Fe-Catalyzed Esterification of Amides via C-N Bond Activation

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A. General information

All manipulations were carried out under air atmosphere unless otherwise specified. The reactions were monitored by GC (7820A, Hubei University of Science and Technology) and GC-MS (QP2010, Hunan University). The $^1$H NMR and $^{13}$C NMR spectra were recorded on a Brucker ADVANCE III spectrometer at 400 MHz and 100 MHz, respectively (Hubei University of Science and Technology). Flash column chromatography was performed using silica gel 40-70 μm (200-300 μm). Amides were purchased from Energy Chemical, Alfa Aesar, Aladdin or Maya Reagent, alcohols or esters were purchased from Energy Chemical.

B. General information

A 25 mL Schlenk-type tube equipped with a magnetic stir bar was charged with FeCl$_3$.6H$_2$O (0.04 mmol, 20 mol%), then amide 2 (0.24 mmol), alcohol or ester (0.24 mmol), HCl (0.24 mmol, 36%-38%), n-hexane (1.0 mL), was added at room temperature, and then the reaction mixture was stirred at 80 ºC for 14 h. The reaction was monitored by GC. After completion of the reaction, the resulting solution was neutralized with saturated NaCl solution. The product was extracted with EtOAc or CHCl$_3$, dried over anhydrous Na$_2$SO$_4$ and concentrated in vacuo. The crude product was purified by flash column chromatography on silica gel to give analytically pure product.

C. $^1$H NMR and $^{13}$C NMR data of products

Ethyl benzoate (3a)$^\dagger$: eluent: petroleum ether; colorless oil; yield: 85%. $^1$H NMR (400 MHz, CDCl$_3$) δ: 8.05 (d, $J$ = 8.0 Hz, 2H), 7.54 (t, $J$ = 7.4 Hz, 1H), 7.43 (t, $J$ = 7.6 Hz, 2H), 4.37 (q, $J$ = 7.2 Hz, 2H), 1.39 (t, $J$ = 7.2 Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ: 166.6, 132.8, 130.5, 129.5, 128.3, 60.9, 14.3; GC-MS: m/z = 150.

Propyl benzoate (3b)$^\dagger$: eluent: petroleum ether; colorless oil; yield: 88%. $^1$H NMR (400 MHz, CDCl$_3$) δ: 8.05 (d, $J$ = 7.2 Hz, 2H), 7.55 (t, $J$ = 7.4 Hz, 1H), 7.44 (t, $J$ = 7.2 Hz, 2H),
4.28 (t, $J = 6.6$ Hz, 2H), 1.75-1.84 (m, 2H), 1.03 (t, $J = 7.4$ Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$: 166.7, 132.8, 130.5, 129.5, 128.3, 66.5, 22.1, 10.5; GC-MS: m/z = 164.

Octyl benzoate (3c): eluent: petroleum ether; colorless oil; yield: 82%. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$: 8.05 (d, $J = 7.2$ Hz, 2H), 7.55 (t, $J = 7.4$ Hz, 1H), 7.44 (t, $J = 7.0$ Hz, 2H), 4.32 (t, $J = 6.8$ Hz, 2H), 1.73-1.80 (m, 2H), 1.41-1.46 (m, 2H), 1.28-1.34 (m, 8H), 0.89 (t, $J = 7.2$ Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$: 166.7, 132.8, 130.5, 129.5, 128.3, 65.1, 31.8, 29.23, 29.17, 28.7, 26.0, 22.6, 14.1; GC-MS: m/z = 234.

Isopropyl benzoate (3d): eluent: petroleum ether; colorless oil; yield: 91%. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$: 8.04 (d, $J = 7.6$ Hz, 2H), 7.53 (t, $J = 7.4$ Hz, 1H), 7.42 (t, $J = 7.8$ Hz, 2H), 5.21-5.30 (m, 1H), 1.36 (d, $J = 6.4$ Hz, 6H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$: 166.1, 132.7, 130.9, 129.5, 128.3, 68.3, 21.9; GC-MS: m/z = 164.

tert-Butyl benzoate (3e): eluent: petroleum ether; colorless oil; yield: 81%. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$: 8.00 (d, $J = 8.8$ Hz, 2H), 7.52 (t, $J = 6.6$ Hz, 1H), 7.42 (t, $J = 7.0$ Hz, 2H), 1.60 (s, 9H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$: 165.7, 132.4, 132.0, 129.3, 128.1, 80.9, 28.1; GC-MS: m/z = 178.

Cyclohexyl benzoate (3f): eluent: petroleum ether; colorless oil; yield: 80%. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$: 8.04 (d, $J = 7.2$ Hz, 2H), 7.51 (t, $J = 7.4$ Hz, 1H), 7.40 (t, $J = 7.8$ Hz, 2H), 5.00-5.06 (m, 1H), 1.92-1.94 (m, 2H), 1.76-1.79 (m, 2H), 1.54-1.59 (m, 3H), 1.34-1.44 (m, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$: 165.9, 132.6, 131.0, 129.5, 128.2, 72.9, 31.6, 25.5, 23.7; GC-MS: m/z = 204.

Phenethyl benzoate (3g): eluent: petroleum ether/ethyl acetate (200: 1); colorless oil; yield: 83%. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$: 8.01 (d, $J = 7.6$ Hz, 2H), 7.54 (t, $J = 7.4$ Hz, 1H), 7.42 (t, $J = 7.8$ Hz, 2H), 7.22-7.34 (m, 5H), 4.53 (t, $J = 7.0$ Hz, 2H), 3.08 (t, $J = 7.0$ Hz, 2H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$: 166.6, 137.9, 132.9, 130.3, 129.6, 129.0, 128.6, 128.4, 126.6, 65.5, 35.3; GC-MS: m/z = 226.

3-Phenylpropyl benzoate (3h): eluent: petroleum ether; colorless oil;
yield: 81%. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$: 8.03 (d, $J$ = 7.6 Hz, 2H), 7.55 (t, $J$ = 7.2 Hz, 1H), 7.43 (t, $J$ = 7.8 Hz, 2H), 7.29 (t, $J$ = 7.4 Hz, 2H), 7.17-7.22 (m, 3H), 4.34 (t, $J$ = 6.6 Hz, 2H), 2.79 (t, $J$ = 7.6 Hz, 2H), 2.07-2.14 (m, 2H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$: 166.6, 141.2, 132.9, 130.4, 129.6, 128.52, 128.49, 128.39, 126.1, 64.3, 32.4, 30.3; GC-MS: m/z =240.

2,2,2-Trifluoroethyl benzoate (3i)$^5$: eluent: petroleum ether/ethylacetate (30: 1); yield: 81%. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$: 8.07 (t, $J$ = 6.2 Hz, 2H), 7.56-7.63 (m, 1H), 7.43-7.49 (m, 2H), 4.71 (q, $J$ = 8.4 Hz, 2H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$: 164.9, 133.9 (d, $J_{F-C}$ = 62 Hz), 130.0, 129.8 (q, $J_{F-C}$ = 69 Hz), 128.6, 127.3 (q, $J_{F-C}$ = 275 Hz), 61.3 (q, $J_{F-C}$ = 37 Hz); GC-MS: m/z =204.

2-Hydroxyethyl benzoate (3j)$^6$: eluent: petroleum ether/ethylacetate (10: 1); colorless oil; yield: 85%. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$: 8.07 (d, $J$ = 8.0 Hz, 2H), 7.57 (t, $J$ = 7.4 Hz, 1H), 7.45 (t, $J$ = 7.6 Hz, 2H), 4.57 (t, $J$ = 5.6 Hz, 2H), 3.81 (t, $J$ = 5.6 Hz, 2H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$: 166.2, 133.3, 129.8, 129.6, 128.5, 64.5, 41.7; GC-MS: m/z =166.

Ethyl 4-methylbenzoate (3k)$^7$: eluent: petroleum ether/ethylacetate (50:1); Colorless oil; yield: 86%. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$: 7.94 (d, $J$ = 8.0 Hz, 2H), 7.23 (d, $J$ = 8.0 Hz, 2H), 4.37 (q, $J$ = 7.2 Hz, 2H), 2.40 (s, 3H), 1.38 (t, $J$ = 7.2 Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$: 166.7, 143.4, 129.6, 129.0, 127.8, 60.8, 21.6, 14.4; GC-MS: m/z =164.

Ethyl 4-methoxybenzoate (3l)$^7$: eluent: petroleum ether/ethylacetate (50:1); colorless oil; yield: 85%. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$: 7.98 (d, $J$ = 8.4 Hz, 2H), 6.89 (d, $J$ = 8.0 Hz, 2H), 4.34 (q, $J$ = 7.0 Hz, 2H), 3.84 (s, 3H), 1.37 (t, $J$ = 7.0 Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$: 166.4, 163.3, 131.5, 123.0, 113.5, 60.6, 55.4, 14.4; GC-MS: m/z =180.

Ethyl 4-hydroxybenzoate (3m)$^7$: eluent: petroleum ether/ethylacetate (10:1); colorless oil; yield: 78%. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$: 7.96 (d, $J$ = 8.4 Hz, 2H), 7.40 (s, 1H), 6.91 (d, $J$ = 8.4 Hz, 2H), 4.37 (q, $J$ = 7.2 Hz, 2H), 1.38 (t, $J$ = 7.2 Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$: 167.5, 160.8, 132.0, 122.1, 115.4, 61.2, 14.3; GC-MS: m/z =166.
Ethyl 4-aminobenzoate (3n): eluent: petroleum ether/ethyl acetate (10:1); colorless oil; yield: 75%. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\): 7.86 (d, \(J = 8.0\) Hz, 2H), 6.63 (d, \(J = 8.4\) Hz, 2H), 4.32 (q, \(J = 7.0\) Hz, 2H), 4.09 (s, 2H), 1.35 (t, \(J = 7.2\) Hz, 3H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\): 166.8, 151.0, 131.6, 119.9, 113.8, 60.4, 14.4; GC-MS: m/z = 165.

Ethyl 4-chlorobenzoate (3o): eluent: petroleum ether/ethyl acetate (100:1); colorless oil; yield: 86%. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\): 7.97 (d, \(J = 8.8\) Hz, 2H), 7.40 (d, \(J = 8.4\) Hz, 2H), 4.38 (q, \(J = 7.2\) Hz, 2H), 1.39 (t, \(J = 7.2\) Hz, 3H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\): 165.7, 139.2, 130.9, 128.9, 128.6, 61.2, 14.3; GC-MS: m/z = 184.

Ethyl 4-bromobenzoate (3p): eluent: petroleum ether/ethyl acetate (100:1); colorless oil, yield: 84%. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\): 7.89 (d, \(J = 8.4\) Hz, 2H), 7.56 (d, \(J = 8.4\) Hz, 2H), 4.37 (q, \(J = 7.2\) Hz, 2H), 1.38 (t, \(J = 7.2\) Hz, 3H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\): 165.9, 131.7, 131.1, 129.4, 127.9, 61.2, 14.3; GC-MS: m/z = 227.

Ethyl 4-nitrobenzoate (3q): eluent: petroleum ether; mp: 56.3-57.1°C, white solid; yield: 90%. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\): 8.25 (d, \(J = 8.4\) Hz, 2H), 8.18 (d, \(J = 8.8\) Hz, 2H), 4.42 (q, \(J = 7.2\) Hz, 2H), 1.40 (t, \(J = 7.2\) Hz, 3H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\): 164.7, 150.5, 135.8, 130.6, 123.5, 61.9, 14.2; GC-MS: m/z = 195.

Ethyl 2-naphthoate (3r): eluent: petroleum ether; colorless oil; yield: 86%. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\): 8.62 (s, 1H), 8.08 (d, \(J = 8.8\) Hz, 1H), 7.95 (d, \(J = 8.0\) Hz, 1H), 7.87 (d, \(J = 8.4\) Hz, 2H), 7.52-7.60 (m, 2H), 4.46 (q, \(J = 7.2\) Hz, 2H), 1.46 (t, \(J = 7.2\) Hz, 3H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\): 166.8, 135.5, 132.5, 131.0, 129.4, 128.17, 128.10, 127.8, 126.6, 125.2, 61.1, 14.4; GC-MS: m/z = 200.

Ethyl thiophene-2-carboxylate (3s): eluent: petroleum ether; colorless oil; yield: 84%. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\): 7.79 (d, \(J = 4.0\) Hz, 1H), 7.53 (d, \(J = 4.8\) Hz, 1H), 7.09 (t, \(J = 4.4\) Hz, 1H), 4.36 (q, \(J = 7.0\) Hz, 2H), 1.37 (t, \(J = 7.2\) Hz, 3H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\): 162.3, 134.1, 133.3, 132.2, 127.7, 61.1, 14.3; GC-MS: m/z = 156.
Ethyl 2-(1H-indol-3-yl)acetate (3t): eluent: petroleum ether; colorless oil; yield: 55%. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\): 8.14 (s, 1H), 7.60 (d, \(J = 8.0 \text{ Hz}, 1H\)), 7.23 (d, \(J = 8.0 \text{ Hz}, 1H\)), 7.09-7.20 (m, 2H), 6.98 (d, \(J = 2.0 \text{ Hz}, 1H\)), 4.14 (q, \(J = 7.0 \text{ Hz}, 2H\)), 3.74 (s, 1H), 1.23 (t, \(J = 7.0 \text{ Hz}, 3H\)); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\): 172.3, 136.2, 127.3, 123.3, 122.1, 119.6, 118.9, 111.4, 108.3, 60.9, 31.5, 14.3; GC-MS: m/z =203.

Ethyl cinnamate (3u): eluent: petroleum ether; colorless oil; yield: 84%. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\): 7.70 (d, \(J = 16.0 \text{ Hz}, 1H\)), 7.52-7.54 (m, 2H), 7.38-7.39 (m, 3H), 6.43 (d, \(J = 16.0 \text{ Hz}, 1H\)), 4.26 (q, \(J = 7.0 \text{ Hz}, 2H\)), 1.34 (t, \(J = 7.0 \text{ Hz}, 3H\)); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\): 167.0, 144.6, 134.5, 130.2, 128.9, 128.1, 118.3, 60.5, 14.3; GC-MS: m/z =176.

Ethyl 3-methylbenzoate (3v): eluent: petroleum ether; colorless oil; yield: 85%. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\): 7.86 (s, 1H), 7.83 (s, 1H), 7.30-7.35 (m, 2H), 4.38 (q, \(J = 7.0 \text{ Hz}, 2H\)), 2.40 (s, 3H), 1.39 (t, \(J = 7.0 \text{ Hz}, 3H\)); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\): 166.8, 138.1, 133.6, 130.4, 130.1, 128.2, 126.7, 60.9, 21.3, 14.4; GC-MS: m/z =164.

Ethyl 2-methylbenzoate (3w): eluent: petroleum ether; colorless oil; yield: 81%. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\): 7.90 (d, \(J = 8.4 \text{ Hz}, 1H\)), 7.38 (t, \(J = 7.4 \text{ Hz}, 1H\)), 7.22-7.25 (m, 2H), 4.36 (q, \(J = 7.2 \text{ Hz}, 2H\)), 2.60 (s, 3H), 1.39 (t, \(J = 7.2 \text{ Hz}, 3H\)); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\): 167.7, 140.0, 131.8, 131.6, 130.5, 130.0, 125.7, 60.7, 21.7, 14.3; GC-MS: m/z =164.

Benzyl benzoate (3x): eluent: petroleum ether; colorless oil; yield: 78%. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\): 8.08 (d, \(J = 8.0 \text{ Hz}, 2H\)), 7.56 (t, \(J = 7.2 \text{ Hz}, 1H\)), 7.33-7.46 (m, 7H), 5.37 (s, 2H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\): 166.4, 136.1, 133.0, 130.1, 129.7, 128.6, 128.4, 128.2, 128.15, 66.7; GC-MS: m/z =212.

Ethyl 2-phenylacetate (3y): eluent: petroleum ether; colorless oil; yield: 86%. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\): 7.24-7.34 (m, 5H), 4.15 (q, \(J = 7.0 \text{ Hz}, 2H\)), 3.60 (s, 3H), 1.24 (t, \(J =
7.2 Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$: 171.6, 134.2, 129.3, 128.6, 127.1, 60.9, 41.5, 14.2; GC-MS: m/z = 164.

![Butyl acetate (3x)]: eluent: petroleum ether; colorless oil; yield: 79%. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$: 4.03 (t, $J$ = 6.6 Hz, 2H), 2.00 (s, 3H), 1.54-1.61 (m, 2H), 1.30-1.39 (m, 2H), 0.90 (t, $J$ = 7.4 Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$: 171.1, 64.3, 30.6, 20.9, 19.1, 13.6. GC-MS: m/z = 116.

![Benzyl formate (3z)]: eluent: petroleum ether; colorless oil; yield: 82%. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$: 8.15 (s, 1H), 7.35-7.39 (m, 5H), 5.21 (s, 2H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$: 160.8, 135.3, 128.7, 128.5, 128.4, 65.7; GC-MS: m/z = 136.

D. References