Supporting Information for:

**Endoperoxide Synthesis by Photocatalytic Aerobic [2+2+2] Cycloaditions**
Jonathan D. Parrish,† Michael A. Ischay,† Zhan Lu,† Song Guo,‡ Noël R. Peters,‡ and Tehshik P. Yoon*†

†Department of Chemistry, University of Wisconsin–Madison, 1101 University Avenue, Madison, Wisconsin 53706
‡University of Wisconsin Small Molecule Screening Facility, Paul P. Carbone Cancer Center, Wisconsin Institutes for Medical Research, 1111 Highland Avenue, Madison, Wisconsin 53792

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I. General information

THF and CH₂Cl₂ were purified by elution through alumina as described by Grubbs.¹ MeNO₂ was purified by distillation from MgSO₄ prior to use. A 200 W (3980 lumens) GE Crystal Clear light bulb was used for all photochemical reactions depicted in Tables 1 and 2. Flash column chromatography was performed with Silicycle 40-63 Å silica (230-400 mesh). 9,10-Dicyanoanthracene (DCA), 5,10,15,20-tetraphenyl-21H,23H-porphine (TPP) and 2,4,6-triphenylpyrylium tetrafluoroborate (TP⁺) were purchased from Aldrich and used without further purification. Ru(bpz)₃(PF₆)₂ and Ru(bpy)₃(PF₆)₂ were prepared as previously described. Diastereomer ratios for all compounds were determined by ¹H NMR analysis of the unpurified reaction mixture. ¹H and ¹³C NMR data for all previously uncharacterized compounds were obtained using Varian Inova-500 and Varian Unity-500 spectrometers and are referenced to TMS (0.0 ppm), CDCl₃ (77.0 ppm), and CD₃CN (118.6 ppm), respectively. IR spectral data were obtained using a Bruker Vector 22 spectrometer (thin film on NaCl). Melting points were obtained using a Mel-Temp II (Laboratory Devices, Inc., USA) melting point apparatus. Mass spectrometry was performed with a Waters (Micromass) AutoSpec®. These facilities are funded by the NSF (CHE-9974839, CHE-9304546) and the University of Wisconsin.

II. Synthesis of cyclization substrates

The substrates for entries 1–4, 7, 8, 10, 11, 13, and 15 were prepared as previously described.³ The substrate for entry 6 was prepared as described by Nair.⁴
**o,p-Dimethoxycinnamyl alcohol.** A solution of ethyl 2,4-dimethoxycinnamate (4.39 g, 18.5 mmol) in 37 mL CH₂Cl₂ was placed in a 250 mL round-bottomed flask. The solution was cooled to –78 °C, and a 1.0 M solution of DIBAL-H in hexanes (46.3 mL, 46.3 mmol) was added over 5 minutes. The reaction was then stirred for 2 h at –78 °C. After warming to 0 °C, the reaction was quenched with a saturated aqueous solution of Rochelle’s salt. The mixture was stirred and allowed to warm to room temperature overnight. The layers were separated, and the aqueous layer was extracted with three portions of Et₂O. The combined organic fractions were dried over MgSO₄ and concentrated via rotary evaporation. The residue was purified by chromatography on SiO₂ (8:1 to 2:1 hexanes:EtOAc) to give 3.39 g (17.4 mmol, 94% yield) of a yellow oil. IR (neat) 3477, 2939, 1110 cm⁻¹.¹ H NMR: (500 MHz, CDCl₃) δ 7.39–7.20 (m, 6H), 6.86 (d, J = 16.0 Hz, 1H), 6.62 (d, J = 16.0 Hz, 1H), 6.46 (dd, J = 8.6, 2.5 Hz, 1H), 6.42 (d, J = 2.5 Hz, 1H), 6.32 (dt, J = 16.0, 6.2 Hz, 1H), 6.23 (dt, J = 16.0, 6.2 Hz, 1H), 4.18 (d, J = 6.2 Hz, 4H), 3.8 (s, 3H), 3.78 (s, 3H).¹³C NMR: (125 MHz, CDCl₃) δ 160.4, 157.8, 136.7, 132.3, 128.4, 127.7, 127.6, 127.5, 126.4, 126.2, 124.2, 118.7, 104.7, 98.3, 71.5, 70.4, 55.3, 55.2. HRMS (EI) calculated for [C₁₁H₁₄O₃]⁺ requires m/z 194.0938, found m/z 194.0939.

**Nitrocinnamyl (E)-cinnamyl ether (Table 2, Entry 5).** A 50 mL round-bottomed flask was charged with 60% NaH (575 mg, 14.4 mmol) and 5 mL THF. A solution of 2,4-dimethoxycinnamyl alcohol (2.00 g, 10.3 mmol) in 7.5 mL THF was added slowly. The reaction was stirred at room temperature for 30 min and then cooled to 0 °C. A solution of cinnamyl bromide (2.42 g, 12.3 mmol) in 8 mL of THF was added, and the reaction was warmed to room temperature. After 24 h, the reaction was quenched with water and the aqueous layer was extracted with two portions of Et₂O. The combined organic fractions were dried over MgSO₄ and concentrated via rotary evaporation. Purification by chromatography on SiO₂ (10:1 to 4:1 hexanes:EtOAc) afforded 2.91 g (9.40 mmol, 91% yield) of a yellow oil. IR (neat) 3003, 2938, 1209 cm⁻¹.¹ H NMR: (500 MHz, CDCl₃) δ 7.39–7.20 (m, 6H), 6.86 (d, J = 16.0 Hz, 1H), 6.62 (d, J = 16.0 Hz, 1H), 6.46 (dd, J = 8.6, 2.5 Hz, 1H), 6.42 (d, J = 2.5 Hz, 1H), 6.32 (dt, J = 16.0, 6.2 Hz, 1H), 6.23 (dt, J = 16.0, 6.2 Hz, 1H), 4.18 (d, J = 6.2 Hz, 4H), 3.8 (s, 3H), 3.78 (s, 3H).¹³C NMR: (125 MHz, CDCl₃) δ 160.4, 157.8, 136.7, 132.3, 128.4, 127.7, 127.6, 127.5, 126.4, 126.2, 124.2, 118.7, 104.7, 98.3, 71.5, 70.4, 55.3, 55.2. HRMS (EI) calculated for [C₂₀H₂₂O₃]⁺ requires m/z 310.1564, found m/z 310.1549.

**p-Nitrocinamyl (E)-cinnamyl ether.** A solution of 4-nitrocinamyl alcohol (1.20 g, 6.70 mmol) and cinnamyl bromide (1.98 g, 10.0 mmol) in 27 mL DMF was placed in a 100 mL round-bottomed flask. The solution was cooled to 0 °C and 60% NaH (402 mg, 10.0 mmol) was added slowly. The mixture was allowed to warm to room temperature and stirred for 7 h. The reaction was quenched by slowly adding a saturated aqueous solution of NH₄Cl and the aqueous layer was extracted with two portions of Et₂O. The combined organic fractions were dried over MgSO₄ and concentrated via rotary evaporation. Purification by chromatography on SiO₂ (20:1 to 4:1 hexanes:EtOAc) gave 885 mg (3.00 mmol, 45% yield) of a red oil. IR (neat) 3080, 1343, 1110 cm⁻¹.¹ H NMR: (500 MHz, CDCl₃) δ 8.11 (d, J = 9.3 Hz, 2H), 7.44 (d, J = 9.3 Hz, 2H), 7.40–7.20 (m, 5H), 6.68 (d, J = 16.0 Hz, 1H), 6.45 (dt, J = 16.0, 5.5 Hz, 1H), 6.31 (dt, J = 16.0, 5.5 Hz, 1H), 4.22–4.19 (m, 4H).¹³C NMR: (125 MHz, CDCl₃) δ 146.6, 143.0, 136.4, 132.5, 131.1, 129.2, 128.4, 127.6, 126.7, 126.3, 125.5, 123.7, 71.0, 69.8. HRMS (EI) calculated for [C₁₈H₁₅NO₃]⁺ requires m/z 195.1208, found m/z 195.1215.

**N-Boc-Aminocinnamyl (E)-cinnamyl ether (Table 2, Entry 9).** A solution of Cu(acac)₂ (213 mg, 0.81 mmol) in 10 mL EtOH was placed in a 100 mL round-bottomed flask. NaBH₄ (300 mg, 7.93 mmol) was added, and the mixture was stirred for 10 min. The flask was then placed
in a water bath and vigorously stirred while a suspension of (E)-p-nitrocinnamyl (E)-cinnamyl ether (1.20 g, 4.06 mmol) in 15 mL of EtOH was added dropwise. After 1 h, additional NaBH₄ (161 mg, 4.25 mmol) was added, and the mixture was stirred for 12 h before being quenched with water. The aqueous phase was extracted with two portions of EtOAc, and the combined organic fractions were dried over MgSO₄ and concentrated via rotary evaporation. Purification by flash column chromatography (20:1 to 1:1 hexanes:EtOAc) afforded the free amine. This material was dissolved in 20 mL 1,4-dioxane in a 100 mL round-bottomed flask. Triethylamine (0.54 mL, 3.90 mmol) and Boc₂O (851 mg, 3.90 mmol) were added, and the reaction was stirred at room temperature for 18 h. The solution was concentrated via rotary evaporation, and the residue was eluted through a short plug of SiO₂ with Et₂O. The eluent was concentrated by rotary evaporation, and the residue was purified by chromatography on SiO₂ (20:1 to 4:1 hexanes:EtOAc) to afford 325 mg (0.912 mmol, 22% yield) of a yellow solid (mp = 82–84 °C). IR (neat) 3329, 1727, 1522 cm⁻¹. ¹H NMR: (500 MHz, CDCl₃) δ 7.40–7.22 (m, 9H), 6.64 (d, J = 15.9 Hz, 1H), 6.57 (d, J = 15.9 Hz, 1H), 6.51 (s, 1H), 6.32 (dt, J = 15.9, 5.9 Hz, 1H), 6.23 (dt, J = 15.9, 5.9 Hz, 1H), 4.21–4.18 (m, 4H), 1.52 (s, 9H). ¹³C NMR: (125 MHz, CDCl₃) δ 152.6, 137.8, 136.7, 132.5, 132.2, 131.6, 128.5, 127.6, 127.1, 126.5, 126.0, 124.5, 118.4, 80.6, 70.8, 70.7, 28.3. HRMS (EI) calculated for [C₅H₇O₂N⁺Na⁺] requires m/z 388.1884, found m/z 388.1880.

(E)-p-Methoxy cinnamyl (E)-p-trifluoromethyl cinnamyl ether (Table 2, Entry 12). A solution of 2-trifluoromethyl cinnamyl alcohol⁵ (1.69 g, 8.36 mmol) in 20 mL THF was placed in a 250 mL round-bottomed flask. 60% NaH (402 mg, 10.1 mmol) was added, and the reaction was stirred for 1 h. The flask was then cooled to 0 °C, and a solution of p-methoxycinnamyl bromide (2.85 g, 12.5 mmol) in 15 mL of THF was added slowly. The solution was allowed to warm to room temperature and stirred for 48 h. The reaction was quenched with water and the aqueous layer was extracted with two portions of Et₂O. The combined organic fractions were washed with brine, dried over MgSO₄, and concentrated via rotary evaporation. Purification by chromatography on SiO₂ (20:1 to 10:1 hexanes:EtOAc) afforded 1.45 g (4.2 mmol, 50% yield) of a colorless oil. IR (neat) 3004, 1514, 1315 cm⁻¹. ¹H NMR: (500 MHz, CDCl₃) δ 7.62 (m, 2H), 7.47 (t, J = 7.5 Hz, 1H), 7.34–7.20 (m, 3H), 7.02 (d, J = 15.7 Hz, 1H), 6.85 (d, J = 8.6 Hz, 2H), 6.58 (d, J = 15.7 Hz, 1H), 6.28 (dt, J = 15.7, 5.9 Hz, 1H), 6.18 (dt, J = 15.7, 5.9 Hz, 1H), 4.22 (d, J = 5.9 Hz, 2H), 4.18 (d, J = 5.9 Hz, 2H), 3.78 (s, 3H). ¹³C NMR: (125 MHz, CDCl₃) δ 159.3, 135.9, 132.5, 131.8, 130.6, 129.4, 128.2, 127.7, 127.5, 127.3, 127.0, 125.7 (q, J = 5.8 Hz), 124.3 (q, J = 273.9 Hz), 123.5, 114.0, 70.9, 70.2, 55.2. HRMS (EI) calculated for [C₂₀H₁₉F₃]⁺ requires m/z 348.1332, found m/z 348.1346.

(E)-p-Methoxy cinnamyl (E)-5-phenylpent-2-en-4-yn-1-yl ether (Table 2, Entry 14). A suspension of 60% NaH (290 mg, 7.20 mmol) in 20 mL THF was placed in a 100 mL round-bottomed flask. The flask was cooled to 0 °C, and (E)-5-phenylpent-2-en-4-yn-1-ol⁶ (1.14 g, 7.20 mmol) was added. The mixture was stirred for 30 min before adding p-methoxycinnamyl bromide (1.63 g, 7.20 mmol). The reaction was allowed to warm to room temperature. After stirring for 12 h, the reaction was cooled to 0 °C and quenched by adding a saturated aqueous solution of NH₄Cl. The aqueous layer was extracted with two portions of EtOAc. The combined organic fractions were washed with brine, dried over MgSO₄, and concentrated via rotary evaporation. Purification by chromatography on SiO₂ (20:1 to 8:1 hexanes:EtOAc) afforded 1.65 g (5.42 mmol, 75% yield) of the title product as a yellow solid (mp = 49–51 °C). IR (neat) 2935, 2198, 1513 cm⁻¹. ¹H NMR: (500 MHz, CDCl₃) δ 7.45–7.30 (m, 7H), 6.86 (d, J = 9.0 Hz, 2H), 6.57 (d, J = 16.1 Hz, 1H), 6.3 (dt, J = 16.01, 5.6 Hz, 1H), 6.16 (dt, J = 16.0, 6.0 Hz, 1H), 5.98 (dt, J = 16.0, 1.7 Hz, 1H), 4.16 (dd, J = 6.0, 1.3 Hz, 2H), 4.13 (dd, J = 5.6, 1.7 Hz, 2H), 3.81 (s, 3H). ¹³C NMR: (125 MHz, CDCl₃) δ 159.3, 139.5, 132.4, 131.5, 129.4, 128.3, 128.2, 127.7, 123.4, 123.2, 114.0, 111.7, 90.0, 87.4, 71.1, 69.7, 55.3. HRMS (EI) calculated for [C₂₅H₂₆O₂⁺] requires m/z 304.1458, found m/z 304.1469.
(E,E)-N,N-Bis-(p-methoxycinnamyl) toluenesulfonamide (Table 2, Entry 16). A suspension of 60% NaH (568 mg, 14.2 mmol) in 30 mL DMF was placed in a 250 mL round-bottomed flask. The mixture was cooled to 0 ºC and a solution of N-p-methoxycinnamyl p-toluene sulfonamide (1.5 g, 4.73 mmol) in 30 mL of DMF was added dropwise over 10 min. The reaction was warmed to room temperature and stirred for 30 min before a solution of p-methoxycinnamyl bromide (2.69 g, 11.8 mmol) in 35 mL of DMF was added. After 24 h, the reaction was carefully quenched with a saturated aqueous solution of NH₄Cl and the aqueous layer was extracted with two portions of Et₂O. The combined organic fractions were dried over MgSO₄ and concentrated via rotary evaporation. Purification by flash column chromatography on SiO₂ (20:1 to 1:2 hexanes:EtOAc) afforded 1.29 g (2.8 mmol, 59% yield) of the title product as a yellow solid (mp = 92–94 ºC). IR (neat) 3033, 1512, 1251 cm⁻¹. ¹H NMR: (500 MHz, CDCl₃) δ 7.32 (d, J = 9.1 Hz, 4H), 6.83 (d, J = 9.1 Hz, 4H), 6.39 (d, J = 15.7 Hz, 2H), 5.93 (dt, J = 15.9, 7.6 Hz, 2H), 4.20 (q, J = 7.2 Hz, 4H), 3.80 (s, 6H), 2.81 (dd, J = 7.6, 1 Hz, 4H), 1.24 (t, J = 7.2 Hz, 6H). ¹³C NMR: (125 MHz, CDCl₃) δ 170.9, 159.1, 133.4, 130.0, 127.3, 121.6, 114.0, 55.3, 49.0, 21.5. HRMS (EI) calculated for [C₂₅H₂₉NO₅S+Na]⁺ requires m/z 486.1710, found m/z 486.1700.

(D,E)-Diethyl 2,2-bis(p-methoxycinnamyl)malonate (Table 2, Entry 17). Diethyl malonate (1.00 g, 6.24 mmol) was added to a suspension of 60% NaH (929 mg, 23.2 mmol) in 16 mL THF. The mixture was stirred for 1 h then cooled to 0 ºC. A solution of p-methoxycinnamyl bromide (3.54 g, 15.6 mmol) in 15 mL of DMF was added. After 1 h, the reaction was quenched with water and the aqueous layer was extracted with two portions of Et₂O. The combined organic fractions were dried over MgSO₄ and concentrated via rotary evaporation. Purification by chromatography on SiO₂ (15:1 to 1:10 hexanes:EtOAc) afforded 2.45 g (5.41 mmol, 87% yield) of a white solid (mp = 74–75 ºC). IR (neat) 3033, 1512, 1251 cm⁻¹. ¹H NMR: (500 MHz, CDCl₃) δ 7.32 (d, J = 9.1 Hz, 4H), 6.83 (d, J = 9.1 Hz, 4H), 6.39 (d, J = 15.7 Hz, 2H), 5.93 (dt, J = 15.9, 7.6 Hz, 2H), 4.20 (q, J = 7.2 Hz, 4H), 3.80 (s, 6H), 2.81 (dd, J = 7.6, 1 Hz, 4H), 1.24 (t, J = 7.2 Hz, 6H). ¹³C NMR: (125 MHz, CDCl₃) δ 170.9, 159.1, 133.4, 130.0, 127.3, 121.7, 113.9, 61.3, 58.1, 55.3, 36.5, 14.2. HRMS (EI) calculated for [C₂₇H₃₅O₆]+ requires m/z 453.2272, found m/z 453.2276.

(E,E)-1,7-bis(4-methoxyphenyl)hepta-1,6-diene (Table 2, Entry 18). An aqueous solution of glutaraldehyde (50% w/w, 1.00 g, 4.99 mmol) and a solution of 4-methoxybenzyl triphenylphosphonium bromide (5.80 g, 12.5 mmol) in 20 mL THF were placed in a 100 mL round-bottomed flask and cooled to 0 ºC. KOt-Bu (1.68 g, 15.0 mmol) was added slowly over 5 min. The resulting orange suspension was stirred at room temperature for 18 h before being diluted with water and extracted with three portions of EtO₂. The combined organic fractions were dried over MgSO₄ and concentrated via rotary evaporation. Purification by chromatography on SiO₂ (20:1 to 10:1 hexanes:EtOAc) afforded a mixture of isomeric bis(styrenes). This material was dissolved in 50 mL of benzene in 100 mL round-bottomed flask, to which was added thiophenol (0.022 mL, 0.211 mmol) and AIBN (34.7 mg, 0.211 mmol). The solution was heated at reflux for 24 h. Upon cooling to room temperature, the solution was diluted with hexanes and washed with two portions of saturated aqueous NaHCO₃ and one portion of brine. The organic layer was then dried over MgSO₄ and concentrated by rotary evaporation. Purification by chromatography on SiO₂ (gradient, 25:1 to 20:1 hexanes/EtOAc) gave 207 mg (0.670 mmol, 13% yield) of the title product as a white solid (mp = 91–93 ºC). IR (neat) 3004, 2916, 1512 cm⁻¹. ¹H NMR: (500 MHz, CDCl₃) δ 7.24 (d, J = 8.9 Hz, 4H), 6.80 (d, J = 8.9 Hz, 4H), 6.32 (d, J = 15.9 Hz, 2H), 6.06 (dt, J = 15.9, 7 Hz, 2H), 3.72 (s, 6H), 2.21 (q, J = 7 Hz, 4H), 1.60 (p, J = 7.3 Hz,
III. Photocycloadditions

**General Procedure**: An oven-dried 135 mL glass pressure vessel containing a magnetic stir bar was charged with bis(alkene) substrate, Ru(bpz)$_3$(PF$_6$)$_2$ (0.005 or 0.02 equiv), and MeNO$_2$. The vessel was fitted with a regulator and pressurized to 60 psi with O$_2$ gas. The reaction was cooled in a 5 °C water bath and irradiated with a 200 W incandescent bulb. After consumption of the substrate, the reaction mixture was eluted through a short pad of SiO$_2$ using EtOAc and CH$_2$Cl$_2$. The solvent was removed by rotary evaporation, and purification of the residue by chromatography on SiO$_2$ (8:1 to 2:1 hexanes:EtOAc) afforded the [2+2+2] cycloadduct.

For the first experiment, a 100 mg (0.357 mmol) of bis(alkene), 1.5 mg (1.8 µmol) of Ru(bpz)$_3$(PF$_6$)$_2$, 17.8 mL of MeNO$_2$ and an irradiation time of 30 min. Purification by flash column chromatography afforded the cycloadduct as an oil. Experiment 1: 100.6 mg (0.322 mmol, 90% yield, dr = 6:1), Experiment 2: 104.0 mg (0.333 mmol, 94% yield, dr = 6:1). IR (neat) 1253, 732, 702 cm$^{-1}$. $^1$H NMR: (500 MHz) $\delta$ 7.50 (d, J = 7.8 Hz, 2H), 7.39-7.35 (m, 2H), 7.33-7.30 (m, 3H), 6.91 (d, J = 8.8 Hz, 2H), 5.56 (d, J = 5.8 Hz, 1H), 5.04 (d, J = 10 Hz, 1H), 4.17 (t, J = 7.4 Hz, 1H), 3.82-3.77 (m, 4H), 3.43 (dd, J = 10.8, 8.0 Hz, 1H), 3.25 (dd, J = 11.4, 7.6 Hz, 1H), 2.88-2.79 (m, 1H), 2.66-2.57 (m, 1H). $^{13}$C NMR: (125 MHz, CD$_2$CN) $\delta$ 161.8, 139.1, 130.72, 130.66, 129.5, 128.9, 128.7, 115.4, 88.5, 84.4, 69.8, 68.7, 56.4, 47.7, 42.3; HRMS (EI) calculated for [C$_{19}$H$_{20}$O$_4$]$^+$ requires m/z 312.1456, found m/z 312.1457.

For the third experiment, a 100 mg (0.357 mmol) of bis(alkene), 6.2 mg (7.0 µmol) of Ru(bpz)$_3$(PF$_6$)$_2$, 17.8 mL of MeNO$_2$ and an irradiation time of 24 h. Purification by flash column chromatography afforded the cycloadduct as an oil. Experiment 1: 52.0 mg (0.167 mmol, 47% yield, dr = 10:1). IR (neat) 756, 735, 702 cm$^{-1}$. $^1$H NMR: (500 MHz) $\delta$ 7.50–7.28 (m, 7H), 7.00 (t, J = 7.9 Hz, 1H), 6.90 (d, J = 8.3 Hz, 1H), 5.62 (d, J = 6.3 Hz, 1H), 5.54 (d, J = 9.8 Hz, 1H), 4.10 (t, J = 7.3 Hz, 1H), 3.85–3.76 (m, 4H), 3.56 (dd, J = 10.9, 8.1 Hz, 1H), 3.13 (dd, J = 11.2, 7.7 Hz, 1H), 2.92 (m, 1H), 2.64 (m, 1H). $^{13}$C NMR: (125 MHz, CDCl$_3$) $\delta$ 156.7, 136.7, 129.9, 128.3, 127.8, 127.3, 127.0, 120.8, 120.5, 83.1, 81.7, 68.72, 68.69, 55.3, 46.0, 41.8; HRMS (EI) calculated for [C$_{19}$H$_{20}$O$_4$]$^+$ requires m/z 312.1456, found m/z 312.1437.

For the fifth experiment, a 100 mg (0.322 mmol) of bis(alkene), 1.4 mg (1.6 µmol) of Ru(bpz)$_3$(PF$_6$)$_2$, 16 mL of MeNO$_2$ and an irradiation time of 2 h. Purification by flash column chromatography afforded the cycloadduct as an oil. Experiment 1: 75.4 mg (0.220 mmol, 68% yield, dr = 4:1), Experiment 2: 71.7 mg (0.209 mmol, 65% yield, dr = 4:1). IR (neat) 1210, 735, 702 cm$^{-1}$. $^1$H NMR: (500 MHz, CDCl$_3$) $\delta$ 7.49 (d, J = 7.2 Hz, 2H), 7.40–7.28 (m, 4H), 6.51 (dd, J = 8.5, 2.4 Hz, 1H), 6.46 (d, J = 2.4 Hz, 1H), 5.58 (d, J = 6 Hz, 1H), 5.48 (d, J = 9.7 Hz, 1H), 4.14 (t, J = 7.4 Hz, 1H), 3.86–3.81 (m, 7H), 3.48 (dd, J = 10.8, 8.1 Hz, 1H), 3.20 (dd, J = 11.3, 7.6 Hz, 1H), 2.92–2.83 (m, 1H), 2.71–2.61 (m, 1H). $^{13}$C NMR: (125 MHz, CDCl$_3$) $\delta$ 161.5, 158.5, 137.0, 128.6, 128.1, 127.6, 127.1, 118.2, 104.4, 98.5, 83.1, 81.4, 68.8, 68.4, 55.43, 55.35, 46.4, 40.9; HRMS (EI) calculated for [C$_{20}$H$_{22}$O$_5$]$^+$ requires m/z 342.1462, found m/z 342.1444.
(Table 2, entry 6). Prepared according to the General Procedure using 100 mg (0.322 mmol) of bis(alkene), 1.4 mg (1.6 µmol) of Ru(bpz)$_2$(PF$_6$)$_2$, 16 mL of MeNO$_2$ and an irradiation time of 1 h. Purification by flash column chromatography afforded the cycloadduct as an oil. Experiment 1: 100.9 mg (0.295 mg, 92% yield, dr = 7:1), Experiment 2: 99.5 mg (0.291 mg, 90% yield, dr = 7:1). IR (neat) 1261, 731, 702 cm$^{-1}$.$^1$H NMR: (500 MHz) δ 7.50 (d, J = 7.5 Hz, 2H), 7.39–7.29 (m, 3H), 6.96–6.91 (m, 2H), 6.87 (d, J = 8.2 Hz, 1H), 5.58 (d, J = 5.8 Hz, 1H), 5.05 (d, J = 9.9 Hz, 1H), 4.18 (t, J = 7.3 Hz, 1H), 3.90 (s, 3H), 3.88 (s, 3H), 3.83 (t, J = 7.8 Hz, 1H), 3.46 (dd, J = 10.8, 7.9 Hz, 1H), 3.26 (dd, J = 11.3, 7.6 Hz, 1H), 2.85 (m, 1H), δ 2.63 (m, 1H).$^{13}$C NMR: (125 MHz, CDCl$_3$) δ 149.9, 149.2, 137.0, 129.3, 128.2, 127.7, 127.1, 120.0, 111.1, 111.0, 87.6, 83.1, 68.9, 68.2, 55.91, 55.89, 46.4, 41.1. HRMS (EI) calculated for [C$_{20}$H$_{22}$O$_{5}$]$^+$ requires m/z 342.1462, found m/z 342.1472.

(114, 114 Signet), found m/z 342.1462, found m/z 342.1472.

$^{13}$C NMR: (125 MHz, CDCl$_3$) δ 149.9, 149.2, 137.0, 129.3, 128.2, 127.7, 127.1, 120.0, 111.1, 111.0, 87.6, 83.1, 68.9, 68.2, 55.91, 55.89, 46.4, 41.1. HRMS (EI) calculated for [C$_{20}$H$_{22}$O$_{5}$]$^+$ requires m/z 342.1462, found m/z 342.1461.

(TipSO$_3$)$_2$O

(114, 114 Signet), found m/z 342.1462, found m/z 342.1472.

$^{13}$C NMR: (125 MHz, CDCl$_3$) δ 157.0, 137.1, 129.4, 128.9, 128.2, 127.6, 127.1, 120.1, 87.5, 83.2, 68.9, 68.1, 46.5, 41.4, 17.9, 12.6. HRMS (EI) calculated for [C$_{7}$H$_{8}$O$_{5}$Si]$^+$ requires m/z 454.2534, found m/z 454.2549.

(TipSO$_3$)$_2$O

(114, 114 Signet), found m/z 342.1462, found m/z 342.1472.

$^{13}$C NMR: (125 MHz, CDCl$_3$) δ 157.0, 137.1, 129.4, 128.9, 128.2, 127.6, 127.1, 120.1, 87.5, 83.2, 68.9, 68.1, 46.5, 41.4, 17.9, 12.6. HRMS (EI) calculated for [C$_{7}$H$_{8}$O$_{5}$Si]$^+$ requires m/z 454.2534, found m/z 454.2549.

(114, 114 Signet), found m/z 342.1462, found m/z 342.1472.

$^{13}$C NMR: (125 MHz, CDCl$_3$) δ 157.0, 137.1, 129.4, 128.9, 128.2, 127.6, 127.1, 120.1, 87.5, 83.2, 68.9, 68.1, 46.5, 41.4, 17.9, 12.6. HRMS (EI) calculated for [C$_{7}$H$_{8}$O$_{5}$Si]$^+$ requires m/z 454.2534, found m/z 454.2549.
80.8, 68.9, 68.1, 46.4, 41.3, 28.3. HRMS (EI) calculated for \([\text{C}_{23}\text{H}_{27}\text{O}_3\text{N}+\text{Na}]^+\) requires m/z 420.1782, found m/z 420.1790.

(114.2, 1)

Experiment 2: 82.1 mg (0.239 mmol, 74% yield, dr >10:1).

Purification by flash column chromatography afforded the cycloaduct as an oil. Experiment 1: 83.0 mg (0.242 mmol, 75% yield, dr >10:1).

Prepared according to the General Procedure using 100 mg (0.322 mmol) of bis(alkene), 1.4 mg (1.6 µmol) of \(\text{Ru(bpz)}_3(\text{PF}_6)_2\), 16.1 mL of \(\text{MeNO}_2\) and an irradiation time of 30 min. Purification by flash column chromatography afforded the cycloaduct as an oil. Experiment 1: 90.3 mg (0.237 mmol, 83% yield, dr = 4:1). IR (neat) 1315, 1253, 1037 cm\(^{-1}\). \(^1\)H NMR: (500 MHz) δ 7.42 (d, J = 8.6 Hz, 2H), 7.32 (d, J = 8.6 Hz, 2H), 6.91 (d, J = 8.6 Hz, 2H), 6.90 (d, J = 8.6 Hz, 2H), 5.52 (d, J = 5.7 Hz, 1H), 5.04 (d, J = 9.9 Hz, 1H), 4.14 (t, J = 7.3 Hz, 1H), 3.83–3.80 (m, 7H), 3.44 (dd, J = 10.8, 8 Hz, 1H), 3.23 (dd, J = 11.2, 7.5 Hz, 1H), 2.86–2.77 (m, 1H), 2.69–2.60 (m, 1H). \(^{13}\)C NMR: (125 MHz, CDCl\(_3\)) δ 160.3, 159.0, 129.1, 129.03, 128.95, 128.4, 114.2, 113.6, 87.3, 82.9, 68.9, 68.1, 55.3, 55.2, 46.7, 41.1. HRMS (EI) calculated for \([\text{C}_{20}\text{H}_{22}\text{O}_3]^+\) requires m/z 342.1462, found m/z 342.1453.

(7.35, 7.7, 1.7

Prepared according to the General Procedure using 100 mg (0.287 mmol) of bis(alkene), 1.2 mg (1.4 µmol) \(\text{Ru(bpz)}_3(\text{PF}_6)_2\), 14.4 mL of \(\text{MeNO}_2\) and an irradiation time of 2 h. Purification by flash column chromatography afforded the cycloaduct as an oil. Experiment 1: 90.3 mg (0.237 mmol, 83% yield, dr = 4:1). IR (neat) 1312, 1120, 773 cm\(^{-1}\). \(^1\)H NMR: (500 MHz) δ 8.22 (d, J = 7.5 Hz, 1H), 7.68 (d, J = 7.8 Hz, 1H), 7.59 (t, J = 7.5 Hz, 1H), 7.45 (t, J = 7.5 Hz, 1H), 7.40 (d, J = 8.6 Hz, 2H), 6.97 (2, J = 8.8 Hz, 2H), 5.99 (d, J = 7.2 Hz, 1H), 5.07 (d, J = 9.7 Hz, 1H), 4.02 (td, J = 7.7, 1.7 Hz, 1H), 3.93 (t, J = 7.7 Hz, 1H), 3.84 (s, 3H), 3.53 (dd, J = 10.6, 7.9 Hz, 1H), 3.00 (m, 1H), 2.91–2.79 (m, 2H). \(^{13}\)C NMR: (125 MHz, CDCl\(_3\)) δ 160.2, 135.3, 132.1, 130.3, 128.8, 128.4, 128.2, 127.4 (q, J = 30.2 Hz), 126.2 (q, J = 5.8 Hz), 124.1 (t, J = 274.5 Hz), 114.3, 86.8, 78.8 (q, J = 2.7 Hz), 68.9 (q, J = 3.9 Hz), 68.7, 55.3, 45.5, 41.3. HRMS (EI) calculated for \([\text{C}_{20}\text{H}_{19}\text{O}_3\text{F}_3]^+\) requires m/z 380.1230, found m/z 380.1237.

(1.4, 13

Prepared according to the General Procedure using 100 mg (0.318 mmol) of bis(alkene), 1.4 mg (1.6 µmol) of \(\text{Ru(bpz)}_3(\text{PF}_6)_2\), 15.9 mL of \(\text{MeNO}_2\) and an irradiation time of 2 h. Purification by flash column chromatography afforded the cycloaduct as an oil. Experiment 1: 94.0 mg (0.271 mmol, 85% yield, dr = 5:1). IR (neat) 1252, 1062, 848 cm\(^{-1}\). \(^1\)H NMR: (500 MHz) δ 7.44 (d, J = 8.6 Hz, 2H), 7.35 (2, J = 8.6 Hz, 2H), 7.29 (d, J = 8.6 Hz, 2H), 6.91 (d, J = 8.6 Hz, 2H), 5.53 (d, J = 5.9 Hz, 1H), 5.04 (d, J = 10.0 Hz, 1H), 4.18 (t, J = 7.3 Hz, 1H), 3.83–3.77 (m, 4H), 3.43 (dd, J = 10.9, 8.1 Hz, 1H), 3.24 (dd, J = 11.4, 7.6 Hz, 1H), 2.82 (m, 1H), 2.55 (m, 1H). \(^{13}\)C NMR:
(125 MHz, CD$_3$CN) $\delta$ 161.9, 138.0, 134.2, 130.8, 130.45, 130.39, 129.5, 115.4, 88.6, 83.8, 69.7, 68.6, 56.4, 47.6, 42.2. HRMS (EI) calculated for [C$_{19}$H$_{16}$O$_5$Cl]$^+$ requires m/z 346.0967, found m/z 346.0985.

(Table 2, entry 14). Prepared according to the General Procedure using 100 mg (0.329 mmol) of bis(alkene), 1.4 mg (1.6 $\mu$mol) of Ru(bpz)$_3$(PF$_6$)$_2$, 16.6 mL of MeNO$_2$ and an irradiation time of 2 h. Purification by flash column chromatography afforded the cycloaduct as an oil. Experiment 1: 88 mg (0.262 mmol, 80% yield, $dr = 2:1$), Experiment 2: 92.1 mg (0.274 mmol, 83% yield, $dr = 2:1$). IR (neat) 1253, 758, 691 cm$^{-1}$. $^1$H NMR: (500 MHz) $\delta$ 7.51 (m, 2H), 7.38–7.30 (m, 5H), 6.89 (d, $J = 8.7$ Hz, 2H), 5.34 (d, $J = 4.7$ Hz, 1H), 5.02 (d, $J = 10.0$ Hz, 1H), 4.17 (t, $J = 7.4$ Hz, 1H), 3.89 (t, $J = 7.7$ Hz, 1H), 3.80 (s, 3H), 3.74 (dd, $J = 11.0$, 7.1 Hz, 1H), 3.46 (dd, $J = 11.4$, 7.9 Hz, 1H), 2.96 (m, 1H), 2.65 (m, 1H). $^{13}$C NMR: (125 MHz, CDCl$_3$) $\delta$ 160.5, 132.0, 129.2, 128.9, 128.4, 128.3, 122.0, 114.1, 89.0, 87.2, 82.8, 73.3, 68.8, 68.0, 55.3, 46.6, 43.5. HRMS (EI) calculated for [C$_{21}$H$_{25}$O$_3$]$^+$ requires m/z 336.1456, found m/z 336.1464.

(Table 2, entry 14, minor diastereomer). IR (neat) 1252, 759, 691 cm$^{-1}$. $^1$H NMR: (500 MHz) $\delta$ 7.46 (m, 2H), 7.38–7.28 (m, 5H), 6.90 (d, $J = 8.7$ Hz, 2H), 5.05 (d, $J = 9.5$ Hz, 2H), 4.23 (t, $J = 7.3$ Hz, 1H), 3.92 (t, $J = 7.3$ Hz, 1H), 3.81 (s, 3H), 3.69 (dd, $J = 10.7$, 7.8 Hz, 1H), 3.51 (dd, $J = 10.7$, 7.9 Hz, 1H), 2.55 (m, 2H). $^{13}$C NMR: (125 MHz, CDCl$_3$) $\delta$ 160.6, 132.0, 129.21, 129.17, 128.4, 127.7, 121.5, 114.2, 88.8, 86.8, 82.7, 75.1, 68.4, 68.3, 55.3, 49.8, 48.1. HRMS (EI) calculated for [C$_{21}$H$_{25}$O$_3$]$^+$ requires m/z 336.1464, found m/z 336.1461.

(Table 2, entry 15). Prepared according to the General Procedure using 100 mg (0.340 mmol) of bis(alkene), 5.9 mg (6.8 $\mu$mol) of Ru(bpz)$_3$(PF$_6$)$_2$, 17 mL of MeNO$_2$ and an irradiation time of 2 h. Purification by flash column chromatography afforded the cycloaduct as an oil. Experiment 1: 88.1 mg (0.270 mmol, 79% yield, $dr >10:1$), Experiment 2: 90.5 mg (0.277 mmol, 82% yield, $dr >10:1$). IR (neat) 1251, 738, 704 cm$^{-1}$. $^1$H NMR: (500 MHz) $\delta$ 7.49 (m, 2H), 7.37 (m, 2H), 7.29 (m, 1H), 7.21 (d, $J = 8.6$ Hz, 2H), 6.86 (d, $J = 8.6$ Hz, 2H), 4.97 (d, $J = 9.9$ Hz, 1H), 4.28 (t, $J = 7.0$ Hz, 1H), 3.78 (s, 3H), 3.72 (t, $J = 8.0$ Hz, 1H), 3.66 (dd, $J = 11.4$, 7.4 Hz, 1H), 3.42 (dd, $J = 10.6$, 8.1 Hz, 1H), 2.51 (m, 1H), 2.30 (m, 1H), 1.61 (s, 3H). $^{13}$C NMR: (125 MHz, CDCl$_3$) $\delta$ 160.3, 140.6, 129.1, 128.6, 127.9, 127.1, 126.9, 114.1, 87.3, 86.1, 68.8, 68.2, 55.2, 53.4, 43.0, 28.5. HRMS (EI) calculated for [C$_{20}$H$_{24}$O$_4$]$^+$ requires m/z 326.1613, found m/z 326.1616.

(Table 2, entry 16). Prepared according to the General Procedure using 100 mg (0.230 mmol) of bis(alkene), 1.0 mg (1.1 $\mu$mol) of Ru(bpz)$_3$(PF$_6$)$_2$, 11.5 mL of MeNO$_2$ and an irradiation time of 2 h. Purification by flash column chromatography afforded the cycloaduct as an oil. Experiment 1: 80.0 mg (0.171 mmol, 75% yield, $dr >10:1$), Experiment 2: 76.2 mg (0.163 mmol, 71% yield, $dr >10:1$). IR (neat) 1163, 733, 665 cm$^{-1}$. $^1$H NMR: (500 MHz) $\delta$ 7.57 (d, $J = 8.2$ Hz, 2H), 7.35 (d, $J = 8.6$ Hz, 2H), 7.25 (d, $J = 8.2$ Hz, 2H), 7.20 (d, $J = 8.6$ Hz, 2H), 6.91–6.86 (m, 4H), 5.32 (d, $J = 5.7$ Hz, 1H), 4.86 (d, $J = 9.9$ Hz, 1H), 3.83 (s, 3H), 3.82 (s, 3H), 3.66 (dd, $J = 8.9$, 7.5 Hz, 1H), 3.34 (dd, $J = 9.8$, 7.2 Hz, 1H), 2.82 (m, 2H), 2.47 (m, 1H), 2.43 (s, 3H), 2.28 (m, 1H). $^{13}$C NMR: (125 MHz, CDCl$_3$) $\delta$ 160.5, 159.2, 143.5, 134.2, 129.7, 129.05, 128.96, 128.5, 128.4, 127.1, 114.2, 113.7, 87.0, 82.7, 55.3, 55.2, 49.5, 48.9, 45.1, 39.7, 21.4. HRMS (EI) calculated for [C$_{72}$H$_{32}$NO$_6$S$^+$Na]$^+$ requires m/z 518.1608, found m/z 518.1614.
(Table 2, entry 17). Prepared according to the General Procedure using 100 mg (0.220 mmol) of bis(alkene), 1.0 mg (1.1 µmol) of Ru(bpz)2(PF6)3, 11 mL of MeNO2 and an irradiation time of 2 h. Purification by flash column chromatography afforded the cycloadduct as an oil. Experiment 1: 97.4 mg (0.201 mmol, 91% yield, dr >10:1), Experiment 2: 98.8 mg (0.204 mmol, 92% yield, dr >10:1). IR (neat) 1253, 1034, 733 cm⁻¹. ¹H NMR: (500 MHz) δ 7.49 (d, J = 8.6 Hz, 2H), 7.32 (d, J = 8.6 Hz, 2H), 6.93–6.87 (m, 4H), 5.37 (d, J = 5.7 Hz, 1H), 4.93 (d, J = 9.8 Hz, 1H), 4.18 (m, 2H), 4.06 (m, 2H), 3.82 (s, 3H), 3.81 (s, 3H), 2.64 (dd, J = 12.8, 6.1 Hz, 1H), 2.49 (m, 1H), 2.33 (dd, J = 13.1, 7.1 Hz, 1H), 2.26 (m, 1H), 1.74 (dd, J = 13.0, 11.6 Hz, 1H), 1.53 (t, J = 13.0 Hz, 1H), 1.23 (t, J = 7.2 Hz, 3H), 1.13 (t, J = 7.2 Hz, 3H). ¹³C NMR: (125 MHz, CDCl3) δ 172.2, 171.9, 160.2, 158.9, 129.4, 129.3, 128.9, 128.8, 114.1, 113.5, 89.5, 84.8, 61.6, 61.5, 57.4, 55.2, 55.2, 54.5, 46.2, 40.8, 36.5, 35.1, 14.0, 13.8. HRMS (EI) calculated for [C₂H₅O₅+Na]⁺ requires m/z 507.1990, found m/z 507.2000.

(As shown above).

(As shown above).

IV. Endoperoxide opening reactions

**Compound 6.** A 2 dram vial equipped with a stirbar was charged with 139 mg (0.440 mmol) of 5. AcOH (2.2 mL) and zinc dust (144 mg, 2.2 mmol) were added, the vial was sealed with a Teflon cap, and the reaction was stirred at room temperature. After 2 h, the reaction mixture was concentrated and eluted through a short plug of silica using EtOAc. The eluent was concentrated by rotary evaporation, and the residue was purified by chromatography on SiO₂ (2:1 to 1:1 hexanes/EtOAc) to afford 126 mg (0.40 mmol, 91% yield) of the desired product as a colorless solid (mp = 150–151 °C). ¹H NMR: (500 MHz, CDCl₃) δ 7.34 (m, 4H), 7.28 (m, 1H), 7.19 (d, J = 8.6 Hz, 2H), 6.85 (d, J = 8.6 Hz, 2H), 4.79 (s, 1H), 4.48 (d, J = 9.0 Hz, 1H), 3.88 (dd, J = 9.0, 7.7 Hz, 1H), 3.80 (m, 4H), 3.79 (d, J = 9.1, 6.6 Hz, 1H), 3.43 (dd, J = 9.1, 7.8 Hz, 1H), 3.39 (dd, J = 9.3, 6.1 Hz, 1H), 3.03 (s, 3H), 2.77 (m, 1H), 2.53 (m, 1H). ¹³C NMR: (125 MHz, CDCl₃) δ 159.4, 142.4, 134.9, 128.4, 127.7, 127.6, 126.7, 114.0, 76.3, 74.4, 71.0, 70.2, 55.3, 49.8, 48.1. HRMS (EI) calculated for [C₁₉H₂₅O₄+Na]⁺ requires m/z 337.1411, found m/z 337.1409.

**Compound 7.** A 2 dram vial equipped with a stirbar was charged with 74.0 mg (0.240 mmol) of endoperoxide 5. Dry CH₂Cl₂ (1.2 mL) and NEt₃ (10 µL, 0.07 mmol) were added sequentially, the vial was sealed with a Teflon cap, and the reaction was stirred at room temperature. After 13 h, the reaction mixture was concentrated by rotary evaporation and the crude reaction mixture was purified by chromatography on SiO₂ (2:1 to 1:1 hexanes/EtOAc) to afford 69.0 mg (0.22 mmol, 92% yield) of a colorless oil. ¹H NMR: (500 MHz, CDCl₃) δ 7.95 (d, J = 7.8 Hz, 2H), 7.56 (t, J = 7.2 Hz, 1H), 7.44 (t, J = 7.5 Hz, 2H), 7.27 (d, J = 8.7 Hz, 2H), 6.85 (d, J = 8.7 Hz, 2H), 4.61 (d, J = 9.0 Hz, 1H), 4.26 (m, 2H), 3.89 (m, 1H), 3.78 (s, 3H), 3.74 (dd,
\[ J = 9.0, 7.2 \text{ Hz}, \text{1H} \], 3.60 (dd, \( J = 9.0, 4.6 \text{ Hz}, \text{1H} \)), 3.16 (m, \text{1H}), 2.33 (s, \text{1H}). \]^1C NMR: (125 MHz, CDCl\(_3\)) \( \delta \) 200.0, 159.4, 136.4, 134.9, 133.2, 128.6, 128.6, 127.6, 114.0, 75.7, 71.3, 70.8, 55.2, 50.6, 49.7. HRMS (E1) calculated for \([\text{C}_{19}\text{H}_{20}\text{O}_4+\text{Na}]^+\) requires m/z 335.1254, found m/z 335.1256.

V. Representative NOE data

\[
\begin{align*}
\text{Table 2, entry 1} & : 3.3\% \\
\text{Table 2, entry 12} & : 3.8\% \\
\text{Table 2, entry 14} & : 3.0\% \\
\text{Table 2, entry 15} & : 2.8\% \\
\text{Table 2, entry 17} & : 2.3\%
\end{align*}
\]

VI. Cytotoxicity screening data

Table S-1. Tabulated cytotoxicity data for representative endoperoxides from Table 2.

<table>
<thead>
<tr>
<th>Compound</th>
<th>IC50 ((\mu\text{M}))</th>
<th>SE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Table 2, Entry 1</td>
<td>&gt;100</td>
<td>NA</td>
</tr>
<tr>
<td>Table 2, Entry 3</td>
<td>27.64</td>
<td>1.27</td>
</tr>
<tr>
<td>Table 2, Entry 5</td>
<td>&gt;100</td>
<td>NA</td>
</tr>
<tr>
<td>Table 2, Entry 6</td>
<td>77.72</td>
<td>1.82</td>
</tr>
<tr>
<td>Table 2, Entry 7</td>
<td>38.71</td>
<td>2.66</td>
</tr>
<tr>
<td>Table 2, Entry 11</td>
<td>&gt;100</td>
<td>NA</td>
</tr>
<tr>
<td>Table 2, Entry 12</td>
<td>13.18</td>
<td>0.63</td>
</tr>
<tr>
<td>Table 2, Entry 13</td>
<td>44.30</td>
<td>1.89</td>
</tr>
<tr>
<td>Table 2, Entry 14</td>
<td>4.56</td>
<td>0.19</td>
</tr>
<tr>
<td>Table 2, Entry 16</td>
<td>17.00</td>
<td>0.46</td>
</tr>
</tbody>
</table>

As an initial demonstration of their potential biological activity, a selection of the compounds reported in Table 2 were assayed for cytotoxicity in human prostate cancer cells (Du145s). Cells were treated for 72 hours with each test compound and then the amount of live cells was quantified using an ATP determining assay reagent, Cell Titer Glo (Promega). The IC\(_{50}\) was determined using curve fitting software, xIfit 5.0 (IDBS), to determine the concentration at which point 50% cytotoxicity was observed. Working stocks were prepared at a final concentration of 100X in anhydrous DMSO. Serial dilutions were made in DMSO in 96-well polypropylene plates using the Precision XS liquid handler (BioTek, Inc.). Compounds were divided equally into the corresponding wells of a 384-well plate in all 4 quadrants using a Biomek FX liquid handler with 96 channel pipetting head (Beckman-Coulter, Inc.). Compounds
were stored at –20 °C in 100% DMSO until the day of the assay(s). Freeze-thaw cycles are minimized to a maximum of 10 per plate.

All cell lines were maintained as previously reported.\(^8\) Cells were harvested by trypsinization using 0.25% trypsin and 0.1% EDTA and then counted in a Cellometer Auto T4 cell counter (Nexcelom, inc), before dilution for assay plating. Cell plating, compound handling and assay set up were performed as previously reported (Langenhan, et al) except that the cells were plated in 50 µL volumes in 384-well clear bottom, tissue culture plates (Corning-Costar, Inc). Compounds were added from the 384-well compound stock plates at a 1:100 dilution using a Biomek FX liquid handler equipped with a 384-channel head (Beckman Coulter, Inc.). 15 µL of cell titer-glo reagent (Promega Corporation, Inc.) was added and incubated for 10 min at room temperature with gentle agitation to lyse the cells.

IC\(_{50}\)s for cytotoxicity assays were determined cell-titer glo using xlfit 5.0 as previously reported in Langenhan, et al. The IC\(_{50}\) determined using the best fit curve for dosage response is reported as the final IC\(_{50}\). The best fit curve is defined as the curve that has the lowest standard error. If the standard error exceeds 10% of the IC\(_{50}\), the assay is deemed a failure and repeated.

VII. References

**o,p-Dimethoxycinnamyl alcohol**

\[
\text{MeO} \quad \text{O} \quad \text{Me}
\]

**\(^1\)H NMR**

500 MHz

CDCl\(_3\)
$o,p$-Dimethoxycinnamyl alcohol

$\begin{array}{c}
\text{MeO} \\
\downarrow \\
\text{O} \\
\downarrow \\
\text{OH} \\
\end{array}$

$^{13}$C NMR
125 MHz
CDCl$_3$
Substrate for Table 2, entry 5

\[ \text{MeO} - \text{O} - \text{O} - \text{Me} \]

\( ^1 \text{H NMR} \)
500 MHz
CDCl\(_3 \)
Substrate for Table 2, entry 5

\( \text{MeO} \)\( \text{O} \)\( \text{O} \)\( \text{Me} \)

\( ^{13} \text{C NMR} \)

125 MHz

\( \text{CDCl}_3 \)
(E)-p-Nitrocinnamyl (E)-cinnamyl ether

\[ \text{O}_2\text{N} \]
\[ \begin{array}{c} \text{H} \\ \text{H} \\ \text{H} \\ \text{H} \end{array} \]
\[ \text{O} \]
\[ \begin{array}{c} \text{H} \\ \text{H} \\ \text{H} \\ \text{H} \end{array} \]

$^1$H NMR
500 MHz
CDCl$_3$
(E)-p-Nitrocinamyl (E)-cinnamyl ether

\[
\text{O}_2\text{N} \quad \text{O} \quad \text{O} 
\]

\[13^C \text{ NMR} \]
125 MHz
CDCl\textsubscript{3}
Substrate for Table 2, entry 9

Boc\text{H-N-} \begin{array}{c} \text{O} \end{array} \text{O-} \text{Boc}

$^1$H NMR
500 MHz
CDCl$_3$
Substrate for Table 2, entry 9

BocHNN

\( ^{13}\text{C NMR} \)

125 MHz

CDCl\(_3\)
Substrate for Table 2, entry 12

MeO-\(\text{CF}_3\)-O-\(\text{CF}_3\)

\(^1\)H NMR
500 MHz
CDCl\(_3\)
Substrate for Table 2, entry 12

$\text{MeO-} \equiv \text{O-} \equiv \text{O-} \equiv \text{OF}_3$

$^{13}\text{C NMR}$

125 MHz

CDCl$_3$
Substrate for Table 2, entry 14

\[ \text{MeO-} \begin{array}{c} \text{O} \\ \text{C-C} \end{array} \text{MeO-} \]

\(^1\text{H NMR}\)
500 MHz
CDCl\(_3\)
Substrate for Table 2, entry 14

MeO

\[ \text{\textsuperscript{13}C NMR} \]

125 MHz

CDCl\textsubscript{3}
Substrate for Table 2, entry 16

\[
\begin{array}{c}
\text{MeO} \\
\text{Ts} \\
\text{OMe}
\end{array}
\]

$^1$H NMR
500 MHz
CDCl$_3$
Substrate for Table 2, entry 16

MeO-\begin{array}{c}
\text{Ts} \\
\text{N}
\end{array} \begin{array}{c}
\text{OMe}
\end{array}

$^{13}$C NMR
125 MHz
CDCl$_3$
Substrate for Table 2, entry 17

\[ \text{MeO} \quad \text{CO}_2\text{Et} \quad \text{CO}_2\text{Et} \quad \text{OMe} \]

$^1$H NMR
500 MHz
CDCl$_3$
Substrate for Table 2, entry 17

\[
\text{MeO} \quad \text{CO}_2\text{Et} \quad \text{CO}_2\text{Et} \quad \text{MeO}
\]

$^{13}$C NMR
125 MHz
CDCl$_3$
Substrate for Table 2, entry 18

\[
\begin{align*}
\text{MeO} &- \text{C} - \text{C} - \text{C} - \text{C} - \text{OMe} \\
\end{align*}
\]

\(^1H\) NMR
500 MHz
CDCl\(_3\)
Substrate for Table 2, entry 18

\[ \text{MeO} \quad \text{MeO} \]

$^{13}$C NMR
125 MHz
CDCl$_3$
Major product for Table 2, entry 1

^{1}H NMR
500 MHz
CDCl_{3}
Major product for Table 2, entry 1

MeO-aryl-O-aryl-Ph

$^{13}$C NMR
125 MHz
CD$_3$CN
Major product for Table 2, entry 3

OMe
O

Ph

$^1$H NMR
500 MHz
CDCl$_3$
Major product for Table 2, entry 3

\[
\begin{align*}
\text{OMe} & \quad \text{Ph} \\
\text{O} & \quad \text{O}
\end{align*}
\]

$^{13}$C NMR
125 MHz
CDCl$_3$
Major product for Table 2, entry 5

\chem{\text{MeO-}C_{\text{aryl}}-O-\text{Ph}^\text{OMe}}

$^1$H NMR
500 MHz
CDCl$_3$
Major product for Table 2, entry 5

\[
\text{MeO-}\overset{\text{O}}{\text{-}}\overset{\text{O}}{\text{-}}\overset{\text{O}}{\text{-}}\overset{\text{Ph}}{\text{-}}
\]

$^{13}$C NMR
125 MHz
CDCl$_3$
Major product for Table 2, entry 6

![Chemical Structure]

$^1$H NMR
500 MHz
CDCl$_3$
Major product for Table 2, entry 6

![Chemical Structure Image]

\(^{13}\text{C NMR}

125 MHz

CDCl\textsubscript{3}
Major product for Table 2, entry 7

MeO-Br

\(^1\)H NMR
500 MHz
CDCl\(_3\)
Major product for Table 2, entry 7

\[ \text{MeO-} \]
\[ \text{Br-} \]
\[ \text{O-} \]
\[ \text{O-} \]
\[ \text{Ph} \]

$^{13}$C NMR
125 MHz
CDCl$_3$
Major product for Table 2, entry 8

TIPSO

$^1$H NMR
500 MHz
CDCl$_3$
Major product for Table 2, entry 8

\[
\text{TIPSO-}
\]

\[
\text{O-O-}
\]

\[
\text{CDCl}_3
\]

$^{13}$C NMR
125 MHz
CDCl$_3$
Major product for Table 2, entry 9

\[ \text{BocHN} - \text{O} - \text{O} - \text{Ph} \]

$^1\text{H NMR}$
500 MHz
CDCl$_3$
Major product for Table 2, entry 9

\[ \text{BocHN-} \overset{\text{O}}{\text{O}} \overset{\text{O}}{\text{O}} \text{Ph} \]

\[ ^{13}\text{C NMR} \]

125 MHz

CDC\textsubscript{3}
Major product for Table 2, entry 11

\[ \text{MeO-} \begin{array}{c} \text{O} \\ \text{O} \\ \text{MeO} \end{array} \]

$^1$H NMR
500 MHz
CDCl$_3$
Major product for Table 2, entry 11

MeO-\[
\begin{array}{c}
| & | \ \\
| & | \ \\
\end{array}
\]
-OMe

$^{13}$C NMR
125 MHz
CDCl$_3$
Major product for Table 2, entry 12

![Chemical structure](image)

$^1$H NMR
500 MHz
CDCl$_3$
Major product for Table 2, entry 12

$^{13}$C NMR
125 MHz
CDCl$_3$
Minor product for Table 2, entry 12

$^1$H NMR
500 MHz
CDCl$_3$
Minor product for Table 2, entry 12

\[
\text{MeO} \quad \text{O} \quad \text{O} \quad \text{CF}_3
\]

\[13\text{C NMR}\]

125 MHz

CDCl\textsubscript{3}
Major product for Table 2, entry 13

MeO

O

O

Cl

\[ ^1H \text{ NMR} \]

500 MHz

CDCl\textsubscript{3}
Major product for Table 2, entry 13

\[
\text{MeO-} - \overset{\text{O}}{\underset{\text{O}}{\text{O}}} - \text{Cl}
\]

\(^{13}\text{C NMR}
\]

125 MHz

CD$_3$CN
Major product for Table 2, entry 14

\[ \text{MeO} \quad \text{O} \quad \text{O} \quad \text{O} \quad \text{C} \]

$^1$H NMR
500 MHz
CDCl$_3$
Major product for Table 2, entry 14

$^{13}$C NMR
125 MHz
CDCl$_3$
Minor product for Table 2, entry 14

$^1$H NMR
500 MHz
CDCl$_3$
Minor product for Table 2, entry 14

$^{13}$C NMR
125 MHz
CDCl$_3$
Major product for Table 2, entry 15

MeO
\[ \begin{array}{c}
\mathrm{O} \\
\mathrm{O}
\end{array} \]
\[ \begin{array}{c}
\mathrm{MeO} \\
\mathrm{MeO}
\end{array} \]

$^1$H NMR
500 MHz
CDCl$_3$
Major product for Table 2, entry 15

$^{13}$C NMR
125 MHz
CDCl$_3$
Major product for Table 2, entry 16

\[
\text{MeO} \quad \text{O} \quad \text{O} \quad \text{OMe}
\]

\[
\text{Ts}
\]

\[
\text{\textsuperscript{1}H NMR, C NMR}
\]

\[
\text{500 MHz, 125 MHz}
\]

\[
\text{CDCl} \_3
\]

\[
\text{CDCl}_3
\]
**Major product for Table 2, entry 17**

**Major product for Table 2, entry 17**

MeO

![Chemical structure](image)

$^{13}$C NMR
125 MHz
CDCl$_3$

**H NMR**
500 MHz
CDCl$_3$

**1** H!NMR
500 MHz
CDCl$_3$

**C!NMR**
125 MHz
CDCl$_3$
Major product for Table 2, entry 18

\begin{center}
\includegraphics[width=\textwidth]{nmr_spectrum.png}
\end{center}

$^1$H NMR
500 MHz
CDCl$_3$
Major product for Table 2, entry 18

\[ \text{MeO-} \begin{array}{c} \text{O} \end{array} \begin{array}{c} \text{O} \end{array} \text{OMe} \]

$^{13}$C NMR
125 MHz
CDCl$_3$
Compound 7

\[ \text{MeO} \begin{array}{c}
\text{OH} \\
\text{O}
\end{array} \]

\(^1\text{H NMR}
500 MHz
CDCl\textsubscript{3}
Compound 7

\[ \text{MeO} \]

\[ \text{OH} \quad \text{O} \quad \text{O} \]

\[ \text{MeO} \]

$^{13}$C NMR

125 MHz

CDCl$_3$
Compound 6

$^1$H NMR
500 MHz
CDCl$_3$
Compound 6

$^{13}$C NMR
125 MHz
CDCl$_3$