

Supporting Information

Microwave-accelerated cross-dehydrogenative-coupling (CDC) of *N*-(quinolin-8-yl)amides with acetone/acetonitrile under metal-free conditions

Chao Zhou, Yunwei Liu, Qi Luo, Yicheng Zhang,* Jingwen Zhou, Haoyu Zhang, and
Jie Liu*

Key Laboratory of Green and Precise Synthetic Chemistry, Ministry of Education, Huaibei
Normal University, Huaibei, Anhui 235000, P. R. China; E-mail: jieliu_1024@163.com;
lbqzhych@163.com.

Table of Contents

1. General Information	2
2. Experimental Section	2
(1) The optimization of reaction conditions	2
(2) Typical procedure for 1a and 2a	5
(3) The radical inhibiting experiments.....	5
3. Characterization data for the products.....	7
4. Copies of ¹ H, ¹³ C NMR and ¹⁹ F NMR spectra.....	21

1. General Information

The following starting materials *N*-(quinolin-8-yl)amides **1** were synthesized according to previously described procedure (F. Doraghi, E. Kianmehr and A. Foroumadi, *Org. Chem. Front.*, **2021**, *8*, 5424–5431). Other starting materials were purchased from commercial suppliers. Analytical thin layer chromatography (TLC) was performed on pre-coated silica gel 60 F₂₅₄ plates. Compounds were visualized by exposure to UV light. Flash column chromatography was performed with silica gel (200 – 300 meshes). NMR spectra were recorded on a 600 MHz spectrometer at ambient temperature, and chemical shifts were given in dimensionless δ values and were frequency referenced relative to TMS in ¹H and ¹³C NMR spectroscopy. The peak patterns are indicated as follows: **s**, singlet; **d**, doublet; **t**, triplet; **q**, quartet; **m**, multiplet; **dd**, doublet of doublet. The coupling constants, *J*, are reported in Hertz (Hz). HRMS data were recorded on an Agilent Technologies 6540 UHD ESI-TOF mass spectrometer. All MW reactions were carried out under microwave irradiation conditions and air atmosphere in a Discover SP (CEM) microwave reactor.



2. Experimental Section

(1) The optimization of reaction conditions

Table S1. Screening oxidants

Entry	Oxidant	Yield 3a (%)
1	H ₂ O ₂	n.r.
2	DTBP	n.r.
3	LPO	trace
4	TBHP	n.r.
5	BPO	62

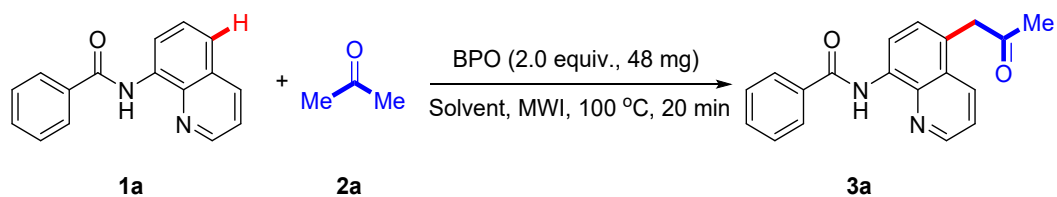
All reactions were carried out with **1a** (0.10 mmol), **2a** (3.0 mL) and oxidant (1.5 equiv.) at 100 °C under microwave irradiation for 20 min; Isolated yield; n.r. = no reaction.

Table S2. Screening the loading of BPO

Entry	BPO (x equiv.)	Yield 3a (%)
1	3.0	72
2	2.5	73
3	2.0	71
4	1.5	62
5	1.0	41
6	0.2	trace
7	0	n.r.

All reactions were carried out with **1a** (0.10 mmol), **2a** (3.0 mL) and BPO (x equiv.) at 100 °C under microwave irradiation for 20 min; isolated yield. n.r. = no reaction.

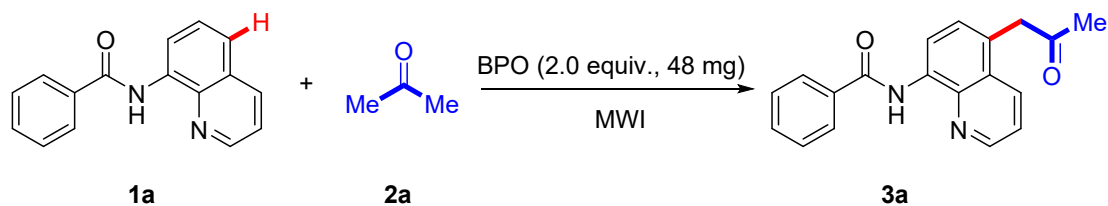
Table S3. Screening solvents



Entry	Solvent	Yield 3a (%)
1	MeCN	53
2	1,4-dioxane	18
3	THF	25
4	DCE	42
5	Cyclohexane	48
6	DCM	39
7	DMSO	20
8	neat	71

All reactions were carried out with **1a** (0.10 mmol), **2a** (2.0 equiv.), BPO (2.0 equiv., 48.0 mg) and solvent (3.0 mL) at 100 °C under microwave irradiation for 20 min; isolated yield.

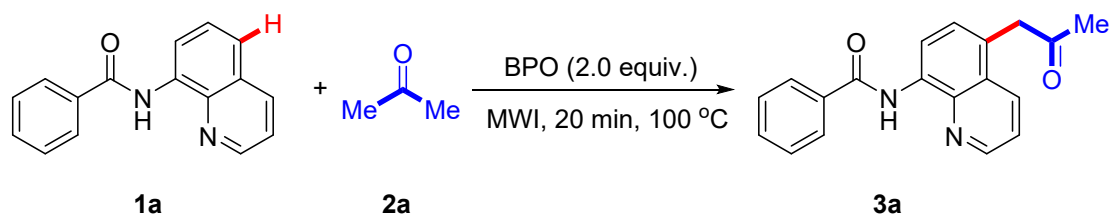
Table S4. Screening reaction time and temperature



Entry	Temp. (°C)	Time	Yield 3a (%)
1	120	20 min	71
2	110	20 min	70
3	100	20 min	71
4	100	30 min	69
5	100	15 min	60
6	100	10 min	47
7	90	20 min	40
8	80	20 min	32
9	70	20 min	trace
10 ^[a]	100	12 h	18

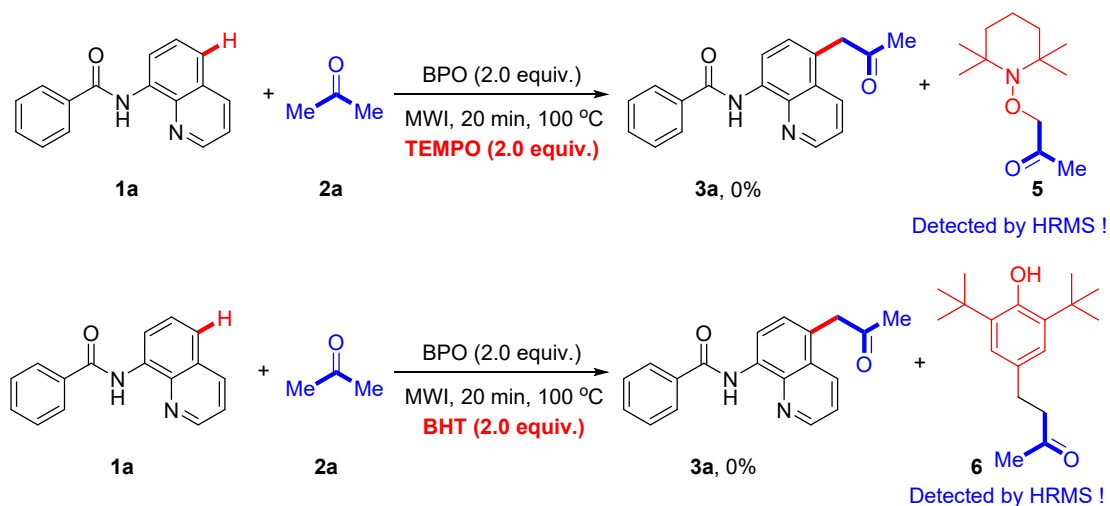
All the reactions were carried out with **1a** (0.10 mmol), **2a** (3.0 mL) and BPO (2.0 equiv., 48 mg) under microwave irradiation; isolated yield. ^[a]In an oil bath.

(2) Typical procedure for 1a and 2a



In the microwave tube was charged with *N*-(quinolin-8-yl)benzamide (**1a**, 0.1 mmol), acetone (**2a**, 3.0 mL) and BPO (2.0 equiv., 48.0 mg). The reaction vessel was placed in a Discover SP (CEM) microwave reactor and the reaction mixture was irradiated at 150 W and 100 °C for 20 min. After completion of the reaction, the mixture was concentrated to yield the crude product, which was further purified by flash chromatography (petroleum ether / ethyl acetate = 5 :1) to give the product **3a** (white solid, 21.6 mg, 71% yield).

(3) The Radical Inhibiting Experiments



In a microwave tube was charged with *N*-(quinolin-8-yl)benzamide (**1a**, 0.1 mmol), acetone (**2a**, 3.0 mL), BPO (2.0 equiv., 48.0 mg) and TEMPO or BHT (2.0 equiv.). The reaction vessel was placed in a Discover SP (CEM) microwave reactor, and the reaction mixture was irradiated at 150 W and 100 °C for 20 min. In the reaction mixture, no desired product **3a** was detected, while an adduct of TEMPO or BHT with

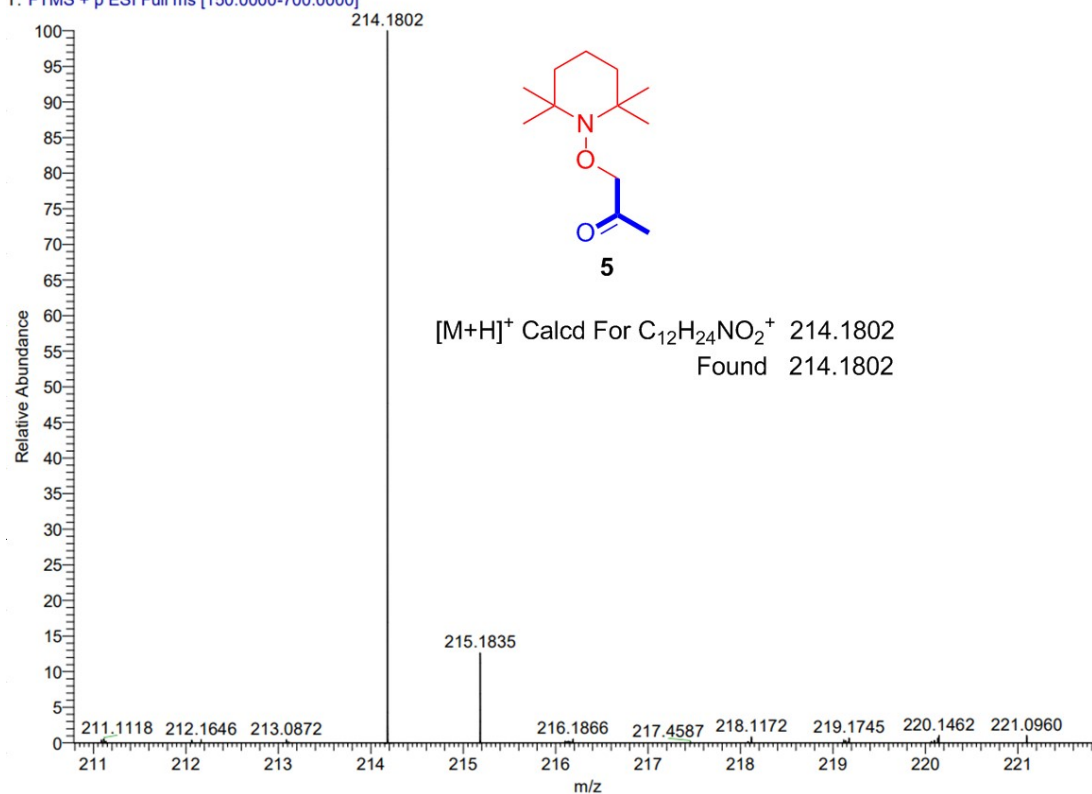
an acetyl radical was formed, which was detected by HPLC-HRMS.

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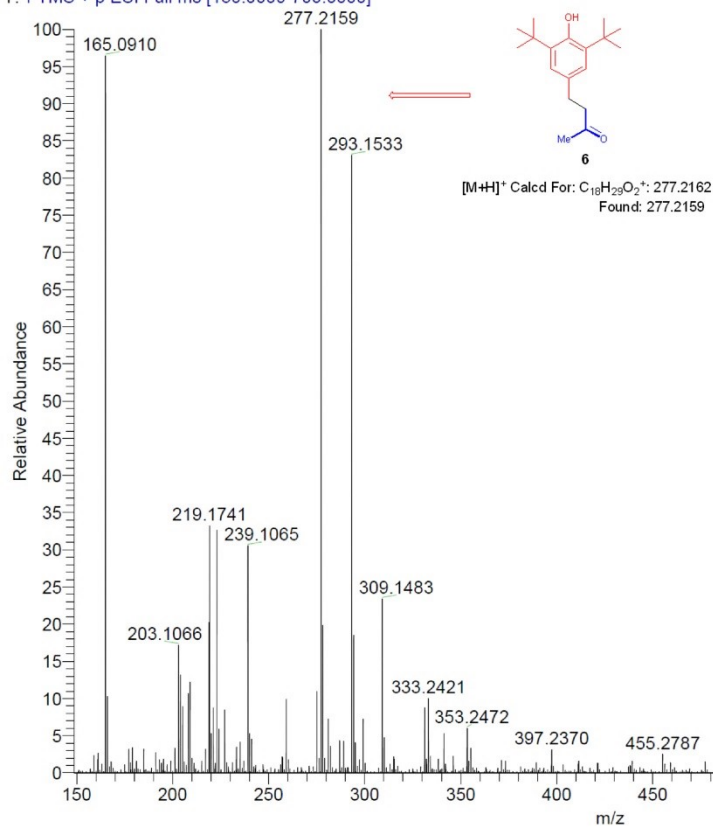
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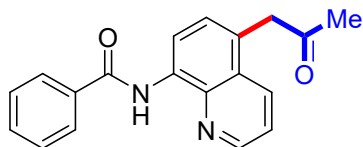
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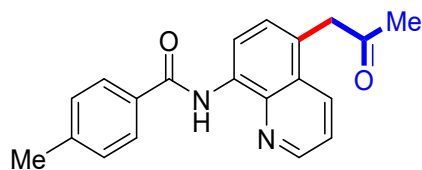
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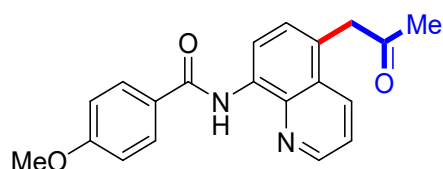
3. Characterization data for the products



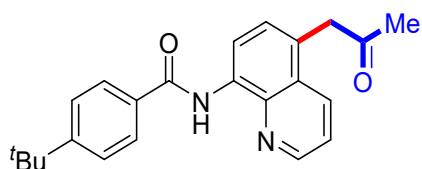
***N*-(5-(2-oxopropyl)quinolin-8-yl)benzamide (3a)**. White solid; 21.6 mg, 71% yield; ¹H NMR (600 MHz, CDCl₃) δ: 10.79 (s, 1H), 8.91 (d, *J* = 7.8 Hz, 1H), 8.87–8.86 (m, 1H), 8.28 (d, *J* = 7.0 Hz, 1H), 8.10–8.08 (m, 2H), 7.59–7.54 (m, 3H), 7.52–7.49 (m, 2H), 4.09 (s, 2H), 2.16 (s, 3H); ¹³C NMR (151 MHz, CDCl₃) δ: 206.3, 165.5, 148.1, 139.0, 135.0, 134.3, 133.2, 131.9, 129.4, 128.8, 127.3, 127.1, 125.0, 121.9, 116.3, 48.3, 28.9. HRMS (ESI) ([M+H]⁺) Calcd For C₁₉H₁₇N₂O₂⁺: 305.1285, Found: 305.1280. The NMR data are consistent with the reported values (See: Liu, D.; Xia, Z.; Xiao, Y.; Yu, Y.; Yu, L.; Song, Z.; Wu, Q.; Zhang, J.; Tan, Z. *Eur. J. Org. Chem.* **2021**, *2021*, 5012–5016).



4-methyl-*N*-(5-(2-oxopropyl)quinolin-8-yl)benzamide (3b). White solid; 21.0 mg, 66% yield; ^1H NMR (600 MHz, CDCl_3) δ : 10.76 (s, 1H), 8.90 (d, $J = 7.8$ Hz, 1H), 8.87–8.86 (m, 1H), 8.28–8.26 (m, 1H), 7.98 (d, $J = 7.9$ Hz, 2H), 7.51–7.49 (m, 2H), 7.35–7.34 (m, 2H), 4.08 (s, 2H), 2.45 (s, 3H), 2.16 (s, 3H); ^{13}C NMR (151 MHz, CDCl_3) δ : 206.3, 165.5, 148.0, 142.4, 139.0, 134.4, 133.2, 132.2, 129.4, 129.4, 127.3, 127.1, 124.9, 121.8, 116.3, 48.3, 28.9, 21.5. HRMS (ESI) ($[\text{M}+\text{H}]^+$) Calcd For $\text{C}_{20}\text{H}_{19}\text{N}_2\text{O}_2^+$: 319.1441, Found: 319.1438.

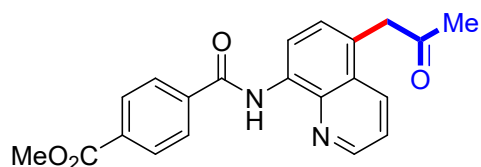


4-methoxy-*N*-(5-(2-oxopropyl)quinolin-8-yl)benzamide (3c). White solid; 23.4 mg, 70% yield; ^1H NMR (600 MHz, CDCl_3) δ : 10.71 (s, 1H), 8.88 (d, $J = 7.8$ Hz, 1H), 8.86–8.85 (m, 1H), 8.26–8.25 (m, 1H), 8.06–8.04 (m, 2H), 7.50–7.47 (m, 2H), 7.04–7.03 (m, 2H), 4.07 (s, 2H), 3.89 (s, 3H), 2.15 (s, 3H); ^{13}C NMR (151 MHz, CDCl_3) δ : 206.3, 165.0, 162.5, 148.0, 139.0, 134.5, 133.1, 129.4, 129.1, 127.3, 127.1, 124.7, 121.8, 116.0, 114.0, 55.4, 48.3, 28.9. HRMS (ESI) ($[\text{M}+\text{H}]^+$) Calcd For $\text{C}_{20}\text{H}_{19}\text{N}_2\text{O}_3^+$: 335.1390, Found: 335.1387.

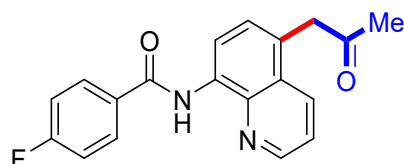


4-(*tert*-butyl)-*N*-(5-(2-oxopropyl)quinolin-8-yl)benzamide (3d). White solid; 27.0 mg, 75% yield; ^1H NMR (600 MHz, CDCl_3) δ : 10.76 (s, 1H), 8.90 (d, $J = 7.9$ Hz, 1H), 8.85–8.84 (m, 1H), 8.25 (d, $J = 6.9$ Hz, 1H), 8.02 (d, $J = 8.4$ Hz, 2H), 7.58–7.56 (m,

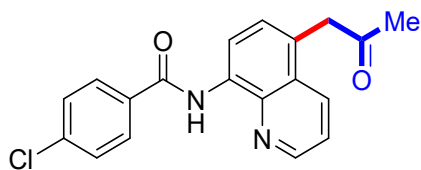
2H), 7.50–7.47 (m, 2H), 4.07 (s, 2H), 2.15 (s, 3H), 1.38 (s, 9H); ^{13}C NMR (151 MHz, CDCl_3) δ : 206.3, 165.4, 155.4, 148.0, 139.0, 134.4, 133.0, 132.2, 129.3, 127.1, 127.0, 125.7, 124.8, 121.8, 116.0, 48.2, 34.9, 31.1, 28.9. HRMS (ESI) ($[\text{M}+\text{H}]^+$) Calcd For $\text{C}_{23}\text{H}_{25}\text{N}_2\text{O}_2^+$: 361.1911, Found: 361.1907.



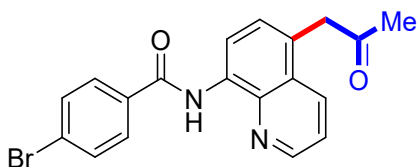
Methyl 4-((5-(2-oxopropyl)quinolin-8-yl)carbamoyl)benzoate (3e). White solid; 25.0 mg, 69% yield; ^1H NMR (600 MHz, CDCl_3) δ : 10.81 (s, 1H), 8.89–8.86 (m, 2H), 8.26 (d, $J = 8.5$ Hz, 1H), 8.21–8.20 (m, 2H), 8.13–8.11 (m, 2H), 7.52–7.50 (m, 1H), 7.49 (d, $J = 7.8$ Hz, 1H), 4.09 (s, 2H), 3.97 (s, 3H), 2.18 (s, 3H); ^{13}C NMR (151 MHz, CDCl_3) δ : 206.1, 166.2, 164.3, 148.2, 138.9, 138.8, 133.9, 133.1, 132.9, 130.0, 129.2, 127.2, 127.0, 125.4, 121.9, 116.3, 52.4, 48.2, 29.0. HRMS (ESI) ($[\text{M}+\text{H}]^+$) Calcd For $\text{C}_{21}\text{H}_{19}\text{N}_2\text{O}_4^+$: 363.1339, Found: 363.1334.



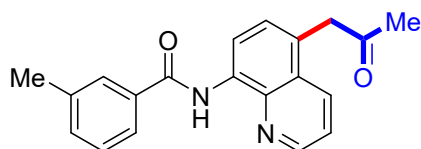
4-fluoro-N-(5-(2-oxopropyl)quinolin-8-yl)benzamide (3f). White solid; 19.3 mg, 60% yield; ^1H NMR (600 MHz, $\text{DMSO}-d_6$) δ : 10.66 (s, 1H), 8.98–8.97 (m, 1H), 8.64 (d, $J = 7.8$ Hz, 1H), 8.40–8.39 (m, 1H), 8.13–8.10 (m, 2H), 7.68–7.66 (m, 1H), 7.50 (d, $J = 7.9$ Hz, 1H), 7.45 (t, $J = 8.8$ Hz, 2H), 4.30 (s, 2H), 2.25 (s, 3H); ^{13}C NMR (151 MHz, $\text{DMSO}-d_6$) δ : 201.46 (d, $J = 7.2$ Hz), 160.64, 158.98 (d, $J = 2.2$ Hz), 144.20, 134.06, 129.52, 128.60, 126.52 (d, $J = 2.7$ Hz), 125.33 (d, $J = 9.2$ Hz), 124.08, 122.61 (d, $J = 9.6$ Hz), 117.53, 111.87, 111.55, 111.41, 41.76, 24.98; HRMS (ESI) ($[\text{M}+\text{H}]^+$) Calcd For $\text{C}_{19}\text{H}_{16}\text{FN}_2\text{O}_2^+$: 323.1190, Found: 323.1190.



4-chloro-*N*-(5-(2-oxopropyl)quinolin-8-yl)benzamide (3g). White solid; 24.7 mg, 73% yield; ^1H NMR (600 MHz, CDCl_3) δ : 10.73 (s, 1H), 8.86–8.84 (m, 2H), 8.26–8.24 (m, 1H), 8.01–7.99 (m, 2H), 7.51–7.49 (m, 3H), 7.47 (d, $J = 8.1$ Hz, 1H), 4.08 (s, 2H), 2.17 (s, 3H); ^{13}C NMR (151 MHz, CDCl_3) δ : 206.1, 164.2, 148.1, 138.9, 138.1, 133.9, 133.3, 133.1, 129.2, 129.0, 128.6, 127.0, 125.2, 121.9, 116.2, 48.1, 28.9. HRMS (ESI) ($[\text{M}+\text{H}]^+$) Calcd For $\text{C}_{19}\text{H}_{16}^{35}\text{ClN}_2\text{O}_2^+$: 339.0895, Found: 339.0895.

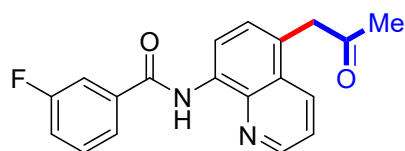


4-bromo-*N*-(5-(2-oxopropyl)quinolin-8-yl)benzamide (3h). White solid; 24.4 mg, 64% yield; ^1H NMR (600 MHz, CDCl_3) δ : 10.74 (s, 1H), 8.87–8.85 (m, 2H), 8.27 (d, $J = 6.9$ Hz, 1H), 7.95–7.93 (m, 2H), 7.68–7.67 (m, 2H), 7.53–7.51 (m, 1H), 7.49 (d, $J = 7.8$ Hz, 1H), 4.09 (s, 2H), 2.17 (s, 3H); ^{13}C NMR (151 MHz, CDCl_3) δ : 206.1, 164.4, 148.1, 138.9, 134.0, 133.8, 133.2, 132.0, 129.3, 128.8, 127.1, 126.6, 125.3, 121.9, 116.3, 48.2, 29.0. HRMS (ESI) ($[\text{M}+\text{H}]^+$) Calcd For $\text{C}_{19}\text{H}_{16}^{79}\text{BrN}_2\text{O}_2^+$: 383.0390, Found: 383.0388.

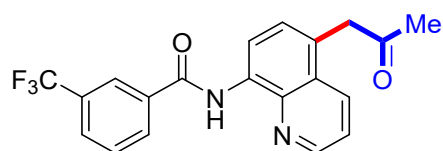


3-methyl-*N*-(5-(2-oxopropyl)quinolin-8-yl)benzamide (3i). White solid; 14.6 mg, 46% yield; ^1H NMR (600 MHz, CDCl_3) δ : 10.75 (s, 1H), 8.91 (d, $J = 7.8$ Hz, 1H), 8.88–8.87 (m, 1H), 8.28–8.27 (m, 1H), 7.89–7.86 (m, 2H), 7.53–7.50 (m, 2H), 7.45–7.43 (m, 1H), 7.40–7.39 (m, 1H), 4.09 (s, 2H), 2.49 (s, 3H), 2.16 (s, 3H); ^{13}C NMR

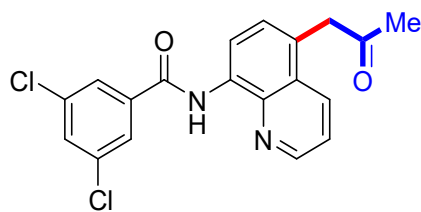
(151 MHz, CDCl₃) δ : 206.3, 165.7, 148.1, 139.1, 138.7, 135.1, 134.4, 133.1, 132.6, 129.4, 128.6, 128.0, 127.1, 124.9, 124.2, 121.9, 116.2, 48.4, 28.9, 21.5. HRMS (ESI) ([M+H]⁺) Calcd For C₂₀H₁₉N₂O₂⁺: 319.1441, Found: 319.1441. The NMR data are consistent with the reported values (See: Liu, D.; Xia, Z.; Xiao, Y.; Yu, Y.; Yu, L.; Song, Z.; Wu, Q.; Zhang, J.; Tan, Z. *Eur. J. Org. Chem.* **2021**, 2021, 5012–5016).



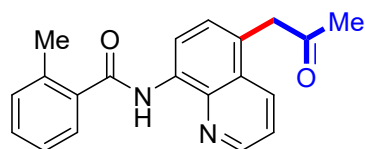
3-fluoro-N-(5-(2-oxopropyl)quinolin-8-yl)benzamide (3j). White solid; 15.8 mg, 49% yield; ¹H NMR (600 MHz, CDCl₃) δ : 10.76 (s, 1H), 8.87–8.86 (m, 2H), 8.28–8.26 (m, 1H), 7.85 (d, *J* = 7.6 Hz, 1H), 7.79–7.77 (m, 1H), 7.53–7.49 (m, 3H), 7.30–7.27 (m, 1H), 4.10 (s, 2H), 2.17 (s, 3H); ¹³C NMR (151 MHz, CDCl₃) δ : 206.13, 164.02 (d, *J* = 2.7 Hz), 163.73, 148.16, 138.96, 137.28 (d, *J* = 6.9 Hz), 133.95, 133.19, 130.45 (d, *J* = 7.9 Hz), 129.27, 127.09, 125.37, 122.68 (d, *J* = 3.1 Hz), 121.94, 118.88 (d, *J* = 21.3 Hz), 116.36, 114.66 (d, *J* = 23.0 Hz), 48.24, 28.97; ¹⁹F NMR (565 MHz, CDCl₃) δ : –111.50. HRMS (ESI) ([M+H]⁺) Calcd For C₁₉H₁₆FN₂O₂⁺: 323.1190, Found: 323.1186.



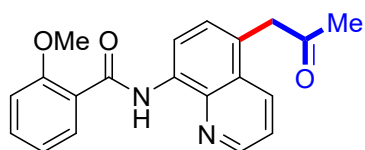
N-(5-(2-oxopropyl)quinolin-8-yl)-3-(trifluoromethyl)benzamide (3k). White solid; 19.7 mg, 53% yield; ¹H NMR (600 MHz, CDCl₃) δ : 10.81 (s, 1H), 8.88–8.87 (m, 2H), 8.34 (s, 1H), 8.27 (d, *J* = 8.5 Hz, 1H), 8.24 (d, *J* = 7.8 Hz, 1H), 7.85–7.83 (m, 1H), 7.69 (t, *J* = 7.8 Hz, 1H), 7.53–7.51 (m, 1H), 7.50 (d, *J* = 7.9 Hz, 1H), 4.10 (s, 2H), 2.18 (s, 3H); ¹³C NMR (151 MHz, CDCl₃) δ : 206.04, 163.83, 148.23, 138.95, 135.85, 133.83, 133.19, 131.40 (q, *J* = 32.9 Hz), 130.18, 129.39, 129.22, 128.40 (q, *J* = 3.7 Hz), 127.08, 125.55, 124.54 (q, *J* = 3.9 Hz), 123.71 (d, *J* = 272.6 Hz), 121.97, 116.41, 48.19, 28.99; ¹⁹F NMR (565 MHz, CDCl₃) δ : –62.69. HRMS (ESI) ([M+H]⁺) Calcd For C₂₀H₁₆F₃N₂O₂⁺: 373.1158, Found: 373.1153.



3,5-dichloro-*N*-(5-(2-oxopropyl)quinolin-8-yl)benzamide (3l). White solid; 14.9 mg, 40% yield; ^1H NMR (600 MHz, CDCl_3) δ : 10.70 (s, 1H), 8.90 (d, $J = 4.2$ Hz, 1H), 8.83 (d, $J = 7.8$ Hz, 1H), 8.28 (d, $J = 8.5$ Hz, 1H), 7.92 (s, 2H), 7.56–7.57 (m, 1H), 7.54 (dd, $J = 8.5, 4.2$ Hz, 1H), 7.50 (d, $J = 7.8$ Hz, 1H), 4.11 (s, 2H), 2.18 (s, 3H); ^{13}C NMR (151 MHz, CDCl_3) δ : 206.0, 162.7, 148.3, 138.9, 137.9, 135.7, 133.6, 133.3, 131.7, 129.2, 127.1, 125.9, 125.8, 122.1, 116.6, 48.3, 29.0. HRMS (ESI) ($[\text{M}+\text{H}]^+$) Calcd For $\text{C}_{19}\text{H}_{15}^{35}\text{Cl}_2\text{N}_2\text{O}_2^+$: 373.0505, Found: 373.0507.

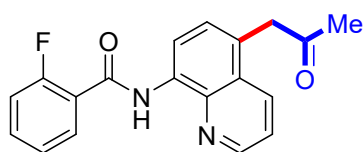


2-methyl-*N*-(5-(2-oxopropyl)quinolin-8-yl)benzamide (3m). White solid; 17.8 mg, 56% yield; ^1H NMR (600 MHz, CDCl_3) δ : 10.27 (s, 1H), 8.91 (d, $J = 7.8$ Hz, 1H), 8.80–8.79 (m, 1H), 8.28–8.26 (m, 1H), 7.68 (d, $J = 5.8$ Hz, 1H), 7.51–7.48 (m, 2H), 7.42–7.39 (m, 1H), 7.34–7.31 (m, 2H), 4.10 (s, 2H), 2.60 (s, 3H), 2.17 (s, 3H); ^{13}C NMR (151 MHz, CDCl_3) δ : 206.2, 168.2, 148.0, 138.8, 136.7, 136.5, 134.4, 133.2, 131.4, 130.4, 129.3, 127.3, 127.1, 126.0, 125.1, 121.8, 116.3, 48.3, 28.9, 20.2. HRMS (ESI) ($[\text{M}+\text{H}]^+$) Calcd For $\text{C}_{20}\text{H}_{19}\text{N}_2\text{O}_2^+$: 319.1441, Found: 319.1439. The NMR data are consistent with the reported values (See: Liu, D.; Xia, Z.; Xiao, Y.; Yu, Y.; Yu, L.; Song, Z.; Wu, Q.; Zhang, J.; Tan, Z. *Eur. J. Org. Chem.* **2021**, 2021, 5012–5016).

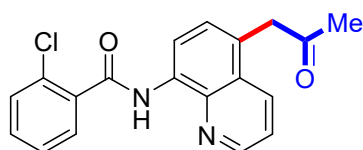


2-methoxy-*N*-(5-(2-oxopropyl)quinolin-8-yl)benzamide (3n). White solid; 16.4 mg,

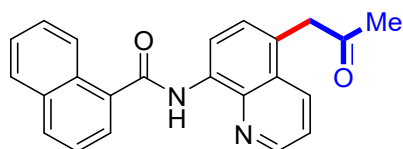
49% yield; ^1H NMR (600 MHz, CDCl_3) δ : 12.35 (s, 1H), 8.99 (d, $J = 7.8$ Hz, 1H), 8.87–8.87 (m, 1H), 8.35–8.33 (m, 1H), 8.24 (d, $J = 8.6$ Hz, 1H), 7.52–7.46 (m, 3H), 7.14 (t, 1H), 7.08–7.06 (m, 1H), 4.18 (s, 3H), 4.06 (s, 2H), 2.14 (s, 3H); ^{13}C NMR (151 MHz, CDCl_3) δ : 206.5, 163.6, 157.7, 148.0, 139.5, 135.5, 133.1, 132.8, 132.3, 129.5, 127.1, 124.7, 122.2, 121.6, 121.2, 117.0, 111.6, 56.1, 48.4, 28.8. HRMS (ESI) ($[\text{M}+\text{H}]^+$) Calcd For $\text{C}_{20}\text{H}_{19}\text{N}_2\text{O}_3^+$: 335.1390, Found: 335.1385.



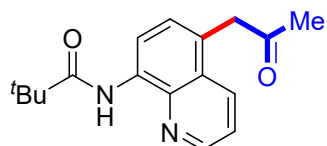
2-fluoro-*N*-(5-(2-oxopropyl)quinolin-8-yl)benzamide (3o). White solid; 19.3 mg, 60% yield; ^1H NMR (600 MHz, CDCl_3) δ : 11.19 (d, $J = 11.3$ Hz, 1H), 8.94–8.92 (m, 1H), 8.88–8.88 (m, 1H), 8.26–8.25 (m, 1H), 8.23–8.20 (m, 1H), 7.54–7.53 (m, 1H), 7.49–7.49 (m, 2H), 7.35–7.32 (m, 1H), 7.27–7.23 (m, 1H), 4.08 (s, 2H), 2.16 (s, 3H); ^{13}C NMR (151 MHz, CDCl_3) δ : 206.24, 161.61, 160.52 (d, $J = 249.2$ Hz), 148.25, 139.05, 134.53, 133.59 (d, $J = 9.2$ Hz), 132.94, 131.95, 129.26, 127.04, 125.38, 124.83 (d, $J = 3.4$ Hz), 121.97 (d, $J = 11.5$ Hz), 121.85, 116.92, 116.32 (d, $J = 24.4$ Hz), 48.25, 28.92; ^{19}F NMR (565 MHz, CDCl_3) δ : -112.09. HRMS (ESI) ($[\text{M}+\text{H}]^+$) Calcd For $\text{C}_{19}\text{H}_{16}\text{FN}_2\text{O}_2^+$: 323.1190, Found: 323.1186.



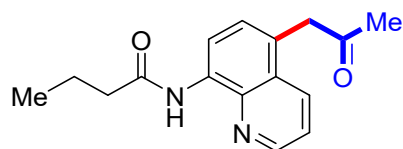
2-chloro-*N*-(5-(2-oxopropyl)quinolin-8-yl)benzamide (3p). White solid; 24.0 mg, 71% yield; ^1H NMR (600 MHz, CDCl_3) δ : 10.54 (s, 1H), 8.92 (d, $J = 7.8$ Hz, 1H), 8.81–8.80 (m, 1H), 8.26–8.24 (m, 1H), 7.81–7.80z (m, 1H), 7.51–7.47 (m, 3H), 7.45–7.39 (m, 2H), 4.09 (s, 2H), 2.17 (s, 3H). ^{13}C NMR (151 MHz, CDCl_3) δ : 206.1, 164.8, 148.1, 138.9, 135.7, 134.1, 133.0, 131.5, 131.1, 130.5, 130.0, 129.2, 127.1, 127.0, 125.5, 121.9, 116.6, 48.2, 28.9. HRMS (ESI) ($[\text{M}+\text{H}]^+$) Calcd For $\text{C}_{19}\text{H}_{16}^{35}\text{ClN}_2\text{O}_2^+$: 339.0895, Found: 339.0891.



***N*-(5-(2-oxopropyl)quinolin-8-yl)-1-naphthamide (3q).** White solid; 15.2 mg, 43% yield; ^1H NMR (600 MHz, CDCl_3) δ : 10.47 (s, 1H), 9.02 (d, $J = 7.8$ Hz, 1H), 8.76 (d, $J = 2.6$ Hz, 1H), 8.53–8.51 (m, 1H), 8.27–8.26 (m, 1H), 8.01 (d, $J = 8.2$ Hz, 1H), 7.94–7.91 (m, 2H), 7.59–7.54 (m, 4H), 7.49–7.47 (m, 1H), 4.11 (s, 2H), 2.18 (s, 3H); ^{13}C NMR (151 MHz, CDCl_3) δ : 206.2, 167.7, 148.1, 138.9, 134.5, 133.9, 133.1, 131.2, 130.3, 129.3, 128.4, 127.3, 127.1, 126.5, 125.5, 125.5, 125.3, 124.9, 121.9, 116.4, 48.3, 29.0. HRMS (ESI) ($[\text{M}+\text{H}]^+$) Calcd For $\text{C}_{23}\text{H}_{19}\text{N}_2\text{O}_2^+$: 355.1441, Found: 355.1437.

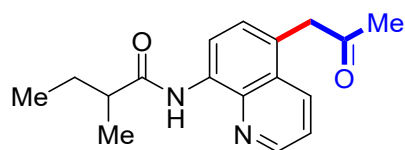


***N*-(5-(2-oxopropyl)quinolin-8-yl)pivalamide (3r).** Colorless liquid; 20.7 mg, 73% yield; ^1H NMR (600 MHz, CDCl_3) δ : 10.31 (s, 1H), 8.83 (d, $J = 2.6$ Hz, 1H), 8.77 (d, $J = 7.9$ Hz, 1H), 8.25–8.24 (m, 1H), 7.50–7.48 (m, 1H), 7.44 (d, $J = 7.9$ Hz, 1H), 4.06 (s, 2H), 2.13 (s, 3H), 1.43 (s, 9H); ^{13}C NMR (151 MHz, CDCl_3) δ : 206.4, 177.3, 148.0, 139.0, 134.4, 133.0, 129.3, 127.0, 124.5, 121.7, 115.9, 48.3, 40.3, 28.8, 27.7. HRMS (ESI) ($[\text{M}+\text{H}]^+$) Calcd For $\text{C}_{17}\text{H}_{21}\text{N}_2\text{O}_2^+$: 285.1598, Found: 285.1597.

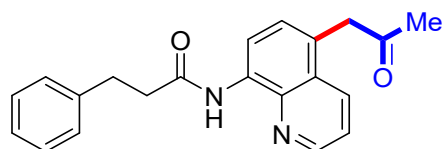


***N*-(5-(2-oxopropyl)quinolin-8-yl)butyramide (3s).** Colorless liquid; 20.3 mg, 75% yield; ^1H NMR (600 MHz, CDCl_3) δ : 9.86 (s, 1H), 8.82–8.81 (m, 1H), 8.76 (d, $J = 7.9$ Hz, 1H), 8.25–8.23 (m, 1H), 7.49–7.47 (m, 1H), 7.43 (d, $J = 7.9$ Hz, 1H), 4.06 (s, 2H), 2.55 (t, $J = 7.5$ Hz, 2H), 2.14 (s, 3H), 1.86 (h, $J = 7.4$ Hz, 2H), 1.06 (t, $J = 7.4$ Hz, 3H); ^{13}C NMR (151 MHz, CDCl_3) δ : 206.3, 171.8, 147.9, 138.6, 134.2, 133.0, 129.3, 127.0,

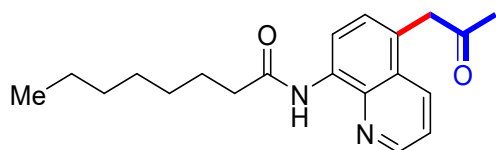
124.6, 121.7, 116.1, 48.2, 40.1, 28.9, 19.1, 13.8. HRMS (ESI) ($[M+H]^+$) Calcd For $C_{16}H_{19}N_2O_2^+$: 271.1441, Found: 271.1440.



2-methyl-*N*-(5-(2-oxopropyl)quinolin-8-yl)butanamide (3t). Colorless liquid; 21.9 mg, 77% yield; 1H NMR (600 MHz, $CDCl_3$) δ : 9.92 (s, 1H), 8.83–8.82 (m, 1H), 8.78 (d, $J = 7.9$ Hz, 1H), 8.25–8.23 (m, 1H), 7.49–7.47 (m, 1H), 7.44 (d, $J = 7.9$ Hz, 1H), 4.06 (s, 2H), 2.55 (q, 1H), 2.14 (s, 3H), 1.87 (h, 1H), 1.62 (h, 1H), 1.33 (d, $J = 6.8$ Hz, 3H), 1.02 (t, $J = 7.4$ Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ : 206.3, 175.3, 147.9, 138.7, 134.3, 133.0, 129.3, 127.0, 124.6, 121.7, 116.1, 48.2, 44.5, 28.8, 27.4, 17.5, 11.9. HRMS (ESI) ($[M+H]^+$) Calcd For $C_{17}H_{21}N_2O_2^+$: 285.1598, Found: 285.1595.

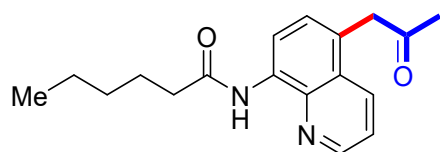


***N*-(5-(2-oxopropyl)quinolin-8-yl)-3-phenylpropanamide (3u).** Colorless solid; 22.9 mg, 69% yield; 1H NMR (600 MHz, $CDCl_3$) δ : 9.85 (s, 1H), 8.78–8.77 (m, 1H), 8.75 (d, $J = 7.9$ Hz, 1H), 8.24–8.23 (m, 1H), 7.47 (dd, $J = 8.5, 4.2$ Hz, 1H), 7.43 (d, $J = 7.9$ Hz, 1H), 7.30–7.29 (m, 4H), 7.21–7.19 (m, 1H), 4.05 (s, 2H), 3.14 (t, 2H), 2.91–2.88 (m, 2H), 2.14 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ : 206.2, 170.8, 147.8, 140.7, 138.5, 134.1, 133.2, 129.3, 128.5, 128.4, 127.0, 126.2, 124.8, 121.7, 116.3, 48.2, 39.6, 31.4, 28.9. HRMS (ESI) ($[M+H]^+$) Calcd For $C_{21}H_{21}N_2O_2^+$: 333.1598, Found: 333.1597.

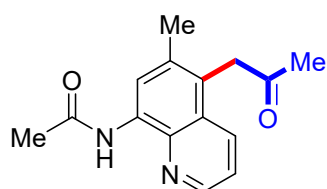


***N*-(5-(2-oxopropyl)quinolin-8-yl)octanamide (3v).** Colorless liquid; 26.4 mg, 81%

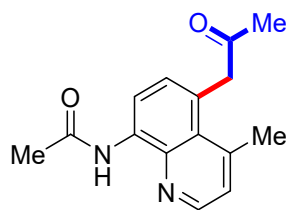
yield; ^1H NMR (600 MHz, CDCl_3) δ : 9.86 (s, 1H), 8.82–8.81 (m, 1H), 8.76 (d, $J = 7.9$ Hz, 1H), 8.25–8.23 (m, 1H), 7.49–7.47 (m, 1H), 7.43 (d, $J = 7.9$ Hz, 1H), 4.05 (s, 2H), 2.56 (t, $J = 7.6$ Hz, 2H), 2.14 (s, 3H), 1.82 (p, $J = 7.6$ Hz, 2H), 1.46–1.26 (m, 8H), 0.92–0.85 (m, 3H); ^{13}C NMR (151 MHz, CDCl_3) δ : 206.3, 171.9, 147.8, 138.6, 134.2, 133.1, 129.3, 127.0, 124.6, 121.7, 116.1, 48.2, 38.2, 31.6, 29.2, 29.0, 28.9, 25.6, 22.6, 14.0. HRMS (ESI) ($[\text{M}+\text{H}]^+$) Calcd For $\text{C}_{20}\text{H}_{27}\text{N}_2\text{O}_2^+$: 327.2067, Found: 327.2063.



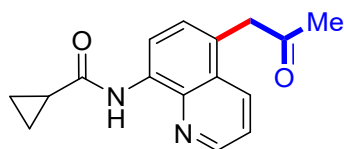
***N*-(5-(2-oxopropyl)quinolin-8-yl)hexanamide (3w)**. Colorless liquid; 23.9 mg, 80% yield; ^1H NMR (600 MHz, CDCl_3) δ : 9.85 (s, 1H), 8.81–8.80 (m, 1H), 8.75 (d, $J = 7.9$ Hz, 1H), 8.24–8.22 (m, 1H), 7.48–7.46 (m, 1H), 7.42 (d, $J = 7.9$ Hz, 1H), 4.05 (s, 2H), 2.56 (t, $J = 7.6$ Hz, 2H), 2.14 (s, 3H), 1.82 (p, $J = 7.5$ Hz, 2H), 1.43–1.38 (m, 4H), 0.92 (t, 3H); ^{13}C NMR (151 MHz, CDCl_3) δ : 206.2, 171.9, 147.8, 138.5, 134.2, 133.0, 129.2, 126.9, 124.5, 121.7, 116.0, 48.1, 38.1, 31.3, 28.8, 25.2, 22.4, 13.9. HRMS (ESI) ($[\text{M}+\text{H}]^+$) Calcd For $\text{C}_{18}\text{H}_{23}\text{N}_2\text{O}_2^+$: 299.1754, Found: 299.1751.



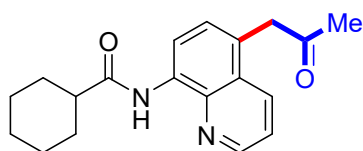
***N*-(6-methyl-5-(2-oxopropyl)quinolin-8-yl)acetamide (3x)**. White solid; 13.8 mg, 54% yield; ^1H NMR (600 MHz, CDCl_3) δ : 9.80 (s, 1H), 8.74–8.74 (m, 1H), 8.68 (s, 1H), 8.21–8.20 (m, 1H), 7.47–7.45 (m, 1H), 4.09 (s, 2H), 2.52 (s, 3H), 2.35 (s, 3H), 2.13 (s, 3H); ^{13}C NMR (151 MHz, CDCl_3) δ : 206.2, 168.8, 146.8, 137.4, 136.2, 133.5, 132.4, 127.3, 122.1, 121.8, 119.6, 43.7, 29.2, 25.1, 21.0. HRMS (ESI) ($[\text{M}+\text{H}]^+$) Calcd For $\text{C}_{15}\text{H}_{17}\text{N}_2\text{O}_2^+$: 257.1285, Found: 257.1281.



***N*-(4-methyl-5-(2-oxopropyl)quinolin-8-yl)acetamide (3y).** White solid; 17.7 mg, 69% yield; ^1H NMR (600 MHz, CDCl_3) δ : 10.05 (s, 1H), 8.68 (d, $J = 8.0$ Hz, 1H), 8.58 (d, $J = 4.3$ Hz, 1H), 7.28–7.26 (m, 1H), 7.21–7.20 (m, 1H), 4.26 (s, 2H), 2.73 (s, 3H), 2.33 (s, 3H), 2.17 (s, 3H); ^{13}C NMR (151 MHz, CDCl_3) δ : 207.0, 168.7, 146.9, 145.0, 139.3, 134.7, 131.9, 127.8, 125.1, 125.1, 115.6, 52.1, 29.3, 25.1, 24.2. HRMS (ESI) ($[\text{M}+\text{H}]^+$) Calcd For $\text{C}_{15}\text{H}_{17}\text{N}_2\text{O}_2^+$: 257.1285, Found: 257.1281.

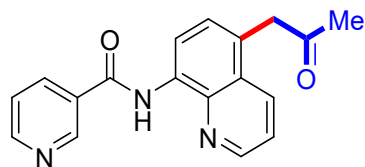


***N*-(5-(2-oxopropyl)quinolin-8-yl)cyclopropanecarboxamide (3z).** Colorless liquid; 19.0 mg, 71% yield; ^1H NMR (600 MHz, CDCl_3) δ : 10.07 (s, 1H), 8.83–8.82 (m, 1H), 8.70 (d, $J = 7.9$ Hz, 1H), 8.25–8.24 (m, 1H), 7.50–7.48 (m, 1H), 7.42 (d, $J = 7.9$ Hz, 1H), 4.05 (s, 2H), 2.13 (s, 3H), 1.84–1.80 (m, 1H), 1.17–1.14 (m, 2H), 0.93–0.90 (m, 2H); ^{13}C NMR (151 MHz, CDCl_3) δ : 206.4, 172.3, 147.8, 138.5, 134.4, 133.1, 129.3, 127.0, 124.4, 121.7, 116.1, 48.3, 28.9, 16.2, 8.2. HRMS (ESI) ($[\text{M}+\text{H}]^+$) Calcd For $\text{C}_{16}\text{H}_{17}\text{N}_2\text{O}_2^+$: 269.1285, Found: 269.1281.

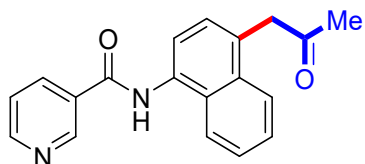


***N*-(5-(2-oxopropyl)quinolin-8-yl)cyclohexanecarboxamide (3aa).** Colorless liquid; 25.7 mg, 83% yield; ^1H NMR (600 MHz, CDCl_3) δ : 9.94 (s, 1H), 8.83–8.82 (m, 1H), 8.77–8.76 (m, 1H), 8.25–8.23 (m, 1H), 7.49–7.47 (m, 1H), 7.44–7.42 (m, 1H), 4.05 (s, 2H), 2.50–2.46 (m, 1H), 2.13 (s, 3H), 2.09–2.07 (m, 2H), 1.89–1.86 (m, 2H), 1.75–

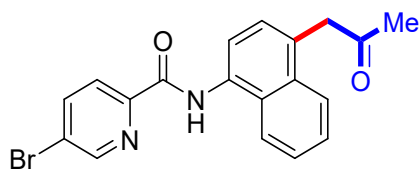
1.73 (m, 1H), 1.67–1.60 (m, 2H), 1.41–1.31 (m, 3H); ^{13}C NMR (151 MHz, CDCl_3) δ : 206.3, 174.9, 147.8, 138.7, 134.3, 133.0, 129.3, 127.0, 124.5, 121.7, 116.1, 48.2, 46.8, 29.7, 28.8, 25.7, 25.7. HRMS (ESI) ($[\text{M}+\text{H}]^+$) Calcd For $\text{C}_{19}\text{H}_{23}\text{N}_2\text{O}_2^+$: 311.1754, Found: 311.1750.



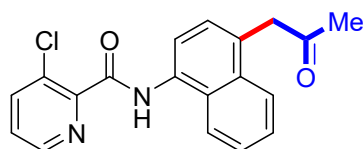
***N*-(5-(2-oxopropyl)quinolin-8-yl)nicotinamide (3ab)**. White solid; 18.3 mg, 60% yield; ^1H NMR (600 MHz, CDCl_3) δ : 10.82 (s, 1H), 9.32 (d, $J = 2.0$ Hz, 1H), 8.87–8.85 (m, 2H), 8.82–8.81 (m, 1H), 8.38–8.36 (m, 1H), 8.27 (d, $J = 6.9$ Hz, 1H), 7.53–7.49 (m, 3H), 4.10 (s, 2H), 2.18 (s, 3H). ^{13}C NMR (151 MHz, CDCl_3) δ : 206.0, 163.4, 152.5, 148.3, 148.2, 138.9, 135.1, 133.7, 133.1, 130.6, 129.2, 127.0, 125.6, 123.6, 122.0, 116.3, 48.1, 29.0. HRMS (ESI) ($[\text{M}+\text{H}]^+$) Calcd For $\text{C}_{18}\text{H}_{16}\text{N}_3\text{O}_2^+$: 306.1237, Found: 306.1234.



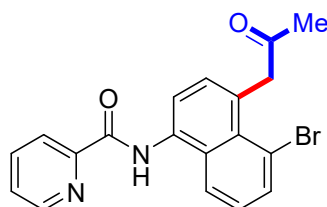
***N*-(4-(2-oxopropyl)naphthalen-1-yl)nicotinamide (3ac)**, White solid; 18.6 mg, 61% yield; ^1H NMR (600 MHz, CDCl_3) δ : 10.75 (s, 1H), 8.69–8.68 (m, 1H), 8.37 (d, $J = 7.7$ Hz, 1H), 8.35–8.33 (m, 1H), 8.12 (d, $J = 7.0$ Hz, 1H), 7.94–7.91 (m, 2H), 7.61–7.55 (m, 2H), 7.52–7.49 (m, 1H), 7.45 (d, $J = 7.7$ Hz, 1H), 4.10 (s, 2H), 2.12 (s, 3H); ^{13}C NMR (151 MHz, CDCl_3) δ : 206.9, 162.2, 149.8, 148.1, 137.7, 132.6, 132.2, 128.4, 127.9, 126.7, 126.5, 126.5, 126.2, 124.7, 122.4, 121.1, 118.3, 49.2, 28.8. HRMS (ESI) ($[\text{M}+\text{H}]^+$) Calcd For $\text{C}_{19}\text{H}_{17}\text{N}_2\text{O}_2^+$: 305.1285, Found: 305.1283.



5-bromo-*N*-(4-(2-oxopropyl)naphthalen-1-yl)picolinamide (3ad). White solid; 24.8 mg, 65% yield; ^1H NMR (600 MHz, CDCl_3) δ : 10.51 (s, 1H), 8.74 (d, $J = 2.2$ Hz, 1H), 8.32 (d, $J = 7.7$ Hz, 1H), 8.22–8.21 (m, 1H), 8.07–8.05 (m, 2H), 7.93–7.92 (m, 1H), 7.62–7.56 (m, 2H), 7.46–7.44 (m, 1H), 4.11 (s, 2H), 2.12 (s, 3H); ^{13}C NMR (151 MHz, CDCl_3) δ : 206.8, 161.5, 149.3, 148.3, 140.4, 132.6, 131.9, 128.3, 128.2, 126.7, 126.6, 126.3, 124.8, 124.4, 123.8, 121.0, 118.5, 49.2, 28.9. HRMS (ESI) ($[\text{M}+\text{H}]^+$) Calcd For $\text{C}_{19}\text{H}_{16}^{79}\text{BrN}_2\text{O}_2^+$: 383.0390, Found: 383.0391.

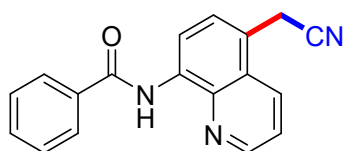


3-chloro-*N*-(4-(2-oxopropyl)naphthalen-1-yl)picolinamide (3ae). White solid; 19.9 mg, 59% yield; ^1H NMR (600 MHz, CDCl_3) δ : 10.65 (s, 1H), 8.62–8.61 (m, 1H), 8.37 (d, $J = 7.7$ Hz, 1H), 8.08–8.07 (m, 1H), 7.94–7.91 (m, 2H), 7.61–7.55 (m, 2H), 7.48–7.45 (m, 2H), 4.11 (s, 2H), 2.12 (s, 3H); ^{13}C NMR (151 MHz, CDCl_3) δ : 207.0, 161.0, 146.0, 145.5, 141.1, 132.7, 132.7, 132.1, 128.4, 128.1, 126.9, 126.9, 126.6, 126.3, 124.8, 121.1, 118.6, 49.3, 28.9. HRMS (ESI) ($[\text{M}+\text{H}]^+$) Calcd For $\text{C}_{19}\text{H}_{16}^{35}\text{ClN}_2\text{O}_2^+$: 339.0895, Found: 339.0892.

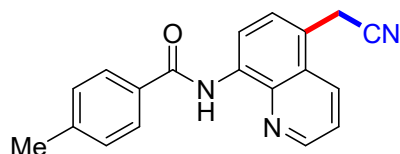


***N*-(4-acetyl-5-bromonaphthalen-1-yl)picolinamide (3af).** White solid; 16.4 mg, 43% yield; ^1H NMR (600 MHz, CDCl_3) δ : 10.52 (s, 1H), 8.76–8.75 (m, 1H), 8.33 (d, $J = 7.7$ Hz, 1H), 8.24–8.23 (m, 1H), 8.08–8.06 (m, 2H), 7.94–7.92 (m, 1H), 7.62–7.57 (m,

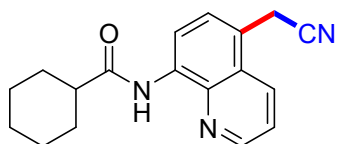
2H), 7.46 (d, $J = 7.7$ Hz, 1H), 4.11 (s, 2H), 2.13 (s, 3H); ^{13}C NMR (151 MHz, CDCl_3) δ : 206.8, 161.5, 149.4, 148.4, 140.4, 132.7, 131.9, 128.4, 128.3, 126.8, 126.7, 126.4, 124.9, 124.4, 123.9, 121.0, 118.5, 49.2, 28.9. HRMS (ESI) ($[\text{M}+\text{H}]^+$) Calcd For $\text{C}_{19}\text{H}_{16}^{79}\text{BrN}_2\text{O}_2^+$: 383.0390, Found: 383.0385.



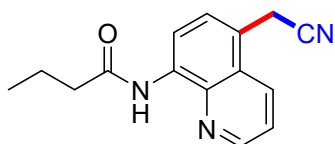
***N*-(5-(cyanomethyl)quinolin-8-yl)benzamide (4a)**. White solid; 20.4 mg, 71% yield; ^1H NMR (600 MHz, CDCl_3) δ : 10.77 (s, 1H), 8.93–8.91 (m, 2H), 8.30 (d, $J = 8.5$ Hz, 1H), 8.09–8.07 (m, 2H), 7.65–7.55 (m, 5H), 4.09 (s, 2H); ^{13}C NMR (151 MHz, CDCl_3) δ : 165.5, 148.4, 138.9, 135.3, 134.8, 132.0, 131.7, 128.8, 128.3, 127.3, 125.8, 122.3, 119.6, 117.3, 116.0, 20.9. HRMS (ESI) ($[\text{M}+\text{H}]^+$) Calcd For $\text{C}_{18}\text{H}_{14}\text{N}_3\text{O}^+$: 288.1131, Found: 288.1132. The NMR data are consistent with the reported values (See: Liu, D.; Xia, Z.; Xiao, Y.; Yu, Y.; Yu, L.; Song, Z.; Wu, Q.; Zhang, J.; Tan, Z. *Eur. J. Org. Chem.* **2021**, 2021, 5012–5016).



***N*-(5-(cyanomethyl)quinolin-8-yl)-4-methylbenzamide (4b)**. White solid; 19.9 mg, 66% yield; ^1H NMR (600 MHz, CDCl_3) δ : 10.73 (s, 1H), 8.92–8.89 (m, 2H), 8.29–8.27 (m, 1H), 7.97 (d, $J = 7.9$ Hz, 2H), 7.63–7.58 (m, 2H), 7.35 (d, $J = 7.9$ Hz, 2H), 4.07 (s, 2H), 2.46 (s, 3H); ^{13}C NMR (151 MHz, CDCl_3) δ : 165.44, 148.38, 142.58, 138.98, 135.40, 131.99, 131.53, 129.49, 128.30, 127.28, 125.77, 122.26, 119.36, 117.30, 115.80, 21.53, 20.90. HRMS (ESI) ($[\text{M}+\text{H}]^+$) Calcd For $\text{C}_{19}\text{H}_{16}\text{N}_3\text{O}^+$: 302.1288, Found: 302.1284. The NMR data are consistent with the reported values (See: Liu, D.; Xia, Z.; Xiao, Y.; Yu, Y.; Yu, L.; Song, Z.; Wu, Q.; Zhang, J.; Tan, Z. *Eur. J. Org. Chem.* **2021**, 2021, 5012–5016).



***N*-(5-(cyanomethyl)quinolin-8-yl)cyclohexanecarboxamide (4c)**. White solid; 22.0 mg, 75% yield; ^1H NMR (600 MHz, CDCl_3) δ : 9.94 (s, 1H), 8.90–8.89 (m, 1H), 8.77 (d, $J = 8.0$ Hz, 1H), 8.29–8.27 (m, 1H), 7.60–7.57 (m, 2H), 4.06 (s, 2H), 2.49 (tt, $J = 11.7, 3.6$ Hz, 1H), 2.10–2.07 (m, 2H), 1.90–1.87 (m, 2H), 1.76–1.73 (m, 1H), 1.67–1.60 (m, 2H), 1.43–1.29 (m, 3H); ^{13}C NMR (151 MHz, CDCl_3) δ : 175.00, 148.18, 138.66, 135.36, 131.60, 128.35, 125.74, 122.15, 119.08, 117.30, 115.86, 46.83, 29.68, 25.72, 25.69, 20.87. HRMS (ESI) ($[\text{M}+\text{H}]^+$) Calcd For $\text{C}_{18}\text{H}_{20}\text{N}_3\text{O}^+$: 294.1601, Found: 294.1597.



***N*-(5-(cyanomethyl)quinolin-8-yl)butyramide (4d)**. White solid; 17.0 mg, 67% yield; ^1H NMR (600 MHz, CDCl_3) δ : 9.86 (s, 1H), 8.88–8.87 (m, 1H), 8.76 (d, $J = 7.9$ Hz, 1H), 8.28–8.26 (m, 1H), 7.60–7.56 (m, 2H), 4.05 (s, 2H), 2.57–2.54 (m, 2H), 1.86 (h, $J = 7.4$ Hz, 2H), 1.08–1.05 (m, 3H); ^{13}C NMR (151 MHz, CDCl_3) δ : 171.86, 148.18, 138.49, 135.23, 131.57, 128.30, 125.71, 122.16, 119.17, 117.28, 115.79, 40.08, 20.85, 19.01, 13.76. HRMS (ESI) ($[\text{M}+\text{H}]^+$) Calcd For $\text{C}_{15}\text{H}_{16}\text{N}_3\text{O}^+$: 254.1288, Found: 254.1289.

4. Copies of ^1H , ^{13}C NMR and ^{19}F NMR spectra