Supporting Information for "Synthesis of C(3) Benzofuran Derived Bis-Aryl Quaternary Centers: Approaches to Diazonamide A"

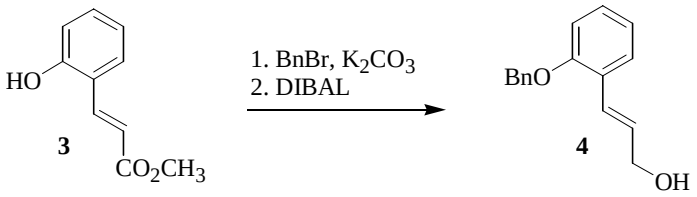
Douglas E. Fuerst, Brian M. Stoltz, and John L. Wood*

Sterling Chemistry Laboratory, Department of Chemistry, Yale University, New Haven, Connecticut 06520-8107

Material and Methods

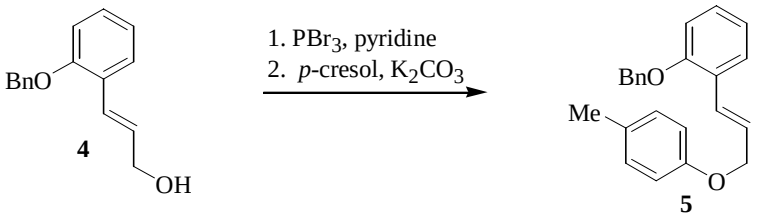
Unless otherwise stated, reactions were performed under a nitrogen atmosphere using freshly distilled solvents. Diethyl ether (Et_2O) and tetrahydrofuran (THF) were distilled from sodium/benzophenone. Methylene chloride (CH_2Cl_2), and benzene were distilled from calcium hydride. Methanol (MeOH) was distilled from magnesium. All other commercially obtained reagents were used as received. All reactions were magnetically stirred and monitored by thin-layer chromatography (TLC) using E. Merck silica gel 60 F254 pre-coated plates (0.25-mm). Column or flash chromatography was performed with the indicated solvents using silica gel (particle size 0.032-0.063 nm) purchased from Bodman. ^{1}H and ^{13}C NMR spectra were recorded on Bruker Avance DPX-500 or Bruker Avance DPX-400 spectrometers. Chemical shifts are reported relative to internal chloroform (^{1}H, δ 7.27 ppm, ^{13}C δ 77.0 ppm), benzene (^{1}H, δ 7.30 ppm), dimethyl sulfoxide (^{13}C, δ 40.5 ppm), or methanol (^{13}C, δ 49.9 ppm). Infrared spectra were recorded on a Midac M-1200 FTIR. High resolution mass spectra were acquired at The University of Illinois Mass Spectrometry Center.

Preparation of allylic alcohol 4.



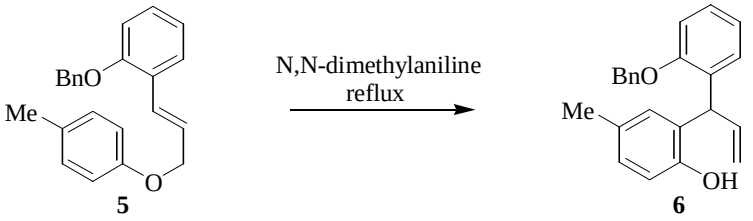
To a solution of phenol **3** (27.0 g, 151.5 mmol) in acetone (250 mL) was added benzyl bromide (21.0 mL, 176.6 mmol) and K_2CO_3 (41.0 g, 296.7 mmol). The reaction mixture was heated to reflux for 12 h. After this time the reaction mixture was concentrated *in vacuo* and the crude mixture taken up in ether (250 mL). Filtration of the residual solids and removal of the solvent in vacuo gave a light yellow oil that was taken up in THF (350 mL). This solution was cooled to –78 °C and treated with DIBAL (67.5 mL, 378.8 mmol). After 30 min. the reaction was carefully quenched with a saturated solution of Rochelle's salt (600 mL) and allowed to stir at room temperature for 2 h. The organic layer was separated, and the aqueous layer extracted with CH_2Cl_2 (3 x 250 mL). The combined organic layers were washed with brine (250 mL) and dried ($MgSO_4$). After solvent removal *in vacuo* the residue was purified by silica gel column chromatography (hexanes:EtOAc, 6:1 then 3:1) to afford allylic alcohol **4** (34.0 g, 93% yield) as a clear oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.50 (dd, *J*=1.5, 7.5 Hz, 1H), 7.47-7.35 (cm, 5H), 7.22 (m, 1H), 7.02 (d, *J*=16.0 Hz, 1H), 6.96 (m, 2H), 6.41 (dt, *J*=6.0, 16.0 Hz, 1H), 5.12 (s, 2H), 4.32 (dd, *J*=1.5, 5.5 Hz, 2H), 1.58 (br s, 1H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 155.9, 137.0, 129.2, 128.7, 128.5, 127.9, 127.3, 126.9, 126.2, 126.1, 121.0, 112.5, 70.4, 64.2; **IR** (thin film/NaCl) 3355 (br w), 3032 (w), 2918 (w), 2865 (w), 1487 (m), 1451 (m), 1381 (w), 1239 (s), 1013 (m), 750 (s) cm^{-1}; **HRMS** (EI) *m/z* found: 240.1147, [calc'd for $C_{16}H_{16}O_2$ (M+H): 240.1150].

Preparation of allyl ether 5.



To a solution of PBr_3 (10.3 mL, 108.3 mmol) and pyridine (4.4 mL, 54.0 mmol) in Et_2O (50 mL) was added allylic alcohol **4** (26.0 g, 108.3 mmol) in Et_2O (50 mL) over 1 h at –15 °C. After stirring for an additional 1 h the reaction mixture was carefully quenched with distilled H_2O (100 mL). The organic layer was separated, and the aqueous layer extracted with Et_2O (50 mL) . The combined organic layers were washed with brine (100 mL) and dried ($MgSO_4$). After solvent removal *in vacuo* the crude pink residue was taken up in acetone (1000 mL) and treated with *p*-cresol (12.3 g, 113.6 mmol) and K_2CO_3 (26.2 g, 189.4 mmol). The reaction mixture was heated to reflux for 12 h. After this time the reaction mixture was concentrated *in vacuo* and the crude mixture taken up in ether (500 mL). After filtration of the residual solids and removal of the solvent *in vacuo* the residue was purified by silica gel column chromatography (hexanes:EtOAc, 10:1) to afford allyl ether **5** (36.2 g, 80% yield) as a clear oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.53 (dd, *J*=1.5, 7.5 Hz, 1H), 7.46-7.35 (cm, 5H), 7.23 (m, 1H), 7.15 (d, *J*=16.0 Hz, 1H), 7.10 (m, 2H), 6.96 (m, 2H), 6.88 (m, 2H), 6.47 (dt, *J*=6.0, 16.0 Hz, 1H), 5.12 (s, 2H), 4.69 (dd, *J*=1.5. 6.0 Hz, 2H), 2.31 (s, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 156.6, 155.9, 137.0, 129.9, 129.8, 128.9, 128.5, 127.9, 127.8, 127.2, 127.1, 125.9, 125.3, 121.0, 114.7, 112.5, 70.3, 69.3, 20.5; **IR** (thin film/NaCl) 3031 (w), 2020 (w), 2862 (w), 1510 (s), 1452 (m), 1293 (m), 1241 (s), 1176 (w), 1015 (m), 750 (m) cm^{-1}; **HRMS** (FAB) *m/z* found: 330.1621, [calc'd for $C_{23}H_{22}O_2$ (M+): 330.1620].

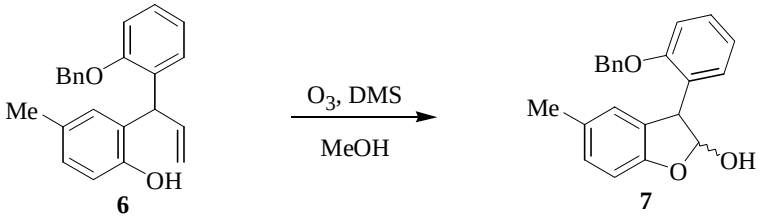
Preparation of olefin 6.



5 **6**

A solution of allyl ether **5** (400 mg, 1.20 mmol) in *N*,*N*-dimethylaniline (12 mL) was submersed into an oil bath preheated to 200 °C. The solution was refluxed for 16 hours, cooled and diluted with Et_2O (25 mL). The ethereal solution was washed with 1N HCl (6 x 10mL) and dried ($MgSO_4$). After solvent removal *in vacuo* the residue was purified by silica gel column chromatography (hexanes:EtOAc, 20:1 then 10:1) to afford olefin **6** (312 mg, 78% yield) as a clear oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.40-7.33 (cm, 5H), 7.23 (m, 2H), 7.00-6.93 (cm, 4H), 6.74 (m, 1H), 6.36 (ddd, *J*=6.0, 10.0, 17.0 Hz, 1H), 5.42 (br s, 1H), 5.33 (d, *J*=6.0 Hz, 1H), 5.30 (dt, *J*=1.5, 10.5 Hz, 1H), 5.11 (s, 2H), 5.02 (dt, *J*=1.5, 17.0 Hz, 1H), 2.25 (s, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 158.4, 154.7, 142.4, 139.8, 134.1, 131.8, 131.3, 131.3, 130.1, 129.9, 129.3, 129.2, 129.1, 129.0, 122.2, 116.7, 116.5, 114.2, 71.7, 43.3, 21.6; **IR** (thin film/NaCl) 3449 (w), 3031 (w), 2920 (w), 1598 (w), 1498 (s), 1451 (m), 1238 (s), 1103 (w), 918 (w), 753 (s) cm^{-1}; **HRMS** (FAB) *m/z* found: 330.1621, [calc'd for $C_{23}H_{22}O_2$ (M+): 330.1620].

Preparation of hemi-acetal 7.

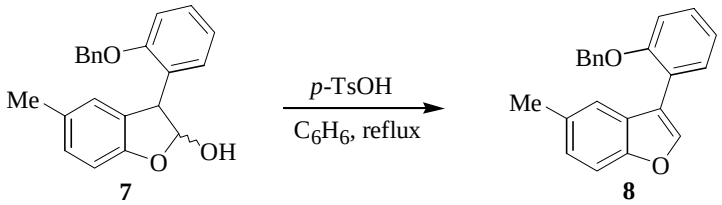


6 **7**

A solution of **6** (8.8 g, 26.7 mmol) in MeOH (200 mL) was cooled to –78 °C and treated with O_3 until TLC showed the disappearance of starting material (about 30 min). The mixture was purged with nitrogen for 15 min at –78 °C, and dimethyl sulfide (27.0 mL) was added at that temperature. The dry ice bath was removed and the solution allowed to stir at room temperature for 12 h. After solvent removal *in vacuo* the residue was

purified by silica gel column chromatography (hexanes:EtOAc, 20:1 then 10:1) to afford hemi-acetal **7** (5.86 g, 66% yield) as a viscous light yellow oil (2:1 mixture of diastereomers). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.46-7.22 (cm, 6H), 7.02 (m, 2H), 6.95 (s, 1H), 6.90-6.80 (cm, 3H), 6.10 (d, *J*=7.0 Hz, 1H), 5.85 (d, *J*=2 Hz, 1H), 5.16 (s, 2H), 5.09 (d, *J*=11.5 Hz, 1H), 5.05 (s, 1H), 5.02 (d, *J*=11.5 Hz, 2H), 4.82 (d, *J*=1.0 Hz, 1H), 3.09 (br s, 1H), 2.30 (s, 3H), 2.29 (s, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 156.8, 156.2, 156.1, 156.0, 136.8, 136.3, 130.6, 130.3, 129.1, 129.0, 128.8, 128.6, 128.5, 128.5, 128.3, 128.1, 128.0, 127.8, 127.4, 127.2, 127.1, 126.1, 125.7, 124.7, 121.3, 121.0, 112.3, 111.9, 109.6, 109.6, 107.0, 102.0, 70.4, 70.0, 50.7, 20.8; **IR** (neat) 3434 (w), 2862 (w), 1599 (w), 1490 (s), 1451 (m), 1240 (m), 1096 (w), 917 (w), 810 (w), 753 (m) cm^{-1}; **HRMS** (FAB) *m/z* found: 332.1411, [calc'd for $C_{22}H_{20}O_3$ (M+): 332.1412].

Preparation of benzofuran 8.

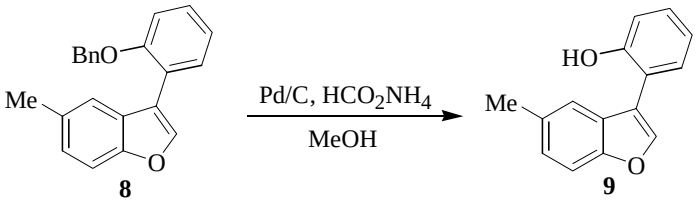


7 **8**

To a solution of hemi-acetal **7** (465 mg, 1.40 mmol) in benzene (50 mL) was added *p*-toluenesulfonic acid (13.3 mg, 0.07 mmol). The reaction mixture was refluxed for 3 h while the solvent was passed through a soxlet extractor containing 4Å molecular sieves. After this time the reaction mixture was cooled, washed with sat. $NaHCO_3$ (3 x 25 mL), and dried ($MgSO_4$). After solvent removal *in vacuo* the residue was purified by silica gel column chromatography (hexanes:EtOAc, 40:1) to afford benzofuran **8** (395 mg, 90% yield) as a clear colorless oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.05 (s, 1H), 7.82 (dd, *J*=1.5, 7.5 Hz, 1H), 7.71 (s, 1H), 7.52 (d, *J*=8.5 Hz, 1H), 7.46-7.38 (cm, 6H), 7.22 (qd, *J*=1.0, 7.5 Hz, 2H), 7.18 (d, *J*=8.5 Hz, 1H), 5.20 (s, 2H), 2.55 (s, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 155.9, 135.5, 144.2, 136.8, 132.0, 129.9, 128.4, 128.2, 127.8, 127.2, 127.2, 125.3, 121.6, 121.1, 120.9, 116.9, 112.9, 111.0, 70.5, 21.4; **IR** (thin film/NaCl) 3032 (w), 2919 (w), 1578 (w), 1494 (s), 1447 (m), 1241 (s), 1109 (m), 1023 (m), 855 (w),

750 (s) cm^{-1}; **HRMS** (FAB) *m/z* found: 314.1307, [calc'd for $C_{22}H_{18}O_2$ (M+): 314.1307].

Preparation of phenol 9.



To a solution of benzofuran **8** (455 mg, 1.45 mmol) in MeOH (25 mL) was added 10% Pd/C (290 mg) and HCO_2NH_4 (457 mg, 7.25 mmol). The reaction mixture was heated to reflux for 15 min after which time TLC showed the complete disappearance of starting material. After cooling to room temperature the reaction mixture was filtered over a pad of celite and washed with ethyl acetate (150 mL). This solution was concentrated *in vacuo*, dissolved in ethyl acetate (50 mL), washed with H_2O (2 x 25 mL), and dried ($MgSO_4$). Solvent removal *in vacuo* afforded analytically pure phenol **9** (310 mg, 95% yield) as a colorless oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.80 (s, 1H), 7.48 (d, *J*=8.5 Hz, 1H), 7.44 (dd, *J*=1.5, 8.0 Hz, 1H), 7.41 (s, 1H), 7.33 (m, 1H), 7.21 (dd, *J*=1.5, 8.5 Hz, 1H), 7.07-7.04 (cm, 2H), 5.19 (s, 1H), 2.47 (s, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 154.0, 153.3, 143.0, 132.9, 130.4, 129.4, 126.7, 126.4, 120.8, 120.2, 117.8, 116.5, 115.9, 111.4, 21.4; **IR** (thin film/NaCl) 3522 (br m), 1578 (m), 1471 (s), 1335 (m), 1279 (m), 1230 (s), 1186 (s), 1102 (s), 969 (w), 757 (s) cm^{-1}; **HRMS** (EI) *m/z* found: 224.0837, [calc'd for $C_{15}H_{12}O_2$ (M+): 224.0837].

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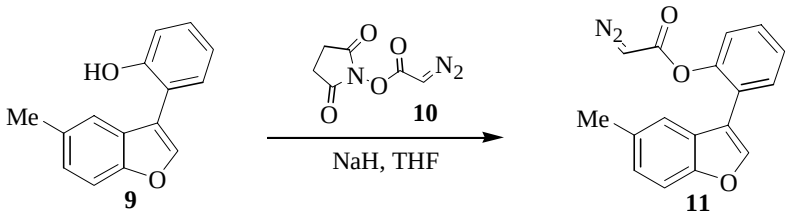
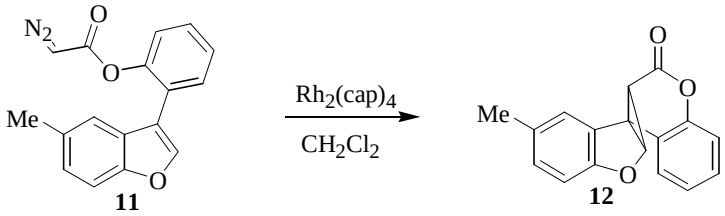
Preparation of α-diazo ester 11.



To a solution of phenol **9** (200 mg, 0.893 mmol) in THF (10 mL) at 0°C was added

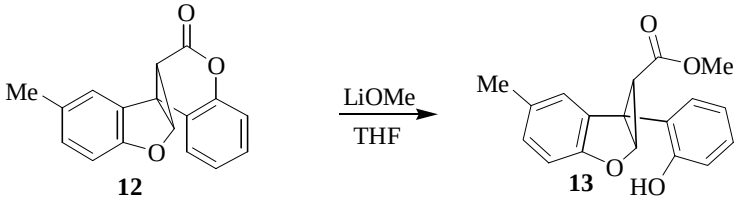
succinimide **10** (172 mg, 0.938 mmol) in THF (5 mL) via cannula over 5 minutes. The reaction mixture was warmed to room temperature during which time a brown precipitate formed. After 15 min the solvent was removed *in vacuo* and the crude mixture taken up ethyl acetate. After filtration of the brown precipitate over a plug of cotton and solvent removal *in vacuo* the residue was purified by silica gel column chromatography (hexanes:EtOAc, 10:1) to afford α-diazo ester **11** (211 mg, 81% yield) as a bright yellow oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.70 (s, 1H), 7.61 (dd, *J*=1.5, 7.5 Hz, 1H), 7.45-7.42(cm, 3H), 7.37 (td, *J*=1.5, 7.5 Hz, 1H), 7.31 (m, 1H), 7.17 (m, 1H), 4.77 (br s, 1H), 2.46 (s, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 153.6, 148.0, 142.8, 130.7, 128.6, 126.9, 126.4, 125.8, 125.3, 123.3, 120.4, 111.1, 21.4; **IR** (thin film/NaCl) 3115 (w), 2116 (s), 1707 (s), 1470 (w), 1366 (s), 1189 (s), 1145 (s), 1112 (m), 968 (w), 798 (m) cm^{-1}; **HRMS** (EI) *m/z* found: 293.0927, [calc'd for $C_{17}H_{13}N_2O_3$ (M+H): 293.0926].

Preparation of cyclopropyl lactone 12.



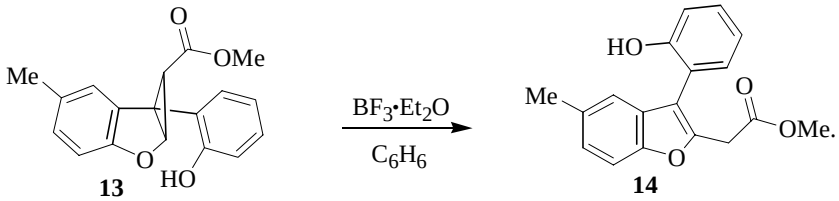
A solution of α-diazo ester **11** (160 mg, 0.548 mmol) in CH_2Cl_2 (7.5 mL) was added to a refluxing suspension of $Rh_2(cap)_4$ (4.0 mg, 0.00548 mmol) in CH_2Cl_2 (7.5 mL) over 12 h via syringe pump. After solvent removal *in vacuo* the residue was purified by silica gel column chromatography (hexanes:EtOAc, 20:1) to afford lactone **12** (88 mg, 61% yield) as a clear colorless oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.64 (dd, *J*=1.5, 7.5 Hz, 1H), 7.39 (s, 1H), 7.34 (m, 1H), 7.22 (td, *J*=1.0, 7.5 Hz, 1H), 7.12 (dd, *J*=1.0, 8.0 Hz, 2H), 6.94 (d, *J*=8.0 Hz, 1H), 4.94 (d, *J*=1.0 Hz, 1H), 2.40 (s, 3H), 1.88 (d, *J*=1.0 Hz, 1H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 164.0, 157.3, 150.3, 131.6, 129.7, 128.9, 126.4, 126.4, 124.7, 124.6, 117.7, 117.3, 111.3, 69.3, 38.1, 28.0, 21.0; **IR** (thin film/NaCl) 3065 (w), 2919 (w), 1754 (s), 1480 (m), 1265 (m), 1187 (s), 1077 (m), 1037 (w), 936 (m), 760 (m) cm^{-1}; HRMS (FAB) *m/z* found: 265.0866, [calc'd for $C_{17}H_{13}O_3$ (M+H): 265.0865].

Preparation of ester 13.



To a solution of lactone **12** (22 mg, 0.83 mmol) in THF (3 mL) at –78 °C was added LiOMe (2 mL, 0.084M in MeOH). After 15 min the reaction was quenched with sat. NH_4Cl (5 mL) and the layers separated. The aqueous layer was extracted with ethyl acetate (2 x 10 mL) and the combined organic layers dried ($MgSO_4$). After solvent removal *in vacuo* the residue was purified by silica gel column chromatography (hexanes:EtOAc, 6:1) to afford ester **13** (22 mg, 88% yield) as a clear colorless oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.25-7.22 (cm, 2H), 7.00-6.93 (cm, 3H), 6.87-6.85 (cm, 2H), 5.45 (d, *J*=1.5 Hz, 1H), 5.11 (br s, 1H), 3.55 (s, 3H), 2.24 (s, 3H), 1.83 (d, *J*=1.5 Hz, 1H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 170.3, 156.4, 154.8, 131.1, 131.1, 131.0, 129.5, 128.9, 124.4, 120.9, 119.6, 115.9, 110.4, 70.0, 51.9, 41.2, 29.2, 20.8; **IR** (thin film/NaCl) 3399 (br m), 2951 (w), 1701 (s), 1595 (w), 1483 (s), 1453 (s), 1277 (s), 1188 (s), 1079 (s), 911. m cm^{-1}; **HRMS** (EI) *m/z* found: 297.1127, [calc'd for $C_{18}H_{17}O_4$ (M+H): 297.1127].

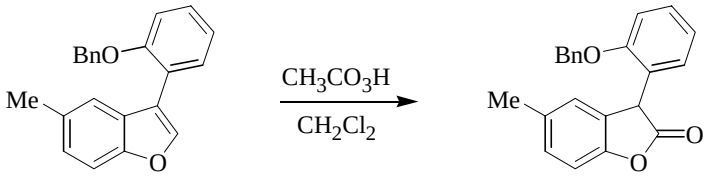
Preparation of benzofuran 14.



To a solution of ester **13** (5.0 mg, 0.017 mmol) in benzene (2 mL) at 0°C was added $BF_3{\cdot}Et_2O$ (0.002 mL, 0.0170 mmol). After stirring for 15 min. the entire reaction mixture was poured onto a silica gel column and chromatographed (hexanes:EtOAc, 10:1 then 6:1) to afford benzofuran **14** (3.4 mg, 68% yield) as a clear colorless oil. **^{1}H NMR** (500 MHz, C_6D_6) δ 7.44-7.37 (cm, 2H), 7.30-7.28 (cm, 3H), 7.04-7.01 (cm, 2H), 6.31 (s, 1H), 3.52 (s, 2H), 3.26 (s, 3H), 2.26 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 170.4, 154.1,

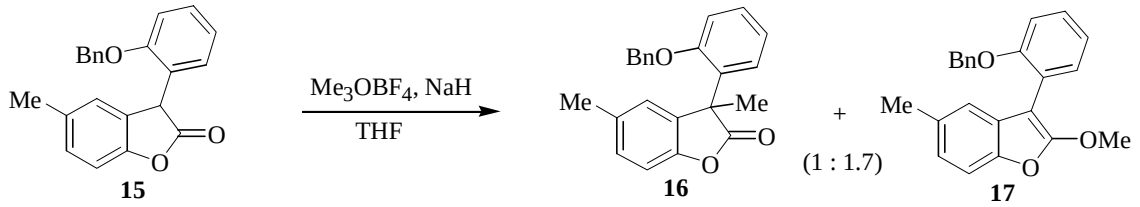
153.2, 148.0, 132.8, 131.1, 129.9, 128.6, 126.2, 120.5, 112.0, 117.0, 116.4, 114.5, 110.8, 52.9, 33.1, 21.3; **IR** (thin film/NaCl) 3427 (br m), 2953 (m), 2923 (s), 1739 (s), 1602 (w), 1450 (s), 1199 (s), 1011 (w), 802 (w), 757 (m) cm^{-1}; **HRMS** (EI) *m/z* found: 296.1043, [calc'd for $C_{18}H_{16}O_4$ (M+): 296.1049].

Preparation of lactone 15.



The procedure of Vedejs was used without modification. Peracetic acid (7.13 mL, 36.5 mmol, Aldrich) was gradually added to a solution of benzofuran **8** (387 mg, 1.23 mmol) in 72 mL of CH_2Cl_2. The mixture was stirred for 16 h and diluted with CH_2Cl_2 to a volume of 150 mL. The organic layer was washed with H_2O (75 mL), 10% $NaHSO_3$ (75 mL), 5% $NaHCO_3$ (75 mL), and dried ($MgSO_4$). After solvent removal *in vacuo* the residue was purified by silica gel column chromatography (hexanes:EtOAc, 20:1) to afford lactone **15** (250 mg, 62% yield) as a clear oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.32-7.28 (cm, 5H), 7.09 (m, 2H), 7.06 (m, 1H), 7.00 (td, *J*=1.0, 7.0 Hz, 1H), 6.93 (d, *J*=8.0 Hz, 1H), 6.86 (m, 2H), 5.00 (d, *J*=11.5 Hz, 1H), 4.93 (d, *J*=1.5 Hz, 1H), 4.93 (3, 1H), 2.29 (s, 3H); **^{13}C NMR** (125 MHz, DMSO-d_6) δ 176.6, 156.2, 152.2, 137.1, 133.9, 132.6, 130.5, 129.5, 129.2, 129.0, 128.5, 128.1, 125.5, 125.2, 121.7, 113.5, 110.6, 70.0, 47.7, 21.4; **IR** (neat) 3033 (w), 2922 (w), 1815 (s), 1600 (m), 1486 (s), 1233 (s), 1065 (s), 1017 (m), 753 (s), 620 (w) cm^{-1}; **HRMS** (EI) *m/z* found: 330.1251, [calc'd for $C_{22}H_{18}O_3$ (M+): 330.1256].

Preparation of lactone 16 and benzofuran 17.



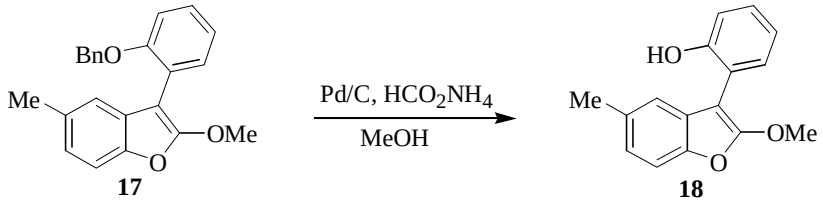
To a solution of lactone **15** (145 mg, 0.439 mmol) in THF (3 mL) at 0°C was added NaH (25 mg, 0.615 mmol; 60% dispersion in mineral oil, Aldrich) in one portion under N_2. The reaction was stirred at 0°C for 1 h before the granular NaH completely disappeared (the solution became dark yellow). Trimethyloxonium tetrafluoroborate (78 mg, 0.527 mmol) was added as a single portion and the mixture allowed to warm to room temperature. After stirring for 2 h the reaction was quenched with sat. NH_4Cl (5 mL) and diluted with ether (20 mL). The organic layer was washed with brine (2 x 10 mL) and dried ($MgSO_4$). After solvent removal *in vacuo* the residue was purified by silica gel column chromatography (hexanes:EtOAc, 40:1) to afford benzofuran **17** (87 mg, 58% yield) as a clear colorless oil and lactone **16** (51 mg, 34% yield) as a white solid.

The first compound to elute was benzofuran **17**. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.54 (dd, *J*=1.5, 8.0 Hz, 1H), 7.38-7.30 (cm, 7H), 7.25 (s, 1H), 7.13 (m, 2H), 7.03 (dd, *J*=1.5, 8.0 Hz, 1H), 5.16 (s, 2H), 4.02 (s, 3H), 2.43 (s, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 158.4, 156.4, 146.7, 137.2, 132.1, 131.6, 130.2, 128.3, 128.3, 127.5, 127.1, 122.6, 120.9, 120.9, 119.7, 113.1, 109.6, 91.2, 70.3, 58.3, 21.4; **IR** (thin film/NaCl) 2858 (w), 1640 (s), 1497 (s), 1366 (s), 1288 (m), 1241 (s), 1117 (w), 1038 (s), 945 (w), 752 (s) cm^{-1}; **HRMS** (FAB) *m/z* found: 344.1411, [calc'd for $C_{23}H_{20}O_3$ (M+): 344.1412].

The second compound to elute was lactone **16**. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.61 (dd, *J*=1.5, 8.0 Hz, 1H), 7.30-7.24 (cm, 4H), 7.07 (dt, *J*=0.5, 7.5 Hz, 1H), 7.00 (dd, *J*=1.0, 8.0 Hz, 1H), 6.95 (m, 2H), 6.82 (d, *J*=7.5 Hz, 1H), 6.74 (d, *J*=8.0 Hz, 1H), 6.69 (d, *J*=1.5 Hz, 1H), 4.92 (d, *J*=12.0 Hz, 1H), 4.78 (d, *J*=12.0 Hz, 1H), 2.27 (s, 3H), 1.83 (s, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 179.9, 155.3, 151.2, 135.7, 133.7, 133.2, 129.2, 128.2, 128.2,

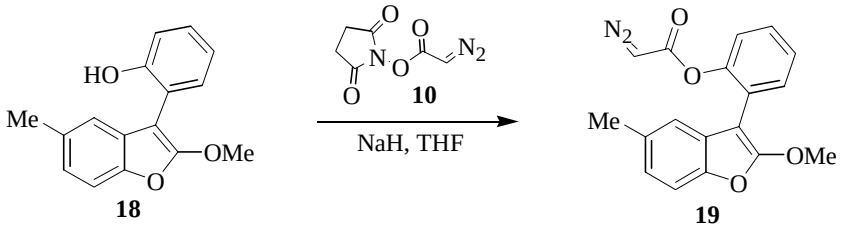
127.7, 127.6, 127.0, 123.0, 120.7, 112.0, 109.9, 70.0, 48.3, 23.9, 21.0; **IR** (thin film/NaCl) 2917 (w), 1797 (s), 1488 (s), 1378 (w), 1261 (m), 1228 (m), 1145 (m), 1031 (s), 749 (m), 701 (w) cm^{-1}; **HRMS** (EI) *m/z* found: 345.1492, [calc'd for $C_{23}H_{21}O_3$ (M+H): 345.1491].

Preparation of phenol 18.



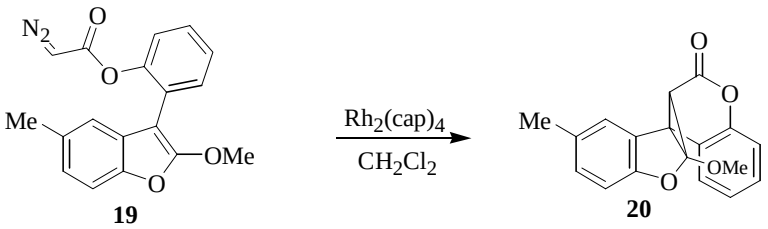
To a solution of benzofuran **17** (49 mg, 1.45 mmol) in MeOH (10 mL) was added 10% Pd/C (28 mg) and HCO_2NH_4 (45 mg, 0.71 mmol). The reaction mixture was heated to reflux for 15 min after which time TLC showed the complete disappearance of starting material. After cooling to room temperature the reaction mixture was filtered over a pad of celite and washed with ethyl acetate (150 mL). This solution was concentrated *in vacuo*, dissolved in ethyl acetate (50 mL), washed with H_2O (2 x 25 mL), and dried ($MgSO_4$). Solvent removal *in vacuo* afforded analytically pure phenol **18** (34 mg, 95% yield) as a colorless oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.45 (dd, *J*=1.0, 7.5 Hz, 1H), 7.30 (d, *J*=8.0 Hz, 2H), 7.24 (m, 1H), 7.08 (dd, *J*=1.0, 8.0 Hz, 1H), 7.06-7.03 (cm, 2H), 5.58 (s, 1H), 4.12 (s, 3H), 2.42 (s, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 157.6, 153.6, 147.2, 133.1, 130.5, 129.1, 129.0, 123.7, 120.7, 119.0, 117.3, 116.6, 110.1, 89.5, 59.0, 21.4; **IR** (thin film/NaCl) 3541 (br w), 2953 (w), 2926 (w), 1634 (m), 1611 (m), 1493 (m), 1371 (m), 1118 (w), 911 (s), 742 (s) cm^{-1}; **HRMS** (EI) *m/z* found: 254.0942, [calc'd for $C_{16}H_{14}O_3$ (M+): 254.0943].

Preparation of α-diazo ester 19.



To a solution of phenol **18** (36 mg, 0.142 mmol) in THF (5 mL) at 0°C was added succinimide **10** (29 mg, 0.156 mmol) in THF (3 mL) via cannula over 5 minutes. The reaction mixture was warmed to room temperature during which time a brown precipitate formed. After 15 min. the solvent was removed *in vacuo* and the crude mixture taken up ethyl acetate. After filtration of the brown precipitate over a plug of cotton and solvent removal *in vacuo* the residue was purified by silica gel column chromatography (hexanes:EtOAc, 10:1) to afford α-diazo ester **11** (37 mg, 85% yield) as a bright yellow oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.65 (dd, *J*=1.5, 7.5 Hz, 1H), 7.50-7.34 (cm, 5H), 7.09 (dd, *J*=1.0, 8.5 Hz, 1H), 4.78 (br s, 1H), 4.13 (s, 3H), 2.50 (s, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 158.8, 148.3, 146.6, 132.6, 131.4, 129.3, 128.1, 126.0, 124.6, 123.1, 123.0, 119.1, 109.7, 90.2, 58.7, 21.4; **IR** (thin film/NaCl) 3112 (w), 2856 (w), 2114 (s), 1709 (s), 1493 (m), 1366 (s), 1287 (w), 1145 (s), 944 (m), 795 (m) cm^{-1}; **HRMS** (EI) *m/z* found: 322.0954, [calc'd for $C_{18}H_{14}N_2O_4$ (M+): 322.0954].

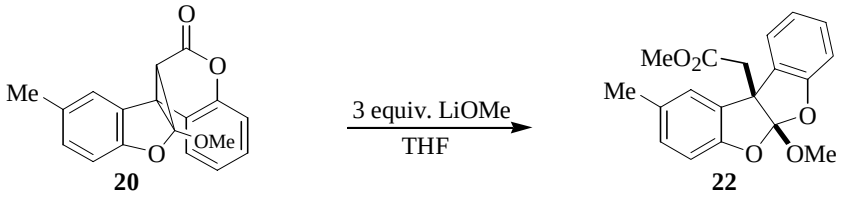
Preparation of lactone 20.



A solution of α-diazo ester **19** (11 mg, 0.036 mmol) in CH_2Cl_2 (2 mL) was added to a refluxing suspension of $Rh_2(cap)_4$ (0.3 mg, 0.000458 mmol) in CH_2Cl_2 (2 mL) over 4 h via syringe pump. After solvent removal *in vacuo* the residue was purified by silica gel column chromatography (hexanes:EtOAc, 20:1) to afford lactone **20** (9.4 mg, 89% yield)

as a clear colorless oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.60 (dd, *J*=1.5, 7.5 Hz, 1H), 7.39-7.35 (cm, 2H), 7.24-7.13 (cm, 3H), 7.00 (d, *J*=8.0 Hz, 1H), 3.35 (s, 3H), 2.39 (s, 3H), 2.12 (s, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 162.2, 155.4, 150.3, 131.6, 129.5, 129.0, 126.7, 126.6, 124.7, 124.5, 117.8, 114.0, 110.9, 98.3, 56.4, 40.4, 32.2, 21.0; **IR** (thin film/NaCl) 2926 (w), 2857 (w), 1757 (s), 1481 (m), 1454 (m), 1375 (w), 1285 (m), 1205 (s), 1101 (m), 757 (w) cm^{-1}; **HRMS** (EI) *m/z* found: 295.0969, [calc'd for $C_{18}H_{15}O_4$ (M+H): 295.0970].

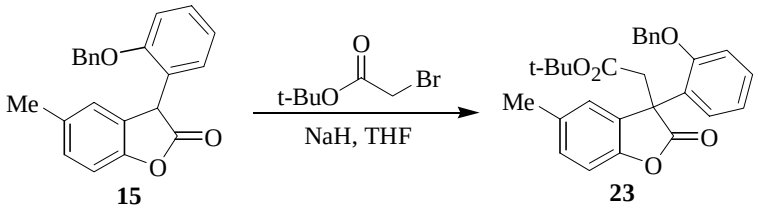
Preparation of orthoester 22.



20 **22**

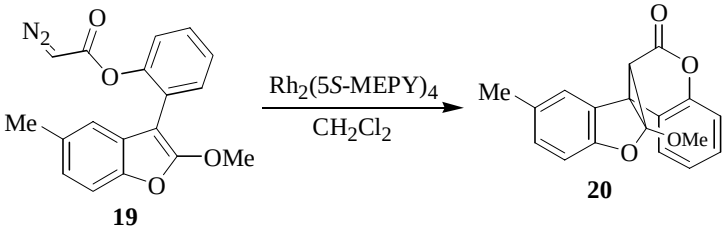
To a solution of lactone **20** (9.0 mg, 0.0306 mmol) in THF (4 mL) at 0 °C was added LiOMe (1 mL, 0.092M in MeOH). After 30 min the reaction was quenched with sat. NH_4Cl (5 mL) and the layers separated. The aqueous layer was extracted with ethyl acetate (2 x 10 mL) and the combined organic layers dried ($MgSO_4$). After solvent removal *in vacuo* the residue was purified by silica gel column chromatography (hexanes:EtOAc, 20:1) to afford orthoester **13** (7.6 mg, 76% yield) as a clear colorless oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.39 (dd, *J*=1.0, 7.5 Hz, 1H), 7.19-7.15 (cm, 2H), 6.97-6.94 (cm, 2H), 6.86 (d, *J*=8.0 Hz, 1H), 6.76 (d, *J*=8.0 Hz, 1H), 3.80 (s, 3H), 3.5 (s, 3H), 3.13 (s, 2H), 2.29 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 170.3, 156.1, 154.0, 131.5, 130.1, 129.9, 129.5, 129.0, 123.8, 123.4, 122.0, 110.1, 109.7, 57.0, 52.0, 51.6, 37.6, 29.7, 21.0; **IR** (thin film/NaCl) 2952 (m), 2924 (m), 1744 (s), 1492 (s), 1462 (m), 1268 (s), 1223 (s), 1043 (s), 936 (s), 811 (w) cm^{-1}; **HRMS** (EI) *m/z* found: 327.1233, [calc'd for $C_{19}H_{19}O_5$ (M+H): 327.1232].

Preparation of lactone 23.



To a solution of lactone **15** (30 mg, 0.091 mmol) in THF (5 mL) at 0°C was added NaH (8.0 mg, 0.109 mmol; 60% dispersion in mineral oil, Aldrich) in one portion under N_2. The reaction was stirred at 0°C for 1 h before the granular NaH completely disappeared (the solution became dark yellow). t-butylbromo acetate (0.016 mL, 0.109 mmol) was added as a single portion and the mixture allowed to warm to room temperature. After stirring for 2 h the reaction was quenched with sat. NH_4Cl (5 mL) and diluted with ether (20 mL). The organic layer was washed with brine (2 x 10 mL) and dried ($MgSO_4$). After solvent removal *in vacuo* the residue was purified by silica gel column chromatography (hexanes:EtOAc, 20:1) to afford lactone **23** (35 mg, 90% yield) as a clear oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.43 (dd, *J*=1.0, 9.0 Hz, 1H), 7.27-7.24 (cm, 4H), 7.01-6.97 (cm, 4H), 6.79 (m, 2H), 6.68 (d, *J*=8.0 Hz, 1H), 4.95 (d, *J*=12.0 Hz, 1H), 4.80 (d, *J*=12.0 Hz, 1H), 3.38 (d, *J*=14.5 Hz, 1H), 3.33 (d, *J*=14.0 Hz, 1H), 2.25 (s, 3H), 1.2 (s, 9H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 178.3, 168.0, 155.5, 152.4, 135.7, 133.0, 130.0, 129.4, 128.8, 128.3, 127.8, 127.7, 127.7, 126.7, 123.9, 120.7, 112.6, 109.7, 81.8, 70.1, 50.5, 42.7, 27.5, 21.0; **IR** (thin film/NaCl) 2978 (w), 228 (w), 1807 (s), 1728 (s), 1597 (w), 1488 (s), 1368 (m), 1157 (s), 1127 (m), 844 (w) cm^{-1}; **HRMS** (EI) *m/z* found: 444.1928, [calc'd for $C_{28}H_{28}O_5$ (M+): 444.1937].

Preparation of enantioenriched cyclopropane 20.



19 **20**

A solution of α-diazo ester **19** (14 mg, 0.0434 mmol) in CH_2Cl_2 (2 mL) was added to a refluxing suspension of Rh_2(5*S*-MEPY)$_4$ (0.4 mg, 0.0005 mmol) in CH_2Cl_2 (2 mL) over 4 h via syringe pump. After solvent removal in vacuo the residue was purified by silica gel column chromatography (hexanes:EtOAc, 20:1) to afford lactone **20** (10.8 mg, 84% yield) as a clear colorless oil. Optically active **20** was spectrally identical (^{1}H, ^{13}C NMR, FT-IR) to racemic **20** prepared from $Rh_2(cap)_4$ with $[\alpha]^{20}_D$ +184.7 (*c* 0.15, $CHCl_3$). The enantioselectivity was determined by portion wise addition of the chiral shift reagent europium tris[3-(hepta-fluoropropylhydroxymethylene)-(+)camphorate (20mg, 0.0168 mmol) to a solution of **20** (6 mg, 0.02 mmol) in approximately 1 mL of $CDCl_3$. Sufficient resolution of the OMe peak for integration purposes was seen after the addition of the 4th portion (80 mg total) of the chiral shift reagent.