

Supporting Information for:
Catalytic, Enantioselective [4+2]-Cycloadditions of Ketene Enolates and *o*-Quinones:
Efficient Entry to Chiral, α,α -Oxygenated Carboxylic Acid Derivatives

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General. Unless otherwise stated, all reactions were carried out under anhydrous, air-free conditions. All solvents were dried and distilled by standard procedures. The ^1H and ^{13}C NMR spectra were acquired on a Bruker Avance400 MHz spectrometer. The ^1H (400 MHz) and ^{13}C (101 MHz) chemical shifts are given in parts per million (δ) with respect to TMS standards and residual chloroform. FTIR spectra were recorded on a Bruker IFS-55 spectrometer and optical rotations were recorded on a Perkin Elmer 120 polarimeter at room temperature. Enantiomeric ratios were obtained using a Regis Technologies (*R,R*)-Whelk-01 Chiral HPLC column or Chiracel OD column. Benzoylquinidine (**3**) was formed from quinidine (Sigma) and benzoyl chloride according to the method of Pracejus.¹ All other chemicals were purchased from Aldrich Chemical Corporation and Acros Organics.

General procedure for the synthesis of *o*-chloranil cycloadducts from aromatic acid chlorides (4c,e,f**):**

Benzoylquinidine (0.055 mmol) was placed into a 25 mL round bottom flask equipped with a magnetic stir bar and was dissolved in 3 mL of THF. The reaction was cooled to $-78\text{ }^\circ\text{C}$ and Hünig's base (0.55 mmol) was added followed by *o*-Chloranil (0.55 mmol) as a solution in 4 mL of THF. The acid chloride (0.55 mmol), as a solution in 3 mL of THF, was then added to the reaction over 5 h via syringe pump. The reaction was kept at $-78\text{ }^\circ\text{C}$ during the entire addition and for 2 h thereafter. The reaction was monitored by TLC and stopped once all of the quinone was consumed. The reaction mixture was then filtered through a plug of silica, and the plug is then flushed thoroughly with hexanes. Concentration of the filtrate *in vacuo* yielded pure product.

General procedure for the synthesis of *o*-chloranil cycloadducts from aliphatic acid chlorides (4a,b,d**):**

Benzoylquinidine (0.055 mmol) was placed into a 25 mL round bottom flask equipped with a magnetic stir bar and was dissolved in 3 mL of THF. The flask was cooled to $-78\text{ }^\circ\text{C}$ and Hünig's base (0.55 mmol) was added followed by *o*-Chloranil (0.55 mmol) as a solution in 4 mL of THF. The acid chloride (0.55 mmol), as a solution in 3 mL of THF, was then added to the reaction. The reaction was monitored by TLC and stopped once all of the quinone was consumed, about 5 h. The reaction mixture was then filtered through a plug of silica, and the plug is then flushed thoroughly with hexanes. Concentration of the filtrate *in vacuo* yielded pure product.

Procedure for the synthesis of *o*-bromanil cycloadduct (4g**):**

Benzoylquinidine (0.055 mmol) was placed into a 25 mL round bottom flask equipped with a magnetic stir bar and was dissolved in 8 mL of THF. The reaction was cooled to $-78\text{ }^\circ\text{C}$ and Hünig's base (0.55 mmol) was added followed by butyryl chloride (0.55 mmol), as a solution in 2 mL of THF. *o*-Bromanil (0.55 mmol) as a solution in 3 mL of THF, was then added to the reaction over 5 h via syringe pump. The reaction mixture was then filtered through a plug of silica, and the plug is then flushed thoroughly with hexanes. Concentration of the filtrate *in vacuo* yielded pure product.

(1) Pracejus, H.; Maetje, H. *J. Prakt. Chem.* **1964**, *24*, 195.

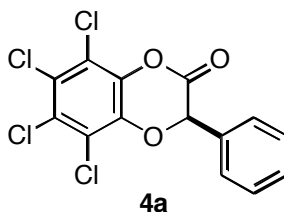
Procedure for the synthesis of phenanthrenequinone cycloadduct (4h):

Benzoylquinidine (0.055 mmol) was placed into a 25 mL round bottom flask equipped with a magnetic stir bar and was dissolved in 8 mL of THF. The reaction was cooled to -78°C and Hünig's base (0.55 mmol) was added followed by butyryl chloride (0.55 mmol), as a solution in 2 mL of THF. Phenanthrenequinone (0.55 mmol) as a solution in 3 mL of THF was then added to the reaction over 5 h via syringe pump. The reaction mixture was then filtered through a plug of silica, and the plug is then flushed thoroughly with hexanes. Concentration of the filtrate *in vacuo* yielded crude product, which was purified by column chromatography on silica gel (hexanes/EtOAc eluent).

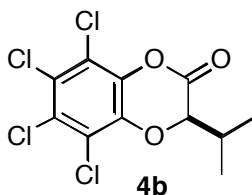
General procedure for the synthesis of α -hydroxy esters (8):

The cyclized product **4(a-d)** (0.14 mmol) was placed into a 25 mL round bottom flask equipped with a magnetic stir bar and was dissolved in 3 mL of 5:1 (MeOH/CH₂Cl₂). The reaction, as determined by TLC was completed in times varying from 30 min to 2 h at room temperature. Upon completion, the reaction mixture was concentrated down under reduced pressure. The residue was then dissolved in 2.6 mL of 4:1 (CH₃CN/H₂O) in a round bottom flask equipped with a magnetic stir bar. Cerium ammonium nitrate (0.14 mmol) was added to the reaction at 0°C and stirred overnight. Water was then added and the mixture was extracted 3X with EtOAc. The organic layer was dried over MgSO₄ and concentrated *in vacuo*. The crude product was then filtered through a plug of Florisil, and the plug is then flushed thoroughly with hexanes. Concentration of the filtrate *in vacuo* yielded pure product. The optical rotations for **8a-8d**² are known in literature and the results confirmed that the (R)-enantiomer is in excess.

Characterization Data:

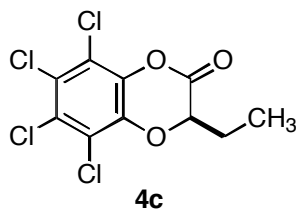


5,6,7,8-Tetrachloro-3-phenyl-benzo[1,4]dioxin-2-one (4a). White crystalline solid: % yield = 90; % ee = 99; mp = $181-183^{\circ}\text{C}$; $[\alpha]_{\text{D}}^{25} = -21.5^{\circ}$ ($c = 0.010$, CHCl₃); ¹H NMR (CDCl₃) δ 7.41 (m, 5H), 6.00 (s, 1H) ppm; ¹³C NMR (CDCl₃) δ 160.3, 138.2, 137.6, 131.0, 130.1, 129.4, 129.2, 127.5, 126.2, 121.7, 120.7, 76.6 ppm; IR (CH₂Cl₂) 1794 cm^{-1} . HPLC (Whelk-01, 1% *i*-PrOH/hexanes, 1.0 mL/min) (R) = 9.16, (S) = 10.64. Anal Calcd for C₁₄H₆Cl₄O₃ C, 46.2; H, 1.66. Found C, 46.4; H, 1.71.

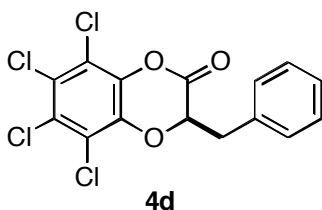


5,6,7,8-Tetrachloro-3-isopropyl-benzo[1,4]dioxin-2-one (4b). White crystalline solid: % yield = 75, % ee = 93; mp = $102-105^{\circ}\text{C}$; $[\alpha]_{\text{D}}^{25} = -6.8^{\circ}$ ($c = 0.010$, CHCl₃); ¹H NMR (CDCl₃) δ 4.51 (d, 1H), 2.29 (m, 1H), 1.15 (d, 3H), 1.12 (d, 3H) ppm; ¹³C NMR (CDCl₃) δ 161.1, 137.5, 128.8, 126.9, 125.8, 121.3, 120.4, 80.0, 29.8, 18.3, 17.4 ppm; IR (CH₂Cl₂) 1775 cm^{-1} . HPLC (Whelk-01, 1% *i*-PrOH/hexanes, 1.0 mL/min) (R) = 5.79, (S) = 6.72. Anal Calcd for C₁₁H₈Cl₄O₃ C, 40.0; H, 2.44. Found C, 39.8; H, 2.42.

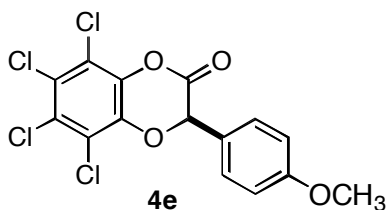
(2) (a) Barrow, R. A.; Moore, R.; Li, L.-H.; Tius, M. A.; *Tetrahedron*, **2000**, *56*, 3339-3352. (b) Moore, Wilner J.; Marel, Gijs A. Van der; Liskamp, Rob J.; *J. Org. Chem.* **1995**, *60*, 5157-5169. (c) Caglioti, L. *Tetrahedron* **1969**, *25*, 2193-2221. (c) Burk, M. J.; Kalberg, C. S.; Pizzano, A. *J. Am. Chem. Soc.* **1998**, *120*, 4345-4353.



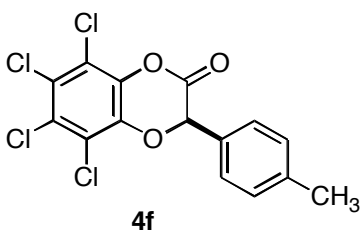
5,6,7,8-Tetrachloro-3-ethyl-benzo[1,4]dioxin-2-one (4c). White crystalline solid: % yield = 90; % ee = 90; mp = 120-122° C; $[\alpha]_D^{25} = +7.3^\circ$ (c = 0.005, CHCl₃); ¹H NMR (CDCl₃) δ 4.65 (m, 1H), 2.01 (m, 2H), 1.17 (m, 3H) ppm; ¹³C NMR (CDCl₃) δ 161.9, 138.7, 137.7, 129.0, 127.1, 121.5, 120.6, 60.3, 23.8, 9.18 ppm; IR (CH₂Cl₂) 1778 cm⁻¹. HPLC (Chiracel OD, 7% *i*-PrOH/hexanes, 1.0 mL/min) (S) = 6.95, (R) = 7.34. Anal Calcd for C₁₀H₆Cl₄O₃ C, 38.0; H, 1.91. Found C, 37.8; H, 1.92.



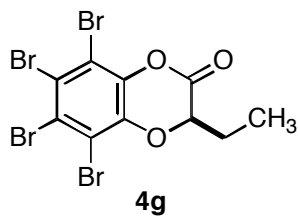
3-Benzyl-5,6,7,8-tetrachloro-benzo[1,4]dioxin-2-one (4d). White crystalline solid: % yield = 72; % ee = 99; mp = 154-156° C; $[\alpha]_D^{25} = +29.0^\circ$ (c = 0.010, CHCl₃); ¹H NMR (CDCl₃) δ 7.27 (m, 5H), 4.97 (m, 1H), 3.39 (m, 1H), 3.29 (m, 1H) ppm; ¹³C NMR (CDCl₃) δ 161.6, 138.6, 137.3, 133.9, 129.5, 129.0, 128.7, 127.7, 127.0, 121.3, 120.5, 75.9, 37.1 ppm; IR (CH₂Cl₂) 1789 cm⁻¹. HPLC (Whelk-01, 1% *i*-PrOH/hexanes, 1.0 mL/min) (R) = 8.84, (S) = 9.34. Anal Calcd for C₁₅H₈Cl₄O₃ C, 47.6; H, 2.12. Found C, 47.4; H, 2.11.



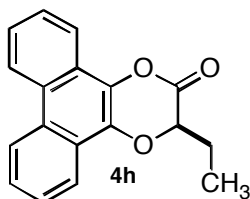
5,6,7,8-Tetrachloro-3-(4-methoxy-phenyl)-benzo[1,4]dioxin-2-one (4e). White crystalline solid: % yield = 58; % ee = 99; mp = 173-175° C; $[\alpha]_D^{25} = +1.6^\circ$ (c = 0.007, CHCl₃); ¹H NMR (CDCl₃) δ 7.30 (m, 2H), 6.92 (m, 2H), 5.94 (s, 1H), 3.80 (s, 3H) ppm; ¹³C NMR (CDCl₃) δ 161.2, 138.5, 138.0, 133.9, 129.4, 128.3, 123.2, 122.1, 120.8, 115.0, 114.3, 76.6, 55.6 ppm; IR (CH₂Cl₂) 1775 cm⁻¹. HPLC (Whelk-01, 1% *i*-PrOH/hexanes, 1.0 mL/min) (R) = 17.73, (S) = 19.38. Anal Calcd for C₁₅H₈Cl₄O₄ C, 45.7; H, 2.05. Found C, 45.4; H, 2.08.



5,6,7,8-Tetrachloro-3-p-tolyl-benzo[1,4]dioxin-2-one (4f). Clear viscous oil: % yield = 75; % ee = 93; $[\alpha]_D^{25} = +0.4^\circ$ (c = 0.003, CHCl₃); ¹H NMR (CDCl₃) δ 7.72 (m, 1H), 7.53 (m, 1H), 7.28 (m, 2H), 5.91 (s, 1H), 2.41 (s, 3H) ppm; ¹³C NMR (CDCl₃) δ 161.2, 137.7, 137.2, 131.9, 130.5, 129.1, 129.0, 128.5, 126.8, 121.2, 120.0, 76.1, 21.1 ppm; IR (CH₂Cl₂) 1781 cm⁻¹. HPLC (Whelk-01, 1% *i*-PrOH/hexanes, 1.0 mL/min) (R) = 9.15, (S) = 12.35. Anal Calcd for C₁₅H₈Cl₄O₃ C, 47.7; H, 2.13. Found C, 47.6; H, 2.14.



5,6,7,8-Tetrabromo-3-ethyl-benzo[1,4]dioxin-2-one (4g). Yellow crystalline solid: % yield = 90, % ee = 95; $[\alpha]_D^{25} = +1.4^\circ$ ($c = 0.003$, CHCl_3); ^1H NMR (CDCl_3) δ 4.62 (m, 1H), 2.02 (m, 2H), 1.05 (m, 3H) ppm; ^{13}C NMR (CDCl_3) δ 161.0, 137.2, 137.1, 133.9, 131.5, 129.3, 129.1, 58.3, 23.1, 10.1 ppm; IR (CH_2Cl_2) 1771 cm^{-1} . HPLC (Whelk-01, 1% *i*-PrOH/hexanes, 1.0 mL/min) (R) = 9.15, (S) = 10.35. Anal Calcd for $\text{C}_{10}\text{H}_6\text{Br}_4\text{O}_3$ C, 24.3; H, 1.22. Found C, 24.5; H, 1.20.



3-Ethylphenanthro[9,10-b][1,4]dioxin-2-one (3H, 4aH, 12bH)-one (4h). Yellow wax: % yield = 60, % ee = 89; ^1H NMR (CDCl_3) δ 8.85 (d, 2H), 7.85 (t, 2H), 7.77 (t, 2H), 7.52 (t, 2H), 4.45 (t, 1H), 1.94 (m, 2H), 0.91 (t, 3H) ppm; ^{13}C NMR (CDCl_3) δ 171.5, 149.7, 133.2, 129.7, 128.9, 128.7, 126.3, 126.1, 123.8, 123.4, 122.8, 122.1, 121.4, 120.8, 120.4, 90.3, 23.1, 8.1 ppm; IR (CH_2Cl_2) 1771 cm^{-1} . HPLC (1% *i*-PrOH/hexanes, 1.0 mL/min) (R) = 15.25, (S) = 16.76. Anal Calcd for $\text{C}_{18}\text{H}_{14}\text{O}_3$ C, 77.7; H, 5.07. Found C, 77.5; H, 5.10.