Supporting Information

Novel Highly Regioselective VO(acac)₂/TBHP Mediated Oxidation of *o*-Alkenyl Phenols to *o*-Hydroxybenzyl Ketones

Alessandra Lattanzi,* Antonello Senatore, Antonio Massa, and Arrigo Scettri

Dipartimento di Chimica, Universita' di Salerno, Via S. Allende, I- 84081, Baronissi, Salerno, Italy

lattanzi@unisa.it

Experimental Section

Materials and Methods. CH₂Cl₂ was dried over calcium hydride and distilled before use. Petrol refers to the fraction of petroleum ether boiling in the range 40–60 °C. All the reactions were carried out under argon atmosphere using flame dried glassware. Flash chromatography was performed on Merk Kieselgel (230–400) mesh. ¹H NMR and ¹³C NMR spectra were recorded at 400 MHz in CDCl₃ as solvent. Chemical shifts (δ) are quoted in ppm relative to internal CDCl₃ δ 7.26 for ¹H NMR and CDCl₃ δ 77.0 for ¹³C NMR. IR absorptions are reported in cm⁻¹. Unless otherwise noted, materials were obtained from commercial suppliers and were used without further purification. Spectroscopic data for compounds **1b**,¹ **1c**,² **1d**,³ **1e**,³ **1f**,⁴ **1g**,³ **1h**,⁵ **1i**,⁶ **2a**,⁷ **2e**,⁸ **4a**,⁷ **4b**,⁹ **4d**,⁹ and **4e**⁸ are in agreement with literature data.

General procedure for 2 and 3. To a stirred solution of dry CH₂Cl₂ (4 mL), under argon atmosphere, were added VO(acac)₂ (5.2 mg, 0.02 mmol) and **1** (1 mmol); then after 5 min TBHP (212 μL, 1.2 mmol of 5.5 M decane solution) was added. The mixture was stirred at 40 °C for 1–7 h. At the end of the reaction, the solvent of the crude reaction mixture was partially removed in vacuo and the concentrated

crude mixture was filtered through a small pad of silica gel before ^1H NMR analysis. Then the reaction mixture was purified by flash chromatography eluting with petrol–Et₂O mixtures from 80:20 to 70:30.

1-(2-Hydroxyphenyl)propan-2-one (2a).⁷ ^1H NMR (400 MHz, CDCl₃) δ 7.18–7.16 (m, 1H), 7.09–7.07 (m, 1H), 6.99 (s, 1H), 6.93–6.86 (m, 2H), 3.75 (s, 2H), 2.30 (s, 3H). ^{13}C NMR (100 MHz, CDCl₃) δ 210.3, 154.7, 130.9, 128.8, 121.0, 120.6, 116.6, 46.0, 29.8. MS (EI) m/z 150 (M^+ , 35%), 108 (24), 107 (100), 77 (26).

1-(2-Hydroxyphenyl)hexan-2-one (2b). Dark yellow dense oil. IR (KBr) 3383.3, 2958.2, 2932.1, 2872.2, 1699.0, 1457.3, 1237.9, 753.3 cm⁻¹. ^1H NMR (400 MHz, CDCl₃) δ 7.55 (s, 1H), 7.19–7.15 (m, 1H), 7.07–7.05 (m, 1H), 6.93–6.91 (m, 1H), 6.88–6.85 (m, 1H), 3.72 (s, 2H), 2.61 (t, J = 7.4 Hz, 2H), 1.60–1.53 (quintet, J = 7.4 Hz, 2H), 1.33–1.24 (sx, J = 7.4 Hz, 2H), 0.88 (t, J = 7.4 Hz, 3H). ^{13}C NMR (100 MHz, CDCl₃) δ 213.0, 155.2, 130.8, 128.9, 121.1, 120.7, 117.3, 45.6, 42.7, 25.5, 22.1, 13.7. MS (EI) m/z 192 (M^+ , 62%), 175 (32), 131 (84), 121 (58), 108 (36), 107 (100), 91 (36), 77 (38), 57 (36).

1-(2-Hydroxyphenyl)-3-methylpentan-1-one (2c). Yellow dense oil. IR (KBr) 3368.3, 2965.5, 2932.3, 2876.0, 1699.0, 1456.7, 1238.4, 752.8 cm⁻¹. ^1H NMR (400 MHz, CDCl₃) δ 7.89 (s, 1H), 7.18–7.14 (m, 1H), 7.06–7.04 (m, 1H), 6.94–6.91 (m, 1H), 6.87–6.83 (m, 1H), 3.77 (s, 2H), 2.70–2.63 (sx, J = 7.0 Hz, 1H), 1.77–1.72 (m, 1H), 1.48–1.42 (m, 1H), 1.13 (d, J = 7.0 Hz, 3H), 0.85 (t, J = 7.0 Hz, 3H). ^{13}C NMR (100 MHz, CDCl₃) δ 216.7, 155.4, 130.7, 128.9, 121.2, 120.6, 117.6, 48.4, 44.1, 25.4, 15.3, 11.4. MS (EI) m/z 192 (M^+ , 100%), 175 (26), 147 (38), 133 (52), 121 (74), 108 (32), 107 (76), 91 (26), 77 (36), 57 (34).

1-(2-Hydroxyphenyl)-3,3-dimethylbutan-2-one (2d). Pale brown dense oil. IR (KBr) 3391.2, 2968.4, 2871.5, 1700.6, 1478.9, 1239.8, 752.7 cm⁻¹. ^1H NMR (400 MHz, CDCl₃) δ 8.33 (s, 1H), 7.17–7.13 (m, 1H), 7.05–7.03 (m, 1H), 6.95–6.93 (m, 1H), 6.86–6.83 (m, 1H), 3.83 (s, 2H), 1.23 (s, 9H). ^{13}C NMR (100 MHz, CDCl₃) δ 218.5, 155.6, 130.7, 128.8, 121.1, 120.5, 117.8, 40.0, 25.7. MS (EI) m/z 192 (M^+ , 100%), 175 (22), 149 (36), 133 (71), 121 (68), 108 (42), 107 (92), 105 (33), 91 (30), 77 (42), 57 (76).

2-(2-Hydroxyphenyl)-1-phenylethanone (2e).⁸ IR (KBr) 3370.2, 2961.2, 2932.1, 1692.0, 1457.3, 1230.9, 752.0 cm^{-1} . ¹H NMR (400 MHz, CDCl_3) δ 8.07–8.09 (m, 2H), 7.64–7.62 (m, 2H), 7.45–7.50 (m, 2H), 7.12–7.16 (m, 2H), 6.90–6.92 (m, 1H), 6.82–6.85 (m, 1H), 4.27 (s, 2H). MS (EI) m/z 212 (M^+ , 26%), 157 (38), 105 (100), 77 (65).

2-(3-Methyl-3-phenyloxiranyl)phenol (3f). Pale yellow dense oil. IR (KBr) 3374.5, 3061.6, 2930.5, 1599.1, 1455.6, 1235.0, 752.1 cm^{-1} . ¹H NMR (400 MHz, CDCl_3) δ 8.13 (s, 1H), 7.45–7.36 (m, 5H), 7.24–7.22 (m, 1H), 7.13–7.11 (m, 1H), 6.90–6.87 (m, 2H), 4.14 (s, 1H), 1.62 (s, 3H). ¹³C NMR (100 MHz, CDCl_3) δ 155.6, 140.6, 129.3, 128.6, 127.9, 127.7, 125.1, 119.8, 117.9, 117.0, 68.1, 63.4, 17.3. MS (EI) m/z 226 (M^+ , 50%), 209 (100), 208 (60), 183 (96), 165 (48), 153 (24), 115 (8). Anal. Calcd for $\text{C}_{15}\text{H}_{14}\text{O}_2$: C, 79.62; H, 6.24. Found: C, 79.83; H, 6.38.

2-(3-*tert*-Butyl-3-methyloxiranyl) phenol (3g). Yellow dense oil. IR (KBr) 3366.8, 2965., 2930.5, 1455.7, 1363.7, 1157.5, 756.2 cm^{-1} . ¹H NMR (400 MHz, CDCl_3) δ 8.19 (s, 1H), 7.16–7.13 (m, 1H), 7.03–7.01 (m, 1H), 6.85–6.80 (m, 2H), 4.23 (s, 1H), 1.16 (s, 3H), 1.04 (s, 9H). ¹³C NMR (100 MHz, CDCl_3) δ 156.1, 128.7, 127.1, 119.5, 118.5, 116.8, 117.0, 68.5, 62.0, 25.8, 13.6. MS (EI) m/z 206 (M^+ , 100%), 189 (30), 188 (24), 150 (19), 121 (8), 107 (6). Anal. Calcd for $\text{C}_{13}\text{H}_{18}\text{O}_2$: C, 75.69, H, 8.80. Found: C, 75.85; H, 8.66.

Acetic Acid *trans*-(2-Propenyl)phenyl Ester (1i). To a stirred solution of neat commercial **1a** (268 mg, 2 mmol) was added pyridine (2.5 mL, 32 mmol) and then Ac_2O (1.5 mL, 16 mmol) at room temperature. Stirring was maintained for 2 h, then the pyridine was removed in vacuo until a yellow oil was obtained. The crude mixture was purified by flash chromatography (95:5 petrol– Et_2O) to afford **1i** as a pale yellow oil (330 mg, 94%).⁶ ¹H NMR (400 MHz, CDCl_3) δ 7.52–7.49 (m, 1H), 7.22–7.18 (m, 2H), 7.02–7.00 (m, 1H), 6.41 (d, J = 15.8 Hz, 1H), 6.25 (dq, J = 15.8, 6.8 Hz, 1H), 2.34 (s, 3H), 1.90 (d, J = 6.8 Hz, 3H).

Acetic Acid *trans*-2-(3-Methyloxiranyl)phenyl Ester (3i). The oxidation reaction on **1i** (176 mg, 1 mmol) was carried out following the procedure described above. The mixture was stirred at room

temperature for 7 h. The crude mixture was purified by flash chromatography (80:20 petrol-Et₂O) to give **3i** (71 mg, 37%) as a pale yellow oil. IR (KBr) 2977.6, 2929.9, 1765.7, 1370.3, 1206.1, 754.8 cm⁻¹. ¹H NMR (400 MHz, CDCl₃) δ 7.29–7.22 (m, 3H), 7.06–7.04 (m, 1H), 3.62 (d, *J* = 2.0 Hz, 1H), 2.95 (dq, *J* = 5.1, 2.0 Hz, 1H), 2.33 (s, 3H), 1.43 (d, *J* = 5.1 Hz, 3H). ¹³C NMR (100 MHz, CDCl₃) δ 169.1, 149.0, 130.1, 128.6, 126.3, 125.7, 121.8, 58.1, 55.1, 20.7, 17.7. MS (EI) *m/z* 192 (M⁺, 100%), 163 (18), 149 (20), 133 (53), 121 (48), 105 (16), 77 (8). Anal. Calcd for C₁₁H₁₂O₃: C, 68.74; H, 6.29. Found: C, 68.59, H, 6.14.

General procedure for 4. To a stirred solution of dry CH₂Cl₂ (4 mL), under argon atmosphere, were added VO(acac)₂ (5.2 mg, 0.02 mmol) and **1** (1 mmol); then after 5 min. TBHP (212 μL, 1.2 mmol of 5.5 M decane solution) was added. The mixture was stirred at 40 °C until the complete formation of **2** (TLC analysis). Then, TFA (112 μL, 1.5 mmol) was added and the reaction mixture was stirred for 2–19 h. At the end of the reaction, the solvent was evaporated under reduced pressure and the crude mixture was purified by flash chromatography eluting with petrol–Et₂O = 99:1.

2-Methylbenzofuran (4a).⁷ ¹H NMR (400 MHz, CDCl₃) δ 7.46–7.44 (m, 1H), 7.40–7.38 (m, 1H), 7.20–7.17 (m, 2H), 6.36 (s, 1H), 2.46 (s, 3H). ¹³C NMR (400 MHz, CDCl₃) δ 155.3, 154.7, 128.9, 123.0, 122.4, 120.0, 110.6, 102.5, 14.1. MS (EI) *m/z* 132 (M⁺, 87%), 131 (100), 77 (11), 51 (14), 44 (16).

2-Butylbenzofuran (4b).⁹ ¹H NMR (400 MHz, CDCl₃) δ 7.47–7.44 (m, 1H), 7.40–7.37 (m, 1H), 7.20–7.15 (m, 2H), 6.37 (s, 1H), 2.77 (t, *J* = 7.5 Hz, 2H), 1.75–1.68 (quintet, *J* = 7.5 Hz, 2H), 1.38–1.48 (sx, *J* = 7.5 Hz, 2H), 0.96 (t, *J* = 7.5 Hz, 3H). ¹³C NMR (400 MHz, CDCl₃) δ 159.7, 154.6, 129.0, 123.0, 122.4, 120.1, 110.7, 101.7, 29.8, 28.1, 22.3, 13.8. MS (EI) *m/z* 174 (M⁺, 20%), 131 (100), 121 (18), 107 (36), 91 (14), 77 (18), 57 (16).

2-sec-Butylbenzofuran (4c). Yellow oil. IR (KBr) 2964.8, 2930.4, 1455.3, 1254.1, 1167.6, 750.5 cm⁻¹. ¹H NMR (400 MHz, CDCl₃) δ 7.50–7.48 (m, 1H), 7.43–7.41 (m, 1H), 7.26–7.15 (m, 2H), 6.37 (s, 1H), 2.90–2.83 (sx, *J* = 7.0 Hz, 1H), 1.85–1.78 (m, 1H), 1.70–1.62 (m, 1H), 1.33 (d, *J* = 7.0 Hz, 3H), 0.93 (t, *J* = 7.0 Hz, 3H). ¹³C NMR (100 MHz, CDCl₃) δ 163.7, 154.5, 128.8, 122.9, 122.2, 120.1, 110.7, 100.7,

35.0, 28.2, 18.4, 11.5. MS (EI) m/z 174 (M^+ , 38%), 145 (94), 131 (100), 115 (48), 107 (26), 91 (16), 77 (10), 57 (12). Anal. Calcd for $C_{12}H_{14}O$: C, 82.72; H, 8.10. Found: C, 82.57; H, 8.00.

2-tert-Butylbenzofuran (4d).⁹ 1H NMR (400 MHz, $CDCl_3$) δ 7.50–7.48 (m, 1H), 7.44–7.42 (m, 1H), 7.21–7.17 (m, 2H), 6.35 (s, 1H), 1.38 (s, 9H). MS (EI) m/z 174 (M^+ , 22%), 145 (48), 131 (100), 115 (32), 107 (22), 91 (18), 77 (32), 57 (14).

2-Phenylbenzofuran (4e).⁸ 1H NMR (400 MHz, $CDCl_3$) δ 7.83–7.89 (m, 2H), 7.22–7.59 (m, 7H), 7.02 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.9, 154.9, 130.5, 129.2, 128.8, 128.5, 124.9, 124.2, 122.9, 120.9, 111.2, 101.3. MS (EI) m/z 194 (M^+ , 100%), 165 (48), 139 (10), 115 (12), 77 (11), 63 (50).

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