

Supporting Information
for
Arylglycine-derivative synthesis via oxidative sp^3
C–H functionalization of α -amino esters

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**General methods, characterization data and NMR spectra of all
synthesized compounds**

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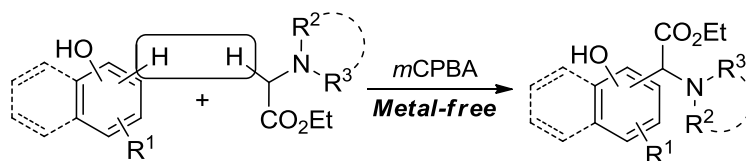
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1. General information

NMR spectra were run in CDCl₃ on a 400 MHz instrument and recorded at the following frequencies: proton (¹H, 400 MHz), carbon (¹³C, 100 MHz).

2. General procedure for the coupling reaction

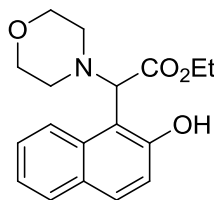
To a solution of ethyl 2-(disubstituted amino)acetate (**2**, 0.6 mmol) in CH₂Cl₂ (3.0 mL), *m*CPBA (0.6 mmol, 121.8 mg, 85% purity) and naphthalenol or phenol (**1**, 0.5 mmol) were added. After the resulting mixture had been stirred under ambient conditions for a period (the reaction progress was monitored by TLC), the solvent was removed under reduced pressure. The residue obtained was purified by silica gel chromatography (eluent: petroleum ether/ethyl acetate = 3:1) to afford arylglycine derivatives **3**.



Scheme S1: Oxidative coupling of naphthalenols or phenols with ethyl 2-(disubstituted amino)acetates.

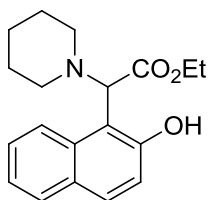
3. Characterization data for all products

Ethyl 2-(2-hydroxynaphthalen-1-yl)-2-morpholinoacetate (**3a**) [1]



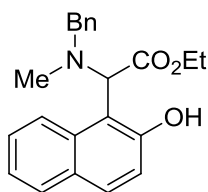
Yield: 79%, 124.5 mg, colorless oil. ¹H NMR (CDCl₃, 400 MHz) δ 1.11–1.13 (m, 3H), 2.64 (br, 4H), 3.78–3.82 (m, 4H), 4.02–4.18 (m, 2H), 4.87 (s, 1H), 7.08 (d, *J* = 8.9 Hz, 1H), 7.29–7.33 (m, 1H), 7.47–7.51 (m, 1H), 7.70–7.75 (m, 2H), 8.03 (d, *J* = 8.6 Hz, 1H), 11.27 (br, 1H); ¹³C NMR (CDCl₃, 100 MHz) δ 14.1, 51.7, 61.6, 66.8, 108.6, 119.5, 121.7, 123.0, 127.1, 128.9, 129.0, 131.0, 132.7, 156.4, 169.3.

Ethyl 2-(2-hydroxynaphthalen-1-yl)-2-(piperidin-1-yl)acetate (3b)



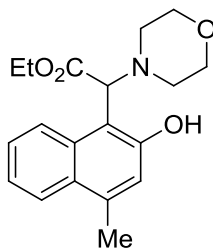
Yield: 64%, 100.3 mg, colorless oil. ^1H NMR (CDCl_3 , 400 MHz) δ 1.11 (t, J = 7.1 Hz, 3H), 1.53–1.71 (m, 6H), 2.60 (br, 4H), 4.04–4.13 (m, 2H), 4.83 (s, 1H), 7.09 (d, J = 8.9 Hz, 1H), 7.30–7.73 (m, 4H), 8.02 (d, J = 8.6 Hz, 1H), 12.03 (br, 1H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 14.1, 24.3, 25.9, 52.5, 61.3, 69.5, 69.6, 109.5, 119.7, 121.7, 122.7, 126.8, 128.7, 128.9, 130.6, 132.7, 157.0, 169.9; IR (neat) 747, 824, 1027, 1117, 1208, 1239, 1301, 1468, 1601, 1623, 1739, 2813, 2855, 2937, 3054 cm^{-1} ; HRMS (ES) calcd for $\text{C}_{19}\text{H}_{23}\text{NO}_3\text{Na}$: 336.1576 $[\text{M} + \text{Na}]^+$; found: 336.1592.

Ethyl 2-(benzyl(methyl)amino)-2-(2-hydroxynaphthalen-1-yl)acetate (3c) [1]



Yield: 64%, 111.8 mg, colorless oil. ^1H NMR (CDCl_3 , 400 MHz) δ 1.13 (t, J = 7.1 Hz, 3H), 2.27 (s, 1H), 3.68 (br, 2H), 4.06–4.18 (m, 2H), 4.99 (s, 1H), 7.14 (d, J = 8.9 Hz, 1H), 7.27–7.37 (m, 6H), 7.49–7.53 (m, 1H), 7.72–7.77 (m, 2H), 8.06 (d, J = 8.6 Hz, 1H), 11.74 (br, 1H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 14.1, 39.3, 59.6, 61.6, 68.7, 109.8, 119.7, 121.8, 122.9, 127.0, 127.9, 128.7, 128.9, 129.0, 129.7, 130.9, 132.6, 136.4, 156.8, 169.9.

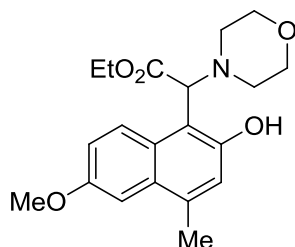
Ethyl 2-(2-hydroxy-4-methylnaphthalen-1-yl)-2-morpholinoacetate (3d)



Yield: 79%, 130.1 mg, colorless oil. ^1H NMR (CDCl_3 , 400 MHz) δ 1.12 (t, J = 7.1 Hz, 3H), 2.62–2.64 (m, 7H), 3.77–3.81 (m, 4H), 4.01–4.15 (m, 2H), 4.85 (s, 1H), 6.96 (s, 1H), 7.35 (dd, J = 7.4, 7.7 Hz, 1H), 7.50 (dd, J = 7.5, 7.8 Hz, 1H), 7.91 (d, J = 7.5 Hz, 1H), 8.04 (d, J = 8.5 Hz, 1H), 11.17 (br, 1H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 14.2, 19.7, 51.7, 61.6, 66.8,

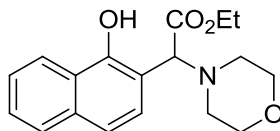
68.9, 106.8, 120.3, 122.2, 122.8, 125.0, 126.8, 128.3, 133.0, 137.7, 155.8, 169.5; IR (neat) 754, 1030, 1118, 1186, 1267, 1390, 1466, 1604, 1616, 1737, 2854, 2966, 3029 cm^{-1} ; HRMS (ES) calcd for $\text{C}_{19}\text{H}_{23}\text{NO}_4\text{Na}$: 352.1525 $[\text{M} + \text{Na}]^+$; found: 352.1520.

Ethyl 2-(2-hydroxy-6-methoxy-4-methylnaphthalen-1-yl)-2-morpholinoacetate (3e)

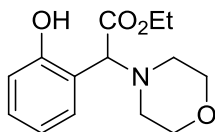


Yield: 75%, 134.8 mg, yellow solid, m.p. 134–136 °C. ^1H NMR (CDCl_3 , 400 MHz) δ 1.12 (t, $J = 7.1$ Hz, 3H), 2.58–2.63 (m, 7H), 3.77–3.84 (m, 4H), 3.92 (s, 1H), 4.03–4.17 (m, 2H), 4.80 (s, 1H), 6.95 (s, 1H), 7.19–7.21 (m, 2H), 7.97 (d, $J = 10.0$ Hz, 1H), 10.92 (br, 1H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 14.2, 19.9, 51.7, 55.6, 61.6, 66.9, 104.5, 107.1, 118.4, 120.8, 123.8, 128.0, 129.3, 136.2, 154.0, 155.5, 169.5; IR (KBr) 732, 1032, 1118, 1152, 1193, 1237, 1267, 1452, 1525, 1607, 1737, 2854, 2963, 3095 cm^{-1} ; HRMS (ES) calcd for $\text{C}_{20}\text{H}_{25}\text{NO}_5\text{Na}$: 382.1630 $[\text{M} + \text{Na}]^+$; found: 382.1624.

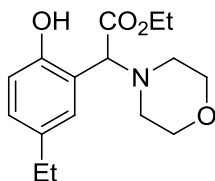
Ethyl 2-(1-hydroxynaphthalen-2-yl)-2-morpholinoacetate (3f)



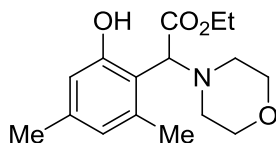
Yield: 66%, 104.1 mg, colorless oil. ^1H NMR (CDCl_3 , 400 MHz) δ 1.18 (t, $J = 7.1$ Hz, 3H), 2.64–2.65 (m, 4H), 3.76–3.86 (m, 4H), 4.07–4.20 (m, 3H), 7.13 (d, $J = 8.4$ Hz, 1H), 7.30 (d, $J = 8.4$ Hz, 1H), 7.43–7.48 (m, 2H), 7.72–7.74 (m, 1H), 8.26–8.29 (m, 1H), 10.83 (br, 1H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 14.2, 51.6, 61.5, 66.8, 69.4, 114.0, 115.7, 115.8, 123.0, 123.1, 137.7, 139.9, 157.6, 169.6; IR (neat) 799, 888, 1029, 1118, 1152, 1199, 1393, 1453, 1578, 1736, 2854, 2915, 2965, 3055 cm^{-1} ; HRMS (ES) calcd for $\text{C}_{18}\text{H}_{21}\text{NO}_4\text{Na}$: 338.1368 $[\text{M} + \text{Na}]^+$; found: 338.1361.

Ethyl 2-(2-hydroxyphenyl)-2-morpholinoacetate (3g)

Yield: 30%, 39.8 mg, colorless oil. ^1H NMR (CDCl_3 , 400 MHz) δ 1.21 (t, J = 7.1 Hz, 3H), 2.60–2.61 (m, 4H), 3.77–3.79 (m, 4H), 4.08 (s, 1H), 4.11–4.23 (m, 2H), 6.79–6.85 (m, 2H), 7.06 (d, J = 7.6 Hz, 1H), 7.19–7.23 (m, 1H), 9.99 (br, 1H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 14.2, 51.2, 61.6, 66.9, 74.0, 117.1, 118.5, 119.8, 129.7, 130.3, 157.1, 169.6; IR (neat) 755, 885, 1029, 1118, 1154, 1192, 1267, 1488, 1587, 1739, 2854, 2963, 3049 cm^{-1} ; HRMS (ES) calcd for $\text{C}_{14}\text{H}_{19}\text{NO}_4\text{Na}$: 288.1212 $[\text{M} + \text{Na}]^+$; found: 288.1219.

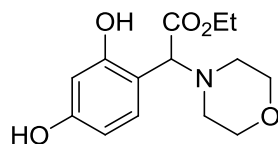
Ethyl 2-(5-ethyl-2-hydroxyphenyl)-2-morpholinoacetate (3h)

Yield: 30%, 44.1 mg, colorless oil. ^1H NMR (CDCl_3 , 400 MHz) δ 1.16–1.23 (m, 6H), 2.51–2.60 (m, 6H), 3.76–3.78 (m, 4H), 4.04 (s, 1H), 4.14–4.20 (m, 2H), 6.76 (d, J = 8.3 Hz, 1H), 6.87 (s, 1H), 7.03 (dd, J = 1.6, 8.2 Hz, 1H), 9.77 (br, 1H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 14.2, 15.9, 28.0, 51.3, 61.5, 66.9, 74.1, 116.8, 118.1, 128.9, 129.5, 135.4, 154.8, 169.7; IR (neat) 830, 889, 1030, 1071, 1212, 1331, 1455, 1501, 1596, 1621, 1739, 2855, 2963, 3171 cm^{-1} ; HRMS (ES) calcd for $\text{C}_{16}\text{H}_{23}\text{NO}_4\text{Na}$: 316.1525 $[\text{M} + \text{Na}]^+$; found: 316.1534.

Ethyl 2-(2-hydroxy-4,6-dimethylphenyl)-2-morpholinoacetate (3i)

Yield: 35%, 51.4 mg, colorless oil. ^1H NMR (CDCl_3 , 400 MHz) δ 1.20 (t, J = 7.1 Hz, 3H), 2.22 (s, 3H), 2.34 (s, 3H), 2.55 (br, 1H), 3.76–3.78 (m, 4H), 4.09–4.18 (m, 2H), 4.28 (s, 1H), 6.49 (s, 1H), 6.52 (s, 1H), 10.37 (br, 1H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 14.2, 51.5, 61.6, 67.0, 74.19, 74.23, 111.1, 119.3, 122.78, 122.82, 125.1, 125.3, 126.9, 127.4, 134.6, 153.4, 169.6; IR (neat) 839, 887, 1031, 1118, 1189, 1257, 1319, 1453, 1578, 1625, 1740, 2855, 2916, 2966, 3130 cm^{-1} ; HRMS (ES) calcd for $\text{C}_{16}\text{H}_{23}\text{NO}_4\text{Na}$: 316.1525 $[\text{M} + \text{Na}]^+$; found: 316.1519.

Ethyl 2-(2,4-dihydroxyphenyl)-2-morpholinoacetate (3j)



Yield: 55%, 77.4 mg, colorless oil. ^1H NMR (CDCl_3 , 400 MHz) δ 1.21 (t, J = 7.1 Hz, 3H), 2.60 (br, 4H), 3.78 (br, 4H), 4.00 (s, 1H), 4.11–4.23 (m, 2H), 6.29–6.34 (m, 2H), 6.89 (d, J = 8.2 Hz, 1H), 7.94 (br, 1H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 14.1, 51.2, 61.7, 66.9, 73.4, 103.9, 107.4, 110.5, 130.7, 158.0, 158.1, 170.1; IR (neat) 733, 886, 977, 1029, 1116, 1175, 1268, 1312, 1454, 1516, 1601, 1627, 1732, 2856, 2917, 2968, 3346 cm^{-1} ; HRMS (ES) calcd for $\text{C}_{14}\text{H}_{19}\text{NO}_5\text{Na}$: 304.1161 $[\text{M} + \text{Na}]^+$; found: 304.1157.

4. Reference

[1] Hwang, D.-R.; Uang, B.-J. *Org. Lett.* **2002**, 4, 463–466.

5. Copies of ^1H and ^{13}C NMR spectra

