Development of a Catalytic Aromatic Decarboxylation Reaction

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General Considerations

Unless otherwise stated all solvents and reagents were ACS reagent grade and were used without further purification. DMSO and DMF were distilled from BaO. Palladium (II) trifluoroacetate was purchased from either Acros or Strem. Analytical thin layer chromatography (TLC) was performed on EM Reagents 1.00 mm silica-gel plates. Due to the volatility of the products, rotary evaporation was avoided. Instead, the solvent was slowly evaporated on the bench-top. In addition, chromatography was performed with the most volatile solvent system possible and the fractions were also concentrated by slow evaporation on the bench-top.

^1H NMR and ^{13}C NMR spectra were recorded on a Bruker AM-500 (500 MHz) spectrometer. Chemical shifts are reported in parts per million (ppm) from tetramethylsilane (0 ppm) or from the solvent resonance (CDCl_3 7.26 ppm, DMSO- d_6 2.54 ppm, Acetone- d_6 2.09 ppm). Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, dd = doublet of doublets, br = broad, m = multiplet), coupling constants, and number of protons. Mass spectra were obtained on a high resonance VG autospec with an ionization mode of either CI or ES. IR spectra were taken on an ASI ReactIR 1000 FT-IR spectrometer. GC analysis for reactions was conducted with an Agilent 6850 gas chromatograph with an HP-1 column (Agilent): length = 30 m, ID = 0.32 mm, film = 0.25 mm, flow = 2 mL/min, 80 °C to 130 °C. Carrier gas: N_2 ; Detector: FID; Injector: 250 °C; Pressure 21.25 psi). Melting points were obtained on Thomas Scientific Unimelt apparatus and are uncorrected. Yields refer to isolated material judged to be $\geq 95\%$ pure by ^1H NMR spectroscopy following silica gel chromatography with Silia-P flash silica gel (50-63 μm mesh particle size).

Synthesis of Decarboxylation Substrates

1,3,7-trimethoxynaphthalene-2-carboxylic acid (2b). To a solution of methyl 1,3-dihydroxy-7-methoxynaphthalene-2-carboxylate (200 mg, 0.85 mmol) in 3.9 mL of THF: H_2O (1.0:0.3), Bu_4NBr (28 mg, 0.085 mmol) and KOH (478 mg, 8.4 mmol) was added. To this solution dimethyl sulfate (810 μL , 8.4 mmol) was added and the reaction was stirred at room temperature for 4 h. The reaction was quenched with 30% NH_4OH for 30 min. The resultant mixture was extracted with Et_2O and washed three times with 30% NH_4OH and one time with H_2O and brine. The organic phase was dried over Na_2SO_4 and concentrated. The resulting residue was chromatographed in 5% EtOAc /Hexanes to afford methyl 1,3,7-trimethoxynaphthalene-2-carboxylate (90 mg) in 38% yield. mp 98-101 °C; ^1H NMR (500 MHz, CDCl_3) δ 7.62 (d, J = 9.0 Hz, 1H), 7.33

(d, $J = 2.6$ Hz, 1H), 7.16 (dd, $J = 9.0, 2.7$ Hz, 1H), 6.91 (s, 1H), 4.01 (s, 3H), 3.98 (s, 3H), 3.90 (s, 3H), 3.89 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 167.2, 156.7, 153.4, 152.6, 130.7, 128.6, 123.8, 120.4, 117.7, 102.2, 101.1, 62.7, 56.0, 55.4, 52.6; IR (film) 3003, 2949, 2907, 2841, 1733, 1606, 1583, 1505 cm^{-1} ; HRMS (CI) calcd for $\text{C}_{15}\text{H}_{16}\text{O}_5$ (M^+) 276.0998, found 276.0996.

To a solution of methyl 1,3,7-trimethoxynaphthalene-2-carboxylate (90 mg, 0.33 mmol) in ethylene glycol was added KOH (500 mg, 8.9 mmol). The suspension was then heated to 130 $^{\circ}\text{C}$ for 24 h under N_2 . The brown mixture was then acidified with concentrated HCl at 0 $^{\circ}\text{C}$ and extracted with EtOAc three times. The organic extracts were then washed with brine and dried over Na_2SO_4 , filtered and concentrated. The resultant solid was dissolved in CH_2Cl_2 and extracted twice with 1M NaOH. The aqueous phase was then acidified and extracted three times with EtOAc. The organic extracts were then washed with brine, dried over Na_2SO_4 , filtered and concentrated to afford **2b** (77 mg) in 90% yield. White powder; mp 204-205 $^{\circ}\text{C}$; ^1H NMR (500 MHz, CDCl_3) δ 7.66 (d, $J = 8.9$ Hz, 1H), 7.37 (d, $J = 2.4$ Hz, 1H), 7.21 (dd, $J = 8.9, 2.5$ Hz, 1H), 6.98 (s, 1H), 4.08 (s, 3H), 3.98 (s, 3H), 3.94 (s, 3H); ^{13}C NMR (125 MHz, DMSO) δ 166.9, 156.3, 151.9, 151.6, 129.8, 128.8, 123.2, 119.8, 119.4, 102.4, 100.7, 62.3, 55.7, 55.2; IR (thin film) 3105, 2972, 2887 (br), 1076, 1610, 1239, 1108 cm^{-1} ; HRMS (ESI) calcd for $\text{C}_{14}\text{H}_{13}\text{O}_4$ ($\text{M}-\text{OH}$) 245.0814, found 245.0820.

1,3,6,8-tetramethoxynaphthalene-2-carboxylic acid (2c). To a solution of methyl 1,3-diacetoxy-6,8-dimethoxynaphthalene-2-carboxylate (200 mg, 0.55 mmol) in 20 mL of $\text{MeOH}:\text{CH}_2\text{Cl}_2$ (1:1), potassium carbonate (1.0 g) was added. The solution was then heated to 40 $^{\circ}\text{C}$ for 30 min. The reaction mixture was then extracted into CH_2Cl_2 twice and then washed with 1M HCl twice. The organic phase was then dried over Na_2SO_4 , filtered, and concentrated to afford methyl 1-acetoxy-3-hydroxy-6,8-dimethoxynaphthalene-2-carboxylate (174 mg) in 98% yield. ^1H NMR (500 MHz, CDCl_3) δ 10.82 (s, 1H), 7.04 (s, 1H), 6.50 (d, $J = 2.2$ Hz, 1H), 6.27 (d, $J = 2.2$ Hz, 1H), 3.95 (s, 3H), 3.86 (s, 3H), 3.85 (s, 3H), 2.35 (s, 3H).

To a solution of methyl 1-acetoxy-3-hydroxy-6,8-dimethoxynaphthalene-2-carboxylate (174 mg, 0.54 mmol) in DMF (5 mL), 60% NaH (430 mg, 11 mmol) and MeI (840 μL , 14 mmol) was added under N_2 . The reaction was stirred at room temperature for 2 h and then quenched with 30% NH_4OH . The reaction mixture was then extracted into Et_2O and washed twice with 30% NH_4OH and once with brine. The organic extracts were then

dried over Na₂SO₄ and concentrated. The resulting residue was chromatographed in 20% EtOAc/Hexanes to afford methyl 1-hydroxy-3,6,8-trimethoxynaphthalene-2-carboxylate (78 mg) in 49% yield.

To a solution of methyl 1-hydroxy-3,6,8-trimethoxynaphthalene-2-carboxylate (78 mg, 0.27 mmol) in 2.6 mL of THF:H₂O (1.0:0.3), Bu₄NBr (8.6 mg, 0.027 mmol) and KOH (150 mg, 2.7 mmol) was added. The solution was cooled to 0 °C and dimethyl sulfate (250 μL, 2.7 mmol) was added and the reaction was stirred at 0 °C for 4 h. The reaction was quenched with 30% NH₄OH for 30 min. The resultant mixture was extracted with Et₂O and washed three times with 30% NH₄OH and one time with H₂O and brine. The organic phase was dried over Na₂SO₄, filtered, and concentrated to afford methyl 1,3,6,8-tetramethoxynaphthalene-2-carboxylate (66 mg) in 81% yield. mp 137-137.5 °C; ¹H NMR (500 MHz, CDCl₃) δ 6.81 (s, 1H), 6.64 (d, *J* = 2.2 Hz, 1H), 6.39 (d, *J* = 2.2 Hz, 1H), 3.94 (s, 3H), 3.93 (s, 3H), 3.88 (s, 3H), 3.877 (s, 3H), 3.86 (s, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 167.2, 159.5, 157.7, 155.4, 154.9, 139.3, 117.1, 110.6, 102.1, 98.6, 97.4, 63.9, 56.0, 55.8, 55.4, 52.5; IR (film) 2995, 2937, 2837, 1729, 1621, 1583, 1447 cm⁻¹; HRMS (CI) calcd for C₁₆H₁₈O₆ (M⁺) 306.1103, found 306.1095.

To a solution of methyl 1,3,6,8-tetramethoxynaphthalene-2-carboxylate (58 mg, 0.19 mmol) in 10 mL of dioxane, 10 mL of conc. LiOH/H₂O was added. The resulting solution was heated to reflux for 24 h. The reaction mixture was then acidified with concentrated HCl and extracted with CH₂Cl₂ three times. The organic extracts were then washed with brine and dried over Na₂SO₄, filtered and concentrated. The resultant solid was dissolved in CH₂Cl₂ and extracted twice with 1M NaOH. This solution was then acidified and extracted three times with EtOAc. The organic extracts were then washed with brine, dried over Na₂SO₄, filtered and concentrated to afford **2c** (41 mg) in 75% yield. White crystalline solid; mp 154-158 °C; ¹H NMR (500 MHz, CDCl₃) δ 6.67 (s, 1H), 6.55 (d, *J* = 2.0 Hz, 1H), 6.35 (d, *J* = 2.1 Hz, 1H), 3.93 (s, 3H), 3.90 (s, 3H), 3.89 (s, 3H), 3.88 (s, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 169.8, 159.7, 157.6, 155.1, 154.7, 139.3, 116.2, 110.3, 102.3, 98.5, 97.3, 64.1, 56.0, 55.9, 55.4; IR (film) 3069, 3003, 2934, 2856, 2660, 2559, 1698, 1621, 1583, 1455, 1432 cm⁻¹; HRMS (ES) calcd for C₁₅H₁₆O₆ (MH⁺) 293.1025, found 293.1027.

1,3,6,7-tetramethoxynaphthalene-2-carboxylic acid (2d). To a solution of methyl 1,3-dihydroxy-6,7-dimethoxynaphthalene-2-carboxylate (200 mg, 0.72 mmol) in 6.5 mL of THF:H₂O (1.0:0.3), Bu₄NBr (23 mg, 0.072 mmol) and KOH (400 mg, 7.2 mmol) was

added. To this solution dimethyl sulfate (680 μ L, 7.2 mmol) was added and the reaction was stirred at room temperature for 4 h. The reaction was quenched with 30% NH_4OH for 30 min. The resultant mixture was extracted with Et_2O and washed three times with 30% NH_4OH and once with H_2O and brine. The organic phase was dried over Na_2SO_4 and concentrated. The resulting residue was chromatographed in 30% EtOAc /Hexanes to afford methyl 1,3,6,7-tetramethoxynaphthalene-2-carboxylate (57 mg) in 25% yield. mp 114-117 $^\circ\text{C}$; ^1H NMR (500 MHz, CDCl_3) δ 7.29 (s, 1H), 7.03 (s, 1H), 6.84 (s, 1H), 3.98 (s, 3H), 3.97 (s, 6H), 3.96 (s, 3H), 3.88 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 167.3, 153.6, 153.4, 151.1, 148.3, 131.6, 117.8, 115.2, 106.0, 101.5, 101.4, 62.8, 56.0 (2), 55.9, 52.6; IR (film) 2999, 2949, 2872, 2845, 1729, 1625, 1602, 1583 cm^{-1} .

To a solution of methyl 1,3,6,7-tetramethoxynaphthalene-2-carboxylate (58 mg, 0.19 mmol) in MeOH (3 mL), concentrated NaOH (3 mL) was added. The solution was then heated to 40 $^\circ\text{C}$ for 1 day. The reaction mixture was then acidified with concentrated HCl and then extracted with CH_2Cl_2 three times. The organic extracts were then washed with brine and dried over Na_2SO_4 , filtered, and concentrated to afford **2d** (55 mg) in quantitative yield. White crystalline solid; mp 168-171 $^\circ\text{C}$; ^1H NMR (500 MHz, CDCl_3) δ 7.34 (s, 1H), 7.04 (s, 1H), 6.90 (s, 1H), 4.07 (s, 3H), 4.003 (s, 3H), 3.999 (s, 3H), 3.96 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 169.7, 155.2, 153.6, 151.6, 148.6, 132.1, 118.3, 113.6, 106.0, 101.9, 101.8, 63.2, 56.3, 56.1, 56.0; IR (film) 3532, 3003, 2937, 2853, 2625, 2023, 1702, 1629, 1610, 1583, 1509, 1482 cm^{-1} ; HRMS (ES) calcd for $\text{C}_{15}\text{H}_{16}\text{O}_6$ (MNa^+) 315.0845, found 315.0838.

1,3,6,7-tetramethoxy-4-methylnaphthalene-2-carboxylic acid (2e). To a solution of methyl 1,3-dihydroxy-6,7-dimethoxynaphthalene-2-carboxylate (200 mg, 0.72 mmol) in 6.5 mL of $\text{THF}:\text{H}_2\text{O}$ (1.0:0.3), Bu_4NBr (23 mg, 0.072 mmol) and KOH (400 mg, 7.2 mmol) was added. To this solution dimethyl sulfate (680 μ L, 7.2 mmol) was added and the reaction was stirred at room temperature for 4 h. The reaction was quenched with 30% NH_4OH for 30 min. The resultant mixture was extracted with Et_2O and washed three times with 30% NH_4OH and one time with H_2O and brine. The organic phase was dried over Na_2SO_4 and concentrated. The resulting residue was chromatographed in 30% EtOAc /Hexanes to afford methyl 1,3,6,7-tetramethoxy-4-methylnaphthalene-2-carboxylate (58 mg) in 26% yield. mp 124-126 $^\circ\text{C}$; ^1H NMR (500 MHz, CDCl_3) δ 7.37 (s, 1H), 7.15 (s, 1H), 4.01 (s, 3H), 4.00 (s, 3H), 3.98 (s, 3H), 3.97 (s, 3H), 3.81 (s, 3H), 2.49 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 167.5, 151.4, 150.9, 150.8, 149.0, 130.8, 120.2, 120.1, 118.6, 103.4, 101.7, 62.8, 62.6, 56.0, 55.9, 52.5, 11.5; IR (film) 3003,

2949, 2907, 2837, 1729, 1620, 1610 cm^{-1} ; HRMS (ES) calcd for $\text{C}_{17}\text{H}_{20}\text{O}_6$ (MNa^+) 343.1158, found 343.1167.

To a solution of methyl 1,3,6,7-tetramethoxy-4-methylnaphthalene-2-carboxylate (55 mg, 0.17 mmol) in 10 mL of dioxane, 10 mL of conc. $\text{LiOH}/\text{H}_2\text{O}$ was added. The resulting solution was heated to reflux for 24 h. The reaction mixture was then acidified with concentrated HCl and extracted with CH_2Cl_2 three times. The organic extracts were then washed with brine and dried over Na_2SO_4 , filtered and concentrated. The resultant solid was dissolved in CH_2Cl_2 and extracted twice with 1M NaOH . This solution was then acidified and extracted three times with EtOAc . The organic extracts were then washed with brine, dried over Na_2SO_4 , filtered and concentrated to afford **2e** (51 mg) in 97% yield. White crystalline solid; mp 174-179 $^\circ\text{C}$; ^1H NMR (500 MHz, CDCl_3) δ 7.38 (s, 1H), 7.13 (s, 1H), 4.05 (s, 3H), 4.03 (s, 3H), 4.02 (s, 3H), 3.89 (s, 3H), 2.50 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 170.4, 152.6, 151.2, 151.0, 149.2, 131.3, 120.6, 120.5, 117.1, 103.4, 101.9, 63.3, 62.9, 56.1, 56.0, 11.6; IR (film) 3516, 2999, 2941, 2872, 2837, 2636, 2602, 1729, 1702, 1625, 1602, 1583, 1509, 1475, 1428 cm^{-1} ; HRMS (ES) calcd for $\text{C}_{16}\text{H}_{18}\text{O}_6$ (MNa^+) 329.1001, found 329.1016.

5,5'-bis-benzyloxy-2,4,6,2',4',6'-hexamethoxy-7,7'-dipropyl-[1,1']-binaphthalenyl-3,3'-dicarboxylic acid (4). To a solution of 68% ee 5,5'-2,4,6,2',4',6'-hexamethoxy-7,7'-dipropyl-[1,1']-binaphthalenyl-3,3'-dicarboxylic acid dimethyl ester (37 mg, 0.055 mmol) and benzyl bromide (46 μL , 0.38 mmol) in DMF (1.0 mL) under an Ar atmosphere was added 60% NaH (13 mg, 0.31 mmol). The dark green mixture was stirred for 15 h, quenched with H_2O , and washed with EtOAc . The organic phase was washed with H_2O and brine, and dried (Na_2SO_4) and the solvent evaporated to yield an orange oil. Purification was accomplished by chromatography (15% $\text{EtOAc}/\text{Hexanes}$) to yield 5,5'-bis-benzyloxy-2,4,6,2',4',6'-hexamethoxy-7,7'-dipropyl-[1,1']-binaphthalenyl-3,3'-dicarboxylic acid dimethyl ester (36 mg) in 78% yield as a yellow resin; $[\alpha]_{\text{D}}^{20}$ -24.7 (c 1.0, CHCl_3 , 68% ee); ^1H NMR (500 MHz, CDCl_3) δ 7.63 (d, J = 7.0 Hz, 4H), 7.44 (t, J = 7.3 Hz, 4H), 7.38 (t, J = 7.3 Hz, 2H), 6.76 (s, 2H), 5.09 (m, 4H), 4.00 (s, 6H), 3.98 (s, 6H), 3.95 (s, 6H), 3.39 (s, 6H), 2.49-2.54 (m, 4H), 1.39-1.43 (m, 4H), 0.75 (t, J = 7.4 Hz, 6H); ^{13}C NMR (125 MHz, CDCl_3) δ 167.8, 154.4, 152.6, 146.8, 138.9, 138.4, 133.8, 129.2, 128.8, 128.3, 127.4, 123.1, 120.7, 120.3, 114.2, 77.1, 64.6, 62.3, 60.9, 53.2, 33.2, 23.9, 14.2; IR (thin film) 2939, 1735, 1330, 1094 cm^{-1} ; HRMS (ESI) calcd for $\text{C}_{50}\text{H}_{54}\text{O}_{12}\text{Na}$ (MNa^+) 869.3513, found 869.3541.

To a suspension of 5,5'-bis-benzyloxy-2,4,6,2',4',6'-hexamethoxy-7,7'-dipropyl-[1,1']-binaphthalenyl-3,3'-dicarboxylic acid dimethyl ester (163 mg, 0.19 mmol) in dioxane (8 mL) and H₂O (9 mL) was added LiOH·H₂O (402 mg, 9.6 mmol) and the mixture was heated to reflux for 24 h. The brown mixture was cooled to room temperature and diluted with H₂O. The aqueous phase was washed with EtOAc and this organic phase was washed with H₂O and brine, dried (Na₂SO₄), and the solvent evaporated to recover 73 mg (0.086 mmol, 45%) of the starting material. The aqueous phase was acidified with 1N HCl, extracted with EtOAc, and the organic phase was washed with H₂O and brine, dried (Na₂SO₄), and the solvent evaporated to yield **4** (81 mg) in 54% yield as an orange resin that was used without further purification; ¹H NMR (500 MHz, CDCl₃) δ 9.00 (br s, 2H), 7.64 (d, *J* = 7.0 Hz, 4H), 7.43 (t, *J* = 7.3 Hz, 4H), 7.36 (t, *J* = 7.3 Hz, 2H), 6.80 (s, 2H), 5.11 (dd, *J* = 9.8, 14.9 Hz, 4H), 3.99 (s, 6H), 3.98 (s, 6H), 3.44 (s, 6H), 2.50-2.54 (m, 4H), 1.40-1.44 (m, 4H), 0.76 (t, *J* = 7.3 Hz, 6H); HRMS (ESI) calcd for C₄₈H₅₀O₁₂Na (MNa⁺) 841.3200, found 841.3240.

Typical Decarboxylation Procedures

Typical procedure for substituted aromatics 3a, 3c, and 3d (Table 1: entries 1, 3, and 4). To a solution of **2d** (20 mg, 0.068 mmol) in 5% DMSO/DMF (1 mL), palladium (II) trifluoroacetate (4.6 mg, 0.014 mmol) was added. To this solution was added trifluoroacetic acid (51 μL, 0.68 mmol). The reaction mixture was heated at 70 °C for 24 h. After cooling, the mixture was diluted with Et₂O, and washed sequentially with 1 M HCl, saturated NH₄Cl, H₂O, and brine. The organic extracts were dried over Na₂SO₄ and concentrated at ambient temperature and pressure by slow evaporation on the bench-top. The resulting residue was chromatographed in 10% Et₂O/pentane to afford **3d** (13.0 mg) in 74% yield.

Typical procedure for substituted aromatics 3b and 3e (Table 1: entries 2 and 5). To a solution of **2b** (10 mg, 0.038 mmol) in 5% DMSO/DMF (0.5 mL), palladium (II) trifluoroacetate (2.5 mg, 0.0076 mmol) was added. To this solution was added trifluoroacetic acid (28 μL, 0.38 mmol). The reaction mixture was heated at 80 °C for 24 h. After cooling, the mixture was diluted with Et₂O, and washed sequentially with 1 M HCl, saturated NH₄Cl, H₂O, and brine. The organic extracts were then dried over Na₂SO₄ and concentrated at ambient temperature and pressure by slow evaporation on the bench-top. The resulting residue was chromatographed in 10% Et₂O/pentane to afford **3b** (6.0 mg) in 71% yield.

Typical procedure for substituted benzenes 3f and 3g (Table 2: entries 6 and 7). To a solution of 2,4,5-trimethoxybenzoic acid (300 mg, 1.4 mmol) in MeOH (15 mL) was added potassium *tert*-butoxide (160 mg, 1.4 mmol). The suspension was then stirred at room temperature for 4 h and then concentrated by rotary evaporation to afford **2f** (344 mg) in 97% yield and was used without further purification.

To a solution of **2f** (150 mg, 0.60 mmol) in DMSO (4.5 mL), palladium (II) trifluoroacetate (240 mg, 0.72 mmol) was added. This solution was heated to 80 °C for 30 min. Then trifluoroacetic acid (450 μ L, 6.00 mmol) was added and the solution was heated at 70 °C overnight. After cooling, the mixture was diluted with Et₂O and washed three times with saturated NH₄Cl, three times with H₂O, and once with brine. The organic extracts were dried over Na₂SO₄ and concentrated at ambient temperature and pressure by slow evaporation on the bench-top. The resultant residue was chromatographed in 20% Et₂O/Pentane to afford **3f** (55 mg) in 55% yield.

Typical procedure for compounds 3h and 3i (Table 2: entries 8 and 9). To a solution of **2h** (15 mg, 0.021 mmol, >99% ee (S)) in 5% DMSO-DMF (1 mL) was added palladium (II) trifluoroacetate (17 mg, 0.052 mmol) and Ag₂CO₃ (35 mg, 0.13 mmol). The mixture was heated in a 75 °C oil bath for 1 h. The reaction was removed from the oil bath and quenched with NaBH₄ (4.0 mg, 0.11 mmol). The black mixture was diluted with EtOAc, and the organic phase washed with 1N HCl and brine, dried (Na₂SO₄), and the solvent was evaporated. Purification was accomplished via chromatography (50% EtOAc/Hexanes) to yield **3h** (8.5 mg, 64%) as an oil (>99% ee).

Typical procedure for compounds 3b and 5 (Scheme 2). To a solution of **4** (27 mg, 0.033 mmol) in 5% DMSO/DMF (0.3 mL) was added palladium (II) trifluoroacetate (23 mg, 0.074 mmol). The mixture was then heated to 90 °C for 1 h. After cooling, 1 N HCl was added and the mixture was extracted with EtOAc. The organic phase was washed with H₂O and brine, dried over Na₂SO₄ and concentrated to yield a brown oil. This material was then dissolved in THF (1.0 mL) and stirred under a H₂ atmosphere for 5 min. After filtration through Celite®, the material was chromatographed in 20% EtOAc/Hexanes to afford **5** (21 mg) in 87% yield.

GC Reaction Monitoring

Monitoring the conversion of 2a to 3a. To a solution of **2a** (60 mg, 0.33 mmol) in 5% DMSO/DMF (3 mL), palladium (II) trifluoroacetate (110 mg, 0.33 mmol) and biphenyl

(51 mg, 0.33 mmol) was added. To this solution was added trifluoroacetic acid (250 μ L, 3.3 mmol). The reaction mixture was then heated at 70 °C for 24 h. At regular intervals, aliquots ($\sim$ 100 μ L) removed. To this aliquot was added 1M HCl and EtOAc. The solution was then shaken and the organic phase was filtered through SiO₂ (10% MeOH/CH₂Cl₂). The reaction progress was monitored by gas chromatography (GC). Retention times; **2a**: 9.93 min, **3a**: 1.60 min, **Biphenyl** (Internal Standard): 5.50 min. Correction factor for **2a**; $y = 1.8x + 0.085$. Correction factor for **3a**; $y = 1.74x + 0.11$.

NMR Reaction Monitoring

Procedure for NMR experiment 1. To a solution of **2a** (12 mg, 0.066 mmol) in DMSO-d₆ (0.75 ml) was added palladium (II) trifluoroacetate (26 mg, 0.079 mmol) and methanesulfonic acid (43 μ L, 0.66 mmol). A ¹H NMR spectrum was then taken. The mixture was then warmed to 65 °C and a spectrum was taken every 20 min for 7 h. The mixture was then cooled after 13 h at 65 °C and a final spectrum was taken.

Procedure for NMR experiment 2. To a solution of 2,6-dimethoxybenzoic acid **2a** (12 mg, 0.066 mmol) in DMSO-d₆ (0.75 mL) was added palladium (II) trifluoroacetate (26 mg, 0.079 mmol) was added. The mixture was then heated at 70 °C for 6 h. The mixture was cooled and methanesulfonic acid (43 μ L, 0.66 mmol) was added. A ¹H NMR spectrum was then taken. The mixture was then warmed to 65 °C and a spectrum was taken every 20 min for 9 h. The mixture was then cooled after 12 h at 65 °C and a final spectrum was taken.

Analytical Data for Decarboxylation Products

1,3-Dimethoxybenzene (3a): Pale yellow oil; ¹H NMR (500 MHz, CDCl₃) δ 7.19 (t, $J = 8.2$ Hz, 1H), 6.52 (dd, $J = 2.4, 8.2$ Hz, 2H), 6.48 (t, $J = 2.4$ Hz, 1H), 3.80 (s, 6H). Spectral data agreed with those reported previously: Saa, J. M.; Dopico, M.; Martonell, G.; Garcia-Raso, A. *J. Org. Chem.* **1994**, 55, 991-995.

3b

1,3,7-Trimethoxynaphthalene (3b): Brown amorphous solid; mp 69-71 °C; ^1H NMR (500 MHz, CDCl_3) δ 7.59 (d, J = 8.9 Hz, 1H), 7.47 (d, J = 2.6 Hz, 1H), 7.13 (dd, J = 8.9, 2.6 Hz, 1H), 6.70 (d, J = 2.1 Hz, 1H), 6.52 (d, J = 2.2 Hz, 1H), 3.98 (s, 3H), 3.91 (s, 3H), 3.89 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 156.6, 156.0, 155.7, 130.2, 128.1, 122.3, 119.5, 100.9, 98.2, 98.1, 55.7, 55.5, 55.4; IR (film) 2988, 2945, 2907, 1737, 1606 cm^{-1} ; HRMS (CI) calcd for $\text{C}_{13}\text{H}_{14}\text{O}_3$ (M^+) 218.0943, found 218.0939.

3c

1,3,6,8-tetramethoxynaphthalene (3c): Black crystalline solid; ^1H NMR (500 MHz, CDCl_3) δ 6.63 (d, J = 2.2 Hz, 2H), 6.37 (d, J = 2.2 Hz, 2H), 3.92 (s, 6H), 3.88 (s, 6H). Spectral data agreed with those reported previously: McCulloch M. W. B.; Malcolm, W. B.; Barrow, R. A. *Tetrahedron Lett.* **2005**, 46, 7619-7621.

3d

1,3,6,7-tetramethoxynaphthalene (3d): Dark brown amorphous solid; mp 120-125 °C; ^1H NMR (500 MHz, CDCl_3) δ 7.45 (s, 1H), 7.02 (s, 1H), 6.66 (d, J = 2.1 Hz, 1H), 6.42 (d, J = 2.2 Hz, 1H), 3.99 (s, 3H), 3.98 (s, 3H), 3.96 (s, 3H), 3.89 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 157.3, 155.7, 150.4, 147.4, 130.8, 116.1, 105.9, 101.5, 97.7, 96.1, 56.0, 55.9, 55.6, 55.5; IR (film) 2999, 2937, 2833, 1633, 1610, 1513 cm^{-1} ; HRMS (ESI) calcd for $\text{C}_{14}\text{H}_{17}\text{O}_4$ (MH^+) 249.1127, found 249.1137.

3e

2,4,6,7-tetramethoxy-1-methylnaphthalene (3e): Orange amorphous solid; mp 134-140 °C; ^1H NMR (500 MHz, CDCl_3) δ 7.49 (s, 1H), 7.12 (s, 1H), 6.57 (s, 1H), 4.02 (s, 3H), 4.00 (s, 3H), 3.996 (s, 3H), 3.92 (s, 3H), 2.43 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 153.9, 150.3, 147.4, 130.1, 116.3, 110.9, 103.8, 102.8, 101.5, 93.4, 57.6, 56.0, 55.9, 55.7, 10.6; IR (film) 2991, 2930, 2833, 16299, 1598, 1513, 1494 cm^{-1} ; HRMS (CI) calcd for $\text{C}_{15}\text{H}_{18}\text{O}_4$ (M^+) 262.1205, found 262.1204.

3f

1,2,4-trimethoxybenzene (3f): Yellow oil; ^1H NMR (500 MHz, CDCl_3) δ 6.78 (d, J = 8.7 Hz, 1H), 6.51 (d, J = 2.8 Hz, 1H), 6.39 (dd, J = 8.7, 2.8 Hz, 1H), 3.85 (s, 3H), 3.83 (s, 3H), 3.76 (s, 3H). Spectral data agreed with those reported previously: Mathivanan, N.; Cozens, F.; McClelland, R. A.; Steenken, S. *J. Am. Chem. Soc.* **1992**, 114, 2198-2203 and Buchanan, G. L.; Raphael, R. A.; Taylor, R. *J. Chem. Soc., Perkins Trans. I* **1973**, 4, 373-375.

3g

1,3,5-trimethylbenzene (3g): Brown amorphous solid; ^1H NMR (500 MHz, CDCl_3) δ 6.90 (s, 3H), 2.43 (s, 9H). Spectral data agreed with those reported previously: Kim, E. K.; Kochi J. K. *J. Am. Chem. Soc.* **1991**, 113, 4962-4974 and Hunt, D. F.; Sethi S. K. *J. Am. Chem. Soc.* **1980**, 102, 6953-6963.

3h

2-((1-(1-2,6,8-trimethoxy-3-((2-methyl-1,3-dioxolan-2-yl)methyl)naphthalen-5-yl)-2,4,6-trimethoxynaphthalen-7-yl)methyl)-2-methyl-1,3-dioxolane (3h): $[\alpha]_D^{20} -17.8$ (c 0.53, CH_2Cl_2 , >99% ee); IR (thin film) 2933, 2839, 1595, 1503, 1463 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 1.18 (s, 6H), 2.75 (d, $J = 13.5$, 2H), 2.99 (d, $J = 13.5$, 2H), 3.44-3.55 (m, 4H), 3.65-3.74 (m, 4H), 3.70 (s, 6H), 3.92 (s, 6H), 4.11 (s, 6H), 6.78 (s, 2H), 7.01 (s, 2H), 7.51 (s, 2H); ^{13}C NMR (500 MHz, CDCl_3) δ 24.6, 37.9, 55.7, 55.8, 57.8, 64.7, 64.8, 95.4, 99.8, 110.3, 112.7, 121.6, 127.9, 129.2, 130.1, 154.1, 155.3, 155.4; HRMS (ESI) calcd for $\text{C}_{36}\text{H}_{42}\text{O}_{10}$ (MH^+) 635.2832, found 635.2843; CSP HPLC (Chiralpak AD, 1.0 mL/min, 95:5 hexanes: *i*PrOH) t_R (S) = 14.7 min, t_R (R) 17.5 min.

3i

(2''*R*,*R*_a,2'''*R*)-5,5'-Bis-benzyloxy-2,2',4,4',6,6'-hexamethoxy-7,7'-bis(2-propyloxy(*tert*-butyl)dimethyl silane)-[1,1']binaphthalenyl (3i): ^1H NMR (500 MHz, CDCl_3) δ -0.23 (s, 6H), -0.11 (s, 6H), 0.73 (s, 18H), 1.00 (d, $J = 6.0$ Hz, 6H), 2.46-2.42 (dd, $J = 7.1$ Hz, 12.7 Hz, 2H), 2.83-2.79 (dd, $J = 6.3$ Hz, 12.7 Hz, 2H), 3.70 (s, 6H), 3.95 (s, 6H), 4.00-4.02 (m, 2H), 4.00 (s, 6H), 5.08 (br s, 4H), 6.74 (s, 2H), 6.76 (s, 2H), 7.37-7.47 (m, 6H), 7.64-7.66 (m, 4H).

5,5'-Bis-benzyloxy-2,2',4,4',6,6'-hexamethoxy-7,7'-dipropyl-[1,1']-binaphthalene

(5): Resin; ^1H NMR (500 MHz, CDCl_3) δ 7.62 (d, $J = 7.0$ Hz, 4H), 7.43 (t, $J = 7.3$ Hz, 4H), 7.37 (t, $J = 7.3$ Hz, 2H), 6.76 (s, 2H), 6.64 (s, 2H), 5.10 (m, 4H), 3.99 (s, 6H), 3.92 (s, 6H), 3.74 (s, 6H), 2.46-2.53 (m, 4H), 1.35-1.42 (m, 4H), 0.75 (t, $J = 7.2$ Hz, 6H); ^{13}C NMR (125 MHz, CDCl_3) δ 157.1, 154.9, 148.8, 147.2, 138.9, 137.0, 133.7, 129.0, 128.5, 127.8, 122.1, 116.5, 112.5, 95.9, 76.2, 61.4, 57.5, 56.1, 32.8, 23.6, 14.0; IR (film) 2933, 1338 cm^{-1} ; HRMS (ESI) calcd for $\text{C}_{46}\text{H}_{50}\text{O}_8\text{Na}$ (MNa^+) 753.3403, found 753.3427.

Scheme 3. 500 MHz ¹H NMR Spectrum of Compound **3a** in CDCl₃

Scheme 2. 500 MHz ^1H NMR Spectrum of Compound **3b** in CDCl_3

Scheme 2. 125 MHz ^{13}C NMR Spectrum of Compound **3b** in CDCl_3

Table 1. 500 MHz ¹H NMR Spectrum of Compound **3c** in CDCl₃

Table 1. 125 MHz ^{13}C NMR Spectrum of Compound **3c** in CDCl_3

Table 1. 500 MHz ^1H NMR Spectrum of Compound **3d** in CDCl_3

Table 1. 125 MHz ^{13}C NMR Spectrum of Compound **3d** in CDCl_3

Table 1. 500 MHz ¹H NMR Spectrum of Compound **3e** in CDCl₃

Table 1. 125 MHz ^{13}C NMR Spectrum of Compound **3e** in CDCl_3

Table 2. 500 MHz ¹H NMR Spectrum of Compound **3f** in CDCl₃

Table 2. 500 MHz ^1H NMR Spectrum of Compound **3g** in CDCl_3

Table 2. 500 MHz ^1H NMR Spectrum of Compound **3h** in CDCl_3

Table 2. 125 MHz ^{13}C NMR Spectrum of Compound **3h** in CDCl_3

Table 2. 500 MHz ^1H NMR Spectrum of Compound **3i** in CDCl_3

Scheme 2. 500 MHz ^1H NMR Spectrum of Compound **5** in CDCl_3

Scheme 2. 125 MHz ^{13}C NMR Spectrum of Compound **5** in CDCl_3