Supporting Information

Simple and efficient copper-catalyzed cascade synthesis of naphthols containing multifunctional groups under mild conditions

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General experimental procedures

All reactions were carried out under nitrogen atmosphere. Proton magnetic resonance spectra (1H NMR) were recorded using tetramethylsilane (TMS) (at 0.00 ppm) in the solvent, remaining CHCl₃ in CDCl₃ (at 7.26 ppm) or remaining DMSO in DMSO-d₆ (at 2.50 ppm) as the internal standard. Carbon magnetic resonance spectra (13C NMR) were recorded using CDCl₃ (at 77.2 ppm) or DMSO-d₆ at 39.5 ppm) as the internal standard.

Synthesis of compounds 1a-d: Compounds 1a-d was synthesized according to the known methods.¹,²

General procedure for synthesis of compounds 3a-t. A 10 mL round bottom flask was charged with a magnetic stirrer and dry DMF (2 mL), substituted methyl 3-(2-halophenyl)-3-oxopropanoate or 3-(2-bromo-5-chlorophenyl)-3-oxopropanenitrile (1) (0.5 mmol), β-keto ester, acetylacetone, alkyl 2-cyanoacetate, 3-oxo-3-phenylpropanenitrile or malononitrile (2) (0.6 mmol), Cs₂CO₃ (1 mmol, 326 mg), after stirring of the mixture for 10 min under nitrogen atmosphere, and CuCl (0.05 mmol, 5 mg) was added to the flask. The mixture was stirred at the shown temperature in Table 2 in text for a time under nitrogen atmosphere. The resulting mixture was filtered, the solid was washed with ethyl acetate two times (2 × 3 mL), and the combined filtrate was concentrated by the rotary evaporator, and the residue was purified by column chromatography on silica gel using petroleum ether/ethyl acetate as eluent to give the desired product.

Dimethyl 4-hydroxy-2-methylnaphthalene-1,3-dicarboxylate (3a). Eluent: petroleum ether/ethyl acetate (15:1). Yield 123 mg (90%) using methyl 3-(2-bromophenyl)-3-oxopropanoate as the substrate; 71 mg (52%) using methyl
3-(2-chlorophenyl)-3-oxopropanoate as the substrate. White solid, mp 95-97 °C. $^1$H NMR (CDCl$_3$, 300 MHz) δ 12.79 (s, 1H), 8.41 (d, 1H, $J = 8.3$ Hz), 7.65-7.53 (m, 2H), 7.52-7.45 (m, 1H), 4.01 (s, 3H), 4.00 (s, 3H), 2.57 (s, 3H). $^{13}$C NMR (CDCl$_3$, 75 MHz) δ 172.9, 170.6, 163.0, 132.7, 132.6, 130.7, 125.8, 124.4, 124.1, 123.5, 106.1, 52.6, 52.5, 21.2. HR-MS [M-H]$^-$ m/z Calcd for C$_{15}$H$_{13}$O$_5$: 273.0763. Found: 273.0755.

![3b](image)

1-Ethyl 3-methyl 4-hydroxy-2-methyl naphthalene-1,3-dicarboxylate (3b). Eluent: petroleum ether/ethyl acetate (15:1). Yield 95 mg (66%). White solid, mp 86-88 °C. $^1$H NMR (CDCl$_3$, 300 MHz) δ 12.77 (s, 1H), 8.40 (d, 1H, $J = 8.3$ Hz), 7.64-7.59 (m, 2H), 7.52-7.44 (m, 1H), 4.50 (q, 2H, $J = 7.2$ Hz), 4.00 (s, 3H), 2.58 (s, 3H), 1.44 (t, 3H, $J = 7.2$ Hz). $^{13}$C NMR (CDCl$_3$, 75 MHz) δ 172.9, 170.1, 162.9, 132.6, 132.5, 130.7, 125.7, 124.8, 124.4, 124.1, 123.5, 106.1, 61.5, 52.6, 21.0, 14.4. HR-MS [M-H]$^-$ m/z Calcd for C$_{16}$H$_{15}$O$_5$: 287.0919. Found: 287.0913.

![3c](image)

1-tert-Butyl 3-methyl 4-hydroxy-2-methyl naphthalene-1,3-dicarboxylate (3c). Eluent: petroleum ether/ethyl acetate (15:1). Yield 119 mg (75%). White solid, mp 161-163 °C. $^1$H NMR (CDCl$_3$, 300 MHz) δ 12.71 (s, 1H), 8.40 (d, 1H, $J = 8.3$ Hz), 7.71-7.58 (m, 2H), 7.52-7.44 (m, 1H), 4.00 (s, 3H), 2.61 (s, 3H), 1.67 (s, 9H). $^{13}$C NMR (CDCl$_3$, 75 MHz) δ 173.0, 169.4, 162.6, 132.6, 131.6, 130.6, 126.1, 125.6, 124.4, 124.0, 123.5, 106.1, 82.4, 52.5, 28.4, 20.7. HR-MS [M-H]$^-$ m/z Calcd for C$_{18}$H$_{19}$O$_5$: 315.1232. Found: 315.1228.

![3d](image)

1-Benzyl 3-methyl 4-hydroxy-2-methyl naphthalene-1,3-dicarboxylate (3d). Eluent:
petroleum ether/ethyl acetate (10:1). Yield 166 mg (95%). White solid, mp 96-97 °C. 

\(^1\)H NMR (CDCl\(_3\), 300 MHz) \(\delta\) 12.78 (s, 1H), 8.39 (d, 1H, \(J = 8.4\) Hz), 7.57-7.34 (m, 8H), 5.47 (s, 2H), 3.98 (s, 3H), 2.53 (s, 3H). \(^1^3\)C NMR (CDCl\(_3\), 75 MHz) \(\delta\) 172.9, 169.9, 163.1, 135.6, 132.7, 132.6, 130.7, 128.8, 128.7, 128.6, 125.7, 124.4, 124.3, 124.1, 123.5, 106.1, 67.4, 52.6, 21.1. HR-MS [M-H] \(m/z\) Calcd for C\(_{21}\)H\(_{17}\)O\(_5\): 349.1076. Found: 349.1076.

1-Ethyl 3-methyl 4-hydroxy-2-propynaphthalene-1,3-dicarboxylate (3e). Eluent: petroleum ether/ethyl acetate (15:1). Yield 107 mg (68%). White solid, mp 57-59 °C. 

\(^1\)H NMR (CDCl\(_3\), 300 MHz) \(\delta\) 12.76 (s, 1H), 8.41 (d, 1H, \(J = 8.6\) Hz), 7.65-7.55 (m, 2H), 7.52-7.44 (m, 1H), 4.51 (q, 2H, \(J = 7.2\) Hz), 4.02 (s, 3H), 2.96 (t, 2H, \(J = 7.9\) Hz), 1.69-1.54 (m, 2H), 1.44 (t, 2H, \(J = 6.9\) Hz), 0.98 (t, 3H, \(J = 7.2\) Hz). \(^1^3\)C NMR (CDCl\(_3\), 75 MHz) \(\delta\) 172.8, 170.1, 163.2, 136.9, 132.6, 130.6, 125.8, 124.7, 124.5, 124.2, 123.7, 105.3, 61.5, 52.7, 36.0, 25.4, 14.8, 14.5. HR-MS [M-H] \(m/z\) Calcd for C\(_{18}\)H\(_{19}\)O\(_5\): 315.1232. Found: 315.1230.

1-Ethyl 3-methyl 4-hydroxy-2-phenynaphthalene-1,3-dicarboxylate (3f). Eluent: petroleum ether/ethyl acetate (15:1). Yield 158 mg (90%). White solid, mp 123-125 °C. 

\(^1\)H NMR (CDCl\(_3\), 300 MHz) \(\delta\) 12.46 (s, 1H), 8.49 (d, 1H, \(J = 8.3\) Hz), 7.80 (d, 1H, \(J = 8.3\) Hz), 7.72-7.63 (m, 1H), 7.62-7.54 (m, 1H), 7.37-7.22 (m, 5H), 3.99 (q, 2H, \(J = 7.2\) Hz), 3.45 (s, 3H), 0.90 (t, 3H, \(J = 7.2\) Hz). \(^1^3\)C NMR (CDCl\(_3\), 75 MHz) \(\delta\) 172.1, 168.9, 162.1, 140.7, 137.2, 132.3, 130.9, 128.9, 127.4, 127.1, 126.5, 125.1, 124.8, 124.4, 124.1, 105.7, 61.3, 52.1, 13.8. HR-MS [M-H] \(m/z\) Calcd for C\(_{21}\)H\(_{17}\)O\(_5\): 349.1076. Found: 349.1075.
Methyl 4-acetyl-1-hydroxy-3-methyl-2-naphthoate (3g). Eluent: petroleum ether/ethyl acetate (10:1). Yield 123 mg (95%). White solid, mp 124-126°C. $^1$H NMR (CDCl$_3$, 300 MHz) $\delta$ 12.74 (s, 1H), 8.43 (d, 1H, $J = 8.3$ Hz), 7.65-7.57 (m, 1H), 7.54-7.44 (m, 2H), 4.02 (s, 3H), 2.59 (s, 3H), 2.53 (s, 3H). $^{13}$C NMR (CDCl$_3$, 75 MHz) $\delta$ 208.4, 173.0, 162.6, 132.3, 131.7, 130.7, 129.5, 125.7, 124.7, 123.7, 123.6, 106.1, 52.6, 33.7, 20.6. HR-MS [M-H]$^-$ m/z Calcd for C$_{15}$H$_{13}$O$_4$: 257.0814. Found: 257.0808.

Dimethyl 2-amino-4-hydroxynaphthalene-1,3-dicarboxylate (3h). Eluent: petroleum ether/ethyl acetate (4:1). Yield 84 mg (61%). Yellow solid, mp 129-131°C. $^1$H NMR (CDCl$_3$, 300 MHz) $\delta$ 13.27 (s, 1H), 8.30-8.21 (m, 2H), 7.77 (s, 2H), 7.54-7.47 (m, 1H), 7.23-7.15 (m, 1H), 4.08 (s, 3H), 3.96 (s, 3H). $^{13}$C NMR (CDCl$_3$, 75 MHz) $\delta$ 171.9, 170.3, 167.5, 151.0, 136.8, 131.6, 124.8, 124.7, 122.0, 119.0, 96.5, 96.3, 53.1, 51.4. HR-MS [M-H]$^-$ m/z Calcd for C$_{14}$H$_{12}$NO$_5$: 274.0716. Found: 274.0718.

1-Ethyl 3-methyl 2-amino-4-hydroxynaphthalene-1,3-dicarboxylate (3i). Eluent: petroleum ether/ethyl acetate (4:1). Yield 151 mg (66%). Yellow solid, mp 69-70°C. $^1$H NMR (CDCl$_3$, 300 MHz) $\delta$ 13.21 (s, 1H), 8.30-8.20 (m, 2H), 7.67 (s, 2H), 7.52-7.43 (m, 1H), 7.20-7.12 (m, 1H), 4.44 (q, 2H, $J = 7.2$ Hz), 4.00 (s, 3H), 1.44 (t, 3H, $J = 7.2$ Hz). $^{13}$C NMR (CDCl$_3$, 75 MHz) $\delta$ 171.9, 169.8, 167.3, 150.8, 136.8, 131.5, 124.7, 124.6, 121.9, 118.9, 96.8, 96.3, 60.5, 53.0, 14.6. HR-MS [M-H]$^-$ m/z Calcd for C$_{15}$H$_{14}$NO$_5$: 288.0872. Found: 288.0876.
1-Butyl 3-methyl 2-amino-4-hydroxynaphthalene-1,3-dicarboxylate (3j). Eluent: petroleum ether/ethyl acetate (4:1). Yield 102 mg (64%) using methyl 3-(2-bromophenyl)-3-oxopropanoate as the substrate; 92 mg (58%) using methyl 3-(2-chlorophenyl)-3-oxopropanoate as the substrate. Yellow solid, mp 58-61 °C. $^1$H NMR (CDCl$_3$, 300 MHz) δ 13.25 (s, 1H), 8.31-8.23 (m, 2H), 7.71 (s, 2H), 7.53-7.46 (m, 1H), 7.22-7.15 (m, 1H), 4.39 (t, 2H, $J$ = 6.9 Hz), 4.08 (s, 3H), 1.86-1.74 (m, 2H), 1.58-1.43 (m, 2H), 0.99 (t, 3H, $J$ = 7.2 Hz). $^{13}$C NMR (CDCl$_3$, 75 MHz) δ 172.0, 170.0, 168.4, 150.8, 136.9, 131.5, 124.8, 124.7, 122.0, 119.0, 96.9, 96.3, 64.6, 53.1, 31.0, 19.7, 13.9. HR-MS [M-H] m/z Calcd for C$_{17}$H$_{18}$NO$_5$: 316.1185. Found: 316.1178.

Methyl 4-cyano-1-hydroxy-3-phenyl-2-naphthoate (3k). Eluent: petroleum ether/ethyl acetate (10:1). Yield 96 mg (63%) using methyl 3-(2-bromophenyl)-3-oxopropanoate as the substrate; 62 mg (41%) using methyl 3-(2-chlorophenyl)-3-oxopropanoate as the substrate. White solid, mp 153-154 °C. $^1$H NMR (CDCl$_3$, 600 MHz) δ 8.51 (d, 1H, $J$ = 6.9 Hz), 8.20 (d, 1H, $J$ = 6.9 Hz), 7.83 (s, 1H), 7.67 (s, 1H), 7.52-7.39 (m, 3H), 7.36-7.28 (m, 2H), 3.49 (s, 3H). $^{13}$C NMR (CDCl$_3$, 150 MHz) δ 171.4, 164.6, 147.4, 139.7, 134.5, 132.3, 128.4, 128.3, 128.0, 127.4, 125.4, 124.7, 124.0, 117.0, 106.4, 103.4, 52.5. HR-MS [M-H] m/z Calcd for C$_{19}$H$_{12}$NO$_3$: 302.0817. Found: 302.0809.

Methyl 3-amino-4-cyano-1-hydroxy-2-naphthoate (3l). Eluent: petroleum
ether/ethyl acetate (4:1). Yield 101 mg (83%). Light yellow solid, mp 198-200°C. $^1$H NMR (CDCl$_3$, 300 MHz) δ 13.20 (s, 1H), 8.21 (d, 1H, $J = 8.3$ Hz), 7.74 (d, 1H, $J = 8.3$ Hz), 7.65-7.56 (m, 1H), 7.32-7.21 (m, 1H), 6.12 (s, 2H), 4.09 (s, 3H). $^{13}$C NMR (CDCl$_3$, 75 MHz) δ 171.2, 167.7, 150.9, 136.4, 132.8, 125.1, 123.3, 122.8, 118.7, 117.9, 96.0, 80.6, 53.4. HR-MS [M-H] m/z Calcd for C$_{13}$H$_9$N$_2$O$_3$: 241.0613. Found: 241.0610.

![3m](image)

**Dimethyl 6-chloro-4-hydroxy-2-methyl-naphthalene-1,3-dicarboxylate (3m).**
Eluent: petroleum ether/ethyl acetate (10:1). Yield 130 mg (84%). White solid, mp 117-119°C. $^1$H NMR (CDCl$_3$, 300 MHz) δ 12.72 (s, 1H), 8.36 (s, 1H), 7.56-7.50 (m, 2H), 4.01 (s, 3H), 4.00 (s, 3H), 2.55 (s, 3H). $^{13}$C NMR (CDCl$_3$, 75 MHz) δ 172.6, 170.1, 161.9, 133.3, 131.9, 131.3, 130.8, 125.9, 124.3, 123.6, 107.1, 52.8, 52.6, 21.2. HR-MS [M-H] m/z Calcd for C$_{15}$H$_{12}$ClO$_5$: 307.0373. Found: 307.0373.

![3n](image)

**1-tert-butyl 3-methyl 6-chloro-4-hydroxy-2-methyl-naphthalene-1,3-dicarboxylate (3n).**
Eluent: petroleum ether/ethyl acetate (10:1). Yield 119 mg (68%). White solid, mp 126-128°C. $^1$H NMR (CDCl$_3$, 300 MHz) δ 12.65 (s, 1H), 8.36 (s, 1H), 7.65-7.50 (m, 2H), 4.01 (s, 3H), 2.60 (s, 3H), 1.67 (s, 9H). $^{13}$C NMR (CDCl$_3$, 75 MHz) δ 172.7, 168.9, 161.5, 132.1, 131.7, 130.8, 125.9, 125.8, 124.3, 123.5, 107.0, 82.7, 52.7, 28.4, 20.7. HR-MS [M-H] m/z Calcd for C$_{18}$H$_{18}$ClO$_5$: 349.0843. Found: 349.0847.

![3o](image)

**1-Ethyl 3-methyl 6-chloro-4-hydroxy-2-propyl-naphthalene-1,3-dicarboxylate (3o).**
Eluent: petroleum ether/ethyl acetate (10:1). Yield 130 mg (74%). White solid,
Methyl 7-chloro-4-cyano-1-hydroxy-3-phenyl-2-naphthoate (3p). Eluent: petroleum ether/ethyl acetate (8:1). Yield 105 mg (62%). White solid, mp 162 °C (decomposed point). $^1$H NMR (CDCl$_3$, 300 MHz) $\delta$ 12.90 (s, 1H), 8.48 (s, 1H), 8.14 (d, 1H, $J = 8.9$ Hz), 7.81-7.71 (m, 1H), 7.51-7.42 (m, 3H), 7.35-7.28 (m, 2H), 3.50 (s, 3H). $^{13}$C NMR (CDCl$_3$, 75 MHz) $\delta$ 171.2, 163.4, 147.5, 139.3, 133.8, 133.0, 132.8, 128.5, 128.3, 128.1, 127.2, 124.9, 123.9, 116.6, 107.4, 103.3, 52.7. HR-MS [M-H]'- m/z Calcd for C$_{19}$H$_{11}$ClNO$_3$: 336.0428. Found: 336.0429.

Methyl 3-amino-7-chloro-4-cyano-1-hydroxy-2-naphthoate (3q). Eluent: petroleum ether/ethyl acetate (5:1). Yield 94 mg (68%). Yellow solid, mp 231-233 °C. $^1$H NMR (DMSO-$d_6$, 300 MHz) $\delta$ 12.68 (s, 1H), 8.04 (d, 1H, $J = 5.2$ Hz), 7.79-7.49 (m, 2H), 7.00 (s, 2H), 3.99 (s, 3H). $^{13}$C NMR (DMSO-$d_6$, 75 MHz) $\delta$ 169.3, 162.9, 151.6, 134.4, 132.5, 127.1, 124.0, 123.1, 118.5, 117.1, 98.7, 78.4, 53.4. HR-MS [M-H]'- m/z Calcd for C$_{13}$H$_8$ClN$_2$O$_3$: 275.0223. Found: 275.0221.

tert-Butyl 6-chloro-3-cyano-4-hydroxy-2-methyl-1-naphthoate (3r). Eluent: ethyl
acetate and then washed with ethyl ether. Yield 92 mg (58%). White solid, dp 193°C (decomposed point). \(^1\)H NMR (CDCl\(_3\), 300 MHz) \(\delta\) 8.20 (d, 1H, \(J = 2.1\) Hz), 7.74 (d, 1H, \(J = 9.3\) Hz), 7.59 (dd, 1H, \(J = 2.1\) Hz, \(J = 9.3\) Hz), 6.87 (s, 1H), 2.59 (s, 3H), 1.68 (s, 9H). \(^{13}\)C NMR (CDCl\(_3\), 75 MHz) \(\delta\) 167.5, 157.2, 132.7, 132.6, 131.5, 131.0, 126.4, 126.1, 122.9, 122.3, 115.4, 96.0, 83.7, 28.4, 18.9. HR-MS [M-H] \(m/z\) Calcd for C\(_{17}\)H\(_{15}\)ClNO\(_3\): 316.0740. Found: 316.0739.

Methyl 6-chloro-3-cyano-4-hydroxy-2-propyl-1-naphthoate (3s). Eluent: ethyl acetate and then washed with ethyl ether. Yield 87 mg (55%). White solid, mp 100-102°C. \(^1\)H NMR (DMSO-\(d_6\), 300 MHz) \(\delta\) 8.41 (s, 1H), 7.82-7.69 (m, 2H), 4.45 (q, 2H, \(J = 6.9\) Hz), 2.81-2.71 (m, 2H), 1.74-1.57 (m, 2H), 1.36 (t, 3H, \(J = 6.9\) Hz), 0.97 (t, 3H, \(J = 7.2\) Hz). \(^{13}\)C NMR (DMSO-\(d_6\), 150 MHz) \(\delta\) 167.5, 160.2, 138.9, 130.9, 130.6, 127.1, 124.1, 122.2, 116.1, 96.2, 61.5, 34.6, 23.7, 14.0, 13.9. HR-MS [M-H] \(m/z\) Calcd for C\(_{17}\)H\(_{15}\)ClNO\(_3\): 316.0740. Found: 316.0742.

2-Amino-6-chloro-4-hydroxynaphthalene-1,3-dicarbonitrile (3t). Eluent: ethyl acetate/methanol (20:1) and then recrystallization from ethyl acetate/hexane. Yield 94 mg (77%). White solid, mp >300°C. \(^1\)H NMR (DMSO-\(d_6\), 300 MHz) \(\delta\) 7.95 (s, 1H), 7.48-7.29 (m, 2H), 5.62 (s, 1H). \(^{13}\)C NMR (DMSO-\(d_6\), 75 MHz) \(\delta\) 174.5, 156.0, 135.4, 130.2, 126.8, 125.2, 124.9, 124.7, 120.1, 120.0, 82.0, 68.1. HR-MS [M-H] \(m/z\) Calcd for C\(_{12}\)H\(_{5}\)ClN\(_3\)O: 242.0121. Found: 242.0118.
References


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