Supporting Information

for

The Total Synthesis of (±)-Ginkgolide B

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Materials and Methods: "Dry" solvents were dried immediately prior to use. Diethyl ether, tetrahydrofuran (THF), and dichloromethane were dried by passing through an activated neutral alumina column immediately prior to use. Alkylamines, chlorotrimethylsilane and acetonitrile were distilled from calcium hydride. Hexamethylphosphoramide (HMPA) was distilled under reduced pressure from calcium hydride and stored over 4Å molecular sieves. Melting points are uncorrected. Infrared (IR) spectra were obtained using a Mattson FT-IR 5000 Galaxy series infrared spectrometer. Proton and carbon nuclear magnetic resonance (^1H , ^{13}C NMR) spectra were recorded on the following instruments: Bruker Model AC-200 (^1H at 200 MHz; ^{13}C at 50 MHz), Bruker Model WM-250 (^1H at 250 MHz), Bruker Model DRX-400 (^1H at 400 MHz, ^{13}C at 100 MHz) and a Bruker Model DRX-500 (^1H at 500 MHz, ^{13}C at 125 MHz). Elemental analyses were performed by Atlantic Microlab, Inc., Norcross, Georgia. High resolution mass spectral analysis were performed at the North Carolina State University Mass Spectrometry Facility, Raleigh, N.C. or by Glaxo-Wellcome Co., Research Triangle Park, N.C. Single crystal X-ray analyses were performed by Peter White at the University of North Carolina.

(E,Z)-Ethyl 3-(3-Furyl) prop-2,3-enoate **7**.

To a stirring solution of 25 g (0.26 mol) of 3-furaldehyde in 200 mL methylene chloride was added 90.48 g (0.26 mol) of (carbethoxymethylene)triphenylphosphorane in one portion. The

mixture was then heated to reflux and allowed to stir overnight. The mixture was then cooled and the solvent removed at reduced pressure. The crude residue was taken up in a minimum amount of methylene chloride and this diluted with methyl butane until precipitation ceased. This mixture was cooled to 0°C and then filtered and the residue washed with ice cold methyl butane. This process was repeated once more and the filtrate was reduced *in vacuo* and then chromatographed to provide 40.56 g (94%) of ester **7** as white crystals, m.p. 38-38.5°C. ¹H NMR (200 MHz, CDCl₃), *E*-isomer: δ 1.27 (t, J= 6.6 Hz, 3H, CO₂CH₂CH₃), 4.18 (q, J= 6.6 Hz, 2H, CO₂CH₂CH₃), 6.12(d, J= 15.5 Hz, 1H, CH=CH-CO₂Et), 6.53 (m, 1H, CH=CH-O), 7.37 (m, 1H, CH=CH-O), 7.53 (d, J= 15.5 Hz, 1H, CH=CH-CO₂Et), 7.60 (m, 1H, C=CH-O). IR (CHCl₃): 3115, 2985, 1710, 1665, 1320, 1225, 1160, 918 cm⁻¹. ¹³C NMR (CDCl₃): 14.335; 60.391; 107.452; 118.060; 122.650; 134.540; 144.393; 144.436; 166.990. HRMS (70 eV), Calc for C₉H₁₀O₃: 166.0629. Found: 166.0627.

Ethyl 4,4-dimethyl, 3-(3-Furyl) pentanoate 8. To a slurry of CuCN (77.0 g, 0.860 mol, 1.5 eq) in 2.5 L of diethyl ether at -78 °C was added *t*-BuLi (1.02 L of a 1.7M solution in hexanes, 1.73 mol, 3 eq) dropwise via addition funnel. This solution was stirred at -78 °C for 15 min and then allowed to warm to -45 °C at which temperature it was stirred for 30 min. The mixture was recooled to -78 °C and ethyl-3-furyl crotonate **7** (95.5 g, 0.575 mol) in 300 mL of diethyl ether was added via cannula. The red solution was warmed to -45 °C and trimethylsilyl chloride (146 mL, 1.15 mol, 2 eq) was added via syringe. The mixture was stirred at -45 °C for 30 min and then warmed to 0 °C and quenched via the dropwise addition of 10% aqueous HCl. The layers were separated and the aqueous layer was extracted twice with 100 mL of diethyl ether. The combined organic extracts were washed twice with 200 mL 10% aqueous NH₄OH and 100 mL brine. The combined aqueous layers were extracted with 100 mL of diethyl ether. The combined organic extracts were dried over Na₂SO₄, filtered and concentrated to give 129 g (0.575

mol, 100%) of the ester **8**. ^1H NMR (200 MHz, CDCl_3): δ 0.91 (s, 9H), 1.11 (t, $J = 6.6$ Hz, 3H), 2.67 (m, 3H), 4.00 (q, $J = 6.6$ Hz, 2H), 6.27 (m, 1H), 7.20 (m, 1H), 7.33 (t, $J = 1.8$ Hz, 1H). ^{13}C NMR (100 MHz, CDCl_3): δ 14.03, 27.72, 33.09, 36.07, 43.28, 60.17, 111.26, 124.84, 140.09, 141.99, 173.04. IR (neat): 2965, 1740, 1160, 1032, 873 cm^{-1} . HRMS (70 eV), calcd for $\text{C}_{13}\text{H}_{20}\text{O}_3$: 224.1412, Found: 224.1410.

4,4 Dimethyl 3-(3-Furyl) pentan-1-al (9). A solution of the ester **8** from above (5.15 g, 23.0 mmol) in 50 mL toluene was cooled to -78°C . A solution of *i*- Bu_2AlH (27.6 mL of a 1.0M solution in hexanes, 27.6 mmol, 1.2 eq) in 40 mL toluene was added dropwise over 1 h via cannula. The solution was stirred at -78°C for an additional 15 min after the addition was complete whereupon water was added dropwise to quench the reaction. The solution was warmed to 23°C , the layers were separated, and the aqueous layer was extracted twice with 25 mL of diethyl ether. The combined organic extracts were washed with 20 mL brine, then dried over Na_2SO_4 , filtered, and concentrated to give 3.92 g (0.022 mol, 95%) of aldehyde **9**. B.P. $92\text{--}98^\circ\text{C}$ (1-2 mm Hg). ^1H NMR (200 MHz, CDCl_3): δ 0.92 (s, 9H), 2.68 (m, 2H), 2.92 (dd, $J = 4.5$, 9.6 Hz, 1H), 6.26 (m, 1H), 7.21 (br s, 1H), 7.34 (t, $J = 2.4$ Hz, 1H), 9.54 (m, 1H). ^{13}C NMR (100 MHz, CDCl_3): δ 27.68, 33.16, 41.14, 44.44, 111.09, 124.74, 140.17, 142.60, 202.64. IR (neat): 2960, 2715, 1726, 1029, 866 cm^{-1} . HRMS (70 eV), calcd for $\text{C}_{11}\text{H}_{16}\text{O}_2$: 180.1149, Found: 180.1148.

Propiolate Adducts 10 and 11. To a stirred solution of 0.23 mL (1.66 mmol) of diisopropylamine in 5 mL THF at -78°C was added 0.66 mL (1.66 mmol) of *n*-BuLi (2.5M in hexanes) dropwise and quickly *via* syringe. This was allowed to stir 20 min and then a solution of

150 mg (1.52 mmol) of ethyl propiolate in 10 mL THF was added slowly dropwise from a pressure equalized addition funnel. The resulting mixture was allowed to stir for 20 min at -78°C and then aldehyde **9**, 0.25 g (1.39 mmol) in 10 mL THF was added in the same manner; the stirring was continued for an additional hour. At the end of this period, the cooling bath was removed and the solution was quenched with vigorous stirring by addition of half saturated ammonium chloride solution. The crude reaction mixture was then diluted with an equal volume of ethyl ether and the organic layer washed with 10% HCl, water, saturated sodium bicarbonate, water and finally saturated sodium chloride solution. The various washes were independently back extracted with fresh ether and the extract combined with the bulk organic phase. After drying (magnesium sulfate) and solvent removal *in vacuo*, the resinous material was purified by repetitive flash chromatography (20% ethyl acetate/ hexanes) to give 255 mg of *anti* adduct **10** and 77 mg of *syn* adduct **11** (3.3 : 1, 86%).

Anti acetylenic ester 10 : ^1H NMR (200 MHz, CDCl_3) δ 0.9 (s, 9H, *t*Bu), 1.32 (t, $J = 7.6$ Hz, 3H, $\text{CO}_2\text{CH}_2\text{CH}_3$), 1.68 (broad s, 1H, OH), 1.88 to 2.18 (band, 2H, $\text{CH}_2\text{CH}(\textit{t}\text{Bu})$), 2.45 (dd, $J = 12.4$ Hz, 4 Hz, 1H, $\text{CH}_2\text{CH}(\textit{t}\text{Bu})$), 4.1 to 4.27 (band, 1H, CHOH), 4.24 (q, $J = 7.6$ Hz, 2H, $\text{CO}_2\text{CH}_2\text{CH}_3$), 6.27 (m, 1H, $\text{OCH}=\text{CH}$), 7.23 (m, 1H, $\text{OCH}=\text{CH}$), 7.36 (m, 1H, $\text{OCH}=\text{C}-\text{C}$). ^{13}C NMR (CDCl_3) δ 13.6; 27.48; 32.72; 37.04; 42.72; 61.43; 61.81; 76.68; 87.69; 110.3; 124.28; 140.07; 142.24; 153.34. IR(CH_2Cl_2): 3400 (broad), 2955, 2220, 1705, 1360, 1245 cm^{-1} . Anal. calcd for $\text{C}_{16}\text{H}_{22}\text{O}_4$: C, 69.04; H, 7.97. Found: C, 68.97; H, 8.02.

Syn acetylenic ester 11 : ^1H NMR (200 MHz, CDCl_3) δ 0.88 (s, 9H, *t*Bu), 1.3 (t, $J = 7.3$ Hz, 3H, $\text{CO}_2\text{CH}_2\text{CH}_3$), 1.64 (broad s, 1H, OH), 1.76 to 2.2 (band, 2H, $\text{CH}_2\text{CH}(\textit{t}\text{Bu})$), 2.62 (dd, $J = 12.7$ Hz, 4 Hz, 1H, $\text{CH}_2\text{CH}(\textit{t}\text{Bu})$), 4.12 to 4.28 (band, 1H, CHOH), 4.23 (q, $J = 7.6$ Hz, 2H, $\text{CO}_2\text{CH}_2\text{CH}_3$), 6.23 (m, 1H, $\text{OCH}=\text{CH}$), 7.22 (m, 1H, $\text{OCH}=\text{CH}$), 7.38 (m, 1H, $\text{OCH}=\text{C}-\text{C}$). ^{13}C NMR (CDCl_3) δ 13.91; 27.85; 32.90; 37.54; 42.01; 59.93; 62.11; 75.98; 88.55; 110.72; 124.25; 140.70; 142.6; 153.46. IR(CH_2Cl_2): 3430 (broad), 2960, 2220, 1710, 1360, 1250 cm^{-1} . Anal. calcd for $\text{C}_{16}\text{H}_{22}\text{O}_4$: C, 69.04; H, 7.97. Found: C, 68.94; H, 7.99.

Anti TMS-acetylenic ester. The anti propiolate adduct **10** (33.77 g, 120 mmol), 32.2 g (470 mmol) of imidazole and a catalytic amount of 4-dimethyl aminopyridine were combined in 650 mL of CH_2Cl_2 . TMSCl (20 mL, 150 mmol) was slowly added *via* syringe. The reaction mixture was then stirred at 25 °C for 10 min and quenched with a saturated solution of NaHCO_3 . The organic layer was separated and washed with a saturated solution of NaHCO_3 and with a mixture of brine and sodium bicarbonate. The aqueous layer was back extracted with methylene chloride and the combined organic layer was dried on sodium sulfate. Removal of the solvent under reduced pressure and flash chromatography provided the TMS-acetylenic ester (38.31 g) in 90% yield. The product must be used immediately in the next reaction.

Anti TMS-cyclopentenone 5.

To a stirring solution of 20.2 mL (100 mmol) of [(1-ethoxycyclopropyl)oxy] trimethylsilane (purchased from Aldrich) in 76 mL diethyl ether was added 76 mL (76 mmol) of zinc chloride (1.0 M in ethyl ether, purchased from Aldrich) *via* syringe in one portion at room temperature. This mixture was then irradiated with ultrasound for 40 min followed by stirring at room temperature for an additional 10 min. At this point the heterogeneous mixture was cooled to 0°C and to this was added successively 2.15 g (10.5 mmol) of copper (I) bromide dimethyl sulfide complex, 14.7 g (41.94 mmol) of TMS-acetylenic ester in 152 mL THF and 17.5 mL (100 mmol) of hexamethylphosphoramide (HMPA). After addition, the mixture was allowed to stir 5 min at 0°C and then the ice bath was removed and the stirring was continued for 3 hours. The reaction was quenched with saturated ammonium chloride solution and the organic layer was washed with half saturated ammonium hydroxide solution until no blue color appeared in the wash. The resulting

organic layer was washed with water, saturated sodium chloride solution and dried over magnesium sulfate. Concentration followed by chromatography of the crude product gave the corresponding TMS-cyclopentenone **5** (13.98 g) in 82% yield.

^1H NMR (200 MHz, CDCl_3) δ 0.06 (s, 9H, TMS), 0.82 (s, 9H, *t*-Bu), 1.15 to 1.4 (band, 1H, $\text{CH}_2\text{CH}(t\text{-Bu})$), 1.22 (t, $J = 6.6$ Hz, 3H, $\text{CO}_2\text{CH}_2\text{CH}_3$), 1.82 to 2.18 (band, 2H, $\text{CH}_2\text{CH}(t\text{-Bu})$), 2.43 (X of ABX_2 , t, $J = 5.25$ Hz, 2H, COCH_2CH_2), 2.67 (AB of ABX_2 , $\Delta\nu = 50$ Hz, $J = 20.3$ Hz, 5.25 Hz, 2H, COCH_2CH_2), 4.16 (m, 2H, $\text{CO}_2\text{CH}_2\text{CH}_3$), 5.0 (m, 1H, CHOTMS), 6.24 (m, 1H, $\text{OCH}=\text{CH}$), 7.1 (m, 1H, $\text{OCH}=\text{CH}$), 7.34 (m, 1H, $\text{OCH}=\text{C}-\text{C}$). ^{13}C NMR (CDCl_3) δ -0.54; 13.7; 24.43; 27.33; 32.86; 34.14; 36.66; 41.73; 60.53; 67.93; 110.46; 124.58; 132.53; 140.32; 142.87; 162.48; 183.16; 203.54. IR(CH_2Cl_2): 1750, 1725, 1640 cm^{-1} . Anal. calcd for $\text{C}_{22}\text{H}_{34}\text{O}_5\text{Si}$: C, 64.99; H, 8.43. Found: C, 65.08; H, 8.45.

Photocycloadduct 23. To a toroidal photochemical reactor (30 mL) equipped with a reflux condenser and a water cooled Pyrex immersion well was added a solution of 50 mg (0.14 mmol) of cyclopentenone **5** in 30 mL hexanes. A uranium glass filter sleeve was placed in the immersion well and a 450 watt Hanovia medium pressure mercury vapor lamp was lowered inside the filter sleeve. The solution was irradiated for 5.5 h whereupon it was concentrated to give 55 mg (100%) of cycloadduct **23**. ^1H NMR (200 MHz, CDCl_3) δ 0.10 (s, 9H), 0.95 (s, 9H), 1.25 (t, $J = 7.2$ Hz, 3H), 1.96 (band, 5H), 2.53 (X of ABXX' , t, $J = 1.7, 10.4, 19.4$ Hz, 1H), 2.92 (B of ABXX' , $J = 9.8, 19.4$ Hz, 1H), 3.91 (m, 1H), 3.98 (dq, $J = 1.4, 7.2$ Hz, 2H); 5.08 (d, $J = 2.9$ Hz, 1H), 5.36, (s, 1H), 6.30 (d, $J = 2.9$ Hz, 1H). ^{13}C NMR (CDCl_3) δ 0.1; 14.6, 25.7, 29.8, 32.8, 38.6, 40.8, 50.6, 61.4, 64.8, 68.0, 73.6, 80.0, 92.0, 107.8, 148.8, 168.3, 212.1.

Anti cyclopentenone 25 (free OH). TMS-cyclopentenone **5** (3.9 g, 9.59 mmol) was dissolved in 150 mL of THF and 30 mL of water. To this solution was added a catalytic amount of PPTS and the mixture was stirred at rt for 2.5 h. The reaction mixture was diluted with diethyl ether, washed with water, saturated sodium bicarbonate, water and brine. The aqueous layer was back extracted with diethyl ether. The combined organic layer was dried over magnesium sulfate. Concentration under reduced pressure provided the cyclopentenone **25** (3.08 g) in 96% yield. ^1H NMR (200 MHz, CDCl_3): 0.86 (s, 9H, *t*-Bu), 1.32 (t, $J = 7.5$ Hz, 3H, $\text{CO}_2\text{CH}_2\text{CH}_3$), 1.85 to 2.32 (band, 3H, $\text{CHCH}_2\text{CH}(\text{OH})$), 2.45 (X of ABX_2 , t, $J = 5.25$ Hz, 2H, $\text{C}(\text{O})\text{CH}_2\text{CH}_2$), 2.7 (AB of ABX_2 , $\Delta\nu = 33.8$ Hz, dt, $J = 20.5$ Hz, 5.25 Hz, 2H, $\text{C}(\text{O})\text{CH}_2\text{CH}_2$), 4.26 (q, $J = 7.5$ Hz, 2H, $\text{CO}_2\text{CH}_2\text{CH}_3$), 4.87 (m, 1H, CHOH), 6.30 (m, 1H, O-CH=CH), 7.21 (m, 1H, O-CH=CH), 7.38 (m, 1H, O-CH=C-C). IR (CH_2Cl_2): 3435, 2961, 1739, 1714, 1631, 1394, 1368, 1031, 872 cm^{-1} .

Lactone 28. To a submersion well type photochemical photoreactor (540 mL) equipped with a reflux condenser and a water cooled Pyrex immersion well was added a solution of 1.54 g (4.6 mmol) of cyclopentenone **25** in 50 mL CH_2Cl_2 and 490 mL hexanes. A uranium glass cutoff filter sleeve was placed in the immersion well and 450 watt Hanovia medium pressure mercury vapor lamp was lowered inside the filter sleeve. The solution was irradiated for 7 h. The process was repeated a second time with the same quantities. The two resulting solutions were combined, concentrated under reduced pressure and flash chromatographed to provide 2.37 g (77%) of photoadducts **27:26** in a 1 : 1.3 ratio (correct isomer : epi isomer).

The previous mixture (2.37 g) was dissolved in 100 mL dry benzene. A catalytic amount of PPTS was added and the resulting solution was heat at reflux until disappearance of the correct isomer in the ^1H NMR spectrum (small aliquots are taken from the reaction and analyzed by ^1H NMR after the solvent has been removed). The reaction was complete after ca. 10 h. After cooling to rt the solution was diluted with diethyl ether and methylene chloride, washed with a saturated solution of sodium bicarbonate, with water and with brine. The aqueous layer was back extracted with methylene chloride and the combined organic layer was dried over magnesium sulfate. Concentration under reduced pressure and flash chromatography of the residue provided 760 mg (74%) of lactone **28** (25% from enone **25**). ^1H NMR (200 MHz, CDCl_3): δ 0.98 (s, 9H), 1.8 to 2.4 (m, 5H), 2.66 (m, 2H), 4.63 (s, 1H), 4.84 (dd, $J = 2.4, 5.4$ Hz, 1H), 5.32 (d, $J = 3.3$ Hz, 1H), 6.54 (d, $J = 3.3$ Hz, 1H). ^{13}C NMR (62.5 MHz, CDCl_3) δ 23.54, 28.67, 32.73, 37.42, 42.67, 55.29, 58.87, 62.26, 62.53, 88.31, 88.40, 102.82, 149.90, 166.80, 204.94. IR (CH_2Cl_2): 2960, 1785, 1738, 1690, 1210, 990 cm^{-1} . HRMS-ES, calcd for $\text{C}_{17}\text{H}_{20}\text{O}_4\text{Na}$ ($\text{M}+\text{Na}$) $^+$: 311.1259, Found: 311.1261.

Cyclopentenone amide 29. To a solution of the acetylene **36** (1.696 g, 5.29 mmol) in 40 mL of THF at -78 $^{\circ}\text{C}$ was added *n*-BuLi (3.97 mL of a 1.6M solution in hexanes, 0.635 mmol, 1.2 eq). The mixture was stirred for 15 min and dimethylcarbamoyl chloride (0.585 mL, 0.635 mmol, 1.2 eq) was added via syringe. After addition, the dry-ice/acetone bath was remove and the solution was allowed to warm to 25 $^{\circ}\text{C}$ for 45 min after which time the mixture was quenched with a 50% saturated, aqueous solution of NaHCO_3 . The layers were separated and the organic layer was washed twice with 20 mL H_2O and 20 mL brine, dried over Na_2SO_4 , filtered, and concentrated to afford 1.864 g of the acetylenic amide (90%). ^1H NMR (250 MHz, CDCl_3): δ 0.54 (m 6H), 0.85(s, 9H), 0.90 (t, $J = 7.9$ Hz, 9H), 1.82 (ddd, $J = 14.0, 12.5, 6$ Hz, 1H), 2.12

(m, 1H), 2.42 (dd, $J = 12.5, 2.5$ Hz), 2.96 (s, 3H), 31.6 (s, 3H), 4.12 (dd, $J = 12.5, 6$ Hz 1H), 6.21 (m, 1H), 7.19 (m, 1H), 7.34 (m, 1H). ^{13}C NMR (62.5 MHz, CDCl_3): δ 4.5, 6.59, 27.8, 33.02, 33.94, 38.1, 38.93, 42.81, 62.47, 77.43, 92.0, , 110.4, 124.8, 140.3, 142.5, 154.0.

Anal. calcd for $\text{C}_{22}\text{H}_{36}\text{O}_4\text{Si}$: C, 67.47; H, 9.52, N 3.58. Found: C, 67.56; H, 9.53, N, 3.54.

A solution of [(1-ethoxycyclopropyl)oxy]trimethylsilane (2.95 mL, 14.7 mmol, Salaün, J.; Marguerite, J. *Org. Synth., Coll. Vol. VII*, **1990**, 131) and ZnCl_2 (11 mL of a 1.0 M solution in diethyl ether, 11 mmol, Nakamura, E.; Kuwajima, I. *Org. Synth., Coll. Vol. VIII*, **1993**, 277-281.) in 11 mL diethyl ether was placed in a flame dried, three-neck, 100 mL round bottom flask under nitrogen. The solution was irradiated in an ultrasonic cleaner for 45 min. The resulting heterogeneous mixture was transferred via cannula to a solution of $\text{CuBr}\cdot\text{SMe}_2$ (300 mg, 1.46 mmol) in 20 mL THF at 0 °C. The mixture was stirred for 10 min and the ice bath was removed. The acetylenic ester **36** (2.00 g, 4.57 mmol) in 2 mL THF was added via cannula while hexamethylphosphoramide (HMPA) (2.6 mL, 14.8 mmol) was added via syringe. The reaction mixture was stirred for 4 h at 23 °C and then quenched by the addition of saturated aqueous NH_4Cl . The layers were separated and the organic layer was washed with concentrated NH_4OH until the aqueous washes were no longer blue. The organic layer was washed with 10 mL H_2O and 10 mL brine. The combined aqueous layers were extracted with 20 mL of diethyl ether and the combined organic extracts were dried over Na_2SO_4 , filtered and concentrated. The residue was purified via flash column chromatography (15% EtOAc/hexanes) to give 1.81 g (79%) of the cyclopentenone. ^1H NMR (200 MHz, CDCl_3): δ 0.50 (m 6H), 0.81(s, 9H), 0.87 (t, $J = 7.9$ Hz, 9H), 1.83 (m, 1H), 1.90 - 2.80 (band, 6H), 2.87 (s, 3H), 2.99 (s, 3H), 4.68 (dd, $J = 9.6, 5$ Hz 1H), 6.22 (brs, 1H), 7.14 (brs, 1H), 7.30 (brs, 1H). ^{13}C NMR (62.5 MHz, CDCl_3): δ 4.5, 6.59, 27.8, 29.0, 33.02, 34.0, 34.5, 38.0, 41.5, 69.0, 111.0, 124.8, 137.0, 140.1, 141.0, 164.2, 205.0. IR (neat) 1630, 1710 cm^{-1} . Anal. calcd for $\text{C}_{22}\text{H}_{36}\text{O}_4\text{Si}$: C, 67.07; H, 9.23, N 3.13. Found: C, 67.22; H, 9.23, N, 3.06.

A solution of the triethylsilylether (1.0 g, 2.23 mmol) and 20 mg of PPTS in 40 mL of THF and 10 mL of water was stirred at rt for 2.5 h. The reaction mixture was diluted with diethyl ether, washed with water, saturated sodium bicarbonate, water and brine. The aqueous layer was back

extracted with diethyl ether. The combined organic layer was dried over magnesium sulfate. Concentration under reduced pressure provided 633 mg of the hydroxycyclopentenone **29** (85%). ^1H NMR (200 MHz, CDCl_3): 0.83 (s, 9H), 1.97 (m, 1H), 2.15 (m, 2H), 2.42 (m, 2H), 2.60 (m, 2H), 2.88 (s, 3H), 2.99 (s, 3H), 3.70 (s, 1H), 4.38 (m, 1H), 6.25 (brs, 1H), 7.15 (brs, 1H), 7.33 (brs, 1H). ^{13}C NMR (62.5 MHz, CDCl_3): δ 26.5, 33.43, 34.57, 34.8, 35.43, 38.42, 43.41, 70.03, 110.9, 112.3, 125.2, 140.2, 142.7, 165.5, 182.3, 204.3. IR (neat) 3380, 2960, 1710, 1620, 1400 cm^{-1} . Anal. calcd for $\text{C}_{19}\text{H}_{27}\text{NO}_4$ C, 68.44; H, 8.16; N, 4.20; Found: C, 68.29; H, 8.23, N, 4.16.

Photocycloadducts 30 and 31. A solution of 200 mg (0.60 mmol) of hydroxycyclopentenone **29** in 100 mL of 5:1 hexanes:benzene was placed in a toroidal photochemical photoreactor (100 mL) equipped with a reflux condenser and a water cooled Pyrex immersion. A uranium glass filter sleeve was placed in the immersion well and 450 watt Hanovia medium pressure mercury vapor lamp was lowered inside the filter sleeve. The solution was irradiated for 7 h. The solution was concentrated under reduced pressure. Analysis of the crude product indicated a 3:1 mixture of diastereomers **30:31** based on integration of the vinyl ether protons and the methine adjacent to the vinyl ether oxygen. The product was purified by flash chromatography to provide 127 mg (21%) minor photoadduct **31**. 0.90 (s, 1H), 1.80 - 2.05 (m, 5H), 2.27- 2.58 (m, 3H), 2.85 (m, 1H), 2.90 (s, 3H), 3.16 (s, 3H), 3.12 (s, 1H), 4.30 (m, 1H), 5.04 (d, $J = 3$ Hz, 1H), 5.32 (s, 1H), 6.24 (d, $J = 3$ Hz, 1H). and 382 mg (64%) major photoadduct **30**. ^1H NMR (250 MHz, CDCl_3): 0.81 (s, 9H), 1.72 (ddd, $J = 5, 12, 12$, 1H), 1.84 - 2.18 (m, 4H), 2.31- 2.89 (m, 3H), 2.90 (s, 3H), 3.25 (s, 3H), 3.82 (s, 1H), 4.28 (m,

1H), 4.88 (s, 1H), 5.24 (d, $J = 3$ Hz, 1H), 6.24 (d, $J = 3$ Hz, 1H). Anal. calcd for $C_{19}H_{27}NO_4$ C, 68.44; H, 8.16; N, 4.20; Found: C, 68.65; H, 8.33, N, 4.41.

Acetylenes 34 and 35. A solution of aldehyde **5** (52 g, 0.289 mol) in 200 mL THF was added dropwise to a solution of ethynylmagnesium bromide (650 mL of a 0.5M solution in THF, 0.325 mol) at -60 °C. The mixture was stirred at -60 °C for 30 min and then quenched by the addition of saturated aqueous NH_4Cl . The layers were separated and the aqueous layer was extracted twice with 100 mL of diethyl ether. The combined organic extracts were washed with 50 mL brine, dried over Na_2SO_4 , filtered and concentrated. The residue was purified by flash chromatography by elution with 10% EtOAc in hexanes to produce 31.6 g of the *anti* product, **34** (0.154 mol, 53%) and 26.4 g of the *syn* product, **35** (0.128 mol, 44%). **Data for *syn* isomer 35:** 1H NMR (400 MHz, $CDCl_3$): δ 0.87 (s, 9H), 1.82 (m, 2H), 2.06 (ddd, $J = 13.8, 10.4, 2.7$ Hz, 1H), 2.40 (d, $J = 2.1$ Hz, 1H), 2.61 (dd, $J = 12.4, 2.7$ Hz, 1H), 4.07 (m, 1H), 6.23 (m, 1H), 7.20 (m, 1H), 7.34 (m, 1H). ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 27.93, 32.91, 38.46, 42.18, 60.17, 72.29, 85.70, 110.96, 124.77, 140.63, 142.50. IR(neat): 3420, 3300, 2950, 2905, 2880, 1727 cm^{-1} . HRMS (x eV), Calcd for $C_{13}H_{18}O_2$: 206.1307, Found: **Data for *anti* isomer 34** 1H NMR (400 MHz, $CDCl_3$): δ 0.87 (s, 9H), 1.91 (td, $J = 12.4, 4.8$ Hz, 1H), 2.00 (td, $J = 12.6, 2.7$ Hz, 1H), 2.12 (br d, $J = 2.8$ Hz, 1H), 2.44 (d, $J = 2.0$ Hz, 1H), 2.44 (dd, $J = 12.1, 2.7$ Hz, 1H), 4.01 (m, 1H), 6.24 (m, 1H), 7.18 (m, 1H), 7.32 (m, 1H). ^{13}C NMR (62.5 MHz, $CDCl_3$): δ 27.90, 33.03, 38.19, 43.37, 62.23, 73.51, 84.64, 110.75, 124.95, 140.26, 142.46. IR (thin film): 3360, 3300, 2950, 2900, 2880, 1360, 1020 cm^{-1} . HRMS (x eV), calcd for $C_{13}H_{18}O_2$: 206.1307, Found: 206.1313.

Mitsunobu inversion of 34. To a mechanically stirred solution of *anti* alcohol **34** (120.7 g, 0.586 mol), triphenylphosphine (184.4 g, 0.703 mol, 1.2 eq), and *p*-nitrobenzoic acid (117.5 g, 0.703 mol, 1.2 eq) in 3 L of toluene at 0 °C, was added diethyl azodicarboxylate (110.7

mL, 0.703 mol, 1.2 eq). The reaction mixture was warmed to 23 °C and allowed to stir for 1 h. The solution was then concentrated and the residue taken up in a 15% EtOAc/hexanes solution and filtered through a pad of Celite topped with silica gel. The filtrate was concentrated and the residue was dissolved in a solution of 800 mL MeOH, 300 mL THF, 300 mL H₂O and 62 g NaOH. This mixture was stirred for 1 h and the solvents were removed under reduced pressure. The aqueous residue was extracted with three times with 200 mL of diethyl ether and the combined organic extracts were dried over Na₂SO₄, filtered and concentrated to give *syn* alcohol **35** (120 g, 0.583 mol, 99%).

Acetylenic ester 36. To a solution of alcohol **35** (56.5 g, 0.274 mol) and triethylamine (42.0 mL, 0.301 mol, 1.1 eq) in 500 mL CH₂Cl₂ at 0 °C was added triethylsilyl chloride (51.0 mL, 0.301 mol, 1.1 eq) via syringe. The mixture was allowed to warm to 23 °C and stir for 45 min. The reaction mixture was then quenched with water and the layers were separated. The organic layer was dried over Na₂SO₄, filtered and concentrated. The residue was dissolved in hexanes and filtered through a pad of Celite topped with silica gel. The filtrate was concentrated to give 83.7 g of the silyl ether **36** (0.261 mol, 95%). ¹H NMR (400 MHz, CDCl₃): δ 0.56 (m, 6H), 0.85 (s, 9H), 0.91 (t, *J* = 7.9 Hz, 9H), 1.73 (m, 1H), 2.10 (ddd, *J* = 13.5, 10.6, 2.4 Hz, 1H), 2.33 (d, *J* = 2.0 Hz, 1H), 2.51 (dd, *J* = 12.1, 2.3 Hz, 1H), 4.02 (dt, *J* = 10.6, 1.9 Hz, 1H), 6.21 (m, 1H), 7.14 (m, 1H), 7.34 (m, 1H). ¹³C NMR (62.5 MHz, CDCl₃): δ 4.85, 6.79, 28.00, 32.90, 39.71, 42.34, 60.37, 71.55, 86.44, 111.30, 124.90, 140.52, 142.23. IR (neat): 3310, 2950, 2880, 1090 cm⁻¹. HRMS-ES, calcd for C₁₉H₃₂O₂NaSi (M+Na)⁺: 343.2069, Found: 343.2054.

To a solution of the silyl ether acetylene above (257.64 g, 0.804 mol) in 1.5 L of THF at -78 °C was added *n*-BuLi (603.1 mL of a 1.6M solution in hexanes, 0.965 mol, 1.2 eq). The mixture was stirred for 15 min and ethyl chloroformate (92.3 mL, 0.965 mol, 1.2 eq) was added via syringe. After addition, the dry-ice/acetone bath was remove and the solution was allowed to

warm to 25 °C for 45 min after which time the mixture was quenched with a 50% saturated, aqueous solution of NaHCO₃. The layers were separated and the organic layer was washed twice with 100 mL H₂O and 100 mL brine, dried over Na₂SO₄, filtered, and concentrated to afford 315.5 g of **36** (0.804 mol, 100%). ¹H NMR (400 MHz, CDCl₃): δ 0.56 (q, *J* = 7.9 Hz, 6H), 0.86 (s, 9H), 0.94 (t, *J* = 7.9 Hz, 9H), 1.28 (t, *J* = 7.1 Hz, 3H), 1.82 (ddd, *J* = 14.0, 12.5, 2.5 Hz, 1H), 2.11 (m, 1H), 2.60 (dd, *J* = 12.5, 2.5 Hz), 4.15 (m, 1H), 4.20 (q, *J* = 7.1 Hz, 2H), 6.21 (m, 1H), 7.20 (m, 1H), 7.34 (m, 1H). ¹³C NMR (62.5 MHz, CDCl₃): δ 4.74, 6.70, 13.98, 27.96, 32.93, 38.76, 42.24, 60.27, 61.87, 75.76, 89.33, 111.11, 124.48, 140.59, 142.42, 153.47. IR (neat): 2950, 2880, 1720 cm⁻¹. Anal. calcd for C₂₂H₃₆O₄Si: C, 67.30; H, 9.24. Found: C, 67.36; H, 9.19.

Cyclopentenone 37. A solution of [(1-ethoxycyclopropyl)oxy]trimethylsilane (75.5 mL, 0.376 mol, 2.4 eq, Salaün, J.; Marguerite, J. *Org. Synth., Coll. Vol. VII*, **1990**, 131) and ZnCl₂ (333 mL of a 0.84 M solution in diethyl ether, 0.279 mol, 1.8 eq, Nakamura, E.; Kuwajima, I. *Org. Synth., Coll. Vol. VIII*, **1993**, 277-281.) in 570 mL diethyl ether was placed in a flame dried, three-neck, 1L round bottom flask under nitrogen. The solution was irradiated in an ultrasonic cleaner for 45 min. The resulting heterogeneous mixture was transferred via cannula to a solution of CuBr•SMe₂ (8.08 g, 38.8 mmol, 0.25eq) in 200 mL THF at 0 °C. The mixture was stirred for 10 min and the ice bath was removed. The acetylenic ester **36** (61 g, 0.155 mol) in 370 mL THF was added via cannula while hexamethylphosphoramide (HMPA) (65.6 mL, 0.377 mol, 2.4 eq) was added via syringe. The reaction mixture was stirred for 4 h at 23 °C and then quenched by the addition of saturated aqueous NH₄Cl. The layers were separated and the organic layer was washed with concentrated NH₄OH until the aqueous washes were no longer blue. The organic layer was washed with 100 mL H₂O and 100 mL brine. The combined aqueous layers were extracted with 200 mL of diethyl ether and the combined organic extracts were dried over

Na₂SO₄, filtered and concentrated. The residue was purified via flash column chromatography (15% EtOAc/hexanes) to give 56.8 g (0.126 mol, 82%) of **37**. ¹H NMR (400 MHz, CDCl₃) δ 0.47 (q, *J* = 7.9 Hz, 6H), 0.82 (s, 9H), 0.85 (t, *J* = 7.9 Hz, 9H), 1.17 (t, *J* = 7.1 Hz, 3H), 1.56 (ddd, *J* = 13.6, 11.7, 3.3 Hz, 1H), 2.00 (ddd, *J* = 11.6, 9.5, 1.9 Hz, 1H), 2.35 (dt, *J* = 6.9, 1.7 Hz, 1H), 2.49 (m, 2H), 2.55 (ddd, *J* = 19.8, 6.7, 3.4 Hz, 1H), 2.76 (ddd, *J* = 19.8, 6.9, 3.3 Hz, 1H), 4.15 (m, 2H), 4.91 (dd, *J* = 9.5, 3.2 Hz, 1H), 6.18 (m, 1H), 7.14 (m, 1H), 7.31 (m, 1H). ¹³C NMR (62.5 MHz, CDCl₃) δ 5.04, 7.13, 14.45, 25.87, 28.36, 33.67, 34.86, 37.84, 42.87, 61.42, 68.96, 112.14, 125.36, 131.51, 140.94, 142.44, 163.29, 186.98, 204.34. IR(CH₂Cl₂): 2980, 1750, 1720, 1215, 1080, 1025 cm⁻¹. HRMS (ES), calcd for C₂₅H₄₀O₅SiNa: (M+Na⁺) 471.2543, Found: 471.2562.

Photoadduct 38. To a submersion well type photochemical reactor (540 mL) equipped with a reflux condenser and a water cooled Pyrex immersion well was added a solution of 20 g (44.6 mmol) of cyclopentenone **37** in 540 mL hexanes. A uranium glass filter sleeve was placed in the immersion well and a 450 watt Hanovia medium pressure mercury vapor lamp was lowered inside the filter sleeve. The solution was irradiated for 17 h whereupon it was concentrated to give 20 g of cycloadduct **38** (44.6 mol, 100%). ¹H NMR (400 MHz, CDCl₃): δ 0.57 (m, 6H), 0.93 (s, 9H), 0.93 (t, *J* = 7.7 Hz, 9H), 1.22 (t, *J* = 7.1 Hz, 3H), 1.73 (ddd, *J* = 12.9, 8.5, 6.9 Hz, 1H), 1.93 (m, 2H), 2.04 (ddd, *J* = 12.8, 6.8, 6.8 Hz, 1H), 2.36 (ddd, *J* = 14.3, 11.7, 9.4 Hz, 1H), 2.55 (ddd, *J* = 19.7, 11.7, 3.1 Hz, 1H), 2.83 (ddd, *J* = 19.6, 9.7, 9.7 Hz, 1H), 4.04 (m, 2H), 4.24 (m, 1H), 4.94 (s, 1H), 5.23 (d, *J* = 2.9 Hz, 1H), 6.29 (d, *J* = 2.9 Hz, 1H). ¹³C NMR (62.5 MHz, CDCl₃): δ 4.94, 6.77, 13.99, 22.56, 29.30, 32.36, 39.26, 40.26, 55.26, 61.45, 63.43, 66.40, 73.93, 85.81, 105.21, 149.60, 168.46, 211.52. IR(thin film): 2950, 2910, 2885, 1740, 1598 cm⁻¹. Anal. calcd for C₂₅H₄₀O₅Si: C, 66.92; H, 8.99. Found: C, 66.67; H, 9.02.

Lactone 28. To a solution of the silyl ether **38** (14.2 g, 0.032 mol) in 65 mL acetonitrile at 0 °C was added 6.5 mL of a 48% aqueous HF solution dropwise via syringe. After the addition was complete, the reaction mixture was allowed to warm to 23 °C and stir for 1 h. The solution was then cooled to 0 °C, diluted with 100 mL Et₂O and quenched by the addition of saturated aqueous NaHCO₃. The layers were separated, the aqueous layer was extracted twice with 50 mL of diethyl ether, and the combined organic extracts were washed with 50 mL brine, dried over Na₂SO₄, filtered, and concentrated to give the crude alcohol **39**. **Data for alcohol 39:** ¹H NMR (250 MHz, CDCl₃) δ 0.90 (s, 9H), 1.24 (t, *J* = 6.9 Hz, 3H), 1.67 (m, 1H), 1.8 to 2.15 (m, 3H), 2.23 (broad s, 1H) 2.3 to 2.63 (m, 2H), 2.87 (m, 1H), 4.0 to 4.23 (m, 3H), 4.89 (s, 1H), 5.24 (d, *J* = 2.9 Hz, 1H), 6.27 (d, *J* = 2.9 Hz, 1H). ¹³C NMR (62.5 MHz, CDCl₃) δ 13.68, 20.72, 28.54, 31.65, 37.66, 39.91, 53.97, 61.14, 62.38, 63.09, 64.41, 72.92, 86.65, 104.90, 148.99, 168.07, 210.29. IR (CDCl₃): 3520, 2240, 1740, 1715, 1595 cm⁻¹. Anal. calcd for C₁₉H₂₆O₅: C, 68.24; H, 7.84. Found: C, 68.00; H, 7.86.

Methanesulfonyl chloride (2.97 mL, 0.038 mol, 1.2 eq) was added dropwise to a solution of the crude alcohol **39** (0.032 mol) and Et₃N (5.8 mL, 0.042 mol, 1.3eq) in 110 mL CH₂Cl₂ at 0 °C. This solution was stirred for 45 min at 0 °C and then the reaction was quenched by the addition of saturated aqueous NaHCO₃. The layers were separated, the aqueous layer was extracted twice with 50 mL CH₂Cl₂, and the combined organic layers were washed with 50 mL H₂O, dried over Na₂SO₄, filtered and concentrated. The resulting mesylate was carried on directly to the lactonization. **Data for mesylate 40:** ¹H NMR (250 MHz, CDCl₃) δ 0.92 (s, 9H), 1.22 (t, *J* = 7.1 Hz, 3H), 1.91 to 2.03 (m, 3H), 2.2 to 2.38 (m, 2H), 2.58 (m, 1H), 2.87 (m, 1H), 3.01 (s, 3H), 4.03 to 4.27 (m, 2H), 4.91 (s, 1H), 4.93 (m, 1H), 5.24 (d, *J* = 2.9 Hz, 1H), 6.33 (d, *J* = 2.9 Hz, 1H). ¹³C NMR (100 MHz, CDCl₃) δ 13.64, 22.53, 28.75, 32.10, 36.34, 38.26, 39.58, 54.27, 61.74, 62.84, 63.12, 63.53, 81.06, 85.62, 103.82, 149.98, 167.16, 208.92. IR(CDCl₃):

2260, 1750, 1725, 1600 cm^{-1} . Anal. calcd for $\text{C}_{20}\text{H}_{28}\text{O}_7\text{S}$: C, 58.23; H, 6.84. Found: C, 58.29; H, 6.85.

A mixture of mesylate **40** (0.032 mol) and ~70 g $4\text{\AA}$ powdered molecular sieves in 1 L of EtOH was stirred at reflux for 26 h at which time no mesylate remained (by ^1H NMR). 1.8 mL H_2O was added and the mixture was heated at reflux for an additional 8 h. The mixture was cooled to 23 $^\circ\text{C}$, filtered through Celite and concentrated to give a mixture of lactone **28** and the corresponding hydroxy ester **42** (by ^1H -NMR). The residue was dissolved in 1 L of benzene in a 2 L round bottom flask equipped with a Dean-Stark trap and a condenser and 1 g pyridinium *p*-toluenesulfonic acid was added. The solution was heated at reflux for 16 h with 100 mL portions being drained from the Dean-Stark trap three times (about every 4 h). At this point, no hydroxy ester remained by ^1H NMR. The solution was cooled to 23 $^\circ\text{C}$ and concentrated. The residue was dissolved in CH_2Cl_2 , washed with 100 mL NaHCO_3 and 100 mL H_2O . The aqueous layers were extracted twice with 50 mL CH_2Cl_2 , and the combined organic layers were dried over Na_2SO_4 , filtered, and concentrated. The crude product was recrystallized from diethyl ether to give 5.78 g lactone **28** (0.020 mol, 63% from **38**). ^1H NMR (200 MHz, CDCl_3): δ 0.98 (s, 9H), 1.8 to 2.4 (m, 5H), 2.66 (m, 2H), 4.63 (s, 1H), 4.84 (dd, $J = 2.4, 5.4$ Hz, 1H), 5.32 (d, $J = 3.3$ Hz, 1H), 6.54 (d, $J = 3.3$ Hz, 1H). ^{13}C NMR (62.5 MHz, CDCl_3) δ 23.54, 28.67, 32.73, 37.42, 42.67, 55.29, 58.87, 62.26, 62.53, 88.31, 88.40, 102.82, 149.90, 166.80, 204.94. IR (CH_2Cl_2): 2960, 1785, 1738, 1690, 1210, 990 cm^{-1} . HRMS-ES, calcd for $\text{C}_{17}\text{H}_{20}\text{O}_4\text{Na}$ ($\text{M}+\text{Na}$) $^+$: 311.1259, Found: 311.1261.

Enone 43 To a solution of lactone **28** (510 mg, 1.8 mmol) in 20 mL of EtOAc which had been washed with concentrated HCl, was added 340 mg PhSeCl (1.8 mmol, 1 eq). This mixture was stirred at 23 $^\circ\text{C}$ for 1h. Solid NaHCO_3 was added and the mixture was stirred another 5 min.

THF (20 mL) was added followed by NaIO₄ (2.27 g, 10.6 mmol, 6 eq) in 15 mL H₂O via cannula. The mixture was stirred for 2 h whereupon 20 mL of 10% Na₂CO₃ was added. The mixture was filtered and the filtrate was extracted with diethyl ether (50 mL), the layers were separated and the aqueous layer was extracted twice more with 50 mL of diethyl ether. The combined organic extracts were washed with 30 mL Na₂S₂O₃, 30 mL H₂O and 30 mL brine. The organic extracts were dried over Na₂SO₄, filtered and concentrated. The residue was purified via flash column chromatography (50% EtOAc:hexanes) to give 400 mg of enone **43** (1.4 mmol, 78%). ¹H NMR (200 MHz, CDCl₃): δ 1.02 (s, 9H), 2.2 (m, 1H), 2.37 (m, 2H), 4.75 (s, 1H), 4.91 (dd, *J* = 5.1, 1.5 Hz, 1H), 5.11 (d, *J* = 3.0 Hz, 1H), 6.4 (d, *J* = 3 Hz, 1H), 6.52 (d, *J* = 6.7 Hz, 1H), 7.51 (d, *J* = 6.7 Hz, 1H). ¹³C NMR (62.5 MHz, CDCl₃) δ 28.75, 32.91, 38.28, 54.35, 56.77, 63.48, 67.96, 83.31, 86.49, 102.32, 141.50, 150.60, 159.52, 167.58, 194.50. IR (CH₂Cl₂): 2963, 1778, 1715, 1602, 909 cm⁻¹. Anal. calcd for C₁₇H₁₈O₄: C, 71.31; H, 6.34. Found: C, 71.23; H, 6.36.

Triol 52. To the enone **43** (3.9 g, 13.6 mmol) in 50 mL acetone was added 400 mL of a freshly prepared solution of dimethyldioxirane (0.05M in acetone, 20.0 mmol, 1.5 eq), followed by 50 mL H₂O. This mixture was stirred for 8h whereupon 520 mg of *p*-toluenesulfonic acid (2.72 mmol, 0.2 eq) was added and the mixture was stirred for an additional 15h. The solution was then concentrated to 150 mL via rotary evaporation with the temperature of the water bath not exceeding 30 °C. EtOAc (150 mL) was added, the layers were separated and the organic layers were washed with 50 mL H₂O and with 50 mL brine, dried over Na₂SO₄, filtered and concentrated to afford a pale yellow solid which was washed with CH₂Cl₂ and filtered to give 4.34 g (12.8 mmol, 94%) of triol **52** as a mixture of isomers. ¹H NMR (200 MHz, acetone d₆) δ 1.14 (s, 9H), 1.87 (dd, *J* = 14 Hz, 6.7 Hz, 1H), 2.25 (dd, *J* = 14.9, 6.7 Hz, 1H), 2.8 (ddd, *J* = 14.9,

14.0, 7.5 Hz, 1H), 3.67 (s, 1H), 4.58 (m, 1H), 4.86 (d, $J = 7.5$ Hz, 1H), 5.37 (s, 1H), 5.51 (d, $J = 4.5$ Hz, 1H), 6.13 (d, $J = 6.0$ Hz, 1H), 8.04 (d, $J = 6.0$ Hz, 1H). ^{13}C NMR (CDCl_3) δ 31.69, 33.58, 36.03, 52.76, 56.88, 56.91, 66.11, 81.20, 85.43, 103.03, 103.33, 132.71, 165.97, 170.63, 199.03. IR (thin film): 3450, 2950, 1775, 1710, 1360, 1190 cm^{-1} . HRMS (70 eV), calcd for $\text{C}_{17}\text{H}_{23}\text{O}_7$ ($\text{M}+\text{H}$): 339.1444, Found: 339.1440.

Enone bis-methyl acetals 53. To a solution of triol **52** (2.66 g, 7.89 mmol) in 107 mL methanol and 27 mL trimethylorthoformate was added 215 mg *p*-toluenesulfonic acid (1.1 mmol, 0.14eq). The reaction mixture was stirred for 3 h at 23 °C whereupon 125 mL of diethyl ether and 215 mg NaHCO_3 were added. After stirring for an additional 10 min, the solution was filtered and concentrated and the resulting white solid was recrystallized with diethyl ether to give 2.36 g of the bis methyl acetal **53a** (6.4 mmol, 82%). The filtrates were concentrated to give 0.43 g (1.18 mmol, 15%) of a minor diastereomer **53b** of the bis-acetal. **Data for 53a (major isomer):** ^1H NMR (200 MHz, CDCl_3): δ 1.13 (s, 9H), 1.9–2.1 (m, 2H), 2.46 (d, $J = 5.25$ Hz, 1H), 2.67 (m, 1H), 3.18 (s, 3H), 3.34 (s, 1H), 3.47 (s, 3H), 4.52 (dd, $J = 5.25, 5.25$ Hz, 1H), 4.72 (s, 1H), 4.75 (d, $J = 7.5$ Hz, 1H), 5.2 (d, $J = 5.25$ Hz, 1H), 6.2 (d, $J = 5.7$ Hz, 1H), 7.78 (d, $J = 5.7$ Hz, 1H). ^{13}C NMR (100 MHz, CDCl_3) δ 30.21, 33.04, 35.19, 54.97, 56.50, 56.62, 57.14, 63.35, 64.90, 80.06, 85.14, 109.60, 109.86, 132.56, 164.46, 170.12, 197.97. IR (CH_2Cl_2): 2969, 1780, 1736, 1300 cm^{-1} . HRMS (70 eV), calcd for $\text{C}_{19}\text{H}_{27}\text{O}_7$ ($\text{M}+\text{H}$): 367.1757. Found: 367.1758.

Data for minor isomer 53b: ^1H NMR (200 MHz, CDCl_3): 1.12 (s, 9H), 1.9 (m, 1H), 2.35 to 2.75 (m, 2H), 3.38 (s, 3H), 3.41 (s, 1H), 3.87 (s, 3H), 4.03 (d, $J = 5.25$ Hz, 1H), 4.53 (s, 1H), 4.87 (dd, $J = 8.1, 3.0$ Hz, 1H), 5.12 (d, $J = 5.25$ Hz, 1H), 6.31 (d, $J = 5.7$ Hz, 1H), 7.8 (d, $J = 5.7$ Hz, 1H).

Conversion of 53b to 53a. To 0.87 g (2.37 mmol) of the minor diastereomer bis-methyl acetal **53b** in 55 mL acetone and 5.5 mL H₂O was added 5.5 mL 6N HCl. The mixture was stirred at 23 °C for 18 h, then cooled to 0 °C and slowly quenched with solid NaHCO₃. Diethyl ether (60 mL) was added and the aqueous layer was washed twice with 25 mL EtOAc. The combined organic layers were washed with 25 mL H₂O, and 25 mL brine, dried over Na₂SO₄, filtered and concentrated to afford 0.80 g (2.18 mmol, 92%) of acetal **53a**.

Hydroxy bis-methyl acetal 54. To a solution of diethylamine (84 μ L, 0.81 mmol, 0.2 eq) in 70 mL THF at -78 °C was added *t*-BuLi (5.93 mL of a 1.5M solution in hexanes, 8.9 mmol, 2.2 eq) dropwise via syringe. This solution was stirred for 30 min at -78 °C and then the bis-methyl acetal **53a** in 70 mL THF was added via cannula. The mixture was stirred for 30 min at -78 °C and then allowed to warm to -20 °C at which temperature it was stirred until the solution became cloudy and the yellow color faded (approximately 30 min). The solution was recooled to -78 °C and 1.48 g of the Davis oxaziridine in 35 mL THF was added via cannula. The mixture was allowed to gradually warm to 0 °C at which temperature it was stirred for an additional 1h. The reaction mixture was quenched with saturated aqueous NH₄Cl, diluted with 175 mL of diethyl ether and the layers were separated. The organic layer was washed twice with 25 mL brine, dried over Na₂SO₄, filtered, concentrated. The residue was purified via flash column chromatography (50% EtOAc/hexanes) to give 1.51 g (3.95 mmol, 98%) of the alcohol **54**. ¹H NMR (250 MHz, CDCl₃): 1.1 (s, 9H), 1.88 (m, 1H), 2.19 (d, *J* = 5.2 Hz, 1H), 2.52 to 2.8 (m, 2H), 3.1 (s, 3H), 3.45 (s, 3H), 4.0 (s, 1H), 4.51 (dd, *J* = 5.3, 5.2 Hz, 1H), 4.78 (d, *J* = 7.9 Hz, 1H), 5.12 (s, 1H), 5.13 (d, *J* = 5.3 Hz, 1H), 6.28 (d, *J* = 6.1 Hz, 1H), 7.72 (d, *J* = 6.1 Hz, 1H). ¹³C NMR (100MHz, CDCl₃) δ 30.05, 33.08, 34.40, 54.95, 55.03, 56.45, 63.77, 67.16, 81.77, 82.15, 84.79, 107.97, 109.00, 129.84, 163.61, 172.15, 199.62. IR (thin film): 3350, 3250, 2920,

1760, 1710, 1330, 1160 cm^{-1} . HRMS (70 eV), calcd for $\text{C}_{19}\text{H}_{27}\text{O}_8$ ($\text{M}+\text{H}$): 383.1706. Found: 383.1704.

Hydroxy ketone 56. To a solution of 12.4 mg (0.032 mmol) of hydroxy bis-methyl acetal **54** in 23 mL CH_2Cl_2 , containing 4Å molecular sieves was added 35 mg (0.2 mmol, 6.25 eq) of predried *p*-toluenesulfonic acid and the resulting solution was stirred at 23 °C for 55 min. The solution was filtered, diluted with CH_2Cl_2 , washed with 10 mL H_2O and 10 mL brine. The aqueous layers were combined and extracted with 10 mL CH_2Cl_2 . The combined organic extracts were dried over MgSO_4 , filtered and concentrated. The residue was purified via flash column chromatography (50% EtOAc in hexanes) to afford 8.2 mg (0.023 mmol, 73%) hydroxy ketone **56**. ^1H NMR (400 MHz, CDCl_3): δ 0.96 (s, 9H), 2.18 (m, 1H), 2.4 (m, 2H), 3.01 (dd, J = 6.8, 1.8 Hz, 1H), 3.28 (s, 3H), 4.35 (dd, J = 9.4, 1.8 Hz, 1H), 4.43 (dd, J = 9.4, 6.8 Hz, 1H), 4.9 (d, J = 4.3 Hz, 1H), 5.5 (s, 1H), 6.12 (d, J = 6 Hz, 1H), 7.61 (d, J = 6 Hz, 1H). ^{13}C NMR (100 MHz, CDCl_3) δ 29.69, 30.59, 33.08, 35.15, 55.76, 57.52, 69.18, 75.01, 77.23, 84.66, 110.94, 133.00, 159.45, 167.30, 196.50, 209.28. IR (thin film): 3490, 2940, 1780, 1750, 1720, 1100 cm^{-1} .

Mono acetate 57. To a solution of 27.3 mg (0.07 mmol) of hydroxy bis-methyl acetal **54** in 10 mL CH_2Cl_2 was added 31 mg (0.25 mmol) of 4-dimethyl aminopyridine and 12 μL (0.125 mmol) of acetic anhydride. The solution was stirred at rt for 15 h and quenched with saturated sodium bicarbonate (vigorous stirring at rt for 1 h). The resulting mixture was diluted with water and

CH_2Cl_2 and the organic layer was separated, washed with saturated sodium bicarbonate and brine. The aqueous layer was back extracted with methylene chloride and the combined organic layer was dried on magnesium sulfate. Most of the solvent was removed under reduced pressure and the resulting solution was passed through a pad of silica gel, which was rinsed with ethyl acetate. Concentration of the resulting solution under reduced pressure and flash chromatography provided 17.6 mg (58%) of mono acetate **57**. Some di-acetate **69** was also isolated (4.2 mg, 13%).

^1H NMR (200 MHz, CDCl_3): 1.01 (s, 9H, *t*-Bu), 2.06 (m, 2H, $\text{CH}(\text{H})\text{CH}(\text{t-Bu})$), 2.21 (s, 3H, OAc), 2.8 (dd, $J = 12.8$ Hz, 10.5 Hz, 1H, $\text{CH}(\text{H})\text{CH}(\text{t-Bu})$), 3.1 (s, 3H, OMe), 3.42 (s, 3H, OMe), 4.03 (s, 1H, OH), 4.58 (m, 1H, $\text{CHCH}_2\text{CH}(\text{t-Bu})$), 5.19 (d, $J = 4.4$ Hz, 1H, $\text{CH}(\text{OAc})$), 5.3 (s, 1H, $\text{CH}(\text{OMe})\text{-O-CH}(\text{OMe})\text{-CH}(\text{OAc})$), 5.68 (d, $J = 4.4$ Hz, 1H, $\text{CH}(\text{OMe})\text{-O-CH}(\text{OMe})\text{-CH}(\text{OAc})$), 6.33 (d, $J = 6.1$ Hz, 1H, $\text{C}(\text{O})\text{CH}=\text{CH}$), 8.35 (d, $J = 6.1$ Hz, 1H, $\text{C}(\text{O})\text{CH}=\text{CH}$).

Acetate aldehyde 58. ^1H NMR (200 MHz, CDCl_3): 0.97 (s, 9H, *t*-Bu), 2.1 to 2.42 (band, 3H, $\text{CH}_2\text{CH}(\text{t-Bu})$), 2.25 (s, 3H, OAc), 3.31 (s, 3H, OMe), 4.78 (d, $J = 5.3$ Hz, 1H, $\text{CHCH}_2\text{CH}(\text{t-Bu})$), 5.45 (s, 1H, $\text{CH}(\text{OMe})$), 5.51 (s, 1H, $\text{CH}(\text{OAc})$), 6.28 (d, $J = 6$ Hz, 1H, $\text{C}(\text{O})\text{CH}=\text{CH}$), 7.33 (d, $J = 6$ Hz, 1H, $\text{C}(\text{O})\text{CH}=\text{CH}$), 9.5 (s, 1H, CHO).

Ketone 59. A catalytic amount of *p*-toluene sulfonic acid was dissolved in ca. 15 mL dry benzene and the water was azeotropically removed by distilling benzene and adding more benzene several times. Once the *p*-TsOH was considered to be dry (ca. 10 min), a solution of 10 mg

(0.028 mmol) of hydroxy ketone **56** in 5 mL CH_2Cl_2 was added at once. A Dean-Stark trap was then installed and the solution was stirred at reflux for 5h (the trap was emptied frequently and more benzene was added). The solution was cooled to rt, most of the benzene was removed under reduced pressure and the residue was taken up in methylene chloride, washed with water and brine. The aqueous layer was back extracted with methylene chloride and the combined organic layer was dried over magnesium sulfate. Concentration under reduced pressure provided the pentacycle **59**. ^1H NMR (250 MHz, CDCl_3): 1.01 (s, 9H, *t*-Bu), 1.78 to 2.1 (band, 2H, $\text{CH}(\text{H})\text{CH}(\text{t-Bu})$), 2.27 (dd, $J = 13.9$ Hz, 4.6 Hz, 1H, $\text{CH}(\text{H})\text{CH}(\text{t-Bu})$), 2.82 (A of ABX, d, $J = 18.5$ Hz, 1H, $\text{C}(\text{O})-\text{CH}(\text{H})-\text{CH}-\text{O}$), 2.98 (B of ABX, dd, $J = 18.5$ Hz, 5.6 Hz, 1H, $\text{C}(\text{O})-\text{CH}(\text{H})-\text{CH}-\text{O}$), 3.29 (s, 3H, OMe), 3.6 (A of AB, $J = 16.7$ Hz, 1H, $\text{O}-\text{CH}(\text{H})-\text{C}(\text{O})$), 4.12 (B of AB, $J = 16.7$ Hz, 1H, $\text{O}-\text{CH}(\text{H})-\text{C}(\text{O})$), 4.28 (X of ABX, d, $J = 5.6$ Hz, 1H, $\text{C}(\text{O})-\text{CH}_2-\text{CH}-\text{O}$), 4.88 (d, $J = 4.6$ Hz, 1H, $\text{CH}-\text{O}-\text{C}(\text{O})$), 5.38 (s, 1H, $\text{CH}(\text{OMe})$). ^{13}C NMR (CDCl_3) δ 29.37; 32.90; 35.66; 45.17; 55.87; 55.97; 68.52; 71.69; 74.39; 75.14; 85.06; 93.75; 114.40; 168.27; 201.18; 201.54. IR (CH_2Cl_2): 1817, 1794, 1734 cm^{-1} .

Deoxygenated bis-methyl acetal 64. To a solution of alcohol **53a** (0.94 g, 2.57 mmol) in DMF was added 1.53 mL DBU (10.3 mmol, 4 eq) and 3.5 mL of CS_2 . This mixture was stirred for 1 h at 23 °C and then 3.5 mL of MeI was added and the solution was stirred for an additional 1 h. The mixture was concentrated and the residue was dissolved in CH_2Cl_2 . The resulting solution was washed twice with 15 mL H_2O , dried over Na_2SO_4 , filtered and concentrated. The resulting crude xanthate **62** was carried on to the next reaction. **Data for xanthate 62:** ^1H NMR (200 MHz, CDCl_3): 1.1 (s, 9H), 2.0 - 2.3 (m, 3H), 2.67 (s, 3H), 3.20 (s, 3H), 3.33 (s, 1H), 3.42 (s, 3H), 4.59 (m, 1H), 4.92 (s, 1H), 5.28 (d, $J = 3.9$ Hz, 1H), 6.23 (d, $J = 6.0$ Hz, 1H), 6.63 (d, $J = 3.9$ Hz, 1H), 8.35 (d, $J = 6.0$ Hz, 1H). ^{13}C NMR (62.5 MHz, CDCl_3): δ 19.96, 30.43,

33.42, 35.42, 54.01, 56.15, 56.70, 56.95, 64.42, 65.05, 83.70, 87.10, 109.21, 110.33, 133.07, 164.98, 169.61, 197.27, 215.77. IR (thin film): 2920, 1770, 1700, 1250 cm^{-1} . HRMS-ES, calcd for $\text{C}_{21}\text{H}_{28}\text{O}_7\text{S}_2\text{Na}$: $(\text{M}+\text{Na})^+$ 470.1174, Found: 479.1185.

The crude xanthate **62**, (2.57 mmol), Bu_3SnH (6.9 mL, 25.7 mmol, 10 eq) and 200 mg AIBN were combined in 80 mL benzene. The solution was warmed to 65 °C at which temperature it was stirred for 6 h. The mixture was then cooled to 23 °C and concentrated. The residue was purified via flash column chromatography (50% EtOAc in hexanes) to give 0.707 g of the reduction product **63** (2.02 mmol, 78% from **53a**). ^1H NMR (400 MHz, CDCl_3): δ 1.0 (s, 9H), 1.86 - 2.1 (m, 4H), 2.44 (dd, $J = 14.5$ Hz, 6.5 Hz, 1H), 3.17 (s, 3H), 3.35 (s, 1H), 3.39 (s, 3H), 4.57 (d, $J = 6.1$ Hz, 1H), 4.89 (s, 1H), 5.23 (dd, $J = 6.5$, 3.3 Hz, 1H), 6.2 (d, $J = 5.8$ Hz, 1H), 7.75 (d, $J = 5.8$ Hz, 1H). ^{13}C NMR (100 MHz, CDCl_3) δ 29.32, 33.21, 34.26, 54.40, 54.90, 56.01, 56.99, 57.07, 62.41, 64.93, 83.61, 107.45, 109.44, 132.69, 163.92, 169.98, 197.52. IR (thin film): 2940, 1775, 1710, 1180, 1090, 980 cm^{-1} . HRMS-ES, calcd for $\text{C}_{19}\text{H}_{26}\text{O}_6\text{Na}$: $(\text{M}+\text{Na})^+$ 373.1627, Found: 373.1645.

Acetal 67. To 5mL of a saturated solution of camphor sulfonic acid in methanol was added ca. 8 mg of the tertiary alcohol **64**. The solution was stirred at rt for 2 days after which it was passed through a pad of silica gel, concentrated and chromatographed to provide two major fractions. The major product from the first fraction was the unreacted Bu_3SnH reduction product **64**, the minor product was the aldehyde **65**. The second fraction was the ketone **67**. ^1H NMR (250 MHz, CDCl_3): 1.0 (s, 9H, *t*-Bu), 2.0 to 2.2 (band, 2H, $\text{CCH}(\text{H})\text{CH}(\text{t-Bu})$), 2.14 (A of ABX, d, $J = 12$ Hz, 1H, $\text{CH}(\text{H})-\text{CH}(\text{O}-)_2$), 2.25 (B of ABX, dd, $J = 12$ Hz, 3.9 Hz, 1H, $\text{CH}(\text{H})-\text{CH}(\text{O}-)_2$), 2.4 (dd, $J = 13$ Hz, 3.75 Hz, 1H, $\text{CCH}(\text{H})\text{CH}(\text{t-Bu})$), 2.66 (A' of A'B'X', dd, $J = 37$ Hz, 3.1 Hz, 1H, $\text{O}-\text{C}(\text{O})-\text{C}(\text{O})-\text{CH}(\text{H})-\text{CH}-\text{O}$), 2.78 (B' of A'B'X', d, $J = 37$ Hz, 1H, $\text{O}-\text{C}(\text{O})-\text{C}(\text{O})-\text{CH}(\text{H})-$

CH-O), 4.3 (X' of A'B'X', d, $J = 3.1$ Hz, 1H, O-C(O)-C(O)-CH₂-CH-O), 4.85 (d, $J = 4.3$ Hz, 1H, CHCH₂CH(t-Bu)), 5.37 (X of ABX, d, $J = 3.9$ Hz, 1H, CH₂-CH(O-)₂), 5.73 (s, 1H, O-CH-O-CH(O-)-CH₂). ¹³C NMR (CDCl₃) δ 28.82; 30.83; 32.39; 36.54; 47.22; 47.48; 62.05; 63.70; 66.04; 66.88; 82.57; 98.87; 114.61; the ketone and lactone carbonyl signals could not be determined with accuracy because of the poor signal / noise ratio (very dilute sample).

Diacetate 69. To a solution of 3.54 g (6.12 mmol) of hydroxy bis-methyl acetal **54** (used without purification from the hydroxylation reaction) in 100 mL CH₂Cl₂ was added 1.2 g (9.84 mmol) of 4-dimethyl aminopyridine and 5.6 mL (59.06 mmol) of acetic anhydride. The solution was heated to reflux for 30 min. The reaction was cooled to room temperature and the solvent was removed on a rotary evaporator (water bath at 45 °C, reduced pressure). The crude product was purified by flash chromatography to provide 1.24 g (48%) of diacetate **69** from ketoester **54**. ¹H NMR (200 MHz, CDCl₃): 1.02 (s, 9H), 1.95 - 2.32 (band, 3H) 2.18 (s, 3H), 2.30 (s, 3H), 3.19 (2, 3H), 3.41 (s, 3H), 4.52 (d, 6.9 Hz, 1H), 4.96 (s, 1H), 5.17 (d, $J = 4.4$ Hz, 1H), 5.72 (d, $J = 4.4$ Hz, 1H), 6.28 (d, $J = 6.1$ Hz, 1H), 8.18 (d, $J = 6.1$ Hz, 1H). IR (thin film): 1780, 1745, 1740, 1450 cm⁻¹

Lactone 68. To a solution of 2.60 mL (18.62 mmol) of diisopropylamine in 70 mL of THF cooled at -78°C, was added 11.64 mL (18.62 mmol) of a 1.6 M solution of *n*-BuLi in hexanes.

The solution was stirred at -78°C for 20 min after which a precooled (-78°C) solution of 1.24 g (2.66 mmol) of diacetate **69** in 30 mL was added dropwise but fairly fast (ca. 5 min). The resulting solution was stirred at -78°C for 5 min and quenched by the slow, dropwise addition of saturated aqueous ammonium chloride. The mixture was diluted with diethyl ether and the organic layer was separated, washed with water and brine. The aqueous layer was back extracted with methylene chloride and the combined organic layer was dried over magnesium sulfate. Concentration under reduced pressure and flash chromatography provided 1.22 g (99%) of the aldol adduct **68**. ^1H NMR (250 MHz, CDCl_3): 1.08 (s, 9H), 1.82 - 2.20 (band, 3H), 2.12 (s, 3H), 2.81 (d, A of AB, $J = 14$ Hz, 1H), 2.91 (d, B of AB, $J = 14$ Hz, 1H), 3.19 (s, 1H), 3.42 (s, 1H), 4.40 (m, 1H), 5.09 (d, $J = 3.4$ Hz, 1H), 5.23 (s, 1H), 5.72 (d, $J = 3.4$ Hz, 1H), 5.81 (d, $J = 6.7$ Hz, 1H), 6.61 (d, $J = 6.7$ Hz, 1H). IR (thin film): 3420, 2920, 1760, 1735, 1710, 1440, 1350 cm^{-1} .

Enol ether 70. A solution of 270 mg (0.58 mmol) of the acetal **68** in 20 mL of CH_2Cl_2 was cooled to -78°C whereupon 4.05 mL of a 1M solution of boron tribromide in CH_2Cl_2 was added via syringe. The mixture was stirred for 10 min at -78°C and the reaction was quenched by the addition of 2 mL of half-saturated aqueous NaHCO_3 . The layers were separated and the organic layer was washed with brine and then dried over sodium sulfate. The solution was passed through a pad of Celite and silica gel on a fritted funnel and the solvents were removed *in vacuo*. The residual crude bromide **71** was used immediately without purification.

Powdered zinc, 3.8 g (58 mmol) was washed with 5 mL 2% HCl, 5 mL H_2O , 5 mL ethanol and 5 mL of ether and then dried *in vacuo* for 1 h. The zinc was suspended in 75 mL of dry THF and 1 mL (11.6 mmol) of dibromoethane was added. The mixture was warmed with a heat gun until gas evolution was observed. Chlorotrimethylsilane 0.96 mL (7.5 mmol) was added

and the mixture was warmed again. The THF was removed by a cannula and the zinc was washed three times with 7 mL of dimethoxyethane. Dimethoxyethane (5 mL) was added to the activated zinc followed by the crude bromide from above in 5 mL of DME. The mixture was stirred for 18 h at 25 °C whereupon 5 mL of saturated NaHCO₃ was added. The mixture was extracted with ethyl acetate and the extracts were dried over sodium sulfate, filtered and concentrated. The residue was purified by flash chromatography (50% to 70% EtOAc in hexanes) to provide 121 mg (55%) of the enol ether **72** and 100 mg (38%) of the hemiacetal **81**. The hemiacetal **81** was resubjected to the above conditions (bromination followed by reductive elimination) to provide an additional 46 mg of the enol ether **72** (166 mg total; 76% overall yield after one recycle). Enol ether **72** ¹H NMR (200 MHz, CDCl₃): δ 0.92 (s, 9H), 1.95 - 2.20 (band, 3H), 2.84 (s, 2H), 3.17 (s, 3H), 4.62 (m, 1H), 4.92 (d, *J* = 3.0 Hz, 1H), 5.43 (s, 1H), 5.69 (d, *J* = 5.7 Hz, 1H), 5.99 (d, *J* = 5.7 Hz, 1H), 6.34 (d, *J* = 3.0 Hz, 1H). IR (thin film): 3480, 1760, 1710, 1610 cm⁻¹. Anal. calcd for C₂₀H₂₄O₇: C, 63.82; H, 6.43. Found: C, 63.85; H, 6.46.

Hydroxylactone 75. A solution of freshly prepared dimethyldioxirane in acetone (20 mL) was added to a solution of 204 mg of enol ether **72** in 5 mL of acetone. The mixture was stirred for 19 h and 20 mg of *p*-toluenesulfonic acid monohydrate was added. The mixture was stirred for an additional 24 h and the solvents were removed under reduced pressure at room temperature. The residue was dissolved in ethyl acetate and the solution was washed with saturated NaHCO₃, dried over sodium sulfate and concentrated to provide 180 mg (78%) of the hemiacetals **74** which was used without further purification. A solution of 90 mg (0.211 mmol) of hemiacetals **74**, 65 mg (0.405 mmol) of bromine, and 117 mg of sodium acetate in 1.8 mL of H₂O and 2.5 mL of acetic acid was placed in a glass stoppered flask and stirred at room temperature for 13 h. Solid Na₂SO₃ was added and the mixture was extracted with ethyl acetate. The extracts were washed

with half-saturated NaCl, dried over sodium sulfate and concentrated. The residue was purified by flash chromatography to provide 57 mg (64%) of hydroxylactone **75** and 17 mg (19%) of the hemiacetals **74**. ^1H NMR (200 MHz, CDCl_3): δ 0.98 (s, 9H), 1.92 (m, 1H), 2.32 (m, 2H), 2.90 (s, 3H), 2.92 (d, A of AB, $J = 19$ Hz, 1H), 3.22 (d, B of AB, $J = 19$ Hz, 1H), 3.39 (s, 3H), 3.75 (d, $J = 3$ Hz, 1H), 4.71 (d, $J = 5.7$ Hz, 1H), 4.88 (d, $J = 3.0$ Hz, 1H), 5.05 (d, $J = 5.5$ Hz, 1H), 5.19 (s, 1H), 5.58 (s, 1H), 6.23 (d, $J = 5.7$ Hz, 1H).

Epoxide 78. To a solution of enol ether **72** (50 mg, 0.122 mmol) in 1 mL of CH_2Cl_2 was added 5 mL of a 7.4 M solution of $t\text{-BuOOH}$ in CH_2Cl_2 . A small amount of powered 4Å molecular sieves were added and the mixture was stirred for 10 min. The $\text{VO}(\text{acac})_2$ (2.5 mg, 38 μmol , 0.3 equiv) was added and the mixture was stirred for 24 h. The mixture was then diluted with CH_2Cl_2 and filtered through Celite. The filtrate was washed with 2 mL half-saturated aqueous NaHCO_3 . The aqueous layer was extracted twice with 2 mL CH_2Cl_2 and the combined organic extracts were dried over Na_2SO_4 , filtered and concentrated. The residue was purified by flash chromatography (1:1 ethylacetate: hexanes) to provide 48 mg (95%) of the epoxide **78**. ^1H NMR (200 MHz, CDCl_3): δ 0.92 (s, 9H), 1.93 - 2.24 (band, 3H), 2.81 (d, A of AB, $J = 18$ Hz, 1H), 2.93 (d, B of AB, $J = 18$ Hz, 1H), 3.23 (s, 3H), 3.65 (d, $J = 3.5$ Hz, 1H), 3.88 (d, $J = 3.5$ Hz, 1H), 4.97 (d, $J = 3.0$ Hz, 1H), 5.06 (m, 1H), 5.38 (s, 1H), 6.38 (d, $J = 3.0$ Hz, 1H).

N-Methylamide 79. To a solution of 25 mg (0.064 mmol) of lactone **78** in 1 mL of methanol was added 2 mL of a 2.0 M solution of methylamine in methanol. The mixture was stirred for 3 h

and concentrated. The residue was purified by flash chromatography (EtOAc) to produce 19 mg (70%) of the amide **79**. ^1H NMR (200 MHz, CDCl_3): δ 0.90 (s, 9H), 1.97 (m, 2H), 2.36 (m, 1H), 2.53 (d, A of AB, $J = 14$ Hz, 1H), 2.84 (br s, 3H), 3.13 (d, B of AB, $J = 14$ Hz, 1H), 3.23 (s, 3H), 3.38 (s, 3H), 3.43 (d, $J = 3$ Hz, 1H), 3.77 (d, $J = 3$ Hz, 1H), 4.95 (d, $J = 3.0$ Hz, 1H), 4.97 (m, 1H), 5.48 (s, 1H), 6.32 (br s, 1H), 6.34 (d, $J = 3.0$ Hz, 1H), 6.64 (s, 1H). IR (neat) 3360, 2940, 1755, 1620, 1360 cm^{-1} .

Amide 80. A solution of 4.5 mg of amide **79** (0.011 mmol) and 1 mg of *p*-toluenesulfonic acid in 1 mL of CH_2Cl_2 was stirred for 18 h at room temperature. The residue was purified by flash chromatography to give 3 mg (67%) of the amide **80**. ^1H NMR (250 MHz, CDCl_3): δ 0.95 (s, 9H), 1.92 - 2.31 (band, 3H), 2.68 (d, A of AB, $J = 14.8$ Hz, 1H), 2.78 (d, B of AB, $J = 14.8$ Hz, 1H), 2.84 (d, $J = 6$ Hz, 3H), 3.47 (s, 3H), 3.87 (dd, $J = 9.3, 6.5$ Hz, 1H), 3.94 (d, $J = 6.5$ Hz, 1H), 4.04 (d, $J = 9.3$ Hz, 1H), 4.74 (d, $J = 3.5$ Hz, 1H), 5.21 (s, 1H), 5.47 (d, $J = 2.5$ Hz, 1H), 5.78 (s, 1H), 5.88 (br s, 1H), 6.17 (d, $J = 2.5$ Hz, 1H). IR (neat) 3360, 2940, 1755, 1620, 1360 cm^{-1} . IR (neat) 3360, 2940, 1755, 1620, 1360 cm^{-1} . Anal. calcd. for $\text{C}_{21}\text{H}_{29}\text{NO}_8$: C, 59.56; H, 6.90; N, 3.31. Found: C, 59.26; H, 6.90; N, 3.22.

Acetate 88. To a solution of diethylamine (6 μL , 0.058 mmol, 0.2 eq) in 6 mL THF at -78°C was added 0.28 mL *t*-BuLi solution (1.56M solution in hexanes, 0.44 mmol, 1.5 eq). The

solution was stirred for 25 min at $-78\text{ }^{\circ}\text{C}$ and the ketoester **63** (102 mg, 0.29 mmol) in 6 mL THF was added via cannula. The mixture was stirred for 30 min at $-78\text{ }^{\circ}\text{C}$ and then warmed to $-30\text{ }^{\circ}\text{C}$ at which temperature it was stirred for an additional 30 min before being re-cooled to $-78\text{ }^{\circ}\text{C}$. The Davis oxaziridine (150 mg, 0.58 mmol, 2 eq) in 3 mL THF was added via cannula and the mixture was warmed slowly to $0\text{ }^{\circ}\text{C}$ at which temperature it was stirred for 1 h. Saturated aqueous NH_4Cl was added and the aqueous layer was extracted twice with 25 mL of diethyl ether. The combined organic extracts were washed with 5 mL brine, dried over Na_2SO_4 , filtered, and concentrated. The residue 100 mg of crude alcohol **64** was used without purification. To a solution of the alcohol **64** (106 mg, 0.29 mmol), Et_3N (0.81 mL, 5.8 mmol, 20 eq), and DMAP (180 mg, 1.45 mmol, 5 eq) in 4 mL CH_2Cl_2 was added acetic anhydride (0.27 mL, 2.9 mmol, 10 eq). The solution was heated to reflux for 1 h. The mixture was allowed to cool to $23\text{ }^{\circ}\text{C}$ and quenched with half-saturated aqueous NaHCO_3 . The aqueous layer was extracted twice with 15 mL CH_2Cl_2 and the combined organic extracts were dried over Na_2SO_4 , filtered and concentrated. The residue was purified via column chromatography (50% EtOAc in hexanes) to give 61 mg (52% for two steps) acetate **88**. ^1H NMR (200 MHz, CDCl_3): δ 0.91 (s, 9H), 1.97 - 2.23 (m, 2H), 2.24 (s, 3H), 2.48 (dd, $J = 6, 11\text{ Hz}$, 1H), 3.17 (s, 3H), 3.37 (s, 3H), 4.60 (dd, $J = 3.7, 1.8\text{ Hz}$, 1H), 4.93 (s, 1H), 5.19 (dd, $J = 6.4, 3.4\text{ Hz}$, 1H), 6.22 (d, $J = 6.3\text{ Hz}$, 1H), 7.65 (d, $J = 6.3\text{ Hz}$, 1H).

Lactone 89. To a solution of diisopropylamine (0.091 mL, 0.65 mmol, 7eq) in 3 mL THF at $-78\text{ }^{\circ}\text{C}$ was added $n\text{-BuLi}$ (0.41 mL of a 1.59 M solution in hexanes, 0.65 mmol, 7eq) dropwise via syringe. This solution was stirred at $-78\text{ }^{\circ}\text{C}$ for 20 min and a solution of the acetate **88** (38 mg, 0.093 mmol) in 2 mL THF which had been precooled to $-78\text{ }^{\circ}\text{C}$ was added dropwise via a jacketed addition funnel. After the addition was complete, the mixture was stirred at $-78\text{ }^{\circ}\text{C}$ for 15 min and quenched via the dropwise addition of saturated aqueous NH_4Cl . The layers were separated and

the aqueous layer was washed twice with 10 mL of diethyl ether. The combined organic extracts were washed with 5 mL brine, dried over Na₂SO₄, filtered and concentrated. Purification of the residue by flash chromatography provided 25 g lactone **89** (66%). ¹H NMR (200 MHz, CDCl₃): δ 0.93 (s, 9H), 1.97 (m, 4H), 2.35 (dd, *J* = 14.5, 6.8 Hz, 1H), 2.88 (AB, *J*_{AB} = 19 Hz, 2H), 3.08 (s, 3H), 3.40 (s, 3H), 4.45 (m, 1H), 5.12 (dd, *J* = 6.7, 3.2 Hz, 1H), 5.19 (s, 1H), 5.79 (d, *J* = 6.0 Hz, 1H), 6.10 (d, *J* = 6.0 Hz, 1H).

Acetal 91. To a solution of lactone **89** (120 mg, 0.319 mmol) in 15 mL MeOH was added excess 10-camphorsulfonic acid (730 mg). The solution was heated at reflux for 18h and then cooled to room temperature. Solid NaHCO₃ was added and the mixture was filtered. The filtrate was concentrated, and the residue was taken up in 30 mL EtOAc, and filtered through silica gel. Concentration of the filtrates gave 96 mg of ester **91** (80%). ¹H NMR (250 MHz, CDCl₃): δ 1.00 (s, 9H), 1.65 - 2.22 (band, 5H), 2.73 (A of AB, *J* = 17.5 Hz, 1H), 3.12 (B of AB, *J* = 17.5 Hz, 1H), 3.32 (s, 3H), 3.77 (s, 3H), 4.58 (d, *J* = 4.6 Hz, 1H), 4.72 (s, 1H), 4.83 (dd, *J* = 5.4, 5.4 Hz, 1H), 5.79 (s, 1H), 5.80 (d, *J* = 5.8 Hz, 1H), 5.95 (d, *J* = 5.8 Hz, 1H).

Vinyl ether 92. To methyl acetal **91** (60 mg, 0.147 mmol) in 5 mL chlorobenzene was added pyridinium *p*-toluenesulfonic acid (180 mg, 0.73 mmol, 5 eq) and pyridine (30 μL, 0.37mmol, 2.5 eq). This mixture was warmed to reflux and allowed to stir for 16 h. The solution was then cooled to room temperature and concentrated. Purification via flash column

chromatography (50% EtOAc in hexanes) gave 46 mg vinyl ether **92** (83%). ^1H NMR (250 MHz, CDCl_3): δ 0.94 (s, 9H), 1.92 (m, 2H), 2.22 (dd, $J = 7.5$, 1H), 2.73 (A of AB, $J = 17.5$ Hz, 1H), 2.98 (B of AB, $J = 17.5$ Hz, 1H), 3.75 (s, 3H), 4.63 (m, 1H), 5.03 (d, $J = 3.0$ Hz, 1H), 5.68 (d, $J = 5.7$ Hz, 1H), 5.71 (d, $J = 5.7$ Hz, 1H), 6.09 (s, 1H), 6.19 (d, $J = 3.0$ Hz, 1H).

Lactone 94. To alkene **92** (25 mg, 0.066 mmol) in 1 mL of CH_2Cl_2 was added 1 mL of a 7.4 M solution of *t*-BuOOH in CH_2Cl_2 . A small amount of powered 4Å molecular sieves were added and the mixture was stirred for 10 min. The $\text{VO}(\text{acac})_2$ (5 mg, 19 μmol , 0.28 eq) was added and the mixture was stirred for 24 h. An additional 2 mg of $\text{VO}(\text{acac})_2$ was then added and the mixture was stirred an additional 24 h. This was repeated two more times to give a total of 1.56 eq of $\text{VO}(\text{acac})_2$ added and a total reaction time of 3 d. The mixture was then diluted with CH_2Cl_2 and filtered through Celite. The filtrate was washed with 2 mL half-saturated aqueous NaHCO_3 . The aqueous layer was extracted twice with 2 mL CH_2Cl_2 and the combined organic extracts were dried over Na_2SO_4 , filtered and concentrated to give a mixture of **94** and the uncyclized epoxide. This mixture was taken up in CH_2Cl_2 and excess *p*-toluenesulfonic acid was added. The solution was stirred for 8 h and solid NaHCO_3 was added. The mixture was stirred for an additional 5 min and then filtered through Celite. The filtrate was concentrated and the residue was purified via flash column chromatography (66% EtOAc in hexanes) to give 18 mg (0.017 mmol, 72%) of **94**. ^1H NMR (250 MHz, CDCl_3): δ 0.92 (s, 9H), 1.74 - 2.42 (band, 3H), 2.58 (A of AB, $J = 18$ Hz, 1H), 3.17 (B of AB, $J = 18$ Hz, 1H), 3.72 (m, 1H), 3.98 (d, $J = 8.0$, 1H), 4.71 (d, $J = 8.0$ Hz, 1H), 5.17 (d, $J = 2.9$ Hz, 1H), 5.21 (d, $J = 2$ Hz, 1H), 5.98 (s, 1H), 6.39 (d, $J = 2.9$ Hz, 1H).

Propionate 96. To a solution of diethylamine (41 μ L, 0.4 mmol, 0.2 eq) in 35 mL THF at -78°C was added 1.92 mL *t*-BuLi solution (1.56M solution in hexanes, 3 mmol, 1.5 eq). This solution was stirred for 25 min at -78°C and the ketoester **63** (0.70 g, 2 mmol) in 25 mL THF was added via cannula. The mixture was stirred for 30 min at -78°C and then warmed to -30°C at which temperature it was stirred for an additional 30 min before being re-cooled to -78°C . The Davis oxaziridine (1.04 g, 4 mmol, 2 eq) in 15 mL THF was added via cannula and the mixture was warmed slowly to 0°C at which temperature it was stirred for 1 h. Saturated aqueous NH_4Cl was added and the aqueous layer was extracted twice with 25 mL of diethyl ether. The combined organic extracts were washed with 10 mL brine, dried over Na_2SO_4 , filtered, and concentrated. The residue was purified via flash column chromatography (50% EtOAc in hexanes) to give 440 mg (1.2 mmol, 60%) hydroxylated product **64**. ^1H NMR (200 MHz, CDCl_3): δ 0.99 (s, 9H), 1.85 - 2.14 (m, 4H), 2.5 (dd, $J = 14.3$ Hz, 6 Hz, 1H), 3.1 (s, 3H), 3.4 (s, 3H), 4.0 (s, 1H), 4.6 (m, 1H), 5.21 (dd, $J = 6.75$ Hz, 3.75 Hz, 1H), 5.25 (s, 1H), 6.3 (d, $J = 6.9$ Hz, 1H), 7.75 (d, $J = 6.9$ Hz, 1H). ^{13}C NMR (100 MHz, CDCl_3): δ 29.52, 30.11, 33.47, 33.63, 52.59, 55.17, 56.28, 62.66, 67.39, 82.03, 83.88, 106.44, 109.18, 129.82, 164.40, 172.43, 200.08. IR (thin film): 3420, 2920, 1780, 1730, 1450, 1370, 1095 cm^{-1} . HRMS (ES), calcd for $\text{C}_{19}\text{H}_{26}\text{O}_7\text{Na}$: ($\text{M}+\text{Na}^+$) 389.1576, Found: 389.1580.

To a solution of the alcohol **64** (0.44 g, 1.2 mmol), Et_3N (3.33 mL, 24 mmol, 20 eq), and DMAP (0.37 g, 3 mmol, 2.5 eq) in 30 mL CH_2Cl_2 was added propionic anhydride (1.54 mL, 12 mmol, 10 eq). The solution was heated to reflux for 90 min. The mixture was allowed to cool to 23°C and quenched with half-saturated aqueous NaHCO_3 . The aqueous layer was extracted twice with 15 mL CH_2Cl_2 and the combined organic extracts were dried over Na_2SO_4 , filtered and, concentrated. The residue was purified via column chromatography (50% EtOAc in hexanes) to

give 0.335 g (0.79 mmol, 66%) propionate **96**. ^1H NMR (400 MHz, CDCl_3): δ 0.93 (s, 9H), 1.23 (t, $J = 7.5$ Hz, 3H), 1.95 (m, 1H), 2.00 (m, 3H), 2.47 (m, 2H), 2.68 (dd, $J = 9.7, 7.6$ Hz, 1H), 3.17 (s, 3H), 3.37 (s, 3H), 4.60 (dd, $J = 3.7, 1.8$ Hz, 1H), 4.96 (s, 1H), 5.19 (dd, $J = 6.4, 3.4$ Hz, 1H), 6.24 (d, $J = 6.3$ Hz, 1H), 7.65 (d, $J = 6.3$ Hz, 1H). ^{13}C NMR (100 MHz, CDCl_3): δ 9.24, 28.23, 29.56, 33.04, 33.87, 35.30, 54.56, 55.57, 56.25, 62.38, 68.13, 83.71, 84.28, 106.81, 109.92, 130.58, 162.87, 168.39, 173.61, 194.56. IR (thin film): 2930, 1780, 1745, 1740, 1450, 1360, 1110, 1090 cm^{-1} . HRMS (ES), calcd for $\text{C}_{22}\text{H}_{30}\text{O}_8\text{Na}$: ($\text{M}+\text{Na}^+$) 445.1838, Found: 445.1854.

Lactone 97. To a solution of diisopropylamine (0.32 mL, 2.3 mmol, 7eq) in 3 mL THF at -78°C was added $n\text{-BuLi}$ (1.44 mL of a 1.59 M solution in hexanes, 2.3 mmol, 7eq) dropwise via syringe. This solution was stirred at -78°C for 20 min and a solution of the propionate **18** (0.138 g, 0.33 mmol) in 3 mL THF which had been precooled to -78°C was added dropwise via a jacketed addition funnel. After the addition was complete, the mixture was stirred at -78°C for 15 min and quenched via the dropwise addition of saturated aqueous NH_4Cl . The layers were separated and the aqueous layer was washed twice with 10 mL of diethyl ether. The combined organic extracts were washed with 5 mL brine, dried over Na_2SO_4 , filtered and concentrated to give 0.138 g alcohol **97** (0.33 mmol, 100%). ^1H NMR (400 MHz, CDCl_3): δ 0.95 (s, 9H), 1.29 (d, $J = 7.9$ Hz, 3H), 1.93 (m, 4H), 2.35 (dd, $J = 14.5, 6.8$ Hz, 1H), 2.79 (q, $J = 7.9$ Hz, 1H), 3.09 (s, 3H), 3.42 (s, 3H), 4.48 (m, 1H), 5.13 (dd, $J = 6.7, 3.2$ Hz, 1H), 5.21 (s, 1H), 5.77 (d, $J = 6.0$ Hz, 1H), 6.10 (d, $J = 6.0$ Hz, 1H). ^{13}C NMR (100 MHz, CDCl_3): δ 10.65, 29.42, 30.12, 33.46, 39.98, 43.37, 52.46, 53.69, 56.97, 63.71, 69.37, 85.77, 91.34, 93.36, 106.26, 106.99, 132.40, 136.23, 172.66, 178.21. IR (thin film): 3420, 2920, 1760, 1710, 1440, 1350 cm^{-1} . HRMS (ES), calcd for $\text{C}_{22}\text{H}_{30}\text{O}_8\text{Na}$: ($\text{M}+\text{Na}^+$) 445.1838, Found: 445.1853.

Enol ether 101. According to the same procedures described for the conversion of lactone **89** to enol ether **92**, 55 mg (0.13 mmol) of lactone **97** was converted to 30 mg (59% overall) of enol ether **101**. ^1H NMR (250 MHz, CDCl_3): δ 0.94 (s, 9H), 1.31 (d, $J = 7.1$ Hz, 3H), 1.92 (m, 2H), 2.20 (dd, $J = 12, 1$ Hz, 1H), 2.93 (q, $J = 7.1$ Hz, 1H), 3.70 (s, 3H), 4.57 (m, 1H), 4.78 (s, 1H), 5.032 (d, $J = 3.0$ Hz, 1H), 5.68 (d, $J = 5.7$ Hz, 1H), 5.73 (d, $J = 5.7$ Hz, 1H), 6.09 (s, 1H), 6.21 (d, $J = 3.0$ Hz, 1H). IR (thin film): 3480, 2950, 1780, 1720, 1610, 1360, 1240, 1210, 1195, 1140, 1000 cm^{-1} .

Lactone 105. To alkene **101** (30 mg, 0.077 mmol) (also contained about 20% of enol ether **100**) in 1.5 mL of CH_2Cl_2 was added 2.5 mL of a 7.4 M solution of *t*-BuOOH in CH_2Cl_2 . A small amount of powered 4Å molecular sieves were added and the mixture was stirred for 10 min. The $\text{VO}(\text{acac})_2$ (10 mg, 38 μmol) was added and the mixture was stirred for 24 h. An additional 2 mg of $\text{VO}(\text{acac})_2$ (7.5 μmol) was then added and the mixture was stirred an additional 24 h. This was repeated two more times to give a total of reaction time of 3 d. The mixture was then diluted with CH_2Cl_2 and filtered through Celite. The filtrate was washed with 2 mL half-saturated aqueous NaHCO_3 . The aqueous layer was extracted twice with 2 mL CH_2Cl_2 and the combined organic extracts were dried over Na_2SO_4 , filtered and concentrated to give a mixture of **105** and the uncyclized epoxide. This mixture was taken up in CH_2Cl_2 and excess *p*-toluenesulfonic acid was added. The solution was stirred for 2 h and solid NaHCO_3 was added. The mixture was stirred for an additional 5 min and then filtered through Celite. The filtrate was concentrated and

the residue was purified via flash column chromatography (66% EtOAc in hexanes) to give 15 mg (50%) of **105** as well as 17 mg (17%) of lactone **106**. **Data for 105** ^1H NMR (250 MHz, CDCl_3): δ 0.90 (s, 9H), 1.50 (d, $J = 7.1$ Hz, 3H), 1.90 (m, 2H), 2.25 (m, 1H), 2.83 (q, $J = 7.1$ Hz, 1H), 3.69 (s, 1H), 4.18 (m, 1H), 4.50 (s, 1H), 4.69 (s, 1H), 5.08 (d, $J = 2.9$ Hz, 1H), 5.21 (m, 1H), 5.41 (d, $J = 2.6$ Hz, 1H), 5.84 (s, 1H), 6.39 (d, $J = 2.9$ Hz, 1H).

Lactone 107. To a solution of **97** (70 mg, 0.166 mmol) in methanol at ambient temperature was added 0.35 mL of a solution of 50 mg 95% NaH in 2 mL of methanol. This solution was stirred for 2 h and then quenched with NH_4Cl . The mixture was extracted twice with 5 mL EtOAc and the combined extracts were filtered through Celite, dried over Na_2SO_4 , filtered and concentrated to give a 1.4:1 mixture of **97**:**107**. The diastereomers were separated via flash column chromatography (37% diethyl ether in CH_2Cl_2) to give 24 mg of **107** (0.056 mmol, 34%). This process was repeated with recovered **97** to give a total of 35 mg of desired epimer **2** (0.083 mmol, 50%). **Data for 107:** ^1H NMR (400 MHz, CDCl_3): δ 0.96 (s, 9H), 1.30 (d, $J = 7.5$ Hz, 3H), 1.94 (m, 4H), 2.34 (dd, $J = 14.5, 6.8$ Hz, 1H), 2.85 (q, $J = 7.5$ Hz, 1H), 3.05 (s, 3H), 3.43 (s, 3H), 4.49 (m, 1H), 5.13 (dd, $J = 6.7, 3.3$ Hz, 1H), 5.26 (s, 1H), 5.63 (d, $J = 6.0$ Hz, 1H), 6.27 (d, $J = 6.0$ Hz, 1H). ^{13}C NMR (100 MHz, CDCl_3): δ 11.21, 29.41, 33.39, 36.45, 45.08, 52.44, 54.09, 56.92, 63.70, 69.59, 84.94, 92.98, 93.63, 106.01, 106.52, 129.04, 139.16, 172.00, 176.36. IR (thin film): 3400, 2920, 1780, 1700, 1450, 1360, 1110, 1090 cm^{-1} . HRMS (ES), calcd for $\text{C}_{22}\text{H}_{30}\text{O}_8\text{Na}$: 445.1838, Found: 445.1844.

Pentacycle 100. To a solution of lactone **107** (18 mg, 0.043 mmol) in 2 mL MeOH was added excess 10-camphorsulfonic acid (150 mg). The solution was heated at reflux for 18h and then cooled to room temperature. Solid NaHCO₃ was added and the mixture was filtered. The filtrate was concentrated, and the residue was taken up in 30 mL EtOAc, and filtered through silica gel. Concentration of the filtrates gave 16 mg of ester **100** (0.038 mmol, 88%). ¹H NMR (400 MHz, CDCl₃): δ 1.01 (s, 9H), 1.50 (d, *J* = 7.1 Hz, 3H), 1.80 (dt, *J* = 13.9, 4.69 Hz, 1H), 2.02 (m, 1H), 2.21 (m, 3H), 3.15 (q, *J* = 7.1 Hz, 1H), 3.35 (s, 3H), 3.72 (s, 3H), 4.59 (d, *J* = 4.6 Hz, 1H), 4.86 (dd, *J* = 5.4, 5.4 Hz, 1H), 5.79 (s, 1H), 5.80 (d, *J* = 5.8 Hz, 1H), 5.94 (d, *J* = 5.8 Hz, 1H). ¹³C NMR (100 MHz, CDCl₃): δ 13.46, 29.45, 32.73, 34.66, 36.74, 43.24, 49.72, 52.43, 56.66, 68.09, 78.31, 84.16, 87.57, 101.26, 105.56, 115.57, 131.14, 138.34, 172.81, 177.68. IR (thin film): 3460, 2960, 1780, 1740, 1450, 1370, 1250 cm⁻¹. HRMS (ES), calcd for C₂₂H₃₀O₈Na: (M+Na⁺) 445.1838, Found: 445.1825.

Vinyl ether 102. To methyl acetal **100** (8.8 mg, 0.21 mmol) in 2 mL chlorobenzene was added pyridinium *p*-toluenesulfonic acid (30 mg, 0.118 mmol, 5.7 eq) and pyridine (4.8 μL, 0.06 mmol, 2.9 eq). This mixture was warmed to reflux and allowed to stir for 4 h. The solution was then cooled to room temperature and concentrated. Purification via flash column chromatography (50% EtOAc in hexanes) gave 6.9 mg vinyl ether **102** (0.0177 mmol, 85%). ¹H NMR (400 MHz, CDCl₃): δ 0.94 (s, 9H), 1.50 (d, *J* = 7.1 Hz, 3H), 1.97 (m, 2H), 2.24 (dd, *J* = 12.6, 3.8 Hz, 1H), 2.97 (q, *J* = 7.1 Hz, 1H), 3.71 (s, 3H), 4.63 (m, 1H), 5.02 (d, *J* = 3.0 Hz,

1H), 5.66 (d, $J = 5.7$ Hz, 1H), 5.73 (d, $J = 5.7$ Hz, 1H), 6.03 (s, 1H), 6.20 (d, $J = 3.0$ Hz, 1H). ^{13}C NMR (100 MHz, CDCl_3): δ 13.63, 29.35, 30.11, 33.19, 36.78, 43.60, 52.44, 53.63, 70.83, 80.51, 84.09, 86.88, 100.75, 102.56, 119.87, 136.46, 145.39, 173.07, 177.66. IR (thin film): 3480, 2950, 1780, 1720, 1610, 1360, 1240, 1210, 1195, 1140, 1000 cm^{-1} . HRMS (ES), calcd for $\text{C}_{21}\text{H}_{26}\text{O}_7\text{Na}$: ($\text{M}+\text{Na}^+$) 413.1576, Found: 413.1584.

Lactone 106. To alkene **102** (8 mg, 0.020 mmol) in CH_2Cl_2 was added 1.5 mL of a 7.4 M solution of *t*-BuOOH in CH_2Cl_2 . A small amount of powered 4Å molecular sieves were added and the mixture was stirred for 10 min. The $\text{VO}(\text{acac})_2$ (2.5 mg, 9.4 μmol , 0.46 eq) was added and the mixture was stirred for 24 h. An additional 2 mg of $\text{VO}(\text{acac})_2$ (7.5 μmol , 0.37 eq) was then added and the mixture was stirred an additional 24 h. This was repeated two more times to give a total of 1.56 eq of $\text{VO}(\text{acac})_2$ added and a total reaction time of 4 d. The mixture was then diluted with CH_2Cl_2 and filtered through Celite. The filtrate was washed with 2 mL half-saturated aqueous NaHCO_3 . The aqueous layer was extracted twice with 2 mL CH_2Cl_2 and the combined organic extracts were dried over Na_2SO_4 , filtered and concentrated to give a mixture of **106** and the uncyclized epoxide. This mixture was taken up in CH_2Cl_2 and excess *p*-toluenesulfonic acid was added. The solution was stirred for 2 h and solid NaHCO_3 was added. The mixture was stirred for an additional 5 min and then filtered through Celite. The filtrate was concentrated and the residue was purified via flash column chromatography (66% EtOAc in hexanes) to give 6.5 mg (0.017 mmol, 81%) of **106** which was spectroscopically identical to that previously reported by Corey: (Corey, E. J.; Kang, M.; Desai, M. C.; Ghosh, A. K.; Houppis, I. N. *J. Am. Chem. Soc.* **1988**, *110*, 649-651).. ^1H NMR (400 MHz, CDCl_3): δ 0.95 (s, 9H), 1.25 (d, $J = 7.1$ Hz, 3H), 1.88 (m, 2H), 2.31 (m, 1H), 2.74 (d, $J = 3.8$ Hz, 1H), 2.93 (q, $J = 7.1$ Hz, 1H), 4.08 (dd, $J = 8.0, 3.8$ Hz, 1H), 4.65 (d, $J = 8.0$ Hz, 1H), 5.17 (d, $J = 2.9$ Hz, 1H), 5.23 (d, $J = 2.6$ Hz, 1H),

6.00 (s, 1H), 6.41 (d, $J = 2.9$ Hz, 1H). ^{13}C NMR (100 MHz, CDCl_3): δ 7.66, 32.80, 37.32, 41.67, 53.59, 54.98, 71.31, 73.43, 74.59, 79.79, 83.55, 93.35, 95.16, 102.64, 120.07, 146.32, 171.94, 176.89. IR (thin film): 3440, 2960, 1775, 1760, 1365, 1245, 1120, 1000 cm^{-1} .

Ginkgolide B (1). To a solution of vinyl ether **106** (10 mg, 0.025 mmol) in 2 mL acetone was added freshly generated dimethyldioxirane solution (30 mL of 0.05 M solution in acetone, excess). Two drops of H_2O were added and the mixture was stirred for 20 h at ambient temperature. The mixture was then concentrated *in vacuo* and the residue was dissolved in 1.5 mL of acetic acid and 1.5 mL of a solution of Br_2 and NaOAc in H_2O (72 mg Br_2 and 130 mg NaOAc in 2 mL H_2O) was added. This solution was allowed to stir at ambient temperature for 20 h and then quenched with 10% $\text{Na}_2\text{S}_2\text{O}_3$. The mixture was extracted twice with 5 mL EtOAc , and the combined organic extracts were washed with 5 mL H_2O and 5 mL brine, dried over Na_2SO_4 , filtered and concentrated to give crude ginkgolide B **1**. Purification via flash column chromatography (50% EtOAc in hexanes) followed by recrystallization with methylene chloride gave 5.5 mg of pure ginkgolide B **1** (0.013 mmol, 52%). ^1H NMR (400 MHz, acetone- $d_6/\text{D}_2\text{O}$): δ 1.10 (s, 9H), 1.20 (d, $J = 7.1$ Hz, 3H), 1.87 (dd, $J = 14.3, 4.8$ Hz, 1H), 2.07 (ddd, $J = 14.3, 13.6, 4.2$ Hz, 1H), 2.21 (dd, $J = 13.6, 4.8$ Hz, 1H), 2.95 (q, $J = 7.1$ Hz, 1H), 4.16 (d, $J = 7.9$ Hz, 1H), 4.63 (d, $J = 7.9$ Hz, 1H), 5.19 (s, 1H), 5.36 (d, $J = 4.2$ Hz, 1H), 6.07 (s, 1H). ^{13}C NMR (125 MHz; acetone- d_6): δ 8.09, 30.55, 32.99, 37.82, 42.79, 49.82, 68.62, 70.54, 73.04, 75.08, 79.62, 84.48, 92.18, 99.40, 111.17, 170.92, 173.90, 176.66. IR (thin film) 3420, 2950, 1790, 1360, 1090 cm^{-1} .