Supporting Information for

Efficient Microwave Method for the Oxidative Coupling of Phenols

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I. Materials. All compounds were purchased from Aldrich, Alfa Aesar, TCI America, Matrix Scientific, Strem, and/or Fisher. NMR solvents were purchased from Cambridge Isotope Laboratories, Inc. Chlorobenzene (Acros) was used as-received. The flash chromatography of all compounds was performed utilizing silica gel 60 (32-63 micron) purchased from Bodman Industries.

II. Instrumentation. Nuclear magnetic resonance (NMR) spectra were obtained using either a Bruker AvanceIII-500 or Bruker 300 NMR spectrometer. Chemical shifts for protons are reported in parts per million downfield from tetramethylsilane and are referenced to residual protium in the NMR solvent (CHCl_3 : δ 7.26). Chemical shifts for carbon are reported in parts per million downfield from tetramethylsilane and were referenced to the carbon resonances of the solvent (CDCl_3 : δ 77.2). Data are represented as follows: chemical shift, integration, multiplicity (s = singlet, d = doublet, sep = septet, m = multiplet, br = broad), coupling constants in Hertz (Hz), and assignment. Mass spectrometric data were obtained at the Caltech Mass Spectrometry Facility. A Biotage[®] Initiator microwave reactor was used for all microwave experiments. Microwave reactions were conducted in septum-sealed, glass vials equipped with magnetic stirbars; an external surface sensor was used to monitor reaction conditions.

III. Experimental Procedures.

3,3'-di-*tert*-butyl-5,5'-dichloro-6,6'-dimethylbiphenyl-2,2'-diol (2a).

Representative Phenoxy Radical, Microwave Heating Procedure: To a 0.2-5 mL microwave reaction vial equipped with a stirbar, 2-*tert*-butyl-4-chloro-5-methylphenol¹ (590 mg, 1.5 mmol, 1.0 equiv) was dissolved in chlorobenzene (1.5 mL). Di-*tert*-butyl peroxide (287 μ L, 1.58 mmol, 1.05 equiv) was then added. The vial was capped and placed in the microwave reactor. After thoroughly mixing for 5 minutes to ensure that the peroxide was thoroughly distributed throughout the reaction mixture,² the reaction was heated to 200 °C for 10 minutes. Upon cooling, the reaction was directly purified by flash chromatography on silica gel to afford the desired product in 98% isolated yield. Silica TLC: R_f = 0.26 (100% hexanes; UV TLC visualization); IR (pellet, cm^{-1}) 3505 (s), 2969 (m), 1371 (s), 1182 (s); ¹H NMR (300 MHz, CDCl_3 , 20 °C) 7.38 (2H, s, ArH), 4.87 (2H, s, OH), 1.96 (6H, s, CH_3), 1.40 (18H, s, $(\text{CH}_3)_3$); ¹³C NMR (75 MHz, CDCl_3 , 20 °C) δ 150.9, 136.1, 133.5, 128.7, 126.2, 121.3, 34.9, 29.3, 16.8; HRMS (FAB) calcd. for $\text{C}_{22}\text{H}_{28}\text{Cl}_2\text{O}_2$ 394.1466, found m/z: 394.1456.

Representative Phenoxy Radical, Conventional Heating Procedure. Experimental procedure was performed according to Zhang, A. *Tetrahedron* **2000**, 56, 7163-7171 and Gutierrez, E. G.; Moorhead, E. J.; Smith, E. H.; Lin, V.; Ackerman, L. K. G.; Sun, V.; Grant, S.; Wenzel, A. G. *Eur. J. Org. Chem.* **2010**, 3027-3031. To a 50-mL, round-bottomed flask, 2-*tert*-butyl-4-chloro-

¹ Gutierrez, E. G.; Moorhead, E. J.; Smith, E. H.; Lin, V.; Ackerman, L. K. G.; Sun, V.; Grant, S.; Wenzel, A. G. *Eur. J. Org. Chem.* **2010**, 3027-3031.

² Neat di-*tert*-butyl peroxide represents a vial explosion hazard upon heating. To safely execute this reaction, thorough reagent mixing is needed prior to heating.

5-methylphenol¹ (590 mg, 1.5 mmol, 1.0 equiv) was dissolved in chlorobenzene (30 mL). Di-*tert*-butyl peroxide (412 μ L, 2.25 mmol, 1.5 equiv) was then added with stirring. The flask was capped with a reflux condenser and immersed in a 140 °C-oil bath for 2 h. The reaction was then allowed to slowly cool to room temperature over a 3-h period. The volatiles were then removed, and the resulting residue was purified via silica gel chromatography (100% hexanes) to afford the desired product as a white solid in 40% isolated yield.

Representative Iron Trichloride Microwave Heating Procedure. Experimental procedure adapted from Ding, Y.; Liao, J.; Zhang, G.; Liang, X. *Huaxue Shijie* **2004**, 45, 430-432. To a 0.2-5 mL microwave reaction vial, 2-*tert*-butyl-4-chloro-5-methylphenol¹ (590 mg, 1.5 mmol, 1.0 equiv) was combined with water (3.0 mL). FeCl₃·6H₂O (426 mg, 1.58 mmol, 1.05 equiv) was then added with stirring. The vial was capped and placed in the microwave reactor. After irradiating the vial to 150 °C for 20 min, the vial was removed from the microwave reactor, and the reaction contents were partitioned between water and dichloromethane in a separatory funnel. The layers were separated, and the aqueous layer was extracted with dichloromethane until the product was no longer visible in the aqueous layer by TLC (3x's). The combined organics were dried over anhydrous sodium sulfate, filtered, and concentrated. The resulting residue was purified by flash chromatography on silica gel.

Representative Copper-exchanged Montmorillonite Clay Procedure. Experimental procedure was performed according to Kantam, M. L.; Santhi, P. L. *Synth. Commun.* **1996**, 26, 3075-3079. To a 50-mL, 2-neck, round-bottom flask, 2-*tert*-butyl-4-chloro-5-methylphenol¹ (590 mg, 1.5 mmol, 1.0 equiv) was dissolved in chlorobenzene (15 mL). Copper-exchanged Montmorillonite

clay³ was then added in one portion with stirring. The flask was stoppered and capped with a hollow, water-cooled condenser. A 16-G needle connected to an air supply was then passed through the condenser to bubble air through the reaction media. Once the setup was complete, the flask was immersed in a 140 °C-oil bath for 6 h, while maintaining a consistent air flow through the needle. The reaction was then cooled to ambient temperature, and the air stream was stopped. The flask contents were filtered through a Hirsch funnel, and the clay was rinsed with dichloromethane (2 x 15 mL) and acetone (2 x 15 mL). The combined filtrate was concentrated, and the resulting residue was purified by flash chromatography on silica gel.

2-*tert*-butyl-4-fluoro-5-methylphenol (1b). A flame-dried, 500-mL flask was charged with 4-

fluoro-3-methylphenol⁴ (26.6 g, 146 mmol, 1.0 equiv). Dichloromethane (70 mL) was then added with stirring. To this mixture, *tert*-butyl alcohol (14.0 mL, 146 mmol, 1.0 equiv) was added. The reaction was cooled to 0 °C for 5 minutes, and 95% aqueous sulfuric acid (8.2 mL, 146 mmol, 1.0 equiv) was added. The reaction was allowed warm to ambient temperature. After 48 h, an additional 14.0 mL (146 mmol) of *tert*-butyl alcohol and 8.2 mL 95% aqueous sulfuric acid (146 mmol) was added. After an additional 48 h, saturated aqueous sodium bicarbonate was slowly added until gas evolution ceased (~140 mL). The mixture was then partitioned with ethyl acetate (140 mL). The organic layer was washed with saturated aqueous sodium bicarbonate (2 x 100 mL) and brine (1 x 100 mL). Organics were then dried over anhydrous sodium sulfate, filtered, and concentrated to afford analytically pure product as a yellow, crystalline solid in quantitative, isolated yield. Silica TLC: R_f = 0.21 (5% ethyl acetate in hexanes); IR (pellet, cm^{-1}) 3559 (s), 1526 (m), 1409 (s),

³ Laszlo, P.; Mathy, A. *Helv. Chim. Acta.* **1987**, *70*, 577-586.

⁴ 4-Fluoro-3-methylphenol is commercially available from Matrix Scientific (\$69/25 g). <http://www.matrixscientific.com> (accessed July 2014).

1191 (s); ^1H NMR (300 MHz, CDCl_3 , 20 $^\circ\text{C}$) δ 6.92 (1H, d, J = 11.7 Hz, ArH), 6.47 (1H, d, J = 6.7 Hz, ArH), 4.38 (1H, s, OH), 2.18 (3H, s, CH_3), 1.38 (9H, s, $(\text{CH}_3)_3$); ^{13}C NMR (75 MHz, CDCl_3 , 20 $^\circ\text{C}$) δ 153.8, 149.5, 135.1 (d, J = 6.0 Hz), 122.2 (d, J = 18.9 Hz); 118.6 (d, J = 5.31 Hz); 113.6 (d, J = 24.8 Hz), 34.3, 29.4, 13.9; HRMS (FAB) calcd. for $\text{C}_{11}\text{H}_{15}\text{FO}$ 182.1106, found m/z : 182.1102.

3,3'-di-*tert*-butyl-5,5'-difluoro-6,6'-dimethylbiphenyl-2,2'-diol (2b).

Phenoxy Radical, Microwave Heating Procedure: Utilizing the microwave procedure outlined for **1a**, the product was isolated as a cream solid in 89% yield following flash chromatography on silica gel (elution gradient of 100% hexanes $\rightarrow$ 5% ethyl acetate in hexanes). Silica TLC: R_f = 0.29 (5% ethyl acetate in hexanes); IR (pellet, cm^{-1}) 3534 (m), 2960 (w), 1389 (m), 1152 (s); ^1H NMR (300 MHz, CDCl_3 , 20 $^\circ\text{C}$) δ 7.08 (2H, d, J = 11.7 Hz, ArH), 4.74 (2H, s, OH), 1.84 (6H, s, CH_3), 1.37 (9H, s, $(\text{CH}_3)_3$); ^{13}C NMR (75 MHz, CDCl_3 , 20 $^\circ\text{C}$) δ 153.8, 148.1 (d, J = 2.1 Hz), 135.9 (d, J = 6.1 Hz), 121.9 (d, J = 17.9 Hz), 120.3 (d, J = 4.7 Hz), 114.8 (d, J = 25.5 Hz); HRMS (EI^+) calcd. for $\text{C}_{22}\text{H}_{28}\text{F}_2\text{O}_2$ 363.2136 $[\text{M}+\text{H}]$, found m/z : 363.2148.

3,3'-di-*tert*-butyl-5,5'-dimethylbiphenyl-2,2'-diol (2c).

Phenoxy Radical, Microwave Heating Procedure: Utilizing the microwave procedure outlined above for **1a**, the product was isolated in 62% yield following flash chromatography on silica gel. Characterization information was found to correlate with literature values.⁵

⁵ Jiang, Q.; Sheng, W.; Tian, M.; Tang, J.; Guo, C. *Eur. J. Org. Chem.* **2013**, 1861-1866.

1,1'-binaphthyl-2,2'-diol (2d).

Phenoxy Radical, Microwave Heating Procedure: Utilizing the microwave procedure outlined above for **1a**, the product was isolated in quantitative yield following flash chromatography on silica gel. Characterization information was found to correlate with literature values.⁶

6,6'-dibromo-1,1'-binaphthyl-2,2'-diol (2e).

Phenoxy Radical, Microwave Heating Procedure: Utilizing the microwave procedure outlined above for **1a**, the product was isolated in 93% yield following flash chromatography on silica gel. Characterization information was found to correlate with literature values.⁷

6,6'-dimethoxy-1,1'-binaphthyl-2,2'-diol (2f).

Phenoxy Radical, Microwave Heating Procedure: Utilizing the microwave procedure outlined above for **1a**, the product was isolated in quantitative yield following flash chromatography on silica gel. Characterization information was found to correlate with literature values.⁷

7,7'-dimethoxy-1,1'-binaphthyl-2,2'-diol (2g).

Phenoxy Radical, Microwave Heating Procedure: Utilizing the microwave procedure outlined above for **1a**, the product was isolated in 83% yield following flash chromatography on silica gel.

⁶ Matsushita, M.; Kamata, K.; Yamaguchi, K.; Mizuno, N. *J. Am. Chem. Soc.* **2005**, *127*, 6632-6640.

⁷ Lv, N.; Xie, M.; Gu, W.; Ruan, H.; Qiu, S.; Zhou, C.; Cui, Z. *Org. Lett.* **2013**, *15*, 2382-2385.

Characterization information was found to correlate with literature values.⁷

3-*tert*-butyl-5,6,7,8-tetrahydronaphthalen-2-ol (1h). To a flame-dried, 250-mL round-bottom

flask under argon, 5,6,7,8-tetrahydro-2-naphthol (1.84 g, 12.4 mmol, 1.0 equiv) was added, followed by 70 mL of anhydrous dichloromethane. The

mixture was stirred until homogeneous, and then *tert*-butanol (1.35 mL, 12.4

mmol, 1.0 equiv) was added. Boron trifluoride dimethyl etherate (4.6 mL, 49.6 mmol, 4.0 equiv)

was then added dropwise via syringe. The solution was observed to become a cloudy, orange-

brown color. The mixture was allowed to stir for 1.5 h, at which point deionized water (35 mL)

was slowly added to quench the reaction. After allowing the reaction to stir an additional 1.5 h,

the contents of the round-bottom flask were transferred to a 250-mL, separatory funnel. The

organic layer was isolated and washed with saturated, aqueous sodium carbonate (35 mL x 1)

and brine (25 mL x 1). The organics were dried over anhydrous sodium sulfate, filtered, and

concentrated to afford a viscous, brown oil. The product was purified via flash chromatography

on silica gel (2.5% ethyl acetate in hexanes) to afford the desired product as yellow crystals in

59% isolated yield. Silica TLC: R_f = 0.83 (15% ethyl acetate in hexanes; UV TLC visualization);

IR (salt plate, cm^{-1}) 3251 (s), 2995 (m), 2934 (s), 1616 (m), 1412 (s), 1180 (s); ^1H NMR (500

MHz, CDCl_3 , 20 °C) δ 6.98 (1H, s, Ar-**H**), 6.42 (1H, s, Ar-**H**), 4.54 (1H, br s, **OH**), 2.73-2.68

(4H, m, cyclohexyl protons), 1.81-1.78 (4H, m, cyclohexyl protons), 1.43 (9H, s, (**CH**₃)₃); ^{13}C

NMR (75 MHz, CDCl_3 , 20 °C) δ 151.8, 135.6, 133.7, 128.7, 127.7, 116.6, 34.2, 29.8, 28.8, 28.7,

23.6, 23.2; MS (EI^+) calcd. for $\text{C}_{14}\text{H}_{21}\text{O}$ 205.1 [$\text{M}+\text{H}$], found m/z : 205.1.

3,3'-di-*tert*-butyl-5,5',6,6',7,7',8,8'-octahydro-1,1'-binaphthyl-2,2'-diol (2h).

Phenoxy Radical, Microwave Heating Procedure: Utilizing the microwave procedure outlined above for **1a**, the product was isolated as a yellow, crystalline solid in 93% yield following flash chromatography on silica gel (elution gradient of 2.5% ethyl acetate in hexanes $\rightarrow$ 10% ethyl acetate in hexanes). Silica TLC: R_f = 0.78 (15% ethyl acetate in hexanes). IR (salt plate, cm^{-1}) 3510 (s), 2931 (s), 1185.3 (s); ^1H NMR (500 MHz, CDCl_3 , 20 $^\circ\text{C}$) δ 7.09 (2H, s, Ar-**H**), 4.88 (2H, s, **OH**), 2.78-2.74 (4H, m, cyclohexyl protons), 2.24-2.08 (4H, m, cyclohexyl protons), 1.79-1.66 (8H, m, cyclohexyl protons), 1.43 (18H, s, (**CH**₃)₃); ^{13}C NMR (75 MHz, CDCl_3 , 20 $^\circ\text{C}$) δ 150.1, 134.5, 133.8, 129.1, 128.3, 119.5, 34.55, 29.6, 29.5, 26.8, 23.2, 23.1; HRMS (FAB) calcd. for $\text{C}_{28}\text{H}_{37}\text{O}_2$ 405.2794 [$\text{M}+\text{H}-\text{H}_2$], found m/z : 405.2803 [$\text{M}+\text{H}-\text{H}_2$].