Supporting Information

Nickel-catalyzed chelation-assisted direct arylation of unactivated C(sp³)–H bonds with aryl halides

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I. General remarks
NMR spectra were obtained on a Bruker AV II-400 MHz spectrometer. The $^1$H NMR (400 MHz) chemical shifts were measured relative to CDCl$_3$ or TMS as the internal reference (CDCl$_3$: $\delta = 7.26$ ppm; TMS: $\delta = 0.00$ ppm). The $^{13}$C NMR (100 MHz) chemical shifts were given using CDCl$_3$ as the internal standard (CDCl$_3$: $\delta = 77.16$ ppm). High-resolution mass spectra (HRMS) were obtained with a Waters-Q-TOF-Premier (ESI). Melting points were determined with XRC-1 and are uncorrected.

Unless otherwise noted, all reagents were obtained from commercial suppliers and used without further purification. Ni(OAc)$_2$ and NiCl$_2$ were purchased from Chengdu Kelong Chemical Engineering Reagent (China) CO., Ltd. 8-Aminoquinoline was purchased from Sichuan Xieli Biological & Chemical Reagent (China) CO., Ltd. The solvents were dried over CaH$_2$ (for DMF) or sodium (for 1,4-dioxane, toluene, and $t$-AmyLOH). Starting materials 1 were prepared according to the literature procedure.$^{1,2}$

II. Synthesis of nickel(II) trifluoromethanesulfonate
Trifluoromethanesulfonic acid (1.18 mL, 13.3 mmol) was added dropwise to the solution of Ni(OAc)$_2$ (0.72 g, 4.4 mmol) in CH$_3$CN (60 mL). The resulting mixture was stirred at room temperature for 2 h. Then the solvent was evaporated until around 15 mL solution was left. Diethyl ether (100 mL) was added. The suspension was decanted, and the residual powder was washed successively with diethyl ether and hexane, and dried under vacuum at 70 °C to afford Ni(OTf)$_2$ as a light green solid (0.94 g, 60% yield).

III. Optimization of the coupling of aliphatic amide 1a with aryl iodide 2a
An oven-dried Schlenk tube with a magnetic stir bar was charged with 2-benzyl-3-(4-methoxyphenyl)-2-methyl-N-(quinolin-8-yl)propanamide 1a (82.1 mg, 0.2 mmol), 4-iodoanisole 2a (93.6 mg, 0.4 mmol), Ni catalyst (0.02 mmol, 10 mol%), PPh$_3$ (10.4 mg, 0.04 mmol, if required), base (0.4 mmol), additive and 1,4-dioxane (1
mL) under an argon atmosphere. The tube was sealed with a teflon-coated cap and the mixture was stirred at 160 °C for 24 h. After being cooled to ambient temperature, the solution was diluted with 20 mL of EtOAc, filtered through a celite pad, and washed with 10-20 mL of EtOAc. The combined organic phases were concentrated and the residue was purified by column chromatography on silica gel (ethyl acetate/petroleum ether = 1/10, v/v) to give the desired product 3a.

Table S1. Optimization of the nickel-catalyzed arylation of aliphatic amide 1a with 1-iodo-4-methoxybenzene 2a

<table>
<thead>
<tr>
<th>Entry</th>
<th>Ni cat.</th>
<th>Base</th>
<th>Additive (equiv)</th>
<th>Yieldb</th>
</tr>
</thead>
<tbody>
<tr>
<td>1c</td>
<td>Ni(OTf)2</td>
<td>K2CO3</td>
<td>none</td>
<td>24%</td>
</tr>
<tr>
<td>2c</td>
<td>Ni(OTf)2</td>
<td>K3PO4</td>
<td>none</td>
<td>trace</td>
</tr>
<tr>
<td>3c</td>
<td>Ni(OTf)2</td>
<td>Li2CO3</td>
<td>none</td>
<td>15%</td>
</tr>
<tr>
<td>4c</td>
<td>Ni(OTf)2</td>
<td>Na2CO3</td>
<td>none</td>
<td>35%</td>
</tr>
<tr>
<td>5c</td>
<td>Ni(OTf)2</td>
<td>Na2CO3</td>
<td>DMSO (7.0)</td>
<td>48%</td>
</tr>
<tr>
<td>6</td>
<td>Ni(OTf)2</td>
<td>Na2CO3</td>
<td>DMSO (7.0)</td>
<td>57%</td>
</tr>
<tr>
<td>7</td>
<td>Ni(OTf)2</td>
<td>Na2CO3</td>
<td>DMSO (3.5)</td>
<td>68%</td>
</tr>
<tr>
<td>8</td>
<td>Ni(OTf)2</td>
<td>Na2CO3</td>
<td>PivOH (0.2)</td>
<td>52%</td>
</tr>
<tr>
<td>9</td>
<td>Ni(OTf)2</td>
<td>Na2CO3</td>
<td>DMSO (3.5)/PivOH (0.2)</td>
<td>83%</td>
</tr>
<tr>
<td>10d</td>
<td>Ni(OTf)2</td>
<td>Na2CO3</td>
<td>DMSO (3.5)/PivOH (0.2)</td>
<td>54%</td>
</tr>
<tr>
<td>11</td>
<td>Ni(OTf)2</td>
<td>Na2CO3</td>
<td>DMSO (3.5)/PivOH (0.1)</td>
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</tr>
<tr>
<td>12</td>
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<td>Na2CO3</td>
<td>DMSO (3.5)/PivOH (0.4)</td>
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</tr>
<tr>
<td>13</td>
<td>Ni(OAc)2</td>
<td>Na2CO3</td>
<td>DMSO (3.5)/PivOH (0.2)</td>
<td>61%</td>
</tr>
<tr>
<td>14</td>
<td>NiCl2</td>
<td>Na2CO3</td>
<td>DMSO (3.5)/PivOH (0.2)</td>
<td>61%</td>
</tr>
<tr>
<td>15e</td>
<td>Ni(cod)2</td>
<td>Na2CO3</td>
<td>DMSO (3.5)/PivOH (0.2)</td>
<td>62%</td>
</tr>
<tr>
<td>16</td>
<td>Ni(cod)2</td>
<td>Na2CO3</td>
<td>DMSO (3.5)/PivOH (0.2)</td>
<td>50%</td>
</tr>
<tr>
<td>17f</td>
<td>Ni(OTf)2</td>
<td>Na2CO3</td>
<td>DMSO (3.5)/PivOH (0.2)</td>
<td>85%</td>
</tr>
</tbody>
</table>

*a* Reactions were carried out using nickel catalyst (10 mol%), PPh3 (20 mol%), additive, base (2.0 equiv), amide 1a (0.2 mmol) and 1-iodo-4-methoxybenzene 2a (2.0 equiv) in dry 1,4-dioxane (1 mL) at 160 °C for 24 h. 

*b* Isolated yields. 

*c* 140 °C. 

*d* In the absence of PPh3. 

*e* PPh3 (40 mol%). 

*f* 1-Iodo-4-methoxybenzene 2a (3.0 equiv).

IV. General procedure for the coupling of aliphatic amides with aryl iodides
An oven-dried Schlenk tube with a magnetic stir bar was charged with aliphatic amide 1 (0.2 mmol, 1 equiv), aryl iodide 2 (0.4 mmol or 0.6 mmol), Ni(OTf)$_2$ (7.2 mg, 0.02 mmol), PPh$_3$ (10.4 mg, 0.04 mmol), Na$_2$CO$_3$ (42 mg, 0.4 mmol), and PivOH (4.2 mg, 0.04 mmol). The tube was then taken to a Schlenk line and DMSO (50 µL, 0.7 mmol) and 1,4-dioxane (1 mL) were added under an argon atmosphere. The tube was sealed with a teflon-coated cap and the resulting mixture was stirred at 160 °C for 36 h. After being cooled to ambient temperature, the solution was diluted with 20 mL of EtOAc, filtered through a celite pad, and washed with 10-20 mL of EtOAc. The combined organic phases were concentrated and the residue was purified by column chromatography on silica gel using hexane/ethyl acetate as the eluent to give the desired product.

V. General procedure for the coupling of aliphatic amides with aryl bromides

An oven-dried Schlenk tube with a magnetic stir bar was charged with aliphatic amide 1 (0.2 mmol, 1 equiv), aryl bromide (0.8 mmol), Ni(OTf)$_2$ (7.2 mg, 0.02 mmol), PPh$_3$ (10.4 mg, 0.04 mmol), Na$_2$CO$_3$ (42 mg, 0.4 mmol), and PivOH (4.2 mg, 0.04 mmol) (6.7 mg, 0.04 mmol). The tube was then taken to a Schlenk line and DMSO (50 µL, 0.7 mmol) and 1,4-dioxane (1 mL) were added under an argon atmosphere. The tube was sealed with a teflon-coated cap and the resulting mixture was stirred at 160 °C for 36 h. After being cooled to ambient temperature, the solution was diluted with 20 mL of EtOAc, filtered through a celite pad, and washed with 10-20 mL of EtOAc. The combined organic phases were concentrated and the residue was purified by column chromatography on silica gel using hexane/ethyl acetate as the eluent to give the desired product.

VI. Plausible mechanism

Although the detailed mechanism is not clear at this stage, a plausible catalytic cycle is proposed in Scheme S1. First, aliphatic amide 1 coordinates with nickel(II) complex via a chelation of an 8-aminoquinoline residue to generate the intermediate IM1, which then undergoes an intramolecular C(sp$^3$)–H activation with the
assistance of Na₂CO₃ to form the metallocycle IM₂. Subsequently, oxidative addition of IM₂ with aryl halide affords the key intermediate IM₃.⁴⁵ Upon reductive elimination of IM₃, the desired product 3 is obtained and the nickel catalyst is regenerated. When nickel(0) catalyst is used, we suspected that the oxidative addition of aryl iodide with Ni(0) might form Ar–Ni–I complex. The resulting Ni(II) species further reacts with the amide 1 to generate the intermediate IM₁.⁵

![Scheme S1 Plausible mechanism.](image)

VII. Experimental data for the described substances

2-Benzyl-2-(4-methoxybenzyl)-3-(4-methoxyphenyl)-N-(quinolin-8-yl)propanamide (3a)

Following the general procedure except that the reaction time was 24 h. 2-Benzyl-3-(4-methoxyphenyl)-2-methyl-N-(quinolin-8-yl)propanamide (82.1 mg, 0.2 mmol) and 4-iodoanisole (93.6 mg, 0.4 mmol) were used. Purification via column chromatography on silica gel (ethyl acetate/petroleum ether = 1/10, v/v) afforded 3a.
as a white solid (85 mg, 83% yield). When 4-bromoanisole (100 μL, 0.8 mmol) was used as the coupling partner, 3a was obtained in 76% yield (79 mg). M.p.: 43-47 °C. 

\[ \text{H NMR (400 MHz, CDCl}_3\text{): } \delta = 3.17 (s, 4H), 3.23 (s, 2H), 3.68 (s, 6H), 6.68-6.71 (m, 4H), 7.08-7.10 (m, 4H), 7.13-7.21 (m, 5H), 7.34 (dd, } J = 8.4 \text{ Hz, } 4.0 \text{ Hz, 1H}, 7.48 (dd, } J = 8.4 \text{ Hz, 0.8 Hz, 1H}, 7.56 (t, } J = 8.0 \text{ Hz, 1H}, 8.09 (dd, } J = 8.4 \text{ Hz, 1.6 Hz, 1H}, 8.47 (dd, } J = 4.0 \text{ Hz, 1.6 Hz, 1H}, 8.84 (dd, } J = 7.6 \text{ Hz, 0.8 Hz, 1H}, 9.95 (s, 1H) \text{ ppm.} \]

\[ \text{C NMR (100 MHz, CDCl}_3\text{): } \delta = 41.0, 41.5, 52.4, 55.2, 113.6, 116.3, 121.4, 121.5, 126.4, 127.5, 127.8, 128.2, 129.3, 130.7, 131.6, 134.3, 136.0, 137.6, 138.7, 147.9, 158.2, 174.2 \text{ ppm.} \]

HRMS (ESI\(^+\)): calcd for C\(_{34}\)H\(_{32}\)N\(_2\)O\(_3\) [M+Na]\(^+\) 539.2311, found 539.2313.

![Chemical structure of 2-Benzyl-2-(3-methoxybenzyl)-3-(4-methoxyphenyl)-N-(quinolin-8-yl)propanamide (3b)](image)

2-Benzyl-2-(3-methoxybenzyl)-3-(4-methoxyphenyl)-N-(quinolin-8-yl)propanamide (3b)

Following the general procedure. 2-Benzyl-3-(4-methoxyphenyl)-2-methyl-N-(quinolin-8-yl)propanamide (82.1 mg, 0.2 mmol) and 3-iodoanisole (71.4 μL, 0.6 mmol) were used. Purification via column chromatography on silica gel (ethyl acetate/petroleum ether = 1/10, v/v) afforded 3b as an off-white solid (75 mg, 73% yield). When 3-bromoanisole (100.4 μL, 0.8 mmol) was used as the coupling partner, 3b was obtained in 50% yield (51 mg). M.p.: 38-40 °C. \[ \text{H NMR (400 MHz, CDCl}_3\text{): } \delta = 3.21 (s, 2H), 3.23 (s, 2H), 3.26 (s, 2H), 3.53 (s, 3H), 3.69 (s, 3H), 6.66-6.72 (m, 4H), 6.82 (d, } J = 7.6 \text{ Hz, 1H}, 7.09-7.12 (m, 3H), 7.15-7.23 (m, 5H), 7.34 (dd, } J = 8.0 \text{ Hz, 4.0 Hz, 1H}, 7.49 (dd, } J = 8.4 \text{ Hz, 1.2 Hz, 1H}, 7.57 (t, } J = 8.0 \text{ Hz, 1H}, 8.09 (dd, } J = 8.4 \text{ Hz, 1.6 Hz, 1H}, 8.48 (dd, } J = 4.0 \text{ Hz, 1.6 Hz, 1H}, 8.87 (d, } J = 7.6 \text{ Hz, 1H}, 9.99 (s, 1H) \text{ ppm.} \]

\[ \text{C NMR (100 MHz, CDCl}_3\text{): } \delta = 41.1, 41.5, 41.9, 52.4, 55.0, 55.2, 112.5, 113.6, 115.8, 116.3, 121.4, 121.5, 123.0, 126.5, 127.4, 127.8, 128.2, 129.0, 129.2, 130.6, 131.6, 134.3, 136.0, 137.5, 138.6, 139.0, 148.0, 158.3, 159.3, 174.1 \text{ ppm.} \]
2-Benzyl-2-(2-methoxybenzyl)-3-(4-methoxyphenyl)-N-(quinolin-8-yl)propanamide (3c)

Following the general procedure. 2-Benzyl-3-(4-methoxyphenyl)-2-methyl-N-(quinolin-8-yl)propanamide (82.1 mg, 0.2 mmol) and 2-iodoanisole (78.0 μL, 0.6 mmol) were used. Purification via column chromatography on silica gel (ethyl acetate/petroleum ether = 1/15, v/v) afforded 3c as an off-white solid (36 mg, 35% yield). M.p.: 44-47 °C. 1H NMR (400 MHz, CDCl3): δ = 3.14-3.33 (m, 6H), 3.50 (s, 3H), 3.69 (s, 3H), 6.58 (d, J = 8.4 Hz, 1H), 6.68-6.71 (m, 2H), 6.78 (td, J = 7.6 Hz, 1.2 Hz, 1H), 7.04-7.09 (m, 3H), 7.11-7.19 (m, 6H), 7.31 (dd, J = 8.4 Hz, 4.4 Hz, 1H), 7.45 (dd, J = 8.4 Hz, 1.2 Hz, 1H), 7.54 (t, J = 8.0 Hz, 1H), 8.07 (dd, J = 8.0 Hz, 1.6 Hz, 1H), 8.42 (dd, J = 4.4 Hz, 1.6 Hz, 1H), 8.85 (dd, J = 7.6 Hz, 1.2 Hz, 1H), 9.90 (s, 1H) ppm. 13C NMR (100 MHz, CDCl3): δ = 35.9, 40.7, 41.2, 52.0, 55.15, 55.23, 110.1, 113.5, 116.2, 120.1, 121.1, 121.4, 125.9, 126.3, 127.5, 127.7, 128.1, 129.8, 130.8, 131.5, 131.7, 134.6, 135.9, 138.0, 138.6, 147.8, 158.15, 158.22, 174.4 ppm. HRMS (ESI+): calcd for C34H32N2NaO3 [M+Na]+ 539.2311, found 539.2321.

2-(4-Aminobenzyl)-2-benzyl-3-(4-methoxyphenyl)-N-(quinolin-8-yl)propanamide (3d)

Following the general procedure. 2-Benzyl-3-(4-methoxyphenyl)-2-methyl-N-(quinolin-8-yl)propanamide (82.1 mg, 0.2 mmol) and 4-iodoaniline (131.4 mg, 0.6 mmol) were used. Purification via column chromatography on silica gel (ethyl acetate/petroleum ether = 1/3, v/v) afforded 3d as an off-white solid (55 mg, 55%
yield). When 4-bromoaniline (137.6 mg, 0.8 mmol) was used as the coupling partner, 3d was obtained in 46% yield (46 mg). M.p.: 70-74 °C. ¹H NMR (400 MHz, CDCl₃): δ = 3.14 (s, 2H), 3.16 (s, 2H), 3.22 (s, 2H), 3.53 (br. s, 2H), 3.68 (s, 3H), 6.50-6.52 (m, 2H), 6.68-6.71 (m, 2H), 6.96-6.98 (m, 2H), 7.08-7.11 (m, 2H), 7.13-7.21 (m, 5H), 7.33 (dd, J = 8.0 Hz, 4.0 Hz, 1H), 7.48 (dd, J = 8.4 Hz, 1.2 Hz, 1H), 7.56 (t, J = 8.0 Hz, 1H), 8.08 (dd, J = 8.4 Hz, 1.6 Hz, 1H), 8.50 (dd, J = 4.0 Hz, 1.6 Hz, 1H), 8.86 (dd, J = 7.6 Hz, 1.2 Hz, 1H), 9.99 (s, 1H) ppm. ¹³C NMR (100 MHz, CDCl₃): δ = 40.8, 41.1, 41.6, 52.4, 55.2, 113.5, 115.0, 116.3, 121.3, 121.4, 126.4, 127.1, 127.5, 127.8, 128.1, 129.4, 130.7, 131.5, 131.6, 134.4, 136.0, 137.7, 138.7, 144.8, 147.9, 158.2, 174.4 ppm. HRMS (ESI⁺): calcd for C₃₃H₃₁N₃NaO₂ [M+Na]⁺ 524.2314, found 524.2314.

2-(4-Acetamidobenzyl)-2-benzyl-3-(4-methoxyphenyl)-N-(quinolin-8-yl)propanamide (3e)

Following the general procedure. 2-Benzyl-3-(4-methoxyphenyl)-2-methyl-N-(quinolin-8-yl)propanamide (82.1 mg, 0.2 mmol) and N-(4-iodophenyl)acetamide (156.6 mg, 0.6 mmol) were used. Purification via column chromatography on silica gel (ethyl acetate/petroleum ether = 1/1, v/v) afforded 3e as an off-white solid (75 mg, 69% yield). M.p.: 82-88 °C. ¹H NMR (400 MHz, CDCl₃): δ = 2.06 (s, 3H), 3.15 (s, 2H), 3.18 (s, 2H), 3.21 (s, 2H), 3.66 (s, 3H), 6.67-6.69 (m, 2H), 7.05-7.10 (m, 4H), 7.12-7.17 (m, 5H), 7.30-7.33 (m, 3H), 7.46 (d, J = 7.6 Hz, 1H), 7.52 (t, J = 7.6 Hz, 1H), 7.70-7.72 (m, 1H), 8.06 (dd, J = 8.4 Hz, 1.2 Hz, 1H), 8.48 (dd, J = 4.4 Hz, 1.6 Hz, 1H), 8.81 (dd, J = 7.6 Hz, 1.2 Hz, 1H), 10.01 (s, 1H) ppm. ¹³C NMR (100 MHz, CDCl₃): δ = 24.5, 41.0, 41.1, 41.6, 52.3, 55.2, 113.5, 116.3, 119.5, 121.47, 121.51, 126.5, 127.4, 127.8, 128.2, 129.1, 130.6, 131.0, 131.6, 133.1, 134.1, 136.0, 136.6, 137.3, 138.6, 148.0, 158.2, 168.6, 174.1 ppm. HRMS (ESI⁺): calcd for C₃₅H₃₃N₃NaO₃ [M+Na]⁺ 566.2420, found 566.2428.
2-(4-Acetylbenezyl)-2-benzyl-3-(4-methoxyphenyl)-N-(quinolin-8-yl)propanamide (3f)

Following the general procedure. 2-Benzyl-3-(4-methoxyphenyl)-2-methyl-N-(quinolin-8-yl)propanamide (82.1 mg, 0.2 mmol) and 1-(4-iodophenyl)ethanone (147.6 mg, 0.6 mmol) were used. Purification via column chromatography on silica gel (ethyl acetate/petroleum ether = 1/8, v/v) afforded 3f as a white solid (58 mg, 55% yield). When 2-(4-acetylbenzyl)-2-methyl-3-phenyl-N-(quinolin-8-yl)propanamide (84.5 mg, 0.2 mmol) and 4-iodoanisole (140.4 mg, 0.6 mmol) were used as the starting materials, 3f was obtained in 71% yield (75 mg). M.p.: 65-68 °C. 1H NMR (400 MHz, CDCl3): δ = 2.48 (s, 3H), 3.19 (s, 2H), 3.25 (s, 4H), 3.69 (s, 3H), 6.68-6.72 (m, 2H), 7.06-7.09 (m, 2H), 7.14-7.19 (m, 5H), 7.26 (d, J = 8.4 Hz, 2H), 7.33 (dd, J = 8.4 Hz, 4.0 Hz, 1H), 7.50 (dd, J = 8.4 Hz, 1.2 Hz, 1H), 7.57 (t, J = 8.0 Hz, 1H), 7.74 (d, J = 8.4 Hz, 2H), 8.09 (dd, J = 8.4 Hz, 1.6 Hz, 1H), 8.45 (dd, J = 4.4 Hz, 1.6 Hz, 1H), 8.83 (dd, J = 7.6 Hz, 1.2 Hz, 1H), 9.95 (s, 1H) ppm. 13C NMR (100 MHz, CDCl3): δ = 26.6, 41.1, 41.6, 42.0, 52.4, 55.2, 113.7, 116.4, 121.5, 121.6, 126.7, 127.5, 127.8, 128.2, 128.8, 130.6, 130.8, 131.6, 134.1, 135.4, 136.1, 137.1, 138.6, 143.6, 148.0, 158.4, 173.7, 198.0 ppm. HRMS (ESI+): calcd for C35H33N2O3 [M+H]+ 529.2491, found 529.2485.

Methyl 4-(2-benzyl-2-(4-methoxybenzyl)-3-oxo-3-(quinolin-8-ylamino)propyl) benzoate (3g)

Following the general procedure. 2-Benzyl-3-(4-methoxyphenyl)-2-methyl-N-(quinolin-8-yl)propanamide (82.1 mg, 0.2 mmol) and methyl 4-iodobenzoate (157.0
mg, 0.6 mmol) were used. Purification via column chromatography on silica gel (ethyl acetate/petroleum ether = 1/10, v/v) afforded 3g as a white solid (65 mg, 60% yield). When methyl 4-(2-benzyl-2-methyl-3-oxo-3-(quinolin-8-ylamino)propyl) benzoate (87.7 mg, 0.2 mmol) and 4-iodoanisole (140.4 mg, 0.6 mmol) were used as the starting materials, 3g was obtained in 50% yield (54 mg). M.p.: 55-59 °C. 

1H NMR (400 MHz, CDCl3): δ = 3.19 (s, 2H), 3.24-3.26 (m, 4H), 3.68 (s, 3H), 3.86 (s, 3H), 6.70 (d, J = 8.4 Hz, 2H), 7.07 (d, J = 8.8 Hz, 2H), 7.13-7.18 (m, 5H), 7.25 (d, J = 8.8 Hz, 2H), 7.33 (dd, J = 8.4 Hz, 4.4 Hz, 1H), 7.49 (dd, J = 8.4 Hz, 1.2 Hz, 1H), 7.57 (t, J = 8.0 Hz, 1H), 7.83 (d, J = 8.4 Hz, 2H), 8.09 (dd, J = 8.4 Hz, 1.6 Hz, 1H), 8.46 (dd, J = 4.4 Hz, 1.6 Hz, 1H), 8.84 (dd, J = 7.6 Hz, 1.2 Hz, 1H), 9.96 (s, 1H) ppm. 

13C NMR (100 MHz, CDCl3): δ = 41.2, 41.7, 41.8, 52.1, 52.4, 55.2, 113.7, 116.4, 121.5, 121.6, 126.6, 127.5, 127.9, 128.3, 128.4, 128.9, 129.4, 130.6, 130.7, 131.6, 134.1, 136.1, 137.2, 138.7, 143.3, 148.0, 158.4, 167.1, 173.7 ppm. HRMS (ESI+): calcd for C35H33N2O4 [M+H]+ 545.2440, found 545.2433.

MeO

N

H

O

Et2NOC

4-(2-Benzyl-2-(4-methoxybenzyl)-3-oxo-3-(quinolin-8-ylamino)propyl)-N,N-diethylbenzamide (3h)

Following the general procedure. 2-Benzyl-3-(4-methoxyphenyl)-2-methyl-N-(quinolin-8-yl)propanamide (82.1 mg, 0.2 mmol) and N,N-diethyl-4-iodobenzamide (181.8 mg, 0.6 mmol) were used. Purification via column chromatography on silica gel (ethyl acetate/petroleum ether = 1/1, v/v) afforded 3h as a white solid (72 mg, 62% yield). When 4-(2-benzyl-2-methyl-3-oxo-3-(quinolin-8-ylamino)propyl)-N,N-diethylbenzamide (95.9 mg, 0.2 mmol) and 4-iodoanisole (140.4 mg, 0.6 mmol) were used as the starting materials, 3h was obtained in 73% yield (85 mg). M.p.: 39-40 °C. 

1H NMR (400 MHz, CDCl3): δ = 0.97 (m, 3H), 1.19 (m, 3H), 3.09 (m, 2H), 3.18 (s, 2H), 3.23-3.28 (m, 4H), 3.49 (m, 2H), 3.67 (s, 3H), 6.67-6.70 (m, 2H), 7.05-7.09 (m, 2H), 7.13-7.18 (m, 5H), 7.21 (m, 4H), 7.34 (dd, J = 8.4 Hz, 4.4 Hz, 1H), 7.48 (dd, J =
8.4 Hz, 1.6 Hz, 1H), 7.56 (t, J = 8.0 Hz, 1H), 8.08 (dd, J = 8.0 Hz, 1.6 Hz, 1H), 8.49 (dd, J = 4.0 Hz, 1.6 Hz, 1H), 8.84 (dd, J = 7.6 Hz, 1.6 Hz, 1H), 9.99 (s, 1H) ppm. $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ = 13.0, 14.2, 41.2, 41.3, 41.6, 52.3, 55.2, 113.6, 116.3, 121.48, 121.53, 126.3, 126.5, 127.4, 127.8, 128.2, 129.0, 130.58, 130.60, 131.6, 134.2, 135.3, 136.0, 137.3, 138.6, 138.9, 148.1, 158.3, 171.3, 173.9 ppm. HRMS (ESI$^+$): calcd for C$_{38}$H$_{40}$N$_3$O$_3$ [M+H]$^+$ 586.3070, found 586.3074.

2-Benzyl-2-(4-cyanobenzyl)-3-(4-methoxyphenyl)-N-(quinolin-8-yl)propanamide (3i)

Following the general procedure. 2-Benzyl-3-(4-cyanophenyl)-2-methyl-N-(quinolin-8-yl)propanamide (81.1 mg, 0.2 mmol) and 4-iodoanisole (140.4 mg, 0.6 mmol) were used. Purification via column chromatography on silica gel (ethyl acetate/petroleum ether = 1/8, v/v) afforded 3i as a white solid (60 mg, 59% yield). M.p.: 57-60 °C. $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ = 3.18 (s, 2H), 3.228 (s, 2H), 3.234 (s, 2H), 3.69 (s, 3H), 6.69-6.73 (m, 2H), 7.05-7.07 (m, 2H), 7.14-7.22 (m, 5H), 7.25-7.27 (m, 2H), 7.38 (dd, J = 8.0 Hz, 4.0 Hz, 1H), 7.42 (d, J = 8.0 Hz, 2H), 7.51 (dd, J = 8.0 Hz, 1.2 Hz, 1H), 7.57 (t, J = 8.0 Hz, 1H), 8.12 (dd, J = 8.0 Hz, 1.2 Hz, 1H), 8.49 (dd, J = 4.4 Hz, 1.6 Hz, 1H), 8.81 (dd, J = 7.6 Hz, 1.2 Hz, 1H), 9.94 (s, 1H) ppm. $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ = 41.2, 41.7, 42.3, 52.5, 55.2, 110.3, 113.7, 116.4, 119.0, 121.7, 121.8, 126.8, 127.5, 127.9, 128.4, 128.6, 130.5, 131.4, 131.6, 131.8, 133.9, 136.2, 136.9, 138.6, 143.7, 148.1, 158.5, 173.4 ppm. HRMS (ESI$^+$): calcd for C$_{34}$H$_{30}$N$_3$O$_2$ [M+H]$^+$ 512.2338, found 512.2336.

2-Benzyl-2-(4-formylbenzyl)-3-(4-methoxyphenyl)-N-(quinolin-8-yl)propanamide
(3j)
Following the general procedure. 2-Benzyl-3-(4-formylphenyl)-2-methyl-N-(quinolin-8-yl)propanamide (81.7 mg, 0.2 mmol) and 4-iodoanisole (140.4 mg, 0.6 mmol) were used. Purification via column chromatography on silica gel (ethyl acetate/petroleum ether = 1/8, v/v) afforded 3j as a white solid (56 mg, 55% yield).
M.p.: 50-52 °C. $^1$H NMR (400 MHz, CDCl$_3$): $\delta = 3.20$ (s, 2H), 3.26 (s, 2H), 3.27 (s, 2H), 3.69 (s, 3H), 6.69-6.72 (m, 2H), 7.06-7.08 (m, 2H), 7.14-7.21 (m, 5H), 7.32-7.35 (m, 3H), 7.50 (dd, $J = 8.4$ Hz, 1.2 Hz, 1H), 7.57 (t, $J = 8.0$ Hz, 1H), 7.66 (d, $J = 8.0$ Hz, 2H), 8.10 (dd, $J = 8.0$ Hz, 1.6 Hz, 1H), 8.45 (dd, $J = 4.4$ Hz, 1.6 Hz, 1H), 8.83 (dd, $J = 7.6$ Hz, 1.2 Hz, 1H), 9.87 (s, 1H), 9.96 (s, 1H) ppm. $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta = 41.2, 41.7, 42.3, 52.5, 55.2, 113.7, 116.4, 121.6, 121.7, 126.7, 127.5, 127.9, 128.3, 128.8, 129.6, 130.6, 131.3, 131.6, 134.1, 134.9, 136.1, 137.0, 138.6, 145.4, 148.0, 158.5, 173.6, 192.1 ppm. HRMS (ESI$^+$): calcd for C$_{34}$H$_{31}$N$_2$O$_3$ [M+H]$^+$ 515.2335, found 515.2338.

2-Benzyl-2-(3-formylbenzyl)-3-(4-methoxyphenyl)-N-(quinolin-8-yl)propanamide (3k)
Following the general procedure. 2-Benzyl-3-(3-formylphenyl)-2-methyl-N-(quinolin-8-yl)propanamide (81.7 mg, 0.2 mmol) and 4-iodoanisole (140.4 mg, 0.6 mmol) were used. Purification via column chromatography on silica gel (ethyl acetate/petroleum ether = 1/8, v/v) afforded 3k as a white solid (60 mg, 59% yield).
M.p.: 48-50 °C. $^1$H NMR (400 MHz, CDCl$_3$): $\delta = 3.19$ (s, 2H), 3.24-3.27 (m, 4H), 3.69 (s, 3H), 6.69-6.73 (m, 2H), 7.07-7.10 (m, 2H), 7.13-7.21 (m, 5H), 7.30 (t, $J = 7.6$ Hz, 1H), 7.35 (dd, $J = 8.0$ Hz, 4.0 Hz, 1H), 7.45 (d, $J = 7.6$ Hz, 1H), 7.50 (dd, $J = 8.0$ Hz, 1.2 Hz, 1H), 7.57 (t, $J = 8.0$ Hz, 1H), 7.61-7.64 (m, 2H), 8.10 (dd, $J = 8.4$ Hz, 1.6 Hz, 1H), 8.45 (dd, $J = 4.0$ Hz, 1.6 Hz, 1H), 8.83 (dd, $J = 7.6$ Hz, 1.2 Hz, 1H), 9.76 (s,
$\delta = 41.2, 41.6, 41.9, 52.5, 55.3, 113.7, 116.4, 121.6, 121.7, 126.7, 127.4, 127.5, 127.9, 128.4, 128.8, 130.6, 131.6, 132.8, 134.1, 136.1, 136.3, 136.8, 137.1, 138.6, 138.8, 148.0, 158.4, 173.7, 192.4$ ppm. HRMS (ESI$^+$): calcd for C$_{34}$H$_{31}$N$_2$O$_3$ [M+H]$^+$ 515.2335, found 515.2327.

2,2-Dibenzyl-3-(4-methoxyphenyl)-N-(quinolin-8-yl)propanamide (3l)

Following the general procedure. 2-Benzyl-2-methyl-3-phenyl-N-(quinolin-8-yl)propanamide (76.1 mg, 0.2 mmol) and 4-iodoanisole (140.4 mg, 0.6 mmol) were used. Purification via column chromatography on silica gel (ethyl acetate/petroleum ether = 1/10, v/v) afforded 3l as an off-white solid (66 mg, 68% yield). M.p.: 39-42 °C. $^1$H NMR (400 MHz, CDCl$_3$): $\delta = 3.19$ (s, 2H), 3.25 (s, 4H), 3.68 (s, 3H), 6.67-6.71 (m, 2H), 7.08-7.10 (m, 2H), 7.12-7.20 (m, 10H), 7.33 (dd, $J = 8.4$ Hz, 4.0 Hz, 1H), 7.49 (dd, $J = 8.4$ Hz, 1.2 Hz, 1H), 7.57 (t, $J = 8.0$ Hz, 1H), 8.09 (dd, $J = 8.0$ Hz, 1.6 Hz, 1H), 8.47 (dd, $J = 4.4$ Hz, 1.6 Hz, 1H), 8.86 (dd, $J = 7.6$ Hz, 1.2 Hz, 1H), 9.97 (s, 1H) ppm. $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta = 41.2, 41.6, 52.3, 55.2, 113.6, 116.3, 121.4, 121.5, 126.5, 127.5, 127.8, 128.2, 129.2, 130.7, 131.6, 134.3, 136.0, 137.5, 138.7, 147.9, 158.3, 174.1$ ppm. HRMS (ESI$^+$): calcd for C$_{33}$H$_{30}$N$_2$O$_2$ [M+Na]$^+$ 509.2205, found 509.2206.

2-Benzyl-2-(4-methoxybenzyl)-3-(naphthalen-1-yl)-N-(quinolin-8-yl)propanamide (3m)

Following the general procedure. 2-Benzyl-2-methyl-3-(naphthalen-1-yl)-N-(quinolin-8-yl)propanamide (86.1 mg, 0.2 mmol) and 4-iodoanisole (140.4 mg, 0.6 mmol) were used. Purification via column chromatography on silica gel (ethyl acetate/petroleum ether = 1/10, v/v) afforded 3m as an off-white solid (68 mg, 73% yield). M.p.: 194-196 °C. $^1$H NMR (400 MHz, CDCl$_3$): $\delta = 3.19$ (s, 2H), 3.25 (s, 4H), 3.68 (s, 3H), 6.67-6.71 (m, 2H), 7.08-7.10 (m, 2H), 7.12-7.20 (m, 10H), 7.33 (dd, $J = 8.4$ Hz, 4.0 Hz, 1H), 7.49 (dd, $J = 8.4$ Hz, 1.2 Hz, 1H), 7.57 (t, $J = 8.0$ Hz, 1H), 8.09 (dd, $J = 8.0$ Hz, 1.6 Hz, 1H), 8.47 (dd, $J = 4.4$ Hz, 1.6 Hz, 1H), 8.86 (dd, $J = 7.6$ Hz, 1.2 Hz, 1H), 9.97 (s, 1H) ppm. $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta = 41.2, 41.6, 52.3, 55.2, 113.6, 116.3, 121.4, 121.5, 126.5, 127.5, 127.8, 128.2, 129.2, 130.7, 131.6, 134.3, 136.0, 137.5, 138.7, 147.9, 158.3, 174.1$ ppm. HRMS (ESI$^+$): calcd for C$_{32}$H$_{29}$N$_2$O$_2$ [M+Na]$^+$ 509.2205, found 509.2206.
acetate/petroleum ether = 1/8, v/v) afforded 3m as an off-white solid (84 mg, 79% yield). M.p.: 63-66 °C. $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ = 3.34 (s, 2H), 3.40 (d, $J$ = 3.2 Hz, 2H), 3.59 (s, 2H), 3.67 (s, 3H), 6.66-6.69 (m, 2H), 7.08 (d, $J$ = 8.4 Hz, 2H), 7.12-7.29 (m, 8H), 7.32 (t, $J$ = 7.6 Hz, 1H), 7.40 (dd, $J$ = 8.4 Hz, 1.2 Hz, 1H), 7.47 (d, $J$ = 8.0 Hz, 1H), 7.50 (t, $J$ = 8.0 Hz, 1H), 7.59 (t, $J$ = 8.0 Hz, 2H), 7.95 (d, $J$ = 8.4 Hz, 1H), 7.98 (dd, $J$ = 8.0 Hz, 1.2 Hz, 1H), 8.22 (dd, $J$ = 4.4 Hz, 1.6 Hz, 1H), 8.78 (dd, $J$ = 7.6 Hz, 1.2 Hz, 1H), 9.74 (s, 1H) ppm. $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ = 37.7, 41.0, 41.6, 51.9, 55.2, 113.6, 116.1, 121.2, 123.8, 125.11, 125.13, 125.8, 126.5, 127.27, 127.29, 127.5, 127.6, 128.2, 128.4, 129.3, 130.8, 131.7, 133.3, 133.4, 133.9, 134.2, 135.7, 137.6, 138.4, 147.6, 158.3, 174.3 ppm. HRMS (ESI$^+$): calcd for C$_{37}$H$_{32}$N$_2$NaO$_2$ [M+Na]$^+$ 559.2361, found 559.2364.

2-(4-Methoxybenzyl)-3-phenyl-N-(quinolin-8-yl)acrylamide (4)

Following the general procedure. 2-Methyl-3-phenyl-N-(quinolin-8-yl)acrylamide (57.7 mg, 0.2 mmol), and 4-iodoanisole (140.4 mg, 0.6 mmol) were used. Purification via column chromatography on silica gel (ethyl acetate/petroleum ether = 1/10, v/v) afforded 4 as a mixture of (E)- and (Z)-isomers (46 mg, 58% yield). The ratio of (E)-4/(Z)-4 was 8:1 as determined by $^1$H NMR. $^1$H NMR (400 MHz, CDCl$_3$, a mixture of two isomers): $\delta$ = 3.77 (s, OCH$_3$, major isomer), 3.83 (s, OCH$_3$, minor isomer), 4.12 (s, major isomer), 4.21 (s, minor isomer), 6.60 (d, $J$ = 8.8 Hz, minor isomer), 6.88 (d, $J$ = 8.8 Hz, major isomer), 6.92 (d, $J$ = 8.8 Hz, minor isomer), 7.18-7.23 (m), 7.28-7.44 (m), 7.48 (d, $J$ = 8.4 Hz, major isomer), 7.53 (t, $J$ = 7.6 Hz, major isomer), 7.91 (s, minor isomer), 7.93 (s, major isomer), 8.06 (dd, $J$ = 8.4 Hz, 1.6 Hz, minor isomer), 8.12 (dd, $J$ = 8.4 Hz, 1.6 Hz, major isomer), 8.53 (dd, $J$ = 4.4 Hz, 1.6 Hz, minor isomer), 8.68 (dd, $J$ = 4.0 Hz, 1.6 Hz, major isomer), 8.75 (d, $J$ = 7.6 Hz, minor isomer), 8.83 (dd, $J$ = 7.6 Hz, 1.2 Hz, major isomer), 9.58 (s, minor isomer), 10.40 (s,
major isomer) ppm. $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ = 32.9, 33.8, 55.4, 55.5, 113.6, 114.2, 114.3, 116.7, 121.6, 121.7, 126.7, 127.5, 128.0, 128.3, 128.5, 128.7, 129.2, 129.5, 130.0, 130.2, 130.8, 130.9, 134.9, 135.4, 135.9, 136.3, 137.19, 137.23, 138.8, 148.1, 158.5, 167.0 ppm. HRMS (ESI$^+$): calcd for C$_{26}$H$_{22}$N$_2$NaO$_2$ [M+Na]$^+$ 417.1579, found 417.1575.

2-Benzyl-3-(4-methoxyphenyl)-2-methyl-N-(quinolin-8-yl)propanamide (5)

Following the general procedure except that the reaction temperature was 150 °C and 2-nitrobenzoic acid (6.7 mg, 0.04 mmol) instead of PivOH was added. 2,2-Dimethyl-3-phenyl-N-(quinolin-8-yl)propanamide (60.9 mg, 0.2 mmol) and 4-iodoanisole (140.4 mg, 0.6 mmol) were used. Purification via column chromatography on silica gel (ethyl acetate/petroleum ether = 1/20, v/v) afforded 5 as a white solid (49 mg, 60% yield). M.p.: 80-82 °C. $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ = 1.31 (s, 3H), 2.74 (d, $J$ = 13.2 Hz, 1H), 2.78 (d, $J$ = 13.2 Hz, 1H), 3.43 (d, $J$ = 13.6 Hz, 1H), 3.49 (d, $J$ = 13.2 Hz, 1H), 3.67 (s, 3H), 6.69-6.71 (m, 2H), 7.10-7.23 (m, 7H), 7.36 (dd, $J$ = 8.4 Hz, 4.4 Hz, 1H), 7.48 (dd, $J$ = 8.4 Hz, 1.2 Hz, 1H), 7.56 (t, $J$ = 7.6 Hz, 1H), 8.09 (dd, $J$ = 8.4 Hz, 1.6 Hz, 1H), 8.62 (dd, $J$ = 4.4 Hz, 1.6 Hz, 1H), 8.88 (d, $J$ = 7.6 Hz, 1H), 9.92 (s, 1H) ppm. $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ = 19.7, 45.9, 46.6, 50.2, 55.2, 113.5, 116.4, 121.49, 121.52, 126.5, 127.4, 127.9, 128.1, 129.7, 130.5, 131.4, 134.4, 136.2, 137.8, 138.8, 148.2, 158.3, 174.8 ppm. HRMS (ESI$^+$): calcd for C$_{27}$H$_{26}$N$_2$NaO$_2$ [M+Na]$^+$ 433.1892, found 433.1891.

2-(4-Methoxybenzyl)-2-methyl-N-(quinolin-8-yl)butanamide (6)

Following the general procedure except that the reaction temperature was 150 °C. 2,2-Dimethyl-N-(quinolin-8-yl)butanamide (48.5 mg, 0.2 mmol) and 4-idoanisole (140.4 mg, 0.6 mmol) were used. Purification via column chromatography on silica
gel (ethyl acetate/petroleum ether = 1/20, v/v) afforded 6 as colourless oil (45 mg, 64% yield). $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ = 0.99 (t, $J$ = 7.6 Hz, 3H), 1.34 (s, 3H), 1.54-1.63 (m, 1H), 2.00-2.09 (m, 1H), 2.77 (d, $J$ = 13.2 Hz, 1H), 3.20 (d, $J$ = 13.6 Hz, 1H), 3.68 (s, 3H), 6.69-6.73 (m, 2H), 7.09-7.11 (m, 2H), 7.41 (dd, $J$ = 8.0 Hz, 4.0 Hz, 1H), 7.49 (dd, $J$ = 8.4 Hz, 1.2 Hz, 1H), 7.55 (t, $J$ = 7.6 Hz, 1H), 8.13 (dd, $J$ = 8.0 Hz, 0.8 Hz, 1H), 8.74 (dd, $J$ = 4.4 Hz, 1.6 Hz, 1H), 8.85 (d, $J$ = 7.6 Hz, 1H), 10.12 (s, 1H) ppm. $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ = 9.3, 20.3, 45.3, 49.2, 55.2, 113.5, 116.3, 121.4, 121.6, 127.5, 128.0, 130.0, 131.3, 134.6, 136.3, 138.9, 148.3, 158.2, 175.5 ppm. HRMS (ESI$^+$): calcd for C$_{22}$H$_{24}$N$_2$NaO$_2$ [M+Na]$^+$ 371.1735, found 371.1732.

2,2-Bis(4-methoxybenzyl)-N-(quinolin-8-yl)undecanamide (7)

Following the general procedure. 2,2-Dimethyl-N-(quinolin-8-yl)undecanamide (68.1 mg, 0.2 mmol) and 4-iodoanisole (187.2 mg, 0.8 mmol) were used. Purification via column chromatography on silica gel (ethyl acetate/petroleum ether = 1/20, v/v) afforded 7 as colourless oil (64 mg, 58% yield). $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ = 0.89 (t, $J$ = 6.8 Hz, 3H), 1.27-1.35 (m, 12H), 1.66 (m, 4H), 2.95 (d, $J$ = 14.0 Hz, 2H), 3.23 (d, $J$ = 14.0 Hz, 2H), 3.67 (s, 6H), 6.70 (d, $J$ = 8.4 Hz, 4H), 7.12 (d, $J$ = 8.4 Hz, 4H), 7.37 (dd, $J$ = 8.4 Hz, 4.4 Hz, 1H), 7.49 (d, $J$ = 8.0 Hz, 1H), 7.57 (t, $J$ = 8.0 Hz, 1H), 8.11 (d, $J$ = 8.4 Hz, 1H), 8.63 (d, $J$ = 3.2 Hz, 1H), 8.87 (d, $J$ = 7.2 Hz, 1H), 9.99 (s, 1H) ppm. $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ = 14.3, 22.8, 24.2, 29.4, 29.6, 29.7, 30.2, 32.0, 32.1, 41.3, 53.1, 55.1, 113.5, 116.3, 121.3, 121.5, 127.5, 127.9, 129.8, 131.2, 134.4, 136.1, 138.8, 148.1, 158.1, 174.8 ppm. HRMS (ESI$^+$): calcd for C$_{36}$H$_{44}$N$_2$NaO$_3$ [M+Na]$^+$ 575.3250, found 575.3242.
2-(4-Methoxybenzyl)-3-(4-methoxyphenyl)-2-phenyl-N-(quinolin-8-yl)propanamide (8)

Following the general procedure. 2-Methyl-2-phenyl-N-(quinolin-8-yl)propanamide (58.1 mg, 0.2 mmol) and 4-iodoanisole (187.2 mg, 0.8 mmol) were used. Purification via column chromatography on silica gel (ethyl acetate/petroleum ether = 1/10, v/v) afforded 8 as a white solid (57 mg, 57% yield). M.p.: 146-148 °C. $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ = 3.38-3.47 (m, 4H), 3.71 (s, 6H), 6.63-6.67 (m, 4H), 6.85-6.88 (m, 4H), 7.28-7.39 (m, 6H), 7.47 (dd, $J$ = 8.4 Hz, 1.2 Hz, 1H), 7.54 (t, $J$ = 8.0 Hz, 1H), 8.09 (dd, $J$ = 8.4 Hz, 1.6 Hz, 1H), 8.54 (dd, $J$ = 4.4 Hz, 1.6 Hz, 1H), 8.74 (dd, $J$ = 7.6 Hz, 1.2 Hz, 1H), 9.87 (s, 1H) ppm. $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ = 41.1, 55.2, 58.4, 113.3, 116.2, 121.3, 121.6, 127.3, 127.5, 128.0, 128.3, 128.6, 129.3, 131.7, 134.6, 136.1, 138.7, 142.6, 148.2, 158.2, 174.0 ppm. HRMS (ESI$^+$): calcd for C$_{33}$H$_{30}$N$_2$NaO$_3$ [M+Na]$^+$ 525.2154, found 525.2154.

3-(4-Methoxyphenyl)-2-methyl-N-(quinolin-8-yl)propanamide (9)

Following the general procedure. N-(Quinolin-8-yl)isobutyramide (42.9 mg, 0.2 mmol) and 4-iodoanisole (140.4 mg, 0.6 mmol) were used. Purification via column chromatography on silica gel (ethyl acetate/petroleum ether = 1/20, v/v) afforded 9 as colourless oil (32 mg, 50% yield). $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ = 1.33 (d, $J$ = 6.4 Hz, 3H), 2.74-2.79 (m, 1H), 2.81-2.90 (m, 1H), 3.14 (dd, $J$ = 13.2 Hz, 7.2 Hz, 1H), 3.72 (s, 3H), 6.77-6.80 (m, 2H), 7.16-7.19 (m, 2H), 7.43 (dd, $J$ = 8.4 Hz, 4.4 Hz, 1H), 7.48 (dd, $J$ = 8.4 Hz, 1.6 Hz, 1H), 7.53 (t, $J$ = 8.0 Hz, 1H), 8.14 (dd, $J$ = 8.0 Hz, 1.6 Hz, 1H), 8.75 (dd, $J$ = 4.4 Hz, 1.6 Hz, 1H), 8.79 (dd, $J$ = 7.6 Hz, 1.6 Hz, 1H), 9.75 (s, 1H) ppm. $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ = 17.8, 39.6, 45.2, 55.3, 113.9, 116.6, 121.5, 121.6, 127.5, 128.0, 130.1, 131.8, 134.6, 136.4, 138.5, 148.2, 158.2, 174.7 ppm.
HRMS (ESI\(^+\)): calcd for C\(_{20}\)H\(_{20}\)N\(_2\)NaO\(_2\) [M+Na]\(^+\) 343.1422, found 343.1427.

**VIII. References**


IX. Copy of $^1$H-$^1$H NOESY spectrum of 4
X. Copies of $^1$H and $^{13}$C NMR spectra

![NMR spectra image]

- $^1$H NMR spectra
  - δ (ppm): 7.05, 7.54, 7.82, 8.07
  - δ (ppm): 7.05, 7.54, 7.82, 8.07

- $^{13}$C NMR spectra
  - δ (ppm): 121.46, 121.36
  - δ (ppm): 121.46, 121.36

These spectra provide detailed information about the chemical shifts and proton/resonance assignments for the molecules of interest.