# Supporting Information

## Chemo- and Regioselective Nucleophilic Hydrofunctionalization of Unactivated Aliphatic Alkenes under Transition-Metal-Free Catalyst

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## I. General

$^{1}H$ NMR spectra were acquired on Jeol 400 MHz spectrometers and chemical shifts were recorded relative to tetramethylsilane (δ 0.00) or residual protiated solvent ($CDCl_3$: δ 7.26). Multiplicities were given as: s (singlet), d (doublet), t (triplet), q (quartet) and m (multiplet). The number of protons (n) for a given resonance was indicated by nH. Coupling constants were reported as a *J* value in Hz. $^{13}C$ NMR spectra were obtained at 100 MHz on 400 MHz instruments and chemical shifts were recorded relative to solvent resonance ($CDCl_3$: δ 77.16). $^{31}P$ NMR spectra were obtained at 162 MHz on 400 MHz instrument. Proof of purity of new compounds was demonstrated with copies of $^{1}H$, $^{13}C$, $^{31}P$ and $^{19}F$ NMR spectra.

Glassware was dried in an oven at 120 $^{o}C$ for at least 2 hours before use. Unless noted otherwise, commercially available chemicals were used without further purification. The GC standard, *n*-dodecane was degassed with argon bubbling and dried over activated 4 Å molecular sieve beads for a few days in the glove box before use.

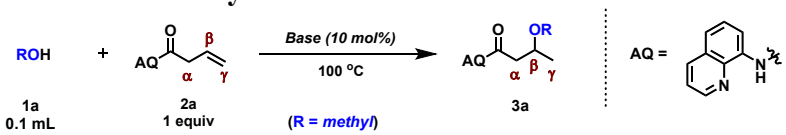
Thin-layer chromatography (TLC) was conducted with Merck 60 F254 coated silica gel plate (0.2 mm thickness). Flash chromatography was performed using Merck silica gel 60 (0.040-0.063 mm) or SiliCycle silica gel F60 (0.040-0.063 mm). The dilute solvents usually used Ethyl Acetate/Petroleum Ether, which was abbreviated as EA:PE.

GCMS analysis was conducted on a Thermo Scientific DSQ II single quadrupole GC/MS instrument with Agilent J & W GC column DB-5MS-UI. ESI/MS analysis was conducted on a ThermoFinnigan LCQ Fleet MS spectrometer. Gas chromatographic (GC) analysis was performed on a SHIMADZU GC-2010 plus instrument equipped with an FID detector and a Agilent J & W GC column DB-5MS-UI.

## II. Condition optimization for the Model Reaction

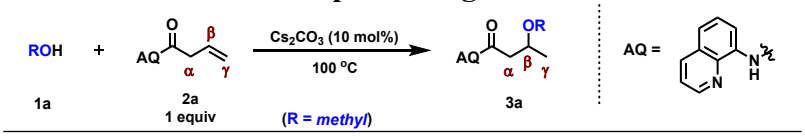
*Typical procedure for condition optimization:* To a dry 10-mL Schlenk tube containing a magnetic stir bar was added alkenes **2a** (1 equiv, 0.1 mmol, 21.2 mg), catalytic base (10 mol%, 0.01 mmol, 3.3 mg), nucleophilic reagent **1a** (0.1 mL) were added sequentially. The tube was capped tightly and the mixture was vigorously stirred in a *pre*-warmed 100 °C oil bath. After 24 hours, 10 uL dodecane was added in the tube. After filtering, the filtrate was subjected to GC analysis to determine the conversion of alkenes **2a**, calibrated GC yield of the coupling product. The major byproducts from alkene are the mixture of isomerized cis/trans alkenes and removed 8-aminoquinoline group.

**Table S1 Effect of base catalysts**




| Entry | Base | Alkene/Conversion (%) | Yield (%) |
|---|---|---|---|
| 1 | LiOH | 100 | 92 |
| 2 | NaOH | 100 | 90 |
| 3 | KOH | 100 | 95 |
| 4 | $CsOH·H_2O$ | 100 | 92 |
| 5 | $Li_2CO_3$ | 36 | 0 |
| 6 | $Na_2CO_3$ | 100 | 72 |
| 7 | $K_2CO_3$ | 100 | 93 |
| **8** | **$Cs_2CO_3$** | **100** | **99** |
| 9 | NaOAc | 59 | 0 |
| 10 | KOAc | 31 | 0 |
| 11 | CsOAc | 8 | 0 |
| 12 | $CH_3OK$ | 100 | 93 |
| 13 | $^t$BuOK | 100 | 90 |
| 14 | CsF | 100 | 32 |
| 15 | $K_3PO_4$ | 100 | 91 |
| 16 | KHMDS | 100 | 94 |
| 17 | $Et_3N$ | 94 | 0 |
| 18 | DMAP | 95 | 0 |
| 19 | TMEDA | 100 | 0 |
| 20 | DIPEA | 100 | 0 |
| 21 | Pyridine | 0 | 0 |
| 22 | / | 2 | 0 |

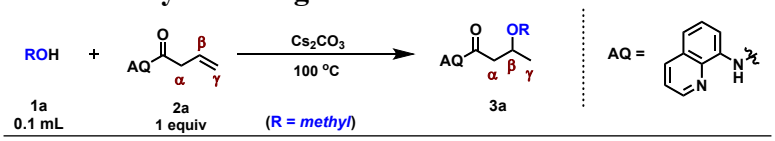
**Table S2 Effect of volume of nucleophilic reagent**




| Entry | ROH/μL | Alkene/Conversion (%) | Yield (%) |
|---|---|---|---|
| 1 | 5 | 100 | 35 |
| 2 | 10 | 100 | 44 |
| 3 | 20 | 100 | 55 |
| 4 | 50 | 100 | 78 |
| **5** | **100** | **100** | **99** |

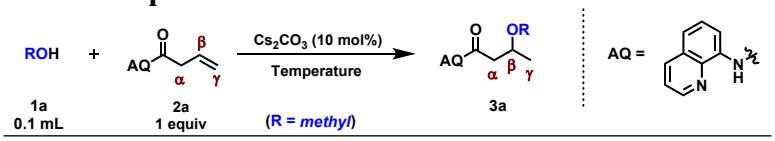
| | | | |
|---|---|---|---|
| 6 | 200 | 100 | 99 |
| 7 | 500 | 100 | 99 |
| 8 | 1000 | 100 | 95 |

## Table S3 Effect of Catalyst loading




| Entry | Catalyst loading | Alkene/Conversion (%) | Yield (%) |
|---|---|---|---|
| 2 | 0.5% | 100 | 26 |
| 3 | 1% | 100 | 84 |
| 4 | 2% | 100 | 87 |
| 5 | 3% | 100 | 92 |
| 6 | 4% | 100 | 93 |
| 7 | 5% | 100 | 99 |
| **8** | **10%** | **100** | **99** |
| 9 | 20% | 100 | 99 |

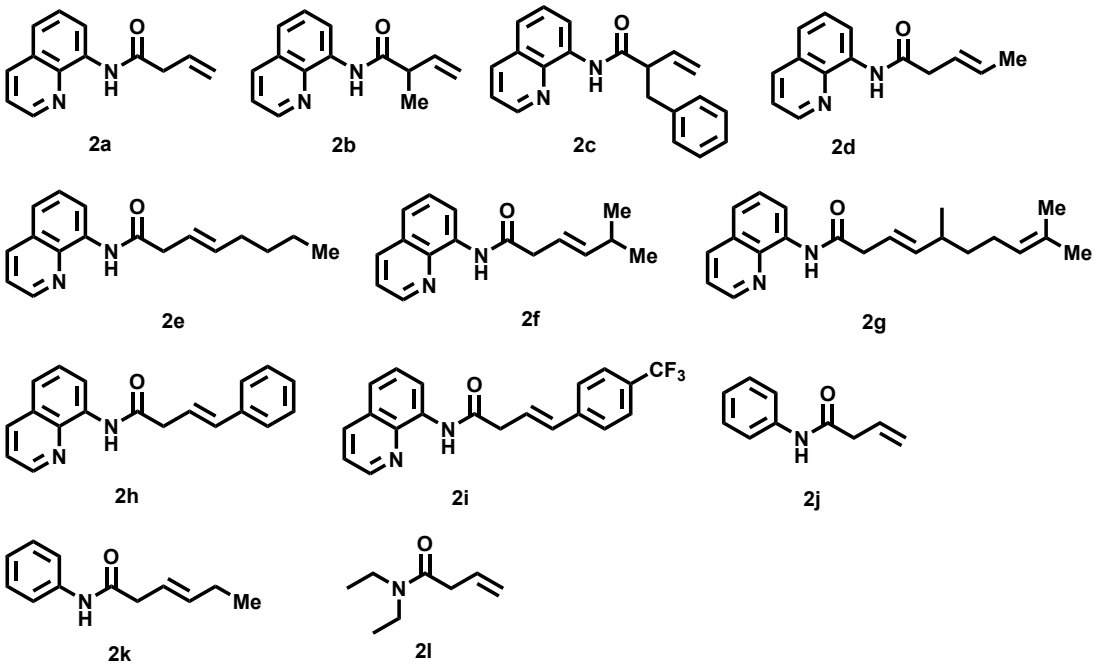
## Table S4 Effect of Temperature




| Entry | Temperature | Alkene/Conversion (%) | Yield (%) |
|---|---|---|---|
| 1 | 60 | 100 | 76 |
| 2 | 70 | 100 | 85 |
| 3 | 80 | 100 | 93 |
| 4 | 90 | 100 | 99 |
| **5** | **100** | **100** | **99** |
| 6 | 110 | 100 | 76 |
| 7 | 120 | 100 | 52 |
| 9 | 130 | 100 | 39 |

## III. Synthesis of alkene substrates

**Table S5. Alkene substrates 2a-2l**



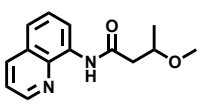

Note: alkene substrates 2a-2f[1], 2g[2], 2h-2i[1], 2j[3], 2k[4], 2l[5] were prepared according to the corresponding literature methods.

## IV. Base-catalyzed addition of various nucleophiles

*General Procedure A:* To a dry 10-mL Schlenk tube containing a magnetic stir bar was charged with alkenes 2a (1 equiv, 0.1 mmol, 21.2 mg), catalytic base, nucleophilic reagent 1a (0.1 mL) sequentially. The tube was capped tightly and the mixture was vigorously stirred in a pre-warmed 100 $^{o}$C oil bath. After alkenes was almost fully consumed (monitored by GC), the reaction mixture was concentrated on a rotary evaporator, then the resulting residue was directly subjected to preparative TLC. The structure of the desired product was confirmed by $^{1}$H and $^{13}$C NMR spectroscopy of the purified sample. The typical procedure using 0.1 mmol of alkenes was applied for all the isolation, unless stated otherwise.

*General Procedure B:* To a dry 10-mL Schlenk tube containing a magnetic stir bar was charged with alkenes 2a (1 equiv, 0.1 mmol, 21.2 mg), catalytic base, nucleophilic reagent 1a (2 equiv, 0.2 mmol) and THF (0.1 mL) sequentially. The tube was capped tightly and the mixture was vigorously stirred in a pre-warmed 100 $^{o}$C oil bath. After alkenes was almost fully consumed (monitored by GC), the reaction mixture was concentrated on a rotary evaporator, then the resulting residue was directly subjected to preparative TLC. The structure of the desired product was confirmed by $^{1}$H and $^{13}$C NMR spectroscopy of the purified sample. The typical procedure using 0.1 mmol of alkenes was applied for all the isolation, unless stated otherwise.

*General Procedure C:* To a dry 10-mL Schlenk tube containing a magnetic stir bar was charged with alkenes 2a (1 equiv, 0.1 mmol, 21.2 mg), catalytic base, nucleophilic reagent 1a (2 equiv, 0.2 mmol) and MeCN (0.1 mL) sequentially. The tube was capped tightly and the mixture was vigorously stirred in a pre-warmed 100 $^{o}$C oil bath. After alkenes was almost fully consumed (monitored by GC), the reaction mixture was concentrated on a rotary evaporator, then the resulting residue was directly subjected to preparative TLC. The structure of the desired product was confirmed by $^{1}$H and $^{13}$C NMR spectroscopy of the purified sample. The typical procedure using 0.1 mmol of alkenes was applied for all the isolation, unless stated otherwise.

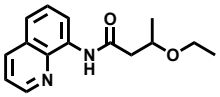


**3-Methoxy-*N*-(quinolin-8-yl)butanamide (3a).** The reaction was conducted according to general procedure A, $Cs_2CO_3$ (10 mol%, 0.01 mmol, 3.3 mg) was added, the reaction mixture was stirred at 100 °C for 24 hours. The product was purified by preparative TLC (1:20 EA:PE) as yellow oil (24 mg, 99%).

$^1$H NMR (400 MHz, $CDCl_3$): δ 10.57 (s, 1H), 8.82-8.77 (m, 2H), δ 8.15 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.55-7.42 (m, 3H), 3.95-3.88 (m, 1H), 3.50 (s, 3H), 2.81-2.59 (m, 2H), 1.31 (d, *J* = 6.1, 3H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ 170.04, 148.32, 138.71, 136.35, 134.93, 128.05, 127.48, 121.65, 121.54, 116.69, 74.26, 56.67, 45.54, 19.25.

HRMS (ESI): Calcd for $C_{14}H_{16}N_2O_2$ $[M+H]^+$: 245.1290, Found: 245.1290.

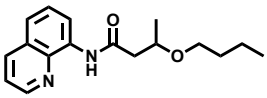


**3-Ethoxy-*N*-(quinolin-8-yl)butanamide (3b).** The reaction was conducted according to general procedure A, $Cs_2CO_3$ (10 mol%, 0.01 mmol, 3.3 mg) was added, the reaction mixture was stirred at 80 °C for 24 hours. The product was purified by preparative TLC (1:20 EA:PE) as yellow oil (25 mg, 95%).

$^1$H NMR (400 MHz, $CDCl_3$): δ 10.55 (s, 1H), 8.82-8.79 (m, 2H), 8.16-8.13 (m, 1H), 7.55-7.42 (m, 3H), 4.03-3.96 (m, 1H), 3.75-3.57 (m, 2H), 2.79-2.63 (m, 2H), 1.36-1.30 (m, 6H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ 170.28, 148.18, 138.79, 136.33, 135.12, 128.10, 127.50, 121.63, 121.52, 116.82, 72.40, 64.34, 45.81, 19.90, 15.58.

HRMS (ESI): Calcd for $C_{15}H_{18}N_2O_2$ $[M+H]^+$: 259.1447, Found: 259.1442.

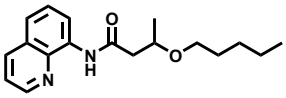


**3-Butoxy-*N*-(quinolin-8-yl)butanamide (3c).** The reaction was conducted according to general procedure A, $Cs_2CO_3$ (10 mol%, 0.01 mmol, 3.3 mg) was added, the reaction mixture was stirred at 80 °C for 24 hours. The product was purified by preparative TLC (1:20 EA:PE) as yellow oil (27 mg, 95%).

$^1$H NMR (400 MHz, $CDCl_3$): δ 10.47 (s, 1H), 8.81-8.79 (m, 2H), 8.15 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.55-7.43 (m, 3H), 3.93-4.01 (m, 1H), 3.64-3.50 (m, 2H), 2.78-2.63 (m, 2H), 1.73-1.66 (m, 2H), 1.43-1.34 (m, 2H), 1.30 (d, *J* = 6.2 Hz, 3H), 0.87 (t, *J* = 7.4 Hz, 3H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ 170.31, 148.14, 138.77, 136.34, 135.09, 128.10, 127.51, 121.63, 121.52, 116.81, 72.64, 68.93, 45.89, 32.17, 19.85, 19.49, 14.10.

HRMS (ESI): Calcd for $C_{17}H_{22}N_2O_2$ $[M+H]^+$: 287.1760, Found: 287.1761.

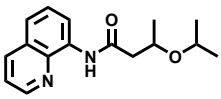


**3-(Pentyloxy)-*N*-(quinolin-8-yl)butanamide (3d).** The reaction was conducted according to general procedure A, $Cs_2CO_3$ (10 mol%, 0.01 mmol, 3.3 mg) was added, the reaction mixture was stirred at 100 °C for 24 hours. The product was purified by preparative TLC (1:20 EA:PE) as yellow oil (28 mg, 92%).

$^1$H NMR (400 MHz, $CDCl_3$): δ 10.46 (s, 1H), 8.82-8.79 (m, 2H), 8.16-8.14 (m, 1H), 7.55-7.43 (m, 3H), 4.01-3.94 (m, 1H), 3.64-3.49 (m, 2H), 2.78-2.63 (m, 2H), 1.74-1.67 (m, 2H), 1.36-1.24 (m, 7H), 0.79 (t, $J$ = 7.1 Hz, 3H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ 170.31, 148.15, 138.76, 136.34, 135.06, 128.09, 127.50, 121.63, 121.52, 116.80, 72.67, 69.26, 45.92, 29.82, 28.49, 22.72, 19.87, 14.14.

HRMS (ESI): Calcd for $C_{18}H_{24}N_2O_2$ $[M+H]^+$: 301.1916, Found: 301.1915.

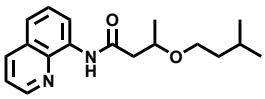


**3-Isopropoxy-*N*-(quinolin-8-yl)butanamide (3e).** The reaction was conducted according to general procedure A, $Cs_2CO_3$ (10 mol%, 0.01 mmol, 3.3 mg) was added, the reaction mixture was stirred at 60 °C for 24 hours. The product was purified by preparative TLC (1:20 EA:PE) as yellow oil (23 mg, 83%).

$^1$H NMR (400 MHz, $CDCl_3$): δ 10.44 (s, 1H), 9.13-8.57 (m, 2H), 8.14 (dd, $J$ = 8.3, 1.7 Hz, 1H), 7.60-7.38 (m, 3H), 4.17-3.98 (m, 1H), 3.81 (m, 1H), 2.83-2.50 (m, 2H), 1.28 (t, $J$ = 6.3 Hz, 6H), 1.15 (d, $J$ = 6.1 Hz, 3H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ 170.34, 148.14, 138.67, 136.29, 135.06, 128.06, 127.48, 121.63, 121.48, 116.72, 69.50, 46.45, 23.25, 21.91, 20.69.

HRMS (ESI): Calcd for $C_{16}H_{20}N_2O_2$ $[M+H]^+$: 273.1603, Found: 273.1605.

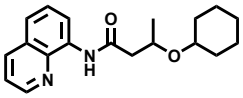


**3-(Isopentyloxy)-*N*-(quinolin-8-yl)butanamide (3f).** The reaction was conducted according to general procedure A, $Cs_2CO_3$ (10 mol%, 0.01 mmol, 3.3 mg) was added, the reaction mixture was stirred at 100 °C for 24 hours. The product was purified by preparative TLC (1:20 EA:PE) as yellow oil (25 mg, 82%).

$^1$H NMR (400 MHz, $CDCl_3$): δ 10.45 (s, 1H), 8.81-8.79 (m, 2H), 8.15 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.55-7.55 (m, 3H), 4.01-3.93 (m, 1H), 3.67-3.50 (m, 2H), 2.77-2.63 (m, 2H), 1.77-1.66 (m, 1H), 1.63-1.57 (m, 2H), 1.31 (d, *J* = 6.2 Hz, 3H), 0.84 (dd, *J* = 6.6, 2.5 Hz, 6H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ 170.31, 148.15, 138.76, 136.34, 135.07, 128.09, 127.50, 121.62, 121.52, 116.81, 72.70, 67.54, 45.94, 38.85, 25.13, 22.83, 22.70, 19.85.

HRMS (ESI): Calcd for $C_{18}H_{24}N_2O_2$ $[M+H]^+$: 301.1916, Found: 301.1915.

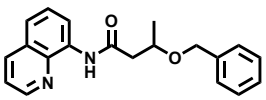


**3-(Cyclohexyloxy)-*N*-(quinolin-8-yl)butanamide (3g).** The reaction was conducted according to general procedure A, $Cs_2CO_3$ (10 mol%, 0.01 mmol, 3.3 mg) was added, the reaction mixture was stirred at 100 °C for 24 hours. The product was purified by preparative TLC (1:20 EA:PE) as yellow oil (19 mg, 60%).

$^1$H NMR (400 MHz, $CDCl_3$): δ 10.42 (s, 1H), 8.81-8.79 (m, 2H), 8.15 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.55-7.43 (m, 3H), 4.19-4.11 (m, 1H), 3.48-3.41 (m, 1H), 2.74-2.64 (m, 2H), 1.96-1.92 (m, 2H), 1.80-1.65 (m, 2H), 1.53-1.44 (m, 2H), 1.34-1.11 (m, 7H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ 170.39, 148.14, 138.73, 136.30, 135.10, 128.09, 127.52, 121.64, 121.48, 116.76, 75.70, 69.29, 46.52, 33.44, 32.11, 25.93, 24.53, 24.33, 20.79.

HRMS (ESI): Calcd for $C_{19}H_{24}N_2O_2$ $[M+H]^+$: 313.1916, Found: 313.1915.

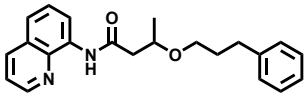


**3-(Benzyloxy)-*N*-(quinolin-8-yl)butanamide (3h).** The reaction was conducted according to general procedure A, $Cs_2CO_3$ (10 mol%, 0.01 mmol, 3.3 mg) was added, the reaction mixture was stirred at 100 °C for 24 hours. The product was purified by preparative TLC (1:20 EA:PE) as dark green oil (29 mg, 90%).

$^1$H NMR (400 MHz, $CDCl_3$): δ 10.41 (s, 1H), 8.80 (dd, *J* = 7.4, 1.6 Hz, 1H), 8.55 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.13 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.56-7.48 (m, 2H), 7.41-7.37 (m, 3H), 7.25-7.22 (m, 3H), 4.72-4.65 (m, 2H), 4.20-4.12 (m, 1H), 2.87-2.70 (m, 2H), 1.38 (d, *J* = 6.1 Hz, 3H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ 169.97, 148.26, 138.66, 138.57, 136.26, 134.92, 128.37, 128.04, 127.73, 127.55, 127.46, 121.60, 121.56, 116.73, 72.73, 71.08, 45.98, 19.91.

HRMS (ESI): Calcd for $C_{20}H_{20}N_2O_2$ $[M+H]^+$: 321.1603, Found: 321.1597.

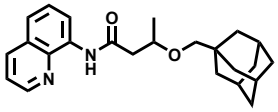


**3-(3-Phenylpropoxy)-*N*-(quinolin-8-yl)butanamide (3i).** The reaction was conducted according to general procedure A, $Cs_2CO_3$ (10 mol%, 0.01 mmol, 3.3 mg) was added, the reaction mixture was stirred at 100 °C for 24 hours. The product was purified by preparative TLC (1:20 EA:PE) as yellow oil (26 mg, 86%).

$^1$H NMR (400 MHz, $CDCl_3$): δ 10.46 (s, 1H), 8.81 (dd, *J* = 7.3, 1.7 Hz, 1H), 8.71 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.14 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.55-7.39 (m, 3H), 7.25-7.21 (m, 2H), 7.17-7.10 (m, 3H), 4.02-3.95 (m, 1H), 3.66-3.51 (m, 2H), 2.79-2.65 (m, 4H), 2.09-1.96 (m, 2H), 1.31 (d, *J* = 6.2 Hz, 3H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ 170.24, 148.23, 142.15, 138.73, 136.35, 135.04, 128.58, 128.39, 128.11, 127.52, 125.82, 121.63, 121.56, 116.82, 72.79, 68.18, 46.00, 32.45, 31.62, 19.83.

HRMS (ESI): Calcd for $C_{22}H_{24}N_2O_2$ $[M+H]^+$: 301.1916, Found: 301.1915.

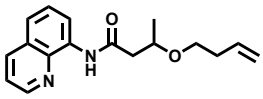


**3-(Adamantan-1-ylmethoxy)-*N*-(quinolin-8-yl)butanamide (3j).** The reaction was conducted according to general procedure B, $Cs_2CO_3$ (10 mol%, 0.01 mmol, 3.3 mg) was added, the reaction mixture was stirred at 100 °C for 24 hours. The product was purified by preparative TLC (1:20 EA:PE) as yellow oil (15 mg, 40%).

$^1$H NMR (400 MHz, $CDCl_3$): δ 10.16 (s, 1H), 8.81-8.78 (m, 2H), 8.16-8.13 (m, 1H), 7.55-7.42 (m, 3H), 3.93-3.86 (m, 1H), 3.16-3.03 (m, 2H), 2.74-2.65 (m, 2H), 1.80 (s, 3H), 1.66-1.57 (m, 3H), 1.53-1.44 (m, 9H), 1.28 (d, *J* = 6.2 Hz, 3H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ 170.44, 148.18, 138.65, 136.32, 134.94, 128.06, 127.50, 121.63, 121.53, 116.80, 80.16, 73.67, 46.25, 39.62, 39.14, 37.29, 37.21, 34.11, 28.34, 19.65.

HRMS (ESI): Calcd for $C_{24}H_{30}N_2O_2$ $[M+H]^+$: 379.2386, Found: 378.2387.

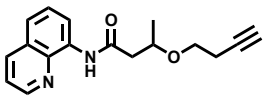


**3-(But-3-en-1-yloxy)-*N*-(quinolin-8-yl)butanamide (3k).** The reaction was conducted according to general procedure A, $Cs_2CO_3$ (10 mol%, 0.01 mmol, 3.3 mg) was added, the reaction mixture was stirred at 100 °C for 24 hours. The product was purified by preparative TLC (1:20 EA:PE) as yellow oil (25 mg, 86%).

$^1$H NMR (400 MHz, $CDCl_3$): δ 10.47 (s, 1H), 8.81-8.79 (m, 2H), 8.16-8.13 (m, 1H), 7.55-7.42 (m, 3H), 5.91-5.81 (m, 1H), 5.09-4.95 (m, 2H), 4.03-3.96 (m, 1H), 3.70-3.56 (m, 2H), 2.79-2.63 (m, 2H), 2.49 (q, $J$ = 6.8 Hz, 2H), 1.31 (d, $J$ = 6.2 Hz, 3H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ 170.17, 148.16, 138.70, 136.35, 135.40, 135.02, 128.06, 127.48, 121.64, 121.54, 116.78, 116.41, 72.74, 68.42, 45.82, 34.47, 19.77.

HRMS (ESI): Calcd for $C_{17}H_{20}N_2O_2$ $[M+H]^+$: 285.1603, Found: 285.1603.

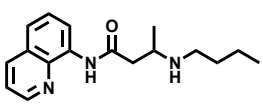


**3-(But-3-yn-1-yloxy)-*N*-(quinolin-8-yl)butanamide (3l).** The reaction was conducted according to general procedure A, $Cs_2CO_3$ (20 mol%, 0.02 mmol, 6.6 mg) was added, the reaction mixture was stirred at 100 °C for 24 hours. The product was purified by preparative TLC (1:20 EA:PE) as yellow oil (24 mg, 85%).

$^1$H NMR (400 MHz, $CDCl_3$): δ 10.44 (s, 1H), 8.82-8.77 (m, 2H), 8.13 (dd, $J$ = 8.3, 1.7 Hz, 1H), 7.54-7.42 (m, 3H), 4.06-3.99 (m, 1H), 3.80-3.64 (m, 2H), 2.80-2.76 (m, 1H), 2.76-2.56 (m, 3H), 1.92 (t, $J$ = 2.7 Hz, 1H), 1.31 (d, $J$ = 6.2 Hz, 3H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ 169.93, 148.22, 138.69, 136.39, 134.96, 128.09, 127.49, 121.67, 121.58, 116.82, 81.39, 72.97, 69.44, 67.11, 45.74, 20.11, 19.75.

HRMS (ESI): Calcd for $C_{17}H_{18}N_2O_2$ $[M+H]^+$: 283.1447, Found: 283.1447.

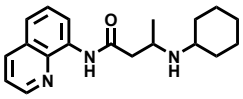


**3-(Butylamino)-*N*-(quinolin-8-yl)butanamide (3m).** The reaction was conducted according to general procedure A, $Cs_2CO_3$ (10 mol%, 0.01 mmol, 3.3 mg) was added, the reaction mixture was stirred at 100 °C for 24 hours. The product was purified by preparative TLC (1:10 EA:PE) as yellow solid (27 mg, 95%).

$^1$H NMR (400 MHz, $CDCl_3$): δ 11.33 (s, 1H), 8.82-8.78 (m, 2H), 8.14 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.55-7.42 (m, 3H), 3.25-3.18 (m, 1H), 2.80-2.67 (m, 2H), 2.65-2.52 (m, 2H), 1.75-1.55 (m, 2H), 1.46-1.39 (m, 2H), 1.22 (d, *J* = 6.4 Hz, 3H), 0.93 (t, *J* = 7.4 Hz, 3H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ 171.16, 148.15, 139.07, 136.32, 135.44, 128.18, 127.52, 121.56, 121.51, 117.19, 50.86, 47.14, 44.64, 32.57, 20.80, 20.77, 14.28.

HRMS (ESI): Calcd for $C_{17}H_{23}N_3O$ $[M+H]^+$: 286.1919, Found: 286.1912.

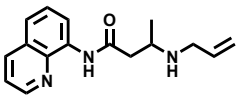


**3-(Cyclohexylamino)-*N*-(quinolin-8-yl)butanamide (3n).** The reaction was conducted according to general procedure A, $Cs_2CO_3$ (10 mol%, 0.01 mmol, 3.3 mg) was added, the reaction mixture was stirred at 100 °C for 24 hours. The product was purified by preparative TLC (1:10 EA:PE) as yellow solid (26 mg, 85%).

$^1$H NMR (400 MHz, $CDCl_3$): δ 11.56 (s, 1H), 9.84-8.80 (m, 2H), 8.13 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.54-7.41 (m, 3H), 3.43-3.35 (m, 1H), 2.70-2.49 (m, 3H), 2.01-1.90 (m, 2H), 1.80-1.64 (m, 2H), 1.41-1.14 (m, 9H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ 171.28, 148.07, 139.08, 136.26, 135.58, 128.17, 127.50, 121.50, 121.42, 117.23, 53.54, 46.62, 45.36, 34.39, 32.86, 26.38, 25.41, 25.13, 21.17.

HRMS (ESI): Calcd for $C_{19}H_{25}N_3O$ $[M+H]^+$: 312.2076, Found: 312.2076.

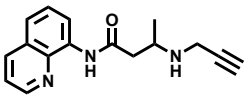


**3-(Allylamino)-*N*-(quinolin-8-yl)butanamide (3o).** The reaction was conducted according to general procedure A, $Cs_2CO_3$ (10 mol%, 0.01 mmol, 3.3 mg) was added, the reaction mixture was stirred at 100 °C for 24 hours. The product was purified by preparative TLC (1:5 EA:PE) as yellow oil (24 mg, 89%).

$^1$H NMR (400 MHz, $CDCl_3$): δ 11.25 (s, 1H), 8.81-8.79 (m, 2H), 8.14 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.54-7.41 (m, 3H), 6.15-6.01 (m, 1H), 5.30-5.11 (m, 2H), 3.47-3.37 (m, 2H), 3.30-3.23 (m, 1H), 2.66-2.55 (m, 2H), 1.24 (d, *J* = 6.3 Hz, 3H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ 170.94, 148.24, 138.95, 136.99, 136.32, 135.27, 128.12, 127.47, 121.55, 117.09, 116.15, 50.14, 50.02, 44.74, 20.65.

HRMS (ESI): Calcd for $C_{16}H_{19}N_3O$ $[M+H]^+$: 270.1606, Found: 270.1605.

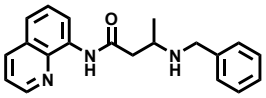


**3-(Prop-2-yn-1-ylamino)-*N*-(quinolin-8-yl)butanamide (3p).** The reaction was conducted according to general procedure A, $Cs_2CO_3$ (10 mol%, 0.01 mmol, 3.3 mg) was added, the reaction mixture was stirred at 100 °C for 24 hours. The product was purified by preparative TLC (1:5 EA:PE) as yellow oil (20 mg, 73%).

$^1$H NMR (400 MHz, $CDCl_3$): δ 10.76 (s, 1H), 8.82-8.76 (m, 2H), 8.14 (dd, *J* = 8.2, 1.7 Hz, 1H), 7.54-7.41 (m, 3H), 3.59 (d, *J* = 2.4 Hz, 2H), 3.48-3.41 (m, 1H), 2.67-2.58 (m, 2H), 2.24 (s, 1H), 1.80 (s, 1H), 1.25 (d, *J* = 6.4 Hz, 3H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ 170.39, 148.30, 138.79, 136.32, 134.94, 128.07, 127.44, 121.59, 121.57, 116.90, 82.08, 71.61, 49.48, 44.59, 35.86, 20.22.

HRMS (ESI): Calcd for $C_{16}H_{17}N_3O$ $[M+H]^+$: 268.1450, Found: 268.1450.

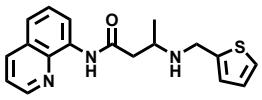


**3-(Benzylamino)-*N*-(quinolin-8-yl)butanamide (3q).** The reaction was conducted according to general procedure A, $Cs_2CO_3$ (10 mol%, 0.01 mmol, 3.3 mg) was added, the reaction mixture was stirred at 100 °C for 24 hours. The product was purified by preparative TLC (1:10 EA:PE) as yellow oil (30 mg, 95%).

$^1$H NMR (400 MHz, $CDCl_3$): δ 11.07 (s, 1H), 8.82 (dd, *J* = 7.4, 1.6 Hz, 1H), 8.68 (dd, *J* = 4.3, 1.7 Hz, 1H), 8.14 (dd, *J* = 8.3, 1.6 Hz, 1H), 7.56-7.40 (m, 5H), 7.32-7.23 (m, 3H), 4.01-3.92 (m, 2H), 3.37-3.29 (m, 1H), 2.74-2.60 (m, 2H), 1.73 (s, 1H), 1.29 (d, *J* = 6.4 Hz, 3H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ 170.84, 148.27, 140.30, 138.97, 136.29, 135.23, 128.49, 128.35, 128.15, 127.48, 127.08, 121.56, 117.17, 51.62, 50.58, 44.68, 20.64.

HRMS (ESI): Calcd for $C_{20}H_{21}N_3O$ $[M+H]^+$: 321.1603, Found: 321.1599.

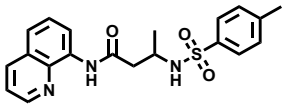


***N*-(Quinolin-8-yl)-3-((thiophen-2-ylmethyl)amino)butanamide (3r).** The reaction was conducted according to general procedure A, $Cs_2CO_3$ (10 mol%, 0.01 mmol, 3.3 mg) was added, the reaction mixture was stirred at 100 °C for 24 hours. The product was purified by preparative TLC (1:10 EA:PE) as yellow oil (31 mg, 95%).

$^1$H NMR (400 MHz, $CDCl_3$): δ 10.81 (s, 1H), 8.80-8.74 (m, 2H), 8.14 (dd, *J* = 8.3, 1.8 Hz, 1H), 7.55-7.41 (m, 3H), 7.18 (dd, *J* = 5.0, 1.3 Hz, 1H), 7.04-6.93 (m, 2H), 4.15 (d, *J* = 0.7 Hz, 2H), 3.40-3.30 (m, 1H), 2.70-2.61 (m, 2H), 1.78 (s, 1H), 1.27 (d, *J* = 6.4 Hz, 3H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ 170.61, 148.34, 143.81, 138.88, 136.31, 135.05, 128.12, 127.46, 126.75, 125.16, 124.44, 121.60, 117.05, 50.11, 46.05, 44.82, 20.59.

HRMS (ESI): Calcd for $C_{18}H_{19}N_3OS$ $[M+H]^+$: 326.1327, Found: 326.1326.

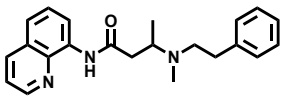


**3-((4-Methylphenyl)sulfonamido)-*N*-(quinolin-8-yl)butanamide (3s).** The reaction was conducted according to general procedure C, $Cs_2CO_3$ (10 mol%, 0.01 mmol, 3.3 mg) was added, the reaction mixture was stirred at 100 °C for 24 hours. The product was purified by preparative TLC (1:2 EA:PE) as yellow solid (25 mg, 66%).

$^1$H NMR (400 MHz, $CDCl_3$): δ 9.69 (s, 1H), 8.75 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.63-8.59 (m, 1H), 8.13 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.77-7.74 (m, 2H), 7.51-7.41 (m, 3H), 7.13-7.11 (m, 2H), 5.95 (d, *J* = 7.9 Hz, 1H), 3.87-3.77 (m, 1H), 2.61 (d, *J* = 5.5 Hz, 2H), 2.23 (s, 3H), 1.27 (d, *J* = 6.7 Hz, 3H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ 169.15, 148.34, 143.15, 138.22, 137.92, 136.43, 133.94, 129.63, 127.92, 127.24, 127.07, 122.02, 121.79, 116.78, 47.53, 43.55, 21.57, 21.43.

HRMS (ESI): Calcd for $C_{20}H_{21}N_3O_3S$ $[M+H]^+$: 384.1382, Found: 384.1380.



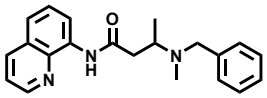
**3-(Methyl(phenethyl)amino)-*N*-(quinolin-8-yl)butanamide (3t).** The reaction was conducted according to general procedure A, CsOAc (20 mol%, 0.02 mmol, 3.8 mg)

was added, the reaction mixture was stirred at 100 °C for 24 hours. The product was purified by preparative TLC (1:10 EA:PE) as dark green oil (29 mg, 84%).

$^1$H NMR (400 MHz, $CDCl_3$): δ 12.10 (s, 1H), 8.85-8.80 (m, 2H), 8.14 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.56-7.40 (m, 3H), 7.23-7.11 (m, 5H), 3.42-3.36 (m, 1H), 3.09-2.66 (m, 5H), 2.54 (s, 3H), 2.38 (dd, *J* = 16.3, 3.9 Hz, 1H), 1.08 (d, *J* = 6.6 Hz, 3H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ 171.27, 148.08, 140.56, 139.35, 136.18, 135.82, 128.80, 128.44, 128.21, 127.49, 126.09, 121.44, 117.46, 55.80, 54.55, 41.50, 37.24, 34.74, 13.16.

HRMS (ESI): Calcd for $C_{22}H_{25}N_3O$ $[M+H]^+$: 348.2076, Found: 348.2076.

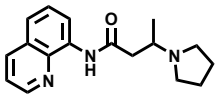


**3-(Benzyl(methyl)amino)-*N*-(quinolin-8-yl)butanamide (3u).** The reaction was conducted according to general procedure A, CsOAc (20 mol%, 0.02 mmol, 3.8 mg) was added, the reaction mixture was stirred at 100 °C for 24 hours. The product was purified by preparative TLC (1:10 EA:PE) as dark green oil (20 mg, 61%).

$^1$H NMR (400 MHz, $CDCl_3$): δ 11.60 (s, 1H), 8.83 (dd, *J* = 7.4, 1.5 Hz, 1H), 8.60 (dd, *J* = 4.3, 1.8 Hz, 1H), 8.14 (dd, *J* = 8.4, 1.7 Hz, 1H), 7.57-7.49 (m, 2H), 7.40-7.37 (m, 3H), 7.17-7.10 (m, 3H), 3.88 (d, *J* = 13.1 Hz, 1H), 3.53 (d, *J* = 13.2 Hz, 1H), 3.47-3.39 (m, 1H), 2.91-2.84 (m, 1H), 2.47-2.39 (m, 1H), 2.39 (s, 3H), 1.16 (d, *J* = 6.6 Hz, 3H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ 171.24, 148.12, 139.12, 136.15, 135.55, 129.31, 128.19, 128.16, 127.52, 126.97, 121.47, 121.45, 117.22, 56.70, 55.55, 42.00, 37.58, 13.54.

HRMS (ESI): Calcd for $C_{21}H_{23}N_3O$ $[M+H]^+$: 334.1919, Found: 334.1917.



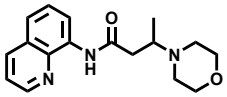
**3-(Pyrrolidin-1-yl)-*N*-(quinolin-8-yl)butanamide (3v).** The reaction was conducted according to general procedure A, CsOAc (20 mol%, 0.02 mmol, 3.8 mg) was added, the reaction mixture was stirred at 100 °C for 24 hours. The product was purified by preparative TLC (1:10 EA:PE) as brown solid (24 mg, 84%).

$^1$H NMR (400 MHz, $CDCl_3$): δ 12.26 (s, 1H), 8.83 (dd, *J* = 7.6, 1.5 Hz, 1H), 8.76 (dd, *J* = 4.3, 1.8 Hz, 1H), 8.10 (dd, *J* = 8.3, 1.8 Hz, 1H), 7.52-7.37 (m, 3H), 3.12-3.05 (m,

1H), 2.82-2.73 (m, 4H), 2.70-2.61 (m, 2H), 1.98-1.92 (m, 4H), 1.22 (d, *J* = 6.6 Hz, 3H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ 171.03, 147.84, 139.37, 136.09, 135.96, 128.16, 127.40, 121.34, 121.32, 117.40, 54.40, 49.67, 42.91, 23.89, 16.34.

HRMS (ESI): Calcd for $C_{17}H_{21}N_3O$ $[M+H]^+$: 284.1763, Found: 284.1763.

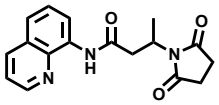


**3-Morpholino-*N*-(quinolin-8-yl)butanamide (3w).** The reaction was conducted according to general procedure A, CsOAc (20 mol%, 0.02 mmol, 3.8 mg) was added, the reaction mixture was stirred at 100 °C for 24 hours. The product was purified by preparative TLC (1:5 EA:PE) as colorless solid (30 mg, 99%).

$^1$H NMR (400 MHz, $CDCl_3$): δ 11.70 (s, 1H), 8.85-8.82 (m, 2H), 8.14 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.55-7.42 (m, 3H), 4.05-4.00 (m, 2H), 3.96-3.91 (m, 2H), 3.22-3.13 (m, 1H), 2.82-2.75 (m, 3H), 2.65-2.60 (m, 2H), 2.49-2.44 (m, 1H), 1.13 (d, *J* = 6.7 Hz, 3H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ 171.06, 148.05, 139.17, 136.37, 135.66, 128.22, 127.48, 121.67, 121.53, 117.81, 66.84, 56.69, 40.94, 13.87.

HRMS (ESI): Calcd for $C_{17}H_{21}N_3O_2$ $[M+H]^+$: 300.1712, Found: 300.1711.

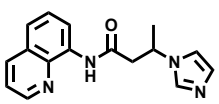


**3-(2,5-Dioxopyrrolidin-1-yl)-*N*-(quinolin-8-yl)butanamide (3x).** The reaction was conducted according to general procedure C, CsOAc (50 mol%, 0.05 mmol, 9.5 mg) was added, the reaction mixture was stirred at 100 °C for 24 hours. The product was purified by preparative TLC (1:10 EA:PE) as yellow oil (18 mg, 58%).

$^1$H NMR (400 MHz, $CDCl_3$): δ 9.75 (s, 1H), 8.79-8.67 (m, 2H), 8.13 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.51-741 (m, 3H), 4.92-4.83 (m, 1H), 3.37 (dd, *J* = 15.2, 9.1 Hz, 1H), 2.94 (dd, *J* = 15.2, 6.0 Hz, 1H), 2.63 (s, 4H), 1.46 (d, *J* = 6.9 Hz, 3H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ 177.44, 168.56, 148.33, 138.39, 136.47, 134.32, 128.02, 127.47, 121.78, 116.74, 44.89, 40.47, 28.22, 18.19.

HRMS (ESI): Calcd for $C_{17}H_{17}N_3O_3$ $[M+H]^+$: 312.1348, Found: 312.1346.

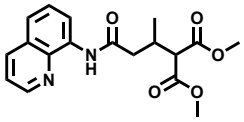


**3-(1H-Imidazol-1-yl)-*N*-(quinolin-8-yl)butanamide (3y).** The reaction was conducted according to general procedure C, CsOAc (20 mol%, 0.02 mmol, 3.8 mg) was added, the reaction mixture was stirred at 100 °C for 24 hours. The product was purified by preparative TLC (1:10 EA:PE) as yellow oil (18 mg, 64%).

$^1$H NMR (400 MHz, $CDCl_3$): δ 9.73 (s, 1H), 8.74-8.65 (m, 2H), 8.12 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.62 (s, 1H), 7.51-7.40 (m, 3H), 7.02 (d, *J* = 4.1 Hz, 2H), 4.97-4.88 (m, 1H), 3.02-2.90 (m, 2H), 1.61 (d, *J* = 6.9 Hz, 3H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ 167.58, 148.32, 138.22, 136.51, 133.93, 129.59, 127.96, 127.35, 122.11, 121.81, 116.81, 116.78, 50.34, 46.23, 21.65.

HRMS (ESI): Calcd for $C_{16}H_{16}N_4O$ $[M+H]^+$: 281.1402, Found: 281.1400.

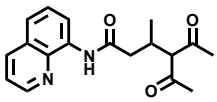


**Dimethyl 2-(4-oxo-4-(quinolin-8-ylamino)butan-2-yl)malonate (3z).** The reaction was conducted according to general procedure A, $Cs_2CO_3$ (20 mol%, 0.02 mmol, 6.6 mg) were added, the reaction mixture was stirred at 100 °C for 24 hours. The product was purified by preparative TLC (1:20 EA:PE) as yellow oil (34 mg, 99%).

$^1$H NMR (400 MHz, $CDCl_3$): δ 9.85 (s, 1H), 8.81-8.76 (m, 2H), 8.16 (dd, *J* = 8.3, 1.5 Hz, 1H), 7.55-7.44 (m, 3H), 3.76 (s, 6H), 3.61 (d, *J* = 6.5 Hz, 1H), 3.02-2.91 (m, 1H), 2.80 (dd, *J* = 14.9, 5.4 Hz, 1H), 2.57 (dd, *J* = 14.9, 8.3 Hz, 1H), 1.18 (d, *J* = 6.8 Hz, 3H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ 170.02, 169.20, 169.12, 148.32, 138.39, 136.48, 134.48, 128.03, 127.49, 121.77, 121.69, 116.56, 55.91, 52.62, 52.59, 42.24, 30.89, 17.70.

HRMS (ESI): Calcd for $C_{18}H_{20}N_2O_5$ $[M+H]^+$: 345.1450, Found: 345.1451.



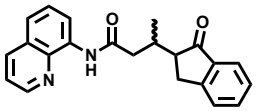
**4-Acetyl-3-methyl-5-oxo-*N*-(quinolin-8-yl)hexanamide (3aa).** The reaction was conducted according to general procedure A, $Cs_2CO_3$ (50 mol%, 0.05 mmol, 16.5 mg) were added, the reaction mixture was stirred at 100 °C for 24 hours. The product was purified by preparative TLC (1:20 EA:PE) as yellow oil (17 mg, 53%).

$^1$H NMR (400 MHz, $CDCl_3$): δ 9.81 (s, 1H), 8.80 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.74 (dd, *J* = 6.6, 2.5 Hz, 1H), 8.15 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.55-7.44 (m, 3H), 3.92 (d, *J* =

9.0 Hz, 1H), 3.04-2.94 (m, 1H), 2.62-2.44 (m, 2H), 2.27 (s, 3H), 2.22 (s, 3H), 1.09 (d, *J* = 6.8 Hz, 3H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ 204.50, 204.27, 169.88, 148.37, 138.35, 136.48, 134.31, 128.02, 127.43, 121.82, 121.81, 116.54, 73.38, 42.14, 31.03, 30.41, 30.12, 17.70.

HRMS (ESI): Calcd for $C_{18}H_{20}N_2O_3$ $[M+H]^+$: 313.1552, Found: 313.1552.

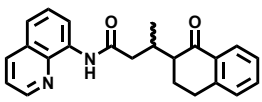


**3-(1-Oxo-2,3-dihydro-1*H*-inden-2-yl)-*N*-(quinolin-8-yl)butanamide (3ab).** The reaction was conducted according to general procedure B, KOH (50 mol%, 0.05 mmol, 2.8 mg) was added, the reaction mixture was stirred at 100 °C for 24 hours. The product was purified by preparative TLC (1:20 EA:PE) as brown oil (31 mg, 90%). The dr value is 1.3:1 analysis by GCMS.

$^{1}$H NMR (400 MHz, $CDCl_3$): δ 9.94 (d, *J* = 40.6 Hz, 1H), 8.83-8.76(m, 2H), 8.14 (m, 1H), 7.75 (t, *J* = 6.9 Hz, 1H), 7.59-7.42 (m, 5H), 7.37-7.33 (m, 1H), 3.38-3.27 (m, 1H), 3.07-2.90 (m, 3H), 2.82-2.57 (m, 2H), 1.01 (dd, *J* = 6.7, 2.8 Hz, 3H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ 208.51, 208.03, 171.06, 170.47, 154.03, 153.88, 148.35, 148.29, 138.48, 138.39, 137.85, 137.49, 136.44, 136.31, 134.88, 134.82, 134.63, 134.49, 128.00, 127.99, 127.47, 127.45, 127.44, 127.38, 126.61, 126.53, 123.83, 123.62, 121.71, 121.67, 121.62, 121.57, 116.56, 116.52, 51.17, 50.47, 43.48, 42.41, 32.91, 32.01, 31.28, 28.86, 15.96, 15.81.

HRMS (ESI): Calcd for $C_{22}H_{20}N_2O_2$ $[M+H]^+$: 345.1603, Found: 345.1602.



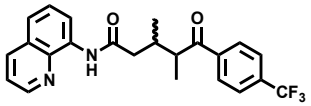
**3-(1-Oxo-1,2,3,4-tetrahydronaphthalen-2-yl)-*N*-(quinolin-8-yl)butanamide (3ac).** The reaction was conducted according to general procedure B, KOH (50 mol%, 0.05 mmol, 2.8 mg) was added, the reaction mixture was stirred at 100 °C for 24 hours. The product was purified by preparative TLC (1:20 EA:PE) as yellow oil (35 mg, 97%). The dr value is 1.3:1 analysis by GCMS.

$^{1}$H NMR (400 MHz, $CDCl_3$): δ 9.92 (d, *J* = 17.9 Hz, 1H), 8.82-8.75 (m, 2H), 8.15-8.02 (m, 2H), 7.54-7.43 (m, 4H), 7.31-7.21 (m, 2H), 3.14-2.88 (m, 3H), 2.86-2.65 (m,

1H), 2.67-2.55 (m, 2H), 2.29-2.20 (m, 1H), 2.12-1.98 (m, 1H), 1.13 (dd, *J* = 27.5, 6.8 Hz, 3H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ 199.66, 199.27, 171.50, 170.91, 148.33, 148.30, 143.97, 138.50, 138.42, 136.44, 136.35, 134.73, 134.58, 133.29, 132.97, 128.75, 128.01, 127.57, 127.47, 127.43, 126.68, 121.72, 121.67, 121.56, 121.47, 116.51, 52.13, 51.63, 43.14, 43.06, 31.62, 29.81, 29.38, 28.87, 26.36, 24.18, 16.85, 16.64.

HRMS (ESI): Calcd for $C_{23}H_{22}N_2O_2$ $[M+H]^+$: 359.1760, Found: 359.1760.



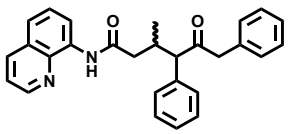
**3,4-Dimethyl-5-oxo-*N*-(quinolin-8-yl)-5-(4-(trifluoromethyl)phenyl)pentanamide (3ad).** The reaction was conducted according to general procedure B, KOH (50 mol%, 0.05 mmol, 2.8 mg) was added, the reaction mixture was stirred at 100 °C for 24 hours. The product was purified by preparative TLC (1:10 EA:PE) as yellow oil (30 mg, 73%). The dr value is 2:1 analysis by GCMS.

$^{1}$H NMR (400 MHz, $CDCl_3$): δ 9.79 (d, *J* = 35.6 Hz, 1H), 8.82-8.72 (m, 2H), 8.18-8.04 (m, 3H), 7.69-7.65 (m, 2H), 7.58-7.42 (m, 3H), 3.83-3.64 (m, 1H), 2.80-2.39 (m, 3H), 1.28-1.17 (m, 4H), 0.97 (d, *J* = 6.9 Hz, 2H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ 203.17, 202.89, 170.54, 170.51, 148.34, 148.28, 139.29 (m), 138.36 (d, *J* = 1.9 Hz), 136.53, 136.48, 134.43 (m), 129.04, 128.74, 128.07, 128.03, 127.50, 127.47, 125.91, 125.87, 125.84, 125.83, 125.81, 125.77, 125.73, 121.81, 121.76, 121.68, 116.56, 116.47, 45.08, 44.05, 43.06, 41.27, 33.32, 32.39, 18.46, 15.51, 13.80, 11.10.

$^{19}$F NMR (376 MHz, $CDCl_3$): δ -62.98, -62.99.

HRMS (ESI): Calcd for $C_{23}H_{21}F_3N_2O_2$ $[M+H]^+$: 415.1633, Found: 415.1633.

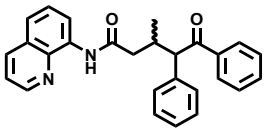


**3-Methyl-5-oxo-4,6-diphenyl-*N*-(quinolin-8-yl)hexanamide (3ae).** The reaction was conducted according to general procedure B, KOH (50 mol%, 0.05 mmol, 2.8 mg) was added, the reaction mixture was stirred at 100 °C for 24 hours. The product was purified by preparative TLC (1:10 EA:PE) as yellow oil (24 mg, 57%). The dr value is 1:1 analysis by GCMS.

$^1$H NMR (400 MHz, $CDCl_3$): δ 9.69 (d, *J* = 81.6 Hz, 1H), 8.83-8.70 (m, 2H), 8.17-8.12 (m, 1H), 7.56-7.41 (m, 3H), 7.36-7.17 (m, 8H), 7.08-7.05 (m, 2H), 3.87 (dd, *J* = 29.1, 9.9 Hz, 1H), 3.72 (s, 1H), 3.67 (d, *J* = 3.0 Hz, 1H), 3.03-2.84 (m, 1H), 2.61 (dd, *J* = 14.2, 4.3 Hz, 0.5H), 2.41-2.33 (m, 1H), 2.07 (dd, *J* = 14.6, 9.2 Hz, 0.5H), 0.95 (dd, *J* = 74.0, 6.7 Hz, 3H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ 207.54, 207.02, 170.72, 148.33, 148.17, 138.46, 138.33, 136.94, 136.44, 134.60, 134.51, 134.12, 133.92, 129.76, 129.41, 129.30, 129.21, 129.03, 128.71, 128.63, 128.05, 128.00, 127.78, 127.66, 127.49, 127.09, 126.99, 121.73, 121.67, 121.58, 121.48, 116.55, 116.44, 63.38, 62.88, 50.00, 49.58, 43.22, 42.40, 33.24, 33.00, 18.55, 17.54.

HRMS (ESI): Calcd for $C_{28}H_{26}N_2O_2$ $[M+H]^+$: 423.2073, Found: 423.2072.

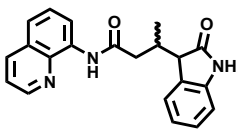


**3-Methyl-5-oxo-4,5-diphenyl-*N*-(quinolin-8-yl)pentanamide (3af).** The reaction was conducted according to general procedure B, KOH (50 mol%, 0.05 mmol, 2.8 mg) was added, the reaction mixture was stirred at 100 $^o$C for 24 hours. The product was purified by preparative TLC (1:10 EA:PE) as yellow oil (38 mg, 93%). The dr value is 1:1 analysis by GCMS.

$^1$H NMR (400 MHz, $CDCl_3$): δ 9.74 (d, *J* = 61.7 Hz, 1H), 8.80-8.75 (m, 2H), 8.15-8.12 (m, 1H), 8.03-7.99 (m, 2H), 7.54-7.16 (m, 11H), 4.75 (dd, *J* = 9.6, 2.9 Hz, 1H), 3.22-3.06 (m, 1H), 2.76 (dd, *J* = 14.4, 4.3 Hz, 0.5H), 2.56-2.50 (m, 1H), 2.24 (dd, *J* = 14.7, 8.7 Hz, 0.5H), 1.10 (dd, *J* = 89.0, 6.7 Hz, 3H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ 200.06, 199.95, 170.85, 170.74, 148.25, 148.19, 138.40, 138.35, 137.75, 137.68, 137.47, 137.22, 136.43, 136.36, 134.57, 134.54, 133.05, 132.95, 129.24, 129.19, 129.11, 128.94, 128.80, 128.71, 128.65, 128.56, 127.99, 127.49, 127.44, 127.37, 121.67, 121.51, 121.48, 116.49, 116.45, 58.60, 58.37, 43.43, 42.33, 34.73, 34.23, 18.79, 17.69.

HRMS (ESI): Calcd for $C_{27}H_{24}N_2O_2$ $[M+H]^+$: 409.1916, Found: 409.1916.



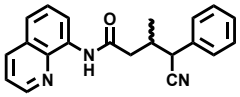
**3-(2-Oxoindolin-3-yl)-*N*-(quinolin-8-yl)butanamide (3ag).** The reaction was conducted according to general procedure B, KOH (50 mol%, 0.05 mmol, 2.8 mg)

was added, the reaction mixture was stirred at 100 °C for 24 hours. The product was purified by preparative TLC (1:5 EA:PE) as brown solid (20 mg, 58%). The dr value is 1.3:1 analysis by GCMS.

$^1$H NMR (400 MHz, $CDCl_3$): δ 9.97 (d, *J* = 97.5 Hz, 1H), 9.09 (d, *J* = 48.4 Hz, 1H), 8.83-8.73 (m, 2H), 8.14-8.11 (m, 1H), 7.54-7.29 (m, 4H), 7.21-7.16 (m, 1H), 7.06-6.88 (m, 2H), 3.67-3.65 (m, 1H), 3.22-3.16 (m, 0.5H), 3.09-3.01 (m, 1H), 2.81-2.76 (m, 0.5H), 2.71-2.59 (m, 1H), 1.05 (dd, *J* = 94.4, 6.8 Hz, 3H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ 179.75, 179.54, 171.11, 170.23, 148.37, 148.27, 142.15, 141.97, 138.57, 138.38, 136.44, 136.35, 134.64, 134.41, 128.92, 128.19, 128.04, 128.02, 127.98, 127.75, 127.44, 127.40, 125.02, 124.16, 122.57, 122.46, 121.72, 121.70, 121.69, 116.71, 116.63, 109.89, 109.75, 50.51, 49.66, 41.99, 41.90, 33.24, 33.03, 16.62, 15.41.

HRMS (ESI): Calcd for $C_{21}H_{19}N_3O_2$ $[M+H]^+$: 346.1556, Found: 346.1556.

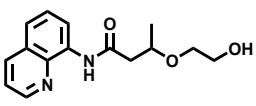



**4-Cyano-3-methyl-5-oxo-5-phenyl-*N*-(quinolin-8-yl)pentanamide (3ah).** The reaction was conducted according to general procedure A, KOH (50 mol%, 0.05 mmol, 2.8 mg) was added, the reaction mixture was stirred at 100 °C for 24 hours. The product was purified by preparative TLC (1:20 EA:PE) as yellow oil (33 mg, 99%). The dr value is 1.3:1 analysis by GCMS.

$^1$H NMR (400 MHz, $CDCl_3$): δ 9.84 (d, *J* = 34.6 Hz, 1H), 8.83-8.69 (m, 2H), 8.18-8.14 (m, 1H), 7.55-7.30 (m, 8H), 4.20 (dd, *J* = 85.3, 5.1 Hz, 1H), 2.85-2.68 (m, 2H), 2.65-2.46 (m, 1H), 1.18 (dd, *J* = 58.7, 6.6 Hz, 3H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ 169.39, 169.38, 148.40, 148.34, 138.33, 138.30, 136.47, 134.57, 134.24, 133.62, 129.12, 129.03, 128.40, 128.21, 128.16, 128.03, 127.99, 127.91, 127.39, 121.94, 121.85, 121.81, 119.77, 119.25, 116.61, 116.54, 43.12, 42.67, 42.63, 40.60, 35.74, 35.48, 18.22, 15.67.

HRMS (ESI): Calcd for $C_{21}H_{19}N_3O$ $[M+H]^+$: 330.1616, Found: 330.1613.



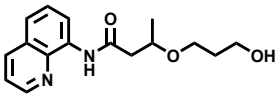

**3-(2-Hydroxyethoxy)-*N*-(quinolin-8-yl)butanamide (5a).** The reaction was conducted according to general procedure A, $Cs_2CO_3$ (10 mol%, 0.01 mmol, 3.3 mg)

was added, the reaction mixture was stirred at 100 °C for 24 hours. The product was purified by preparative TLC (1:5 EA:PE) as yellow oil (19 mg, 68%).

$^1$H NMR (400 MHz, $CDCl_3$): δ 10.41 (s, 1H), 8.86-8.82 (m, 2H), 8.17 (dd, *J* = 8.3, 1.6 Hz, 1H), 7.56-7.44 (m, 3H), 4.20 (t, *J* = 6.8 Hz, 1H), 4.08-4.01 (m, 1H), 3.91-3.85 (m, 2H), 3.83-3.78 (m, 1H), 3.66-3.61 (m, 1H), 2.88 (dd, *J* = 15.2, 3.1 Hz, 1H), 2.67 (dd, *J* = 15.2, 7.0 Hz, 1H), 1.34 (d, *J* = 6.3 Hz, 3H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ 170.05, 148.72, 138.41, 137.08, 134.66, 128.34, 127.60, 121.85, 121.66, 117.45, 72.64, 70.44, 62.08, 45.05, 19.18.

HRMS (ESI): Calcd for $C_{15}H_{18}N_2O_3$ $[M+H]^+$: 275.1396, Found: 275.1394.

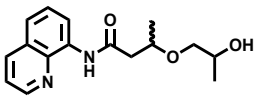



**3-(3-Hydroxypropoxy)-*N*-(quinolin-8-yl)butanamide (5b).** The reaction was conducted according to general procedure A, $Cs_2CO_3$ (10 mol%, 0.01 mmol, 3.3 mg) was added, the reaction mixture was stirred at 100 °C for 24 hours. The product was purified by preparative TLC (1:5 EA:PE) as yellow oil (22 mg, 76%).

$^1$H NMR (400 MHz, $CDCl_3$): δ 10.25 (s, 1H), 8.82-8.78 (m, 2H), 8.15 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.55-7.43 (m, 3H), 4.06-3.99 (m, 1H), 3.82-3.69 (m, 4H), 2.77-2.67 (m, 2H), 2.52 (s, 1H), 2.00-1.82 (m, 2H), 1.32 (d, *J* = 6.2 Hz, 3H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ 169.98, 148.31, 138.62, 136.50, 134.74, 128.12, 127.54, 121.73, 121.70, 116.92, 73.12, 67.29, 61.17, 45.53, 32.42, 19.74.

HRMS (ESI): Calcd for $C_{16}H_{20}N_2O_3$ $[M+H]^+$: 289.1552, Found: 289.1552.

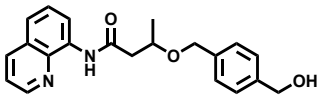



**3-(2-Hydroxypropoxy)-*N*-(quinolin-8-yl)butanamide (5c).** The reaction was conducted according to general procedure A, $Cs_2CO_3$ (10 mol%, 0.01 mmol, 3.3 mg) was added, the reaction mixture was stirred at 100 °C for 24 hours. The product was purified by preparative TLC (1:5 EA:PE) as yellow oil (19 mg, 66%). The dr value is 1.1:1 analysis by GCMS.

$^1$H NMR (400 MHz, $CDCl_3$): δ 10.50-10.21 (m, 1H), 8.83-8.77 (m, 2H), 8.16-8.14 (m, 1H), 7.54-7.42 (m, 3H), 4.18-4.09 (m, 1H), 4.05-3.98 (m, 1H), 3.66-3.63 (m, 1H), 3.53-3.31 (m, 1H), 2.91-2.83 (m, 1H), 2.70-2.56 (m, 1H), 1.34-1.30 (m, 3H), 1.21-1.12 (m, 3H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ 170.27, 169.94, 169.91, 148.71, 148.33, 138.43, 138.35, 137.03, 136.93, 136.84, 134.70, 134.59, 134.42, 128.27, 128.26, 128.25, 127.63, 127.54, 127.50, 121.84, 121.77, 121.76, 121.63, 121.63, 121.58, 117.50, 117.33, 117.24, 75.86, 75.24, 74.44, 73.03, 72.48, 71.09, 66.96, 66.82, 66.37, 45.40, 44.86, 44.44, 20.45, 19.35, 18.76, 18.56, 18.52, 17.18.

HRMS (ESI): Calcd for $C_{16}H_{20}N_2O_3$ $[M+H]^+$: 289.1552, Found: 289.1549.

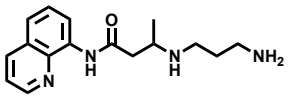



**3-((4-(Hydroxymethyl)benzyl)oxy)-*N*-(quinolin-8-yl)butanamide (5d).** The reaction was conducted according to general procedure B, $Cs_2CO_3$ (10 mol%, 0.01 mmol, 3.3 mg) was added, the reaction mixture was stirred at 100 °C for 24 hours. The product was purified by preparative TLC (1:10 EA:PE) as yellow oil (20 mg, 58%).

$^1$H NMR (400 MHz, $CDCl_3$): δ 10.34 (s, 1H), 8.78 (dd, *J* = 7.3, 1.8 Hz, 1H), 8.60 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.13 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.55-7.48 (m, 2H), 7.41-7.37 (m, 1H), 7.36 (d, *J* = 8.0 Hz, 2H), 7.22 (d, *J* = 8.0 Hz, 2H), 4.70-4.62 (m, 4H), 4.18-4.11 (m, 1H), 2.82 (dd, *J* = 14.7, 7.8 Hz, 1H), 2.70 (dd, *J* = 14.7, 4.0 Hz, 1H), 1.36 (d, *J* = 6.2 Hz, 3H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ 169.97, 148.25, 140.24, 138.63, 138.00, 136.31, 134.85, 128.02, 127.47, 127.03, 121.61, 116.75, 72.71, 70.83, 65.22, 46.00, 19.93.

HRMS (ESI): Calcd for $C_{21}H_{22}N_2O_3$ $[M+H]^+$: 351.1709, Found: 351.1709.

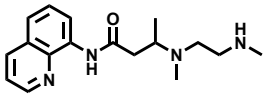



**3-((3-Aminopropyl)amino)-*N*-(quinolin-8-yl)butanamide (5e).** The reaction was conducted according to general procedure A, CsOAc (10 mol%, 0.01 mmol, 1.9 mg) was added, the reaction mixture was stirred at 100 °C for 24 hours. The product was purified by preparative TLC (1:10 MeOH:DCM) as yellow oil (23 mg, 80%).

$^1$H NMR (400 MHz, $CDCl_3$): δ 11.08 (s, 1H), 8.77-8.75 (m, 2H), 8.08 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.49-7.36 (m, 3H), 3.21-3.14 (m, 1H), 2.83-2.69 (m, 4H), 2.62-2.49 (m, 2H), 1.82-1.67 (m, 2H), 1.19 (d, *J* = 6.4 Hz, 3H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ 170.87, 148.08, 138.85, 136.22, 135.16, 128.04, 127.34, 121.46, 117.04, 50.82, 45.01, 44.46, 40.52, 33.93, 20.58.

HRMS (ESI): Calcd for $C_{16}H_{22}N_4O$ $[M+H]^+$: 287.1872, Found: 287.1872.

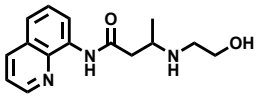


**3-(Methyl(2-(methylamino)ethyl)amino)-*N*-(quinolin-8-yl)butanamide (5f).** The reaction was conducted according to general procedure A, CsOAc (10 mol%, 0.01 mmol, 1.9 mg) was added, the reaction mixture was stirred at 100 °C for 24 hours. The product was purified by preparative TLC (1:5 EA:PE) as yellow oil (20 mg, 65%).

$^1$H NMR (400 MHz, $CDCl_3$): δ 11.51 (s, 1H), 8.81-8.79 (m, 2H), 8.16 (dd, *J* = 8.3, 1.6 Hz, 1H), 7.55-7.43 (m, 3H), 3.35-3.27 (m, 1H), 2.94-2.86 (m, 2H), 2.81-2.76 (m, 2H), 2.55-2.49 (m, 1H), 2.43 (s, 3H), 2.41-2.36 (m, 1H), 2.29 (s, 3H), 1.07 (d, *J* = 6.6 Hz, 3H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ 171.46, 148.20, 138.95, 136.58, 135.30, 128.26, 127.62, 121.64, 121.57, 117.39, 56.00, 49.77, 48.91, 41.77, 38.12, 35.60, 12.85.

HRMS (ESI): Calcd for $C_{17}H_{24}N_4O$ $[M+H]^+$: 301.2028, Found: 301.2028.

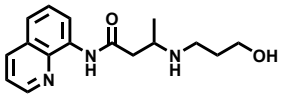


**3-((2-Hydroxyethyl)amino)-*N*-(quinolin-8-yl)butanamide (5g).** The reaction was conducted according to general procedure A, CsOAc (10 mol%, 0.01 mmol, 1.9 mg) was added, the reaction mixture was stirred at 100 °C for 24 hours. The product was purified by preparative TLC (1:20 MeOH:DCM) as yellow oil (24 mg, 88%).

$^1$H NMR (400 MHz, $CDCl_3$): δ 11.62 (s, 1H), 8.85 (dd, *J* = 7.4, 1.6 Hz, 1H), 8.81 (dd, *J* = 4.3, 1.7 Hz, 1H), 8.13 (dd, *J* = 8.3, 1.6 Hz, 1H), 7.53-7.39 (m, 3H), 3.84-3.74 (m, 2H), 3.28-3.20 (m, 1H), 3.02-2.97 (m, 1H), 2.90-2.84 (m, 1H), 2.73 (dd, *J* = 15.8, 3.3 Hz, 1H), 2.50 (dd, *J* = 15.8, 7.2 Hz, 1H), 1.24 (d, *J* = 6.3 Hz, 3H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ 170.88, 148.67, 138.67, 136.97, 135.12, 128.38, 127.53, 121.74, 121.47, 117.81, 62.00, 50.53, 49.07, 43.44, 20.42.

HRMS (ESI): Calcd for $C_{15}H_{19}N_3O_2$ $[M+H]^+$: 274.1556, Found: 274.1556.



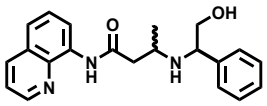
**3-((3-Hydroxypropyl)amino)-*N*-(quinolin-8-yl)butanamide (5h).** The reaction was conducted according to general procedure A, CsOAc (10 mol%, 0.01 mmol, 1.9 mg)

was added, the reaction mixture was stirred at 100 °C for 24 hours. The product was purified by preparative TLC (1:20 MeOH:DCM) as yellow oil (24 mg, 85%).

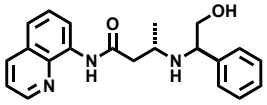
$^1$H NMR (400 MHz, $CDCl_3$): δ 10.46 (s, 1H), 8.79 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.75 (dd, *J* = 7.0, 2.0 Hz, 1H), 8.13 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.53-7.41 (m, 3H), 3.81 (t, *J* = 5.5 Hz, 1H), 3.29-3.21 (m, 1H), 2.99-2.89 (m, 4H), 2.69-2.60 (m, 2H), 1.83-1.77 (m, 2H), 1.24 (d, *J* = 6.4 Hz, 3H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ 170.24, 148.38, 138.60, 136.51, 134.55, 128.11, 127.42, 121.89, 121.71, 117.11, 62.91, 51.22, 46.06, 43.60, 31.32, 19.86.

HRMS (ESI): Calcd for $C_{16}H_{21}N_3O_2$ $[M+H]^+$: 288.1712, Found: 288.1712.



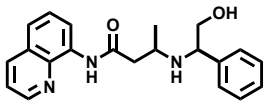
**3-((2-Hydroxy-1-phenylethyl)amino)-*N*-(quinolin-8-yl)butanamide (5i).** 2-amino-1-phenylethanol (2 equiv, 0.2 mmol, 27.4mg) and CsOAc (10 mol%, 0.01 mmol, 1.9 mg) were added, neat condition, the reaction mixture was stirred at 100 °C for 24 hours. The product was purified by preparative TLC (1:10 MeOH:DCM) as yellow oil (30 mg, 86%). The dr value is 1.2:1 analysis by GCMS.



$^1$H NMR (400 MHz, $CDCl_3$): δ 11.86 (s, 1H), 8.93 (dd, *J* = 7.5, 1.6 Hz, 1H), 8.86 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.20 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.58-7.45 (m, 3H), 7.41-7.37 (m, 2H), 7.33-7.29 (m, 3H), 4.10-4.07 (m, 1H), 3.81-3.74 (m, 2H), 3.14-3.07 (m, 1H), 2.99 (dd, *J* = 15.4, 3.6 Hz, 1H), 2.30 (dd, *J* = 15.4, 4.3 Hz, 1H), 1.20 (d, *J* = 6.7 Hz, 3H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ 170.83, 148.62, 140.66, 138.56, 137.32, 135.21, 128.98, 128.53, 127.89, 127.79, 126.79, 121.64, 121.50, 117.81, 67.86, 63.28, 47.63, 41.60, 20.69.

HRMS (ESI): Calcd for $C_{21}H_{23}N_3O_2$ $[M+H]^+$: 350.1869, Found: 350.1868.

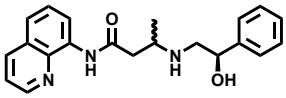


$^1$H NMR (400 MHz, $CDCl_3$): δ 11.21 (s, 1H), 8.87-8.85 (m, 2H), 8.17 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.57-7.43 (m, 3H), 7.35-7.32 (m, 2H), 7.29-7.20 (m, 3H), 4.06 (dd, *J* =

8.6, 4.0 Hz, 1H), 3.81-3.71 (m, 2H), 3.18-3.11 (m, 1H), 2.64-2.54 (m, 2H), 1.20 (d, *J* = 6.4 Hz, 3H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ 170.60, 148.74, 139.85, 138.71, 136.81, 135.00, 128.79, 128.35, 127.77, 127.51, 127.38, 121.82, 121.60, 117.56, 67.61, 61.85, 46.86, 45.99, 18.99.

HRMS (ESI): Calcd for $C_{21}H_{23}N_3O_2$ $[M+H]^+$: 350.1869, Found: 350.1868.

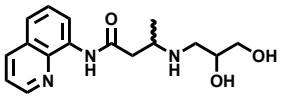


**3-(((*R*)-2-Hydroxy-2-phenylethyl)amino)-*N*-(quinolin-8-yl)butanamide (5j).** (*R*)-2-amino-1-phenylethan-1-ol (2 equiv, 0.2 mmol, 27.4mg) and CsOAc (10 mol%, 0.01 mmol, 1.9 mg) were added, neat condition, the reaction mixture was stirred at 100 °C for 24 hours. The product was purified by preparative TLC (1:10 MeOH:DCM) as yellow oil (32 mg, 92%). The dr value is 1.3:1 analysis by GCMS.

$^1$H NMR (400 MHz, $CDCl_3$): δ 11.57 (d, *J* = 39.7 Hz, 1H), 8.94-8.88 (m, 2H), 8.18-8.15 (m, 1H), 7.57-7.50 (m, 2H), 7.46-7.42 (m, 3H), 7.38-7.34 (m, 2H), 7.30-7.28 (m, 1H), 4.99-4.89 (m, 1H), 3.32-3.23 (m, 1H), 3.14-3.06 (m, 1H), 3.02-2.83 (m, 1H), 2.80-2.69 (m, 1H), 2.58-2.48 (m, 1H), 1.29-1.21 (m, 3H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ 170.78, 170.69, 149.00, 148.85, 142.51, 142.28, 138.72, 138.64, 137.02, 136.94, 135.09, 128.57, 128.53, 128.42, 127.68, 127.55, 126.04, 125.90, 121.83, 121.79, 121.58, 121.56, 117.79, 73.48, 72.49, 55.90, 54.22, 50.97, 50.34, 44.04, 43.48, 20.59, 20.32.

HRMS (ESI): Calcd for $C_{21}H_{23}N_3O_2$ $[M+H]^+$: 350.1869, Found: 350.1866.

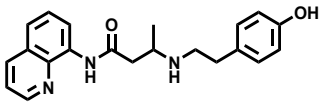


**3-((2,3-Dihydroxypropyl)amino)-*N*-(quinolin-8-yl)butanamide (5k).** The reaction was conducted according to general procedure A, CsOAc (10 mol%, 0.01 mmol, 1.9 mg) was added, the reaction mixture was stirred at 100 °C for 24 hours. The product was purified by preparative TLC (1:5 MeOH:DCM) as yellow oil (23 mg, 77%). The dr value is 1:1 analysis by GCMS.

$^1$H NMR (400 MHz, $CDCl_3$): δ 11.38 (d, *J* = 51.3 Hz, 1H), 8.87-8.82 (m, 2H), 8.17-8.14 (m, 1H), 7.55-7.42 (m, 3H), 3.95-3.88 (m, 1H), 3.78-3.74 (m, 1H), 3.66-3.59 (m, 1H), 3.31-3.18 (m, 1H), 2.99-2.77 (m, 2H), 2.69-2.44 (m, 2H), 1.27-1.23 (m, 3H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ 170.84, 170.77, 148.79, 148.66, 138.65, 138.59, 137.15, 136.98, 134.99, 134.95, 128.44, 128.36, 127.63, 127.58, 121.86, 121.85, 121.59, 121.54, 117.90, 117.74, 71.41, 70.56, 65.41, 65.15, 51.16, 50.52, 50.33, 49.08, 43.87, 43.20, 20.62, 20.34.

HRMS (ESI): Calcd for $C_{16}H_{21}N_3O_3$ $[M+H]^+$: 304.1661, Found: 304.1655.

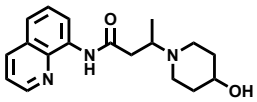


**3-((4-Hydroxyphenethyl)amino)-*N*-(quinolin-8-yl)butanamide (5l).** The reaction was conducted according to general procedure B, $CsOH{\cdot}H_2O$ (10 mol%, 0.01 mmol, 1.9 mg) was added, the reaction mixture was stirred at 100 °C for 24 hours. The product was purified by preparative TLC (1:5 EA:PE) as yellow oil (35 mg, 99%).

$^1$H NMR (400 MHz, $CDCl_3$): δ 10.90 (s, 1H), 8.79 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.74 (dd, *J* = 6.8, 2.2 Hz, 1H), 8.12 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.53-7.39 (m, 3H), 7.01 (d, *J* = 8.5 Hz, 2H), 6.74 (d, *J* = 8.4 Hz, 2H), 4.49 (s, 2H), 3.33-3.25 (m, 1H), 3.04-2.97 (m, 1H), 2.95-2.90 (m, 1H), 2.90-2.81 (m, 2H), 2.66-2.64 (m, 2H), 1.21 (d, *J* = 6.4 Hz, 3H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ 170.88, 155.29, 148.35, 138.85, 136.44, 134.77, 130.44, 129.85, 128.16, 127.43, 121.98, 121.69, 117.41, 115.85, 50.81, 48.32, 43.66, 34.86, 19.86.

HRMS (ESI): Calcd for $C_{21}H_{23}N_3O_2$ $[M+H]^+$: 350.1869, Found: 350.1868.

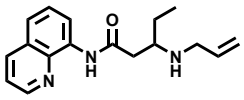


**3-(4-Hydroxypiperidin-1-yl)-*N*-(quinolin-8-yl)butanamide (5m).** The reaction was conducted according to general procedure C, CsOAc (20 mol%, 0.02 mmol, 3.8 mg) was added, the reaction mixture was stirred at 100 °C for 24 hours. The product was purified by preparative TLC (1:2 EA:PE) as white solid (26 mg, 82%).

$^1$H NMR (400 MHz, $CDCl_3$): δ 11.85 (s, 1H), 8.88 (dd, *J* = 4.1, 1.8 Hz, 1H), 8.84 (dd, *J* = 7.3, 1.8 Hz, 1H), 8.13 (dd, *J* = 8.3, 1.8 Hz, 1H), 7.54-7.41 (m, 3H), 3.85-3.79 (m, 1H), 3.30-3.21 (m, 1H), 3.03-2.99 (m, 1H), 2.88-2.78 (m, 2H), 2.65-2.59 (m, 1H), 2.42-2.29 (m, 2H), 2.16-1.93 (m, 4H), 1.08 (d, *J* = 6.6 Hz, 3H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ 171.52, 148.22, 139.34, 136.24, 135.81, 128.22, 127.41, 121.66, 121.54, 117.96, 68.78, 56.39, 43.67, 41.43, 34.10, 34.04, 13.64.

HRMS (ESI): Calcd for $C_{18}H_{23}N_3O_2$ $[M+H]^+$: 314.1869, Found: 314.1868.

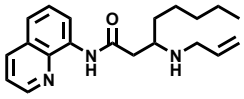


**3-(Allylamino)-*N*-(quinolin-8-yl)pentanamide (7a).** The reaction was conducted according to general procedure A, $Cs_2CO_3$ (10 mol%, 0.01 mmol, 3.3 mg) was added, the reaction mixture was stirred at 100 °C for 24 hours. The product was purified by preparative TLC (1:5 EA:PE) as brown oil (25 mg, 89%).

$^1H$ NMR (400 MHz, $CDCl_3$): δ 11.39 (s, 1H), 8.81-8.78 (m, 2H), 8.13-8.10 (m, 1H), 7.53-7.39 (m, 3H), 6.16-6.06 (m, 1H), 5.31-5.30 (m, 1H), 5.14-5.11 (m, 1H), 3.42-3.40 (m, 2H), 3.08-3.02 (m, 1H), 2.67 (dd, *J* = 15.5, 3.7 Hz, 1H), 2.54 (dd, *J* = 15.5, 7.9 Hz, 1H), 2.02 (s, 1H), 1.71-1.52 (m, 2H), 0.96 (t, *J* = 7.5 Hz, 3H).

$^{13}C$ NMR (100 MHz, $CDCl_3$): δ 171.16, 148.18, 139.03, 136.86, 136.24, 135.39, 128.12, 127.43, 121.48, 121.47, 117.15, 116.23, 55.85, 49.65, 41.47, 26.57, 10.07.

HRMS (ESI): Calcd for $C_{17}H_{21}N_3O$ $[M+H]^+$: 284.1763, Found: 284.1768.

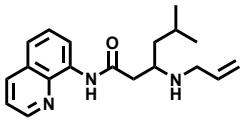


**3-(Allylamino)-*N*-(quinolin-8-yl)octanamide (7b).** The reaction was conducted according to general procedure A, $Cs_2CO_3$ (10 mol%, 0.01 mmol, 3.3 mg) was added, the reaction mixture was stirred at 100 °C for 48 hours. The product was purified by preparative TLC (1:5 EA:PE) as brown oil (25 mg, 78%).

$^1H$ NMR (400 MHz, $CDCl_3$): δ 11.43 (s, 1H), 8.82-8.78 (m, 2H), 8.11 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.53-7.39 (m, 3H), 6.16-6.06 (m, 1H), 5.32-5.26 (m, 1H), 5.14-5.10 (m, 1H), 3.43-3.39 (m, 2H), 3.11-3.05 (m, 1H), 2.69 (dd, *J* = 15.4, 3.7 Hz, 1H), 2.52 (dd, *J* = 15.4, 7.7 Hz, 1H), 1.71 (s, 1H), 1.66-1.46 (m, 2H), 1.43-1.23 (m, 6H), 0.86 (t, *J* = 6.8 Hz, 3H).

$^{13}C$ NMR (100 MHz, $CDCl_3$): δ 171.20, 148.17, 139.06, 137.08, 136.23, 135.46, 128.14, 127.45, 121.47, 121.43, 117.16, 116.06, 54.64, 49.76, 41.98, 34.13, 31.97, 25.60, 22.68, 14.12.

HRMS (ESI): Calcd for $C_{20}H_{27}N_3O$ $[M+H]^+$: 326.2232, Found: 326.2232.

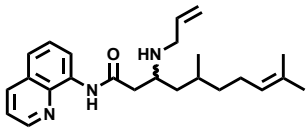


**3-(Allylamino)-5-methyl-*N*-(quinolin-8-yl)hexanamide (7c).** The reaction was conducted according to general procedure A, $Cs_2CO_3$ (10 mol%, 0.01 mmol, 3.3 mg) was added, the reaction mixture was stirred at 100 °C for 48 hours. The product was purified by preparative TLC (1:5 EA:PE) as black oil (15 mg, 48%).

$^1$H NMR (400 MHz, $CDCl_3$): δ 11.42 (s, 1H), 8.81-8.78 (m, 2H), 8.13 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.54-7.40 (m, 3H), 6.16-6.06 (m, 1H), 5.33-5.28 (m, 1H), 5.15-5.12 (m, 1H), 3.49-3.37 (m, 2H), 3.17-3.11 (m, 1H), 2.73 (dd, *J* = 15.4, 3.7 Hz, 1H), 2.51 (dd, *J* = 15.5, 7.3 Hz, 1H), 1.94 (s, 1H), 1.78-1.68 (m, 1H), 1.56-1.49 (m, 1H), 1.42-1.32 (m, 1H), 0.92 (t, *J* = 6.6 Hz, 6H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ 171.11, 148.21, 139.08, 136.85, 136.26, 135.44, 128.16, 127.47, 121.51, 121.48, 117.21, 116.34, 52.69, 49.67, 43.71, 41.89, 25.17, 23.19, 22.62.

HRMS (ESI): Calcd for $C_{19}H_{25}N_3O$ $[M+H]^+$: 312.2076, Found: 312.2075.

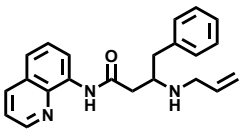


**3-(Allylamino)-5,9-dimethyl-*N*-(quinolin-8-yl)dec-8-enamide (7d).** The reaction was conducted according to general procedure A, $Cs_2CO_3$ (10 mol%, 0.01 mmol, 3.3 mg) was added, the reaction mixture was stirred at 100 °C for 48 hours. The product was purified by preparative TLC (1:5 EA:PE) as yellow oil (21 mg, 54%). The dr value is 1:1 analysis by GCMS.

$^1$H NMR (400 MHz, $CDCl_3$): δ 11.39 (d, *J* = 27.0 Hz, 1H), 8.82-8.78 (m, 2H), 8.13 (dd, *J* = 8.1, 1.7 Hz, 1H), 7.54-7.40 (m, 3H), 6.17-6.05 (m, 1H), 5.33-5.28 (m, 1H), 5.16-5.13 (m, 1H), 5.09-5.04 (m, 1H), 3.48-3.36 (m, 2H), 3.22-3.13 (m, 1H), 2.76-2.70 (m, 1H), 2.57-2.47 (m, 1H), 2.09 (s, 1H), 2.02-1.88 (m, 2H), 1.69-1.55 (m, 7H), 1.51-1.46 (m, 1H), 1.40-1.13 (m, 3H), 0.92 (t, *J* = 6.7 Hz, 3H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ 171.07, 171.06, 148.20, 139.05, 136.76, 136.66, 136.26, 135.38, 131.49, 128.15, 127.46, 124.64, 121.50, 117.23, 117.19, 116.51, 116.41, 52.57, 52.46, 49.67, 49.54, 42.16, 41.90, 41.79, 41.69, 37.61, 37.06, 29.62, 29.48, 25.81, 25.47, 25.41, 20.06, 19.77, 17.77.

HRMS (ESI): Calcd for $C_{24}H_{33}N_3O$ $[M+H]^+$: 380.2702, Found: 380.2707.

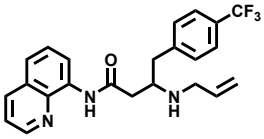


**3-(Allylamino)-4-phenyl-*N*-(quinolin-8-yl)butanamide (7e).** The reaction was conducted according to general procedure A, $Cs_2CO_3$ (10 mol%, 0.01 mmol, 3.3 mg) was added, the reaction mixture was stirred at 100 °C for 48 hours. The product was purified by preparative TLC (1:3 EA:PE) as yellow oil (24 mg, 68%).

$^1$H NMR (400 MHz, $CDCl_3$): δ 11.39 (s, 1H), 8.81-8.79 (m, 2H), 8.14 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.55-7.41 (m, 3H), 7.33-7.30 (m, 2H), 7.25-7.21 (m, 3H), 6.11-6.01 (m, 1H), 5.29-5.24 (m, 1H), 5.14-5.10 (m, 1H), 3.53-3.38 (m, 3H), 2.97 (dd, *J* = 13.5, 6.1 Hz, 1H), 2.86 (dd, *J* = 13.6, 6.8 Hz, 1H), 2.70 (dd, *J* = 15.7, 3.8 Hz, 1H), 2.52 (dd, *J* = 15.7, 7.9 Hz, 1H), 1.86 (s, 1H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ 170.83, 148.21, 138.10, 136.50, 136.27, 135.29, 129.55, 128.73, 127.44, 126.67, 121.58, 121.53, 117.25, 116.49, 55.63, 49.74, 41.44, 40.07.

HRMS (ESI): Calcd for $C_{22}H_{23}N_3O$ $[M+H]^+$: 346.1919, Found: 346.1916.



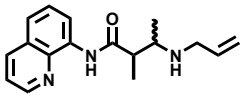
**3-(Allylamino)-*N*-(quinolin-8-yl)-4-(4-(trifluoromethyl)phenyl)butanamide (7f).** The reaction was conducted according to general procedure A, $Cs_2CO_3$ (10 mol%, 0.01 mmol, 3.3 mg) was added, the reaction mixture was stirred at 100 °C for 48 hours. The product was purified by preparative TLC (1:3 EA:PE) as yellow oil (16 mg, 39%).

$^1$H NMR (400 MHz, $CDCl_3$): δ 11.10 (s, 1H), 8.80 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.77 (dd, *J* = 7.0, 2.1 Hz, 1H), 8.15 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.57-7.49 (m, 4H), 7.46-7.43 (m, 1H), 7.35 (d, *J* = 8.0 Hz, 2H), 6.08-5.98 (m, 1H), 5.29-5.24 (m, 1H), 5.16-5.12 (m, 1H), 3.53-3.42 (m, 3H), 3.05 (dd, *J* = 13.6, 6.1 Hz, 1H), 2.90 (dd, *J* = 13.6, 7.1 Hz, 1H), 2.68 (dd, *J* = 15.6, 4.1 Hz, 1H), 2.53 (dd, *J* = 15.6, 7.4 Hz, 1H).

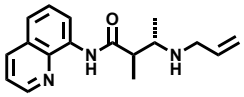
$^{13}$C NMR (100 MHz, $CDCl_3$): δ 170.38, 148.30, 142.53, 138.97, 136.40, 135.08, 129.90, 128.19, 127.49, 125.68 (q, *J* = 3.8 Hz), 121.77, 121.66, 117.24, 116.70, 55.56, 49.80, 41.32, 40.07.

$^{19}$F NMR (376 MHz, $CDCl_3$): δ -62.30.

HRMS (ESI): Calcd for $C_{23}H_{22}F_3N_3O$ $[M+H]^+$: 414.1793, Found: 414.1790.



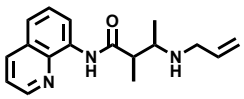
**3-(Allylamino)-2-methyl-*N*-(quinolin-8-yl)butanamide (7g).** The reaction was conducted according to general procedure A, $Cs_2CO_3$ (10 mol%, 0.01 mmol, 3.3 mg) was added, the reaction mixture was stirred at 100 °C for 48 hours. The product was purified by preparative TLC (1:5 EA:PE) as gray solid (17 mg, 60%). The dr value is 7:4 analysis by GCMS.



$^1$H NMR (400 MHz, $CDCl_3$): δ 11.59 (s, 1H), 8.83 (dd, *J* = 7.5, 1.6 Hz, 1H), 8.80 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.13 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.54-7.40 (m, 3H), 6.20-6.10 (m, 1H), 5.37-5.31 (m, 1H), 5.18-5.14 (m, 1H), 3.52-3.40 (m, 2H), 3.06-3.01 (m, 1H), 2.80-2.74 (m, 1H), 1.29 (d, *J* = 7.2 Hz, 3H), 1.15 (d, *J* = 6.5 Hz, 3H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ 174.04, 148.17, 139.30, 137.15, 136.23, 135.73, 128.21, 127.53, 121.45, 121.27, 117.12, 116.00, 55.50, 50.34, 45.34, 16.83, 13.31.

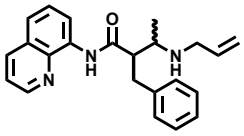
HRMS (ESI): Calcd for $C_{17}H_{21}N_3O$ $[M+H]^+$: 284.1763, Found: 284.1758.



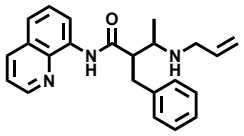
$^1$H NMR (400 MHz, $CDCl_3$): δ 10.74 (s, 1H), 8.81-8.79 (m, 2H), 8.15 (dd, *J* = 8.3, 1.8 Hz, 1H), 7.55-7.42 (m, 3H), 6.01-5.92 (m, 1H), 5.25-5.21 (m, 1H), 5.09-5.06 (m, 1H), 3.45-3.40 (m, 1H), 3.32-3.27 (m, 1H), 3.11-3.04 (m, 1H), 2.66-2.59 (m, 1H), 1.34 (d, *J* = 7.1 Hz, 3H), 1.19 (d, *J* = 6.5 Hz, 3H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ 174.48, 148.28, 138.96, 137.16, 136.38, 135.14, 128.15, 127.54, 121.61, 121.51, 116.95, 115.99, 55.01, 50.41, 48.68, 17.93, 14.55.

HRMS (ESI): Calcd for $C_{17}H_{21}N_3O$ $[M+H]^+$: 284.1763, Found: 284.1758.



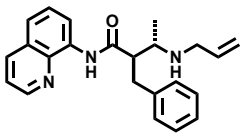
**3-(Allylamino)-2-benzyl-*N*-(quinolin-8-yl)butanamide (7h).** The reaction was conducted according to general procedure A, $Cs_2CO_3$ (10 mol%, 0.01 mmol, 3.3 mg) was added, the reaction mixture was stirred at 100 °C for 24 hours. The product was purified by preparative TLC (1:5 EA:PE) as yellow oil (18 mg, 51%). The dr value is 1.2:1 analysis by GCMS.



$^1$H NMR (400 MHz, $CDCl_3$): δ 11.18 (s, 1H), 8.78-8.75 (m, 2H), 8.13 (dd, *J* = 8.2, 1.6 Hz, 1H), 7.54-7.40 (m, 3H), 7.30-7.24 (m, 4H), 7.21-7.15 (m, 1H), 6.11-6.01 (m, 1H), 5.29-5.24 (m, 1H), 5.15-5.11 (m, 1H), 3.44-3.30 (m, 3H), 3.08-3.00 (m, 2H), 2.83-2.78 (m, 1H), 1.22 (d, *J* = 6.5 Hz, 3H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ 172.34, 148.19, 140.32, 139.26, 136.28, 135.32, 129.08, 128.59, 128.20, 127.49, 126.27, 121.56, 121.50, 117.43, 116.56, 53.92, 52.46, 49.98, 34.32, 16.40.

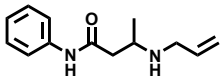
HRMS (ESI): Calcd for $C_{23}H_{25}N_3O$ $[M+H]^+$: 360.2076, Found: 360.2074.



$^1$H NMR (400 MHz, $CDCl_3$): δ 10.47 (s, 1H), 8.75 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.72 (dd, *J* = 7.1, 2.0 Hz, 1H), 8.12 (dd, *J* = 8.2, 1.8 Hz, 1H), 7.53-7.40 (m, 3H), 7.29-7.27 (m, 2H), 7.25-7.21 (m, 2H), 7.15-7.11 (m, 1H), 6.04-5.95 (m, 1H), 5.32-5.27 (m, 1H), 5.15-5.12 (m, 1H), 3.51-3.45 (m, 1H), 3.33-3.27 (m, 1H), 3.24-3.19 (m, 1H), 3.13-3.05 (m, 2H), 2.90-2.85 (m, 1H), 1.28 (d, *J* = 6.6 Hz, 3H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ 172.75, 148.25, 139.71, 138.93, 136.61, 136.31, 134.83, 129.07, 128.60, 128.08, 127.44, 126.39, 121.70, 121.58, 117.19, 116.45, 56.64, 53.34, 50.26, 35.52, 18.23.

HRMS (ESI): Calcd for $C_{23}H_{25}N_3O$ $[M+H]^+$: 360.2076, Found: 360.2074.

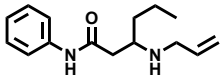


**3-(Allylamino)-*N*-phenylbutanamide (7i).** The reaction was conducted according to general procedure A, $Cs_2CO_3$ (10 mol%, 0.01 mmol, 3.3 mg) was added, the reaction mixture was stirred at 100 °C for 24 hours. The product was purified by preparative TLC (1:20 MeOH:DCM) as yellow oil (19 mg, 89%).

$^1$H NMR (400 MHz, $CDCl_3$): δ 10.78 (s, 1H), 7.54-7.52 (m, 2H), 7.31-7.27 (m, 2H), 7.07-7.03 (m, 1H), 6.00-5.90 (m, 1H), 5.30-5.24 (m, 1H), 5.20-5.16 (m, 1H), 3.45-3.39 (m, 1H), 3.33-3.27 (m, 1H), 3.19-3.11 (m, 1H), 2.54 (dd, *J* = 16.1, 3.4 Hz, 1H), 2.35 (dd, *J* = 16.1, 7.8 Hz, 1H), 2.08 (s, 1H), 1.22 (d, *J* = 6.5 Hz, 3H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ 170.23, 138.65, 135.56, 128.99, 123.73, 119.77, 116.91, 50.09, 48.99, 42.30, 20.30.

HRMS (ESI): Calcd for $C_{13}H_{18}N_2O$ $[M+H]^+$: 219.1497, Found: 219.1499.

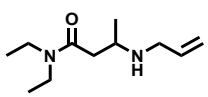


**3-(Allylamino)-*N*-phenylhexanamide (7j).** The reaction was conducted according to general procedure A, $Cs_2CO_3$ (10 mol%, 0.01 mmol, 3.3 mg) was added, the reaction mixture was stirred at 100 °C for 48 hours. The product was purified by preparative TLC (1:20 MeOH:DCM) as yellow oil (17 mg, 69%).

$^1$H NMR (400 MHz, $CDCl_3$): δ 10.89 (s, 1H), 7.54-7.52 (m, 2H), 7.31-7.27 (m, 2H), 7.07-7.03 (m, 1H), 6.01-5.91 (m, 1H), 5.31-5.25 (m, 1H), 5.21-5.17 (m, 1H), 3.41-3.31 (m, 2H), 3.03-2.97 (m, 1H), 2.60 (dd, *J* = 16.1, 3.2 Hz, 1H), 2.34 (dd, *J* = 16.2, 7.4 Hz, 1H), 2.10 (s, 1H), 1.62-1.46 (m, 2H), 1.44-1.30 (m, 2H), 0.93 (t, *J* = 7.3 Hz, 3H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ 170.39, 138.72, 135.53, 129.00, 123.67, 119.74, 117.00, 54.34, 48.64, 39.36, 36.01, 19.18.

HRMS (ESI): Calcd for $C_{15}H_{22}N_2O$ $[M+H]^+$: 247.1810, Found: 247.1816.



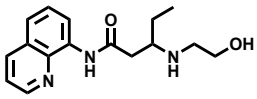
**3-(Allylamino)-*N*,*N*-diethylbutanamide (7k).** The reaction was conducted according to general procedure A, $Cs_2CO_3$ (10 mol%, 0.01 mmol, 3.3 mg) was added, the

reaction mixture was stirred at 100 °C for 24 hours. The product was purified by preparative TLC (1:5 EA:PE) as brown oil (19 mg, 95%).

$^1$H NMR (400 MHz, $CDCl_3$): δ 5.93-5.83 (m, 1H), 5.18-5.14 (m, 1H), 5.08-5.04 (m, 1H), 3.37-3.29 (m, 3H), 3.28-3.23 (m, 2H), 3.23-3.16 (m, 2H), 2.87 (s, 1H), 2.44 (dd, *J* = 15.7, 7.6 Hz, 1H), 2.32 (dd, *J* = 15.7, 5.1 Hz, 1H), 1.15-1.05 (m, 9H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ 170.71, 136.34, 116.39, 49.87, 49.69, 42.04, 40.17, 39.81, 19.95, 14.31, 13.12.

HRMS (ESI): Calcd for $C_{11}H_{22}N_2O$ $[M+H]^+$: 199.1810, Found: 199.1811.

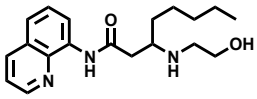



**3-((2-Hydroxyethyl)amino)-*N*-(quinolin-8-yl)pentanamide (7l).** The reaction was conducted according to general procedure A, CsOAc (10 mol%, 0.01 mmol, 1.9 mg) was added, the reaction mixture was stirred at 100 °C for 24 hours. The product was purified by preparative TLC (1:10 MeOH:DCM) as yellow oil (24 mg, 85%).

$^1$H NMR (400 MHz, $CDCl_3$): δ 11.77 (s, 1H), 8.85 (dd, *J* = 7.5, 1.6 Hz, 1H), 8.80 (dd, *J* = 4.3, 1.7 Hz, 1H), 8.13 (dd, *J* = 8.3, 1.8 Hz, 1H), 7.52-7.39 (m, 3H), 3.85-3.76 (m, 2H), 3.02-2.97 (m, 1H), 2.96-2.86 (m, 2H), 2.73 (dd, *J* = 15.8, 3.1 Hz, 1H), 2.51 (dd, *J* = 15.8, 7.1 Hz, 1H), 1.65 -1.53 (m, 2H), 0.95 (t, *J* = 7.4 Hz, 3H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ 171.10, 148.62, 138.65, 137.01, 135.19, 128.40, 127.56, 121.66, 121.44, 117.80, 62.10, 56.48, 48.69, 40.41, 26.57, 10.36.

HRMS (ESI): Calcd for $C_{16}H_{21}N_3O_2$ $[M+H]^+$: 288.1712, Found: 288.1716.



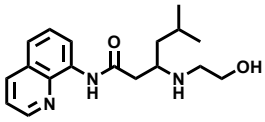

**3-((2-Hydroxyethyl)amino)-*N*-(quinolin-8-yl)octanamide (7m).** The reaction was conducted according to general procedure A, CsOAc (10 mol%, 0.01 mmol, 1.9 mg) was added, the reaction mixture was stirred at 100 °C for 48 hours. The product was purified by preparative TLC (1:10 MeOH:DCM) as yellow oil (24 mg, 72%).

$^1$H NMR (400 MHz, $CDCl_3$): δ 11.83 (s, 1H), 8.87 (dd, *J* = 7.5, 1.6 Hz, 1H), 8.81 (dd, *J* = 4.4, 1.7 Hz, 1H), 8.15-8.13 (m, 1H), 7.52-7.40 (m, 3H), 3.86-3.77 (m, 2H), 3.07-3.01 (m, 1H), 2.99-2.87 (m, 2H), 2.76 (dd, *J* = 15.8, 3.2 Hz, 1H), 2.48 (dd, *J* = 15.7,

6.9 Hz, 1H), 1.60-1.48 (m, 2H), 1.40-1.30 (m, 2H), 1.28-1.22 (m, 4H), 0.85 (t, *J* = 6.9 Hz, 3H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ 171.14, 148.63, 138.66, 137.05, 135.25, 128.43, 127.60, 121.64, 121.44, 117.83, 62.22, 55.16, 48.81, 40.72, 33.88, 31.82, 25.83, 22.63, 14.08.

HRMS (ESI): Calcd for $C_{19}H_{27}N_3O_2$ $[M+H]^+$: 330.2182, Found: 330.2178.

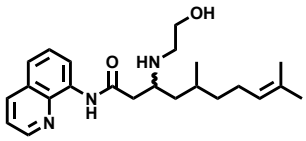


**3-((2-Hydroxyethyl)amino)-5-methyl-*N*-(quinolin-8-yl)hexanamide (7n).** The reaction was conducted according to general procedure A, CsOAc (10 mol%, 0.01 mmol, 1.9 mg) was added, the reaction mixture was stirred at 100 °C for 48 hours. The product was purified by preparative TLC (1:10 MeOH:DCM) as yellow oil (21 mg, 66%).

$^1$H NMR (400 MHz, $CDCl_3$): δ 11.84 (s, 1H), 8.87 (dd, *J* = 7.5, 1.6 Hz, 1H), 8.81 (dd, *J* = 4.3, 1.7 Hz, 1H), 8.14 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.54-7.40 (m, 3H), 3.85-3.77 (m, 2H), 3.14-3.08 (m, 1H), 2.99-2.89 (m, 2H), 2.79 (dd, *J* = 15.7, 3.3 Hz, 1H), 2.45 (dd, *J* = 15.7, 6.4 Hz, 1H), 1.76-1.66 (m, 1H), 1.50-1.34 (m, 2H), 0.90 (d, *J* = 1.8 Hz, 3H), 0.89 (d, *J* = 1.7 Hz, 3H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ 171.07, 148.60, 138.64, 137.06, 135.24, 128.43, 127.60, 121.63, 121.44, 117.81, 62.17, 53.11, 48.86, 43.13, 40.58, 25.07, 22.91, 22.62.

HRMS (ESI): Calcd for $C_{18}H_{25}N_3O_2$ $[M+H]^+$: 315.1947, Found: 315.1940.

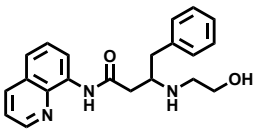


**3-((2-Hydroxyethyl)amino)-5,9-dimethyl-*N*-(quinolin-8-yl)dec-8-enamide (7o).** The reaction was conducted according to general procedure A, CsOAc (10 mol%, 0.01 mmol, 1.9 mg) was added, the reaction mixture was stirred at 100 °C for 48 hours. The product was purified by preparative TLC (1:20 MeOH:DCM) as yellow oil (31 mg, 82%). The dr value is 1.3:1 analysis by GCMS.

$^1$H NMR (400 MHz, $CDCl_3$): δ 11.78 (d, *J* = 21.4 Hz, 1H), 8.88-8.80 (m, 2H), 8.16-8.14 (m, 1H), 7.54-7.41 (m, 3H), 5.07-5.01 (m, 1H), 3.86-3.77 (m, 2H), 3.18-3.12 (m, 1H), 3.02-2.89 (m, 2H), 2.82-2.77 (m, 1H), 2.51-2.44 (m, 1H), 2.04-1.85 (m, 2H), 1.65-1.48 (m, 8H), 1.45-1.24 (m, 2H), 1.21-1.10 (m, 1H), 0.92-0.89 (m, 3H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ 171.06, 170.96, 148.62, 148.58, 138.67, 137.08, 137.05, 135.22, 135.18, 131.57, 128.44, 127.63, 127.62, 124.52, 124.49, 121.68, 121.65, 121.46, 117.83, 62.15, 62.05, 53.07, 52.86, 48.88, 48.71, 41.39, 41.20, 40.93, 40.43, 37.34, 37.04, 29.57, 29.37, 25.78, 25.77, 25.38, 25.33, 19.87, 19.75, 17.76, 17.72.

HRMS (ESI): Calcd for $C_{23}H_{33}N_3O_2$ $[M+H]^+$: 384.2651, Found: 384.2651.

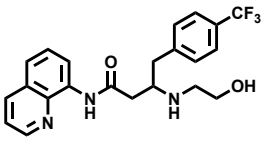



**3-((2-Hydroxyethyl)amino)-4-phenyl-*N*-(quinolin-8-yl)butanamide (7p).** The reaction was conducted according to general procedure A, CsOAc (10 mol%, 0.01 mmol, 1.9 mg) was added, the reaction mixture was stirred at 100 °C for 48 hours. The product was purified by preparative TLC (1:20 MeOH:DCM) as yellow oil (26 mg, 75%).

$^1$H NMR (400 MHz, $CDCl_3$): δ 11.74 (s, 1H), 8.88 (dd, *J* = 7.4, 1.7 Hz, 1H), 8.81 (dd, *J* = 4.3, 1.8 Hz, 1H), 8.16 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.55-7.41 (m, 3H), 7.33-7.29 (m, 2H), 7.25-7.21 (m, 1H), 7.20-7.18 (m, 2H), 3.82-3.72 (m, 2H), 3.41-3.35 (m, 1H), 2.97-2.94 (m, 2H), 2.89 (d, *J* = 6.8 Hz, 2H), 2.81 (dd, *J* = 15.9, 3.3 Hz, 1H), 2.51 (dd, *J* = 15.9, 7.3 Hz, 1H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ 170.79, 148.64, 138.69, 137.84, 137.04, 135.13, 129.31, 128.83, 128.42, 127.58, 126.81, 121.79, 121.49, 117.92, 61.99, 56.25, 48.81, 40.61, 40.08.

HRMS (ESI): Calcd for $C_{21}H_{23}N_3O_2$ $[M+H]^+$: 350.1869, Found: 350.1872.




**3-((2-Hydroxyethyl)amino)-*N*-(quinolin-8-yl)-4-(4-(trifluoromethyl)phenyl)butanamide (7q).** The reaction was conducted according to

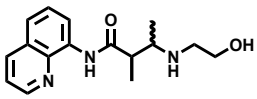
general procedure A, CsOAc (10 mol%, 0.01 mmol, 1.9 mg) was added, the reaction mixture was stirred at 100 °C for 48 hours. The product was purified by preparative TLC (1:10 MeOH:DCM) as yellow oil (21 mg, 51%).

$^1$H NMR (400 MHz, $CDCl_3$): δ 11.58 (s, 1H), 8.86 (dd, *J* = 7.3, 1.8 Hz, 1H), 8.82 (dd, *J* = 4.4, 1.8 Hz, 1H), 8.18 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.58-7.52 (m, 4H), 7.47-7.44 (m, 1H), 7.32 (d, *J* = 8.0 Hz, 2H), 3.83-3.73 (m, 2H), 3.45-3.38 (m, 1H), 3.01-2.90 (m, 4H), 2.80 (dd, *J* = 15.9, 3.4 Hz, 1H), 2.50 (dd, *J* = 15.8, 7.1 Hz, 1H).

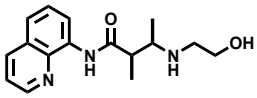
$^{13}$C NMR (100 MHz, $CDCl_3$): δ 170.41, 148.71, 142.22, 138.71, 137.16, 135.03, 129.72, 128.49, 127.66, 125.80 (q, *J* = 3.8 Hz), 125.78, 121.96, 121.61, 117.95, 62.06, 56.21, 48.89, 40.65, 40.18.

$^{19}$F NMR (376 MHz, $CDCl_3$): δ -62.34.

HRMS (ESI): Calcd for $C_{21}H_{22}F_3N_3O_2$ $[M+H]^+$: 418.1742, Found: 418.1737.



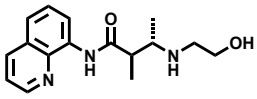
**3-((2-Hydroxyethyl)amino)-2-methyl-*N*-(quinolin-8-yl)butanamide (7r).** The reaction was conducted according to general procedure A, CsOAc (10 mol%, 0.01 mmol, 1.9 mg) was added, the reaction mixture was stirred at 100 °C for 48 hours. The product was purified by preparative TLC (1:10 MeOH:DCM) as yellow oil (27 mg, 93%). The dr value is 2.6:1 analysis by GCMS.



$^1$H NMR (400 MHz, $CDCl_3$): δ 11.14 (s, 1H), 8.86-8.84 (m, 2H), 8.17 (dd, *J* = 8.2, 1.8 Hz, 1H), 7.56-7.43 (m, 3H), 3.80-3.69 (m, 1H), 3.09-3.01 (m, 2H), 2.88-2.83 (m, 1H), 2.67-2.60 (m, 2H), 1.42 (d, *J* = 7.2 Hz, 3H), 1.27 (d, *J* = 6.6 Hz, 3H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ 173.33, 148.60, 138.75, 137.16, 135.46, 128.57, 127.74, 121.42, 117.60, 62.36, 57.08, 50.27, 43.36, 16.25, 13.40.

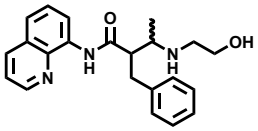
HRMS (ESI): Calcd for $C_{16}H_{21}N_3O_2$ $[M+H]^+$: 288.1712, Found: 288.1716.



$^1$H NMR (400 MHz, $CDCl_3$): δ 11.82 (s, 1H), 8.91 (dd, *J* = 7.7, 1.5 Hz, 1H), 8.83 (dd, *J* = 4.3, 1.7 Hz, 1H), 8.16 (dd, *J* = 8.2, 1.7 Hz, 1H), 7.55-7.42 (m, 3H), 3.88-3.79 (m, 2H), 3.03-2.94 (m, 3H), 2.93-2.87 (m, 1H), 1.25 (d, *J* = 7.1 Hz, 3H), 1.13 (d, *J* = 6.6 Hz, 3H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ 174.55, 148.71, 138.83, 136.91, 135.05, 128.40, 127.61, 121.78, 121.60, 117.52, 61.82, 55.55, 49.97, 49.02, 18.94, 16.26.

HRMS (ESI): Calcd for $C_{16}H_{21}N_3O_2$ $[M+H]^+$: 288.1712, Found: 288.1716.

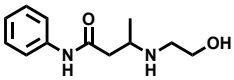



**2-Benzyl-3-((2-hydroxyethyl)amino)-*N*-(quinolin-8-yl)butanamide (7s).** The reaction was conducted according to general procedure A, CsOAc (10 mol%, 0.01 mmol, 1.9 mg) was added, the reaction mixture was stirred at 100 °C for 48 hours. The product was purified by preparative TLC (1:20 MeOH:DCM) as yellow oil (33 mg, 90%). The dr value is 2.3:1 analysis by GCMS.

$^1$H NMR (400 MHz, $CDCl_3$): δ 11.78 (s, 0.6H), 11.10 (s, 0.2H),8.93-8.79 (m, 2H), 8.16-8.12 (m, 1H), 7.55-7.40 (m, 3H), 7.32-7.25 (m, 4H), 7.22-7.14 (m, 1H), 3.81-3.73 (m, 2H), 3.49-3.24 (m, 1H), 3.13-3.06 (m, 1H), 3.02-2.97 (m, 1H), 2.93-2.87 (m, 1H), 2.86-2.76 (m, 2H), 2.68-2.62 (m, 1H), 1.28-1.16 (m, 3H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ 172.97, 172.14, 148.66, 148.50, 140.37, 139.09, 138.68, 138.60, 137.14, 136.79, 135.25, 134.83, 129.00, 128.89, 128.65, 128.56, 128.50, 128.29, 127.67, 127.47, 126.51, 126.22, 121.73, 121.52, 121.42, 121.40, 117.45, 117.38, 62.23, 62.02, 57.23, 54.14, 53.01, 50.35, 50.19, 49.87, 36.91, 33.71, 19.43, 16.12.

HRMS (ESI): Calcd for $C_{22}H_{25}N_3O_2$ $[M+H]^+$: 364.2025, Found: 364.2030.

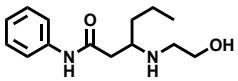



**3-((2-Hydroxyethyl)amino)-*N*-phenylbutanamide (7t).** The reaction was conducted according to general procedure A, CsOAc (10 mol%, 0.01 mmol, 1.9 mg) was added, the reaction mixture was stirred at 100 °C for 24 hours. The product was purified by preparative TLC (1:10 MeOH:DCM) as yellow oil (20 mg, 88%).

$^1$H NMR (400 MHz, $CDCl_3$): δ 10.39 (s, 1H), 7.54-7.52 (m, 2H), 7.27 (t, *J* = 7.3 Hz, 2H), 7.04 (t, *J* = 7.4 Hz, 1H), 3.77-3.69 (m, 2H), 3.17-3.08 (m, 1H), 3.01 (s, 2H), 2.90-2.85(m, 1H), 2.74-2.69 (m, 1H), 2.48 (dd, *J* = 15.8, 4.0 Hz, 1H), 2.35 (dd, *J* = 15.8, 7.7 Hz, 1H), 1.16 (d, *J* = 6.4 Hz, 3H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ 170.55, 138.43, 128.99, 124.03, 120.06, 61.27, 50.44, 48.26, 42.47, 20.08.

HRMS (ESI): Calcd for $C_{12}H_{18}N_2O_2$ $[M+H]^+$: 223.1447, Found: 223.1452.

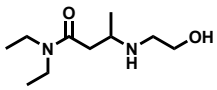


**1-(1-((2-Hydroxyethyl)amino)butyl)-3-phenylurea (7u).** The reaction was conducted according to general procedure A, CsOAc (10 mol%, 0.01 mmol, 1.9 mg) was added, the reaction mixture was stirred at 100 °C for 48 hours. The product was purified by preparative TLC (1:10 MeOH:DCM) as yellow oil (21 mg, 85%).

$^1$H NMR (400 MHz, $CDCl_3$): δ 10.58 (s, 1H), 7.54-7.51 (m, 2H), 7.28-7.23 (m, 2H), 7.05-7.01 (m, 1H), 3.74 (t, *J* = 5.1 Hz, 2H), 3.00-2.94 (m, 1H), 2.87-2.73 (m, 4H), 2.53 (dd, *J* = 16.0, 3.5 Hz, 1H), 2.31 (dd, *J* = 16.0, 7.5 Hz, 1H), 1.57-1.39 (m, 2H), 1.36-1.24 (m, 2H), 0.89 (t, *J* = 7.2 Hz, 3H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ 170.72, 138.52, 128.97, 123.92, 119.99, 61.44, 54.69, 47.89, 39.63, 35.98, 19.15, 14.13.

HRMS (ESI): Calcd for $C_{14}H_{22}N_2O_2$ $[M+H]^+$: 251.1760, Found: 251.1753.

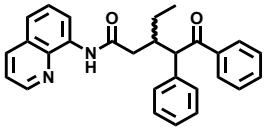


***N*,*N*-Diethyl-3-((2-hydroxyethyl)amino)butanamide (7v).** The reaction was conducted according to general procedure A, CsOAc (10 mol%, 0.01 mmol, 1.9 mg) was added, the reaction mixture was stirred at 100 °C for 24 hours. The product was purified by preparative TLC (1:10 MeOH:DCM) as yellow oil (16 mg, 78%).

$^1$H NMR (400 MHz, $CDCl_3$): δ 3.77-3.71 (m, 1H), 3.62-3.57 (m, 1H), 3.41-3.27 (m, 4H), 3.25-3.21 (m, 3H), 2.87-2.81 (m, 1H), 2.77-2.72 (m, 1H), 2.47-2.33 (m, 2H), 1.16-1.06 (m, 9H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ 170.85, 60.40, 49.19, 48.12, 42.09, 40.37, 39.54, 19.97, 14.27, 13.13.

HRMS (ESI): Calcd for $C_{10}H_{22}N_2O_2$ $[M+H]^+$: 203.1760, Found: 203.1754.

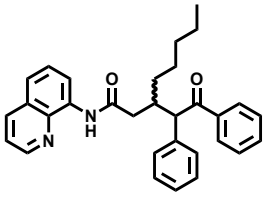


**3-Ethyl-5-oxo-4,5-diphenyl-*N*-(quinolin-8-yl)pentanamide (7w).** The reaction was conducted according to general procedure B, KOH (50 mol%, 0.05 mmol, 2.8 mg) was added, the reaction mixture was stirred at 100 °C for 48 hours. The product was purified by preparative TLC (1:20 EA:PE) as gray oil (36 mg, 85%). The dr value is 1.2:1 analysis by GCMS.

$^1$H NMR (400 MHz, $CDCl_3$): δ 9.83 (s, 0.4H), 9.62 (s, 0.5H), 8.78-8.74 (m, 2H), 8.14-8.10 (m, 1H), 8.04-7.99 (m, 2H), 7.54-7.44 (m, 4H), 7.43-7.37 (m, 3H), 7.33-7.27 (m, 2H), 7.25-7.10 (m, 2H), 5.00 (t, *J* = 9.4 Hz, 1H), 3.09-2.89 (m, 1H), 2.79-2.69 (m, 1H), 2.60 (dd, *J* = 15.2, 4.6 Hz, 0.5H), 2.30 (dd, *J* = 15.2, 6.9 Hz, 0.5H), 1.76-1.57 (m, 1H), 1.53-1.33 (m, 1H), 1.03-0.93 (m, 3H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ 200.32, 200.18, 171.00, 148.21, 148.14, 138.38, 138.33, 137.72, 137.69, 137.40, 137.27, 136.38, 136.30, 134.58, 134.57, 133.01, 132.86, 129.39, 129.34, 129.03, 128.91, 128.78, 128.70, 128.63, 128.49, 127.98, 127.95, 127.44, 127.40, 127.37, 127.28, 121.63, 121.61, 121.46, 121.40, 116.44, 116.39, 56.18, 56.09, 40.69, 40.48, 39.10, 38.35, 25.06, 23.50, 11.68, 11.30.

HRMS (ESI): Calcd for $C_{28}H_{26}N_2O_2$ $[M+H]^+$: 423.2073, Found: 423.2071.



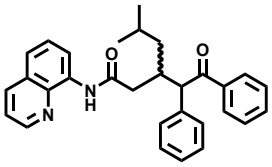
**3-(2-Oxo-1,2-diphenylethyl)-*N*-(quinolin-8-yl)octanamide (7x).** The reaction was conducted according to general procedure B, KOH (50 mol%, 0.05 mmol, 2.8 mg) was added, the reaction mixture was stirred at 100 °C for 48 hours. The product was purified by preparative TLC (1:20 EA:PE) as black oil (34 mg, 73%). The dr value is 1.2:1 analysis by GCMS.

$^1$H NMR (400 MHz, $CDCl_3$): δ 9.82 (s, 0.4H), 9.82 (s, 0.5H), 8.78-8.74 (m, 2H), 8.14-8.10 (m, 1H), 8.04-7.99 (m, 2H), 7.54-7.45 (m, 4H), 7.44-7.37 (m, 3H), 7.33-7.26 (m, 2H), 7.24-7.09 (m, 2H), 5.02 (dd, *J* = 9.5, 2.6 Hz, 1H), 3.10-2.92 (m, 1H),

2.80-2.68 (m, 1H), 2.61 (dd, *J* = 15.2, 4.6 Hz, 0.5H), 2.30 (dd, *J* = 15.2, 6.5 Hz, 0.5H), 1.71-1.62 (m, 0.5H), 1.49-1.35 (m, 2.5H), 1.30-1.10 (m, 5H), 0.80-0.76 (m, 3H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ 200.43, 200.28, 171.05, 171.01, 148.19, 148.11, 138.39, 138.35, 137.74, 137.46, 137.29, 136.38, 136.30, 134.59, 134.56, 132.98, 132.83, 129.42, 129.37, 129.00, 128.88, 128.80, 128.71, 128.61, 128.47, 127.98, 127.95, 127.45, 127.40, 127.34, 127.27, 121.63, 121.62, 121.45, 121.39, 116.45, 116.41, 56.51, 56.28, 39.54, 39.39, 39.06, 38.68, 32.39, 32.02, 31.94, 30.69, 27.03, 26.58, 22.63, 22.60, 14.08.

HRMS (ESI): Calcd for $C_{31}H_{32}N_2O_2$ $[M+H]^+$: 465.2542, Found: 465.2549.

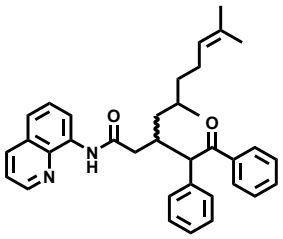


**5-Methyl-3-(2-oxo-1,2-diphenylethyl)-*N*-(quinolin-8-yl)hexanamide (7y).** The reaction was conducted according to general procedure B, KOH (50 mol%, 0.05 mmol, 2.8 mg) was added, the reaction mixture was stirred at 100 °C for 48 hours. The product was purified by preparative TLC (1:20 EA:PE) as gray oil (23 mg, 52%). The dr value is 1.2:1 analysis by GCMS.

$^1$H NMR (400 MHz, $CDCl_3$): δ 9.79 (s, 0.4H), 9.56 (s, 0.5H), 8.78-8.73 (m, 2H), 8.15-8.10 (m, 1H), 8.03-7.98 (m, 2H), 7.55-7.39 (m, 5H), 7.35-7.35 (m, 2H), 7.30-7.27 (m, 2H), 7.24-7.07 (m, 2H), 5.07 (dd, *J* = 9.2, 4.9 Hz, 1H), 3.13-2.94 (m, 1H), 2.80 (dd, *J* = 15.0, 5.5 Hz, 0.5H), 2.71-2.62 (m, 1H), 2.28 (dd, *J* = 15.4, 5.3 Hz, 0.5H), 1.85-1.75 (m, 1H), 1.69-1.62 (m, 1H), 1.46-1.39 (m, 0.5H), 1.29-1.23 (m, 1H), 1.15-1.09 (m, 0.5H), 0.98 (d, *J* = 6.5 Hz, 1.6H), 0.85 (dd, *J* = 11.2, 6.6 Hz, 3H), 0.78 (d, *J* = 6.5 Hz, 1.4H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ 200.65, 200.40, 171.08, 171.00, 148.20, 148.12, 138.40, 138.36, 137.77, 137.76, 137.53, 137.29, 136.39, 136.30, 134.61, 134.54, 132.96, 132.78, 129.51, 129.48, 128.96, 128.86, 128.83, 128.77, 128.60, 128.44, 128.01, 127.96, 127.46, 127.40, 127.29, 127.25, 121.65, 121.63, 121.47, 121.40, 116.46, 116.43, 56.82, 56.44, 42.01, 40.32, 39.51, 38.56, 37.26, 36.97, 26.03, 25.59, 23.92, 23.73, 21.72, 21.69.

HRMS (ESI): Calcd for $C_{30}H_{30}N_2O_2$ $[M+H]^+$: 451.2386, Found: 451.2378.

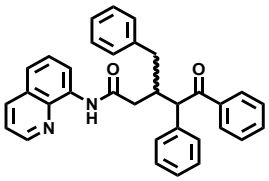


**5,9-Dimethyl-3-(2-oxo-1,2-diphenylethyl)-*N*-(quinolin-8-yl)dec-8-enamide (7z).** The reaction was conducted according to general procedure B, KOH (50 mol%, 0.05 mmol, 2.8 mg) was added, the reaction mixture was stirred at 100 °C for 48 hours. The product was purified by preparative TLC (1:20 EA:PE) as yellow oil (25 mg, 49%). The dr value is 1.3:1 analysis by GCMS.

$^1$H NMR (400 MHz, $CDCl_3$): δ 9.57 (d, *J* = 19.0 Hz, 1H), 8.78-8.72 (m, 2H), 8.15-8.12 (m, 1H), 8.03-8.00 (m, 2H), 7.55-7.40 (m, 6H), 7.38-7.36 (m, 2H), 7.25-7.19 (m, 2H), 7.14-7.05 (m, 1H), 5.12-5.09 (m, 1H), 5.06-4.92 (m, 1H), 3.14-3.06 (m, 1H), 2.70-2.58 (m, 1H), 2.32-2.21 (m, 1H), 2.07-1.84 (m, 2H), 1.77-1.36 (m, 9H), 1.26-1.09 (m, 2H), 1.00-0.86 (m, 3H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ 200.43, 200.38, 171.01, 170.99, 148.15, 148.13, 138.41, 138.38, 137.86, 137.72, 137.61, 137.54, 136.40, 134.66, 134.62, 132.96, 131.23, 131.08, 129.57, 129.53, 128.97, 128.95, 128.79, 128.61, 128.04, 128.03, 127.49, 127.32, 127.29, 125.09, 124.84, 121.66, 121.64, 121.40, 116.48, 116.45, 56.99, 56.61, 40.48, 40.05, 39.00, 38.34, 38.23, 37.20, 36.93, 35.94, 30.58, 30.45, 25.83, 25.65, 25.63, 25.37, 20.56, 19.15, 17.81, 17.62.

HRMS (ESI): Calcd for $C_{35}H_{38}N_2O_2$ $[M+H]^+$: 519.3012, Found: 519.3010.



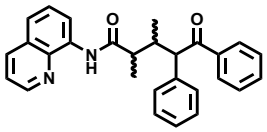
**3-Benzyl-5-oxo-4,5-diphenyl-*N*-(quinolin-8-yl)pentanamide (7aa).** The reaction was conducted according to general procedure B, KOH (50 mol%, 0.05 mmol, 2.8 mg) was added, the reaction mixture was stirred at 100 °C for 48 hours. The product was purified by preparative TLC (1:20 EA:PE) as gray solid (23 mg, 47%). The dr value is 1.1:1 analysis by GCMS.

$^1$H NMR (400 MHz, $CDCl_3$): δ 9.56 (d, *J* = 72.8 Hz, 1H), 8.78-8.71 (m, 2H), 8.15-8.10 (m, 1H), 8.05-7.96 (m, 2H), 7.57-7.46 (m, 3H), 7.44-7.36 (m, 3H), 7.35-7.10 (m,

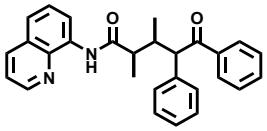
10H), 5.22-5.19 (m, 1H), 3.36-3.15 (m, 1H), 3.02-2.74 (m, 2H), 2.73-2.53 (m, 1H), 2.48-2.19 (m, 1H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ 200.48, 200.15, 170.93, 170.82, 148.11, 140.50, 140.23, 138.34, 137.73, 137.53, 137.29, 137.18, 136.37, 136.27, 134.54, 134.46, 133.07, 132.82, 129.71, 129.42, 129.07, 129.06, 128.85, 128.62, 128.51, 128.46, 128.42, 128.01, 127.94, 127.42, 127.37, 126.23, 126.17, 121.67, 121.63, 121.52, 121.46, 116.43, 55.59, 55.26, 41.60, 41.38, 37.80, 37.62, 37.04, 36.90.

HRMS (ESI): Calcd for $C_{33}H_{28}N_2O_2$ $[M+H]^+$: 485.2229, Found: 485.2229.



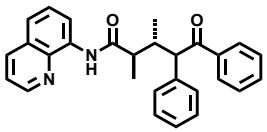
**2,3-Dimethyl-5-oxo-4,5-diphenyl-*N*-(quinolin-8-yl)pentanamide (7ab).** The reaction was conducted according to general procedure B, KOH (50 mol%, 0.05 mmol, 2.8 mg) was added, the reaction mixture was stirred at 100 °C for 48 hours. The product was purified by preparative TLC (1:20 EA:PE) as gray solid (25 mg, 60%). The dr value is 2.2:2.2:1:1 analysis by GCMS.



$^1$H NMR (400 MHz, $CDCl_3$): δ 9.72 (s, 1H), 8.85-8.82 (m, 2H), 8.19 (dd, *J* = 8.3, 1.7 Hz, 1H), 8.01-7.99 (m, 2H), 7.59-7.52 (m, 4H), 7.50-7.44 (m, 2H), 7.38-7.34 (m, 2H), 7.31-7.27 (m, 2H), 7.24-7.20 (m, 1H), 5.07 (d, *J* = 10.7 Hz, 1H), 2.80-2.71 (m, 1H), 2.58-2.50 (m, 1H), 1.34 (d, *J* = 7.1 Hz, 3H), 1.16 (d, *J* = 6.7 Hz, 3H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ 200.57, 173.62, 148.20, 138.73, 137.93, 137.51, 136.51, 134.62, 133.10, 129.51, 129.18, 128.77, 128.64, 128.14, 127.59, 127.45, 121.77, 121.61, 116.75, 57.21, 42.30, 41.82, 17.08, 13.86.

HRMS (ESI): Calcd for $C_{28}H_{26}N_2O_2$ $[M+H]^+$: 423.2073, Found: 423.2066.

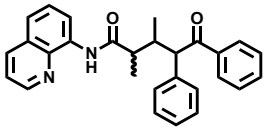


$^1$H NMR (400 MHz, $CDCl_3$): δ 9.77 (s, 1H), 8.79 (dd, *J* = 7.5, 1.5 Hz, 1H), 8.52 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.09 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.98-7.95 (m, 2H), 7.54-7.46 (m,

2H), 7.37-7.31 (m, 3H), 7.26-7.22 (m, 3H), 7.18-7.14 (m, 3H), 4.92 (d, *J* = 10.6 Hz, 1H), 2.96-2.89 (m, 1H), 2.86-2.77 (m, 1H), 1.47 (d, *J* = 7.0 Hz, 3H), 0.87 (d, *J* = 7.1 Hz, 3H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ 200.46, 173.56, 148.11, 138.48, 138.08, 137.09, 136.20, 134.32, 132.74, 129.18, 128.92, 128.88, 128.28, 127.89, 127.39, 127.28, 121.54, 121.51, 116.42, 57.67, 44.69, 40.48, 16.74, 12.87.

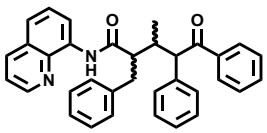
HRMS (ESI): Calcd for $C_{28}H_{26}N_2O_2$ $[M+H]^+$: 423.2073, Found: 423.2066.



$^1$H NMR (400 MHz, $CDCl_3$): δ 10.12 (s, 0.5H), 9.77 (s, 0.5H), 8.94-8.71 (m, 2H), 8.18-8.13 (m, 1H), 8.06-7.96 (m, 2H), 7.56-7.43 (m, 5H), 7.41-7.33 (m, 4H), 7.29-7.26 (m, 1H), 7.24-7.18 (m, 1H), 4.67 (dd, *J* = 9.9, 4.4 Hz, 1H), 3.24-3.12 (m, 1H), 2.92-2.85 (m, 0.5H), 2.54-2.48 (m, 0.5H), 1.25-1.21 (m, 3H), 1.07 (d, *J* = 6.8 Hz, 1.5H), 0.81 (d, *J* = 7.0 Hz, 1.5H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ 200.05, 199.76, 174.44, 174.41, 148.53, 148.24, 138.75, 138.54, 137.82, 137.62, 137.47, 137.01, 136.36, 136.34, 134.92, 134.68, 133.12, 133.07, 129.42, 129.34, 129.09, 128.95, 128.82, 128.71, 128.61, 128.58, 128.09, 127.98, 127.64, 127.48, 127.42, 121.71, 121.65, 121.45, 121.32, 116.57, 116.22, 57.06, 57.02, 44.34, 42.77, 40.17, 38.85, 13.67, 13.09, 11.50, 10.38.

HRMS (ESI): Calcd for $C_{28}H_{26}N_2O_2$ $[M+H]^+$: 423.2073, Found: 423.2066.

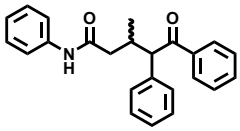


**2-Benzyl-3-methyl-5-oxo-4,5-diphenyl-*N*-(quinolin-8-yl)pentanamide (7ac).** The reaction was conducted according to general procedure B, KOH (50 mol%, 0.05 mmol, 2.8 mg) was added, the reaction mixture was stirred at 100 °C for 48 hours. The product was purified by preparative TLC (1:20 EA:PE) as black solid (29 mg, 58%). The dr value is 1.5:1.5:1:1 analysis by GCMS.

$^1$H NMR (400 MHz, $CDCl_3$): δ 10.06-9.48 (m, 1H), 8.93-8.68 (m, 2H), 8.27-8.05 (m, 1H), 8.00-7.84 (m, 2H), 7.60-7.28 (m, 10H), 7.25-6.96 (m, 6H), 5.01-4.69 (m, 1H), 3.42-3.06 (m, 2H), 3.03-2.69 (m, 2H), 1.26-0.94 (m, 3H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ 200.20, 200.04, 199.99, 199.75, 172.96, 172.77, 172.24, 172.14, 148.48, 148.07, 148.01, 147.80, 140.52, 140.31, 139.62, 139.22, 138.62, 138.61, 138.28, 138.04, 137.84, 137.79, 137.50, 137.37, 137.35, 136.97, 136.68, 136.49, 136.20, 136.15, 135.83, 134.88, 134.57, 134.46, 134.02, 133.11, 133.09, 132.57, 129.49, 129.42, 129.27, 129.24, 129.20, 129.15, 129.07, 129.05, 128.96, 128.92, 128.84, 128.74, 128.63, 128.60, 128.58, 128.55, 128.54, 128.50, 128.42, 128.09, 127.97, 127.84, 127.81, 127.62, 127.56, 127.49, 127.41, 127.31, 127.29, 127.17, 126.36, 126.34, 126.14, 126.14, 121.74, 121.72, 121.62, 121.53, 121.51, 121.41, 121.26, 116.91, 116.50, 116.20, 116.09, 57.72, 57.27, 57.16, 56.91, 52.88, 52.04, 51.26, 49.69, 40.87, 39.32, 39.17, 38.43, 37.61, 36.91, 32.64, 31.90, 14.31, 13.91, 13.72, 12.95.

HRMS (ESI): Calcd for $C_{34}H_{30}N_2O_2$ $[M+H]^+$: 499.2386, Found: 499.2381.

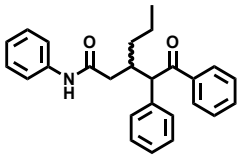


**3-Methyl-5-oxo-*N*,4,5-triphenylpentanamide (7ad).** The reaction was conducted according to general procedure B, KOH (50 mol%, 0.05 mmol, 2.8 mg) was added, the reaction mixture was stirred at 100 °C for 24 hours. The product was purified by preparative TLC (1:5 EA:PE) as yellow solid (33 mg, 93%). The dr value is 1.5:1 analysis by GCMS.

$^1$H NMR (400 MHz, $CDCl_3$): δ 8.00-7.97 (m, 2H), 7.87 (s, 1H), 7.55-7.46 (m, 3H), 7.40-7.36 (m, 3H), 7.33-7.27 (m, 5H), 7.23-7.17 (m, 1H), 7.11-7.06 (m, 1H), 4.64 (dd, *J* = 27.8, 9.7 Hz, 1H), 3.09-2.88 (m, 1H), 2.53 (dd, *J* = 13.9, 3.5 Hz, 0.6H), 2.26 (dd, *J* = 13.8, 8.5 Hz, 0.4H), 2.28-2.23 (m, 0.5H), 2.03-1.97 (m, 0.5H) 1.16 (d, *J* = 6.6 Hz, 1.2H), 0.91 (d, *J* = 6.8 Hz, 1.8H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ 200.68, 200.14, 170.72, 170.66, 138.17, 148.14, 137.99, 137.56, 137.48, 137.27, 136.94, 133.27, 133.13, 129.14, 129.07, 129.04, 129.02, 128.96, 128.86, 128.70, 128.66, 127.55, 127.49, 124.24, 124.20, 120.03, 119.97, 59.04, 58.44, 43.63, 41.73, 34.72, 34.58, 18.79, 17.83.

HRMS (ESI): Calcd for $C_{24}H_{23}NO_2$ $[M+H]^+$: 358.1807, Found: 358.1810.

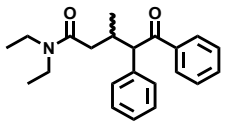


**3-(2-Oxo-1,2-diphenylethyl)-*N*-phenylhexanamide (7ae).** The reaction was conducted according to general procedure B, KOH (50 mol%, 0.05 mmol, 2.8 mg) was added, the reaction mixture was stirred at 100 °C for 24 hours. The product was purified by preparative TLC (1:5 EA:PE) as white solid (34 mg, 87%). The dr value is 1.1:1 analysis by GCMS.

$^1$H NMR (400 MHz, $CDCl_3$): δ 8.06 (s, 1H), 8.02-7.98 (m, 2H), 7.55-7.53 (m, 1H), 7.50-7.44 (m, 2H), 7.40-7.36 (m, 3H), 7.34-7.27 (m, 5H), 7.23-7.17 (m, 1H), 7.11-7.07 (m, 1H), 4.88 (dd, *J* = 36.2, 9.5 Hz, 1H), 2.96-2.78 (m, 1H), 2.47-2.42 (m, 1.4H), 2.02-1.97 (m, 0.6H), 1.68-1.59 (m, 0.4H), 1.48-1.37 (m, 2H), 1.30-1.18 (m, 1.6H), 0.89-0.86 (m, 1.4H), 0.78-0.75 (m, 1.6H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ 201.26, 200.59, 171.14, 170.90, 138.27, 138.07, 137.49, 137.16, 136.95, 133.32, 133.12, 129.42, 129.06, 129.00, 128.98, 128.91, 128.77, 128.70, 128.65, 127.50, 124.12, 124.09, 119.95, 119.91, 57.58, 56.40, 40.82, 39.34, 38.99, 38.43, 35.01, 33.94, 20.62, 19.77, 14.33, 14.23

HRMS (ESI): Calcd for $C_{26}H_{27}NO_2$ $[M+H]^+$: 386.2120, Found: 386.2123.



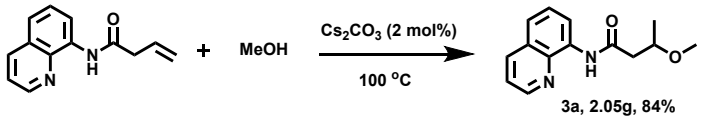
***N*,*N*-Diethyl-3-methyl-5-oxo-4,5-diphenylpentanamide (7af).** The reaction was conducted according to general procedure B, KOH (50 mol%, 0.05 mmol, 2.8 mg) was added, the reaction mixture was stirred at 100 °C for 24 hours. The product was purified by preparative TLC (1:5 EA:PE) as yellow oil (31 mg, 90%). The dr value is 1:1 analysis by GCMS.

$^1$H NMR (400 MHz, $CDCl_3$): δ 7.99-7.97 (m, 2H), 7.48-7.43 (m, 1H), 7.39-7.35 (m, 3H), 7.33-7.31 (m, 1H), 7.28-7.24 (m, 2H), 7.20-7.15 (m, 1H), 4.71 (dd, *J* = 14.5, 9.5 Hz, 1H), 3.45-3.31 (m, 1.5H), 3.29-3.18 (m, 1.5H), 3.14-2.98 (m, 1H), 2.97-2.82 (m, 1H), 2.46 (dd, *J* = 14.4, 4.6 Hz, 0.5H), 2.23-2.17 (m, 1H), 1.95 (dd, *J* = 14.9, 8.8 Hz, 0.5H), 1.13-1.09 (m, 3H), 1.08-1.04 (m, 3H), 0.94-0.90 (m, 1.5H), 0.86 (d, *J* = 6.8 Hz, 1.5H).

$^{13}C$ NMR (100 MHz, $CDCl_3$): δ 200.38, 200.27, 171.16, 171.05, 138.03, 137.70, 137.51, 137.24, 132.97, 132.94, 129.24, 129.03, 128.90, 128.79, 128.73, 128.65, 128.59, 127.32, 127.24, 58.49, 58.33, 42.10, 42.02, 40.14, 40.04, 38.60, 36.93, 34.57, 33.88, 18.66, 17.47, 14.42, 14.18, 13.17.

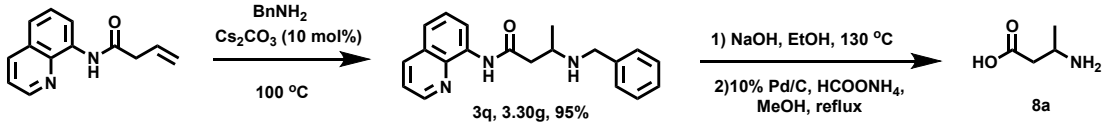
HRMS (ESI): Calcd for $C_{22}H_{27}NO_2$ $[M+H]^+$: 338.2120, Found: 338.2116.

## V. Gram-scale reaction and drug synthesis

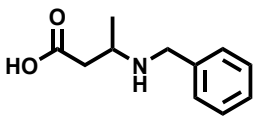



*General procedure for gram-scale reaction:* In a dry 100-mL Schlenk tube containing a magnetic stirbar was charged with $Cs_2CO_3$ (2 mol%, 66 mg, 0.2 mmol), alkene 2a (1 equiv, 2.12 g, 10 mmol) and methanol (10 mL). The mixture was stirred at 100 ºC for 24 h. The reaction mixture was concentrated on a rotary evaporator, then the resulting residue was directly subjected to silica gel flash chromatography (1:10 EA:PE), product was obtained as yellow oil (2.05 g, 84%).

*General procedure for gram-scale reaction:* In a dry 100-mL Schlenk tube containing a magnetic stirbar was charged with $Cs_2CO_3$ (10 mol%, 326 mg, 1 mmol), alkene 2a (1 equiv, 2.12 g, 10 mmol) and methanol (10 mL). The mixture was stirred at 80 ºC for 24 h. The reaction mixture was concentrated on a rotary evaporator, then the resulting residue was directly subjected to silica gel flash chromatography (1:10 EA:PE), product was obtained as yellow oil (2.40 g, 99%).




*The 8-aminoquinoline group was removed by adapting a literature procedure.*[6,7,8] To a flame-dried 48-mL sealed vessel equipped with a Teflon-coated magnetic stir bar was added 3q (9.5 mmol), NaOH (142.5 mmol, 15 equiv), and 39 mL of EtOH. The resulting mixture was stirred at 130 ºC for 16 h. At this time, the reaction mixture was allowed to cool to room temperature and neutralized, the solvent was evaporated under vacuum and the product was washed with $CH_2Cl_2$, filtered and decanted with MeOH to obtain a white solid. (1.77g, 96% yield).



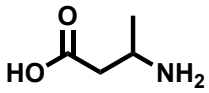
**3-(Benzylamino)butanoic acid.**

$^1$H NMR (400 MHz, $D_2O$): δ 7.34 (s, 5H), 4.16-4.06 (m, 2H), 3.46-3.38 (m, 1H), 2.41-2.40 (m, 2H), 1.23 (d, $J$ = 6.7 Hz, 3H).

$^{13}$C NMR (100 MHz, $D_2O$): δ 177.99, 131.14, 129.52, 129.33, 51.59, 48.07, 38.92, 15.91.

HRMS (ESI): Calcd for $C_{11}H_{15}NO_2$ $[M+H]^+$: 194.1181, Found: 194.1182.

*The benzyl group was removed by adapting a literature procedure.*[9] To a stirred suspension of an appropriate *N*-benzyl compound (9.12 mmol) and an equal weight of 10% Pd-C in dry methanol (60 ml), anhydrous ammonium formate (45.6 mmol) was added in a single portion under nitrogen. The resulting mixture was stirred at 80 ºC for 2 h. The reaction mixture was filtered while hot and the celite pad was washed with boiling water (60 ml), and concentrated in vacuo to give pure free amino acid as a colorless oil (0.90g, 96% yield).



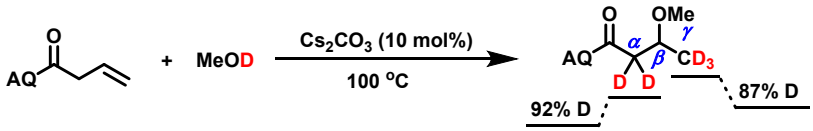

**3-Aminobutanoic acid. (8a)**

$^1$H NMR (400 MHz, $D_2O$): δ 3.49-3.41 (m, 1H), 2.34 (d, *J* = 6.6 Hz, 2H), 1.15 (d, *J* = 6.7 Hz, 2H).

$^{13}$C NMR (100 MHz, $D_2O$): δ 177.83, 45.29, 40.45, 17.71.

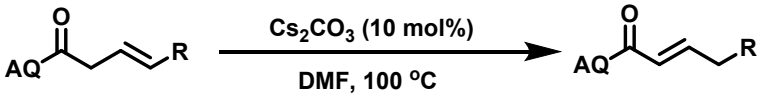
HRMS (ESI): Calcd for $C_4H_9NO_2$ $[M+H]^+$: 104.0712, Found: 104.0714.

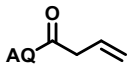
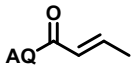
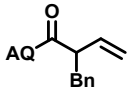
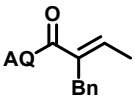
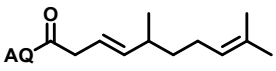
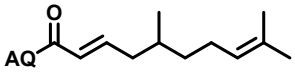
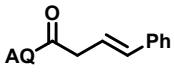
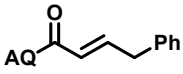
## VI. Study on the Possible Reaction Pathway




*General procedure for deuterium-labelling experiment:* In a dry 10-mL Schlenk tube containing a magnetic stirbar was charged with $Cs_2CO_3$ (10 mol%, 0.01 mmol, 3.3 mg), alkene 2a (1 equiv, 0.1 mmol, 21.2 mg) and $d_1$-methanol (0.1 mL). The mixture was stirred at 100 ºC for 24 h. The reaction mixture was concentrated on a rotary evaporator, then the resulting residue was directly subjected to preparative TLC (1:10 EA:PE), the product was obtained in 76% yield, $\alpha$-position D-incorporation ratio is 92%, $\gamma$-position D-incorporation ratio is 87%.

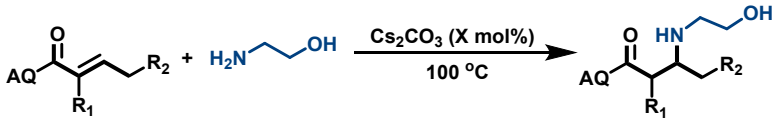
*General procedure for base-catalyzed conjugative isomerization of allyl amide:* In a dry 10-mL Schlenk tube containing a magnetic stirbar was charged with $Cs_2CO_3$ (10 mol%, 0.01 mmol, 3.3 mg), alkene **2a** (1 equiv, 0.1 mmol) and *N,N*-dimethylformamide (0.1 mL). The mixture was stirred at 100 ºC for 24 h. 10 uL dodecane was added in the tube. After filtering, the filtrate was subjected to GC analysis to determine the conversion of alkenes **2a**, calibrated GC yield of the conjugative isomerized product.

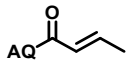
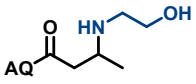
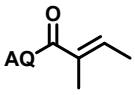
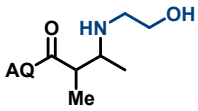
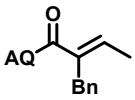
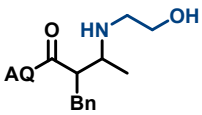
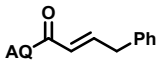
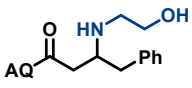



| Entry | Alkene | Product | Yield(%) |
|---|---|---|---|
| 1 |  |  | 75 |
| 2 |  |  | 0 |
| 3 |  |  | 25 |
| 4 |  |  | 0 |

*General procedure for base-catalyzed aza-Michael addition of conjugated amide:* In a dry 10-mL Schlenk tube containing a magnetic stirbar was charged with CsOAc (10 mol%, 0.01 mmol, 1.9 mg), alkene 2a (1 equiv, 0.1 mmol, 21.2 mg) and 2-aminoethan-1-ol (0.1 mL). The mixture was stirred at 100 ºC for 24 h. The reaction

mixture was concentrated on a rotary evaporator, then the resulting residue was directly subjected to preparative TLC (1:20 MeOH:DCM), product was obtained.




| Entry | Alkene | Product | $Cs_2CO_3$ loading | Yield(%) |
|---|---|---|---|---|
| 1 |  |  | 10 mol% | 58 |
| | | | 1 equiv | 43 |
| 2 |  |  | 10 mol% | 53 |
| | | | 1 equiv | 18 |
| 3 |  |  | 10 mol% | 40 |
| | | | 1 equiv | 26 |
| 4 |  |  | 10 mol% | 35 |
| | | | 1 equiv | 32 |

## VII. Reference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