13 C NMR (125 MHz, CDCl₃) δ 179.8, 144.5, 141.5, 128.4, 111.6, 58.4, 23.8, 19.5, 13.5.

Tetrabutylammonium pentafluorophenonate (S39). Pale yellow solid, 1 H NMR (500 MHz, CDCl₃) δ 3.13–3.09 (m, 8 H), 1.53–1.46 (m, 8 H), 1.28 (sx, J = 7.4 Hz, 8 H), 0.87 (t, J =

7.4 Hz, 12 H); 13 C NMR (125 MHz, CDCl₃) δ 147.0, 142.1, 140.3, 139.7, 137.8, 125.1, 58.4, 23.6, 19.4, 13.3.

Tetrabutylammonium 1H-benzo[d][1,2,3]triazol-1-olate (S40). Brown solid, 1 H NMR (500 MHz, CDCl₃) δ 7.67–7.63 (m, 2 H), 7.07–7.01 (m, 2 H), 3.20–3.17 (m, 8 H), 1.55–1.49 (m, 8 H), 1.31 (sx, J = 7.4 Hz, 8 H), 0.89 (t, J = 7.3 Hz, 12 H); 13 C NMR (125 MHz, CDCl₃) δ 143.8, 127.8, 122.2, 121.1, 118.0, 112.4, 58.5, 23.8, 19.6, 13.6.

General procedure for the Pd-based cyclization

To a flame-dried seal tube was added Pd(OAc)₂ (2.2 mg, 0.010 mmol, 0.1 equiv), *t*-BuMephos (4.7 mg, 0.015 mmol, 0.15 equiv), and the desired tetrabutylammonium salt (0.30 mmol, 3.0 equiv). Next, a solution of the desired vinyl triflate (0.10 mmol, 1.0 equiv) in toluene (1 mL) was added at 23 °C. The resultant mixture was then stirred at 90 °C until palladium black completely crashed out, typically after 5 h. Upon completion, the reaction mixture was cooled to 23 °C and filtered through a pad of silica gel (EtOAc). The filtrate was concentrated, and the resultant residue was purified by flash column chromatography (silica gel, hexanes:EtOAc) to provide the desired oxygenated product in the amount and form delineated below.

Product Acetate 18. Pale yellow oil, 28.2 mg, 96% yield; R_f = 0.26 (silica gel, hexanes:EtOAc, 10:1); IR (film) v_{max} 2955, 2930, 2863, 1739, 1729, 1597, 1564, 1448, 1385, 1274, 1218, 1150, 1034 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 5.27 (s, 1 H), 4.00 (dd, J = 27.2, 10.5 Hz, 2 H), 3.65 (s, 3 H), 2.26–2.22 (m, 1 H), 2.20–2.17 (m, 1 H), 2.06 (s, 3 H), 1.56–1.49 (m, 2 H), 1.47–1.40 (m, 2 H), 1.37–1.28 (m, 2 H), 1.09 (s, 3 H), 0.99 (s, 3 H), 0.92 (s, 3 H); ¹³C NMR (125 MHz, CDCl₃) δ 176.7, 144.1, 133.2, 72.4, 55.5, 51.8, 44.0, 35.8, 35.4, 32.5, 31.8, 30.5, 29.7, 29.4, 28.2, 27.4, 26.1, 21.0; HRMS (ESI) calcd for $C_{17}H_{27}O_4^+$ [M + H⁺] 295.1904, found 295.1907.

Product Benzolate 19. Colorless oil, 28.4 mg, 80% yield; $R_f = 0.26$ (silica gel, hexanes:EtOAc, 10:1); IR (film) v_{max} 2955, 2864, 1722, 1451, 1362, 1274, 1205, 1176, 1151, 1114, 1070, 1026, 961, 711; ¹H NMR (500 MHz, CDCl₃) δ 8.07–8.05 (m, 2 H), 7.56 (tt, J = 7.4, 1.3 Hz, 1 H), 7.46–7.43 (m, 2 H), 5.36 (s, 1 H), 4.25 (dd, J = 16.5, 10.5 Hz, 2 H), 3.65 (s, 3 H), 2.30–2.27 (m, 1 H), 2.23–2.20 (m, 1 H), 1.71–1.58 (m, 2 H), 1.51–1.45 (m, 2 H), 1.40–1.25 (m, 2 H), 1.20 (s, 3 H), 1.00 (s, 3 H), 0.94 (s, 3 H); ¹³C NMR (125 MHz, CDCl₃) δ 176.8, 166.7, 144.0, 133.4, 132.7, 130.7, 129.6, 128.3, 72.7, 55.5, 51.9, 44.4, 35.8, 35.6, 34.8, 32.6, 31.9, 30.5, 29.4, 26.2; HRMS (ESI) calcd for $C_{22}H_{28}O_4Na^+$ [M + Na⁺] 379.1880, found 379.1886.

Product 4-Me 20. White oil, 29.2 mg, 79% yield; $R_f = 0.27$ (silica gel, hexanes:EtOAc, 10:1); IR (film) v_{max} 2954, 2864, 1720, 1612, 1458, 1380, 1362, 1273, 1206, 1177, 1151, 1120, 1020, 961, 914, 841; ¹H NMR (500 MHz, CDCl₃) δ 7.94 (d, J = 8.2 Hz, 2 H), 7.24 (d, J = 8.1 Hz, 2 H), 5.34 (s, 1 H), 4.22 (dd, J = 18.6, 10.6 Hz, 2 H), 3.65 (s, 3 H), 2.41 (s, 3 H), 2.30–2.26 (m, 1 H), 2.22–2.19 (m, 1 H), 1.70–1.57 (m, 2 H), 1.49–1.44 (m, 2 H), 1.40–1.27 (m, 2 H), 1.19 (s, 3 H), 1.00 (s, 3 H), 0.94 (s, 3 H); ¹³C NMR (125 MHz, CDCl₃) δ 176.8, 166.8, 144.1, 143.3, 133.3, 129.6, 129.0, 128.0, 72.5, 55.5, 51.9, 44.4, 35.8, 35.6, 34.8, 32.6, 31.9, 30.5, 29.4, 26.2, 21.6; HRMS (ESI) calcd for $C_{23}H_{31}O_4^+$ [M + H⁺] 371.2217, found 371.2226.

Product 4-OMe 21. Pale yellow oil, 14.3 mg, 37% yield; $R_f = 0.25$ (silica gel, hexanes:EtOAc, 10:1); IR (film) v_{max} 2955, 2864, 1716, 1607, 1511, 1459, 1363, 1300, 1256, 1205, 1167, 1102, 1031, 847, 770 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 8.01 (d, J = 8.8 Hz, 2 H), 6.92 (d, J = 8.8 Hz, 2 H), 5.35 (s, 1 H), 4.21 (dd, J = 17.8, 10.5 Hz, 2 H), 3.86 (s, 3 H), 3.65 (s, 3 H), 2.30–2.26 (m, 1 H), 2.22–2.19 (m, 1 H), 1.70–1.57 (m, 2 H), 1.50–1.44 (m, 2 H), 1.40–1.27 (m, 2 H), 1.19 (s, 3 H), 1.00 (s, 3 H), 0.94 (s, 3 H); ¹³C NMR (125 MHz, CDCl₃) δ 176.8, 166.4, 163.2, 144.1, 133.3, 131.5, 123.2, 113.6, 72.4, 55.5, 55.4, 51.8, 44.4, 35.8, 35.6, 34.8, 32.6, 31.9, 30.5, 29.4, 26.2; HRMS (ESI) calcd for $C_{23}H_{31}O_5^+$ [M + H⁺] 387.2166, found 387.2179.

Product 3-OMe 22. Pale yellow oil, 23.2 mg, 60% yield; $R_f = 0.44$ (silica gel, hexanes:EtOAc, 10:1); IR (film) v_{max} 2955, 2864, 2838, 1721, 1587, 1457, 1321, 1278, 1151, 1104, 1046, 977, 756 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 7.65 (dt, J = 7.7, 1.0 Hz, 1 H), 7.58 (dd, J = 2.6, 1.5 Hz, 1 H), 7.35 (t, J = 7.9 Hz), 7.10 (ddd, J = 8.2, 2.6, 0.8 Hz, 1 H), 5.36 (s, 1 H), 4.24 (dd, J = 19.1, 10.5 Hz, 2 H), 3.86 (s, 3 H), 3.65 (s, 3 H), 2.30–2.26 (m, 1 H), 2.23–2.20 (m, 1 H), 1.70–1.58 (m, 2 H), 1.51–1.44 (m, 2 H), 1.40–1.29 (m, 2 H), 1.19 (s, 3 H), 1.00 (s, 3 H), 0.94 (s, 3 H); ¹³C NMR (125 MHz, CDCl₃) δ 176.7, 166.5, 159.6, 144.0, 133.4, 132.0, 129.3, 121.2, 119.2, 114.2, 72.8, 55.5, 55.4, 51.9, 44.4, 35.8, 35.6, 34.8, 32.6, 31.9, 30.5, 29.4, 26.2; HRMS (ESI) calcd for $C_{23}H_{31}O_5^+$ [M + H⁺] 387.2166, found 387.2173.

Product 4-CHO 23. Colorless oil, 34.1 mg, 89% yield; $R_f = 0.28$ (silica gel, hexanes:EtOAc, 10:1); IR (film) v_{max} 2955, 2864, 1723, 1709, 1459, 1275, 1202, 1116, 1016, 759 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 10.1 (s, 1 H), 8.21 (d, J = 8.2 Hz, 2 H), 7.96 (d, J = 8.3 Hz, 2 H), 5.36 (s, 1 H), 4.28 (dd, J = 12.8, 10.6 Hz, 2 H), 3.65 (s, 3 H), 2.31–2.27 (m, 1 H), 2.23–2.20 (m, 1 H), 1.68–1.59 (m, 2 H), 1.52–1.45 (m, 2 H), 1.40–1.25 (m, 2 H), 1.21 (s, 3 H), 0.99 (s, 3 H), 0.94 (s, 3 H); ¹³C NMR (125 MHz, CDCl₃) δ 191.7, 176.6, 165.6, 143.9, 139.1, 135.7, 133.5, 130.1, 129.5, 73.2, 55.6, 51.9, 44.3, 35.8, 35.5, 34.7, 32.6, 31.8, 30.5, 29.3, 26.2; HRMS (ESI) calcd for $C_{23}H_{29}O_5^+$ [M + H⁺] 385.2010, found 385.2009.

Product 4-CN 24. Yellow oil, 29.7 mg, 78% yield; R_f = 0.19 (silica gel, hexanes:EtOAc, 10:1); IR (film) v_{max} 2955, 2864, 2231, 1724, 1458, 1275, 1206, 1152, 1118, 1018, 956, 861, 767 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 8.15–8.14 (m, 2 H), 7.76–7.74 (m, 2 H), 5.34 (s, 1 H), 4.28 (dd, J = 12.0, 10.6 Hz, 2 H), 3.65 (s, 3 H), 2.30–2.27 (m, 1 H), 2.23–2.20 (m, 1 H), 1.70–1.57 (m, 2 H), 1.52–1.45 (m, 2 H), 1.40–1.25 (m, 2 H), 1.19 (s, 3 H), 0.99 (s, 3 H), 0.94 (s, 3 H); ¹³C NMR (125 MHz, CDCl₃) δ 176.6, 165.0, 143.8, 134.5, 133.6, 132.2, 130.0, 118.0, 116.3, 73.4, 55.6, 51.9, 44.3, 35.8, 35.5, 34.7, 32.6, 31.8, 30.5, 29.3, 26.2; HRMS (ESI) calcd for $C_{23}H_{28}O_4N^+$ [M + H⁺] 382.2013, found 382.2017.

Product 4-CF₃ 25. Colorless oil, 41.1 mg, 97% yield; $R_f = 0.50$ (silica gel, hexanes:EtOAc, 10:1); IR (film) v_{max} 2956, 2865, 1726, 1412, 1357, 1281, 1132, 1066, 1018, 862 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 8.16 (d, J = 8.1 Hz, 2 H), 7.71 (d, J = 8.2 Hz, 2 H), 5.36 (s, 1 H), 4.28 (dd, J = 15.2 Hz, 10.6 Hz, 2 H), 3.66 (s, 3 H), 2.31–2.27 (m, 1 H), 2.23–2.20 (m, 1 H), 1.71–1.58 (m, 2 H), 1.52–1.46 (m, 2 H), 1.37–1.25 (m, 2 H), 1.20 (s, 3 H), 1.00 (s, 3 H), 0.94 (s, 3 H); ¹³C NMR (125 MHz, CDCl₃) δ 176.6, 165.4, 143.9, 134.2, 133.9, 133.5, 139.9, 125.39, 125.36, 73.1, 55.6, 51.9, 44.3, 35.8, 35.5, 34.7, 32.6, 30.5, 29.3, 26.2; HRMS (ESI) calcd for $C_{23}H_{28}O_4F_3^+$ [M + H⁺] 425.1934, found 425.1942.

Product 4-COOMe 26. Yellow solid, 30.6 mg, 74% yield; $R_f = 0.37$ (silica gel, hexanes:EtOAc, 10:1); IR (film) v_{max} 2954, 2864, 1724, 1458, 1272, 1117, 1019, 731 cm⁻¹; ¹H

NMR (500 MHz, CDCl₃) δ 8.10 (s, 4 H), 5.35 (s, 1 H), 4.26 (dd, J = 13.7, 10.5 Hz, 2 H), 3.94 (s, 3 H), 3.64 (s, 3 H), 2.30–2.26 (m, 1 H), 2.22–2.19 (m, 1 H), 1.70–1.58 (m, 2 H), 1.51–1.48 (m, 2 H), 1.39–1.24 (m, 2 H), 1.20 (s, 3 H), 0.98 (s, 3 H), 0.93 (s, 3 H); 13 C NMR (125 MHz, CDCl₃) δ 176.6, 166.3, 165.8, 143.9, 134.5, 133.8, 133.5, 129.54, 129.51, 73.1, 55.6, 52.4, 52.0, 44.3, 35.8, 35.5, 34.7, 32.6, 31.8, 30.5, 29.3, 26.2; HRMS (ESI) calcd for $C_{24}H_{31}O_6^+$ [M + H $^+$] 415.2115, found 415.2113.

Product 4-COPh 27. Yellow oil, 42.3 mg, 92% yield; $R_f = 0.37$ (silica gel, hexanes:EtOAc, 10:1); IR (film) v_{max} 2955, 2864, 1710, 1663, 1449, 1297, 1206, 1116, 926, 714 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 8.17–8.15 (m, 2 H), 7.85–7.84 (m, 2 H), 7.81–7.79 (m, 2 H), 7.63–7.60 (m, 1 H), 7.51–7.48 (m, 2 H), 5.37 (s, 1 H), 4.29 (dd, J = 14.7, 10.5 Hz, 2 H), 3.66 (s, 3 H), 2.31–2.27 (m, 1 H), 2.23–2.20 (m, 1 H), 1.71–1.59 (m, 2 H), 1.52–1.46 (m, 2 H), 1.40–1.29 (m, 2 H), 1.22 (s, 3 H), 1.00 (s, 3 H), 0.94 (s, 3 H); ¹³C NMR (125 MHz, CDCl₃) δ 176.7, 165.9, 143.9, 141.2, 137.0, 133.8, 133.5, 132.9, 130.1, 129.8, 129.4, 128.5, 73.1, 55.6, 51.9, 44.4, 35.8, 35.4, 34.7, 32.2, 31.8, 30.5, 29.4, 26.2; HRMS (ESI) calcd for $C_{29}H_{32}O_5Na^+$ [M + Na⁺] 483.2142, found 483.2146.

Product 4-Cl 28. Yellow oil, 27.4 mg, 70% yield; $R_f = 0.54$ (silica gel, hexanes:EtOAc, 10:1); IR (film) v_{max} 2956, 2864, 124, 1595, 1488, 1459, 1400, 1381, 1363, 1272, 1205, 1151, 1116, 1015, 960, 850, 760 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 7.98 (d, J = 8.5 Hz, 2 H), 7.41 (d, J = 8.5 Hz, 2 H), 5.34 (s, 1 H), 4.24 (dd, J = 14.1, 10.6 Hz, 2 H), 3.65 (s, 3 H), 2.30–2.26 (m, 1 H), 2.22–2.19 (m, 1 H), 1.69–1.58 (m, 2 H), 1.51–1.44 (m, 2 H), 1.40–1.28 (m, 2 H), 1.19 (s, 3 H),0.99 (s, 3 H), 0.93 (s, 3 H); ¹³C NMR (125 MHz, CDCl₃) δ 176.6, 165.8, 144.0, 139.2, 133.4, 130.9, 129.6, 129.2, 128.7, 128.3, 72.8, 55.5, 51.9, 44.3, 35.8, 35.5, 34.7, 32.6, 31.8, 30.5, 29.3, 26.2; HRMS (ESI) calcd for $C_{22}H_{28}O_4Cl^+$ [M + H $^+$] 391.1671, found 391.1675.

Product 4-F 29. Pale yellow oil, 33.7 mg, 90% yield; $R_f = 0.51$ (silica gel, hexanes:EtOAc, 10:1); IR (film) v_{max} 2955, 2864, 1724, 1604, 1508, 1458, 1274, 1152, 1116, 854, 767 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 8.08–8.05 (m, 2 H), 7.13–7.09 (m, 2 H), 5.34 (s, 1 H), 4.23 (dd, J = 13.7, 10.6 Hz, 2 H), 3.65 (s, 3 H), 2.30–2.26 (m, 1 H), 2.22–2.19 (m, 1 H), 1.70–1.57 (m, 2 H), 1.51–1.44 (m, 2 H), 1.40–1.25 (m, 2 H), 1.19 (s, 3 H), 0.99 (s, 3 H), 0.94 (s, 3 H); ¹³C NMR (125 MHz, CDCl₃) δ 176.7, 166.7, 165.7, 164.7, 144.0, 133.4, 132.1, 132.0, 127.0, 126.9, 115.5, 115.3, 72.8, 55.5, 51.9, 44.4, 35.8, 35.5, 34.7, 32.6, 31.8, 30.5, 29.4, 26.2; HRMS (ESI) calcd for $C_{22}H_{28}O_4F^+$ [M + H⁺] 375.1966, found 375.1971.

Product 3-F 30. Colorless oil, 29.9 mg, 80% yield; R_f = 0.49 (silica gel, hexanes:EtOAc, 10:1); IR (film) v_{max} 2957, 2864, 1724, 1596, 1561, 1448, 1388, 1276, 1261, 1204, 1151, 1094, 858 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 7.85–7.84 (m, 1 H), 7.74–7.71 (m, 1 H), 7.44–7.40 (m, 1 H), 7.27–7.23 (m, 1 H), 5.35 (s, 1 H), 4.25 (dd, J = 15.8, 10.5 Hz, 2 H), 3.65 (s, 3 H), 2.30–2.26 (m, 1 H), 2.23–2.20 (m, 1 H), 1.70–1.58 (m, 2 H), 1.51–1.45 (m, 2 H), 1.40–1.25 (m, 2 H), 1.19 (s, 3 H), 1.00 (s, 3 H), 0.94 (s, 3 H); ¹³C NMR (125 MHz, CDCl₃) δ 176.7, 165.5, 161.6, 143.9, 133.5, 130.0, 129.9, 125.3, 125.2, 119.9, 119.7, 116.5, 116.3, 73.0, 55.5, 51.9, 44.3, 35.8, 35.5, 34.7, 32.6, 31.8, 30.5, 29.3, 26.2; HRMS (ESI) calcd for $C_{22}H_{28}O_4F^+$ [M + H⁺] 375.1966, found 375.1971.

Product 2-F 31. Colorless oil, 32.6 mg, 87% yield; $R_f = 0.40$ (silica gel, hexanes:EtOAc, 10:1); IR (film) v_{max} 2955, 2864, 1724, 1613, 1486, 1458, 1363, 1297, 1153, 1128, 1033, 960, 758 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 7.95 (td, J = 7.6, 1.8 Hz, 1 H), 7.52–7.48 (m, 1 H), 7.19

(dt, J = 7.8, 0.5 Hz, 1 H), 7.12 (dd, J = 10.6, 8.7 Hz, 1 H), 5.36 (s, 1 H), 4.25 (dd, J = 12.8, 10.6 Hz, 2 H), 3.64 (s, 3 H), 2.28–2.24 (m, 1 H), 2.22–2.19 (m, 1 H), 1.70–1.57 (m, 2 H), 1.50–1.43 (m, 2 H), 1.39–1.24 (m, 2 H), 1.19 (s, 3 H), 0.98 (s, 3 H), 0.93 (s, 3 H); 13 C NMR (125 MHz, CDCl₃) δ 176.8, 164.7, 163.0, 160.9, 143.9, 134.3, 134.2, 133.3, 132.2, 123.9, 123.8, 117.0, 116.8, 73.2, 55.6, 51.9, 44.2, 35.8, 35.6, 34.8, 32.6, 31.8, 30.5, 29.4, 26.2; HRMS (ESI) calcd for $C_{22}H_{28}O_4F^+$ [M + H $^+$] 375.1966, found 375.1959.

Product glycine 32. Colorless oil, 29.8 mg, 68% yield; $R_f = 0.16$ (silica gel, hexanes:EtOAc, 5:1); IR (film) v_{max} 2925, 2857, 1778, 1749, 1724, 1457, 1417, 1388, 1206, 955, 731, 714; ¹H NMR (500 MHz, CDCl₃) δ 7.89 (dd, J = 5.5, 3.0 Hz, 2 H), 7.75 (dd, J = 5.4, 3.1 Hz, 2 H), 5.20 (s, 1 H), 4.46 (d, J = 4.1 Hz, 2 H), 4.09 (s, 1 H), 3.64 (s, 3 H), 2.20–2.16 (m, 2 H), 1.52–1.47 (m, 1H), 1.45–1.37 (m, 3 H), 1.34–1.29 (m, 2 H), 1.04 (s, 3 H), 0.96 (s, 3 H), 0.87 (s, 3 H); ¹³C NMR (125 MHz, CDCl₃) δ 176.6, 167.4, 167.2, 143.8, 134.2, 133.4, 132.1, 123.6, 73.4, 55.5, 51.9, 44.0, 39.0, 35.7, 35.3, 34.8, 32.5, 31.8, 30.4, 29.7, 29.3, 25.9; HRMS (ESI) calcd for $C_{25}H_{29}O_6NNa^+$ [M + Na $^+$] 462.1887, found 462.1889.

Product CH₂Ad 33. Colorless oil, 37.3 mg, 87% yield; $R_f = 0.34$ (silica gel, hexanes:EtOAc, 10:1); IR (film) v_{max} 2953, 2904, 2848, 1730, 1457, 1256, 1201, 1136, 1101, 1003 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 5.28 (s, 1 H), 3.96 (dd, J = 15.3, 10.6 Hz, 2 H), 3.65 (s, 3 H), 2.26–2.22 (m, 1 H), 2.19–2.17 (m, 1 H), 2.08 (s, 2 H), 1.96 (s, 3 H), 1.71–1.62 (m, 12 H), 1.55–1.49 (m, 2 H), 1.47–1.39 (m, 2 H), 1.37–1.27 (m, 2 H), 1.10 (s, 3 H), 0.98 (s, 3 H), 0.92 (s, 3 H); ¹³C NMR (125 MHz, CDCl₃) δ 176.7, 172.1, 144.2, 133.1, 72.1, 55.5, 51.8, 49.3, 43.9, 42.5, 36.8, 35.8, 35.7, 34.8, 32.7, 32.6, 31.9, 30.5, 29.4; HRMS (ESI) calcd for $C_{27}H_{41}O_4^+$ [M + H⁺] 429.2999, found 429.2989.

Product Ad 34. Colorless oil, 38.1 mg, 92% yield; R_f = 0.65 (silica gel, hexanes:EtOAc, 10:1); IR (film) v_{max} 2907, 2854, 1727, 1453, 1234, 1150, 1078, 991, 963, 738 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 5.30 (s, 1 H), 3.93 (dd, J = 12.6, 10.6 Hz, 2 H), 3.64 (s, 3 H), 2.26–2.22 (m, 1 H), 2.19–2.16 (m, 1 H), 2.01 (s, 3 H), 1.91–1.90 (m, 6 H), 1.74–1.66 (m, 6 H), 1.54–1.47 (m, 2 H), 1.45–1.38 (m, 2 H), 1.37–1.24 (m, 2 H), 1.10 (s, 3 H), 0.99 (s, 3 H), 0.92 (s, 3 H); ¹³C NMR (125 MHz, CDCl₃) δ 177.7, 176.8, 144.0, 133.2, 71.8, 55.4, 51.9, 44.2, 40.9, 39.0, 36.6, 35.8, 35.5, 34.7, 32.6, 31.8, 30.6, 29.4, 28.0, 26.0; HRMS calcd for $C_{26}H_{39}O_4^+$ [M + H⁺] 415.2843, found 415.2847.

Product pivalate 35. Pale yellow oil, 25.5 mg, 76% yield; $R_f = 0.37$ (silica gel, hexanes:EtOAc, 10:1); IR (film) v_{max} 2957, 2866, 1728, 1597, 1563, 1481, 1448, 1396, 1286, 1217, 1150, 858, 798 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 5.29 (s, 1 H), 3.94 (dd, J = 12.2, 10.5 Hz, 2 H), 3.64 (s, 3 H), 2.25–2.22 (m, 1 H), 2.19–2.16 (m, 1 H), 1.54–1.48 (m, 2 H), 1.46–1.39 (m, 2 H), 1.37–1.26 (m, 2 H), 1.20 (s, 9 H), 1.10 (s, 3 H), 0.98 (s, 3 H), 0.91 (s, 3 H); ¹³C NMR (125 MHz, CDCl₃) δ 178.6, 176.8, 144.0, 133.2, 76.8, 72.1, 55.5, 51.9, 44.2, 35.7, 35.5, 34.7, 32.6, 31.8, 30.5, 29.4, 27.3, 26.0; HRMS (ESI) calcd for $C_{20}H_{33}O_4^+$ [M + H⁺] 337.2373, found 337.2377.

Product furan 36. Yellow oil, 20.6 mg, 60% yield; $R_f = 0.32$ (silica gel, hexanes:EtOAc, 10:1); IR (film) v_{max} 2955, 2864, 1725, 1579, 1506, 1461, 1304, 1205, 1161, 1076, 980, 874 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 8.01 (dd, J = 1.4, 0.7 Hz, 1 H), 7.43 (t, J = 1.7 Hz, 1 H), 6.75 (dd, J = 1.8, 0.7 Hz, 1 H), 5.32 (s, 1 H), 4.18 (dd, J = 15.2, 10.6 Hz, 2 H), 3.65 (s, 3 H), 2.28–2.25 (m, 1 H), 2.22–2.19 (m, 1 H), 1.67–1.52 (m, 2 H), 1.49–1.42 (m, 2 H), 1.39–1.28 (m, 2 H),

1.15 (s, 3 H), 1.00 (s, 3 H), 0.93 (s, 3 H); 13 C NMR (125 MHz, CDCl₃) δ 176.7, 163.2, 147.5, 144.0, 143.6, 133.3, 119.8, 109.8, 72.1, 55.5, 51.9, 44.3, 35.8, 35.4, 34.7, 32.6, 31.8, 30.5, 29.4, 26.2; HRMS (ESI) calcd for $C_{20}H_{27}O_5^+$ [M + H $^+$] 347.1853, found 347.1854.

Product flourophenol 37. Pale yellow oil, 32.6 mg, 78% yield; R_f = 0.75 (silica gel, hexanes:EtOAc, 10:1); IR (film) v_{max} 2957, 2865, 1728, 1518, 1463, 1381, 1205, 1151, 1027, 996 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 5.34 (s, 1 H), 4.08 (d, J = 8.6 Hz, 1 H). 4.00 (d, J = 8.6 Hz, 1 H), 3.64 (s, 3 H), 2.27–2.23 (m, 1 H), 2.22–2.19 (m, 1 H), 1.69–1.59 (m, 2 H), 1.50–1.44 (m, 2 H), 1.39–1.27 (m, 2 H), 1.26 (s, 3 H), 0.98 (s, 3 H), 0.93 (s, 3 H); ¹³C NMR (125 MHz, CDCl₃) δ 176.6, 143.7, 142.8, 140.7, 139.1, 138.0, 137.1, 136.0, 134.5, 133.6, 83.8, 55.6, 51.8, 45.4, 35.8, 35.3, 34.8, 32.6, 31.6, 30.4, 29.3, 25.5; HRMS (ESI) calcd for $C_{21}H_{24}O_3F_5^+$ [M + H⁺] 419.1640, found 419.1649.

Product Benzotriazole 38. Pale yellow oil, 3.3 mg, 9% yield; $R_f = 0.16$ (silica gel, hexanes:EtOAc, 10:1); IR (film) v_{max} 2956, 2864, 1725, 1462, 1376, 1358, 1263, 1239, 1206 1153, 1088, 952, 744; ¹H NMR (500 MHz, CDCl₃) δ 8.00 (d, J = 8.4 Hz, 1 H), 7.63 (d, J = 8.3 Hz, 1 H), 7.49 (ddd, J = 8.4, 7.0, 0.7 Hz, 1 H), 7.37 (ddd, J = 8.4, 6.9, 0.9 Hz, 1 H), 5.46 (s, 1 H), 4.44 (dd, J = 43.2, 7.8 Hz, 2 H), 3.60 (s, 1 H), 2.33–2.30 (m, 1 H), 2.26–2.23 (m, 1 H), 1.79–1.69 (m, 2 H), 1.56–1.49 (m, 2 H), 1.43–1.30 (m, 2 H), 1.41 (s, 3 H), 1.03 (s, 3 H), 0.96 (s, 3 H); ¹³C NMR (125 MHz, CDCl₃) δ 176.5, 143.7, 134.1, 127.7, 127.2, 124.5, 108.9, 88.5, 55.7, 52.0, 44.3, 35.7, 35.4, 34.7, 32.8, 31.6, 30.5, 29.3, 26.0, 20.3, 13.7; HRMS (ESI) calcd for $C_{21}H_{28}O_3N_3^+$ [M + H⁺] 370.2125, found 370.2113.

Product 39. Colorless oil, 24.0 mg, 96% yield; $R_f = 0.64$ (silica gel, hexanes:EtOAc, 10:1); $[\alpha]_D^{20} = +44.0^\circ$ (c = 0.55 in CHCl₃); IR (film) v_{max} 2955, 2868, 2865, 1744, 1455, 1383, 1370, 1242, 1034 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 5.30 (s, 1 H), 3.84 (d, J = 10.4 Hz, 1 H), 3.72 (d, J = 10.4 Hz, 1 H), 3.71 (s, 3 H), 2.20–2.13 (m, 1 H), 2.12–2.08 (m, 1 H), 2.07 (s, 3 H), 1.88–1.84 (m, 1 H), 1.74–1.68 (m, 1 H), 1.56 (d, J = 13.2 Hz, 1 H), 1.40 (d, J = 13.2 Hz, 1 H), 1.20–1.13 (m, 1 H), 1.16 (s, 3 H), 1.06–1.00 (m, 1 H), 1.03 (s, 3 H), 0.95 (d, J = 7.0 Hz, 3 H), 0.79 (s, 3 H); ¹³C NMR (125 MHz, CDCl₃) δ 171.5, 148.2, 125.7, 73.5, 52.1, 51.0, 42.5, 39.4, 32.0, 31.2, 28.2, 24.4, 23.8, 23.0, 22.3, 21.0; HRMS (CI) calcd for $C_{16}H_{27}O_2^+$ [M + H⁺] 251.2006, found 251.2002.

Product 40. Yellow oil, 24.2 mg, 87% yield; $R_f = 0.26$ (silica gel, hexanes:EtOAc, 10:1); IR (film) v_{max} 2954, 2866, 1742, 1459, 1384, 1370, 1247, 1152, 1034, 848 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 5.34 (s, 1 H), 4.00 (dd, J = 20.2, 10.5 Hz, 2 H), 3.69 (s, 3 H), 2.27–2.23 (m, 1 H), 2.16 (d, J = 12.9 Hz, 1 H), 2.06 (s, 3 H), 1.90 (td, J = 12.9, 6.9 Hz, 1 H), 1.72 (d, J = 13.0 Hz, 1 H), 1.68 (ddd, J = 13.3, 7.5, 1.0 Hz, 1H), 1.44 (td, J = 12.4, 7.5 Hz, 1 H), 1.14 (s, 3 H), 1.10 (s, 6 H); ¹³C NMR (125 MHz, CDCl₃) δ 177.5, 171.2, 10, 134.9, 70.9, 66.2, 52.2, 51.9, 50.9, 40.1, 39.6, 35.7, 30.8, 27.5, 25.9, 21.0; HRMS (CI) calcd for $C_{16}H_{25}O_4^+$ [M + H⁺] 281.1753, found 281.1757.

Product 41. Yellow oil, 26.4 mg, 73% yield; $R_f = 0.29$ (silica gel, hexanes:EtOAc, 10:1); IR (film) v_{max} 2959, 2870, 1742, 1714, 1462, 1384, 1372, 1245, 1036 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 5.29 (s, 1 H), 3.99 (s, 2 H), 2.73 (d, J = 14.2 Hz, 1 H), 2.13 (d, J = 14.2 Hz, 1 H), 2.08 (s, 3 H), 1.90 (td, J = 12.9, 6.8 Hz, 1 H), 1.72 (td, J = 12.6, 7.1 Hz, 1 H), 1.62–1.59 (m, 1 H), 1.53–1.51 (m, 1 H), 1.31 (s, 3 H), 1.17 (s, 3 H), 1.06 (s, 3 H), 1.00 (s, 3H); ¹³C NMR (125

MHz, CDCl₃) δ 213.8, 171.1, 148.6, 130.6, 71.9, 54.2, 49.2, 44.4, 38.8, 33.4, 31.0, 30.9, 30.8, 26.4, 26.0, 20.9; HRMS (ESI) calcd for $C_{16}H_{25}O_{3}^{+}$ [M + H⁺] 265.1798, found 265.1792.

Product O-tethered 42. Yellow oil, 24.5 mg, 83% yield; R_f = 0.18 (silica gel, hexanes: EtOAc = 10:1); IR (film) v_{max} ; ¹H NMR (500 MHz, CDCl₃) δ 5.33 (s, 1H), 3.94 (dd, J = 35.7, 10.9 Hz, 2 H), 3.74 (dd, J = 54.8, 9.4 Hz, 2 H), 3.73 (s, 3 H), 2.19–2.15 (m, 1 H), 2.04 (s, 3 H), 1.64–1.59 (m, 1 H), 1.58–1.48 (m, 2 H), 1.20 (s, 3 H), 1.06 (s, 3 H), 0.98 (s, 3 H); ¹³C NMR (125 MHz, CDCl₃) δ 173.1, 171.0, 140.0, 133.8, 84.8, 76.8, 69.6, 52.3, 44.3, 33.0, 32.9, 30.3, 30.2, 29.1, 23.8, 20.9; HRMS (ESI) calcd for $C_{16}H_{24}O_{5}Na^{+}$ [M + Na⁺] 319.1516, found: 319.1523

Product OBn 43. Pale yellow oil, 27.2 mg, 68% yield; $R_f = 0.31$ (silica gel, hexanes:EtOAc, 10:1); IR (film) v_{max} 2953, 2862, 1727, 1454, 1377, 1360, 1244, 1212, 1151, 1100, 1035, 731, 698 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 7.35–7.27 (m, 5 H), 5.39 (s, 1 H), 4.50 (s, 2 H), 4.14 (dd, J = 21.0, 10.5 Hz, 2 H), 3.66 (s, 3 H), 3.45 (d, J = 8.8 Hz, 1 H), 3.23 (d, J = 8.8 Hz, 1 H), 2.22–2.16 (m, 2 H), 2.00 (s, 3 H), 1.90–1.86 (m, 1 H), 1.47–1.31 (m, 5 H), 0.99 (s, 3 H), 0.92 (s, 3 H); ¹³C NMR (125 MHz, CDCl₃) δ 176.8, 171.0, 140.5, 138.8, 134.0, 128.3, 127.4, 127.2, 74.0, 73.2, 67.6, 55.5, 51.9, 48.1, 36.1, 34.9, 32.6, 31.5, 30.7, 30.5, 29.5, 21.0; HRMS (ESI) calcd for $C_{24}H_{32}O_5Na^+$ [M + Na⁺] 423.2142, found 423.2117.

Product 6-membered ring 44. Pale yellow oil, 7.4 mg, 24% yield; R_f = 0.18 (silica gel, hexanes:EtOAc, 10:1); IR (film) v_{max} 2951, 2863, 1726, 1453, 1386, 1371, 1241, 1154, 1058, 1031, 1000, 976 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 5.47 (s, 1 H), 3.75 (s, 2 H), 3.63 (s, 3 H), 2.44–2.41 (m, 1 H), 2.03 (s, 3 H), 1.78–1.75 (m, 1 H), 1.68–1.64 (m, 1 H), 1.57–1.47 (m, 4 H), 1.33–1.30 (m, 1 H), 1.24–1.18 (m, 1 H), 1.13–1.06 (m, 1 H), 1.09 (s, 3 H), 1.00 (s, 3 H), 0.96 (s, 3 H); ¹³C NMR (125 MHz, CDCl₃) δ 176.7, 171.2, 136.9, 136.4, 69.6, 51.8, 46.6, 39.0, 37.3, 35.5, 35.4, 32.9, 32.5, 30.8, 29.1, 25.8, 20.9, 19.2; HRMS (ESI) calcd for $C_{18}H_{29}O_4^+$ [M + H⁺] 309.2060, found 309.2051.

Mechanism Study

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Bicycle 47. To a solution of cyclized product **18** (0.294 g, 1.00 mmol, 1.0 equiv) in MeOH (10 mL) was added K₂CO₃ (0.690 g, 5.00 mmol, 5.0 equiv). The resultant mixture was then stirred for 12 h at 23 °C. The reaction contents were diluted with EtOAc (10 mL) and quenched by the addition of saturated aqueous NH₄Cl (10 mL). The mixture was poured into a separatory funnel and the layers were separated. The aqueous layer was then extracted with EtOAc (2×10 mL). The combined organic layers were washed with H₂O (10 mL) and brine (10mL) before being dried (Na₂SO₄), filtered, and concentrated. The resultant residue was purified by flash column chromatography (silica gel, hexanes:Et₂O, 20:1→10:1) to provide bicycle 47 (28.4 mg, 13% yield) as a yellow solid. 47: $R_f = 0.66$ (silica gel, hexanes:EtOAc, 5:1); IR (film) v_{max} 2955, 2870, 1743, 1597, 1563, 1467, 1395, 1351, 1219, 1126, 1104, 1054, 1034, 992, 880, 864 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 5.28 (s, 1 H), 4.02 (d, J = 9.6 Hz, 1 H), 3.83 (dd, J = 9.6 Hz, 1.7 Hz, 1 H), 2.60–2.53 (m, 1 H), 2.21 (ddd, J = 13.1, 9.6, 4.4 Hz, 1 H), 1.95 (ddd, J = 13.1) 14.7, 9.5, 5.5 Hz, 1 H), 1.74 (tdd, J = 12.6, 4.3, 2.0 Hz, 1 H), 1.61 (td, J = 18.1 Hz, 5.4 Hz, 1 H), 1.48–1.42 (m, 1 H), 1.40–1.32 (m, 2 H), 1.13 (s, 3 H), 0.99 (s, 3 H), 0.97 (s, 3 H); ¹³C NMR (125 MHz, CDCl₃) δ 174.9, 139.5, 126.6, 82.2, 50.7, 42.2, 36.8, 35.8, 35.0, 31.6, 30.6, 28.1, 26.2, 16.6; HRMS (ESI) calcd for $C_{14}H_{21}O_2^+$ [M + H⁺] 221.1536, found 221.1539. For the 2D NMR, see final section of the Supporting Information Section.

D-labeled 47. The D-labeled variant of **18** was prepared by the described procedure used for **S9**. The D-labeled side chain (*E*)-4-iodo-2-methylbut-1-ene-1-*d* was prepared according to Prof. Brown's method. D-labeled **47** was prepared as described above. **D-labeled 47**: H NMR (500 MHz, CDCl₃) δ 5.28 (s, 1 H), 3.81 (s, 1 H), 2.62–2.54 (m, 1 H), 2.21 (ddd, J = 13.1, 9.6, 4.4 Hz, 1 H), 1.95 (ddd, J = 14.7, 9.5, 5.5 Hz, 1 H), 1.75 (tdd, J = 12.6, 4.3, 2.0 Hz, 1 H), 1.61 (td, J = 18.1 Hz, 5.4 Hz, 1 H), 1.49–1.42 (m, 1 H), 1.40–1.35 (m, 2 H), 1.13 (s, 3 H), 0.99 (s, 3 H), 0.98 (s, 3 H). As shown in COSY and nOe of **47**, the chemical shift of H₁ and H₂ are distinct at 3.83 and 4.02 ppm. In the H NMR of **D-labeled 47**, H₁ is missing; thus, the stereochemistry of **D-labeled 47** is confirmed. See the NMR section itself for the H₁ and H₂ labeled protons.

Cyclopropane S45. Ketone S42 (0.103 g, 46% yield) was prepared as a colorless oil from commercial methyl 2-oxocyclohexane-1-carboxylate (S41, 0.156 g, 1.00 mmol, 1.0 equiv) and 4-iodo-2-methylbut-1-ene (0.216 g, 1.10 mmol, 1.1 equiv) by the procedure described above. **S42**: $R_f = 0.29$ (silica gel, hexanes:EtOAc, 10:1); IR (film) v_{max} 2949, 2865, 1714, 1650, 1450, 1215, 1135, 889 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 4.70 (s, 1 H), 4.68 (s, 1 H), 3.73 (s, 1 H), 2.54–2.51 (m, 1 H), 2.46–2.43 (m, 1 H), 2.05–2.00 (m, 2 H)1.96–1.84 (m, 1 H), 1.78–1.65 (m, 3 H), 1.72 (s, 3 H) 1.50–1.44 (m, 1 H); ¹³C NMR (125 MHz, CDCl₃) δ 207.7, 127.5, 145.3, 110.0, 60.1, 52.2, 41.1, 36.0, 32.9, 32.3, 27.6, 22.54, 22.52; HRMS (ESI) calcd for $C_{13}H_{21}O_3^+$ [M + H⁺] 225.1485, found 225.1472. Next, to a solution of i-Pr₂NH (0.440 mL, 3.20 mmol, 1.6 equiv) in THF (5 mL) at 0 °C was added n-BuLi (1.20 mL, 2.5 M in hexanes, 3.00 mmol, 1.5 equiv), The resultant solution was then stirred for 15 min at 0 °C. The reaction contents were then cooled to – 78 °C and a solution of ketone S42 (0.448 g, 2.00 mmol, 1.0 equiv) in THF (5 mL) was added dropwise. After warming to 0 °C and stirring at that temperature for 90 min, the solution was recooled to -78 °C and TMSCl (0.510 mL, 4.00 mmol, 2.0 equiv) was added. The resultant solution was slowly warmed to 23 °C and stirred for 12 h. Upon completion, the reaction contents were quenched by the addition of saturated aqueous NH₄Cl (10 mL). The mixture was then poured into a separatory funnel and the layers were separated. The aqueous layer was extracted with EtOAc (2 × 10 mL). The combined organic layers were then washed with brine (10 mL) before being dried (Na₂SO₄), filtered, and concentrated to provide the desired crude TMS enol ether intermediate (2.00 mmol assumed) directly used for next step without any further purification. Pressing forward, IBX (2.24 g, 8.00 mmol, 4.0 equiv) and MPO (1.00 g, 5.00 mmol, 2.5 equiv) was dissolved in DMSO (20 mL). This solution was then added to a solution of the crude enol ether (2.00 mmol assumed, 1.0 equiv) in DMSO (2.5 mL) at 23 °C. The resultant mixture was stirred at 23 °C for 6 h. Upon completion, the reaction contents were diluted with Et₂O (10 mL) and quenched by the addition of saturated aqueous NaHCO₃ (10 mL). The mixture was poured into a separatory funnel and the layers were separated. The aqueous layer was then extracted with Et₂O (2 × 10 mL). The combined organic layers were washed with

saturated aqueous NaHCO₃ (10 mL), H₂O (10 mL) and brine (10 mL) before being dried (Na₂SO₄), filtered, and concentrated. The resultant residue was purified by flash column chromatography (silica gel, hexanes:EtOAc, 20:1→10:1) to provide enone S43 (0.242 g, 30% vield from ketone S42)^[9] as a pale yellow oil. S43: $R_f = 0.46$ (silica gel, hexanes:EtOAc, 5:1); IR (film) v_{max} 2953, 1723, 1686, 1449, 1386, 1245, 1205, 1081, 889 cm⁻¹; ¹H NMR (500 MHz, $CDCl_3$) δ 6.91–6.88 (m, 1 H), 6.01 (dt, J = 10.1, 1.7 Hz, 1 H), 4.69 (s, 1 H), 4.68 (s, 1 H), 3.68 (s, 3 H), 2.54–2.46 (m, 2 H), 2.37–2.30 (m, 1 H), 2.09–2.03 (m, 1 H), 1.99–1.94 (m, 1 H), 1.87– 1.81 (m, 1 H), 1.72 (s, 3 H); ¹³C NMR (125 MHz, CDCl₃) δ 196.2, 172.0, 149.5, 145.2, 129.1, 110.2, 56.8, 52.4, 32.6, 31.9, 29.9, 23.6, 22.5; HRMS (ESI) calcd for $C_{13}H_{19}O_3^+$ [M + H⁺] 223.1329, found 223.1333. Next, triflate 51 was prepared as described above starting from S43 (0.111 g, 5.00 mmol, 1.0 equiv) to afford triflate **51** (0.104 g, 60% yield) as a colorless oil. **51**: $R_f = 0.62$ (silica gel, hexanes:EtOAc, 10:1); IR (film) v_{max} 2956, 1714, 1654, 1416, 1213, 1143, 1060, 891, 702 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 6.05–6.04 (m, 1 H), 5.87–5.82 (m, 1 H), 4.73 (s, 1 H), 4.71 (s, 1 H), 3.74 (s, 3 H), 3.07 (dd, J = 17.7, 4.2 Hz, 1 H), 2.53-2.49 (m, 1 H), 2.04–1.98 (m, 3 H), 1.94–1.88 (m, 1 H), 1.72 (s, 3 H); ¹³C NMR (125 MHz, CDCl₃) δ 172.7, 148.1, 144.5, 126.1, 120.8, 115.35, 115.34, 115.33, 110.6, 52.6, 49.5, 33.7, 32.7, 32.5, 22.4; HRMS (ESI) calcd for $C_{14}H_{18}O_5F_3S^+$ [M + H⁺] 355.0822, found 355.0822. Finally, **53** was prepared following the general Pd-cyclization procedure defined above from 51 (35.4 mg, 0.1 mmol) to provide 53 (14.9 mg, 56% yield) as a pale yellow oil. 53: $R_f = 0.29$ (silica gel, hexanes: EtOAc, 10:1); IR (film) v_{max} 2952, 2926, 2863, 1738, 1442, 1370, 1240, 1152, 1113, 1055, 1023 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 5.67–5.65 (m, 1 H), 5.59–5.55 (m, 1 H), 5.36 (dd, J = 10.0, 1.5 Hz, 1 H), 3.69 (s, 3H), 2.35-2.32 (m, 1 H), 2.06 (s, 3 H), 1.92-1.82 (m, 2 H),1.71-1.62 (m, 2 H), 1.53-1.49 (m, 1 H), 1.29 (d, J = 5.8 Hz, 1 H), 1.16 (s, 3 H), 0.62 (d, J = 5.7Hz, 1 H); ¹³C NMR (125 MHz, CDCl₃) δ 176.0, 170.6, 132.2, 126.7, 69.6, 54.2, 51.9, 35.82, 35.76, 32.6, 31.7, 31.3, 22.3, 21.3, 19.6; HRMS (ESI) calcd for $C_{15}H_{20}O_4Na^+$ [M + Na⁺] 287.1254, found 287.1246.

Total Synthesis of Members of the Botrydienal Family of Natural Products

Triflate 55. To a solution of *i*-Pr₂NH (0.440 mL, 3.20 mmol, 3.2 equiv) in THF (3 mL) at 0 °C was added n-BuLi (1.20 mL, 2.5 M in hexanes, 3.00 mmol, 3.0 equiv) and the resultant solution was stirred at 0 °C for 15 min. The reaction contents were then cooled to -78 °C and a solution of 54 (0.208 g, 1.00 mmol, 1.0 equiv) in THF (5 mL) was added dropwise over the course of 5 min. The reaction mixture was then warmed to 0 °C and kept at that temperature for 90 min before being cooled to -78 °C. HMPA (0.50 mL) and a solution of Mander's reagent (0.280 g, 3.30 mmol, 3.3 equiv) in THF (2 mL) were then added sequentially. After stirring the resultant mixture at -78 °C for 1 h, LDA (prepared from n-BuLi and i-Pr₂NH as described, 10.0 mL, 1.0 M in THF, 10.0 mmol, 10 equiv) was added at -78 °C and was followed by the addition of Tf₂O (1.68 mL, 10.0 mmol, 10 equiv). The reaction contents were stirred at -78 °C for 4 h before being quenched by the addition of saturated aqueous NaHCO₃ (10 mL). The mixture was then warmed to 23 °C, H₂O (10 mL) was added to dissolve any remaining solids, and the reaction contents was poured into a separatory funnel and the layers were separated. The aqueous layer was then extracted with Et₂O (2×10 mL). The combined organic layers were washed with saturated aqueous NaHCO₃ (100 mL), H₂O (10 mL), and brine (10 mL), dried (Na₂SO₄), filtered, and concentrated. The resultant residue was purified by flash column chromatography (Et₃Nbuffered silica gel, hexanes) to provide triflate 55 (0.314 g, 79% yield) as a colorless oil. 55: R_f = 0.65 (silica gel, hexanes: EtOAc, 15:1); $[\alpha]_D^{20} = +94.0^\circ$ (c = 0.53, CHCl₃); IR (film) v_{max} 2968, 1731, 1421, 1245, 1203, 1142, 1065, 1048, 961, 891, 810 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 4.91 (s, 1 H), 4.68 (s, 1 H), 3.80 (s, 3 H), 2.75–2.72 (m, 1 H), 2.41–2.39 (m, 1 H), 2.16 (d, J =13.1 Hz, 1 H), 1.98 (d, J = 13.1 Hz, 1 H), 1.91–1.87 (m, 3 H), 1.78 (s, 3 H), 1.38–1.33 (m, 1 H), 1.18 (d, J = 7.0 Hz, 3 H), 1.05 (s, 3 H), 1.01 (s, 3 H); 13 C NMR (125 MHz, CDCl₃) δ 165.6, 151.4, 142.5, 131.9, 122.1, 119.6, 117.0, 115.3, 114.5, 52.0, 48.2, 45.9, 39.0, 31.5, 27.5, 27.2, 26.6, 25.5, 22.3, 20.9; HRMS (ESI) calcd for $C_{17}H_{26}O_5F_3S^+$ [M + H⁺] 399.1448, found 399.1436.

Acetate 56. To a flame-dried sealed tube was added Pd(OAc)₂ (0.112 g, 0.500 mmol, 10 mol %), *t*-BuMephos (0.234 g, 0.75 mmol, 15 mol %), and *n*-Bu₄NOAc (4.52 g, 15.0 mmol, 3.0 equiv). A solution of triflate **55** (1.99 g, 5.00 mmol, 1.0 equiv) in EtOAc (50 mL) was then added at 23 °C. The mixture was heated to 90 °C and stirred at this temperature for 12 h. Upon

completion, the reaction contents were cooled to 23 °C and filtered through a pad of silica gel (EtOAc). The filtrate was concentrated and the resultant residue was purified by flash column chromatography (silica gel, hexanes:EtOAc, 30:1) to provide acetate **56** (1.03 g, 67% yield) as a pale yellow oil. **56**: $R_f = 0.48$ (silica gel, hexanes:EtOAc, 10:1); $[\alpha]_D^{20} = +23.0^\circ$ (c = 1.0 in CHCl₃); IR (film) v_{max} 2932, 2865, 1742, 1726, 1373, 1226, 1061, 1030 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 4.24 (d, J = 10.3 Hz, 1 H), 4.05 (d, J = 10.3 Hz, 1 H), 3.71 (s, 3 H), 2.56–2.48 (m, 1 H), 2.15–2.11 (m, 1 H), 2.06 (s, 3 H), 1.93–1.88 (m, 1 H), 1.73 (d, J = 13.3 Hz, 1 H), 1.71–1.66 (m, 1 H), 1.40 (d, J = 13.2 Hz, 1 H), 1.25–1.06 (m, 2 H), 1.11 (s, 3 H), 1.00 (s, 3 H), 0.91 (d, J = 6.8 Hz, 3 H), 0.78 (s, 3 H); ¹³C NMR (125 MHz, CDCl₃) δ 171.2, 170.8, 149.8, 131.5, 73.1, 53.7, 53.1, 51.1, 44.1, 39.0, 33.1, 31.4, 27.9, 23.7, 22.9, 22.1, 21.0, 20.1; HRMS (ESI) calcd for $C_{18}H_{29}O_4^+[M+H^+]$ 309.2060, found 309.2063.

Lactone 57. To a solution of acetate **56** (0.616 g, 2.00 mmol, 1.0 equiv) in MeOH (20 mL) at 23 °C was added K₂CO₃ (2.76 g, 20 mmol, 10 equiv), and the resultant mixture was stirred at 23 °C for 10 h. Upon completion, the reaction contents were diluted with EtOAc (10 mL) and quenched by the addition of saturated aqueous NH₄Cl (10 mL). The mixture was poured into a separatory funnel and the layers were separated. The aqueous layer was then extracted with EtOAc (2 × 10 mL). The combined organic layers were washed with H₂O (2 × 10 mL) and brine (10 mL) before being dried (Na₂SO₄), filtered, and concentrated. The resultant residue was purified by flash column chromatography (silica gel, hexanes:EtOAc, 20:1→10:1) to provide lactone **57** (0.281 g, 60% yield) as a colorless solid. **57**: R_f = 0.58 (silica gel, hexanes:EtOAc, 5:1); $[\alpha]_D^{20} = -53.0^{\circ}$ (c = 0.30 in CHCl₃); IR (film) v_{max} 2957, 2869, 1714, 1462, 1388, 1368, 1256, 1209, 1165, 1070, 1049, 1000, 974, 788 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 4.08 (d, J = 10.4 Hz, 1 H), 4.01 (d, J = 10.4 Hz, 1 H), 2.78–2.72 (m, 1 H), 2.45 (ddd, J = 10.3, 6.8, 2.3 Hz, 1 H), 1.68–1.58 (m, 1 H), 1.56 (d, J = 14.1 Hz, 1 H), 1.50, (d, J = 13.9 Hz, 1 H), 1.39–1.31 (m, 1 H), 1.24 (s, 3 H), 1.16 (s, 3 H), 1.02, (d, J = 7.0 Hz, 1 H), 0.83 (s, 3 H); ¹³C NMR (125 MHz, CDCl₃) δ 166.5, 124.6, 50.4, 49.1, 41.6, 38.4, 29.3, 29.2, 25.9, 25.1, 25.0, 19.3, 16.1; HRMS (ESI) calcd for C₁₅H₂₃O₂⁺ [M + H⁺] 235.1693, found 235.1700.

10-oxodehydrodihydrobotrydial (58). Lactone **57** (46.8 mg, 0.200 mmol, 1.0 equiv) in 1,4-dioxane (2 mL) was treated with SeO₂ (88.8 mg, 0.800 mmol, 4.0 equiv). The resultant mixture was then heated at 110 °C for 12 h. Upon completion, the resultant mixture was cooled to 23 °C and filtered through a pad of silica gel (EtOAc). The filtrate was then

concentrated and the resultant residue was purified by column chromatography (hexanes: EtOAc = $100:1\rightarrow 50:1$) to provide recovered starting material (24.9 mg) along with 10-oxodehydrodihydrobotrydial (**58**, 13.3 mg, 29% yield, 62% yield brsm) as a white solid. **58**: R_f = 0.68 (silica gel, hexanes: EtOAc = 5:1); $[\alpha]_D^{20} = -95.0^\circ$ (c = 1.0 in CHCl₃); lit: $[\alpha]_D^{28} = -166.5^\circ$ (c = 1.0 in CHCl₃)^[10b]; as such the rotation data showed this should be the enantiomer of the originally proposed structure for **58**, but the same absolute configuration as the reassignment by the Li group following their synthesis; IR (film) v_{max} 2961, 2927, 2867, 1759, 1584, 1484, 1245, 1067, 829, 801, 532 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 7.21 (d, J = 7.7 Hz, 1 H), 7.15 (d, J = 7.7 Hz, 1 H), 4.36 (d, J = 10.0 Hz, 1 H), 4.13 (d, J = 10.0 Hz, 1 H), 2.62 (s, 3 H), 1.98 (d, J = 12.8 Hz, 1 H), 1.86 (d, J = 12.9 Hz, 1 H), 1.51 (s, 3 H), 1.45 (s, 3 H), 1.32 (s, 3 H); ¹³C NMR (125 MHz, CDCl₃) δ 164.0, 151.4, 147.0, 139.6, 131.7, 127.2, 119.6, 79.2, 52.1, 45.1, 40.8, 30.8, 30.7, 24.7, 20.2; HRMS (ESI) calcd for C₁₅H₁₉O₂ [M + H⁺] 231.1380, found 231.1388.

Table S1. Comparison of literature and obtained spectral values for 10-oxodehydrodihydrobotrydial (**58**)^[10a]

¹ H NMR in CDCl ₃		
Natural (Collado, 400 MHz)	Synthetic (This work, 500 MHz)	
7.20 (d, J = 7.8 Hz, 1 H)	7.21 (d, J = 7.7 Hz, 1 H)	
7.14 (d, J = 7.8 Hz, 1 H)	7.15 (d, J = 7.7 Hz, 1 H)	
4.35 (d, J = 10.1 Hz, 1 H)	4.36 (d, J = 10.0 Hz, 1 H)	
4.12 (d, J = 10.1 Hz, 1 H)	4.13 (d, J = 10.0 Hz, 1 H)	
2.61 (s, 3 H)	2.62 (s, 3 H)	
1.96 (d, J = 13.0 Hz, 1 H)	1.98 (d, J = 13.0 Hz, 1 H)	
1.84 (d, J = 13.0 Hz, 1 H)	1.86 (d, J = 13.0 Hz, 1 H)	
1.50 (s, 3 H)	1.50 (s, 3 H)	
1.44 (s, 3 H)	1.45 (s, 3 H)	
1.31 (s, 3 H)	1.32 (s, 3 H)	
¹³ C NMR in CDCl ₃		
Natural (Collado, 100 MHz)	Synthetic (This work, 125 MHz)	
164.0	164.0	
151.4	151.4	
147.0	147.0	
139.6	139.6	
131.7	131.7	
127.3	127.2	
119.6	119.6	
79.2	79.2	

52.1	52.1
45.1	45.1
40.4	40.5
30.7	30.8
30.7	30.7
24.7	24.7
20.3	20.2

Alcohol S44. To a solution of acetate 56 (1.23 g, 4.00 mmol, 1.0 equiv) in MeOH (40 mL) at 23 °C was added K₂CO₃ (0.580 g, 4.20 mmol, 1.05 equiv), and the resultant mixture was stirred at 23 °C for 10 h. Upon completion, the reaction mixture was guenched by the addition of saturated aqueous NH₄Cl (30 mL), poured into a separatory funnel, and the resultant layers were separated. The aqueous layer was then extracted with EtOAc (2 × 30 mL). The combined organic layers were washed with H₂O (30 mL) and brine (30 mL) before being dried (Na₂SO₄), filtered, and concentrated. The resultant residue was purified by flash column chromatography (silica gel, hexanes:EtOAc, 10:1→5:1) to provide alcohol S44 (0.894 g, 84% yield) as a white solid. S44: $R_f = 0.33$ (silica gel, hexanes: EtOAc = 5:1); $[\alpha]_D^{20} = -19.0^\circ$ (c = 0.53 in CHCl₃); IR (film) v_{max} 3438, 2921, 2864, 1718, 1656, 1446, 1366, 1261, 1225, 1060, 981, 750 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) 3.75 (s, 3 H), 3.45–3.40 (m, 2 H), 3.21 (dd, J = 6.6, 5.8 Hz, 1 H), 2.56–2.48 (m, 1 H), 2.14-2.10 (m, 1 H), 1.93-1.88 (m, 1 H), 1.72-1.68 (m, 1 H), 1.59 (d, J = 13.0 Hz, 1 H), 1.40(d, J = 12.9 Hz, 1 H), 1.25-1.08 (m, 2 H), 1.10 (s, 3 H), 1.01 (s, 3 H), 0.93 (d, J = 6.8 Hz, 3 H),0.79 (s, 3 H); ¹³C NMR (125 MHz, CDCl₃) δ 172.2, 151.2, 131.2, 71.7, 54.1, 53.0, 51.6, 46.6, 38.5, 33.2, 31.4, 27.8, 23.9, 22.4, 22.1, 20.2; HRMS (ESI) calcd for $C_{16}H_{27}O_3^+$ [M + H⁺] 267.1955, found 267.1965.

TBS-Protected Ether 59. To a solution of alcohol **S46** (0.266 g, 1.00 mmol, 1.0 equiv) in DMF (10 mL) at 23 °C was sequentially added imidazole (0.109 g, 1.60 mmol, 1.6 equiv) and TBSCl (0.225 g, 1.50 mmol, 1.5 equiv). The resultant solution was stirred at 23 °C for 12 h. Upon completion, the reaction contents were quenched by the addition of saturated aqueous NH₄Cl (10 mL), poured into a separatory funnel, and the resultant layers were separated. The aqueous layer was then extracted with Et_2O (2 × 10 mL). The combined organic layers were

washed with H₂O (4 × 10 mL) and brine (10 mL) before being dried (Na₂SO₄), filtered, and concentrated. The resultant residue was purified by flash column chromatography (silica gel, hexanes:EtOAc, 20:1) to provide **59** (0.380 g, 99% yield). **59**: R_f = 0.39 (silica gel, hexanes:EtOAc, 20:1); $[\alpha]_D^{20} = +30.0^{\circ}$ (c = 1.0 in CHCl₃); IR (film) v_{max} 2930, 2857, 1727, 1432, 1385, 1254, 1226, 1212, 1060, 837 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 3.80 (d, J = 8.7 Hz, 1 H), 3.70 (s, 3 H), 3.39 (d, J = 8.7 Hz, 1 H), 2.54–2.48 (m, 1 H), 2.18–2.14 (m, 1 H), 2.04 (d, J = 12.7 Hz, 1 H), 1.90–1.86 (m, 1 H), 1.68–1.63 (m, 1 H), 1.23 (d, J = 12.8 Hz, 1 H), 1.17–1.08 (m, 2 H), 1.001 (s, 3 H), 0.995 (s, 3 H), 0.90 (d, J = 6.8 Hz, 3 H), 0.88 (s, 9 H), 0.77 (s, 3 H), 0.04 (s, 3 H), 0.03 (s, 3 H); ¹³C NMR (125 MHz, CDCl₃) δ 171.2, 152.2, 129.4, 71.6, 53.9, 52.7, 50.9, 46.3, 38.9, 33.1, 27.9, 24.0, 22.8, 22.3, 20.1, 18.2, –5.3, –5.4; HRMS (ESI) calcd for C₂₂H₄₁O₃Si⁺ [M + H⁺] 381.2819, found 381.2826.

Allylic alcohol S45. To a solution of **59** (0.076 g, 0.200 mmol, 1.0 equiv) in 1,4-dioxane (2 mL) at 23 °C was added SeO₂ (0.089 g, 0.800 mmol, 4.0 equiv). The resultant mixture was then heated at 110 °C for 12 h. Upon completion, the resultant mixture was cooled to 23 °C and filtered through a pad of silica gel (EtOAc). The filtrate was then concentrated and the resultant residue was purified by column chromatography (hexanes: EtOAc = 100:1→50:1) to provide allylic alcohol **S45** (0.039 g, 49% yield) as a colorless oil. **S45**: R_f = 0.53 (silica gel, hexanes:EtOAc, 10:1); $[α]_D^{20}$ = +10.0° (c = 0.21 in CHCl₃); IR (film) v_{max} 3426, 2951, 2931, 2860, 1720, 1471, 1251, 1215, 1065, 782 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 4.59 (d, J = 2.0 Hz, 1 H), 4.02 (d, J = 8.5 Hz, 1 H), 3.72 (s, 3 H), 3.21 (d, J = 8.5 Hz, 1 H), 2.49–2.44 (m, 1 H), 2.20 (d, J = 12.8 Hz, 1 H), 1.73–1.54 (m, 2 H), 1.39–1.34 (m, 1 H), 1.15 (d, J = 12.8 Hz, 1 H), 1.023 (s, 3 H), 1.017 (s, 3 H), 0.93 (d, J = 6.9 Hz, 1 H), 0.92 (s, 3 H), 0.85 (s, 3 H), 0.113 (s, 3 H), 0.111(s, 3 H); ¹³C NMR (125 MHz, CDCl₃) δ 170.8, 148.8, 134.2, 79.6, 71.8, 51.1, 49.7, 45.2, 43.4, 33.7, 27.0, 26.9, 26.7, 25.9, 23.3, 21.6, 19.8, 18.4, -5.5, -5.6; HRMS (ESI) calcd for $C_{22}H_{39}O_3Si^+$ [M + H⁺ − H₂O] 379.2663, found 379.2665.

Diene S46. To a solution of allylic alcohol **S45** (0.070 g, 0.180 mmol, 1.0 equiv) in toluene (8 mL) at 23 °C was added the Burgess reagent (0.120 g, 0.500 mmol, 3.0 equiv). The resultant flask was then immersed in a pre-heated oil bath at 80 °C and stirring of the mixture was continued at 80 °C for 12 h. Upon completion, the reaction contents were cooled to 23 °C, diluted with Et₂O (10 mL), and poured into a separatory funnel. This organic layer was washed with saturated aqueous NaHCO₃ (10 mL) and brine (10 mL). The organic phase was then dried (Na₂SO₄) and concentrated. The resultant residue was purified by flash column chromatography

(silica gel, hexanes:EtOAc, 10:1) to provide diene **S46** (0.064 g, 96% yield) as a pale yellow oil. **S46**: $R_f = 0.62$ (silica gel, hexanes: EtOAc = 10:1); $[\alpha]_D^{20} = +28^\circ$ (c = 1.0 in CHCl₃); IR (film) v_{max} 2955, 2928, 2859, 1711, 1463, 1432, 1230, 1096, 852, 836, 775 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 5.59 (dd, J = 5.6, 3.5 Hz, 1 H), 3.78 (d, J = 9.4 Hz, 1 H), 3.74 (s, 3 H), 3.58 (d, J = 9.4 Hz, 1 H), 2.67–2.62 (m, 1 H), 2.42–2.36 (m, 1 H), 2.20 (d, J = 13.2 Hz, 1 H), 2.06–2.00 (m, 1 H), 1.40 (d, J = 13.2 Hz, 1 H), 1.24 (s, 3 H), 1.16 (s, 3 H), 1.11 (s, 3 H), 1.04 (d, J = 6.9 Hz, 1 H), 0.04 (s, 3 H), 0.02 (s, 3 H); ¹³C NMR (125 MHz, CDCl₃) δ 169.4, 151.4, 151.0, 126.0, 118.5, 67.7, 52.3, 50.69, 47.9, 38.5, 31.4, 31.3, 31.0, 30.2, 25.8, 24.1, 18.4, –5.5, –5.6; HRMS (ESI) calcd for $C_{22}H_{39}O_3Si^+[M + H^+]$ 379.2663, found 379.2669.

Botrydienol (60). To a solution of diene S46 (37.8 mg, 0.100 mmol, 1.0 equiv) in CH₂Cl₂ (0.7 mL) at 0 °C was added DIBAL-H (0.3 mL, 1.0 M in CH₂Cl₂ 0.300 mmol, 3.0 equiv) dropwise over the course of 10 min. The resultant solution was then stirred at 0 °C for 1 h. Next, TBAF (0.500 mL, 1.0 M in THF, 0.500 mmol, 5.0 equiv) was added dropwise over the course of 10 min. The resultant mixture was then warmed to 23 °C and stirred at that temperature for an additional 3 h. Upon completion, the reaction contents were quenched by the slow addition of solid Na₂SO₄•10H₂O at 0 °C until no further gas was released. The mixture was then filtered through Celite and the residual solids were washed with EtOAc (5 \times 1 mL). The combined organic layers were washed with saturated H₂O (3 × 5 mL) and brine (5 mL) before being dried (Na₂SO₄), filtered, and concentrated. The resultant residue was purified by flash column chromatography (silica gel, hexanes:EtOAc, 5:1→1:1) to provide botrydienol (60, 23.6 mg, 99% yield) as a white solid. **60**: $R_f = 0.21$ (silica gel, hexanes: EtOAc, 3:1); $[\alpha]_D^{20} = +53.0^{\circ}$ (c = 0.80in CHCl₃); IR (film) v_{max} 3337, 2955, 2924, 2862, 1597, 1563, 1449, 1395, 1219, 1119, 1034 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 5.38 (dd, J = 5.3, 3.1 Hz, 1 H), 4.35 (d, J = 11.3 Hz, 1 H), 4.20 (d, J = 11.3 Hz, 1 H), 3.65 (d, J = 11.1 Hz, 1 H), 3.53 (d, J = 11.1 Hz, 1 H), 2.42 - 2.30 (m, 2 H)H), 2.02 (dt, J = 17.1, 4.5 Hz, 1 H), 1.95 (d, J = 13.2 Hz, 1 H), 1.46 (d, J = 13.2 Hz, 1 H), 1.25 (s, 3 H), 1.15 (s, 3 H), 1.10 (s, 3 H), 1.08 (d, J = 6.8 Hz, 1 H); ¹³C NMR (125 MHz, CDCl₃) δ 150.3, 141.1, 134.2, 114.1, 70.4, 61.9, 53.1, 47.0, 39.7, 32.6, 31.7, 31.0, 30.7, 25.8, 18.8; HRMS (CI) calcd for $C_{15}H_{23}O^{+}[M + H^{+} - H_{2}O]$ 219.1743, found 219.1746.

Botrydienal (3). To a solution of $(COCl)_2$ (0.110 mL, 1.28 mmol, 20 equiv) in CH_2Cl_2 (0.5 mL) at -78 °C was added DMSO (0.045 mL, 0.64 mmol, 10 equiv) dropwise over the course of 5 min. After stirring the resultant solution at -78 °C for 15 min, a solution of

botrydienol (60, 15.0 mg, 0.064 mmol, 1.0 equiv) in CH₂Cl₂ (0.5 mL) was added dropwise over the course of 10 min. The resultant solution was then stirred at -78 °C for 3 h, at which time Et₃N (0.26 mL, 1.9 mmol, 30 equiv) was added the reaction contents were stirred at -78 °C for another 30 min. Upon completion, the reaction contents were quenched by the addition of H₂O (2 mL), warmed to 23 °C, poured into a separatory funnel, and the resultant layers were separated. The aqueous layer was then extracted with CH₂Cl₂ (2 × 2 mL). The combined organic layers were washed with H₂O (3 mL) before being dried (Na₂SO₄), filtered, and concentrated. The resultant residue was purified by flash column chromatography (silica gel, hexanes:EtOAc, $10:1\rightarrow 5:1$) to provide botrydienal (3, 8.2 mg, 55% yield) as a white solid. 3: $R_f = 0.55$ (silica gel, hexanes: EtOAc, 5:1); $[\alpha]_D^{20} = +167.0^\circ$ (c = 0.18 in *n*-hexane); lit: $[\alpha]_D^{30} = +190^\circ$ (c = 0.18 in *n*-hexane);^[11] IR (film) v_{max} 2959, 2926, 2853, 2819, 2807, 2712, 1723, 1658, 1640, 1570, 1453, 1143, 924, 797, 404 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 9.74 (s, 1 H), 9.67 (s, 1 H), 5.88 (dd, J= 6.3, 2.8 Hz, 1 H), 3.00-2.97 (m, 1 H), 2.45 (ddd, J = 18.4, 8.7, 6.7 Hz, 1 H); 2.23 (d, J = 13.6)Hz, 1H), 2.20 (dd, J = 19.2, 6.3 Hz, 1 H); 1.63 (d, J = 13.7 Hz, 1 H); 1.53 (s, 3 H), 1.26 (s, 3 H), 1.06 (s, 3 H), 0.92 (d, J = 7.0 Hz, 1 H); ¹³C NMR (125 MHz, CDCl₃) δ 199.9, 189.8, 155.2, 149.5, 136.0, 123.7, 56.5, 50.6, 40.5, 30.62, 30.61, 28.8, 25.3, 24.2, 18.3; HRMS (ESI) calcd for $C_{15}H_{21}O_2^+$ [M + H⁺] 233.1536, found 233.1542.

Table S2. Comparison of literature and obtained spectral values for botrydienal (3)^[11]

¹ H NMR in CDCl ₃		
Natural (Marumo, 100 MHz)	Synthetic (this work, 500 MHz)	
9.74 (s, 1 H)	9.74 (s, 1 H)	
9.67 (s, 1 H)	9.67 (s, 1 H)	
5.87 (ddd, J = 6.1, 3.2, 0.5 Hz, 1 H)	5.88 (dd, J = 6.3, 2.8 Hz, 1 H)	
2.98 (m, 1 H)	3.00–2.97 (m, 1 H)	
2.48 (ddd, <i>J</i> = 18, 8.1, 6.1 Hz, 2 H)	2.48 (ddd, J = 18.4, 8.7, 6.7 Hz, 2 H)	
2.24 (d, J = 13.9 Hz, 2 H)	2.24 (d, J = 13.6 Hz, 2 H)	
1.63 (d, J = 13.9 Hz, 3 H)	1.63 (d, J = 13.7 Hz, 3 H)	
1.54 (s, 3 H)	1.53 (s, 3 H)	
1.25 (s, 3 H)	1.26 (s, 3 H)	
1.06 (s, 3 H)	1.06 (s, 3 H)	
¹³ C NMR in CDCl ₃		
Natural (Marumo, 25 MHz)	Synthetic (This work, 125 MHz)	
199.5	199.9	
189.5	189.8	
154.9	155.2	
149.2	149.5	
135.7	136.0	
123.5	123.7	
56.3	56.5	
50.4	50.6	

40.4	40.5
30.5	30.6
30.5	30.5
28.7	28.8
25.3	25.3
24.2	24.2
18.3	18.3

Select Substrate Limitations for a Terminating Oxygenation

EtO₂C

KHMDS (1.5 equiv)

THF, -78 °C to 0 °C, then Comin's reagent (1.2 equiv),
$$-78$$
 °C (75%)

S47

$$\begin{array}{c} \text{EtO}_2\text{C} \\ \text{EtO}_2\text{C} \\ \text{TBuMephos (15 mol%),} \\ \text{tBuMephos (15 mol%),} \\ \text{toluene, 90 °C} \\ \text{(88\%)} \\ \text{Me} \\ \end{array}$$

β-H elimination: S47 was prepared as a colorless oil following the described procedure toward S42 (0.119 g, 50% yield) from ethyl 2-oxocyclohexane-1-carboxylate (0.170 g, 1.00 mmol, 1.0 equiv) and 4-iodo-2-methylbut-1-ene (0.216 g, 1.10 mmol, 1.1 equiv). S47: $R_f = 0.54$ (silica gel, hexanes:EtOAc, 5:1); IR (film) v_{max} 2939, 2866, 1714, 1450, 1214, 1187, 1134, 1094, 1022, 867 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 4.70 (s, 1 H), 4.68 (s, 1 H), 4.21 (q, J = 7.1 Hz, 2 H), 2.55-2.52 (m, 1 H), 2.47-2.44 (m, 2 H), 2.05-1.99 (m, 2 H), 1.98-1.85 (m, 2 H), 1.78-1.62 (m, 4 H), 1.72 (s, 3 H), 1.49–1.43 (m, 1 H), 1.27 (t, J = 7.1 Hz, 3 H); ¹³C NMR (125 MHz, CDCl₃) δ 207.9, 171.9, 145.4, 110.0, 61.2, 60.6, 41.1, 36.1, 33.0, 32.3, 27.6, 22.6, 22.5, 14.2; HRMS (ESI) calcd for $C_{14}H_{23}O_3^+$ [M + H⁺] 239.1642, found 239.1646. **S48** was prepared as a colorless oil following the described procedure (83.2 mg, 75% yield). S48: $R_f = 0.65$ (silica gel, hexanes:EtOAc, 5:1); IR (film) v_{max} 2941, 1734, 1416, 1248, 1210, 1145, 1032, 909 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 5.89 (dd, J = 5.1, 3.1 Hz, 1 H), 4.72 (s, 1 H), 4.69 (s, 1H), 4.25–4.17 (m, 2 H), 2.30–2.25 (m, 2 H), 2.22–2.19 (m, 1 H), 2.04–1.95 (m, 3 H), 1.88–1.83 (m, 1 H), 1.74– 1.70 (m, 1 H), 1.72 (s, 2 H), 1.67–1.60 (m, 2 H), 1.29 (t, J = 7.1 Hz, 3 H); ¹³C NMR (125 MHz, CDCl₃) δ 172.9, 148.3, 144.8, 120.1, 119.6, 110.6, 61.7, 50.2, 33.5, 32.3, 32.0, 24.4, 22.4, 18.8, 14.0; HRMS (ESI) calcd for $C_{15}H_{22}OSF_3^+$ [M + H⁺] 371.1135, found 371.1147. **S49** was prepared as a colorless oil following the described standard cyclization cascade procedure (19.4 mg, 88% yield). **S49**: $R_f = 0.56$ (silica gel, hexanes:EtOAc, 10:1); IR (film) v_{max} 2921, 2860, 1722, 1445, 1264, 1218, 1195, 1170, 1076, 1028, 681 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 5.75– 5.72 (m, 1 H), 5.27–5.24 (m, 1 H), 4.16–4.07 (m, 2 H), 2.21–2.13 (m, 1 H), 2.10–1.99 (m, 2 H), 1.84-1.71 (m, 2 H), 1.63-1.51 (m, 3 H), 1.22 (t, J = 7.1 Hz, 3 H); 1.19 (d, J = 5.5 Hz, 1 H), 1.12(s, 3 H), 0.54 (d, J = 5.5 Hz, 1 H); ¹³C NMR (125 MHz, CDCl₃) δ 176.3, 128.9, 126.6, 125.1, 60.0, 52.5,32.3, 32.3,30.8, 27.0, 23.7, 22.3, 19.6, 14.3; HRMS (ESI) $C_{14}H_{21}O_{2}^{+}$ [M + H⁺] 221.1536, found 221.1534.

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