A Rapid Method to Aromatic Aminoalkyl Esters via the Catalyst-Free Difunctionalization of C-N Bond

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1. General Information

Instruments: NMR spectra were recorded on BRUKER DRX 400 or Bruker Avance-500 spectrometers. Chemical shifts are reported in parts per million (ppm) down field from TMS with the solvent resonance as the internal standard. Coupling constants (J) are reported in Hz and refer to apparent peak multiplications. High resolution mass spectra (HRMS) were recorded on Agilent 6210-TOF or Bruker Daltonics Apex II mass instrument (ESI). Melting points were determined using a Metter FP5 melting apparatus in open capillaries and were uncorrected.

Materials: unless otherwise noted, commercial reagents were purchased from Aldrich, Alfa Aesar, and other commercial suppliers and were used as received.

2. The Procedure for synthesis of aromatic aminoalkyl esters.

General procedure A: carboxylic acids 1 (2 mmol), cyclic tertiary amine 2 (2 mmol) and aryl halide 3 (1 mmol), Cs2CO3 (1 mmol) and DMF (2 mL) were added to a 25 mL reaction vessel under argon atmosphere. The reaction mixture was stirred at 140 °C for 12 h, and then cooled to room temperature. The mixture was poured into water and extracted with ethyl acetate for three times. The organic layer was dried over anhydrous Na2SO4. The obtained organic solutions were concentrated and then purified by flash column chromatography on silica gel using a mixed solution of ethyl acetate and petro ether as eluting solvent (1/100–1/1) to afford the desired product.

General procedure B: anhydride 5 (2 mmol), cyclic tertiary amine 2 (2 mmol) and aryl halide 3 (1 mmol), Cs2CO3 (1 mmol) and DMF (2 mL) were added to a 25 mL reaction vessel under argon atmosphere. The reaction mixture was stirred at 140 °C for 12 h, and then cooled to room
temperature. The mixture was poured into water and extracted with ethyl acetate for three times. The organic layer was dried over anhydrous Na$_2$SO$_4$. The obtained organic solutions were concentrated and then purified by flash column chromatography on silica gel using a mixed solution of ethyl acetate and petro ether as eluting solvent (1/100–1/1) to afford the desired product.

**General procedure C:** carboxylic acids 1 or anhydride 5 (2 mmol), cyclic tertiary amine 6 (2 mmol) and aryl halide 3 (1 mmol), Cs$_2$CO$_3$ (1 mmol) and DMF (2 mL) were added to a 25 mL reaction vessel under argon atmosphere. The reaction mixture was stirred at 100°C for 24 h, and then cooled to room temperature. The mixture was poured into water and extracted with ethyl acetate for three times. The organic layer was dried over anhydrous Na$_2$SO$_4$. The obtained organic solutions were concentrated and then purified by flash column chromatography on silica gel using a mixed solution of ethyl acetate and petro ether as eluting solvent (1/100–1/1) to afford the desired product.

3. Experimental characterization data for products

**2-(4-(Pyridin-2-yl)piperazin-1-yl)ethyl acetate:** The title compound was prepared according to the general procedure A and purified by flash column chromatography to give 229 mg colorless oil, 92 % yield. $^1$H NMR (400 MHz, CDCl$_3$) δ 8.15-8.13 (m, 1H), 7.45-7.40 (m, 1H), 6.61-6.56 (m, 2H), 4.21-4.18 (m, 2H), 3.52-3.49 (m, 4H), 2.65-2.62 (m, 2H), 2.59-2.56 (m, 4H), 2.03 (s, 3H); $^{13}$C NMR (101 MHz, CDCl$_3$) δ 171.0, 159.4, 147.9, 137.5, 113.3, 107.1, 61.7, 56.7, 53.2, 45.1, 21.1. HRMS (ESI) calcd. for C$_{13}$H$_{20}$N$_2$O$_2$ [M+H]: 250.1550, found: 250.1555.

**2-(4-(Pyridin-2-yl)piperazin-1-yl)ethyl propionate:** The title compound was prepared according to the general procedure of three-component reaction and purified by flash column chromatography to give 218 mg colorless oil, 83 % yield. $^1$H NMR (500 MHz, CDCl$_3$) δ 8.11-8.09 (m, 1H), 7.40-7.37 (m, 1H), 6.57-6.52 (m, 2H), 4.17 (t, $J = 6.0$ Hz, 2H), 3.46 (t, $J = 5.0$ Hz, 4H), 2.60 (t, $J = 6.0$ Hz, 2H), 2.54 (t, $J = 5.0$ Hz, 4H), 2.30-2.25 (m, 2H), 1.07 (t, $J = 7.5$ Hz, 3H); $^{13}$C NMR (126 MHz, CDCl$_3$) δ 174.3, 159.4, 147.9, 137.4, 113.3, 107.0, 61.6, 56.7, 53.2, 45.1, 27.5, 9.1. HRMS (ESI) calcd. for C$_{13}$H$_{22}$N$_2$O$_2$ [M+H]: 264.1707, found: 264.1708.

**2-(4-(Pyridin-2-yl)piperazin-1-yl)ethyl butyrate:** The title compound was prepared according to the general procedure A and purified by flash column chromatography to give 238 mg colorless oil, 86 % yield. $^1$H NMR (500 MHz, CDCl$_3$) δ 8.15-8.13 (m, 1H), 7.44-7.41 (m, 1H), 6.61-6.56 (m, 2H), 4.21 (t, $J = 6.0$ Hz, 2H), 3.50 (t, $J = 5.3$ Hz, 4H), 2.64 (t, $J = 6.0$ Hz, 2H), 2.58 (t, $J = 5.0$ Hz, 4H), 2.27 (t, $J = 7.3$ Hz, 2H), 1.64-1.60 (m, 2H), 0.91 (t, $J = 7.5$ Hz, 3H); $^{13}$C NMR (126 MHz, CDCl$_3$) δ 173.6, 159.5, 147.9, 137.4, 113.3, 107.0, 61.5, 56.8, 53.2, 45.1, 36.2, 18.4, 13.7. HRMS (ESI) calcd. for C$_{14}$H$_{24}$N$_2$O$_2$ [M+H]: 278.1863, found: 278.1858.

**2-(4-(Pyridin-2-yl)piperazin-1-yl)ethyl pentanoate:** The title compound was prepared according to the general procedure A and purified by flash column chromatography to give 244 mg colorless oil, 84 % yield. $^1$H NMR (500 MHz, CDCl$_3$) δ 8.14-8.12 (m, 1H), 7.43-7.40 (m, 1H), 6.60-6.55 (m, 2H), 4.20 (t, $J = 6.0$ Hz, 2H), 3.49 (t, $J = 5.0$ Hz, 4H), 2.63 (t, $J = 6.0$ Hz, 2H), 2.57 (t, $J = 5.3$ Hz, 4H), 2.28 (t, $J = 7.5$ Hz, 2H), 2.25 (t, $J = 5.5$ Hz, 2H), 2.03 (s, 3H); $^{13}$C NMR (126 MHz, CDCl$_3$) δ 173.6, 159.5, 147.9, 137.4, 113.3, 107.0, 61.5, 56.8, 53.2, 45.1, 36.2, 18.4, 13.7. HRMS (ESI) calcd. for C$_{15}$H$_{26}$N$_2$O$_2$ [M+H]: 292.2020, found: 292.2015.
Hz, 2H), 1.59-1.53 (m, 2H), 1.34-1.27 (m, 2H), 0.86 (t, J = 7.5 Hz, 3H); $^{13}$C NMR (126 MHz, CDCl$_3$) δ 173.7, 159.5, 147.9, 137.4, 113.3, 107.0, 61.5, 56.8, 53.2, 45.1, 34.0, 27.0, 22.2, 13.7. HRMS (ESI) calcd. for C$_{10}$H$_{12}$N$_2$O$_2$ [M+H]: 292.2020, found: 292.2011.

2-(4-(Pyridin-2-yl)piperazin-1-yl)ethyl isobutyrate: The title compound was prepared according to the general procedure A and purified by flash column chromatography to give 211 mg colorless oil, 76 % yield. $^1$H NMR (500 MHz, CDCl$_3$) δ 8.13-8.12 (m, 1H), 7.43-7.39 (m, 1H), 4.19 (t, J = 5.8 Hz, 2H), 3.48 (t, J = 5.0 Hz, 4H), 7.35 (m, 3H), 6.58-6.54 (m, 2H). $^{13}$C NMR (126 MHz, CDCl$_3$) δ 172.9, 159.5, 147.9, 137.4, 113.3, 107.0, 61.6, 56.7, 53.2, 45.2, 33.9, 19.0. HRMS (ESI) calcd. for C$_{13}$H$_{22}$N$_2$O$_2$ [M+H]: 278.1863, found: 278.1860.

2-(4-(Pyridin-2-yl)piperazin-1-yl)ethyl 3-methylbutanoate: The title compound was prepared according to the general procedure A and purified by flash column chromatography to give 247 mg colorless oil, 85 % yield. $^1$H NMR (500 MHz, CDCl$_3$) δ 8.12-8.11 (m, 1H), 7.41-7.38 (m, 1H), 6.58-6.53 (m, 2H). $^{13}$C NMR (101 MHz, CDCl$_3$) δ 127.4, 129.6, 128.4, 113.3, 107.0, 61.4, 56.8, 53.1, 45.1, 43.4, 25.7, 22.4. HRMS (ESI) calcd. for C$_{10}$H$_{16}$N$_2$O$_2$ [M+H]: 292.2020, found: 292.2008.

2-(4-(Pyridin-2-yl)piperazin-1-yl)ethyl benzoate: The title compound was prepared according to the general procedure A and purified by flash column chromatography to give 264 mg colorless solid, 85 % yield. mp 61-62 °C. $^1$H NMR (400 MHz, CDCl$_3$) δ 8.12-8.10 (m, 1H), 7.98-7.96 (m, 2H), 7.51-7.47 (m, 1H), 7.42-7.35 (m, 3H). $^{13}$C NMR (126 MHz, CDCl$_3$) δ 166.5, 159.5, 148.0, 137.5, 133.0, 130.2, 129.6, 128.4, 113.3, 107.1, 62.6, 56.8, 53.3, 45.2. HRMS (ESI) calcd. for C$_{13}$H$_{22}$N$_2$O$_2$ [M+H]: 312.1707, found: 312.1700.

2-(4-(Pyridin-2-yl)piperazin-1-yl)ethyl 4-methylbenzoate: The title compound was prepared according to the general procedure A and purified by flash column chromatography to give 270 mg colorless solid, 83 % yield. mp 67-68 °C. $^1$H NMR (500 MHz, CDCl$_3$) δ 8.18-8.17 (m, 1H), 7.93-7.91 (m, 2H), 7.47-7.43 (m, 1H). $^{13}$C NMR (126 MHz, CDCl$_3$) δ 166.5, 159.5, 147.9, 143.7, 137.5, 129.6, 127.4, 129.1, 113.4, 107.1, 62.3, 56.7, 53.2, 45.2, 21.7. HRMS (ESI) calcd. for C$_{10}$H$_{22}$N$_2$O$_2$ [M+H]: 326.1863, found: 326.1852.

2-(4-(Pyridin-2-yl)piperazin-1-yl)ethyl 4-methoxybenzoate: The title compound was prepared according to the general procedure A and purified by flash column chromatography to give 252 mg colorless solid, 74 % yield. mp 73-74 °C. $^1$H NMR (500 MHz, CDCl$_3$) δ 8.16 (dd, J = 8.0 Hz, 2H), 7.99-7.96 (m, 2H), 7.46-7.42 (m, 1H), 6.90-6.88 (m, 2H), 6.62-6.57 (m, 2H). $^{13}$C NMR (126 MHz, CDCl$_3$) δ 166.5, 159.5, 148.0, 137.5, 133.0, 130.2, 129.6, 128.4, 113.3, 107.1, 62.6, 56.8, 53.3, 45.2, 21.7. HRMS (ESI) calcd. for C$_{10}$H$_{22}$N$_2$O$_2$ [M+H]: 330.1909, found: 330.1907.
2-(4-(Pyridin-2-yl)piperazin-1-yl)ethyl 2,6-dimethoxybenzoate: The title compound was prepared according to the general procedure A and purified by flash column chromatography to give 275 mg colorless solid, 74 % yield. mp 80-81 °C. 1H NMR (400 MHz, CDCl3) δ 8.19-8.18 (m, 1H), 7.49-7.44 (m, 1H), 7.30-7.26 (m, 1H), 6.65-6.60 (m, 2H), 6.55 (d, J = 8.8 Hz, 2H), 5.05 (t, J = 5.8 Hz, 2H), 3.80 (s, 6H), 3.78 (s, 6H), 2.04 (s, 3H); 13C NMR (126 MHz, CDCl3) δ 170.9, 159.7, 157.3, 147.9, 137.4, 131.1, 114.9, 107.5, 61.7, 56.7, 53.1, 45.2. HRMS (ESI) calcd for C19H24N2O3 [M+H]: 342.1812, found: 342.1817.

2-(4-(5-bromopyridin-2-yl)piperazin-1-yl)ethyl acetate: The title compound was prepared according to the general procedure A and purified by flash column chromatography to give 311 mg colorless oil, 81 % yield. mp 61-62 °C. 1H NMR (500 MHz, CDCl3) δ 8.12 (d, J = 2.5 Hz, 1H), 7.45 (dd, J = 9.0, 2.5 Hz, 1H), 6.47 (d, J = 9.0 Hz, 1H), 4.17 (t, J = 5.8 Hz, 2H), 3.45 (t, J = 5.0 Hz, 4H), 2.61 (t, J = 5.8 Hz, 2H), 2.53 (t, J = 5.3 Hz, 4H), 2.01 (s, 3H); 13C NMR (126 MHz, CDCl3) δ 170.9, 157.9, 148.4, 139.6, 108.3, 107.6, 61.7, 56.7, 53.0, 45.1, 21.0. RMS (ESI) calcd for C19H19BrN2O2 [M+1]: 328.0655, found: 328.0670.

2-(4-(4-Methylpyridin-2-yl)piperazin-1-yl)ethyl acetate: the title compound was prepared according to the general procedure A and purified by flash column chromatography to give 213 mg colorless oil, 81 % yield. 1H NMR (500 MHz, CDCl3) δ 7.98-7.96 (m, 1H), 6.40-6.39 (m, 2H), 4.16 (t, J = 6.0 Hz, 2H), 3.46 (t, J = 5.3 Hz, 4H), 2.60 (t, J = 5.8 Hz, 2H), 2.53 (t, J = 5.0 Hz, 4H), 2.18 (s, 3H), 2.00 (s, 3H); 13C NMR (126 MHz, CDCl3) δ 170.9, 159.7, 148.3, 147.5, 114.9, 107.5, 61.7, 56.7, 53.2, 45.2, 21.4, 21.0. HRMS (ESI) calcd for C15H19N2O2 [M+H]: 264.1707, found: 264.1697.

2-(4-(6-Methylpyridin-2-yl)piperazin-1-yl)ethyl acetate: The title compound was prepared according to the general procedure A and purified by flash column chromatography to give 195 mg colorless oil, 74 % yield. 1H NMR (500 MHz, CDCl3) δ 7.33 (dd, J = 8.5, 7.0 Hz, 1H), 6.46 (d, J = 7.0 Hz, 1H), 6.39 (d, J = 8.5 Hz, 1H), 4.21 (t, J = 5.8 Hz, 2H), 3.51 (t, J = 5.0 Hz, 4H), 2.65 (t, J = 6.0 Hz, 2H), 2.58 (t, J = 5.3 Hz, 4H), 2.36 (s, 3H), 2.04 (s, 3H); 13C NMR (126 MHz, CDCl3) δ 171.0, 159.2, 156.8, 137.7, 112.7, 103.6, 61.8, 56.7, 53.3, 45.2, 24.6, 21.0. HRMS (ESI) calcd for C14H17N2O2 [M+H]: 264.1707, found: 264.1706.

2-(4-(6-Acetylpyridin-2-yl)piperazin-1-yl)ethyl acetate: The title compound was prepared according to the general procedure A and purified by flash column chromatography to give 204 mg colorless oil, 70 % yield. 1H NMR (500 MHz, CDCl3) δ 7.54 (dd, J = 8.5, 7.5 Hz, 1H), 7.31-7.30 (m, 1H), 6.78-6.76 (m, 1H), 4.20 (t, J = 6.0 Hz, 2H), 3.57 (t, J = 5.3 Hz, 4H), 2.65 (t, J = 6.0 Hz, 2H), 2.61-2.59 (m, 7H), 2.04 (s, 3H); 13C NMR (126 MHz, CDCl3) δ 200.9, 171.0, 158.5, 151.7, 138.1,
111.0, 110.6, 61.7, 56.7, 53.1, 45.0, 25.8, 21.0. HRMS (ESI) calcd. for C₁₀H₂₂N₂O₃ [M+H]: 292.1656, found: 292.1658.

**Ethyl 6-(4-(2-acetoxyethyl)piperazin-1-yl)picolinate**: The title compound was prepared according to the general procedure A and purified by flash column chromatography to give 205 mg colorless oil, 64 % yield. ¹H NMR (500 MHz, CDCl₃) δ 7.52-7.49 (m, 1H), 7.34 (d, J = 7.5 Hz, 1H), 6.74 (d, J = 8.5 Hz, 1H), 4.35-4.30 (m, 2H), 4.18 (t, J = 6.0 Hz, 2H), 3.57 (t, J = 5.0 Hz, 4H), 2.62 (t, J = 6.0 Hz, 2H), 2.56 (t, J = 5.0 Hz, 4H), 2.01 (s, 3H), 1.34 (t, J = 7.3 Hz, 3H).¹³C NMR (126 MHz, CDCl₃) δ 171.0, 154.8, 146.4, 138.0, 114.5, 110.2, 61.7, 61.4, 56.7, 53.1, 44.8, 21.0, 14.3. HRMS (ESI) calcd. for C₁₆H₂₆N₂O₄ [M+H]: 322.1761, found: 322.1747.

**2-(4-(Quinolin-2-yl)piperazin-1-yl)ethyl acetate**: The title compound was prepared according to the general procedure A and purified by flash column chromatography to give 236 mg colorless solid, 79 % yield. mp 89-90 °C. ¹H NMR (500 MHz, CDCl₃) δ 7.83 (d, J = 9.0 Hz, 1H), 7.70 (d, J = 8.5 Hz, 1H), 7.56 (dd, J = 8.0, 1.5 Hz, 1H), 7.53-7.49 (m, 1H), 7.19 (t, J = 7.5 Hz, 1H), 6.90 (d, J = 9.0 Hz, 1H), 4.21 (t, J = 5.8 Hz, 2H), 3.72 (t, J = 5.0 Hz, 4H), 2.64 (t, J = 5.8 Hz, 2H), 2.59 (t, J = 5.3 Hz, 4H), 2.05 (s, 3H);¹³C NMR (126 MHz, CDCl₃) δ 171.0, 157.3, 147.9, 137.4, 129.5, 127.2, 126.6, 123.1, 122.4, 109.5, 61.7, 56.7, 53.3, 45.0, 21.1. HRMS (ESI) calcd. for C₁₆H₂₄N₂O₂ [M+H]: 300.1707, found: 300.1702.

**2-(4-(4-Nitrophenyl)piperazin-1-yl)ethyl acetate**: The title compound was prepared according to the general procedure A and purified by flash column chromatography to give 205 mg yellow solid, 70 % yield. mp 126-127 °C. ¹H NMR (400 MHz, CDCl₃) δ 8.15-8.11(m, 2H), 6.85-6.80 (m, 2H), 4.25 (t, J = 5.8 Hz, 2H), 3.44 (t, J = 5.2 Hz, 4H), 2.72-2.65 (m, 6H), 2.09 (s, 3H);¹³C NMR (101 MHz, CDCl₃) δ 171.0, 154.8, 138.5, 126.0, 112.7, 61.6, 56.6, 52.8, 47.0, 21.1. HRMS (ESI) calcd. for C₁₆H₂₀N₂O₄ [M+H]: 294.1448 , found: 294.1453.

**2-(4-(Pyridin-2-yl)piperazin-1-yl)ethyl 4-chlorobenzoate**: The title compound was prepared according to the general procedure B and purified by flash column chromatography to give 242 mg colorless solid, 70 % yield. mp 93-94 °C. ¹H NMR (400 MHz, CDCl₃) δ 8.19 (dd, J = 5.2, 2.0 Hz, 1H), 7.99-7.96 (m, 2H), 7.49-7.41 (m, 3H), 6.65-6.60 (m, 2H), 4.49 (t, J = 5.8 Hz, 2H), 3.56 (t, J = 5.4 Hz, 4H), 2.83 (t, J = 5.8 Hz, 2H), 2.68 (t, J = 5.2 Hz, 4H);¹³C NMR (101 MHz, CDCl₃) δ 165.6, 159.5, 148.0, 139.5, 137.5, 131.0, 128.8, 128.7, 113.4, 107.1, 62.8, 56.7, 53.3, 45.2. HRMS (ESI) calcd. for C₁₆H₁₂ClN₂O₂ [M+H]: 346.1317, found: 346.1325.

**2-(4-(4-Methylpyridin-2-yl)piperazin-1-yl)ethyl pentanoate**: The title compound was prepared according to the general procedure B and purified by flash column chromatography to give 250 mg colorless oil, 82 % yield. ¹H NMR (400 MHz, CDCl₃) δ 8.05 (d, J = 4.8 Hz, 1H), 6.49-6.47 (m, 2H), 4.25 (t, J = 5.8 Hz, 2H), 3.54 (t, J = 5.0 Hz, 4H), 2.69 (t, J = 5.8 Hz, 2H), 2.63 (t, J = 5.2 Hz, 4H), 2.33 (t, J = 7.4 Hz, 2H), 2.26 (s, 3H), 1.63-1.58 (m, 2H), 1.38 -1.33 (m, 2H), 0.92 (t, J =
2-(4-(6-Methylpyridin-2-yl)piperazin-1-yl)ethyl pentanoate: The title compound was prepared according to the general procedure B and purified by flash column chromatography to give 253 mg colorless oil, 83 % yield. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.37 (dd, $J = 8.4, 7.2$ Hz, 1H), 6.49 (d, $J = 7.2$ Hz, 1H), 6.43 (d, $J = 8.4$ Hz, 1H), 4.25 (t, $J = 5.8$ Hz, 2H), 3.53 (t, $J = 5.0$ Hz, 4H), 2.68 (t, $J = 6.0$ Hz, 2H), 2.62 (t, $J = 5.0$ Hz, 4H), 2.40 (s, 3H), 2.33 (t, $J = 7.6$ Hz, 2H), 1.65-1.58 (m, 2H), 1.40-1.31 (m, 2H), 0.92 (t, $J = 7.2$ Hz, 3H); $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 173.8, 159.2, 156.8, 137.7, 112.7, 103.6, 61.6, 56.8, 53.3, 45.2, 34.1, 27.1, 24.6, 22.3, 13.8. HRMS (ESI) calcd. for C$_{17}$H$_{32}$N$_3$O$_2$ [M+H]: 306.2176, found: 306.2171.

2-(4-(Quinolin-2-yl)piperazin-1-yl)ethyl pentanoate: The title compound was prepared according to the general procedure B and purified by flash column chromatography to give 269 mg colorless solid, 79 % yield. mp 110-111 °C. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.89 (d, $J = 9.2$ Hz, 1H), 7.70 (d, $J = 8.4$ Hz, 1H), 7.60 (d, $J = 8.0$ Hz, 1H), 7.54 (t, $J = 7.6$ Hz, 1H), 7.25-7.21 (m, 1H), 6.98 (dd, $J = 9.2, 1.6$ Hz, 1H), 4.27 (t, $J = 5.8$ Hz, 2H), 3.77 (t, $J = 5.0$ Hz, 4H), 2.71 (t, $J = 6.0$ Hz, 2H), 2.67 (t, $J = 5.0$ Hz, 4H), 2.34 (t, $J = 7.6$ Hz, 2H), 1.66-1.58 (m, 2H), 1.39-1.33 (m, 2H), 0.92 (t, $J = 7.4$ Hz, 4H); $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 147.8, 147.6, 115.0, 107.6, 61.6, 56.8, 53.2, 45.0, 34.1, 27.1, 22.3, 13.8. HRMS (ESI) calcd. for C$_{26}$H$_{38}$N$_3$O$_2$ [M+H]: 342.2176, found: 342.2178.

2-(4-(4-Nitrophenyl)piperazin-1-yl)ethyl pentanoate: The title compound was prepared according to the general procedure B and purified by flash column chromatography to give 208 mg colorless oil, 6 % yield. mp 147-148 °C. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.13–8.11 (m, 2H), 6.84–6.81 (m, 2H), 4.25 (t, $J = 5.8$ Hz, 2H), 3.43 (t, $J = 5.2$ Hz, 4H), 2.71–2.65 (m, 6H), 2.34 (t, $J = 7.6$ Hz, 2H), 1.64–1.58 (m, 2H), 1.39–1.33 (m, 2H), 0.92 (t, $J = 7.2$ Hz, 3H); $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 173.8, 154.8, 138.4, 126.0, 112.6, 61.3, 56.6, 52.8, 47.0, 34.0, 27.1, 22.3, 13.8. HRMS (ESI) calcd. for C$_{27}$H$_{32}$N$_3$O$_2$ [M+H]: 336.1918, found: 336.1923.

4-(Methyl(quinolin-2-yl)amino)butyl acetate: The title compound was prepared according to the general procedure C and purified by flash column chromatography to give 176 mg colorless oil, 65 % yield. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.76 (d, $J = 9.2$ Hz, 1H), 7.60 (d, $J = 8.4$ Hz, 1H), 7.49 (dd, $J = 8.0, 1.6$ Hz, 1H), 7.45-7.41 (m, 1H), 7.11-7.07 (m, 1H), 6.77 (d, $J = 9.2$ Hz, 1H), 4.06-4.03 (m, 2H), 3.61 (t, $J = 6.6$ Hz, 2H), 3.11 (s, 3H), 1.97 (s, 3H), 1.65-1.61 (m, 4H); $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 170.2, 155.8, 147.1, 136.2, 128.4, 126.2, 125.2, 121.4, 120.5, 107.9, 63.3, 48.4, 35.2, 25.0, 23.0, 20.0. HRMS (ESI) calcd. for C$_{16}$H$_{22}$N$_2$O$_2$ [M+H]: 273.1598, found: 273.1594.
4-(Methyl(quinolin-2-yl)amino)butyl butyrate: The title compound was prepared according to the general procedure C and purified by flash column chromatography to give 190 mg colorless oil, 63 % yield. $^1$H NMR (400 MHz, CDCl$_3$) δ 7.85-7.82 (m, 1H), 7.68-7.66 (m, 1H), 7.58-7.55 (m, 1H), 7.52-7.48 (m, 1H), 7.19-7.15 (m, 1H), 6.84 (d, $J = 8.8$ Hz, 1H), 4.15-4.12 (m, 2H), 3.70-3.67 (m, 2H), 3.18 (s, 3H), 2.29-2.25 (m, 2H), 1.74-1.59 (m, 6H), 0.93 (t, $J = 7.4$ Hz, 3H); $^{13}$C NMR (101 MHz, CDCl$_3$) δ 173.8, 156.9, 148.2, 129.4, 127.2, 126.4, 122.4, 121.6, 108.9, 64.0, 49.5, 36.3, 26.2, 24.1, 18.5, 13.7. HRMS (ESI) calcd. for C$_{18}$H$_{24}$N$_2$O$_2$: [M+H]: 301.1911, found: 301.1914.

4-(Methyl(quinolin-2-yl)amino)butyl 4-methylbenzoate: The title compound was prepared according to the general procedure C and purified by flash column chromatography to give 210 mg colorless solid, 60 % yield. mp 101-102 ºC. $^1$H NMR (400 MHz, CDCl$_3$) δ 7.93-7.90 (m, 2H), 7.83-7.81 (m, 1H), 7.67 (d, $J = 8.4$ Hz, 1H), 7.56 (dd, $J = 8.0$, 1.6 Hz, 1H), 7.52-7.48 (m, 1H), 7.22-7.14 (m, 3H), 6.85 (d, $J = 8.8$ Hz, 1H), 4.38-4.35 (m, 2H), 3.75-3.71 (m, 2H), 3.19 (s, 3H), 1.85-1.80 (m, 4H); $^{13}$C NMR (101 MHz, CDCl$_3$) δ 166.7, 156.9, 148.2, 143.5, 137.2, 129.6, 129.4, 129.1, 127.6, 127.2, 126.4, 122.4, 121.6, 109.0, 64.5, 49.6, 36.3, 26.3, 24.1, 21.7. HRMS (ESI) calcd. for C$_{32}$H$_{27}$N$_2$O$_3$: [M+H]: 349.1911, found: 349.1922.

4-(Methyl(quinolin-2-yl)amino)butyl benzoate: The title compound was prepared according to the general procedure C and purified by flash column chromatography to give 207 mg colorless solid, 62 % yield. mp 95-96 ºC. $^1$H NMR (400 MHz, CDCl$_3$) δ 8.05-8.02 (m, 2H), 7.83-7.81 (m, 1H), 7.67 (d, $J = 8.4$ Hz, 1H), 7.57-7.48 (m, 3H), 7.43-7.38 (m, 2H), 7.18-7.14 (m, 1H), 6.84 (d, $J = 9.2$ Hz, 1H), 4.40-4.37 (m, 2H), 3.75-3.72 (m, 2H), 3.19 (s, 3H), 1.86-1.79 (m, 4H); $^{13}$C NMR (101 MHz, CDCl$_3$) δ 166.7, 156.9, 148.3, 137.2, 132.9, 130.4, 129.6, 129.4, 128.4, 127.2, 122.5, 121.6, 108.9, 64.7, 49.5, 36.3, 26.3, 24.1. HRMS (ESI) calcd. for C$_{33}$H$_{29}$N$_2$O$_3$: [M+H]: 335.1754, found: 335.1762.

4-(Methyl(quinolin-2-yl)amino)butyl 4-chlorobenzoate: The title compound was prepared according to the general procedure C and purified by flash column chromatography to give 170 mg colorless solid, 46 % yield. mp 122-123 ºC. $^1$H NMR (400 MHz, CDCl$_3$) δ 8.00-7.94 (m, 2H), 7.85-7.82 (m, 1H), 7.69 (d, $J = 8.4$ Hz, 1H), 7.59-7.57 (m, 1H), 7.54-7.49 (m, 1H), 7.40-7.36 (m, 2H), 7.20-7.16 (m, 1H), 6.85 (d, $J = 9.2$ Hz, 1H), 4.40-4.37 (m, 2H), 3.77-3.73 (m, 2H), 3.20 (s, 3H), 1.86-1.80 (m, 4H); $^{13}$C NMR (101 MHz, CDCl$_3$) δ 165.8, 156.9, 148.2, 139.3, 137.2, 131.0, 129.4, 128.8, 128.7, 127.3, 126.4, 122.5, 121.6, 108.9, 65.0, 49.5, 36.4, 26.2, 24.1. HRMS (ESI) calcd. for C$_{23}$H$_{21}$ClN$_2$O$_2$: 369.1364, found: 369.1365.

4. Copies of NMR Spectra of Compounds