Angewandte Chemie
Eine Zeitschrift der Gesellschaft Deutscher Chemiker

Supporting Information

for

Angew. Chem. Int. Ed. Z51196

69451 Weinheim, Germany

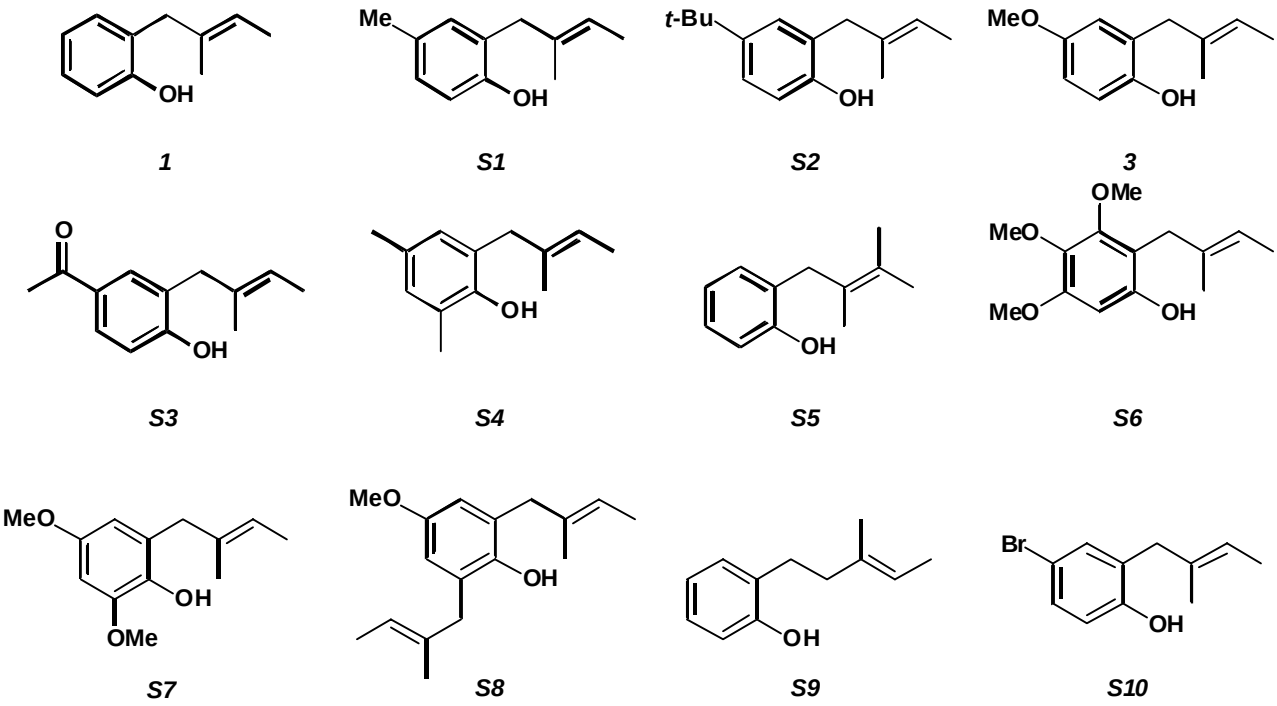
Palladium-Catalyzed Oxidative Wacker Cyclizations in Nonpolar Organic Solvents with Molecular Oxygen: A Stepping Stone to Asymmetric Aerobic Cyclizations

Raissa M. Trend, Yeeman K. Ramtohul, Eric M. Ferreira, and Brian M. Stoltz*

The Arnold and Mabel Beckman Laboratories of Chemical Synthesis, Division of Chemistry and Chemical Engineering, California Institute of Technology, Pasadena, California 91125, USA

Materials and Methods. Unless stated otherwise, reactions were conducted in flame-dried glassware under a nitrogen atmosphere with freshly distilled solvents. All commercially obtained reagents were used as received. Reaction temperatures were controlled by an IKAmag temperature modulator. Thin-layer chromatography (TLC) was conducted with E. Merck silica gel 60 F254 precoated plates (0.25 mm) and visualized via UV and anisaldehyde staining. ICN silica gel (particle size 0.032-0.063 mm) was used for flash column chromatography. Analytical chiral GC was carried out on a Chiraldex G-TA column (30.0 m x 0.25 mm) from Bodman Industries. ^{1}H and ^{13}C NMR spectra were recorded on a Varian Mercury 300 (at 300 MHz and 75 MHz respectively) and are reported relative to Me_4Si (δ 0.0). Data for ^{1}H NMR spectra are reported as follows: chemical shift (δ ppm), multiplicity, coupling constant (Hz) and integration. Data for ^{13}C NMR spectra are reported in terms of chemical shift. IR spectra were recorded on a Perkin Elmer Paragon 1000 spectrometer and are reported in frequency of absorption (cm^{-1}). High resolution mass spectra were obtained from the UC Irvine Mass Spectral Facility and from the California Institute of Technology Mass Spectral Facility. X-Ray crystallographic data were obtained from the California Institiute of Technology Beckman Institute X-Ray Crystallography Laboratory.

Substrates for Phenol/Olefin Cyclizations



1 ***S1*** ***S2*** ***3***

S3 ***S4*** ***S5*** ***S6***

S7 ***S8*** ***S9*** ***S10***

General Procedure for the Preparation of Substituted Phenols. Phenols **1, S1-S2, 3**, **S4**, **S6-S8**, and **S10** were synthesized by the modified procedure of Hurd and Hoffman.[1] To a stirring suspension of NaH (17.5 mmol, 1.1 equiv) in benzene (25 mL) at 0 °C was added a benzene (15 mL) solution of the phenol (15.9 mmol, 1 equiv). The mixture was charged with (*E*)-1-bromo-2-methyl-but-2-ene (17.5 mmol, 1.1 equiv, prepared according to literature procedure[2]) and allowed to warm to 23 °C. After 24 h stirring, benzene was removed under reduced pressure and H_2O (50 mL) and petroleum ether (50 mL) were added. The mixture was extracted with 20% aqueous NaOH (3 x 20 mL) and "Claisen's alkali" (20 mL; 6 g KOH in 5 mL H_2O diluted with 25 mL MeOH). The combined alkali extracts were acidified with 6 N H_2SO_4 and extracted with Et_2O (3 x 50 mL). Combination of the organics, drying over $MgSO_4$, concentration in vacuo and purification by flash column chromatography on silica gel (19:1 hexanes/EtOAc eluent) provided the *o*-substituted phenol.

Phenol 1. 87% yield colorless oil: R_F 0.46 (4:1 hexanes/EtOAc eluent); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.19-7.07 (comp m, 2H), 6.91-6.83 (comp m, 2H), 5.51 (app.qdd, *J* = 6.6, 2.7, 1.7 Hz, 1H), 5.42 (br s, 1H,), 3.34 (s, 2H), 1.66 (d, *J* = 6.6 Hz, 3H), 1.61 (d, *J* = 1.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 155.1, 135.1, 131.1, 128.0, 125.2, 121.4, 120.8, 116.1, 41.7, 15.7, 13.6; IR (film) 3459, 2916, 1454, 1219 cm^{-1}; HRMS (EI$^+$) *m/z* calc'd for $[C_{11}H_{14}O]^+$: 162.1045, found 162.1044.

***p*-Methylphenol S1.** 71% yield colorless oil: R_F 0.40 (4:1 hexanes/EtOAc eluent); ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.95 (d, *J* = 8.2 Hz, 1H,), 6.89 (s, 1H), 6.73 (d, *J* = 8.2 Hz, 1H), 5.49 (app.qd, *J* = 6.7, 0.9 Hz, 1H), 5.23 (s, 1H), 3.33 (s, 2H), 2.27 (s, 3H), 1.66 (d, *J* = 6.5 Hz, 3H), 1.61 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 153.1, 135.3, 131.7, 129.9, 128.6, 124.8, 121.4, 116.0, 42.1, 20.7, 15.8, 13.7; IR (film) 3457, 2918, 1501, 1260, 1196, 1108 cm^{-1}; HRMS (EI$^+$) *m/z* calc'd for $[C_{12}H_{16}O]^+$: 176.1201, found 176.1199.

---

[1] Hurd, C. D.; Hoffman, W. A. *J. Am. Chem. Soc.* **1940**, *62*, 212-222.

[2] Haynes, R. K.; Katsifis, A. G.; Vonwiller, S. C.; Hambley, T. W. *J. Am. Chem. Soc.* **1988**, *110*, 5423-5433.

***p*-*t*-Butylphenol S2.** 47% yield colorless oil: R_F 0.51 (4:1 hexanes/EtOAc eluent); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.16 (dd, *J* = 8.2, 2.2 Hz, 1H), 7.07 (d, *J* = 2.2 Hz, 1H), 6.77 (d, *J* = 8.2 Hz, 1H), 5.49 (app.qd, *J* = 6.6, 1.1 Hz, 1H), 5.24 (s, 1H), 1.66 (dd, *J* = 6.6, 1.1 Hz, 3H), 1.62 (s, 3H), 1.30 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 153.3, 143.8, 135.7, 128.4, 125.2, 124.6, 121.7, 116.0, 43.0, 34.7, 32.3, 16.4, 14.2; IR (film) 3463, 2964, 2909, 2865, 1504, 1364, 1271 cm^{-1}; HRMS (NH_3CI) *m/z* calc'd for $[C_{15}H_{22}O]^+$: 218.1671, found 218.1677.

***p*-Methoxyphenol 3.** 52% yield colorless oil: R_F 0.46 (4:1 hexanes/EtOAc eluent); ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.78-6.65 (comp m, 3H), 5.48 (app.qdd, *J* = 6.6, 2.7, 1.7 Hz, 1H), 5.03 (br s, 1H), 3.77 (s, 3H), 3.33 (s, 2H), 1.65 (dq, *J* = 6.6, 1.1 Hz, 3H), 1.61 (d, *J* = 1.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 153.7, 149.2, 134.9, 126.3, 121.6, 116.7, 112.7, 55.9, 42.2, 15.8, 13.7; IR (film) 3426, 2915, 1504, 1434, 1230, 1206 cm^{-1}; HRMS (NH_3CI) *m/z* calc'd for $[C_{12}H_{16}O]^+$: 192.1150, found 192.1153.

4,6-Dimethylphenol S4. 48% yield colorless oil: R_F 0.72 (4:1 hexanes/EtOAc eluent); ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.85 (s, 1H), 6.75 (s, 1H), 5.54 (app.qdd, *J* = 6.6, 2.7, 1.7 Hz, 1H), 5.33 (s, 1H), 3.34 (s, 2H), 2.25 (s, 3H), 2.21 (s, 3H), 1.67 (dd, *J* = 6.6, 1.1 Hz, 3H), 1.62 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 151.4, 135.6, 130.2, 129.3, 124.6, 124.1, 121.5, 76.5, 42.6, 20.6, 16.0, 15.7, 13.7; IR (film) 3493, 2917, 1485, 1213, 1204 cm^{-1}; HRMS (NH_3CI) *m/z* calc'd for $[C_{13}H_{18}O]^+$: 190.1358, found 190.1355.

4,5,6-Trimethoxyphenol S6. 18% yield white crystalline solid: R_F 0.25 (4:1 hexanes/EtOAc eluent); ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.26 (s, 1H), 5.46 (app.qdd, *J* = 7.0, 3.2, 1.5 Hz, 1H), 5.41 (s, 1H), 3.85 (s, 3H), 3.82 (s, 6H), 3.37 (s, 2H), 1.65 (s, 3H), 1.63 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 152.6, 152.3, 151.9, 136.4, 135.5, 120.8, 110.5, 96.6, 61.4, 61.2, 56.0, 33.9, 15.9, 13.6; IR (film) 3417, 2937, 1607, 1462, 1414, 1126 cm^{-1}; HRMS (EI$^+$) *m/z* calc'd for $[C_{14}H_{20}O_4]^+$: 252.1361, found 252.1352.

4,6-Dimethoxyphenol S7. Phenolic starting material was synthesized by the procedure of Helquist and Bäckvall.[3] 45% yield colorless oil: R_F 0.52 (4:1 hexanes/EtOAc eluent); ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.38 (d, *J* = 2.8 Hz, 1H), 6.26 (d, *J* = 2.8 Hz, 1H), 5.28-5.27 (comp m, 2H), 3.87 (s, 3H), 3.76 (s, 3H), 3.31 (s, 2H), 1.62-1.60 (comp m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 152.8, 147.0, 138.0, 134.6, 126.1, 120.2, 106.1, 97.1, 56.2, 55.9, 39.5, 16.1, 13.8; IR (film) 3521, 2916, 1613, 1497, 1227, 1199 cm^{-1}; HRMS (NH_3CI) *m/z* calc'd for $[C_{13}H_{18}O_3]^+$: 222.1256, found 222.1255.

***p*-Methoxy-*bis*-alkylphenol S8**. 30% yield yellow oil: R_F 0.82 (4:1 hexanes/EtOAc eluent); ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.54 (s, 2H), 5.38 (app.qdd, *J* = 6.6, 2.8, 1.1 Hz, 2H), 5.19 (s, 1H), 3.75 (s, 3H), 3.31 (s, 4H), 1.64 (dd, *J* = 5.5, 1.1 Hz, 6H), 1.31 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 153.1, 147.7, 135.1, 126.9, 121.0, 114.3, 55.8, 41.4, 15.9, 13.7; IR (film) 3490, 2915, 1604, 1478, 1440, 1234, 1193 cm^{-1}; HRMS (NH_3CI) *m/z* calc'd for $[C_{17}H_{24}O_2]^+$: 242.1307, found 242.1310.

***p*-Bromophenol S10**. 49% yield pale green oil: R_F 0.51 (4:1 hexanes/EtOAc eluent); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.09-7.12 (comp m, 2H), 6.61 (d, *J* = 8.8 Hz, 1H), 5.41 (app.qd, *J* = 6.6, 1.7 Hz, 1H), 5.33 (br s, 1H), 3.22 (s, 2H), 1.56 (d, *J* = 6.6 Hz, 3H), 1.50 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 154.5, 134.5, 133.5, 130.9, 127.3, 122.3, 118.0, 112.8, 41.8, 15.7, 13.7; IR (film) 3453, 2916, 1403, 1411, 1263, 1216, 1108 cm^{-1}; HRMS (NH_3CI) *m/z* calc'd for $[C_{11}H_{13}BrO]^+$: 240.0150, found 240.0151.

---

[3] Nikaido, M.; Aslanian, R; Scavo, F.; Helquist, P.; Åkermark, B.; Bäckvall, J-E. *J. Org. Chem.* **1984**, *49*, 4740-4741.

***p*-Acylphenol S3.** Bromophenol **S10** (100 mg, 0.42 mmol, 1.0 equiv) was dissolved in THF and cooled to -78 °C. Upon dropwise addition of *t*-BuLi (1.7 M in pentane, 782 µL, 1.33 mmol, 3.2 equiv), the stirring solution became yellow. After 1.5 h, exchange was complete by TLC and as *N*-methoxy-*N*-methyl acetamide (88 µL, 0.83 mmol, 2.0 equiv) was introduced, the yellow color dissipated. The mixture was allowed to stir at -78 °C for 1 h, then was quenched with 1:1 H_2O/saturated aqueous NH_4Cl (10 mL), warmed to 23 °C, and extracted with Et_2O (3 x 20 mL). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated in vacuo. Purification by flash column chromatography on silica gel (4:1 hexanes/EtOAc eluent) gave the *p*-acyl phenol **S3** (40 mg, 0.20 mmol, 47% yield) as a white crystalline solid: R_F 0.23 (4:1 hexanes/EtOAc eluent); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.81-7.76 (comp m, 2H), 6.87 (d, *J* = 8.3 Hz, 1H), 6.10 (s, 1H), 5.55 (app.qdd, *J* = 6.4, 2.8, 1.4 Hz, 1H), 3.42 (s, 2H), 2.56 (s, 3H), 1.67 (dd, *J* = 6.4, 1.4 Hz, 3H), 1.60 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 197.4, 160.1, 134.8, 131.9, 130.5, 129.6, 125.0, 122.5, 116.1, 42.1, 26.6, 15.7, 13.7; IR (film) 3264, 2917, 1655, 1589, 1280 cm^{-1}; HRMS (EI$^+$) *m/z* calc'd for $[C_{13}H_{16}O_2]^+$: 204.1150, found 204.1152.

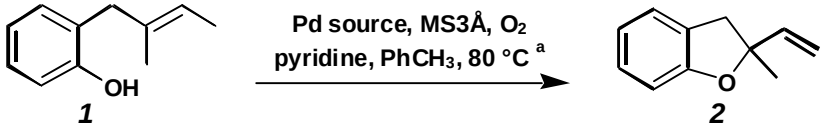
Tetrasubstituted olefin S5. Conversion of known 2,3-dimethyl-but-2-en-1-ol[4] to 1-chloro-2,3-dimethyl-but-2-ene followed Corey's procedure.[5] Dimethyl sulfide (0.63 mL, 8.55 mmol, 1.6 equiv) was added to a solution of *N*-chlorosuccinimide (1.14 g, 8.55 mmol, 1.6 equiv) in CH_2Cl_2 (45 mL) at 0 °C. The mixture was stirred for 30 min and cooled to -20 °C. A solution of 2,3-dimethyl-but-2-en-1-ol (537 mg, 5.34 mmol, 1.0 equiv) in CH_2Cl_2 (5 mL) was introduced dropwise over 5 min. The resulting clear, colorless solution was warmed to 0 °C and allowed to stir for 1 h, then poured into ice-cold brine (20 mL). The layers were separated, and the aqueous portion extracted with Et_2O (3 x 20 mL). The organics were combined, washed with ice-cold brine (2 x 30 mL), dried over $MgSO_4$, filtered, and concentrated in vacuo. The crude, unstable 1-chloro-2,3-dimethyl-but-2-ene was used immediately without further purification. NaH (60% in mineral oil, 214 mg, 5.34 mmol, 1.0 equiv) was suspended in benzene (5 mL), cooled to 0 °C, and subjected to a benzene (5 mL) solution of phenol (401 mg, 4.27 mmol, 0.8 equiv). The prepared allylic chloride was transferred to the phenoxide with additional benzene (10 mL). The mixture was allowed to warm to 23 °C and stirred for 12 h. Benzene was removed by rotary evaporation from the opaque, pink mixture, and H_2O (50 mL) and petroleum ether (50 mL) were added. The mixture was extracted with 20% aqueous NaOH (3 x 20 mL) and "Claisen's alkali" (10 mL; 6 g KOH in 5 mL H_2O diluted with 25 mL MeOH). The combined alkali extracts were acidified with 6 N H_2SO_4 and extracted with Et_2O (3 x 50 mL). The organics were combined, dried over $MgSO_4$, filtered, and concentrated in vacuo. Flash column chromatography on silica gel (19:1 hexanes/EtOAc eluent) afforded **S5** (286 mg, 1.62 mmol, 38% yield from phenol) as a slightly unstable, clear, colorless oil: R_F 0.52 (4:1 hexanes/EtOAc eluent); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.16-6.98 (comp m, 2H), 6.83 (app.td, *J* = 7.4, 1.1 Hz, 1H), 6.62 (d, *J* = 7.7 Hz, 1H), 4.79 (s, 1H), 3.35 (s, 2H), 1.63 (s, 3H), 1.53 (s, 3H), 1.52 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 155.6, 130.7, 128.0, 127.4, 126.6, 126.5, 121.2, 116.1, 35.7, 21.2, 20.9, 18.6; IR (film) 3440, 2917, 2860, 1488, 1454, 1218 cm^{-1}; HRMS (NH_3CI) *m/z* calc'd for $[C_{12}H_{16}O]^+$: 176.1201, found 176.1206.

Homoallylic phenol S9. A solution of MeONHMe•HCl (4.88 g, 50.0 mmol, 2.5 equiv) in CH_2Cl_2 (40 mL) was cooled to -5 °C in an acetone/ice bath. $AlMe_3$ (2.0 M in toluene, 25.0 mL 50.0 mmol, 2.5 equiv) was introduced dropwise over 15 min, and the mixture allowed to stir for 1 h. Bubbling commenced upon addition of dihydrocoumarin (2.53 mL, 20.0 mmol, 1.0 equiv) to the clear, colorless solution and the mixture was quenched after 10 min with saturated aqueous $NaHCO_3$ (15 mL). After extraction with CH_2Cl_2 (3 x 25 mL), the organics were combined, dried over Na_2SO_4, and concentrated to toluene. Following redissolution in THF (40 mL), MeMgBr (3 M in Et_2O, 16.7 mL, 50.0 mmol, 2.5 equiv) was added dropwise at 0 °C and the mixture allowed to stir for 15 min. After quenching with saturated aqueous NH_4Cl (20 mL) and extraction with Et_2O, the combined organics were dried over $MgSO_4$ and concentrated under reduced pressure to yield a pale yellow oil

[4] McCullogh, J. J.; MacInnis, W. K.; Lock, C. J. L; Faggiani, R. *J. Am. Chem. Soc.* **1982**, *104*, 4644-4658.
[5] Corey, E. J.; Kim, C. U.; Takeda, M. *Tetrahedron Lett.* **1972**, *42*, 4339-4342.

which was purified by flash column chromatography on silica gel (9:1 hexanes/EtOAc eluent) to give the methyl ketone (2.56 g,15.6 mmol, 78%) as a colorless oil. Dry potassium *t*-butoxide (4.72 g, 42.1 mmol, 2.7 equiv) was added slowly to a suspension of $EtPPh_3Br$ (15.6 g, 42.1 mmol, 2.7 equiv) in toluene (15 mL) at 0 °C. The mixture became viscous and turned from colorless to yellow to orange. The flask was supplied with additional toluene (15 mL), warmed to 23 °C, and allowed to stir for 2 h. The now red reaction mixture was re-cooled to 0 °C and subjected to a toluene (10 mL) solution of the methyl ketone (2.56 g, 15.6 mmol, 1 equiv). After warming to 23 °C and stirring for 3 h, consumption of the starting material was observed by TLC. The mixture was re-cooled to 0 °C, quenched with 1:1 H_2O/saturated aqueous NH_4Cl, and extracted with EtOAc (3 x 75 mL). The organic layers were combined, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Column chromatography of the yellow residue on silica gel (19:1 hexanes/EtOAc eluent) and removal of the solvents by rotary evaporation provided **S9** (1.15 g, 6.52 mmol, 42% yield) as a colorless oil, and as a mixture of olefin isomers: R_F 0.40 (4:1 hexane/EtOAc eluent); ^1H NMR (data for 3.6:1 mixture of olefin isomers based on the relative integration of peaks at δ 1.64 and 1.54; 300 MHz, $CDCl_3$) δ 7.18-7.09 (comp m, 2H), 7.18-7.09 (comp m, 2H), 6.94-6.89 (comp m, 1H), 6.94-6.89 (comp m, 1H), 6.79 (d, *J* = 7.7 Hz, 1H), 6.79 (d, *J* = 7.7 Hz, 1H), 5.35-5.27 (comp m, 1H), 5.35-5.27 (comp m, 1H), 5.09-5.05 (comp m, 1H), 5.09-5.05 (comp m, 1H), 2.78-2.71 (comp m, 2H), 2.78-2.71 (comp m, 2H), 2.41-2.29 (comp m, 2H), 2.41-2.29 (comp m, 2H), 1.79 (s, 3H), 1.71 (s, 3H), 1.63 (d, *J* = 6.6 Hz, 3H), 1.54 (d, *J* = 7.4 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 153.7, 153.6, 135.9, 130.5, 130.3, 128.7, 127.4, 127.3, 121.0, 120.2, 119.2, 115.5, 39.9, 31.9, 29.2, 28.7, 23.8, 16.1, 13.6, 13.3; IR (film) 3441, 2964, 2928, 2860, 1591, 1502, 1456, 1235 cm^{-1}; MS *m/z* calc'd for $[C_{12}H_{16}O]^+$ HRMS (NH_3CI): 176.1201, found 176.1199.

Table 1. Optimization Studies



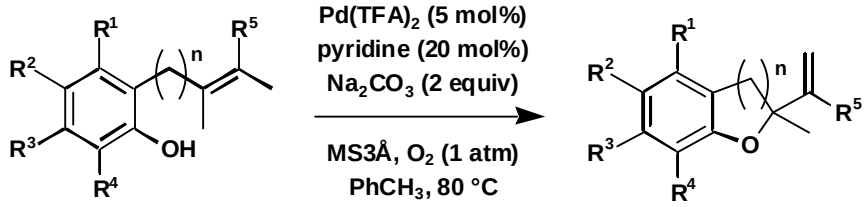
1 ***2***

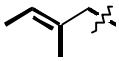
entry	Pd source	Additive	time	yield[b]
1.	$Pd(nbd)Cl_2$	none	24 h	7%
2.	$PdCl_2$	none	24 h	27%
3.	$Pd(OAc)_2$	none	24 h	76%
4.	$Pd(TFA)_2$	none	60 min	87%
5.	$Pd(TFA)_2$	Na_2CO_3 (2 equiv)	20 min	95%
6.	$Pd(TFA)_2$	Na_2CO_3 (2 equiv), no pyridine	24 h	39%

[a] 5 mol% Pd, 20 mol% pyridine, 500 mg/mmol MS3Å, 1 atm O_2, 0.1M in substrate. [b] Isolated yield.

General Procedure for the Racemic Oxidative Cyclization of 1. Palladium Source and Additive Optimization Reactions Shown in Table 1. A thick-walled oven-dried 25 mL 15 cm-long tube equipped with magnetic stir bar was charged with powdered molecular sieves (MS3Å, 125 mg, 500mg/mmol), palladium source (0.0125 mmol, 0.05 equiv), and additive (0.50 mmol, 2.0 equiv), followed by toluene (2.5 mL), pyridine (4.0 μL, 0.050 mmol, 0.20 equiv), and phenol **1** (40.6 mg, 0.25 mmol, 1.0 equiv). The tube was evacuated and back-filled with O_2 (3 x, balloon), heated to 80 °C, and allowed to stir under O_2 (1 atm, balloon). The reaction was monitored by TLC. Upon complete conversion, the crude reaction mixture was filtered over silica gel (1.5 x 10 cm, hexane → 19:1 hexanes/EtOAc eluent). The filtrate was concentrated in vacuo to provide dihydrobenzofuran **2**.

Table 2. Pd-Catalyzed Aerobic Phenol/Olefin Cyclizations



entry	R^1	R^2	R^3	R^4	R^5	n	time, yield
1.	H	H	H	H	H	1	*20 min, 95% yield*
2.	H	Me	H	H	H	1	*20 min, 99% yield*
3.	H	*t*-Bu	H	H	H	1	*25 min, 90% yield*
4.	H	OMe	H	H	H	1	*15 min, 89% yield*
5.	H	$COCH_3$	H	H	H	1	*25 h, 93% yield*
6.	H	Me	H	Me	H	1	*20 min, 85% yield*
7.	H	H	H	H	Me	1	*25 min, 80% yield*
8.	OMe	OMe	OMe	H	H	1	*10 min, 86% yield*
9.	H	OMe	H	OMe	H	1	*40 min, 80% yield*
10.	H	OMe	H		H	1	*2 h, 93% yield*
11.[a]	H	H	H	H	H	2	*75 min, 85% yield*
12.[b]	H	H	H	H	H	1	*14 h, 86% yield*

[a] The starting material was used as a 3.6:1 mixture of olefin isomers. [b] 2 mol% Pd, 8 mol% pyridine.

General Procedure for the Racemic Oxidative Cyclization of Phenols Shown in Table 2. A thick-walled oven-dried 25 mL 15 cm-long tube equipped with magnetic stir bar was charged with powdered molecular sieves (MS3Å, 125 mg, 500mg/mmol), $Pd(TFA)_2$ (4.2 mg, 0.0125 mmol, 0.05 equiv), and additive (0.50 mmol, 2.0 equiv), followed by toluene (2.5 mL), pyridine (4.0 µL, 0.050 mmol, 0.20 equiv), and phenolic substrate (0.25 mmol, 1.0 equiv). The tube was evacuated and back-filled with O_2 (3 x, balloon), heated to 80 °C, and allowed to stir under O_2 (1 atm, balloon). The reaction was monitored by TLC. Upon complete conversion, which varied by substrate, the crude reaction mixture was filtered over silica gel (1.5 x 10 cm, hexane → 19:1 hexanes/EtOAc eluent). Concentration of the filtrate in vacuo provided the cyclized product.

Entry 1, Table 2. 20 min, 95% yield clear, colorless oil: R_F 0.67 (4:1 hexanes/EtOAc eluent); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.16-7.11 (comp m, 2H), 6.87-6.79 (comp m, 2H), 6.06 (dd, *J* = 17.0, 11.0 Hz, 1H), 5.33 (dd, *J* = 17.6, 1.1 Hz, 1H), 5.11 (dd, *J* = 11.0, 1.1 Hz, 1H), 3.19 (d, *J* = 15.4 Hz, 1H), 3.07 (d, *J* = 15.4 Hz, 1H), 15.7 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 158.8, 141.7, 128.1, 126.5, 125.2, 120.4, 112.9, 109.6, 87.7, 42.3, 26.4; IR (film) 1481, 1245 cm^{-1}; HRMS (EI^+) *m/z* calc'd for $[C_{11}H_{12}O]^+$: 160.0888, found 160.0888.

Entry 2, Table 2. 20 min, 99% yield clear, colorless oil: R_F 0.66 (4:1 hexanes/EtOAc eluent); ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.96 (s, 1H), 6.93 (d, *J* = 8.9 Hz, 1H), 6.70 (d, *J* = 7.9 Hz, 1H), 6.05 (dd, *J* = 17.3, 10.9 Hz, 1H), 5.32 (dd, *J* = 17.3, 1.2 Hz, 1H), 5.10 (dd, *J* = 10.6, 1.2 Hz, 1H), 3.16 (d, *J* = 15.5 Hz, 1H), 3.03 (d, *J* = 15.5 Hz, 1H), 2.29 (s, 3H), 1.56 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 156.9, 142.0, 129.7, 128.6, 126.6, 125.9, 112.9, 109.2, 87.7, 42.3, 26.3, 21.0; IR (film) 2975, 2925, 1492, 1249 cm^{-1}; HRMS (EI^+) *m/z* calc'd for $[C_{12}H_{14}O]^+$: 174.1045, found 174.1047.

Entry 3, Table 2. 25 min, 90% yield clear, colorless oil: R_F 0.74 (4:1 hexanes/EtOAc eluent); ^{1}H NMR (300

MHz, $CDCl_3$) δ 7.17-7.14 (comp m, 2H), 6.72 (d, *J* = 8.2 Hz, 1H), 6.06 (dd, *J* = 17.3, 10.4 Hz, 1H), 5.32 (d, *J* = 17.0 Hz, 1H), 5.09 (d, 11.0 Hz, 1H), 3.18 (d, *J* = 15.4 Hz, 1H), 3.06 (d, *J* = 15.4 Hz, 1H), 1.56 (s, 3H), 1.30 (s, 9H); 13C NMR (75 MHz, CDCl3) 156.8, 143.4, 142.1, 126.2, 125.0, 122.3, 112.9, 108.8, 87.7, 42.5, 34.4, 32.0, 26.4; IR (film) 2964, 1494, 1250 cm-1; HRMS (NH_3CI) m/z calc'd for $[C_{15}H_{20}O]^+$: 216.1514, found 216.1515.

Entry 4, Table 2. 15 min, 89% yield clear, colorless oil: RF 0.57 (4:1 hexanes/EtOAc eluent); 1H NMR (300 MHz, CDCl3) 6.74-6.65 (comp m, 3H), 6.04 (dd, J = 17.3, 10.4 Hz, 1H), 5.31 (dd, J = 17.6, 1.1 Hz, 1H), 5.10 (dd, J = 10.4, 1.1 Hz, 1H), 3.76 (s, 3H), 3.04 (d, J = 15.4 Hz, 1H), 3.16 (d, J = 15.4 Hz, 1H), 1.55 (s, 3H); 13C NMR (75 MHz, CDCl3) 154.0, 153.0, 141.8, 127.5, 113.0, 112.9, 111.5, 109.5, 87.8, 56.2, 42.7, 26.3; IR (film) 1488, 1226, 1140 cm-1; HRMS (NH_3CI) m/z calc'd for $[C_{12}H_{14}O_2]^+$: 190.0994, found 190.0999.

Entry 5, Table 2. 25 h, 93% yield clear, colorless oil: RF 0.30 (4:1 hexanes/EtOAc eluent); 1H NMR (300 MHz, CDCl3) 7.83-7.81 (comp m, 2H), 6.81 (d, J = 9.2 Hz, 1H), 6.04 (dd, J = 17.4, 11.0 Hz, 1H), 5.32 (d, J = 17.0 Hz, 1H), 5.13 (d, J = 11.0 Hz, 1H), 3.22 (d, J = 15.6 Hz, 1H), 3.09 (d, J = 15.6 Hz, 1H), 2.54 (s, 3H), 1.58 (s, 3H); 13C NMR (75 MHz, CDCl3) 196.9, 163.3, 141.1, 130.8, 130.7, 127.5, 126.0, 113.5, 109.3, 89.7, 41.5, 26.6, 26.4; IR (film) 2976, 1675, 1608, 1488, 1271 cm^{-1}; HRMS (EI^+) *m/z* calc'd for $[C_{13}H_{14}O_2]^+$: 202.0994, found 202.0995.

Entry 6, Table 2. 20 min, 85% yield clear, colorless oil: R_F 0.75 (4:1 hexanes/EtOAc eluent); ^1H NMR (300 MHz, $CDCl_3$) δ 6.78 (s, 1H), 6.76 (s, 1H), 6.03 (dd, *J* = 17.3, 10.4 Hz, 1H), 5.29 (dd, *J* = 17.0, 1.1 Hz, 1H), 5.07 (dd, *J* = 10.4, 1.1 Hz, 1H), 3.13 (d, *J* = 15.4 Hz, 1H), 3.03 (d, *J* = 15.4 Hz, 1H), 2.25 (s, 3H), 2.20 (s, 3H), 1.55 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 155.5, 142.2, 130.0, 129.5, 125.9, 123.0, 119.3, 112.6, 87.2, 42.6, 26.4, 20.9, 15.5; IR (film) 2973, 2922, 1482, 1233 cm^{-1}; HRMS (EI^+) *m/z* calc'd for $[C_{13}H_{16}O]^+$: 188.1201, found 188.1198.

Entry 7, Table 2. 25 min, 80% yield clear, colorless oil: R_F 0.63 (4:1 hexanes/EtOAc eluent); ^1H NMR (300 MHz, $CDCl_3$) δ 7.16-7.11 (comp m, 2H), 6.79-6.87 (comp m, 2H), 5.10 (s, 1H), 4.86 (s, 1H), 3.27 (d, *J* = 15.4 Hz, 1H), 3.03 (d, *J* = 15.9 Hz, 1H), 1.84 (s, 3H), 1.56 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.1, 147.9, 128.2, 126.8, 125.2, 120.3, 110.2, 109.7, 90.0, 41.6, 26.3, 19.0; IR (film) 1402, 1462, 1249 cm^{-1}; HRMS (NH_3CI) *m/z* calc'd for $[C_{12}H_{14}O]^+$: 173.0967, found 173.0968.

Entry 8, Table 2. 10 min, 86% yield clear, colorless oil: R_F 0.30 (4:1 hexanes/EtOAc eluent); ^1H NMR (300 MHz, $CDCl_3$) δ 7.27 (s, 1H), 6.04 (dd, *J* = 17.4, 10.5 Hz, 1H), 5.32 (dd, *J* = 17.4, 1.4 Hz, 1H), 5.11 (dd, *J* = 10.5, 0.9 Hz, 1H), 3.92 (s, 3H), 3.81 (s, 3H), 3.78 (s, 3H), 3.20 (d, *J* = 14.7 Hz, 1H), 3.07 (d, *J* = 14.7 Hz, 1H), 1.55 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 155.5, 154.0, 150.3, 141.8, 135.1, 113.0, 108.5, 90.2, 88.5, 61.5, 60.2, 56.3, 40.6, 26.4; IR (film) 2935, 1616, 1472, 1196, 1120 cm^{-1}; HRMS (EI^+) *m/z* calc'd for $[C_{14}H_{18}O_4]^+$: 250.1216, found 250.1205.

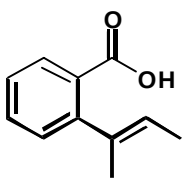
Entry 9, Table 2. 40 min, 80% yield clear, colorless oil: R_F 0.57 (4:1 hexanes/EtOAc eluent); ^1H NMR (300 MHz, $CDCl_3$) δ 6.36 (d, *J* = 10.6 Hz, 1H), 6.35 (d, *J* = 10.6 Hz, 1H), 6.07 (dd, *J* = 17.2, 10.6 Hz, 1H), 5.31 (dd, *J* = 17.2, 1.2 Hz, 1H), 5.09 (dd, *J* = 10.3, 1.2 Hz, 1H), 3.86 (s, 3H), 3.76 (s, 3H), 3.18 (d, *J* = 15.5 Hz, 1H), 3.05 (d, *J* = 15.5 Hz, 1H), 1.58 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 177.7, 154.7, 144.7, 141.6, 141.4, 127.3, 112.9, 101.3, 99.2, 56.2, 56.1, 43.0, 26.4; IR (film) 2972, 2938, 2837, 1617, 1498, 1217, 1150 cm^{-1}; HRMS (NH_3CI) *m/z* calc'd for $[C_{13}H_{16}O_3]^+$: 220.1099, found 220.1101.

Entry 10, Table 2. 2 h, 93% yield, clear, yellow oil: R_F 0.45 (19:1 hexanes/EtOAc eluent); ^1H NMR (300

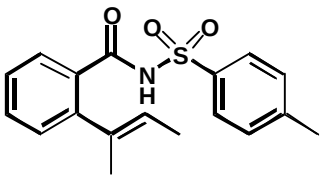
MHz, $CDCl_3$) δ 6.58 (d, *J* = 2.7 Hz, 1H), 6.49 (d, *J* = 2.7 Hz, 1H), 6.02 (dd, *J* = 17.0, 10.4 Hz, 1H), 5.34-5.26 (comp m, 2H), 5.06 (dd, *J* = 10.7, 1.7 Hz, 1H), 3.74 (s, 3H), 3.23 (d, *J* = 2.7 Hz, 2H), 3.14 (d, *J* = 15.4 Hz, 1H), 3.03 (d, *J* = 15.4 Hz, 1H), 1.62-1.60 (comp m, 6H), 1.53 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 154.1, 151.8, 142.3, 134.4, 126.8, 122.7, 120.4, 114.0, 112.6, 108.7, 87.2, 56.1, 43.0, 39.5, 26.5, 16.0, 13.7; IR (film) 2931, 1479, 1440, 1233 cm^{-1}; HRMS (EI^+) *m/z* calc'd for $[C_{17}H_{22}O_2]^+$: 258.1620, found 258.1613.

Entry 11, Table 2. 75 min, 85% yield clear, colorless oil: R_F 0.62 (4:1 hexanes/EtOAc eluent); ^1H NMR (300 MHz, $CDCl_3$) δ 7.13-7.01 (comp m, 2H), 6.87-6.78 (comp m, 2H), 5.86 (dd, *J* = 17.6, 11.0 Hz, 1H), 5.12 (d, *J* = 17.3 Hz, 1H), 5.07 (dd, *J* = 11.0, 1.1 Hz, 1H), 2.73-2.68 (comp m, 2H), 1.97-1.78 (comp m, 2H), 1.46 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 154.2, 141.4, 129.5, 127.5, 121.5, 119.9, 117.0, 114.1, 76.8, 31.9, 27.3, 22.7; IR (film) 1582, 1487, 1456, 1238 cm^{-1}; HRMS (NH_3CI) *m/z* calc'd for $[C_{12}H_{14}O]^+$: 174.1045, found 174.1041.

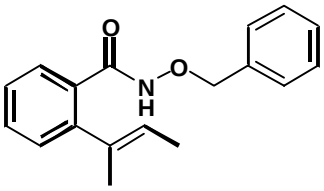
Substrates for Heteroatom/Olefin Cyclization



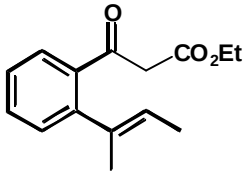
S11



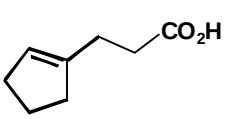
S12



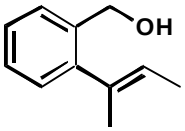
S13



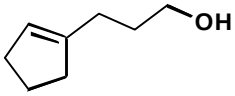
S14



S15

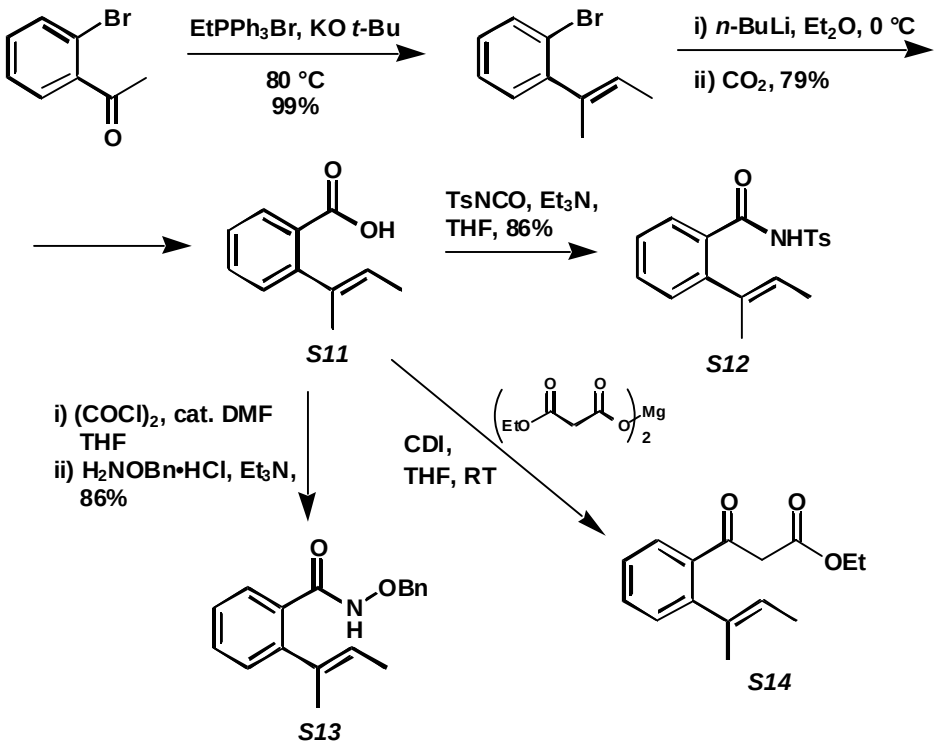


S16



S17

Scheme SM1. Styrenyl Substrate Synthesis



Benzoic acid S11. To a suspension of potassium *t*-butoxide (1.12 g, 10.0 mmol, 2.7 equiv) in toluene (37 mL) was added $EtPPh_3Br$ (3.71 g, 10.0 mmol, 2.7 equiv) and the mixture stirred at 0 °C for 10 min. The resulting orange suspension was warmed to 23 °C and stirred for an additional 1 h. The reaction mixture was cooled to 0 °C and subjected to dropwise addition of 2'-bromoacetophenone (0.5 mL, 3.71 mmol, 1.0 equiv). The mixture was heated at reflux for 8 h, then cooled to 23 °C and quenched with saturated aqueous NH_4Cl (50 mL). The organic layer was separated and the aqueous layer extracted with Et_2O (2 x 50 mL). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated in vacuo. The resulting white solid was triturated with Et_2O and hexane (1:1, 50 mL) to separate $Ph_3P{=}O$ which was removed by filtration. The filtrate was concentrated under reduced pressure. Purification by flash column chromatography on silica gel (hexane as eluent) afforded the bromostyrene as a colorless oil (99% yield). A solution of the bromostyrene (223 mg, 1.06 mmol, 1.0 equiv) in anhydrous Et_2O (2 mL) was treated dropwise with *n*-BuLi (2.5 M in hexane, 0.51 mL, 1.28 mmol, 1.2 equiv) at 0 °C. After 10 min, anhydrous CO_2 gas was bubbled through the reaction mixture for 5 min. The mixture was allowed to warm to 23 °C and stirred for an additional 30 min. The reaction was quenched with saturated aqueous $NaHCO_3$ (10 mL) and washed with Et_2O (2 x 10 mL). The aqueous layer was then acidified with 2N HCl to pH 1 and extracted with Et_2O (3 x 10 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure to furnish benzoic acid **S11** as a white solid (131 mg, 0.74 mmol, 79% yield): R_F 0.23 (4:1 hexanes/EtOAc eluent); ^1H NMR (data for a 1.1:1 mixture of olefin isomers based on the relative integration of peaks at δ 1.79 and 1.40; 300 MHz, $CDCl_3$) δ 12.08 (br s, 1H), 12.08 (br s, 1H), 8.08 (d, *J* = 7.7 Hz, 1H), 7.96 (d, *J* = 7.7 Hz, 1H), 7.58-7.31 (comp m, 2H), 7.58-7.31 (comp m, 2H), 7.25 (d, *J* = 7.7 Hz, 1H), 7.18 (d, *J* = 7.7 Hz, 1H), 5.56-5.46 (comp m, 1H), 5.56-5.46 (comp m, 1H), 2.08-2.02 (comp m, 3H), 2.08-2.02 (comp m, 3H), 1.79 (d, *J* = 6.6 Hz, 3H), 1.40 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.0, 173.1, 148.1, 144.8, 137.6, 133.0, 132.6, 131.2, 130.8, 130.4, 130.2, 128.7, 126.9, 126.7, 123.3, 121.3, 25.6, 18.3, 14.7, 14.3; IR (film) 2979, 1693, 1408 cm^{-1}; HRMS (NH_3CI) *m/z* calc'd for $[C_{11}H_{12}O_2]^+$: 176.0837, found 176.0835.

Tosyl amide S12. To a solution of acid **S11** (2.0 g, 11.3 mmol, 1.0 equiv) in THF (28 mL) was added *p*-toluenesulfonyl isocyanate (2.6 mL, 17.0 mmol, 1.5 equiv) followed by dropwise introduction of Et_3N (2.4 mL,

17.0 mmol, 1.5 equiv). The mixture was then stirred at 60 °C for 1 h. After cooling to 23 °C, The solvent was removed in vacuo and the residue diluted with EtOAc (50 mL) and washed with 2N HCl (20 mL). The organic layer was dried over Na_2SO_4 and the solvents removed by rotary evaporation. Purification by flash column chromatography on silica gel (1:2 hexanes/Et_2O eluent) afforded tosyl amide **S12** as a white foam (3.4 g, 10.3 mmol, 91% yield): R_F 0.15 (1:1 hexanes/Et_2O eluent); ^{1}H NMR (data for a 1:1 mixture of olefin isomers based on the relative integration of peaks at δ 5.72 and 5.50; 300 MHz, $CDCl_3$) δ 9.48 (br s, 1H), 9.18 (br s, 1H), 7.94 (d, *J* = 7.7 Hz, 4H), 7.76 (d, *J* = 7.7 Hz, 1H), 7.51 (d, *J* = 7.7 Hz, 1H), 7.44-7.13 (comp m, 4H), 7.44-7.13 (comp m, 4H), 7.08 (d, *J* = 7.2 Hz, 1H), 7.01 (d, *J* = 7.7 Hz, 1H), 5.72 (app.qd, *J* = 5.5, 1.1 Hz, 1H), 5.50 (app.qd, *J* = 5.5. 1.1 Hz, 1H), 2.36 (s, 3H), 2.35 (s, 3H), 1.86 (s, 3H), 1.75 (s, 3H), 1.66 (d, *J* = 6.6 Hz, 3H), 1.34 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.9, 164.6, 144.9, 144.8, 144.1, 140.5, 136.9, 136.8, 136.0, 135.3, 135.2, 132.5, 131.7, 130.5, 129.7, 129.6, 129.4, 129.3, 129.1, 128.8, 128.3, 128.3, 127.3, 126.9, 126.8, 125.6, 25.9, 21.6, 18.1, 14.8, 14.1; IR (film) 3241, 1699, 1426, 1168 cm^{-1}; HRMS (NH_3CI) *m/z* calc'd for $[C_{18}H_{19}NO_3S + H]^+$: 330.1164, found 330.1157.

Benzyl hydroxamate S13. To a solution of acid **S11** (200 mg, 1.13 mmol, 1.0 equiv) in THF (6 mL) was added oxalyl chloride (0.50 mL, 5.67 mmol, 5 equiv) followed by catalytic DMF (1 drop). After 2 h, the volatiles were removed in vacuo. The residue was diluted with THF (6 mL) and then treated with *O*-benzylhydroxylamine•HCl (362 mg, 2.27 mmol, 2.0 equiv) followed by Et_3N (0.8 mL, 5.67 mmol, 5 equiv). The mixture was stirred for 2 h, quenched by the addition of 2N NaOH (10 mL), and extracted with EtOAc (2 x 10 mL). The combined organic layers were washed with 2N HCl (10 mL), dried over Na_2SO_4 and filtered. Evaporation of the solvents under reduced pressure followed by purification by flash column chromatography on silica gel (4:1 hexanes/EtOAc eluent) gave **S13** (273 mg, 0.95 mmol, 86% yield) as an oil : R_F 0.63 (2:1 hexanes/EtOAc eluent); ^{1}H NMR (data for 3:1 mixture of olefin isomers based on the relative integration of peaks at δ 1.61 and 1.25; 300 MHz, $CDCl_3$) δ 9.23 (s, 1H), 9.08 (s, 1H), 7.69 (d, *J* = 7.7 Hz, 1H), 7.46 (d, *J* = 7.7 Hz, 1H), 7.37-7.10 (comp m, 7H), 7.37-7.10 (comp m, 7H), 7.06 (d, *J* = 7.7 Hz, 1H), 6.97 (d, *J* = 7.7 Hz, 1H), 5.50-5.37 (comp m, 1H), 5.50-5.37 (comp m, 1H), 4.93 (s, 2H), 4.93 (s, 2H), 1.82 (comp m, 3H), 1.82 (comp m, 3H), 1.61 (d, *J* = 7.1 Hz, 3H), 1.25 (app.dd, *J* = 7.1, 1.7 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.3, 166.1, 143.9, 140.0, 137.3, 136.3, 135.4, 131.0, 130.8, 130.4, 129.2, 129.1, 128.7, 128.6, 128.4, 127.0, 126.7, 125.4, 124.1, 77.8, 77.7, 25.8, 17.9, 14.7, 14.2; IR (film) 3189, 1652, 1496, 1023 cm^{-1}; HRMS (NH_3CI) *m/z* calc'd for $[C_{18}H_{19}NO_2 + H]^+$: 282.1494, found 282.1497.

Ketoester S14. Prepared according to the modified procedure of Barco et al.[6] To a solution of acid **S11** (1.4 g, 7.90 mmol, 1.0 equiv) in THF (79 mL) was added *N,N'*-carbonyldiimidazole (1.45 g, 8.74 mmol, 1.1 equiv) and the resulting solution stirred for 1 h. Magnesium monoethyl malonate (2.87 g, 11.9 mmol, 1.5 equiv, prepared according to literature procedure[6]) was introduced and the mixure heated at 80 °C for 24 h. After cooling to 23 °C, the solvent was removed under reduced pressure. The residue was diluted with 5% aqueous citric acid (75 mL) and extracted with EtOAc (3 x 30 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated in vacuo. Purification by flash column chromatography on silica gel (4:1 hexanes/EtOAc eluent) gave ketoester **S14** (1.44 g, 5.8 mmol, 74% yield) as an oil: R_F 0.50 (2:1 hexanes/Et_2O eluent); ^{1}H NMR (isolated as 2.1:1 mixture of olefin isomers and keto-enols, data for the major keto-ester only; 300 MHz, $CDCl_3$) δ 7.62-7.09 (comp m, 4H), 5.45-5.38 (comp m, 1H), 4.14 (q, *J* = 7.3 Hz, 2H), 3.73 (s, 2H), 2.04 (s, 3H), 1.76 (d, *J* = 6.7 Hz, 3H), 1.22 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (data for carbonyl carbons of major keto-ester only; 75 MHz, $CDCl_3$) δ 198.6, 167.5; IR (film) 2980, 1743, 1692 cm^{-1}; HRMS (EI$^+$) *m/z* calc'd for $[C_{15}H_{18}O_3]^+$: 246.1256, found 246.1256.

[6]Barco, A.; Benetti, S.; Pollini, G. P.; *J. Org. Chem.* **1985**, *50*, 5223-5230.

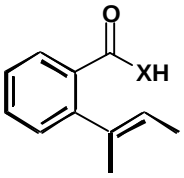
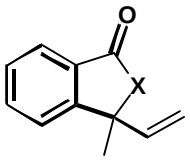
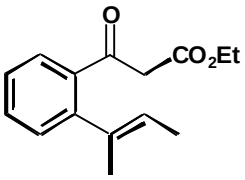
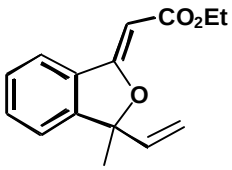
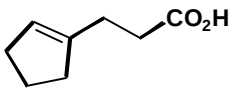
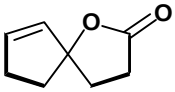
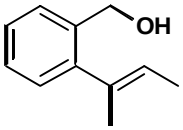
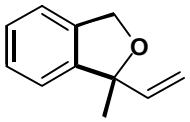
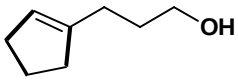
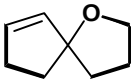
Carboxylic acid S15. See Lokensgard, et al and references therein.[7] R_F 0.35 (2:1 hexanes/EtOAc eluent); ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.36-5.32 (m, 1H), 2.54-2.20 (comp m, 8H), 1.84-1.79 (comp m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 180.2, 142.7, 124.3, 35.5, 33.0, 32.8, 26.4, 23.7; IR (film) 2957, 2895, 2843, 1705, 1446 cm^{-1}; HRMS (EI$^+$) *m/z* calc'd for $[C_8H_{12}O_2 + H]^+$: 140.0837, found 140.0836.

Benzyl alcohol S16. Lithium aluminum hydride (140 mg, 3.69 mmol, 2.6 equiv) was suspended in Et_2O (4 mL) in a two-necked flask equipped with reflux condenser and cooled to 0 °C. A solution of benzoic acid **S11** (250 mg, 1.42 mmol, 1.0 equiv) in Et_2O (6 mL) was added dropwise to the stirring suspension over 5 min. Bubbling was observed, and the mixture was allowed to warm to 23 °C. After 5 h the reaction was recooled to 0 °C, quenched with 5:1 Et_2O/MeOH (20 mL) followed by 3 M HCl (20 mL), and allowed to stir for 12 h. Extraction with Et_2O (3 x 25 mL) was followed by combination of the organics, drying over $MgSO_4$ and removal of the solvents under reduced pressure to provide the yellow oil **S16** (173 mg, 1.07 mmol, 75% yield) as a mixture of olefin isomers: R_F 0.29 (4:1 hexanes/EtOAc eluent); ^{1}H NMR (data for 2.7:1 mixture of olefin isomers based on the relative integration of peaks at δ 5.60 and 5.41; 300 MHz, $CDCl_3$) δ 7.48-7.41 (comp m, 1H), 7.48-7.41 (comp m, 1H), 7.31-7.23 (comp m, 2H), 7.31-7.23 (comp m, 2H), 7.12-7.09 (m, 1H), 7.12-7.09 (m, 1H), 5.60 (app.qdd, *J* = 6.9, 3.2, 1.4 Hz, 1H), 5.41 (app.qdd, *J* = 6.9, 3.2, 1.4 Hz, 1H), 4.65 (d, *J* = 4.1 Hz, 2H), 4.60 (d, *J* = 3.7 Hz, 2H), 1.98-1.95 (m, 3H), 1.98-1.95 (m, 3H), 1.77 (d, *J* = 6.9 Hz, 3H), 1.36 (dq, *J* = 6.9, 1.4 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 158.0, 145.1, 141.1, 138.0, 137.8, 136.5, 135.9, 128.8, 128.2, 127.9, 127.8, 127.7, 127.2, 127.0, 124.6, 122.9, 63.6, 63.4, 26.1, 18.5, 15.0, 14.1; IR (film) 3317, 2967, 2914, 1434, 1029 cm^{-1}; HRMS (EI$^+$) *m/z* calc'd for $[C_{11}H_{14}O]^+$: 162.1045, found 162.1051.

Primary alcohol S17. The methyl ester of **S15** (500 mg, 3.24 mmol, 1.0 equiv) was dissolved in CH_2Cl_2 (6 mL) and cooled to -78 °C. As neat DIBAL (1.27 mL, 7.13 mmol, 2.2 equiv) was slowly added to the mixture, the solution became yellow in color. After 1 h, the reaction was quenched with saturated aqueous Na^+/K^+ tartrate, allowed to warm to 23 °C and stirred for 12 h. The phases were separated and the aqueous layer extracted with CH_2Cl_2 (5 x 15 mL CH_2Cl_2). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude residue was purified by flash column chromatography on silica gel (19:1 hexanes/EtOAc eluent) to afford the known **S17** (90 mg, 0.71 mmol, 22% yield) as a volatile, clear, colorless oil.

Table 3. Aerobic Oxidative Heteroatom/Olefin Cyclizations[a]

[7]Lokensgard, J. P.; O'Dea, J.; Hill, E. A.; *J. Org. Chem.* **1974**, *39*, 3355-3357.

entry	Substrate	Product		time, yield
1.[b]			X = O	*8 h, 90% yield*
2.[b]			X = NTs	*8 h, 88% yield*
3.[b]			X = NOBn	*4 h, 82% yield*
4.[b]				*48 h, 63% yield* [c,d]
5.				*48 h, 62% yield* [e]
6.[b]				*3 h, 87% yield* [f]
7.				*10 h, 93% yield* [f]

[a] 5 mol% $Pd(TFA)_2$, 20 mol% pyridine, MS3Å, 1 atm O_2, 0.25 M in subtrate, $PhCH_3$, 80 °C. [b] The starting material was used as a mixture of olefin isomers. [c] 10 mol% $Pd(TFA)_2$, 40 mol% pyridine, 2 equiv LiOAc. [d] 3:1 *Z:E*. [e] 10 mol% $Pd(TFA)_2$, 40 mol% pyridine. [f] 2 equiv Na_2CO_3, 0.1M in substrate.

General Procedure for the Racemic Heteroatom/Olefin Oxidative Cyclizations Shown in Table 3 (Entries 1-3). To a mixture of $Pd(TFA)_2$ (4.2 mg, 0.0125 mmol, 0.05 equiv) and powdered molecular sieves (MS3Å, 125 mg, 500 mg/mmol) in toluene (1.0 mL) was added pyridine (4.0 µL, 0.050 mmol, 0.20 equiv). The flask was evacuated and back-filled with O_2 (3 x, balloon) and the mixture heated at 80 °C for 10 min. The substrate (0.25 mmol, 1.0 equiv) was introduced and the reaction mixture heated at 80 °C under O_2 (1 atm, balloon) until completion of the reaction as indicated by TLC. The solvent was removed in vacuo and the residue purified directly by flash column chromatography on silica gel (hexane/EtOAc or hexane/Et_2O eluent) to give the cyclized product.

Entry 1, Table 3. 8 h. Purification by flash column chromatography on silica gel (2:1 hexanes/Et_2O eluent) afforded the desired product as an amorphous solid (90% yield): R_F 0.27 (4:1 hexanes/EtOAc eluent); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.86 (d, *J* = 7.2, Hz, 1H), 7.66 (dd, *J* = 7.1, 7.0 Hz, 1H), 7.50 (dd, *J* = 7.1, 6.6, Hz, 1H), 7.38 (d, *J* = 6.6 Hz, 1H), 6.03 (dd, *J* = 17.6, 10.4 Hz, 1H), 5.38 (d, *J* = 17.6 Hz, 1H), 5.19 (d, *J* = 10.4 Hz, 1H), 1.74 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.7, 152.7, 137.9, 134.3, 129.2, 125.9, 125.3, 121.7, 115.6, 86.8, 25.6; IR (film) 1762, 1267 cm^{-1}; HRMS (NH_3CI) *m/z* calc'd for $[C_{11}H_{10}O_2]^+$: 174.0681, found 174.0680.

Entry 2, Table 3. 8 h. Purification by flash column chromatography on silica gel (2:1 hexanes/EtOAc eluent) gave a colorless foam (88% yield): R_F 0.24 (1:1 hexanes/Et_2O eluent); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.04 (d, *J* = 8.1 Hz, 2H), 7.75 (d, *J* = 7.2 Hz, 1H), 7.62 (dd, *J* = 7.2, 6.6 Hz, 1H), 7.43 (dd, *J* = 7.5, 7.5 Hz, 1H), 7.32-7.27 (comp m, 3H), 6.07 (dd, *J* = 17.7, 10.2 Hz, 1H), 5.42 (d, *J* = 17.7 Hz, 1H), 5.38 (d, *J* = 10.5 Hz, 1H), 2.40 (s, 3H), 2.05 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.3, 150.3, 145.0, 138.8, 136.8, 134.4, 129.5, 129.1, 128.9, 128.0, 124.9, 122.7, 117.0, 71.3, 24.9, 22.1; IR (film) 1730, 1466, 1360, 1169 cm^{-1}; HRMS (NH_3CI) *m/z* calc'd for $[C_{18}H_{17}NO_3 + H]^+$: 328.1007, found 328.1008.

Entry 3, Table 3. 4 h. Purification by flash column chromatography on silica gel (4:1 hexanes/EtOAc eluent) furnished the cyclized product as a colorless oil (82% yield): R_F 0.48 (2:1 hexanes/EtOAc eluent); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.85 (d, *J* = 7.7 Hz, 1H), 7.58-7.35 (comp m, 7H), 7.25 (d, *J* = 7.7 Hz, 1H), 5.76 (dd, *J* = 17.6, 10.4 Hz, 1H), 5.41 (d, *J* = 17.0 Hz, 1H), 5.29 (d, *J* = 10.4 Hz, 1H), 5.25 (d, *J* = 10.4 Hz, 1H), 5.15 (d, *J* = 9.9 Hz, 1H), 1.58 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.9, 146.9, 138.3, 135.3, 132.5, 129.7, 128.9, 128.7, 128.6, 128.5, 123.9, 122.0, 117.1, 79.3, 66.9, 21.3; IR (film) 3070, 2979, 1711, 1460 cm^{-1}; HRMS (NH_3CI) *m/z* calc'd for $[C_{18}H_{17}NO_2 + H]^+$: 280.1337, found 280.1330.

Racemic Heteroatom/Olefin Oxidative Cyclizations Shown in Table 3 (Entry 4). To a mixture of $Pd(TFA)_2$ (8.4 mg, 0.025 mmol, 0.10 equiv), LiOAc (33 mg, 0.50 mmol, 2.0 equiv), and powdered molecular sieves (MS3Å, 125 mg, 500 mg/mmol) in toluene (1.0 mL) was added pyridine (8.0 µL, 0.100 mmol, 0.40 equiv). The flask was evacuated and back-filled with O_2 (3 x, balloon) and the mixture heated at 80 °C for 10 min. The substrate (0.25 mmol, 1.0 equiv) and anhydrous LiOAc (33 mg, 0.50 mmol, 2 equiv) were introduced, and the reaction mixture heated at 80 °C under O_2 (1 atm, balloon) until completion of the reaction as indicated by TLC. The solvent was removed in vacuo and the residue purified directly by flash column chromatography on silica gel (4:1 hexanes/Et_2O eluent) to give the cyclized product.

Entry 4, Table 3. 48 h. Purification by flash column chromatography on silica gel (4:1 hexanes/Et_2O eluent) afforded the *E*-isomer (16% yield) and *Z*-isomer (47% yield) as oils. *E*-isomer: R_F 0.53 (2:1 hexanes/Et_2O eluent); ^{1}H NMR (300 MHz, acetone-d_6) δ 9.19 (d, *J* = 7.9 Hz, 1H), 7.63-7.58 (m, 1H), 7.54-7.46 (m, 2H), 6.13 (dd, *J* = 17.4, 10.7 Hz, 1H), 5.58 (s, 1H), 5.34 (dd, *J* = 17.4, 0.9 Hz, 1H), 5.13 (dd, *J* = 10.7, 0.9 Hz, 1H), 4.16 (q, *J* = 7.3 Hz, 2H), 1.68 (s, 3H), 1.26 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (75 MHz, acetone-d_6) δ 169.5, 167.6, 150.6, 140.2, 132.7, 130.5, 129.2, 128.9, 122.1, 114.2, 92.0, 90.3, 59.8, 25.8, 14.9; IR (film) 2978, 1703, 1633 cm^{-1}; HRMS (EI$^+$) *m/z* calc'd for $[C_{15}H_{16}O_3]^+$: 244.1099, found 244.1090. *Z*-isomer: R_F 0.19 (2:1 hexanes/Et_2O eluent); ^{1}H NMR (300 MHz, acetone-d_6) δ 7.82 (dd, *J* =7.7, 1.6 Hz, 1H), 7.61-7.46 (comp m, 3H), 6.17 (dd, *J* = 17.0, 11.0 Hz, 1H), 5.54 (s, 1H), 5.40 (dd, *J* = 17.0, 1.1 Hz, 1H), 5.13 (dd *J* = 11.0, 1.1 Hz, 1H), 4.12 (app.qd, *J* = 7.1, 1.7 Hz, 2H), 1.71 (s, 3H), 1.25 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, acetone-d_6) δ 166.2, 165.5, 148.1, 140.0, 132.9, 132.3, 129.6, 122.5, 122.4, 114.2, 93.4, 86.5, 59.3, 26.0, 14.9; IR (film) 2980, 1706, 1645 cm^{-1}; HRMS (EI$^+$) *m/z* calc'd for $[C_{15}H_{16}O_3]^+$: 244.1099, found 244.1106.

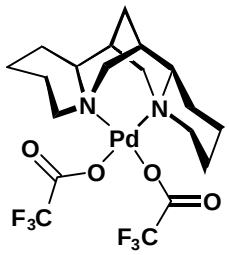
Racemic Heteroatom/Olefin Oxidative Cyclizations Shown in Table 3 (Entry 5). To a mixture of $Pd(TFA)_2$ (8.4 mg, 0.025 mmol, 0.10 equiv) and powdered molecular sieves (MS3Å, 125 mg, 500 mg/mmol) in toluene (1.0 mL) was added pyridine (8.0 µL, 0.100 mmol, 0.40 equiv). The flask was evacuated and back-filled with O_2 (3 x, balloon) and the mixture heated at 80 °C for 10 min. The substrate (0.25 mmol, 1.0 equiv) was introduced and the reaction mixture heated at 80 °C under O_2 (1 atm, balloon) until completion of the reaction as indicated by TLC. The solvent was removed in vacuo and the residue purified directly by flash column chromatography on silica gel (2:1 hexanes/EtOAc eluent) to give the cyclized product.

Entry 5, Table 3. 48 h. Purification by flash column chromatography on silica gel (2:1 hexanes/EtOAc eluent) provided the spiro lactone (62% yield) as a colorless oil: R_F 0.29 (2:1 hexanes/EtOAc eluent); ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.10-6.04 (m, 1H), 5.74-5.66 (m, 1H), 2.64-1.98 (m, 8H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 176.8, 137.7, 131.9, 98.0, 36.4, 33.6, 31.3, 29.9; IR (film) 2938, 1769 cm^{-1}; HRMS (EI$^+$) *m/z* calc'd for $[C_8H_{10}O_2]^+$: 138.0681, found 138.0685.

General Procedure for the Racemic Oxidative Cyclizations of Primary Alcohols Shown in Table 3 (Entries 6-7): A thick-walled oven-dried 25 mL 15 cm-long tube equipped with magnetic stir bar was charged with powdered molecular sieves (MS3Å, 125 mg, 500 mg/mmol), $Pd(TFA)_2$ (4.2 mg, 0.0125 mmol, 0.05 equiv), and Na_2CO_3 (53 mg, 0.50 mmol, 2.0 equiv), followed by toluene (2.5 mL), pyridine (4.0 µL, 0.050 mmol, 0.20 equiv), and primary alcohol substrate (0.25 mmol, 1.0 equiv). The tube was evacuated and back-filled with O_2 (3 x, balloon), heated to 80 °C, and allowed to stir under O_2 (1 atm, balloon). The reaction was monitored for conversion by TLC. Upon complete conversion, which varied by substrate, the crude reaction mixture was filtered over silica gel (1.5 x 10 cm, hexane → 19:1 hexanes/EtOAc eluent). Concentration in vacuo provided the cyclized product.

Entry 6, Table 3. 3 h, 87% yield clear colorless oil: R_F 0.54 (4:1 hexanes/EtOAc eluent); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.30-7.13 (comp m, 3H), 6.06 (dd, *J* = 17.0, 10.4 Hz, 1H), 5.22 (dd, *J* = 17.0, 1.4 Hz, 1H), 5.13 (d, *J* = 12.1 Hz, 1H), 5.08 (d, *J* = 12.6 Hz, 1H), 5.06 (dd, *J* = 10.4, 1.4 Hz, 1H), 1.60 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 144.7, 142.1, 139.0, 127.7, 127.5, 121.6, 121.3, 112.6, 87.8, 71.4, 26.4; IR (film) 2976, 2848, 1029 cm^{-1}; HRMS (HVEI$^+$) *m/z* calc'd for $[C_{11}H_{12}O]^+$: 160.0884, found 160.0888.

Entry 7, Table 3. 10 h, 93% yield volatile clear colorless oil: R_F 0.46 (4:1 hexanes/EtOAc eluent); ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.92-5.89 (m, 1H), 5.71-5.68 (m, 1H), 3.85 (t, *J* = 7.2 Hz, 2H), 2.54-2.44 (m, 1H), 2.35-2.32 (m, 1H), 2.05-1.84 (comp m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 135.1, 133.8, 94.3, 67.4, 37.0, 36.8, 31.2, 26.6; HRMS (EI$^+$) *m/z* calc'd for $[C_8H_{12}O]^+$: 124.0888, found 124.0889.

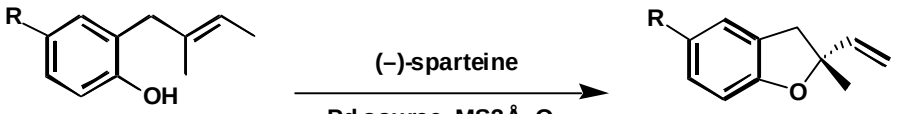


S18

***bis*-Trifluoracetate palladium(II) sparteine (S18) ((–)sparteine)Pd(TFA)$_2$)**[8] $Pd(CH_3CN)_2Cl_2$ (500 mg, 1.93 mmol, 1.0 equiv) was dried under vacuum for 30 min then dissolved in toluene (40 mL). (–)-Sparteine (461 µL, 1.93 mmol, 1.0 equiv) was introduced via syringe, and the orange mixture heated at 60 °C for 2 h. The flask was cooled to 23 °C, opened, and $Ag(OCOCF_3)_2$ (851 mg, 3.85 mmol, 2.0 equiv) quickly added. White/green precipitate formed immediately, and was removed via filtration after 1 h using CH_2Cl_2 (30 mL) to rinse. Heptane (30 mL) was added to the yellow filtrate and the solvents were removed under reduced pressure to afford a bright orange micro-crystalline solid (365 mg, 0.63 mmol, 33% yield). X-ray quality crystals were grown by slow diffusion of hexane into a concentrated CH_2Cl_2 solution of the complex: ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.55 (d, *J* = 11.5 Hz, 1H), 4.33 (d, *J* = 12.6 Hz, 1H), 3.69 (app.qd, *J* = 12.6, 3.3 Hz, 1H), 3.23 (t, *J* = 13.3 Hz, 1H), 3.04 (d, *J* = 13.8 Hz, 1H), 2.89 (d, *J* = 12.4 Hz, 1H), 2.76 (d, *J* = 13.3 Hz, 2H), 2.36-1.26 (comp m, 18H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 70.2, 65.7, 65.6, 63.7, 59.7, 49.0, 34.9, 34.7, 30.2, 27.5, 26.5, 24.2, 24.0, 23.4, 20.6; IR (film) 2942, 1683, 1409, 1194, 1138 cm^{-1}; HRMS (ES$^+$) *m/z* calc'd for $[C_{17}H_{26}N_2O_2F_3Pd - C_2O_2F_3]^+$: 453.0988, found 453.0974.

[8] Cystallographic data have been deposited at the CCDC, 12 Union Road, Cambridge CB2 1EZ, UK, and copies can be obtained on request, free of charge, by quoting the publication citation and the deposition number 192101.

Table 4. The Pd-Catalyzed Asymmetric Aerobic Wacker Cyclization



1, R = H
3, R = OMe

(+)-2, R = H
(+)-4, R = OMe

entry	compd	Pd source	Additive	time	yield[b]	ee
1.	1	$Pd(nbd)Cl_2$[c]	none	36 h	68%	12%
2.	1	$PdBr_2$	none	36 h	32%	8%
3.	1	$PdCl_2$	none	36 h	2%	12%
4.	1	$Pd(CH_3CN)_2Cl_2$	none	36 h	53%	12%
5.	1	$Pd(OAc)_2$	none	36 h	18%	51%
6.	1	$Pd(TFA)_2$	none	36 h	72%	76%
7.	1	(sp)$Pd(TFA)_2$[d]	none[e]	36 h	83%	77%
8.	1	(sp)$Pd(TFA)_2$	Na_2CO_3 (2 equiv)[f]	36 h	53%	76%
9.	1	(sp)$Pd(TFA)_2$	$Ca(OH)_2$ (2 equiv)[f]	36 h	87%[g]	81%
10.	3	(sp)$Pd(TFA)_2$	$Ca(OH)_2$ (2 equiv)[f]	24 h	64%[g,h]	88%
11.	3	(sp)$Pd(TFA)_2$	$Ca(OH)_2$ (2 equiv)[f]	60 h@55 °C	57%[g,h]	90%

[a] 10 mol% Pd, 40 mol% (–)-sparteine, 0.1M in substrate, 1 atm O_2, 500 mg/mmol MS3Å. [b] Measured by GC. [c] nbd=norbornadiene. [d] sp=(–)-sparteine. [e] 30 mol% (–)-sparteine. [f] 100 mol% (–)-sparteine. [g] Isolated yield. [h] Produced with dimeric byproduct **S19**.

General Procedure for Asymmetric Oxidative Cyclization of 1. Palladium Source Screening Trials Shown in Table 4 (Entries 1-6). A thick-walled oven-dried 10 mL 15 cm-long tube equipped with magnetic stir bar was charged with powdered molecular sieves (MS3Å, 50 mg, 500 mg/mmol), and palladium source (0.010 mmol, 0.10 equiv), followed by toluene (1.0 mL), (–)-sparteine (9.2 µL, 0.040 mmol, 0.40 equiv), and pentadecane as a GC internal standard (3.0 µL, 0.011 mmol, 0.11 equiv). The tube was evacuated, back-filled with O_2 (3 x, balloon), and heated to 80 °C for 20 min. Phenol **1** (16.2 mg, 0.10 mmol, 1.0 equiv) was added, and the mixture allowed to stir under O_2 (1 atm, balloon) at 80 °C. The reaction was monitored for % conversion and % enantiomeric excess by chiral GC. Aliquots (0.10 mL) of the reaction mixture were collected at 12 h, 24 h, and 36 h, filtered through a plug of silica gel (EtOAc eluent), and analyzed (see below for details).

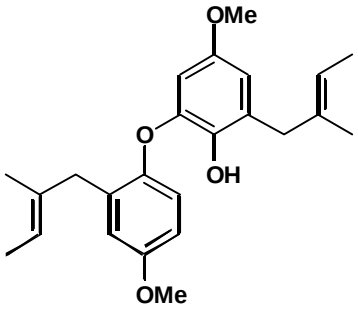
General Procedure for Asymmetric Oxidative Cyclization of 1. Additive Screening Trials Shown in Table 4 (Entries 7-8). A thick-walled oven-dried 10 mL 15 cm-long tube equipped with magnetic stir bar was charged with powdered molecular sieves (MS3Å, 50 mg, 500 mg/mmol), (sp)$Pd(TFA)_2$ (5.7 mg, 0.010 mmol, 0.10 equiv) and additive (0.20 mmol, 2.0 equiv), followed by toluene (1.0 mL), (–)-sparteine (23.9 µL, 0.10 mmol, 1.0 equiv), pentadecane as a GC internal standard (3.0 µL, 0.011 mmol, 0.11 equiv), and phenol **1** (16.2 mg, 0.10 mmol, 1.0 equiv). The tube was evacuated, back-filled with O_2 (3 x balloon), heated to 80 °C, and stirred under O_2 (1 atm, balloon). The reaction was monitored for % conversion and % enantiomeric excess by chiral GC. Aliquots (0.10 mL) of the reaction mixture were collected at 12 h, 24 h, and 36 h, filtered through a plug of silica gel (EtOAc), and analyzed (see below for details).

General Procedure for Asymmetric Oxidative Cyclization of Phenols Shown in Table 4 (Entries 9-11). A thick-walled oven-dried 25 mL 15 cm-long tube equipped with magnetic stir bar was charged with powdered molecular sieves (MS3Å, 125 mg, 500 mg/mmol), (sp)$Pd(TFA)_2$ (14.2 mg, 0.025 mmol, 0.10 equiv), and oven-dried $Ca(OH)_2$ (37 mg, 0.50 mmol, 2.0 equiv), followed by toluene (2.5 mL), (–)-sparteine (60 µL, 0.25 mmol, 1.0 equiv), and phenolic substrate (0.25 mmol, 1.0 equiv). The tube was evacuated and back-filled with O_2 (3 x, balloon), heated to 80 °C, and allowed to stir under O_2 (1 atm, balloon). The reaction was monitored for

conversion by TLC. Upon complete conversion, which varied by substrate, the crude reaction mixture was filtered over silica gel (1.5 x 10 cm, hexane → 19:1 hexanes/EtOAc eluent). Removal of the solvents in vacuo afforded the cyclized product. % enantiomeric excess was determined by chiral GC on a Bodman Chiraldex GT-A column (see below for details).

(+)-2. 36 h, 87% yield: 81% ee; $[\alpha]_D^{23}$ +9.4 (*c* 1.0, $CHCl_3$); R_F 0.67 (4:1 hexanes/EtOAc eluent); ^1H NMR (300 MHz, $CDCl_3$) δ 7.16-7.11 (comp m, 2H), 6.87-6.79 (comp m, 2H), 6.06 (dd, *J* = 17.0, 11.0 Hz, 1H), 5.33 (dd, *J* = 17.6, 1.1 Hz, 1H), 5.11 (dd, *J* = 11.0, 1.1 Hz, 1H), 3.19 (d, *J* = 15.4 Hz, 1H), 3.07 (d, *J* = 15.4 Hz, 1H), 1.57 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 158.8, 141.7, 128.1, 126.5, 125.2, 120.4, 112.9, 109.6, 87.7, 42.3, 26.4; IR (film) 1481, 1245 cm^{-1}; HRMS (EI^+) *m/z* calc'd for $[C_{11}H_{12}O]^+$: 160.0888, found 160.0888.

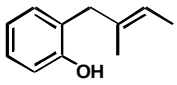
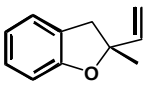
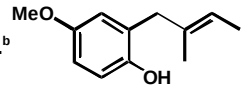
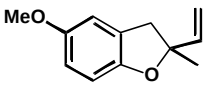
(+)-4. For reaction at 80 °C: 24 h, 64% yield, 1.3:1 dihydrofuran/dimer **S19**: 88% ee For reaction at 55 °C, 60 h, 57% yield, 1:1 dihydrofuran:dimer **S19**: 90% ee; $[\alpha]_D^{22}$ +0.13 (*c* 0.86, $CHCl_3$); R_F 0.57 (4:1 hexanes/EtOAc eluent); ^1H NMR (300 MHz, $CDCl_3$) δ 6.74-6.65 (comp m, 3H), 6.04 (dd, *J* = 17.3, 10.4 Hz, 1H), 5.31 (dd, *J* = 17.6, 1.1 Hz, 1H), 5.10 (dd, *J* = 10.4, 1.1 Hz, 1H), 3.76 (s, 3H), 3.04 (d, *J* = 15.4 Hz, 1H), 3.16 (d, *J* = 15.4 Hz, 1H), 1.55 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 154.0, 153.0, 141.8, 127.5, 113.0, 112.9, 111.5, 109.5, 87.8, 56.2, 42.7, 26.3; IR (film) 1488, 1226, 1140 cm^{-1}; HRMS (NH_3CI) *m/z* calc'd for $[C_{12}H_{14}O_2]^+$: 190.0994, found 190.0999.



S19

Aryl ether dimer S19. Isolated with dihydrofuran **(+)-4** in varying ratios: R_F 0.48 (4:1 hexanes/EtOAc eluent); ^1H NMR (300 MHz, $CDCl_3$) δ 6.87 (d, *J* = 8.7 Hz, 1H), 6.79-6.70 (comp m, 3H), 6.37 (d, *J* = 3.2 Hz, 1H), 6.11 (d, *J* = 3.2 Hz, 1H), 5.39 (s, 1H), 5.32 (app.qd, *J* = 6.4, 1.4 Hz, 1H), 5.24 (app.qd, *J* = 6.9, 1.4 Hz, 1H), 3.80 (s, 3H), 3.64 (s, 3H), 3.35 (s, 2H), 3.25 (s, 2H), 1.65-1.56 (comp m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 156.3, 152.8, 147.7, 145.3, 139.0, 134.6, 134.2, 133.1, 127.7, 121.0, 120.5, 120.4, 116.8, 112.4, 109.2, 101.2, 55.9, 55.8, 40.2, 39.5, 16.1, 16.0, 13.7, 13.6; IR (film) 3458, 2913, 1607, 1492, 1439, 1202 cm^{-1}; HRMS (EI^+) *m/z* calc'd for $[C_{24}H_{30}O_4]^+$: 382.2141, found 382.2144.

Table SM1. Methods employed for the determination of % Conversion and % Enantiomeric excess.

Entry	Substrate	Product	GC Conditions[a]	Retention time of phenol (min)	Retention time of S enationmer (min)	Retention time of R enationmer (min)	Retention time of pentadecane internal standard (min)
1.			50 °C, 0 min; 2.0 °C/min to 150 °C 1.0 mL/min carrier gas flow	63.50	26.93	27.25	36.86
2.[b]			80 °C 5 min; 1.0 °C/min to 140 °C 15.0 °C/min to 180 °C 1.0 mL/min carrier gas flow	-------	48.37	48.79	------

[a] All assays conducted on Bodman Chiraldex GT-A column. [b] Conversion not measured by GC, no internal standard.