Selective Remote Esterification of 8-Aminoquinoline Amides via Copper(II)-Catalyzed C(sp²)-O Cross-Coupling Reactions


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1. General Information
All the chemicals were obtained commercially and used without any prior purification. \(^1\)H NMR spectra were recorded on a Bruker AvanceII 500 spectrometer. All products were isolated by short chromatography on a silica gel (200–300 mesh) column using petroleum ether (60-90°C) and ethyl acetate. Unless otherwise noted. All compounds were characterized by \(^1\)H NMR, \(^{13}\)C NMR and HRGC- HRMS, which are consistent with those reported in the literature.

2. Experimental Section

General procedure for preparation acyloxylation of 8-aminoquinoline amides

A mixture of the 1 (0.2 mmol), PhI(OAc)\(_2\) (96.6 mg, 1.5 eq), Cu(OAc)\(_2\) (3.6 mg, 10 mol %) in AcOH (2.0 mL) was stirred at 45 °C under air atmosphere for 5.0 h. Then the mixture was cooled to room temperature and poured into water (10 mL). The mixture was extracted with EtOAc (6 mL x 3) and the combined organic layer was washed with brine (10 mL), dried with Na\(_2\)SO\(_4\), and the solvent was removed under reduced pressure. The product 2 was purified by flash column chromatography using PE/AcOEt as an eluent.

KIE experiment

The reaction of 1r (62.0 mg, 0.25 mmol), 1r-D\(_2\) (62.5 mg, 0.25 mmol), Cu(OAc)\(_2\) (9.1 mg, 10 mol %), PhI(OAc)\(_2\) (241.5 mg, 1.5 eq) in MeCN (4.0 mL) at 45 °C under air for 1 hour produced 2aa/2aa-D (37% yield). \(^1\)H NMR analysis of the isolated product demonstrated the KIE of 1.0 was resolved for the acyloxylation reaction, this result indicated that the turnover-limiting step does not involve C-H activation.
3. Characterization data of the products

8-(2-methylbenzamido)quinolin-5-yl acetate (2a)

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\text{\begin{center}
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\text{H} \\
\text{O} \\
\text{N} \\
\text{O} \\
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Obtained as a white solid in 80% yield; M.p. 122-123 °C. \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 10.12 (s, 1H), 8.96 (d, \(\text{J} = 8.5\) Hz, 1H), 8.81 (d, \(\text{J} = 2.6\) Hz, 1H), 8.20 (d, \(\text{J} = 6.9\) Hz, 1H), 7.67 (d, \(\text{J} = 7.7\) Hz, 1H), 7.50 (dd, \(\text{J} = 8.5, 4.2\) Hz, 1H), 7.42 – 7.36 (m, 2H), 7.32 (t, \(\text{J} = 7.9\) Hz, 2H), 2.59 (s, 3H), 2.46 (s, 3H). \(^{13}\)C NMR (126 MHz, CDCl\(_3\)) \(\delta\) 169.53, 168.12, 148.65, 140.77, 138.86, 136.72, 136.53, 133.04, 131.40, 130.48, 130.40, 127.25, 126.05, 122.00, 121.89, 119.38, 115.93, 20.92, 20.20. HRMS(ESI\(+\)): Calculated for C\(_{19}\)H\(_{16}\)N\(_2\)O\(_3\)H, [M\(+\)H\(^+\)] \(321.1234\). Found 321.1233.

8-(3-methylbenzamido)quinolin-5-yl acetate (2b)

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\text{H} \\
\text{O} \\
\text{N} \\
\text{OAc}
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Obtained as a white solid in 78% yield; M.p. 148-149 °C. \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 10.61 (s, 1H), 8.95 (d, \(\text{J} = 8.5\) Hz, 1H), 8.88 (d, \(\text{J} = 2.7\) Hz, 1H), 8.21 (d, \(\text{J} = 7.0\) Hz, 1H), 7.88 (s, 2H), 7.53 (d, \(\text{J} = 4.2\) Hz, 1H), 7.44 – 7.36 (m, 3H), 2.48 (s, 3H), 2.46 (s, 3H). \(^{13}\)C NMR (126 MHz, CDCl\(_3\)) \(\delta\) 169.50, 165.62, 148.68, 140.67, 139.05, 138.73, 135.04, 132.98, 132.68, 130.48, 128.68, 128.07, 124.22, 121.99, 121.89, 119.41, 115.93, 21.50, 20.92. HRMS(ESI\(+\)): Calculated for C\(_{19}\)H\(_{16}\)N\(_2\)O\(_3\)H, [M\(+\)H\(^+\)] \(321.1234\). Found 321.1233.

8-(4-methylbenzamido)quinolin-5-yl acetate (2c)

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\text{O} \\
\text{N} \\
\text{OAc}
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]\]

Obtained as a white solid in 81% yield; M.p. 181-182 °C. \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 10.60 (s, 1H), 8.89 (dd, \(\text{J} = 40.7, 5.6\) Hz, 2H), 8.18 (d, \(\text{J} = 8.4\) Hz, 1H), 7.96 (d, \(\text{J} = 8.1\) Hz, 2H), 7.49 (d, \(\text{J} = 4.2\) Hz, 1H), 7.34 (d, \(\text{J} = 2.7\) Hz, 3H), 2.44 (s, 6H). \(^{13}\)C NMR (126 MHz, CDCl\(_3\)) \(\delta\) 169.51, 165.34, 148.63, 142.44, 140.60, 138.99, 132.99, 132.19, 130.46, 129.49, 127.30, 121.97, 121.88, 119.38, 115.81, 21.56, 20.91. HRMS(ESI\(+\)): Calculated for C\(_{19}\)H\(_{16}\)N\(_2\)O\(_3\)H, [M\(+\)H\(^+\)] \(321.1234\). Found 321.1233.

8-(4-methoxylbenzamido)quinolin-5-yl acetate (2d)

\[
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\text{MeO} \\
\text{O} \\
\text{H} \\
\text{OAc}
\end{tabular}
\end{center}
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Obtained as a white solid in 86% yield; M.p. 159-161 °C. \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 10.58 (s, 1H), 8.90 (dd, \(\text{J} = 27.3, 5.5\) Hz, 2H), 8.20 (d, \(\text{J} = 6.9\) Hz, 1H), 8.05 (d, \(\text{J} = 8.8\) Hz, 2H), 7.52 (d, \(\text{J} = 4.2\) Hz, 1H), 7.36 (d, \(\text{J} = 8.5\) Hz, 1H), 7.05 – 7.02 (m, 2H), 3.89 (s, 3H), 2.46 (s, 3H). \(^{13}\)C NMR (126 MHz, CDCl\(_3\)) \(\delta\) 169.52, 164.93, 162.59, 148.58, 140.50, 138.98,
8-(2-fluorobenzamido)quinolin-5-yl acetate (2e)

Obtained as a white solid in 75% yield; M.p. 185-186 °C. $^1$H NMR (500 MHz, CDCl$_3$) δ 11.09 (d, $J = 12.6$ Hz, 1H), 8.94 (d, $J = 39.5$ Hz, 2H), 8.22 (d, $J = 0.9$ Hz, 2H), 7.53 (s, 1H), 7.37 (d, $J = 8.5$ Hz, 2H), 7.26 (s, 2H), 2.46 (s, 3H). $^{13}$C NMR (126 MHz, CDCl$_3$) δ 169.47, 161.60, 160.61 (d, $J = 252.5$ Hz), 148.89, 140.99, 139.11, 133.67 (d, $J = 8.8$ Hz), 133.14, 132.09, 130.36, 130.80, 124.91 (d, $J = 3.8$ Hz), 120.00, 121.94 (d, $J = 12.5$ Hz), 119.31, 116.66, 116.37 (d, $J = 24.0$ Hz), 109.31, 116.37 (d, $J = 24.0$ Hz), 2.46 (s, 3H).

HRMS(ESI+): Calculated for C$_{19}$H$_{16}$N$_2$O$_4$H$^+$$^{[M+H]}$ 337.1183. Found 337.1180.

8-(4-bromobenzamido)quinolin-5-yl acetate (2f)

Obtained as a white solid in 81% yield; M.p. 196-197 °C. $^1$H NMR (500 MHz, CDCl$_3$) δ 10.61 (s, 1H), 8.89 (d, $J = 14.6$ Hz, 2H), 8.21 (s, 1H), 7.94 (d, $J = 8.6$ Hz, 2H), 7.68 (d, $J = 8.6$ Hz, 2H), 7.53 (d, $J = 8.5$ Hz, 1H), 7.37 (d, $J = 8.5$ Hz, 1H), 2.46 (s, 3H). $^{13}$C NMR (126 MHz, CDCl$_3$) δ 169.45, 164.35, 148.73, 140.90, 138.94, 133.84, 132.58, 132.07, 130.59, 128.89, 126.70, 122.01, 121.97, 119.38, 116.05, 20.91. HRMS(ESI+): Calculated for C$_{18}$H$_{13}$BrN$_2$O$_3$H$^+$$^{[M+H]}$ 385.0183. Found 385.0187.

8-acetamidoquinolin-5-yl acetate (2g)

Obtained as a white solid in 63% yield; M.p. 124-126 °C. $^1$H NMR (500 MHz, CDCl$_3$) δ 9.71 (s, 1H), 8.80 (dd, $J = 28.9$, 6.4 Hz, 2H), 8.18 (d, $J = 8.5$ Hz, 1H), 7.51 (d, $J = 4.2$ Hz, 1H), 7.31 (d, $J = 8.5$ Hz, 1H), 2.45 (s, 3H), 2.35 (s, 3H). $^{13}$C NMR (126 MHz, CDCl$_3$) δ 169.49, 168.68, 148.46, 140.48, 138.45, 132.81, 130.51, 121.89, 121.80, 119.35, 115.85, 25.10, 20.90. HRMS(ESI+): Calculated for C$_{13}$H$_{12}$N$_2$O$_3$H$^+$$^{[M+H]}$ 245.0921, Found 245.0926.

8-(cyclopropanecarboxamido)quinolin-5-yl acetate (2h)

Obtained as a white solid in 69% yield; M.p. 143-145 °C. $^1$H NMR (500 MHz, CDCl$_3$) δ 9.93 (s, 1H), 8.74 (d, $J = 8.5$ Hz, 2H), 8.17 (d, $J = 8.5$ Hz, 1H), 7.49 (d, $J = 4.2$ Hz, 1H), 7.29 (d, $J = 8.5$ Hz, 1H), 2.44 (s, 3H), 1.79 (s, 1H), 1.15 (d, $J = 7.2$ Hz, 2H), 0.91 (d, $J = 4.5$ Hz, 2H). $^{13}$C NMR (126 MHz, CDCl$_3$) δ 172.20, 169.50, 148.45, 140.28, 138.45, 133.03, 130.43,
8-(cyclohexanecarboxamido)quinolin-5-yl acetate(2i)

Obtained as a white solid in 75% yield; M.p. 164-165 °C. \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 9.85 (s, 1H), 8.83 (dd, \(J = 16.4, 5.6\) Hz, 2H), 8.21 (d, \(J = 8.5\) Hz, 1H), 7.52 (d, \(J = 4.3\) Hz, 1H), 7.32 (d, \(J = 8.5\) Hz, 1H), 2.50 (s, 1H), 2.44 (s, 3H), 2.08 (d, \(J = 10.9\) Hz, 2H), 1.88 (d, \(J = 13.2\) Hz, 2H), 1.64 (d, \(J = 3.2\) Hz, 5H), 0.88 (s, 1H).

\(^{13}\)C NMR (126 MHz, CDCl\(_3\)) \(\delta\) 174.89, 169.48, 148.23, 140.36, 138.35, 132.82, 130.87, 121.97, 121.71, 119.52, 116.21, 46.81, 29.74, 25.78, 25.74, 20.89. HRMS(ESI+): Calculated for C\(_{18}\)H\(_{20}\)N\(_2\)O\(_3\)H, [M+H]\(^+\) 313.1547, Found 313.1540.

8-(2-methoxyacetamido)quinolin-5-yl acetate(2j)

Obtained as a white solid in 58% yield; M.p. 116-117 °C. \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 10.66 (s, 1H), 8.85 (dd, \(J = 38.2, 5.5\) Hz, 2H), 8.18 (d, \(J = 6.8\) Hz, 1H), 7.50 (dd, \(J = 8.5, 4.2\) Hz, 1H), 7.32 (d, \(J = 8.5\) Hz, 1H), 4.15 (s, 2H), 3.60 (s, 3H), 2.45 (s, 3H).

\(^{13}\)C NMR (126 MHz, CDCl\(_3\)) \(\delta\) 169.46, 168.19, 148.97, 140.92, 139.10, 132.15, 130.26, 121.95, 121.83, 119.16, 116.11, 72.72, 59.56, 20.91. HRMS(ESI+): Calculated for C\(_{14}\)H\(_{14}\)N\(_2\)O\(_4\)H, [M+H]\(^+\) 275.1027, Found 275.1022.

8-(tetrahydrofuran-2-carboxamido)quinolin-5-yl acetate(2k)

Obtained as a white solid in 71% yield; M.p. 166-168 °C. \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 10.83 (s, 1H), 8.85 (dd, \(J = 43.4, 5.6\) Hz, 2H), 8.18 (d, \(J = 6.9\) Hz, 1H), 7.50 (dd, \(J = 8.5, 4.2\) Hz, 1H), 7.32 (d, \(J = 8.5\) Hz, 1H), 4.62 (d, \(J = 2.8\) Hz, 1H), 4.22 (d, \(J = 7.5\) Hz, 1H), 4.07 (d, \(J = 7.5\) Hz, 1H), 2.45 (s, 3H), 2.39 (d, \(J = 8.1\) Hz, 1H), 2.26 (d, \(J = 5.9\) Hz, 1H), 2.01 – 1.96 (m, 2H).

\(^{13}\)C NMR (126 MHz, CDCl\(_3\)) \(\delta\) 172.07, 169.47, 148.96, 140.88, 139.12, 132.23, 130.31, 121.98, 121.81, 119.19, 115.99, 79.13, 69.80, 30.47, 25.56, 20.91. HRMS(ESI+): Calculated for C\(_{16}\)H\(_{16}\)N\(_2\)O\(_4\)H, [M+H]\(^+\) 301.1183, Found 301.1186.

8-(furan-2-carboxamido)quinolin-5-yl acetate(2l)

Obtained as a white solid in 61% yield; M.p. 163-166 °C. \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 10.68 (s, 1H), 8.90 (dd, \(J = 14.3, 5.6\) Hz, 2H), 8.20 (d, \(J = 7.0\) Hz, 1H), 7.62 (d, \(J = 0.8\) Hz,
1H), 7.53 (d, J = 4.2 Hz, 1H), 7.33 (d, J = 30.5 Hz, 2H), 6.59 (d, J = 1.7 Hz, 1H), 2.46 (s, 3H).

$^{13}$C NMR (126 MHz, CDCl$_3$) $\delta$ 169.48, 156.31, 148.80, 148.25, 144.58, 140.82, 138.90, 132.49, 130.43, 122.00, 121.93, 119.33, 116.05, 115.25, 112.49, 20.92. HRMS(ESI+): Calculated for C$_{16}$H$_{12}$N$_2$O$_4$H, [M+H]$^+$ 297.0870, Found 297.0875.

8-(4-cyanobenzamido)quinolin-5-yl acetate(2n)

\[
\text{OAc} \\
\text{N} \\
\text{N}
\]

Obtained as a white solid in 30% yield; M.p. 190-192 °C. $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 10.69 (s, 1H), 8.92 (d, J = 8.5 Hz, 2H), 8.26 – 8.23 (m, 1H), 8.17 (d, J = 8.3 Hz, 1H), 7.86 (d, J = 8.3 Hz, 2H), 7.56 (d, J = 12.7 Hz, 1H), 7.40 (d, J = 8.5 Hz, 1H), 2.47 (s, 3H).

$^{13}$C NMR (126 MHz, CDCl$_3$) $\delta$ 169.42, 163.40, 148.87, 141.30, 138.84, 132.71, 132.32, 132.18, 130.77, 130.61, 127.99, 122.11, 119.40, 118.05, 116.39, 115.46, 20.92. HRMS(ESI+): Calculated for C$_{19}$H$_{13}$N$_3$O$_3$H, [M+H]$^+$ 332.1030, Found 332.1039.

8-benzamido-2methylquinolin-5-yl acetate(2p)

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\text{OAc} \\
\text{N} \\
\text{N}
\]

Obtained as a white solid in 73% yield; M.p. 154-156 °C.$^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 10.64 (s, 1H), 8.83 (d, J = 8.5 Hz, 1H), 8.00 (d, J = 8.2 Hz, 3H), 7.49 (d, J = 7.4 Hz, 3H), 7.31 (d, J = 8.6 Hz, 1H), 7.22 (d, J = 8.5 Hz, 1H), 7.17 (s, 3H), 2.71 (s, 3H), 2.37 (s, 3H). $^{13}$C NMR (126 MHz, CDCl$_3$) $\delta$ 168.49, 164.23, 156.79, 139.86, 137.44, 134.17, 131.19, 130.80, 129.61, 127.80, 126.24, 121.70, 119.06, 117.32, 115.01, 24.34, 19.89. HRMS(ESI+): Calculated for C$_{19}$H$_{16}$N$_2$O$_3$H, [M+H]$^+$ 321.1234, Found 321.1237.

8-benzamido-6-methoxyquinolin-5-yl acetate(2q)

\[
\text{OAc} \\
\text{N} \\
\text{N}
\]

Obtained as a white solid in 75% yield; M.p. 159-161 °C.$^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 10.65 (s, 1H), 8.95 (s, 1H), 8.64 (d, J = 2.6 Hz, 1H), 8.04 (d, J = 8.5 Hz, 1H), 8.00 (d, J = 6.8 Hz, 2H), 7.49 (d, J = 7.4 Hz, 3H), 7.38 (d, J = 4.3 Hz, 1H), 3.98 (s, 3H), 2.38 (s, 3H). $^{13}$C NMR (126 MHz, CDCl$_3$) $\delta$ 168.00, 164.47, 147.47, 145.25, 133.77, 132.86, 132.78, 131.03, 128.18, 127.86, 126.23, 125.94, 121.96, 121.38, 103.93, 55.75, 19.48. HRMS(ESI+): Calculated for C$_{19}$H$_{16}$N$_2$O$_4$H, [M+H]$^+$ 337.1183, Found 337.1189.

4-benzamidonaphthalen-1-yl acetate-3$_3$(2r)
Obtained as a white solid in 82% yield; M.p. 177-178 °C. $^1$H NMR (500 MHz, CDCl$_3$) δ 10.66 (s, 1H), 8.96 (d, $J = 8.5$ Hz, 1H), 8.89 (d, $J = 2.6$ Hz, 1H), 8.21 (s, 1H), 8.08 (d, $J = 6.7$ Hz, 2H), 7.56 (d, $J = 7.3$ Hz, 4H), 7.38 (d, $J = 8.5$ Hz, 1H). HRMS(ESI+): Calculated for C$_{18}$H$_{11}$D$_3$N$_2$O$_3$H, [M+H]$^+$ 310.1266, Found 310.1269.

8-benzamidoquinolin-5-yl formate (2s)

Obtained as a white solid in 58% yield; M.p. 230-231 °C. $^1$H NMR (400 MHz, DMSO) δ 10.34 (s, 1H), 9.94 (s, 1H), 8.78 (d, $J = 2.7$ Hz, 1H), 8.53 (d, $J = 8.5$ Hz, 2H), 7.93 (d, $J = 8.0$ Hz, 2H), 7.48 (d, $J = 7.5$ Hz, 3H), 7.42 (d, $J = 4.2$ Hz, 1H), 6.86 (d, $J = 8.4$ Hz, 1H). $^{13}$C NMR (101 MHz, DMSO) δ 164.31, 161.43, 149.03, 148.85, 139.38, 135.24, 131.87, 131.74, 128.91, 127.03, 126.44, 120.59, 120.02, 117.63, 108.34. HRMS(ESI+): Calculated for C$_{17}$H$_{12}$N$_2$O$_3$, [M+H]$^+$ 293.0921, Found 293.0923.

8-benzamidoquinolin-5-yl isobutyrate (2t)

Obtained as a white solid in 47% yield; M.p. 115-116 °C. $^1$H NMR (400 MHz, DMSO) δ 10.55 (s, 1H), 8.99 (d, $J = 2.8$ Hz, 1H), 8.68 (d, $J = 8.4$ Hz, 1H), 8.30 – 8.26 (m, 1H), 8.01 (d, $J = 6.9$ Hz, 2H), 7.69 (s, 1H), 7.58 (s, 3H), 7.42 (d, $J = 8.4$ Hz, 1H), 3.02 (s, 1H), 1.32 (d, $J = 7.0$ Hz, 6H). $^{13}$C NMR (101 MHz, DMSO) δ 175.75, 164.97, 150.13, 141.43, 139.10, 134.77, 132.73, 132.60, 131.08, 129.44, 127.50, 123.22, 122.27, 119.62, 116.73, 33.81, 19.21. HRMS(ESI+): Calculated for C$_{20}$H$_{18}$N$_2$O$_3$, [M+H]$^+$ 335.1390, Found 335.1398.

8-benzamidoquinolin-5-yl propionate (2u)

Obtained as a white solid in 62% yield; M.p. 108-109 °C. $^1$H NMR (400 MHz, DMSO) δ 10.55 (s, 1H), 8.99 (d, $J = 4.0$ Hz, 1H), 8.68 (d, $J = 8.4$ Hz, 1H), 8.38 (d, $J = 8.4$ Hz, 1H), 8.01 (d, $J = 7.2$ Hz, 2H), 7.69 (dd, $J = 8.5$, 4.2 Hz, 1H), 7.67 – 7.49 (m, 3H), 7.43 (d, $J = 8.4$ Hz, 1H), 2.80 (q, $J = 7.4$ Hz, 2H), 1.18 (t, $J = 7.4$ Hz, 3H). $^{13}$C NMR (101 MHz, DMSO) δ 173.43, 164.97, 150.13, 141.43, 139.10, 134.77, 132.73, 132.60, 131.43, 129.45, 127.51, 123.12, 122.34, 119.68, 116.78, 27.15, 9.31. HRMS(ESI+): Calculated for C$_{19}$H$_{16}$N$_2$O$_3$, [M+H]$^+$ 321.1234, Found 321.1230.

8-(cyclohexanecarboxamido)quinolin-5-yl propionate (2v)
8-(4-bromobenzamido)quinolin-5-yl propionate(2w)

Obtained as a white solid in 48% yield; M.p. 126-127 °C. ¹H NMR (400 MHz, DMSO) δ 10.53 (s, 1H), 8.96 (s, 1H), 8.61 (s, 1H), 8.35 (s, 1H), 7.91 (s, 2H), 7.77 (s, 2H), 7.67 (d, J = 8.3 Hz, 1H), 7.41 (d, J = 8.4 Hz, 1H), 2.79 (d, J = 7.5 Hz, 2H), 1.18 (s, 3H). ¹³C NMR (101 MHz, DMSO) δ 173.37, 164.09, 150.10, 141.60, 139.20, 133.83, 132.44, 132.36, 131.36, 129.65, 126.34, 123.06, 122.32, 119.61, 117.17, 27.16, 9.30. HRMS(ESI+): Calculated for C₁₉H₁₅BrN₂O₃H, [M+H]⁺ 399.0339, Found 399.0332.

8-(2-fluorobenzamido)quinolin-5-yl propionate(2x)

Obtained as a white solid in 51% yield; M.p. 117-118 °C. ¹H NMR (400 MHz, CDCl₃) δ 11.08 (d, J = 12.7 Hz, 1H), 8.92 (d, J = 31.2 Hz, 2H), 8.18 (d, J = 8.5 Hz, 2H), 7.51 (d, J = 5.0 Hz, 2H), 7.29 (d, J = 41.3 Hz, 3H), 2.75 (d, J = 7.6 Hz, 2H), 1.35 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 172.93, 161.78, 160.41 (d, J = 278.5 Hz), 148.77, 141.00, 139.00, 133.61, 132.44, 132.36, 131.36, 129.25, 116.73, 116.32 (d, J = 24.0 Hz), 27.65, 9.23. HRMS(ESI+): Calculated for C₁₉H₁₅FN₂O₃H, [M+H]⁺ 339.1140, Found 339.1148.

4. X-ray Crystal Data for 2c

Crystals of 2c (C₁₉H₁₆N₂O₃) was recrystallized from CDCl₃. The single colourless transparent granular crystal which was suitable for X-ray diffraction measurements was mounted on a glass fiber. Unit cell measurements and intensity data collections were performed on a Rigaku AFC7R diffractometer with graphite monochromated Mo Ka. The data reduction included a correction for Lorentz and polarization effects, with an applied multi-scan absorption correction (SADABS). The crystal structure was solved and refined using the SHELXTL-97 program suite. Direct methods yielded all non-hydrogen atoms which were refined with anisotropic thermal parameters. The obtained crystal structure has been deposited at the Cambridge Crystallographic Data Centre and allocated the deposition number: 1508095 (2c, CCDC NO.). The crystalographic data and refinement parameters of them are listed in Table S1.
<table>
<thead>
<tr>
<th><strong>Table S1</strong> Crystallographic data and structure refinement for 2c.</th>
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<tbody>
<tr>
<td><strong>Empirical formula</strong></td>
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<tr>
<td><strong>Formula weight</strong></td>
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<tr>
<td><strong>Temperature, K</strong></td>
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<tr>
<td><strong>Wavelength, Å</strong></td>
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<tr>
<td><strong>Crystal system</strong></td>
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<td><strong>Space group</strong></td>
</tr>
<tr>
<td><strong>Unit cell dimensions</strong></td>
</tr>
<tr>
<td>a, b, c, Å</td>
</tr>
<tr>
<td>α, β, γ, °</td>
</tr>
<tr>
<td><strong>Volume, Å³</strong></td>
</tr>
<tr>
<td>Z</td>
</tr>
<tr>
<td><strong>Calculated density, Mg/m³</strong></td>
</tr>
<tr>
<td><strong>Absorption coefficient, mm⁻¹</strong></td>
</tr>
<tr>
<td>F (000)</td>
</tr>
<tr>
<td><strong>Crystal size, mm</strong></td>
</tr>
<tr>
<td><strong>Theta range for data collection, °</strong></td>
</tr>
<tr>
<td><strong>Limiting indices</strong></td>
</tr>
<tr>
<td><strong>Absorption correction</strong></td>
</tr>
<tr>
<td><strong>Refinement method</strong></td>
</tr>
<tr>
<td><strong>Data / restraints / parameters</strong></td>
</tr>
<tr>
<td><strong>Goodness of fit on F²</strong></td>
</tr>
<tr>
<td><strong>Final R indices [I&gt;2sigma(I)]</strong></td>
</tr>
<tr>
<td><strong>R indices (all data)</strong></td>
</tr>
</tbody>
</table>
5. $^1$H and $^{13}$C NMR spectra of the products

2a $^1$H NMR

2a $^{13}$C NMR
$2c \ ^1H\ NMR$

$2c \ ^{13}C\ NMR$
2d $^1$H NMR

2d $^{13}$C NMR
2e $^1$H NMR

2e $^{13}$C NMR
2g $^1$H NMR

2g $^{13}$C NMR
2h $^1$H NMR

2h $^{13}$C NMR
2i $^1$H NMR

2i $^{13}$C NMR
2j $^1$H NMR

2j $^{13}$C NMR
2k $^1$H NMR

$^1$H NMR spectrum with peaks at various ppm values.

2k $^{13}$C NMR

$^{13}$C NMR spectrum with peaks at various ppm values.
$2p^1H$ NMR

$2p^{13}C$ NMR
2q $^1$H NMR

2q $^{13}$C NMR
$2^r \text{H NMR}$
2s $^1$H NMR

2s $^{13}$C NMR
$2x$ $^1H$ NMR

$2x$ $^{13}C$ NMR
2aa/2aa-D $^1$H NMR