Supporting Information

Intermolecular Reductive Heck Reaction of Unactivated Aliphatic Alkenes with Organohalides

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I. General

^{1}H NMR spectra were acquired on Bruker 400 MHz or 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). Proof of purity of new compounds was demonstrated with copies of ^{1}H, ^{13}C and ^{19}F NMR spectra.

Glassware was dried in an oven at 120^{o}C for at least 2h before use. Dry 2,3-butanediol was freshly distilled from calcium oxide under argon 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.

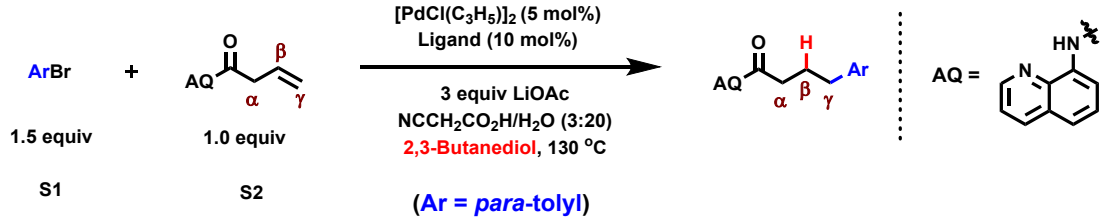
Thin-layer chromatography (TLC) was conducted with Merck 60 F254 coated silica gel plate (0.2 mm thickness). Flash chromatography was performed using Merck silica gel 60 (0.040-0.063 mm) or SiliCycle silica gel F60 (0.040-0.063 mm).The dilute solvents usually used Ethyl Acetate/Petroleum Ether, which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

II. Condition optimization for the Model Reductive Heck Reaction

Typical procedure for condition optimization: In an argon atmosphere, a dry 10-mL Schlenk tube containing a magnetic stirbar was charged with $[PdCl(C_3H_5)]_2$ (5 mol%, 1.9 mg, 0.005 mmol), cataCXium@PCy (10 mol%, 3.4 mg, 0.01 mmol), alkenes (1 equiv, 0.1 mmol, 21.2 mg), LiOAc (3 equiv, 0.3 mmol, 19.8 mg), 4-bromotoluene (1.5 equiv, 0.15 mmol, 44.7 mg), dry 2,3-butanediol (1.0 mL), cyanoacetic acid (3 equiv, 0.3 mmol, 25.6 mg) and H_2O (20 equiv, 2 mmol, 36 uL) sequentially. The tube was capped tightly and the mixture was vigorously stirred in a *pre*-warmed 130°C oil bath. Cooling after 12 h, 10 uL dodecane was added in the tube. After filtering, the filtrate was subjected to GC analysis to determine the conversion of alkenes and ArBr, calibrated GC yield of the coupling product. The major byproducts from alkene are the mixture of isomerized cis/trans alkenes.

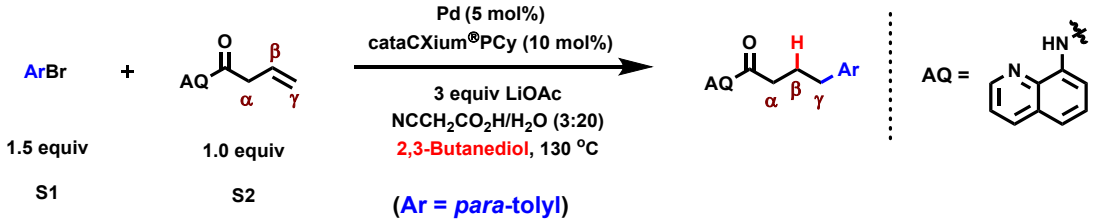
Table S1 Effect of supporting ligands for Pd catalysts



Entry	Ligand	ArBr/Conversion (%)	Alkene/Conversion (%)	Yield (%)
1	NO	17	100	16
2	$^{n}Bu_3PHBF_4$	98	100	59
3	PCy_3HBF_4	95	100	55
4	$^{t}Bu_3PHBF_4$	99	100	44
5	Cy-Johnphos	94	100	66
6	Brettphos	98	100	73
7	X-phos	99	100	74
8	Davephos	78	100	45
9	**cataCXium®PCy**	**98**	**100**	**88**
10	cataCXium®2PoMely	98	100	87
11	cataCXium®RPICy	98	100	80

12	cataCXium®RPINCy	97	100	86
13	DPPP	97	100	6
14	Xantphos	99	100	44

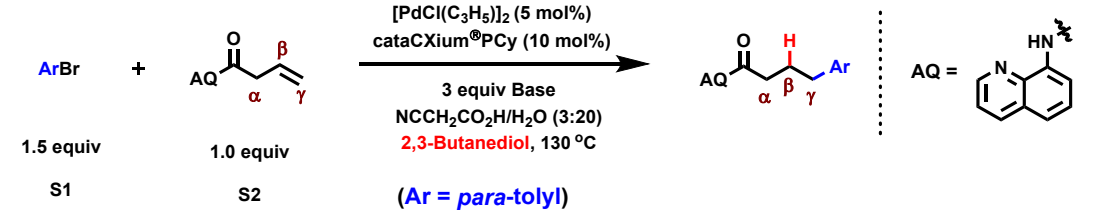
Table S2 Effect of Pd Sources



Entry	Cat.	ArBr/Conversion (%)	Alkene/Conversion (%)	Yield (%)
1	NO	<10	98[a]	-
2	$Pd(OAc)_2$	60	100	51
3	$PdCl_2$	99	100	65
4	$Pd(acac)_2$	73	100	66
5	$Pd(hfacac)_2$	94	100	72
6	$Pd(CF_3COO)_2$	85	100	67
7	$Pd_2(dba)_3$	96	100	69
8	$Pd(dba)_2$	96	100	53
9	**$[PdCl(C_3H_5)]_2$**	**98**	**100**	**88**

[a] Alkene (S2) was isomerized to conjugated alkene in 90% yield.

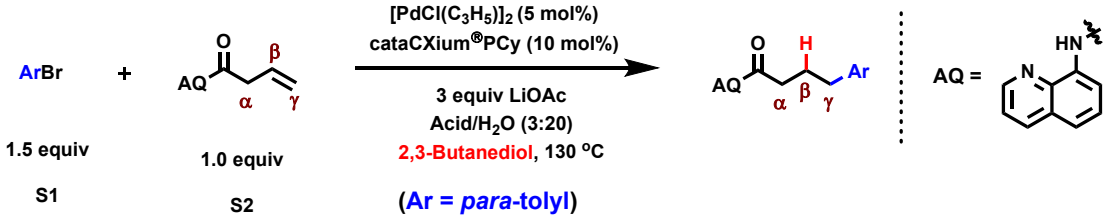
Table S3 Effect of Bases



Entry	Base	ArBr/Conversion (%)	Alkene/Conversion (%)	Yield (%)
1	NO	-	70	-
2	**LiOAc**	**98**	**100**	**88**
3	NaOAc	88	100	86

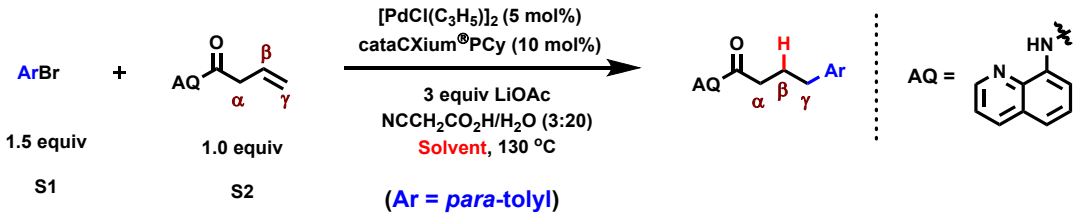
4	KOAc	99	100	86
5	Li_2CO_3	67	100	10
6	^{t}BuOLi	85	100	10
7	K_2CO_3	100	100	5
8	HCOONa	100	100	58
9	PS	-	49	-
10	DIPEA	41	100	5
11	Et_3N	38	100	3
12	DABCO	100	100	3
13	Cy_2NMe	52	100	4

Table S4 Effect of Acids



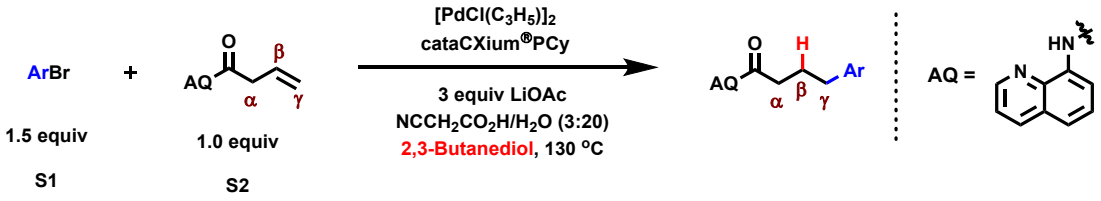
Entry	Acid	ArBr/Conversion (%)	Alkene/Conversion (%)	Yield (%)
1	No	97	100	85
2	HCOOH	99	99	65
3	HOAc	83	100	81
4	TFA	19	71	17
5	**$NCCH_2COOH$**	**98**	**100**	**88**
6	$COOHCH_2COOH$	15	55	12
7	^{i}PrCOOH	75	100	85
8	^{t}BuCOOH	97	99	83
9	PhCOOH	80	100	65
10	*p*-^{t}Bu-PhCOOH	78	100	80
11	*p*-NO_2-PhCOOH	60	99	51
12	*p*-CN-PhCOOH	65	99	70

Table S5 Effect of Solvents



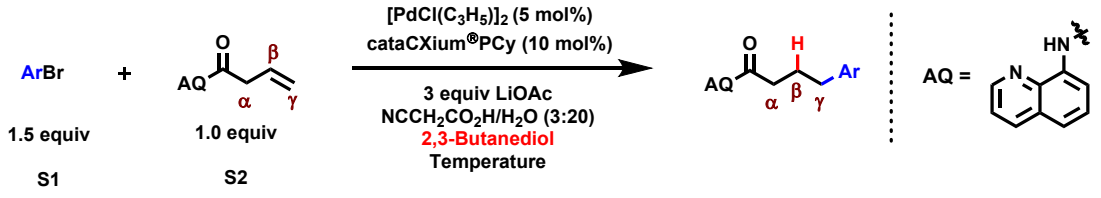
Entry	Solvent	ArBr/Conversion (%)	Alkene/Conversion (%)	Yield (%)
1	MeOH	74	100	23
2	EtOH	74	100	70
3	^{i}PrOH	71	100	58
4	^{n}BuOH	49	100	43
5	^{t}Bu-OH	5	56	5
6	EG	65	100	50
7	Propylene glycol	100	100	79
8	**2,3-Butanediol**	**98**	**100**	**88**
9	1,2-Pentanediol	100	100	80
10	1,2-Hexanediol	100	100	72
11	Tol	-	26	-
12	DMF	3	100	-
13	1,4-Dioxane	-	34	-
14	CPME	-	38	-
15	$PhCF_3$	-	24	-
16	DMPU	3	100	-
17	3-Hydroxy-2-butanone	55	98	46
18	2,3-Butanedione	83	80	-

Table S6 Effect of Catalyst Loading



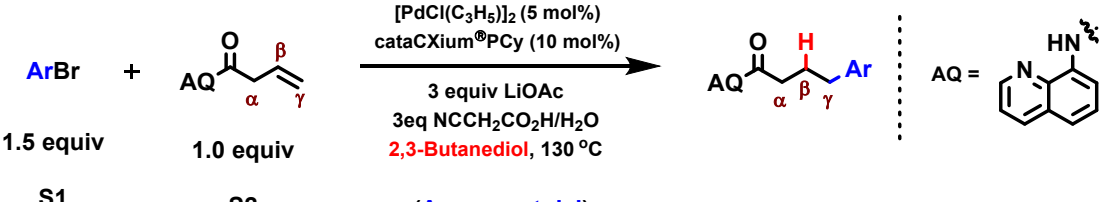
Entry	Catalyst loading	ArBr/Conversion (%)	Alkene/Conversion (%)	Yield (%)
1	2.5%	98	99	75
2	**5.0%**	**98**	**100**	**88**
3	7.5%	100	100	90
4	10%	100	100	92

Table S7 Effect of Temperature



Entry	Temperature/℃	ArBr/Conversion (%)	Alkene/Conversion (%)	Yield (%)
1	80	88	26	5
2	100	95	35	31
3	110	96	100	80
4	120	96	100	85
5	**130**	**98**	**100**	**88**
6	140	99	100	90

Table S8 Effect on Amount of H_2O

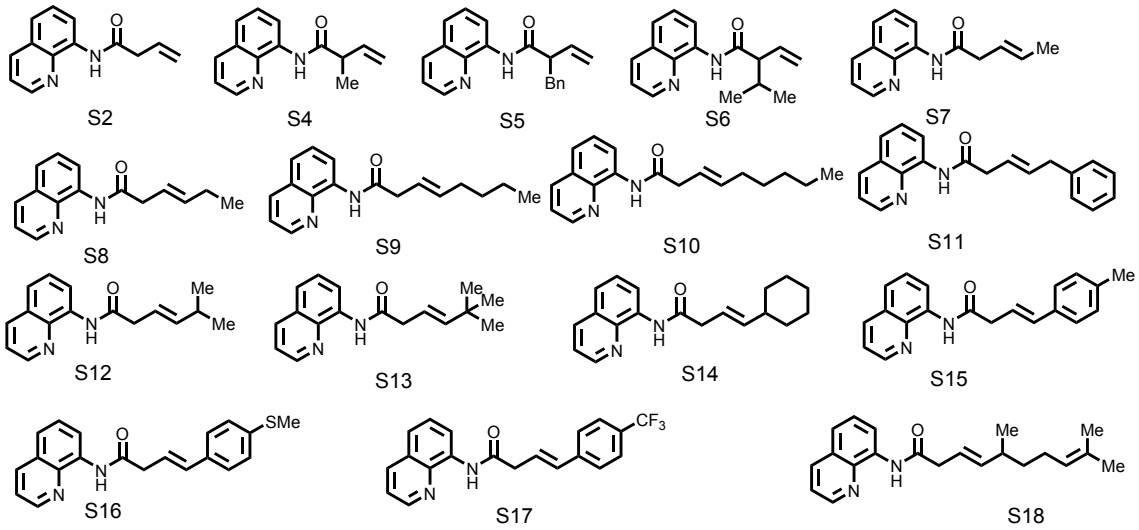


Entry	H_2O/eq	ArBr/Conversion (%)	Alkene/Conversion (%)	Yield (%)
1	NO	98	100	62
2	10	100	100	71

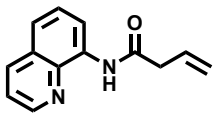
3	**20**	**98**	**100**	**88**
4	50	99	100	60
6	100	99	100	51

III. Synthesis of alkene substrates

Figure S1. 8-Aminoquinoline-containing alkene substrates

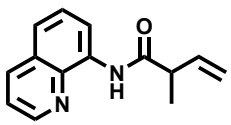


Note: alkene substrates S2[1a], S4-S12[1a], S13[1b] and S14[1a] were prepared according to the corresponding literature methods.



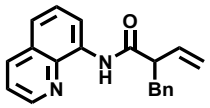
N-(quinolin-8-yl)but-3-enamide (S2): Crude acid (~7.2 mmol) was charged into a 100 mL flask containing 15 mL dry DCM. 8-Aminoquinoline (720 mg, 5 mmol), pyridine (0.8 mL, 10 mmol) and HATU (2.47 g, 6.5 mmol) were added sequentially, the reaction was stirred at ambient temperature for 20 h. The deep brown solution was diluted with 100 mL EtOAc, washed with sat. $NaHCO_3$ (40 mL ×2) and brine (40 mL × 1), and then purified by column chromatography (1:20 EA/PE) to afford **S2** as yellow oil (90%).

^{1}H NMR (400 MHz, $CDCl_3$): δ 9.97 (s, 1H), 8.85-8.72 (m, 2H), 8.15 (d, J = 8.3 Hz, 1H), 7.55-7.43 (m, 3H), 6.20-6.10 (m, 1H), 5.45-5.34 (m, 2H), 3.37 (d, J = 8Hz, 2H).



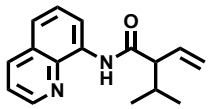
2-methyl-N-(quinolin-8-yl)but-3-enamide (S4):

^{1}H NMR (400 MHz, $CDCl_3$): δ 10.04 (s, 1H), 8.83-8.76 (m, 2H), 8.13 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.58-7.40 (m, 3H), 6.15-6.06 (m, 1H), 5.44-5.27 (m, 2H), 3.36 (m, 1H), 1.50-1.42 (d, *J* = 8.3, 3H).



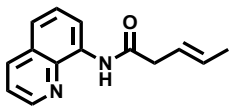
2-benzyl-N-(quinolin-8-yl)but-3-enamide (S5):

^{1}H NMR (400 MHz, $CDCl_3$): δ 9.92 (s, 1H), 8.81-8.74 (m, 2H), 8.13 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.56-7.46 (m, 2H), 7.44-7.41 (m, 1H), 7.27-7.22 (m, 4H), 7.20-7.13 (m, 1H), 6.09-6.0 (m, 1H), 5.33-5.21 (m, 2H), 3.52-3.46 (m, 1H), 3.41-3.36 (m, 1H), 3.0-2.95 (m, 1H).



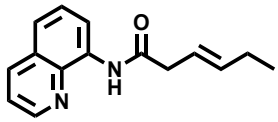
2-isopropyl-N-(quinolin-8-yl)but-3-enamide (S6):

^{1}H NMR (400 MHz, $CDCl_3$): δ 9.92 (s, 1H), 8.82-8.79 (m, 2H), 8.15 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.55-7.43 (m, 3H), 6.08-5.98 (m, 1H), 5.33-5.27 (m, 2H), 2.89-2.84 (m, 1H), 2.28 (m, 1H), 1.04 (d, *J* = 6.7 Hz, 3H), 0.99 (d, *J* = 6.8 Hz, 3H).



(E)-N-(quinolin-8-yl)pent-3-enamide (S7):

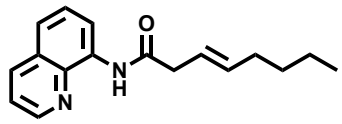
^{1}H NMR (400 MHz, $CDCl_3$): δ 10.14 (s, 1H), 8.84-8.75 (m, 2H), 8.16 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.59-7.43 (m, 3H), 5.90-5.71 (m, 2H), 3.27 (d, *J* = 5.9 Hz, 2H), 1.83 (d, *J* = 6.8 Hz, 3H).



(E)-N-(quinolin-8-yl)hex-3-enamide (S8):

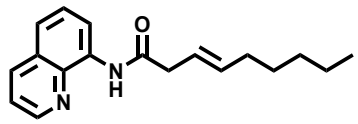
^{1}H NMR (400 MHz, $CDCl_3$): δ 10.10 (s, 1H), 8.79-8.76 (m, 2H), 8.16 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.58-7.41 (m, 3H), 5.91-5.70 (m, 2H), 3.27 (d, *J* = 7.0 Hz, 2H), 2.23-2.15

(m, 2H), 1.13 (t, *J* = 7.5 Hz, 3H).



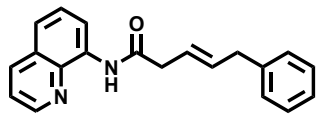
(E)-N-(quinolin-8-yl)oct-3-enamide (S9):

^{1}H NMR (400 MHz, $CDCl_3$): δ 10.08 (s, 1H), 8.80-8.75 (m, 2H), 8.15 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.57-7.41 (m, 3H), 5.89-5.69 (m, 2H), 3.30-3.25 (m, 2H), 2.2-2.14 (m, 2H), 1.54-1.36 (m, 4H), 0.93 (t, *J* = 7.2 Hz, 3H).



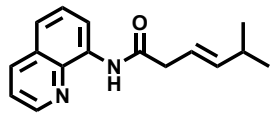
(E)-N-(quinolin-8-yl)non-3-enamide (S10):

^{1}H NMR (400 MHz, $CDCl_3$): δ 10.08 (s, 1H), 8.80-8.75 (m, 2H), 8.14 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.57-7.40 (m, 3H), 5.89-5.68 (m, 2H), 3.31-3.22 (m, 2H), 2.18-2.13 (m, 2H), 1.53-1.47 (m, 2H), 1.37-1.31 (m, 4H), 0.92-0.86 (m, 3H).



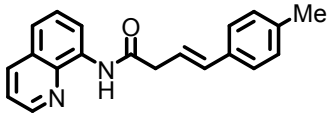
(E)-5-phenyl-N-(quinolin-8-yl)pent-3-enamide (S11):

^{1}H NMR (400 MHz, $CDCl_3$):δ 10.06 (s, 1H), 8.80-8.75 (m, 2H), 8.17 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.57-7.44 (m, 3H), 7.34-7.29 (m, 4H), 7.25-7.19 (m, 1H), 6.04-5.94 (m, 1H), 5.89-5.78 (m,1H), 3.52 (d, *J* =8.0, 1.1 Hz, 2H), 3.33 (d, *J* = 8.0, 1.1 Hz, 2H).



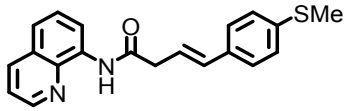
(E)-5-methyl-N-(quinolin-8-yl)hex-3-enamide (S12):

^{1}H NMR (400 MHz, $CDCl_3$):δ 10.15 (s, 1H), 8.81-8.73 (m, 2H), 8.17 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.58-7.40 (m, 3H), 5.87-5.65 (m, 2H), 3.30-3.23 (m, 2H), 2.49-2.51 (m, *J* = 6.7 Hz, 1H), 1.13 (dd, *J* = 6.8, 1.9 Hz, 6H).



(*E*)-*N*-(Quinolin-8-yl)-4-(*p*-tolyl)but-3-enamide (S15): (*E*)-4-(*p*-tolyl)but-3-enoic acid was prepared according to the literature[1c]. The last synthesis step is following the method of synthesizing compound (**S2**).

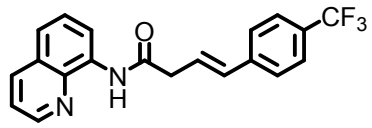
^{1}H NMR (400 MHz, $CDCl_3$): δ 10.09 (s, 1H), 8.8-8.68 (m, 2H), 8.13 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.60-7.47 (m, 2H), 7.46-7.32 (m, 3H), 7.15 (d, *J* = 7.8 Hz, 2H), 6.69 (d, *J* = 15.7 Hz, 1H), 6.48-6.4 (m, 1H), 3.49 (d, *J* = 8, 1.5 Hz, 2H), 2.35 (s, 3H).



(*E*)-4-(4-(Methylthio)phenyl)-*N*-(quinolin-8-yl)but-3-enamide (S16) **:** The compound was prepared according to the literature[1a]. In an argon atmosphere, a dry 25-mL Schlenk tube containing a magnetic stirbar was charged with $Pd_2(dba)_3$ (10 mol%, 27.6 mg, 0.03 mmol), Cy-Johnphos (20 mol%, 21 mg, 0.06 mmol), alkenes S2 (1 equiv, 0.3 mmol, 63.6 mg), Proton Sponge (3 equiv, 0.9 mmol, 192.6 mg), 4-(methylthio)phenyl trifluoromethanesulfonate (1.5 equiv, 0.45 mmol), dry DMPU (5.5 mL) and trifluoroacetic acid (3 equiv, 0.9 mmol, 73 uL) sequentially. The tube was capped tightly and the mixture was vigorously stirred in a *pre*-warmed 130^{o}C oil bath. After alkenes was almost fully consumed (monitored by GCMS), the reaction mixture was concentrated on a rotary evaporator and then distilled under reduced pressure, the resulting residue was directly subjected to flash silica gel chromatography to afford **S16** as white solid (86%, 0.86 g).

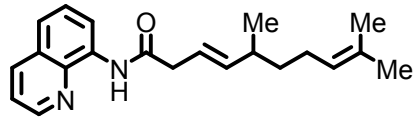
^{1}H NMR (400 MHz, $CDCl_3$): δ 10.07 (s, 1H), 8.77 (dd, *J* = 7.2Hz, 1.6Hz, 1H), 8.73 (dd, *J* = 4.2Hz, 1.5Hz, 1H), 8.15 (dd, *J* = 8.2Hz, 1.5Hz, 1H), 7.56-7.449 (m, 2H), 7.43 (dd, *J* = 8.2Hz, 4.2Hz, 1H), 7.39-7.37 (m, 2H), 7.23-7.21 (m, 2H), 6.69-6.65 (m. 1H), 6.49-6.42 (m, 1H), 3.49 (dd, *J* = 7.3Hz, 0.8Hz, 2H), 2.50 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 169.3, 148.2, 138.4, 137.8, 136.3, 134.3, 134.2, 133.8, 127.8, 127.3, 126.8, 126.5, 121.7, 121.6, 121.6, 116.4, 42.3, 15.7.



(*E*)-*N*-(Quinolin-8-yl)-4-(4-(trifluoromethyl)phenyl)but-3-enamide (S17): (*E*)-4-(4-(trifluoromethyl)phenyl)but-3-enoic acid was prepared according to the literature[1c]. The last synthesis step is following the method of synthesizing compound (**S2**).

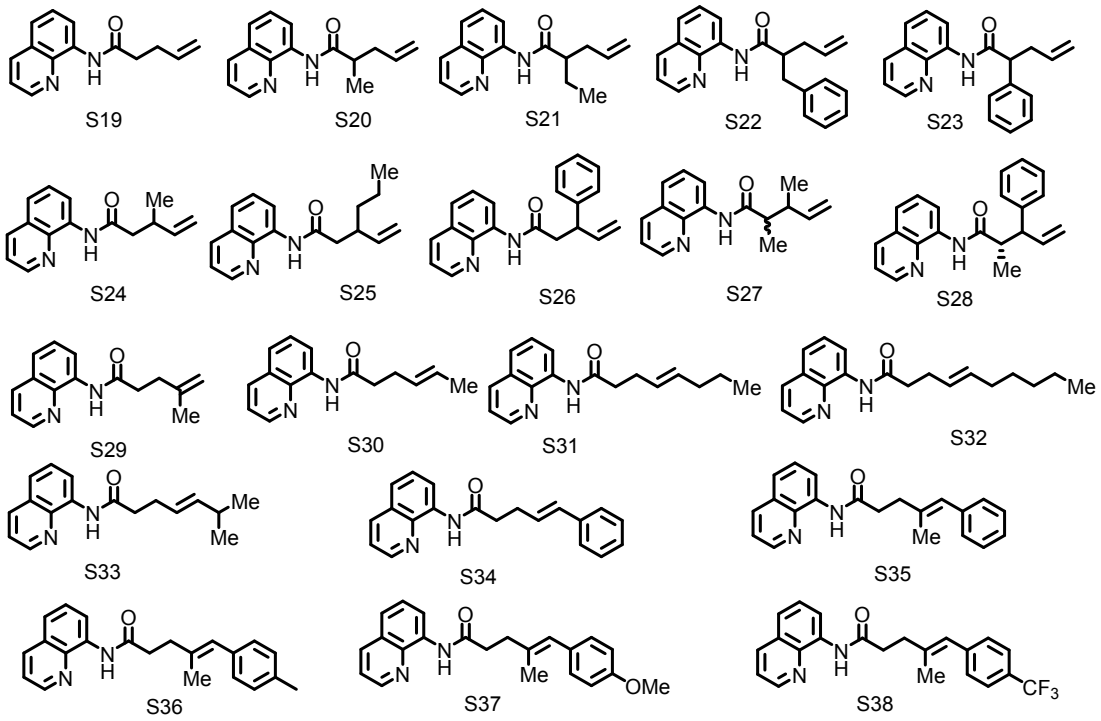
^{1}H NMR (400 MHz, $CDCl_3$): δ 10.05 (s,1H), 8.81-8.71 (m, 2H), 8.16 (m, 1H), 7.63-7.48 (m, 6H), 7.48-7.41 (m, 1H), 6.78-6.69 (m, 1H), 6.64-6.57 (m, 1H), 3.54 (dd, *J* = 7.0, 1.3 Hz, 2H).



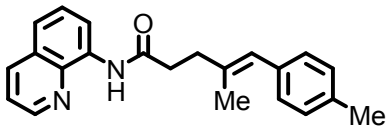
(*E*)-5,9-Dimethyl-*N*-(quinolin-8-yl)deca-3,8-dienamide (S18)： (*E*)-5,9-dimethylde ca-3,8-dienoic acid was prepared according to the literature[1d]. The last synthesis step is following the method of synthesizing compound (**S2**).

^{1}H NMR (400 MHz, $CDCl_3$): δ 10.14 (s, 1H), 8.81-8.72 (m, 2H), 8.15 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.57-7.47 (m, 2H), 7.45-7.42 (m, 4.2 Hz ,1H), 5.73-5.71 (m, 2H), 5.15-5.10 (m, 1H), 3.30-3.25 (m, 2H), 2.35-2.25 (m, 1H), 2.10-2.00 (m, 2H), 1.68 (t, *J* = 1.4 Hz, 3H), 1.56 (d, *J* = 1.4 Hz, 3H), 1.53-1.35 (m, 2H), 1.13 (d, *J* = 6.8 Hz, 3H).

Figure S2. 8-Aminoquinoline-containing alkene substrates



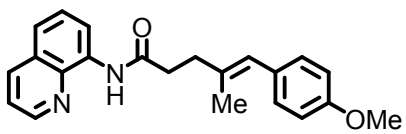
Note: alkene substrates S19-S28[1a], S30[1e] and S33-S34[1e] were prepared according to the corresponding literature methods. For alkene S29, S31, S32, S35, S36, S37 and S38, these corresponding acids are prepared according to the literature[1f], The last synthesis step is following the method of synthesizing compound (**S2**).



(*E*)-4-Methyl-*N*-(quinolin-8-yl)-5-(*p*-tolyl)pent-4-enamide (S36):

^{1}H NMR (400 MHz, $CDCl_3$): δ 9.88 (s, 1H), 8.80-8.77 (m, 2H), 8.16 (dd, *J* = 8.3Hz, 1.6Hz, 1H), 7.56-7.49 (m, 2H), 7.45 (dd, *J* = 8.3Hz, 4.2Hz, 1H), 7.15-7.09 (m, 4H), 6.38 (m, 1H), 2.82-2.78 (m, 2H), 2.71-2.67 (m, 2H), 2.33 (s, 3H), 1.95 (d, *J* = 1.0Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 171.4, 148.3, 138.4, 136.6, 136.5, 135.8, 135.4, 134.6, 128.9, 128.1, 127.6, 125.8, 121.7, 121.6, 116.6, 37.1, 36.4, 21.3, 18.0.



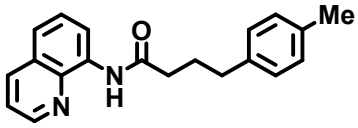
(*E*)-5-(4-Methoxyphenyl)-4-methyl-*N*-(quinolin-8-yl)pent-4-enamide (S37):

^{1}H NMR (400 MHz, $CDCl_3$): δ 9.88 (s, 1H), 8.81-8.77 (m, 2H), 8.16 (dd, *J* = 8.2Hz, 1.2Hz, 1H), 7.57-7.50 (m, 2H), 7.45 (dd, *J* = 8.3Hz, 4.2Hz, 1H), 7.17-7.15 (m, 2H), 6.85-6.83 (m, 2H), 6.36 (s, 1H), 3.80 (s, 3H), 2.81-2.78 (m, 2H), 2.70-2.67 (m, 2H), 1.94 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 171.4, 157.9, 148.3, 138.4, 136.5, 135.8, 134.6, 130.9, 130.1, 128.0, 127.6, 125.4, 121.7, 121.6, 116.6, 113.5, 55.4, 37.1, 36.4, 18.0.

IV. Pd-catalyzed intermolecular reductive Heck reaction of various organohalides

Typical procedure for reductive Heck reaction of various organobromides: In an argon atmosphere, a dry 25-mL Schlenk tube containing a magnetic stirbar was charged with $[PdCl(C_3H_5)]_2$ (5 mol%, 5.7 mg, 0.015 mmol), cataCXium®PCy (10 mol%, 10.2 mg, 0.03 mmol), alkenes **S2** (1 equiv, 0.3 mmol, 63.6 mg), LiOAc (3 equiv, 0.9 mmol, 20 mg), organobromides (1.5 equiv, 0.45 mmol), dry 2,3-butanediol (3 mL) and H_2O (20 equiv, 6 mmol, 108 uL). The tube was capped tightly and the mixture was vigorously stirred in a *pre*-warmed 130°C oil bath. After alkenes was almost fully consumed (monitored by GCMS), the reaction mixture was concentrated on a rotary evaporator and then distilled under vacuum, the resulting residue was directly subjected to flash silica gel chromatography. The structure of the desired product was confirmed by ^1H and ^{13}C NMR spectroscopy of the purified sample. The typical procedure using 0.3 mmol of alkenes was applied for all the isolation, unless stated otherwise.

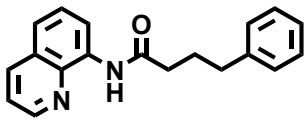


***N*-(Quinolin-8-yl)-4-(*p*-tolyl)butanamide (P1).** The reaction mixture was stirred at 130°C for 18h. The product was purified by flash chromatography (1:20 EA/PE) as yellow oil (81 mg, 88%).

^1H NMR (400 MHz, $CDCl_3$): δ 9.79 (s, 1H), 8.80-8.79 (m, 2H), 8.15 (d, *J* = 8.1Hz, 1H), 7.56-7.44 (m, 3H), 7.12 (q, *J* = 7.2Hz, 4H), 2.74 (t, *J* = 7.5Hz, 2H), 2.58 (t, *J* = 7.4Hz, 2H), 2.33 (s, 3H), 2.19-2.11 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 171.5, 148.1, 138.4, 138.3, 136.3, 135.4, 134.5, 129.1, 128.4, 127.9, 127.4, 121.5, 121.3, 116.4, 37.3, 34.7, 27.1, 21.0.

HRMS (ESI): Calcd for $C_{20}H_{20}N_2O$ $[M+H]^+$: 305.1654, Found: 305.1653.



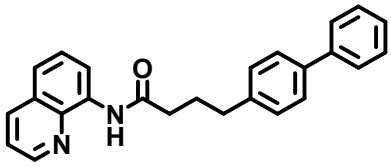
4-Phenyl-*N*-(quinolin-8-yl)butanamide (P2). The reaction mixture was stirred at

130°C for 18h. The product was purified by flash chromatography (1:20 EA/PE) as yellow solid (79 mg, 90%). Mp: 61.2-63.0 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.79 (s, 1H), 8.80-8.78 (m, 2H), 8.15 (dd, *J* = 8.3Hz, 1.7Hz, 1H), 7.55-7.43 (m, 3H), 7.32-7.18 (m, 5H), 2.77 (t, *J* = 7.6Hz, 2H), 2.58 (t, *J* = 7.5Hz, 2H), 2.20-2.12 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 171.5, 148.1, 141.5, 138.3, 136.4, 134.5, 128.6, 128.5, 128.0, 127.5, 126.0, 121.6, 121.4, 116.5, 37.3, 35.2, 27.1.

HRMS (ESI): Calcd for $C_{19}H_{18}N_2O$ $[M+H]^+$: 291.1497, Found: 291.1499.

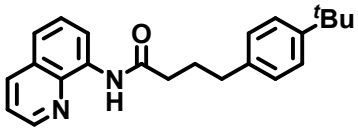


4-([1,1'-Biphenyl]-4-yl)-*N*-(quinolin-8-yl)butanamide (P3). The reaction mixture was stirred at 130°C for 18h. The product was purified by flash chromatography (1:20 EA/PE) as white solid (93 mg, 85%). Mp: 60.2-61.0 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.87 (s, 1H), 8.88-8.81 (m, 2H), 8.15 (dd, *J* =8.3Hz, 1.7Hz, 1H), 7.67-7.55 (m, 5H), 7.51-7.40 (m, 4H), 7.36 (t, *J* = 8.2Hz, 3H), 2.84 (t, *J* = 7.6Hz, 2H), 2.64 (t, *J* = 7.4Hz, 2H), 2.28-2.20 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 171.5, 148.1, 141.1, 140.7, 139.0, 138.3, 136.5, 134.5, 129.1, 128.8, 128.0, 127.5, 127.2, 127.1, 127.0, 121.7, 121.5, 116.6, 37.4, 34.9, 27.1.

HRMS (ESI): Calcd for $C_{25}H_{22}N_2O$ $[M+H]^+$: 367.1810, Found: 367.1810.

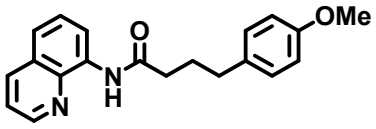


4-(4-(*tert*-Butyl)phenyl)-*N*-(quinolin-8-yl)butanamide (P4). The reaction mixture was stirred at 130°C for 18h. The product was purified by flash chromatography (1:20 EA/PE) as yellow oil (96 mg, 92%).

^{1}H NMR (400 MHz, $CDCl_3$): δ 9.79 (s, 1H), 8.81-8.78 (m, 2H), 8.16 (dd, *J* = 8.3Hz, 1.5Hz, 1H), 7.56-7.44 (m, 3H), 7.32 (d, *J* = 8.2Hz, 2H), 7.18 (d, *J* = 8.2Hz, 2H), 2.75 (t, *J* = 7.5Hz, 2H), 2.59 (t, *J* = 7.5Hz, 2H), 2.20-2.12(m, 2H), 1.31 (s, 9H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 171.7, 148.9, 148.2, 138.5, 138.5, 136.5, 134.7, 128.4, 128.1, 127.6, 125.4, 121.7, 121.5, 116.6, 37.6, 34.8, 34.5, 31.6, 27.1.

HRMS (ESI): Calcd for $C_{23}H_{26}N_2O$ $[M+H]^+$: 347.2123 , found: 347.2121.

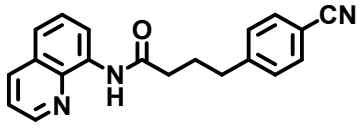


4-(4-Methoxyphenyl)-*N*-(quinolin-8-yl)butanamide (P5). The reaction mixture was stirred at 130^{o}C for 18h. The product was purified by flash chromatography (1:20 EA/PE) as yellow oil (85 mg, 88%).

^{1}H NMR (400 MHz, $CDCl_3$): δ 9.79 (s, 1H), 8.81-8.79 (m, 2H), 8.15 (dd, *J* = 8.3Hz, 1.6Hz, 1H), 7.56-7.43 (m, 3H), 7.16 (d, *J* = 8.6Hz, 2H), 6.85 (d, *J* = 8.8Hz, 2H), 3.79 (s, 3H), 2.72 (t, *J* = 7.5Hz, 2H), 2.57 (t, *J* = 7.5Hz, 2H), 2.17-2.09 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 171.6, 158.0, 148.2, 138.4, 136.5, 134.6, 133.7, 129.6, 128.0, 127.5, 121.7, 121.5, 116.5, 113.9, 55.4, 37.4, 34.4, 27.4.

HRMS (ESI): Calcd for $C_{20}H_{20}N_2O_2$ $[M+H]^+$: 321.1603 , Found: 321.1601

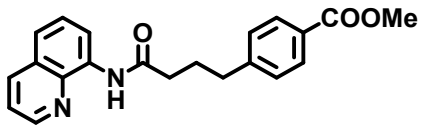


4-(4-Cyanophenyl)-*N*-(quinolin-8-yl)butanamide (P6) . The reaction mixture was stirred at 130^{o}C for 18h. The product was purified by flash chromatography (1:10 EA/PE) as brown solid (79 mg, 83%). Mp: 96.0-97.3 ^{o}C.

^{1}H NMR (400 MHz, $CDCl_3$): δ 9.78 (s, 1H), 8.80-8.75 (m, 2H), 8.16 (dd, *J* = 8.2Hz, 1.6Hz, 1H), 7.57-7.44 (m, 5H), 7.33 (d, *J* = 8.2Hz, 2H), 2.82 (t, *J* = 7.7Hz, 2H), 2.58 (t, *J* = 7.3Hz, 2H), 2.19-2.11 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 170.9, 148.2, 147.3, 138.3, 136.5, 134.3, 132.3, 129.4, 128.0, 127.4, 121.7, 121.6, 119.1, 116.5, 109.9, 37.0, 35.3, 26.5.

HRMS (ESI): Calcd for $C_{20}H_{17}N_3O$ $[M+H]^+$: 316.1450, Found: 316.1448.

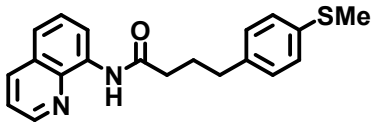


Methyl 4-(4-oxo-4-(quinolin-8-ylamino)butyl)benzoate (P7). The reaction mixture was stirred at 130°C for 18h. The product was purified by flash chromatography (1:20 EA/PE) as yellow oil (32 mg, 30%). While $NCCH_2COOH$ (3 equiv, 0.9 mmol, 77mg) was added, the product was afforded in 68% yield (72 mg).

^1H NMR (400 MHz, $CDCl_3$) δ 9.79 (s, 1H), 8.80-8.77 (m, 2H), 8.15 (dd, *J* = 8.2Hz , 1.7Hz, 1H), 7.98-7.95 (m, 2H), 7.50-7.43 (m, 3H), 7.31 (d, *J* = 8.1Hz, 2H), 3.90 (s, 3H), 2.82 (t, *J* = 7.6Hz, 2H), 2.58 (t, *J* = 7.3Hz, 2H), 2.21-2.13 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 171.2, 167.2, 148.2, 147.1, 138.4, 136.5, 134.5, 129.9, 128.7, 128.1, 128.0, 127.5, 121.7, 121.6, 116.5, 52.1, 37.2, 35.3, 26.7.

HRMS (ESI): Calcd for $C_{21}H_{20}N_2O_3$ $[M+H]^+$: 349.1552, Found: 349.1547.

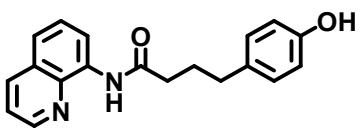


4-(4-(Methylthio)phenyl)-*N*-(quinolin-8-yl)butanamide (P8). The reaction mixture was stirred at 130°C for 18h. The product was purified by flash chromatography (1:20 EA/PE) as yellow oil (81 mg, 80%).

^1H NMR (400 MHz, $CDCl_3$) δ 9.79 (s, 1H), 8.80-8.79 (m, 2H), 8.15 (dd, *J* = 8.3Hz, 1.7Hz, 1H), 7.54-7.43 (m, 3H), 7.19 (q, *J* = 8.4Hz, 4H), 2.73 (t, *J* = 7.5Hz, 2H), 2.57 (t, *J* = 7.4Hz, 2H), 2.47 (s, 3H), 2.17-2.10 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 171.5, 148.2, 138.7, 138.4, 136.5, 135.6, 134.6, 129.2, 128.0, 127.5, 127.2, 121.7, 121.5, 116.5, 37.3, 34.7, 27.1, 16.4.

HRMS (ESI): Calcd for $C_{20}H_{20}N_2OS$ $[M+H]^+$: 337.1375, Found: 337.1373.

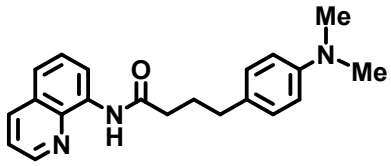


4-(4-Hydroxyphenyl)-*N*-(quinolin-8-yl)butanamide (P9). The title compound was prepared from PhBr (3 equiv). The reaction mixture was stirred at 130°C for 18h. The product was purified by flash chromatography (1:20 EA/PE) as white solid (45 mg, 48%). While $NCCH_2COOH$ (3 equiv, 0.9 mmol, 77mg) was added, the product was afforded in 77% yield (71 mg). Mp: 113.3-115.0 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.80 (s, 1H), 8.80-8.76 (m, 2H)，8.15 (dd, *J* = 8.3Hz, 1.7Hz, 1H), 7.55-7.43 (m, 3H), 7.06 (d, *J* = 8.4Hz, 2H), 6.77(d, *J* = 8.5Hz, 2H), 5.71(s, 1H), 2.67 (t, *J* = 7.4Hz, 2H), 2.56 (t, *J* = 7.3Hz, 2H), 2.14-2.06 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 172.2, 154.4, 148.3, 138.4, 136.6, 134.4, 133.2, 129.7, 128.1, 127.6, 121.8, 121.7, 116.9, 115.4, 37.4, 34.4, 27.4.

HRMS (ESI): Calcd for $C_{19}H_{18}N_2O_2$ $[M+H]^+$: 307.1447, Found: 307.1446.

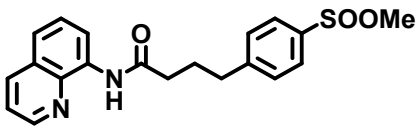


4-(4-(Dimethylamino)phenyl)-*N*-(quinolin-8-yl)butanamide (P10). The reaction mixture was stirred at 130°C for 18h. The product was purified by flash chromatography (1:20 EA/PE) as yellow oil (55 mg, 55%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.79 (s, 1H), 8.81-8.79 (m, 2H), 8.16 (dd, *J* = 8.3Hz, 1.7Hz, 1H), 7.56-7.44 (m, 3H), 7.14-7.12 (m, 2H), 6.72-6.70 (m, 2H), 2.91 (s, 6H), 2.69 (t, *J* = 7.5Hz, 2H), 2.57 (t, *J* = 7.5Hz, 2H), 2.16-2.09 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 171.9, 149.3, 148.2, 138.5, 136.5, 134.7, 129.8, 129.3, 128.1, 127.6, 121.7, 121.4, 116.5, 113.2, 41.0, 37.6, 34.3, 27.5.

HRMS (ESI): Calcd for $C_{21}H_{23}N_3O$ $[M+H]^+$: 334.1919, Found: 334.1915.



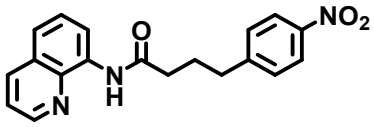
(4-(Methylsulfonyl)phenyl)-*N*-(quinolin-8-yl)butanamide (P11). The reaction mixture was stirred at 130°C for 18h. The product was purified by flash

chromatography (1:20 EA/PE) as yellow solid (37 mg, 33%). While $NCCH_2COOH$ (3 equiv, 0.9 mmol, 77mg) was added, the product was afforded in 75% yield (83 mg). Mp: 106.9-108.5 °C.

^1H NMR (400 MHz, $CDCl_3$) δ 9.78 (s, 1H), 8.78-8.73 (m, 2H), 8.14 (dd, *J* = 8.2Hz, 1.7Hz, 1H), 7.83 (d, *J* = 8.2Hz, 2H), 7.53-7.40 (m, 5H), 3.01 (s, 3H), 2.83 (t, *J* = 7.7Hz, 2H), 2.57 (t, *J* = 7.3Hz, 2H), 2.18-2.11 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 170.9, 148.2, 138.2, 136.5, 134.3, 129.6, 128.0, 127.6, 127.4, 121.7, 121.6, 116.5, 44.6, 37.0, 35.1, 26.6.

HRMS (ESI): Calcd for $C_{20}H_{20}N_2O_3S$ $[M+H]^+$: 369.1273, Found: 369.1279.

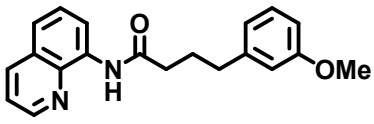


(4-Nitrophenyl)-*N*-(quinolin-8-yl)butanamide (P12). The title compound was prepared from PhBr (3 equiv). The reaction mixture was stirred at 130°C for 18h. The product was purified by flash chromatography (1:20 EA/PE) as yellow solid (41 mg, 41%). While $NCCH_2COOH$ (3 equiv, 0.9 mmol, 77mg) was added, the product was afforded in 63% yield (64 mg). Mp: 89.4-91.0 °C.

4-^1H NMR (401 MHz, $CDCl_3$) δ 9.77 (s, 1H), 8.79-8.73 (m, 2H), 8.15-8.09 (m, 3H), 7.53-7.42 (m, 3H), 7.36 (d, *J* = 8Hz, 2H), 2.85 (t, *J* = 8Hz, 2H), 2.58 (t, *J* = 8Hz, 2H), 2.20-2.12 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 170.8, 148.3, 148.3, 146.6, 138.4, 136.5, 134.4, 129.4, 128.0, 127.5, 123.8, 121.8, 121.7, 116.6, 37.0, 35.1, 26.6.

HRMS (ESI): Calcd for $C_{19}H_{17}N_3O_3$ $[M+H]^+$: 336.1348, Found: 336.1348.

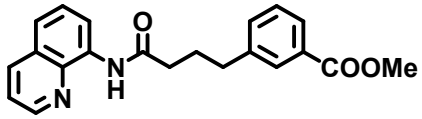


4-(3-Methoxyphenyl)-*N*-(quinolin-8-yl)butanamide (P13). The reaction mixture was stirred at 130°C for 18h. The product was purified by flash chromatography (1:20 EA/PE) as yellow oil (78 mg, 82%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.79 (s, 1H), 8.80-8.78 (m, 2H), 8.14 (dd, *J* = 8.3Hz, 1.7Hz, 1H), 7.55-7.42 (m, 3H), 7.22 (dd, *J* = 15.6Hz, 7.8Hz, 1H), 6.85-6.74 (m, 3H), 3.78 (s, 3H), 2.75 (t, *J* = 7.5Hz, 2H), 2.57 (t, *J* = 7.5Hz, 2H), 2.20-2.12 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 171.5, 159.8, 148.2, 143.2, 138.4, 136.5, 134.6, 129.5, 128.0, 127.5, 121.7, 121.5, 121.1, 116.5, 114.3, 111.5, 55.2, 37.4, 35.3, 27.0.

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

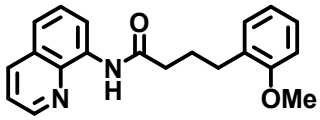


Methyl 3-(4-oxo-4-(quinolin-8-ylamino)butyl)benzoate (P14). The reaction mixture was stirred at 130^{o}C for 18h. The product was purified by flash chromatography (1:30 EA/PE) as yellow oil (34 mg, 32%). While $NCCH_2COOH$ (3 equiv, 0.9 mmol, 77mg) was added, the product was afforded in 72% yield (75 mg).

^{1}H NMR (401 MHz, $CDCl_3$) δ 9.79 (s, 1H), 8.79 (d, *J* = 5.2Hz, 2H), 8.13 (d, *J* = 8.4Hz, 1H), 7.92 (s, 1H), 7.88 (d, *J* = 7.8Hz, 2H), 7.54-7.33 (m, 4H), 7.27 (s, 1H), 3.88 (s, 3H), 2.81 (d, *J* = 7.6Hz, 2H), 2.57 (d, *J* = 7.5Hz, 2H), 2.21-2.13 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 171.3, 167.3, 148.2, 141.9, 138.3, 136.5, 134.5, 133.3, 130.4, 129.7, 128.6, 128.0, 127.5, 127.5, 121.7, 121.6, 116.6, 52.2, 37.3, 35.1, 27.0.

HRMS (ESI): Calcd for $[M+H]^+$: $C_{21}H_{20}N_2O_3$ $[M+H]^+$: 349.1552 , Found: 349.1555.

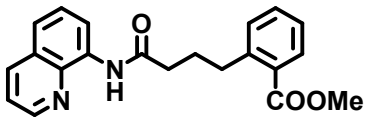


4-(2-Methoxyphenyl)-*N*-(quinolin-8-yl)butanamide (P15). The reaction mixture was stirred at 130^{o}C for 18h. The product was purified by flash chromatography (1:30 EA/PE) as yellow oil (86 mg, 90%).

^{1}H NMR (400 MHz, $CDCl_3$): δ 9.84 (s, 1H), 8.82-8.80 (m, 2H), 8.16 (dd, *J* = 8.3Hz, 1.6Hz, 1H), 7.56-7.43 (m, 3H) , 7.21-7.18 (m, 2H), 6.92-6.84 (m, 2H), 3.80 (s, 3H), 2.78 (t, *J* = 7.7Hz, 2H), 2.58 (t, *J* = 7.6Hz, 2H), 2.18-2.10 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 171.9, 157.7, 148.2, 138.5, 136.5, 134.7, 130.3, 130.0, 128.1, 127.6, 127.4, 121.7, 121.4, 120.5, 116.5, 110.3, 55.3, 37.8, 29.8, 25.7.

HRMS (ESI): Calcd for $C_{20}H_{20}N_2O_2$ $[M+H]^+$: 321.1603, Found: 321.1599.

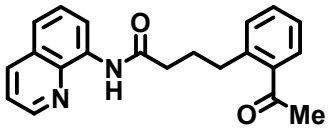


Methyl 2-(4-oxo-4-(quinolin-8-ylamino)butyl)benzoate (P16). The reaction mixture was stirred at 130°C for 18h. The product was purified by flash chromatography (1:30 EA/PE) as yellow oil (71 mg, 68%). While $NCCH_2COOH$ (3 equiv, 0.9 mmol, 77mg) was added, the product was afforded in 81% yield (85 mg).

^1H NMR (400 MHz, $CDCl_3$) δ 9.62 (s, 1H), 8.60-8.58 (m, 2H), 7.95 (dd, *J* = 8.3Hz, 1.7Hz, 1H), 7.70 (dd, *J* = 7.8, 1.4Hz, 1H), 7.36-7.22 (m, 4H), 7.13 (dd, *J* = 7.7Hz, 1.3Hz, 1H), 7.08-7.04 (m, 1H), 3.69 (s, 3H), 2.92 (t, *J* = 7.5Hz, 2H), 2.44 (t, *J* = 7.5Hz, 2H), 1.99-1.91 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 171.6, 168.1, 148.2, 143.7, 138.4, 136.5, 134.7, 132.2, 131.3, 130.9, 129.5, 128.0, 127.5, 126.2, 121.7, 121.5, 116.5, 52.1, 37.9, 33.9, 27.4.

HRMS (ESI): Calcd for $C_{21}H_{20}N_2O_3$ $[M+H]^+$: 349.1552, Found: 349.1549.

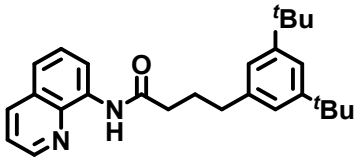


4-(2-Acetylphenyl)-*N*-(quinolin-8-yl)butanamide (P17). The reaction mixture was stirred at 130°C for 18 h. The product was purified by flash chromatography (1:20 EA/PE) as yellow oil (72 mg, 72%). While $NCCH_2COOH$ (3 equiv, 0.9 mmol, 77mg) was added, the product was afforded in 85% yield (85 mg).

^1H NMR (400 MHz, $CDCl_3$) δ 9.81 (s, 1H), 8.81-8.77(m, 2H), 8.15 (dd, *J* = 8.3Hz, 1.7Hz, 1H), 7.68 (dd, *J* = 7.7Hz, 1.3Hz, 1H), 7.55-7.26 (m, 6H), 3.03-2.99 (m, 2H), 2.66-2.60 (m, 5H), 2.16-2.08 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 202.1, 171.7, 148.2, 142.0, 138.4, 137.8, 136.5, 134.7, 131.7, 131.6, 129.5, 128.0, 127.5, 126.1, 121.7, 121.45, 116.5, 37.9, 33.5, 30.0, 27.5.

HRMS (ESI): Calcd for $C_{21}H_{20}N_2O_2$ $[M+H]^+$: 333.1603 , Found: 333.1659.

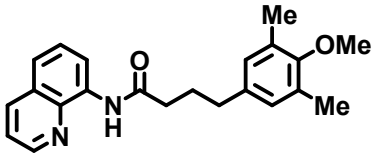


4-(3,5-*di-tert*-Butylphenyl)-*N*-(quinolin-8-yl)butanamide (P18). The reaction mixture was stirred at 130°C for 18h. The product was purified by flash chromatography (1:20 EA/PE) as yellow oil (99 mg, 82%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.86 (s, 1H), 8.85 (dd, *J* = 7.5Hz, 1.5Hz, 2H), 8.16 (dd, *J* = 8.3Hz, 1.7Hz, 1H), 7.58-7.44 (m, 3H), 7.32 (s, 1H), 7.13 (d, *J* = 1.8Hz, 2H), 2.80 (t, *J* = 7.7Hz, 2H), 2.65 (t, *J* = 7.5Hz, 2H), 2.21 (p, *J* = 7.6Hz, 2H), 1.36 (s, 18H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 171.7, 150.8, 148.2, 140.7, 138.4, 136.4, 134.6, 128.0, 127.5, 122.8, 121.6, 121.5, 120.0, 116.5, 37.7, 35.9, 34.8, 31.6, 27.5.

HRMS (ESI): Calcd for $C_{27}H_{34}N_2O$ $[M+H]^+$: 403.2749 , Found: 403.2741.

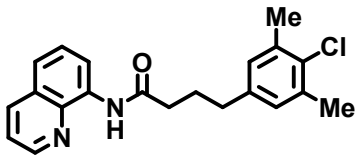


4-(4-Methoxy-3,5-dimethylphenyl)-*N*-(quinolin-8-yl)butanamide (P19). The reaction mixture was stirred at 130°C for 18h. The product was purified by flash chromatography (1:20 EA/PE) as yellow solid (93 mg, 89%). Mp: 119.6-121.0 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.79 (s, 1H), 8.81-8.79 (m, 2H), 8.16 (dd, *J* = 8.3Hz, 1.7Hz, 1H), 7.56-7.44 (m, 3H), 6.88 (s, 2H), 3.69 (s, 3H), 2.65 (t, *J* = 7.5Hz, 2H), 2.57 (t, *J* = 7.4Hz, 2H), 2.26 (s, 6H), 2.19-2.07 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 171.7, 155.3, 148.2, 138.5, 136.8, 136.5, 134.7, 130.7, 129.0, 128.1, 127.6, 121.7, 121.5, 116.6, 59.8, 37.5, 34.6, 27.3, 16.2.

HRMS (ESI): Calcd for $C_{22}H_{24}N_2O_2$ $[M+H]^+$: 349.1916, Found: 349.1913.



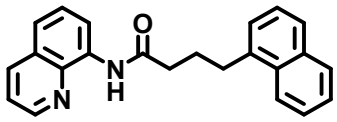
4-(4-Chloro-3,5-dimethylphenyl)-*N*-(quinolin-8-yl)butanamide (P20). The reaction mixture was stirred at 130°C for 18h. The product was purified by flash

chromatography (1:20 EA/PE) as yellow oil (87 mg, 82%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.78 (s, 1H), 8.80-8.78 (m, 2H), 8.16 (dd, *J* = 8.3Hz, 1.7Hz, 1H), 7.56-7.44 (m, 3H), 6.95 (s, 2H), 2.67 (t, *J* = 7.5Hz, 2H), 2.56 (t, *J* = 7.4Hz, 2H), 2.34 (s, 6H), 2.16-2.09 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 171.5, 148.2, 139.3, 138.4, 136.5, 136.2, 134.6, 132.3, 128.8, 128.1, 127.6, 121.7, 121.6, 116.5, 37.3, 34.5, 27.1, 20.8.

HRMS (ESI): Calcd for $C_{21}H_{21}ClN_2O$ $[M+H]^+$: 353.1421, Found: 353.1416.

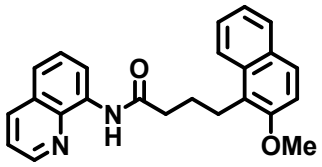


4-(Naphthalen-1-yl)-*N*-(quinolin-8-yl)butanamide (P21). The reaction mixture was stirred at 130^{o}C for 18h. The product was purified by flash chromatography (1:20 EA/PE) as yellow oil (92 mg, 90%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.83 (s, 1H), 8.85-8.79 (m, 2H), 8.16-8.13 (m, 2H), 7.87 (dd, *J* = 7.6Hz, 1.8Hz, 1H), 7.74 (dd, *J* = 7.2Hz, 2.3Hz, 1H), 7.58-7.39 (m, 7H), 3.25 (t, *J* = 7.7Hz, 2H), 2.67 (t, *J* = 7.3Hz, 2H), 2.35-2.28 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 171.4, 148.1, 138.4, 137.7, 136.4, 134.5, 134.0, 131.9, 128.8, 128.0, 127.5, 126.9, 126.3, 125.9, 125.6, 125.5, 123.9, 121.6, 121.5, 116.5, 37.6, 32.4, 26.4.

HRMS (ESI): Calcd for $C_{23}H_{20}N_2O$ $[M+H]^+$: 341.1654, Found: 341.1651.

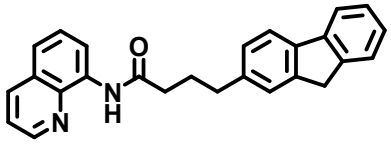


4-(2-Methoxynaphthalen-1-yl)-*N*-(quinolin-8-yl)butanamide (P22). The reaction mixture was stirred at 130^{o}C for 18h. The product was purified by flash chromatography (1:20 EA/PE) as yellow solid (69 mg, 62%). Mp: 61.2-63.0 ^{o}C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.80 (s, 1H), 8.83-8.77 (m, 2H), 8.14 (dd, *J* = 8.3Hz, 1.7Hz, 1H), 8.04 (d, *J* = 8.6Hz, 1H), 7.79-7.72 (m, 2H), 7.56-7.41 (m, 4H), 7.34-7.25 (m, 2H), 3.90 (s, 3H), 3.32-3.12 (m, 2H), 2.65 (t, *J* = 7.4Hz, 2H), 2.22-2.15 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 171.9, 154.5, 148.1, 138.4, 136.4, 134.7, 133.1, 129.2, 128.5, 128.0, 127.8, 127.5, 126.4, 123.3, 123.2, 122.8, 121.6, 121.3, 116.5, 113.2, 56.4, 37.7, 25.6, 24.2.

HRMS (ESI): Calcd for $C_{24}H_{22}N_2O_2$ $[M+H]^+$: 371.1760, Found: 371.1756.

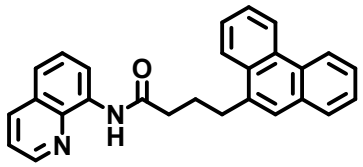


4-(*9H*-Fluoren-2-yl)-*N*-(quinolin-8-yl)butanamide (P23). The reaction mixture was stirred at 130°C for 18h. The product was purified by flash chromatography (1:20 EA/PE) as yellow solid (100 mg, 88%). Mp: 144.0-145.0 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.78 (s, 1H), 8.80-8.76 (m, 2H), 8.13 (dd, *J* = 8.3Hz, 1.7Hz, 1H), 7.74-7.68 (m, 2H) ,7.54-7.41(m, 5H), 7.36-7.33 (m, 1H), 7.28-7.23 (m, 2H), 3.84 (s, 2H), 2.84 (t, *J* = 7.5Hz, 2H), 2.59 (t, *J* = 7.4Hz, 2H), 2.24-2.19 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 171.5, 148.1, 143.6, 143.2 141.7, 140.3, 139.7, 138.4, 136.4, 134.5, 128.0, 127.5, 127.2, 126.7, 126.3, 125.3, 125.0, 121.6, 121.4, 119.8, 119.6, 116.5, 37.3, 36.8, 35.4, 27.3.

HRMS (ESI): Calcd for $C_{26}H_{22}N_2O$ $[M+H]^+$: 379.1810, Found: 379.1806.

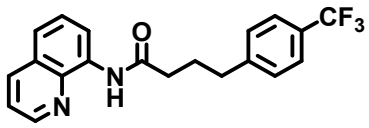


4-(Phenanthren-9-yl)-*N*-(quinolin-8-yl)butanamide (P24). The reaction mixture was stirred at 130°C for 18h. The product was purified by flash chromatography (1:20 EA/PE) as yellow solid (103 mg, 88%). Mp: 115.3-117.0 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.84 (s, 1H), 8.87-8.65 (m, 4H), 8.21-8.12 (m, 2H), 7.82 (d, *J* = 7.6Hz, 1H), 7.65-7.41 (m, 8H), 3.28 (t, *J* = 7.6Hz, 2H), 2.70 (t, *J* = 7.3Hz, 2H), 2.41-2.36 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 171.5, 148.2, 138.4, 136.4, 135.8, 134.6, 131.9, 131.2, 130.8, 129.9, 128.2, 128.0, 127.5, 126.8, 126.7, 126.6, 126.3, 126.1, 124.6, 123.3, 122.5, 121.6, 121.5, 116.6, 37.6, 32.8, 25.8.

HRMS (ESI): Calcd for $C_{27}H_{22}N_2O$ $[M+H]^+$: 391.1810, Found: 391.1807.



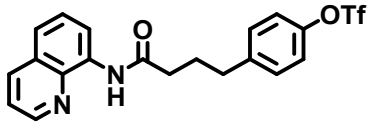
***N*-(Quinolin-8-yl)-4-(4-(trifluoromethyl)phenyl)butanamide (P25).** The reaction mixture was stirred at 130°C for 18h. The product was purified by flash chromatography (1:20 EA/PE) as yellow solid (37 mg, 34%). While $NCCH_2COOH$ (3 equiv, 0.9 mmol, 77mg) was added, the product was afforded in 90% yield (97 mg). Mp: 80.0-81.5 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.79 (s, 1H), 8.80-8.77 (m, 2H), 8.17 (dd, *J* = 8.3Hz, 1.7Hz, 1H), 7.55-7.52 (m, 4H), 7.46 (dd, *J* = 8.3Hz, 4.2Hz, 1H), 7.35 (d, *J* = 7.9Hz, 2H), 2.83 (t, *J* = 7.6Hz, 2H), 2.59 (t, *J* = 7.3Hz, 2H), 2.21-2.14 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 171.2, 148.3, 145.8, 138.4, 136.6, 134.5, 129.0, 128.1, 127.6, 125.5, 125.4 (q, *J* = 3.6Hz), 121.7 (d, *J* = 11.4Hz), 116.6, 37.2, 35.1, 26.8.

^{19}F NMR (376 MHz, $CDCl_3$) δ -62.19.

HRMS (ESI): Calcd for $C_{20}H_{17}F_3N_2O$ $[M+H]^+$: 359.1371, Found: 359.1364.



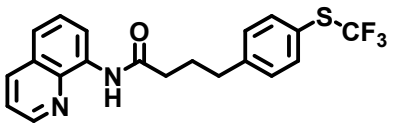
4-(4-Oxo-4-(quinolin-8-ylamino)butyl)phenyl trifluoromethanesulfonate (P26). The reaction mixture was stirred at 130°C for 18h. The product was purified by flash chromatography (1:20 EA/PE) as yellow oil (74 mg, 56%). While $NCCH_2COOH$ (3 equiv, 0.9 mmol, 77mg) was added, the product was afforded in 70% yield (92 mg).

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.80 (s, 1H), 8.80-8.77 (m, 2H), 8.16 (dd, *J* = 8.3Hz, 1.7Hz, 1H), 7.56-7.43(m, 3H), 7.31-7.29 (m, 2H), 7.20-7.18 (m, 2H), 2.79 (dd, *J* = 8.5Hz, 6.8Hz, 2H), 2.59 (t, *J* = 7.3Hz, 2H), 2.18-2.11 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 171.1, 148.3, 148.0, 142.3, 138.4, 136.5, 134.5, 130.3, 128.1, 127.5, 121.7 (d, *J* = 10.4Hz), 121.3, 120.4, 117.3, 116.6, 37.1, 34.6, 26.9.

^{19}F NMR (376 MHz, $CDCl_3$) δ -72.77.

HRMS (ESI): Calcd for $C_{20}H_{17}F_3N_2O_4S$ $[M+H]^+$: 439.0939, Found: 439.0938.



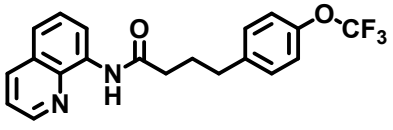
***N*-(Quinolin-8-yl)-4-(4-((trifluoromethyl)thio)phenyl)butanamide (P27)**. The reaction mixture was stirred at 130°C for 18h. The product was purified by flash chromatography (1:20 EA/PE) as yellow solid (66 mg, 55%). While $NCCH_2COOH$ (3 equiv, 0.9 mmol, 77mg) was added, the product was afforded in 85% yield (100 mg). Mp: 91.2-93.0 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.80 (s, 1H), 8.81-8.77 (m, 2H), 8.17 (dd, *J* = 8.2Hz, 1.7Hz, 1H), 7.58-7.45 (m, 5H), 7.29 (d, *J* = 8.2Hz, 2H), 2.80 (t, *J* = 7.4Hz, 2H), 2.59 (t, *J* = 7.3Hz, 2H), 2.21-2.13 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 171.2, 148.3, 145.0, 138.4, 136.6 (d, *J* = 11.8Hz), 134.5, 131.3, 129.9, 128.2, 128.1, 127.6, 121.7 (d, *J* = 12.5Hz), 116.6, 37.2, 35.0, 26.8.

^{19}F NMR (376 MHz, $CDCl_3$) δ -42.99.

HRMS (ESI): Calcd for $C_{20}H_{17}F_3N_2OS$ $[M+H]^+$: 391.1092, Found: 391.1090.



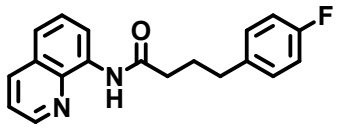
***N*-(Quinolin-8-yl)-4-(4-(trifluoromethoxy)phenyl)butanamide (P28)**. The reaction mixture was stirred at 130°C for 18h. The product was purified by flash chromatography (1:20 EA/PE) as yellow oil (62 mg, 55%). While $NCCH_2COOH$ (3 equiv, 0.9 mmol, 77mg) was added, the product was afforded in 82% yield (92 mg).

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.80 (s, 1H), 8.81-8.77 (m, 2H), 8.17 (dd, *J* = 8.2Hz, 1.7Hz, 1H), 7.57-7.45 (m, 3H), 7.26 (d, *J* = 6.1Hz, 2H), 7.14 (d, *J* = 8Hz ,2H), 2.78 (t, *J* = 7.6Hz, 2H), 2.59 (t, *J* = 7.4Hz, 2H), 2.19-2.11 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 171.3, 148.3, 147.6, 140.4, 138.4, 136.6, 134.6, 129.9, 128.1, 127.6, 121.7 (d, *J* = 14.2Hz), 121.1, 119.4, 116.6, 37.3, 34.6, 27.1.

^{19}F NMR (376 MHz, CDCl3) δ -57.79.

HRMS (ESI): Calcd for $C_{20}H_{17}F_3N_2O_2$ $[M+H]^+$: 375.1320, Found: 375.1317.



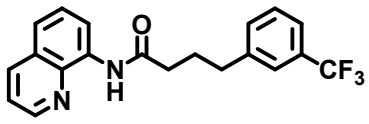
4-(4-Fluorophenyl)-*N*-(quinolin-8-yl)butanamide (P29) . The reaction mixture was stirred at 130^{o}C for 18 h. The product was purified by flash chromatography (1:20 EA/PE) as yellow oil (76 mg, 82%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.79 (s, 1H), 8.80-8.78 (m, 2H), 8.14 (dd, *J* = 8.3Hz, 1.7 Hz, 1H), 7.56-7.42 (m, 3H), 7.20-7.16 (m, 2H), 7.00-6.95 (m, 2H), 2.73 (t, *J* = 7.6Hz, 2H), 2.56 (t, *J* = 7.4Hz, 2H), 2.16-2.09 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 171.3, 161.4 (d, *J* = 243.3Hz), 148.2, 138.3, 137.1 (d, *J* = 3.2Hz), 136.4, 134.5, 130.0 (d, *J* = 7.8Hz), 128.0, 127.4, 121.6 (d, *J* = 13.8Hz), 116.5, 115.3, 115.1, 37.2, 34.4, 27.2.

^{19}F NMR (376 MHz, $CDCl_3$): δ -(117.45-117.53) (m).

HRMS (ESI): Calcd for $C_{19}H_{17}FN_2O$ $[M+H]^+$: 309.1403, Found: 309.1405.



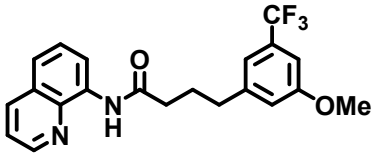
***N*-(Quinolin-8-yl)-4-(3-(trifluoromethyl)phenyl)butanamide (P30).** The reaction mixture was stirred at 130^{o}C for 18h. The product was purified by flash chromatography (1:20 EA/PE) as yellow oil (90 mg, 84%). While $NCCH_2COOH$ (3 equiv, 0.9 mmol, 77mg) was added, the product was afforded in 88% yield (95 mg).

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.82 (s, 1H), 8.81-8.78 (m, 2H), 8.14 (dd, *J* = 8.2Hz, 1.7Hz, 1H), 7.55-7.50 (m, 3H), 7.48-7.37 (m, 4H), 2.81 (t, *J* = 7.4Hz, 2H), 2.59 (t, *J* = 7.4Hz, 2H), 2.20-2.13 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 171.1, 148.1, 142.5, 138.2, 136.5, 134.4, 132.0, 131.2, 130.7(q, *J* = 31.8Hz), 128.9, 128.0, 127.4, 125.2 (q, *J* = 3.6Hz), 122.9 (q, *J* = 3.8Hz), 121.6 (d, *J* = 8.3Hz), 116.5, 37.1, 35.0 , 26.9.

^{19}F NMR (376 MHz, $CDCl_3$) δ -62.42.

HRMS (ESI): Calcd for $C_{20}H_{17}F_3N_2O$ $[M+H]^+$: 359.1371, Found: 359.1370.



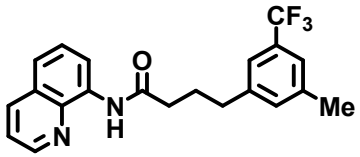
4-(3-Methoxy-5-(trifluoromethyl)phenyl)-*N*-(quinolin-8-yl)butanamide (P31). The reaction mixture was stirred at 130°C for 18h. The product was purified by flash chromatography (1:20 EA/PE) as yellow oil (44 mg, 38%). While $NCCH_2COOH$ (3 equiv, 0.9 mmol, 77mg) was added, the product was afforded in 86% yield (100 mg).

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.81 (s, 1H), 8.79-8.78 (m, 2H), 8.16 (d, *J* = 8.2Hz, 1H), 7.56-7.44 (m, 3H), 7.10 (s, 1H), 6.96 (s, 2H), 3.82 (s, 3H), 2.79 (t, *J* = 7.6Hz, 2H), 2.59 (t, *J* = 7.3Hz, 2H), 2.21-2.13 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 171.2, 160.0, 148.3, 144.2, 138.4, 136.5, 134.5, 131.9 (d, *J* = 31.8Hz), 128.1, 127.5, 125.5, 122.8, 121.7 (d, *J* =12.6 Hz), 117.9, 117.7 (q, *J* = 3.6Hz), 108.5 (q, *J* =3.9Hz), 55.6, 37.2, 35.2, 26.9.

^{19}F NMR (376 MHz, $CDCl_3$) δ -62.44

HRMS (ESI): Calcd for $C_{21}H_{19}F_3N_2O_2$ $[M+H]^+$: 389.1477, Found: 389.1473.



4-(3-Methyl-5-(trifluoromethyl)phenyl)-*N*-(quinolin-8-yl)butanamide (P32). The reaction mixture was stirred at 130°C for 18h. The product was purified by flash

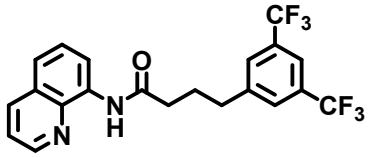
chromatography (1:20 EA/PE) as yellow solid (34 mg, 30%). While $NCCH_2COOH$ (3 equiv, 0.9 mmol, 77mg) was added, the product was afforded in 82% yield (92 mg). Mp: 64.4-65.5 °C.

^1H NMR (400 MHz, $CDCl_3$) δ 9.81 (s, 1H), 8.80-8.78 (m, 2H), 8.16 (d, *J* = 8.2Hz, 1H), 7.56-7.44 (m, 3H), 7.30-7.23 (m, 3H), 2.78 (t, *J* = 7.2Hz, 2H), 2.59 (t, *J* = 7.3Hz, 2H), 2.37 (s, 3H), 2.20-2.12 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 171.2, 148.3, 142.4, 139.0, 138.4, 136.5, 134.5, 132.9, 130.7 (q, *J* = 31.5Hz), 128.1, 127.6, 123.6 (q, *J* = 3.8Hz), 122.5 (q, *J* = 3.8Hz), 121.7 (d, *J* = 13.1Hz), 116.6, 37.3, 35.0, 27.0, 21.4.

^{19}F NMR (376 MHz, $CDCl_3$) δ -62.40.

HRMS (ESI): Calcd for $C_{21}H_{19}F_3N_2O$ $[M+H]^+$: 373.1528, Found: 373.1527.



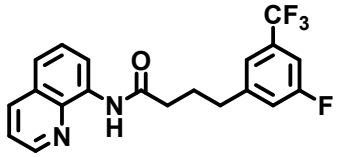
4-(3,5-Bis(trifluoromethyl)phenyl)-*N*-(quinolin-8-yl)butanamide (P33). The reaction mixture was stirred at 130°C for 18h. The product was purified by flash chromatography (1:20 EA/PE) as yellow oil (36 mg, 28%). While $NCCH_2COOH$ (3 equiv, 0.9 mmol, 77mg) was added, the product was afforded in 85% yield (109 mg).

^1H NMR (400 MHz, $CDCl_3$) δ 9.83 (s, 1H), 8.80-8.77 (m, 2H), 8.16 (d, *J* = 8.2Hz, 1H), 7.71 (d, *J* = 8.7Hz, 3H), 7.56-7.44 (m, 3H), 2.90 (t, *J* = 7.9Hz, 2H), 2.63 (t, *J* = 7.2Hz, 2H), 2.23-2.16 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 170.7, 148.3, 144.2, 138.4, 136.5, 134.4, 132.2, 131.7 (q, *J* = 33.1Hz), 128.8, 128.1, 127.5, 124.9, 121.8 (d, *J* = 3.5Hz), 120.3 (q, *J* = 3.9Hz), 116.6, 37.0, 35.0, 26.8.

^{19}F NMR (376 MHz, $CDCl_3$) δ -62.79.

HRMS (ESI): Calcd for $C_{21}H_{16}F_6N_2O$ $[M+H]^+$: 427.1245, Found: 427.1239.



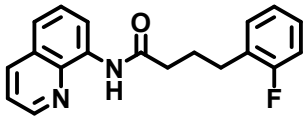
4-(3-Fluoro-5-(trifluoromethyl)phenyl)-*N*-(quinolin-8-yl)butanamide (P34). The reaction mixture was stirred at 130°C for 18h. The product was purified by flash chromatography (1:20 EA/PE) as yellow solid (72 mg, 63%). While $NCCH_2COOH$ (3 equiv, 0.9 mmol, 77mg) was added, the product was afforded in 81% yield (92 mg). Mp: 69.0-71.0 °C.

^1H NMR (400 MHz, $CDCl_3$) δ 9.81 (s, 1H), 8.81-8.77 (m, 2H), 8.16 (dd, *J* = 8.2Hz, 1.6Hz, 1H), 7.56-7.44 (m, 3H), 7.30 (s, 1H), 7.16 (d, *J* = 9.0Hz, 2H), 2.82 (t, *J* = 7.3Hz, 2H), 2.60 (t, *J* = 7.2Hz, 2H), 2.20-2.13(m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 170.9, 162.7 (d, *J* = 248.3Hz), 148.3, 145.5 (d, *J* = 7.5Hz), 138.4, 136.5, 134.4, 132.5 (dd, *J* = 32.8Hz, 8.2Hz), 128.1, 127.5, 121.7 (d, *J* = 7.7 Hz), 121.2 (t, 3.5Hz), 119.1 (d, *J* = 21.0Hz), 116.6, 110.6 (dd, *J* = 24.5Hz, 3.8Hz), 37.0, 34.9, 26.7.

^{19}F NMR (376 MHz, $CDCl_3$) δ -62.66, - (111.33-111.38) (m).

HRMS (ESI): Calcd for $C_{20}H_{16}F_4N_2O$ $[M+H]^+$: 377.1277, Found: 377.1272.



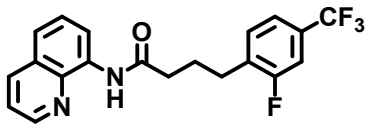
4-(2-Fluorophenyl)-*N*-(quinolin-8-yl)butanamide (P35). The reaction mixture was stirred at 130°C for 18h. The product was purified by flash chromatography (1:20 EA/PE) as yellow oil (75 mg, 81%).

^1H NMR (400 MHz, $CDCl_3$) δ 9.79 (s, 1H), 8.79-8.78 (m, 2H), 8.13 (dd, *J* = 8.3Hz, 1.7Hz, 1H), 7.60-7.38 (m, 3H), 7.26-7.14 (m, 2H), 7.08-6.99 (m, 2H), 2.80 (t, *J* = 7.5Hz, 2H), 2.59 (t, *J* = 7.6Hz, 2H), 2.15 (p, *J* = 7.6Hz, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 171.3, 161.3 (d, *J* = 244.8Hz), 148.1, 138.3, 136.4, 134.5, 130.9 (d, *J* = 5.1Hz), 128.4, 128.2, 128.0, 127.8, 127.7, 127.4, 124.0 (d, *J* = 3.5Hz), 121.5 (d, *J* = 17.7Hz), 116.5, 115.4, 115.2, 37.3, 28.4 (d, *J* = 2.3Hz), 25.8.

^{19}F NMR (376 MHz, $CDCl_3$) δ - (118.55-118.61) (m).

HRMS (ESI): Calcd for $C_{19}H_{17}FN_2O$ $[M+H]^+$: 309.1403, Found: 309.1402.



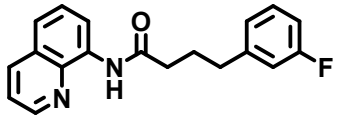
4-(2-Fluoro-4-(trifluoromethyl)phenyl)-*N*-(quinolin-8-yl)butanamide (P36). The reaction mixture was stirred at 130 °C for 18h. The product was purified by flash chromatography (1:20 EA/PE) as yellow solid (98 mg, 86%). Mp: 78.5-79.6 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.80 (s, 1H), 8.79-8.76 (m, 2H), 8.15 (dd, *J* = 8.3Hz, 1.7Hz, 1H), 7.55-7.26 (m, 6H), 2.85 (t, *J* = 7.6Hz, 2H), 2.60 (t, *J* = 7.4Hz, 2H), 2.20-2.12 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 170.9, 160.8 (d, *J* = 247.3Hz), 148.3, 138.4, 136.5, 134.5, 132.7 (d, *J* = 16.3Hz), 131.5 (d, *J* = 5.3Hz), 128.1, 127.5, 121.6 (d, *J* = 10.5Hz), 121.1 (t, *J* = 3.8Hz), 116.6, 112.8 (dd, *J* = 25.6Hz, 3.8Hz), 37.2, 28.5, 28.4 (d, *J* = 1.8Hz), 25.5.

^{19}F NMR (376 MHz, $CDCl_3$) δ -62.49, -(116.12 -116.17) (m).

HRMS (ESI): Calcd for $C_{20}H_{16}F_4N_2O$ $[M+H]^+$: 377.1277, Found: 377.1275.



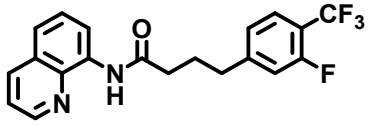
4-(3-Fluorophenyl)-*N*-(quinolin-8-yl)butanamide (P37). The reaction mixture was stirred at 130°C for 18h. The product was purified by flash chromatography (1:20 EA/PE) as yellow oil (73 mg, 79%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.71 (s, 1H), 8.71-8.69 (m, 2H), 8.06 (dd, *J* = 8.3Hz, 1.7Hz, 1H), 7.46-7.33 (m, 3H), 7.18-7.12 (m, 1H), 6.93-6.78 (m, 3H), 2.67 (t, *J* = 7.6Hz, 2H), 2.48 (t, *J* = 7.4Hz, 2H), 2.09-2.02 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 171.2, 163.0 (d, *J* = 245.3Hz), 148.2, 144.1 (d, *J* = 7.1Hz), 138.3, 136.4, 134.4, 129.8 (d, *J* = 8.3Hz), 128.0, 127.4, 124.2 (d, *J* = 2.7Hz), 121.6 (d, *J* = 14.6Hz), 116.5, 115.4 (d, *J* = 20.7Hz), 112.9 (d, *J* = 21.0Hz), 37.1, 34.9 (d, *J* = 1.8Hz), 26.8.

^{19}F NMR (376 MHz, $CDCl_3$) δ - (113.62-113.69) (m).

HRMS (ESI): Calcd for $C_{19}H_{17}FN_2O$ $[M+H]^+$: 309.1403, Found: 309.1403.



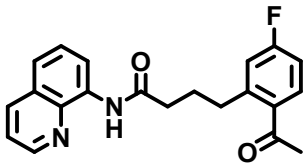
4-(3-Fluoro-4-(trifluoromethyl)phenyl)-*N*-(quinolin-8-yl)butanamide (P38). The reaction mixture was stirred at 130°C for 18h. The product was purified by flash chromatography (1:20 EA/PE) as yellow solid (41 mg, 36%). While $NCCH_2COOH$ (3 equiv, 0.9 mmol, 77mg) was added, the product was afforded in 94% yield (106 mg). Mp: 88.2-89.9 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.80 (s, 1H), 8.81-8.76 (m, 2H), 8.17 (dd, *J* = 8.2Hz, 1.7Hz, 1H), 7.57-7.45 (m, 4H), 7.10 (t, *J* = 8.5Hz, 2H), 2.82 (t, *J* = 7.6Hz, 2H), 2.59 (t, *J* = 7.2Hz, 2H), 2.20-2.13 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 170.9, 159.9 (d, *J* = 252Hz), 148.9 (d, *J* = 7.8Hz), 148.3, 138.4, 136.6, 134.4, 128.1, 127.5, 127.2 (dd, *J* = 4.5Hz, 1.8Hz), 124.3 (d, *J* = 3.5Hz), 121.8 (d, *J* = 7.9Hz), 117.0, 116.8, 116.6, 37.0, 34.9, 26.5.

^{19}F NMR (376 MHz, $CDCl_3$) δ -61.04, -61.08, -(114.93-115.03) (m).

HRMS (ESI): Calcd for $C_{20}H_{16}F_4N_2O$ $[M+H]^+$: 377.1277, Found: 377.1273.



4-(2-Acetyl-5-fluorophenyl)-*N*-(quinolin-8-yl)butanamide (P39). The reaction mixture was stirred at 130°C for 18h. The product was purified by flash chromatography (1:20 EA/PE) as yellow solid (67 mg, 64%). While $NCCH_2COOH$ (3 equiv, 0.9 mmol, 77mg) was added, the product was afforded in 72% yield (76 mg). Mp: 94.2-95.7 °C.

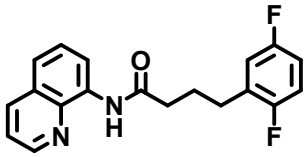
^{1}H NMR (400 MHz, $CDCl_3$) δ 9.81 (s, 1H), 8.79-8.76 (m, 2H), 8.13 (dd, *J* = 8.3Hz, 1.7Hz, 1H), 7.72-7.68 (m, 1H), 7.53-7.41 (m, 3H), 7.05 (dd, *J* = 9.9Hz, 2.7Hz, 1H), 6.96-6.91 (m, 1H), 3.04-3.00 (m, 2H), 2.63 (t, *J* = 7.4Hz, 2H), 2.56 (s, 3H), 2.14-2.06 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 200.2, 171.4, 165.5, 163.0, 148.2, 146.1 (d, *J* = 8.1Hz),

138.4, 136.4, 134.6, 133.7 (d, *J* = 2.9Hz), 132.3 (d, *J* = 9.3Hz), 128.0, 127.5, 121.6 (d, *J* = 19.2Hz), 118.3 (d, *J* = 21.1Hz), 116.5, 113.0 (d, *J* = 21.3Hz), 37.7, 33.6, 29.8, 27.1.

^{19}F NMR (376 MHz, $CDCl_3$) δ - (107.28-107.34) (m).

HRMS (ESI): Calcd for $C_{21}H_{19}FN_2O_2$ $[M+H]^+$: 351.1509, Found: 351.1502.



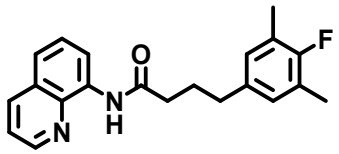
4-(2,5-Difluorophenyl)-*N*-(quinolin-8-yl)butanamide (P40). The title compound was prepared from 1,4-dibromo-2,5-difluorobenzene (1.5 equiv). The reaction mixture was stirred at 130°C for 18h. The product was purified by flash chromatography (1:20 EA/PE) as yellow solid (56 mg, 57%). Mp: 90.4-92.0 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.80 (s, 1H), 8.80-8.77 (m, 2H), 8.16 (dd, *J* = 8.2Hz, 1.7Hz, 1H), 7.56-7.44 (m, 3H), 6.99-6.94 (m, 2H), 6.88-6.82 (m, 1H), 2.77 (t, *J* = 7.6Hz, 2H), 2.60 (t, *J* = 7.5Hz, 2H), 2.18-2.10 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 171.0, 159.2 (dd, *J* = 151Hz, 2.2 Hz), 156.8 (dd, *J* = 150Hz, 2.3Hz), 148.2, 138.3, 136.4, 134.4, 130.0 (q, *J* = 7.0Hz), 128.0, 127.4, 121.6 (d, *J* = 13.7Hz), 117.0 (dd, *J* = 23.5Hz, 5.3Hz), 116.5, 116.2 (dd, *J* = 25.1Hz, 8.8Hz), 114.0 (dd, *J* = 23.9Hz, 8.5Hz), 37.1, 28.4, 25.5.

^{19}F NMR (376 MHz, $CDCl_3$) δ - (119.45-119.55) (m), - (124.62-124.72) (m).

HRMS (ESI): Calcd for $C_{19}H_{16}F_2N_2O$ $[M+H]^+$: 327.1298, Found: 327.1295



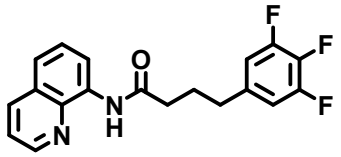
4-(4-Fluoro-3,5-dimethylphenyl)-*N*-(quinolin-8-yl)butanamide (P41). The reaction mixture was stirred at 130°C for 18h. The product was purified by flash chromatography (1:20 EA/PE) as yellow solid (81 mg, 80%). Mp: 58.1-60.0 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.79 (s, 1H), 8.81-8.79 (m, 2H), 8.18-8.15 (m, 1H), 7.57-7.44 (m, 3H), 6.86 (d, *J* = 6.9Hz, 2H), 2.65 (t, *J* = 7.5Hz, 2H), 2.56 (t, *J* = 7.4Hz, 2H), 2.22 (d, *J* = 2.1Hz, 6H), 2.15-2.08 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 171.6, 158.5 (d, *J* = 240Hz), 148.2, 138.4, 136.5, 136.3 (d, *J* = 4.3Hz), 134.6, 128.9 (d, *J* = 4.6Hz), 128.1, 127.6, 124.2 (d, *J* = 17.8Hz), 121.6 (d, *J* = 18.3Hz), 116.6, 37.3, 34.4, 27.3, 14.8 (d, *J* = 4.2Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -126.21.

HRMS (ESI): Calcd for $C_{21}H_{21}FN_2O$ $[M+H]^+$: 337.1716, Found: 337.1711.



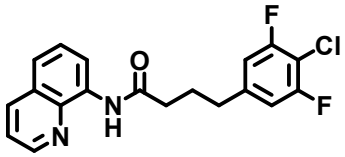
***N*-(Quinolin-8-yl)-4-(3,4,5-trifluorophenyl)butanamide (P42).** The reaction mixture was stirred at 130^{o}C for 18h. The product was purified by flash chromatography (1:20 EA/PE) as yellow solid (86 mg, 83%). Mp: 92.5-93.5 ^{o}C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.80 (s, 1H), 8.81-8.76 (m, 2H), 8.17 (dd, *J* = 8.3Hz, 1.7Hz, 1H), 7.54-7.45 (m, 3H), 6.87-6.83 (m, 2H), 2.70 (t, *J* = 7.6Hz, 2H), 2.57 (t, *J* = 7.2Hz, 2H), 2.15-2.07 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 170.9, 151.2 (dq, *J* = 250.2Hz, 4.1Hz), 148.3, 139.6 (q, *J* = 11Hz), 138.4, 137.9-137.8 (m), 136.6, 134.4, 128.1, 127.5, 121.8 (d, *J* = 8.0 Hz), 116.6, 112.5 (dd, *J* = 15.3Hz, 5.4Hz), 36.9, 34.5, 26.7.

^{19}F NMR (376 MHz, $CDCl_3$) δ - (134.87-134.98) (m), - (164.20-164.35) (m).

HRMS (ESI): Calcd for $C_{19}H_{15}F_3N_2O$ $[M+H]^+$: 345.1215, Found: 345.1212.



4-(4-Chloro-3,5-difluorophenyl)-*N*-(quinolin-8-yl)butanamide (P43). The reaction mixture was stirred at 130^{o}C for 18h. The product was purified by flash chromatography (1:20 EA/PE) as yellow oil (84 mg, 78%).

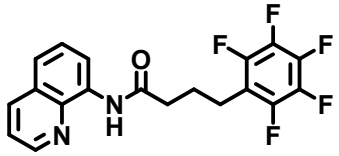
^{1}H NMR (400 MHz, $CDCl_3$) δ 9.79 (s, 1H), 8.81-8.76 (m, 2H), 8.17 (d, *J* = 8.3Hz,

1H), 7.56-7.45 (m, 3H), 6.88 (d, *J* = 8.5Hz, 2H), 2.74 (t, *J* = 7.6Hz, 2H), 2.58 (t, *J* = 7.2Hz, 2H), 2.16-2.09 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 170.9, 158.9 (dd, *J* = 251.0Hz, 3.9Hz), 148.4, 142.6 (t, *J* = 9.0Hz), 138.4, 136.6, 134.4, 128.1, 127.6, 121.8 (d, *J* = 7.0Hz), 116.6, 112.1 (dd, J = 21.8Hz, 2.1Hz), 36.9, 34.7, 26.5.

^{19}F NMR (376 MHz, $CDCl_3$) δ -113.7136 (d, *J* = 7.75Hz).

HRMS (ESI): Calcd for $C_{19}H_{15}ClF_2N_2O$ $[M+H]^+$: 361.0919, Found: 361.0920



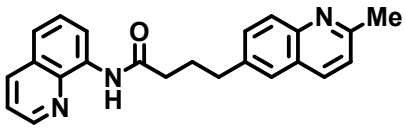
4-(Perfluorophenyl)-*N*-(quinolin-8-yl)butanamide (P44). The reaction mixture was stirred at 130°C for 18h. The product was purified by flash chromatography (1:20 EA/PE) as yellow solid (58 mg, 51%). Mp: 108.2-110.0 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.80 (s, 1H), 8.81-8.74 (m, 2H), 8.17 (dd, *J* = 8.2Hz, 1.7Hz, 1H), 7.56-7.45 (m, 3H), 2.88-2.84 (m, 2H), 2.61 (t, *J* = 7.5Hz, 2H), 2.16-2.09 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 170.4, 148.1, 138.2, 136.5, 134.3, 128.0, 127.4, 121.6 (d, *J* = 3.6Hz), 116.6, 36.9, 24.8, 21.8.

^{19}F NMR (376 MHz, $CDCl_3$) δ -(143.74-143.82) (m), -(157.42-157.53) (m), -(162.58-162.71) (m).

HRMS (ESI): Calcd for $C_{19}H_{13}F_5N_2O$ $[M+H]^+$: 381.1026, Found: 381.1021.

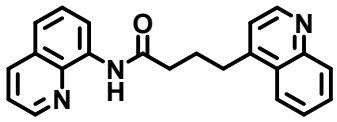


4-(2-Methylquinolin-6-yl)-*N*-(quinolin-8-yl)butanamide (P45). The reaction mixture was stirred at 130°C for 18h. The product was purified by flash chromatography (1:20 EA/PE) as yellow oil (51 mg, 48%). While $NCCH_2COOH$ (3 equiv, 0.9 mmol, 77mg) was added, the product was afforded in 90% yield (96 mg).

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.77 (s, 1H), 8.78-8.75 (m, 2H), 8.13 (dd, *J* = 8.3Hz, 1.7Hz, 1H), 7.97 (dd, *J* = 13.1Hz, 9.2Hz, 2H), 7.59-7.41 (m, 5H), 7.24-7.22 (m, 1H), 2.92 (t, *J* = 7.5Hz, 2H), 2.73 (s, 3H), 2.59 (t, *J* = 7.3Hz, 2H), 2.27-2.20 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 171.3, 158.1, 148.1, 146.2, 139.2, 138.3, 136.4, 136.2, 134.4, 131.1, 128.2, 127.9, 127.4, 126.5, 126.3, 122.1, 121.6, 121.5, 116.5, 37.2, 35.0, 26.8, 25.0.

HRMS (ESI): Calcd for $C_{23}H_{21}N_3O$ $[M+H]^+$: 356.1763, Found: 356.1758.

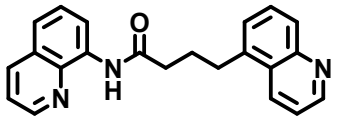


4-(Quinolin-4-yl)-*N*-(quinolin-8-yl)butanamide (P46). The reaction mixture was stirred at 130°C for 18h. The product was purified by flash chromatography (1:20 EA/PE) as yellow oil (64 mg, 62%). While $NCCH_2COOH$ (3 equiv, 0.9 mmol, 77mg) was added, the product was afforded in 78% yield (80 mg).

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.82 (s, 1H), 8.83-8.79 (m, 3H), 8.17-8.11 (m, 3H), 7.70 (t, *J* = 7.7Hz, 1H), 7.57-7.44 (m, 4H), 7.31 (d, *J* = 4.4Hz, 1H), 3.24 (t, *J* = 7.8Hz, 2H), 2.69 (t, *J* = 7.1Hz, 2H), 2.30 (p, *J* = 7.3Hz, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 170.8, 150.1, 148.4 148.2, 147.6, 138.3, 136.4, 134.4, 130.2, 129.1, 128.0, 127.6, 127.4, 126.5, 123.7, 121.7, 121.6, 121.0, 116.5, 37.2, 31.5, 25.6.

HRMS (ESI): Calcd for $C_{22}H_{19}N_3O$ $[M+H]^+$: 342.1606, Found: 342.1604.



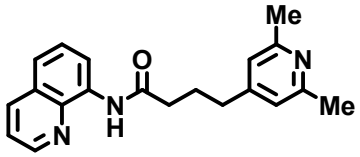
4-(Quinolin-5-yl)-*N*-(quinolin-8-yl)butanamide (P47). The reaction mixture was stirred at 130°C for 18h. The product was purified by flash chromatography (1:20 EA/PE) as yellow oil (51 mg, 50%). While $NCCH_2COOH$ (3 equiv, 0.9 mmol, 77mg) was added, the product was afforded in 83% yield (85 mg).

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.80 (s, 1H), 8.89 (dd, *J* = 4.2Hz, 1.6Hz, 1H), 8.81-8.77 (m, 2H), 8.49 (d, *J* =10.8Hz, 1H), 8.16 (d, *J* = 8.3Hz, 1H), 7.98 (d, *J* =

8.4Hz, 1H), 7.63 (t, *J* = 8.5Hz, 7.0Hz, 1H), 7.57-7.49 (m, 2H), 7.46-7.39 (m, 3H), 3.23-3.19 (m, 2H), 2.67 (t, *J* = 7.1Hz, 2H), 2.28-2.23 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 171.2, 150.0, 148.8, 148.2, 138.3, 138.2, 136.4, 134.4, 132.4, 129.1, 128.2, 128.0, 127.4, 127.0, 126.7, 121.7, 126.6, 120.9, 116.5, 37.3, 31.8, 26.5.

HRMS (ESI): Calcd for $C_{22}H_{19}N_3O$ $[M+H]^+$: 342.1606, Found: 342.1605.

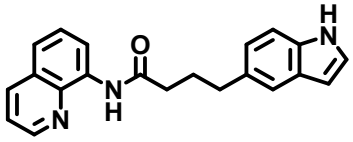


4-(2,6-Dimethylpyridin-4-yl)-*N*-(quinolin-8-yl)butanamide (P48). The reaction mixture was stirred at 130°C for 18h. The product was purified by flash chromatography (1:20 EA/PE) as yellow solid (72 mg, 75 %). Mp: 82.2-84.0 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.77 (s, 1H), 8.79-8.75 (m, 2H), 8.14 (dd, *J* = 8.3Hz, 1.7Hz, 1H), 7.54-7.42 (m, 3H), 6.85 (s, 2H), 2.67 (t, *J* = 7.6Hz, 2H), 2.58-2.53 (m, 2H), 2.49 (s, 6H), 2.16-2.09 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 171.0, 157.4, 151.5, 148.2, 138.3, 136.4, 134.3, 127.9, 127.4, 121.7, 121.6, 120.8, 116.5, 37.0, 34.3, 25.9, 24.1.

HRMS (ESI): Calcd for $C_{20}H_{21}N_3O$ $[M+H]^+$: 320.1763, Found: 320.1765.

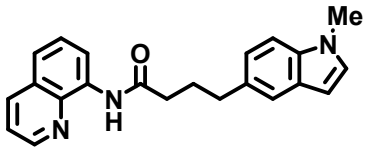


4-(*1H*-Indol-5-yl)-*N*-(quinolin-8-yl)butanamide (P49). The reaction mixture was stirred at 130°C for 18h. The product was purified by flash chromatography (1:20 EA/PE) as yellow oil (64 mg, 65 %).

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.81 (s, 1H), 8.83-8.79 (m, 2H), 8.23-8.14 (m, 2H), 7.56-7.43 (m, 4H), 7.33 (d, *J* = 8.3Hz, 1H), 7.18 (t, *J* = 2.8Hz, 1H), 7.10-7.08 (m, 1H), 6.50 (s, 1H), 2.87 (t, *J* = 7.4Hz, 2H), 2.60 (t, *J* = 7.5Hz, 2H), 2.26-2.18 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 172.0, 148.2, 138.5, 136.5, 134.7, 134.6, 132.9, 128.2, 128.1, 127.6, 124.5, 123.2, 121.7, 121.5, 120.3, 116.5, 111.1, 102.4, 37.5, 35.4, 27.9.

HRMS (ESI): Calcd for $C_{21}H_{19}N_3O$ $[M+H]^+$: 330.1606, Found: 330.1608.

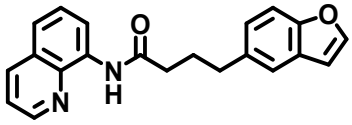


4-(1-Methyl-*1H*-indol-5-yl)-*N*-(quinolin-8-yl)butanamide (P50). The reaction mixture was stirred at 130°C for 18 h. The product was purified by flash chromatography (1:20 EA/PE) as yellow solid (76 mg, 74%). Mp: 62.2-64.0 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.79 (s, 1H), 8.81-8.76 (m, 2H), 8.12 (dd, *J* = 8.2Hz, 1.7Hz, 1H), 7.59-7.31 (m, 4H), 7.29-7.20 (m, 1H), 7.12 (dd, *J* = 8.3Hz, 1.6Hz, 1H), 7.01 (d, *J* = 3.1 Hz, 1H), 6.41 (dd, *J* = 3.1Hz, 0.8 Hz, 1H), 3.75 (s, 3H), 2.86 (t, *J* = 7.4 Hz, 2H), 2.57 (t, *J* = 7.5Hz, 2H), 2.32-2.08 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 171.8, 148.1, 138.4, 136.4, 135.5, 134.6, 132.3, 129.0, 128.7, 128.0, 127.5, 122.6, 121.6, 121.3, 120.3, 116.4, 109.1, 100.5, 37.4, 35.3, 32.9 27.8.

HRMS (ESI): Calcd for $C_{22}H_{21}N_3O$ $[M+H]^+$: 344.1763, Found: 344.1766.

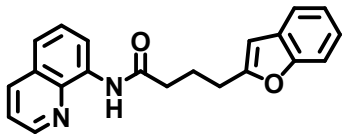


4-(Benzofuran-5-yl)-*N*-(quinolin-8-yl)butanamide (P51). The reaction mixture was stirred at 130°C for 18h. The product was purified by flash chromatography (1:20 EA/PE) as yellow solid (79 mg, 80%). Mp: 97.2-99.0 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.79 (s, 1H), 8.80 (t, *J* = 6.6Hz, 2H), 8.15 (d, *J* = 8.2Hz, 1H), 7.80-7.34 (m, 6H), 7.18 (d, *J* = 8.5Hz, 1H), 6.71 (d, *J* = 2.2Hz, 1H), 2.87 (t, *J* = 7.5Hz, 2H), 2.59 (t, *J* = 7.4Hz, 2H), 2.24-2.17 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 171.5, 153.7, 148.1, 145.1, 138.4, 136.4, 136.0, 134.5, 128.0, 127.6, 127.5, 125.1, 121.6, 121.4, 120.7, 116.5, 111.2, 106.4, 37.3, 35.1, 27.6.

HRMS (ESI): Calcd for $C_{21}H_{18}N_2O_2$ $[M+H]^+$: 331.1447, Found: 331.1446.

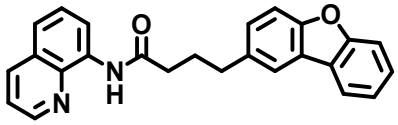


4-(Benzofuran-2-yl)-*N*-(quinolin-8-yl)butanamide (P52). The reaction mixture was stirred at 130°C for 18h. The product was purified by flash chromatography (1:20 EA/PE) as yellow solid (69 mg, 70%). Mp: 72.2-74.0 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.82 (s, 1H), 9.01-8.63 (m, 2H), 8.12 (dd, *J* = 8.3Hz, 1.7Hz, 1H), 7.58-7.34 (m, 5H), 7.29-7.11 (m, 2H), 6.46 (s, 1H), 2.93 (t, *J* = 7.3Hz, 2H), 2.64 (t, *J* = 7.4Hz, 2H), 2.31-2.23 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 171.1, 158.3, 154.8, 148.2, 138.3, 136.4, 134.5, 128.9, 128.0, 127.4, 123.3, 122.5, 121.6, 121.5, 120.3, 116.5, 110.9, 102.7, 37.0 27.8, 23.6.

HRMS (ESI): Calcd for $C_{21}H_{18}N_2O_2$ $[M+H]^+$: 331.1447, Found: 331.1448.

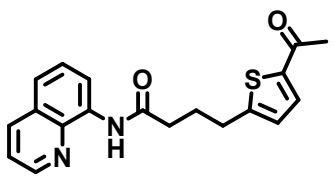


4-(Dibenzo[*b,d*]furan-3-yl)-*N*-(quinolin-8-yl)butanamide (P53). The reaction mixture was stirred at 130°C for 18h. The product was purified by flash chromatography (1:20 EA/PE) as yellow oil (94 mg, 82%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.80 (s, 1H), 8.82-8.74 (m, 2H), 8.14-8.12 (m, 1H), 7.89-7.81 (m, 2H), 7.56-7.40 (m, 6H), 7.34-7.29 (m, 2H), 2.93 (t, *J* = 7.5 Hz, 2H), 2.62 (t, *J* = 7.4 Hz, 2H), 2.29-2.22 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 171.4, 156.5, 154.9, 148.1, 138.3, 136.4, 136.0, 134.5, 127.9, 127.8, 127.4, 127.0, 124.3, 124.2, 122.6, 121.6, 121.5, 120.6, 120.3, 116.4, 111.6, 111.4, 37.2, 35.1, 27.6.

HRMS (ESI): Calcd for $C_{25}H_{20}N_2O_2$ $[M+H]^+$: 381.1603, Found: 381.1603.



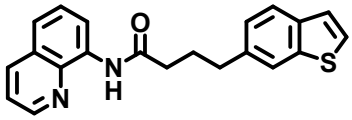
4-(5-Acetylthiophen-2-yl)-N-(quinolin-8-yl)butanamide (P54). The reaction

mixture was stirred at 130°C for 18h. The product was purified by flash chromatography (1:20 EA/PE) as yellow oil (40 mg, 39%). While $NCCH_2COOH$ (3 equiv, 0.9 mmol, 77mg) was added, the product was afforded in 60% yield (61 mg).

^1H NMR (400 MHz, $CDCl_3$) δ 9.81 (s, 1H), 8.81-8.75 (m, 2H), 8.17 (d, *J* = 8.3Hz, 1H), 7.56-7.45 (m, 4H), 6.89 (d, *J* = 3.8Hz, 1H), 3.01 (t, *J* = 7.5Hz, 2H), 2.63 (t, *J* = 7.3Hz, 2H), 2.51 (s, 3H), 2.26-2.18 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 190.5, 170.8, 154.3, 148.1, 142.4, 138.2, 136.5, 134.3, 133.0, 128.0, 127.4, 126.2, 121.7, 121.6, 116.6, 36.7, 29.9, 26.9, 26.5.

HRMS (ESI): Calcd for $C_{19}H_{18}N_2O_2S$ $[M+H]^+$: 339.1167, Found: 339.1168.

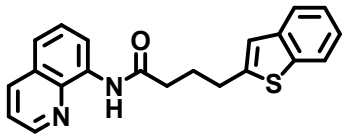


4-(Benzo[*b*]thiophen-6-yl)-*N*-(quinolin-8-yl)butanamide (P55). The reaction mixture was stirred at 130°C for 18h. The product was purified by flash chromatography (1:20 EA/PE) as yellow oil (91 mg, 88%).

^1H NMR (400 MHz, $CDCl_3$) δ 9.79 (s, 1H), 9.02-8.65 (m, 2H), 8.15 (dd, *J* = 8.3Hz, 1.7Hz, 1H), 7.84-7.68 (m, 2H), 7.58-7.20 (m, 6H), 2.89 (t, *J* = 7.5Hz, 2H), 2.59 (t, *J* = 7.4Hz, 2H), 2.26-2.18 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 171.5, 148.3, 140.2, 138.5, 138.0, 137.9, 136.5, 134.6, 128.1, 127.6, 125.7, 125.5, 123.7, 123.6, 122.1, 121.7, 121.5, 116.6, 37.3, 35.3, 27.4.

HRMS (ESI): Calcd for $C_{21}H_{18}N_2OS$ $[M+H]^+$: 347.1218, Found: 347.1224.

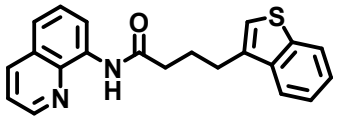


4-(Benzo[*b*]thiophen-2-yl)-*N*-(quinolin-8-yl)butanamide (P56). The reaction mixture was stirred at 130°C for 18h. The product was purified by flash chromatography (1:20 EA/PE) as yellow oil (61 mg, 59%).

^1H NMR (400 MHz, $CDCl_3$) δ 9.98 (s, 1H), 8.98-8.95 (m, 2H), 8.33 (dd, *J* = 8.3Hz, 1.7Hz, 1H), 7.95 (d, *J* = 7.9Hz, 1H), 7.90-7.80 (m, 1H), 7.79-7.59 (m, 3H), 7.56-7.38 (m, 3H), 3.25 (t, *J* = 7.3Hz, 2H), 2.83 (t, *J* = 7.4Hz, 2H), 2.50-2.42 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 171.1, 148.2, 145.3, 140.2, 139.5, 138.3, 136.4, 134.4, 128.0, 127.4, 124.1, 123.6, 122.8, 122.2, 121.6, 121.5, 121.3, 116.5, 36.8, 30.1, 26.7.

HRMS (ESI): Calcd for $C_{21}H_{18}N_2OS$ $[M+H]^+$: 347.1218, Found: 347.1218.

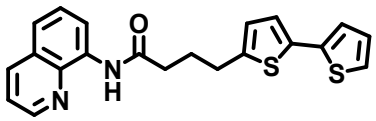


4-(Benzo[*b*]thiophen-3-yl)-*N*-(quinolin-8-yl)butanamide (P57). The reaction mixture was stirred at 130°C for 18h. The product was purified by flash chromatography (1:20 EA/PE) as yellow oil (69 mg, 66%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.91 (s, 1H), 8.83-8.81 (m, 2H), 8.22 (d, *J* = 8.1Hz, 1H), 7.87-7.81 (m, 2H), 7.60-7.47 (m, 3H), 7.39-7.31 (m, 2H), 7.19 (s, 1H), 3.02 (t, *J* = 7.5Hz, 2H), 2.70 (t, *J* = 7.2Hz, 2H), 2.33-2.26 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 171.5, 148.0, 140.6, 139.1, 137.1, 136.1, 134.4, 128.2, 127.8, 124.3, 124.0, 123.0, 121.9, 121.8, 121.7, 117.1, 37.5, 29.1, 25.0.

HRMS (ESI): Calcd for $C_{21}H_{18}N_2OS$ $[M+H]^+$: 347.1218, Found: 347.1218.

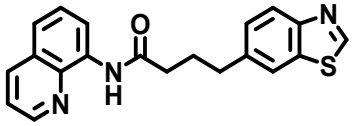


4-([2,2'-Bithiophen]-5-yl)-*N*-(quinolin-8-yl)butanamide (P58). While $NCCH_2COOH$ (3 equiv, 0.9 mmol, 77mg) was added and the reaction mixture was stirred at 130°C for 18h. The product was purified by flash chromatography (1:20 EA/PE) as yellow solid (36 mg, 32%). Without the addition of $NCCH_2COOH$, no title compound was abtained. Mp: 112.2-114.0 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.81 (s, 1H), 8.79-8.77 (m, 2H), 8.15 (d, *J* = 6.6Hz, 1H), 7.56-7.43 (m, 3H), 7.18-7.16 (m, 1H), 7.11-7.10 (m, 1H), 7.00-6.98(m, 2H), 6.75(d, *J* = 3.6Hz, 1H), 2.96 (t, *J* = 7.4Hz, 2H), 2.64 (t, *J* = 7.3Hz, 2H), 2.24-2.16 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 171.2, 148.3, 143.7, 138.4, 137.9, 136.5, 135.4, 134.5, 128.0, 127.8, 127.5, 125.6, 124.0, 123.6, 123.3, 121.7, 121.6, 116.5, 36.9, 29.5, 27.3.

HRMS (ESI): Calcd for $C_{21}H_{18}N_2OS_2$ $[M+H]^+$: 379.0939, Found: 379.0940.

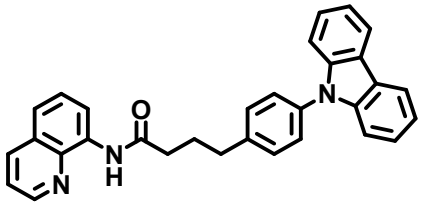


4-(Benzo[*d*]thiazol-6-yl)-*N*-(quinolin-8-yl)butanamide (P59). The reaction mixture was stirred at 130°C for 18h. The product was purified by flash chromatography (1:20 EA/PE) as yellow oil (49 mg, 47%). While $NCCH_2COOH$ (3 equiv, 0.9 mmol, 77mg) was added, the product was afforded in 94% yield (98 mg).

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.79 (s, 1H), 8.92 (s, 1H), 8.83-8.71 (m, 2H), 8.14 (dd, *J* = 8.3Hz, 1.7Hz, 1H), 8.05 (d, *J* = 8.4Hz, 1H), 7.81 (d, *J* = 1.6Hz, 1H), 7.59-7.34 (m, 4H), 2.91 (t, *J* = 7.5Hz, 2H), 2.59 (t, *J* = 7.3Hz, 2H), 2.26-2.18 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 171.2, 153.3, 151.8, 148.2, 139.4, 138.3, 136.4, 134.4, 134.0, 127.9, 127.4, 127.3, 123.4, 121.6, 121.5, 121.3, 116.5, 37.1, 35.1, 27.2.

HRMS (ESI): Calcd for $C_{20}H_{17}N_3OS$ $[M+H]^+$: 348.1171, Found: 348.1168.

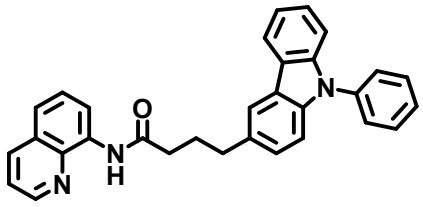


4-(4-(*9H*-Carbazol-9-yl)phenyl)-*N*-(quinolin-8-yl)butanamide (P60). The reaction mixture was stirred at 130°C for 18h. The product was purified by flash chromatography (1:20 EA/PE) as yellow oil (105 mg, 77%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.90 (s, 1H), 8.99-8.77 (m, 2H), 8.26-8.06 (m, 3H), 7.59-7.39 (m, 11H), 7.38-7.28 (m, 2H), 2.91 (t, *J* = 7.6 Hz, 2H), 2.70 (t, *J* = 7.3 Hz, 2H), 2.33-2.26 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 171.4, 148.2, 141.0, 141.0, 138.4, 136.5, 135.6, 134.5, 130.0, 128.0, 127.5, 127.1, 126.0, 123.3, 121.7, 121.6, 120.3, 119.9, 116.6, 109.9, 37.4, 35.0, 27.1.

HRMS (ESI): Calcd for $C_{31}H_{25}N_3O$ $[M+H]^+$: 456.2076, Found: 456.2079.

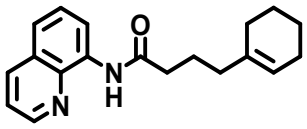


4-(9-Phenyl-*9H*-carbazol-3-yl)-*N*-(quinolin-8-yl)butanamide (P61). The reaction mixture was stirred at 130°C for 18h. The product was purified by flash chromatography (1:20 EA/PE) as yellow oil (109 mg, 80%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.86 (s, 1H), 8.88 (d, *J* = 7.6 Hz, 1H), 8.75 (dd, *J* = 4.3 Hz, 1.7 Hz, 1H), 8.15-8.06 (m, 3H), 7.63-7.54 (m, 5H), 7.49-7.43 (m, 4H), 7.41-7.38 (m, 2H), 7.35-7.29(m, 2H), 3.01 (t, *J* = 7.4 Hz, 2H), 2.67 (t, *J* = 7.3 Hz, 2H), 2.37-2.29 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 171.7, 148.2, 141.1, 139.6, 138.3, 137.9, 136.4, 134.6, 133.2, 129.9, 128.0, 127.5, 127.3, 127.0, 126.8, 125.9, 123.6, 123.3, 121.6, 121.5, 120.4, 120.0, 119.9, 116.5, 109.8, 37.4, 35.3, 27.8.

HRMS (ESI): Calcd for $C_{31}H_{25}N_3O$ $[M+H]^+$: 456.2076, Found: 456.2075.

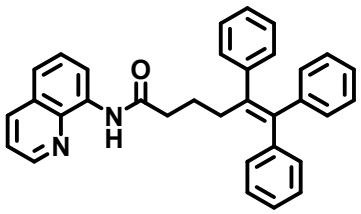


4-(Cyclohex-1-en-1-yl)-*N*-(quinolin-8-yl)butanamide (P62). The reaction mixture was stirred at 130°C for 18h. The product was purified by flash chromatography (1:20 EA/PE) as yellow oil (43 mg, 70%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.80 (s, 1H), 8.81-8.78 (m, 2H), 8.16 (dd, J = 8.4Hz, 1.6Hz, 1H), 7.56-7.44 (m, 3H), 5.47-5.46 (m, 1H), 2.53 (m, J = 7.6 Hz, 2H), 2.10-2.06 (m, 2H), 2.00-1.89 (m, 6H), 1.62-1.60 (m, 2H), 1.58-1.52 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 172.1, 148.2, 138.5, 136.9, 136.5, 134.7, 128.1, 127.6, 122.1, 121.7, 121.5, 116.5, 37.7, 37.6, 28.2, 25.4, 23.6, 23.1, 22.7.

HRMS (ESI): Calcd for $C_{19}H_{22}N_2O$ $[M+H]^+$: 295.1399, Found:295.1398.

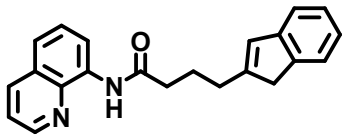


5,6,6-Triphenyl-*N*-(quinolin-8-yl)hex-5-enamide (P63). The reaction mixture was stirred at 130°C for 18h. The product was purified by flash chromatography (1:20 EA/PE) as yellow oil (112 mg, 80%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.66 (s, 1H), 8.80-8.63 (m, 2H), 8.10 (dd, *J* = 8.2Hz, 1.7Hz, 1H), 7.58-7.35 (m, 3H), 7.26-7.05 (m, 10H), 7.03-6.94 (m, 3H), 6.94-6.83 (m, 2H), 2.76-2.56 (m, 2H), 2.43 (t, *J* = 7.7Hz, 2H), 1.89-1.85 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 171.34, 148.1, 143.2, 142.8, 142.0, 140.0, 139.9, 138.30 136.4, 134.5, 130.7, 129.6, 129.4, 128.3, 128.0, 127.9, 127.5, 126.7, 126.4, 125.9, 121.6, 121.4 116.4, 38.1, 35.3, 25.1.

HRMS (ESI): Calcd for $C_{33}H_{28}N_2O$ $[M+H]^+$: 469.2280, Found: 469.2286.

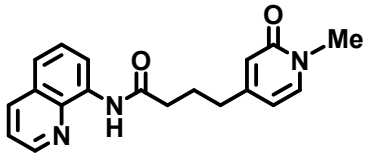


4-(*1H*-Inden-2-yl)-*N*-(quinolin-8-yl)butanamide (P64). The reaction mixture was stirred at 130°C for 18h. The product was purified by flash chromatography (1:20 EA/PE) as yellow oil (65 mg, 66%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.82 (s, 1H), 8.82-8.75 (m, 2H), 8.16 (dd, *J* = 8.3 Hz, 1.7 Hz, 1H), 7.58-7.42 (m, 3H), 7.39 (d, *J* = 7.4 Hz, 1H), 7.32-7.18 (m, 2H), 7.13-7.09 (m, 1H), 6.60 (s, 1H), 3.36 (s, 2H), 2.71-2.53 (m, 4H), 2.19-2.12 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 171.4, 149.4, 148.1, 145.5, 143.1, 138.3, 136.4, 134.5, 128.0, 127.4, 127.1, 126.3, 123.8, 123.5, 121.6, 121.4, 120.0, 116.4, 41.0, 37.5, 30.6, 24.8.

HRMS (ESI): Calcd for $C_{22}H_{20}N_2O$ $[M+H]^+$: 329.1654, Found: 329.1655.

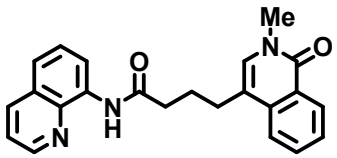


4-(1-Methyl-2-oxo-1,2-dihydropyridin-4-yl)-*N*-(quinolin-8-yl)butanamide (P65). The reaction mixture was stirred at 130°C for 18h. The product was purified by flash chromatography (1:20 EA/PE) as yellow oil (77 mg, 80%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.78 (s, 1H), 8.90-8.54 (m, 2H), 8.12 (dd, *J* = 8.3Hz, 1.7Hz, 1H), 7.61-7.35 (m, 3H), 7.17 (d, *J* = 6.9Hz, 1H), 6.42 (d, *J* = 1.8Hz, 1H), 6.05 (dd, *J* = 6.9Hz, 1.9Hz, 1H), 3.47 (s, 3H), 2.65-2.39 (m, 4H), 2.11-2.03 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 170.9, 163.2, 154.4, 148.2, 138.2, 137.7, 136.4, 134.3, 127.9, 127.3, 121.7, 121.6, 118.7, 116.4, 107.5, 37.3, 36.9, 34.4, 24.8.

HRMS (ESI): Calcd for $C_{19}H_{19}N_3O_2$ $[M+H]^+$: 322.1556, Found: 322.1555.

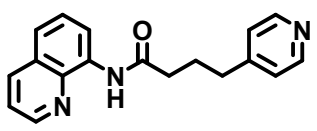


4-(2-Methyl-1-oxo-1,2-dihydroisoquinolin-4-yl)-*N*-(quinolin-8-yl)butanamide (P66). The reaction mixture was stirred at 130°C for 18h. The product was purified by flash chromatography (1:20 EA/PE) as yellow oil (45 mg, 40%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.82 (s, 1H), 8.89-8.69 (m, 2H), 8.47 (dd, *J* = 8.0 Hz, 1.3 Hz, 1H), 8.18 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.74 (d, *J* = 8.1 Hz, 1H), 7.69-7.65 (m, 1H), 7.61-7.40 (m, 4H), 6.97 (s, 1H), 3.55 (s, 3H), 2.84 (t, *J* = 7.6 Hz, 2H), 2.67 (t, *J* = 7.1 Hz, 2H), 2.23-2.16 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 171.1, 162.3, 148.2, 138.3, 136.5, 136.5, 134.3, 132.0, 130.6, 128.3, 128.0, 127.5, 126.6, 126.2, 122.9, 121.7, 121.6, 116.5, 115.4, 37.2, 36.9, 28.8, 25.2.

HRMS (ESI): Calcd for $C_{23}H_{21}N_3O_2$ $[M+H]^+$: 356.1763, Found: 356.1758.



4-(Pyridin-4-yl)-*N*-(quinolin-8-yl)butanamide (P67). The title compound was

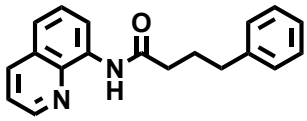
prepared from 1-benzyl-4-bromo-1,2,3,6-tetrahydropyridine (1.5 equiv). The reaction mixture was stirred at 130°C for 18h. The product was purified by flash chromatography (1:20 EA/PE) as yellow oil (53 mg, 60%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.74 (s, 1H), 8.84-8.65 (m, 2H), 8.49 (s, 2H), 8.11 (d, *J* = 8.3Hz, 1H), 7.55-7.34 (m, 3H), 7.29 (d, *J* = 4.7Hz, 2H), 2.79 (t, *J* = 6.8Hz, 2H), 2.55 (t, *J* = 7.2Hz, 2H), 2.22-2.15 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 170.6, 154.0, 148.2, 147.1, 138.2, 136.5, 134.2, 128.0, 127.4, 124.9, 121.7, 116.5, 36.8, 34.7, 25.7.

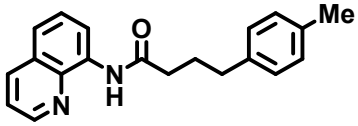
HRMS (ESI): Calcd for $C_{18}H_{17}N_3O$ $[M+H]^+$: 292.1450, Found: 292.1453.

Typical procedure for reductive Heck reaction of various aryl chlorides: In an argon atmosphere, a dry 25-mL Schlenk tube containing a magnetic stirbar was charged with $[PdCl(C_3H_5)]_2$ (5 mol%, 5.7 mg, 0.015 mmol), cataCXium®PCy (10 mol%, 10.2 mg, 0.03 mmol), alkenes **S2** (1 equiv, 0.3 mmol, 63.6 mg), LiOAc (3 equiv, 0.9 mmol, 20 mg), aryl chlorides (1.5 equiv, 0.45 mmol), dry 2,3-butanediol (3 mL) and H_2O (20 equiv, 6 mmol, 108 uL). The tube was capped tightly and the mixture was vigorously stirred in a *pre*-warmed 130°C oil bath. After alkenes was almost fully consumed (monitored by GCMS), the reaction mixture was concentrated on a rotary evaporator and then distilled under vacuum, the resulting residue was directly subjected to flash silica gel chromatography. The structure of the desired product was confirmed by ^{1}H and ^{13}C NMR spectroscopy of the purified sample. The typical procedure using 0.3 mmol of alkenes was applied for all the isolation, unless stated otherwise.



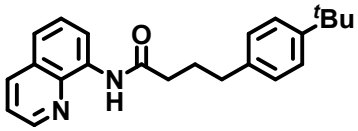
5-**Phenyl-*N*-(quinolin-8-yl)butanamide (P68).** The reaction mixture was stirred at 130°C for 18h. The product was purified by flash chromatography (1:20 EA/PE) as yellow oil (52 mg, 59%).

HRMS (ESI): Calcd for $C_{19}H_{18}N_2O$ $[M+H]^+$: 291.1497, Found: 291.1499.



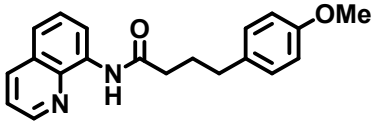
N-**(Quinolin-8-yl)-4-(p-tolyl)butanamide (P69).** The reaction mixture was stirred at 130°C for 18h. The product was purified by flash chromatography (1:20 EA/PE) as yellow oil (44 mg, 48%).

HRMS (ESI): Calcd for $C_{20}H_{20}N_2O$ $[M+H]^+$: 305.1654, Found: 305.1653.



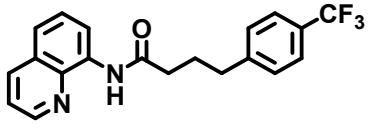
4-**(4-(*tert*-Butyl)phenyl)-*N*-(quinolin-8-yl)butanamide (P70).** The reaction mixture was stirred at 130°C for 18h. The product was purified by flash chromatography (1:20 EA/PE) as yellow oil (75 mg, 72%).

HRMS (ESI): Calcd for $C_{23}H_{26}N_2O$ $[M+H]^+$: 347.2123 , found: 347.2121.



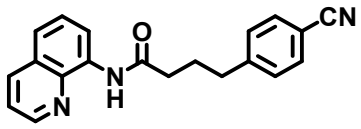
4-(4-Methoxyphenyl)-*N*-(quinolin-8-yl)butanamide (P71). The reaction mixture was stirred at 130°C for 18h. The product was purified by flash chromatography (1:20 EA/PE) as yellow oil (52 mg, 54%).

HRMS (ESI): Calcd for $C_{20}H_{20}N_2O_2$ $[M+H]^+$: 321.1603 , Found: 321.1601.



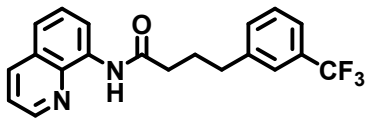
***N*-(Quinolin-8-yl)-4-(4-(trifluoromethyl)phenyl)butanamide (P72).** The reaction mixture was stirred at 130°C for 18h. The product was purified by flash chromatography (1:20 EA/PE) as yellow solid (87 mg, 81%).

HRMS (ESI): Calcd for $C_{20}H_{17}F_3N_2O$ $[M+H]^+$: 359.1371, Found: 359.1364.



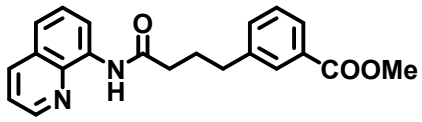
4-(4-Cyanophenyl)-*N*-(quinolin-8-yl)butanamide (P73) . The reaction mixture was stirred at 130°C for 18h. The product was purified by flash chromatography (1:10 EA/PE) as brown solid (36 mg, 38%). While $NCCH_2COOH$ (3 equiv, 0.9 mmol, 77mg) was added, the product was afforded in 74% yield (70 mg).

HRMS (ESI): Calcd for $C_{20}H_{17}N_3O$ $[M+H]^+$: 316.1450, Found: 316.1448.



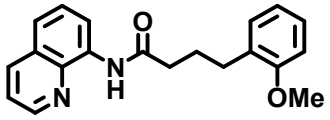
***N*-(Quinolin-8-yl)-4-(3-(trifluoromethyl)phenyl)butanamide (P74).** The reaction mixture was stirred at 130°C for 18h. The product was purified by flash chromatography (1:20 EA/PE) as yellow oil (62 mg, 57%).

HRMS (ESI): Calcd for $C_{20}H_{17}F_3N_2O$ $[M+H]^+$: 359.1371, Found: 359.1370.



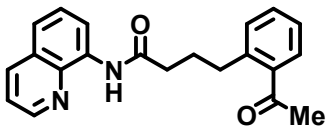
Methyl 3-(4-oxo-4-(quinolin-8-ylamino)butyl)benzoate (P75). The reaction mixture was stirred at 130°C for 18h. The product was purified by flash chromatography (1:30 EA/PE) as yellow oil (52 mg, 50%).

HRMS (ESI): Calcd for $[M+H]^+$: $C_{21}H_{20}N_2O_3$ $[M+H]^+$: 349.1552 , Found: 349.1555.



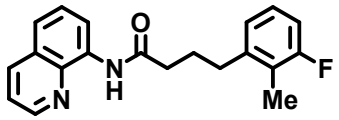
4-(2-Methoxyphenyl)-*N*-(quinolin-8-yl)butanamide (P76). The reaction mixture was stirred at 130°C for 18h. The product was purified by flash chromatography (1:30 EA/PE) as yellow oil (58 mg, 61%).

HRMS (ESI): Calcd for $C_{20}H_{20}N_2O_2$ $[M+H]^+$: 321.1603, Found: 321.1599.



5-**(2-Acetylphenyl)-*N*-(quinolin-8-yl)butanamide (P77).** The reaction mixture was stirred at 130°C for 18h. The product was purified by flash chromatography (1:20 EA/PE) as yellow oil (72 mg, 72%). While $NCCH_2COOH$ (3 equiv, 0.9 mmol, 77mg) was added, the product was afforded in 81% yield (81 mg).

HRMS (ESI): Calcd for $C_{21}H_{20}N_2O_2$ $[M+H]^+$: 333.1603 , Found: 333.1609.



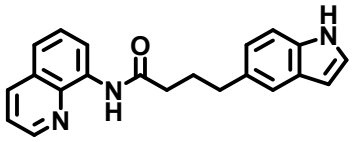
4-(3-Fluoro-2-methylphenyl)-*N*-(quinolin-8-yl)butanamide (P78). The reaction mixture was stirred at 130°C for 18h. The product was purified by flash chromatography (1:20 EA/PE) as yellow oil (77 mg, 68%).

^1H NMR (400 MHz, $CDCl_3$) δ 9.79 (s, 1H), 8.79-8.74 (m, 2H), 8.17-8.08 (m, 1H), 7.54-7.44 (m, 3H), 7.13-7.03 (m, 1H), 6.97 (d, *J* = 8.8Hz, 1H), 6.89-6.84(m, 1H), 2.77 (t, *J* = 6.5Hz, 2H), 2.62 (t, *J* = 4.7Hz, 2H), 2.33 (d, *J* = 1.2Hz, 3H), 2.16-2.04 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 171.3, 161.6 (d, *J* = 242Hz), 148.2, 142.4 (d, *J* = 4.5Hz), 138.4, 136.5, 134.5, 128.0, 127.5, 126.6 (d, *J* = 9.0Hz), 124.6 (d, *J* = 2.6Hz), 123.3 (d, *J* = 16.2Hz), 121.7, 121.6, 116.6, 112.8 (d, *J* = 23Hz) 37.5, 32.6 (d, *J* = 2.8 Hz), 25.9, 10.5 (d, *J* = 5.9 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -116.38.

HRMS (ESI): Calcd for $C_{20}H_{19}FN_2O$ $[M+H]^+$: 323.1560 , Found: 323.1565.



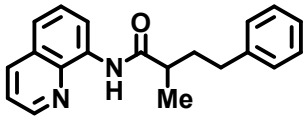
4-(*1H*-Indol-5-yl)-*N*-(quinolin-8-yl)butanamide (P79). The reaction mixture was stirred at 130°C for 18h. The product was purified by flash chromatography (1:20 EA/PE) as yellow oil (59 mg, 60 %).

HRMS (ESI): Calcd for $C_{21}H_{19}N_3O$ $[M+H]^+$: 330.1606, Found: 330.1608.

V. Pd-catalyzed intermolecular reductive Heck reaction of various alkenes

General Procedure A : In an argon atmosphere, a dry 25-mL Schlenk tube containing a magnetic stirbar was charged with $[PdCl(C_3H_5)]_2$ (5 mol%, 5.7 mg, 0.015 mmol), cataCXium@PCy (10 mol%, 10.2 mg, 0.01 mmol), alkenes (1 equiv, 0.3 mmol), LiOAc (3 equiv, 0.9 mmol, 60 mg)，PhBr (1.5 equiv, 0.45 mmol), dry 2,3-butanediol (3 mL) and H_2O (20 equiv, 6 mmol, 108 uL). The tube was capped tightly and the mixture was vigorously stirred in a *pre*-warmed 130°C oil bath. After alkenes was almost fully consumed (monitored by GCMS), the reaction mixture was concentrated on a rotary evaporator and then distilled under reduced pressure and the resulting residue was directly subjected to silica gel flash chromatography. The structure of the desired product was confirmed by ^1H NMR spectroscopy of the purified sample.

General Procedure B : In an argon atmosphere, a dry 25-mL Schlenk tube containing a magnetic stirbar was charged with $[PdCl(C_3H_5)]_2$ (5 mol%, 5.7 mg, 0.015 mmol), cataCXium@PCy (10 mol%, 10.2 mg, 0.03 mmol), alkenes (1 equiv, 0.3 mmol), Cs_2CO_3 (5 equiv, 1.5 mmol)，PhBr (1.5 equiv, 0.45 mmol), dry 2,3-butanediol (3 mL), cyanoacetic acid (3 equiv, 0.9 mmol, 76.8 mg) and H_2O (20 equiv, 6 mmol, 108 uL). The tube was capped tightly and the mixture was vigorously stirred in a *pre*-warmed 130°C oil bath. After alkenes was almost fully consumed (monitored by GCMS), the reaction mixture was concentrated on a rotary evaporator and then distilled under reduced pressure and the resulting residue was directly subjected to silica gel flash chromatography. The structure of the desired product was confirmed by ^1H NMR spectroscopy of the purified sample.

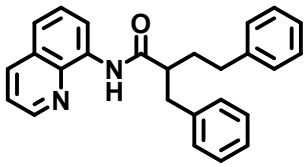


2-Methyl-4-phenyl-*N*-(quinolin-8-yl)butanamide (P80). According to the general procedure A. The reaction mixture was stirred at 130°C for 18h. The product was purified by flash chromatography (1:50 EA/PE) as yellow oil (78 mg, 85%).

^{1}H NMR (400 MHz, $CDCl_3$): δ 9.88 (s, 1H), 8.84-8.81 (m, 2H), 8.18 (dd, *J* = 8.3Hz, 1.6Hz, 1H), 7.58-7.50 (m, 2H), 7.47 (dd, *J* = 8.2Hz, 4.2Hz, 1H), 7.30-7.17 (m, 5H), 2.81-2.59 (m, 3H), 2.26-2.17 (m, 1H), 1.90-1.81 (m, 1H), 1.36 (d, *J* = 6.9Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 175.1, 148.2, 141.8, 138.5, 136.4, 134.6, 128.5, 128.4, 128.0, 127.5, 125.9, 121.6, 121.5, 116.5, 42.3, 36.1, 33.6, 18.3.

HRMS (ESI): Calcd for $C_{20}H_{20}N_2O$ $[M+H]^+$: 305.1654, Found: 305.1654.

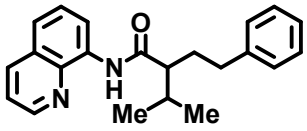


2-Benzyl-4-phenyl-*N*-(quinolin-8-yl)butanamide (P81). According to the general procedure A. The reaction mixture was stirred at 130^{o}C for 18h. The product was purified by flash chromatography (1:50 EA/PE) as yellow oil (96 mg, 84%).

^{1}H NMR (400 MHz, $CDCl_3$): δ 9.70 (s, 1H), 8.82 -8.74 (m, 2H) , 8.13 (dd, *J* = 8.3Hz, 1.5Hz, 1H), 7.55-7.41 (m, 3H), 7.27-7.10 (m, 10H), 3.17 (q, *J* = 7.2Hz, 1H), 2.92-2.74 (m, 3H), 2.69-2.61 (m, 1H), 2.26-2.16 (m, 1H), 2.00-1.88 (m, 1H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 173.6, 148.1, 141.6, 139.4, 138.4, 136.3, 134.3, 129.0, 128.5, 128.4(4), 128.4(2), 127.9, 127.4, 126.3, 125.9, 121.6, 121.5, 116.6, 50.4, 39.3, 34.2, 33.6.

HRMS (ESI): Calcd for $C_{26}H_{24}N_2O$ $[M+H]^+$: 381.1967, Found: 381.1960.

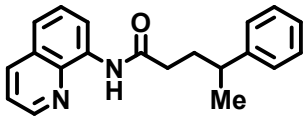


2-Isopropyl-4-phenyl-*N*-(quinolin-8-yl)butanamide (P82). According to the general procedure A. The reaction mixture was stirred at 130^{o}C for 18h. The product was purified by flash chromatography (1:50 EA/PE) as yellow oil (90 mg, 90 %).

^{1}H NMR (400 MHz, $CDCl_3$): δ 9.84 (s, 1H), 8.89-8.81 (m, 2H), 8.17 (dd, *J* = 8.2Hz, 1H), 7.58-7.45 (m, 3H), 7.28-7.24 (m, 2H), 7.22-7.16 (m, 3H), 2.83-2.76 (m, 1H), 2.62-2.55 (m, 1H), 2.24-1.91 (m, 4H), 1.03 (d, *J* = 3.3Hz, 6H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 174.1, 148.2, 142.0, 138.5, 136.4, 134.4, 128.6, 128.4, 128.0, 127.5, 125.9, 121.6, 121.5, 116.5, 55.7, 34.0, 32.1, 31.3, 21.0, 20.4.

HRMS (ESI): Calcd for $C_{22}H_{24}N_2O$ $[M+H]^+$: 333.1967, Found: 333.1966.

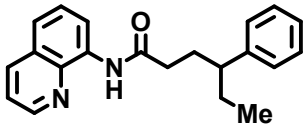


4-Phenyl-*N*-(quinolin-8-yl)pentanamide (P83). According to the general procedure A. The reaction mixture was stirred at 130°C for 18h. The product was purified by flash chromatography (1:50 EA/PE) as yellow oil (84 mg, 92%).

^{1}H NMR (400 MHz, $CDCl_3$): δ 9.47 (s, 1H), 8.56-8.54(m, 2H), 7.92 (dd, *J* = 8.3Hz, 1.6Hz, 1H), 7.32-7.25 (m, 2H), 7.21 (dd, *J* = 8.3Hz, 4.2Hz, 1H), 7.12-7.08 (m, 2H), 7.04-6.98 (m, 3H), 2.64-2.59 (m, 1H), 2.21 (t, *J* = 7.7Hz, 2H), 2.00-1.80 (m, 2H), 1.11 (d, *J* = 7.0Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 171.7, 148.1, 146.4, 138.3, 136.4, 134.5, 128.6, 127.9, 127.5, 127.2, 126.3, 121.6, 121.4, 116.4, 39.6, 36.2, 33.7, 22.6.

HRMS (ESI): Calcd for $C_{20}H_{20}N_2O$ $[M+H]^+$: 305.1654, Found: 305.1654.

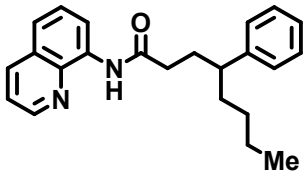


4-Phenyl-*N*-(quinolin-8-yl)hexanamide (P84). According to the general procedure A. The reaction mixture was stirred at 130°C for 18h. The product was purified by flash chromatography (1:50 EA/PE) as yellow oil (84 mg, 88%).

^{1}H NMR (400 MHz, $CDCl_3$): δ 9.57 (s, 1H), 8.69-8.68 (m, 2H), 8.06 (d, *J* = 8.3Hz, 1.6Hz, 1H), 7.46-7.33 (m, 3H), 7.25-7.22 (m, 2H), 7.17-7.11 (m, 3H), 2.49-2.14 (m, 4H), 1.97-1.88 (m, 1H), 1.71-1.50 (m, 2H), 0.72 (t, *J* = 7.4Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 171.8, 148.1, 144.6, 138.3, 136.4, 134.6, 128.5, 128.0, 127.9, 127.5, 126.2, 121.6, 121.3, 116.4, 47.4, 36.1, 31.9, 30.0, 12.2.

HRMS (ESI): Calcd for $C_{21}H_{22}N_2O$ $[M+H]^+$: 319.1810, Found: 319.1815.

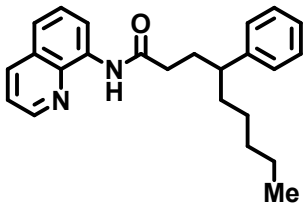


4-Phenyl-*N*-(quinolin-8-yl) octanamide (P85). According to the general procedure A. The reaction mixture was stirred at 130°C for 18h. The product was purified by flash chromatography (1:40 EA/PE) as yellow oil (93 mg, 90%).

^{1}H NMR (400 MHz, $CDCl_3$): δ 9.65 (s, 1H), 8.77-8.75 (m, 2H), 8.13 (dd, *J* = 8.3Hz, 1.5Hz, 1H), 7.54-7.41 (m, 3H), 7.33-7.19 (m, 5H), 2.65-2.58 (m, 1H), 2.41-2.21 (m, 3H), 2.04-1.95 (m, 1H), 1.75-1.58 (m, 2H), 1.34-1.06 (m, 4H), 0.82 (t, *J* = 7.1Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 171.8, 148.1, 145.0, 138.3, 136.4, 134.6, 128.5, 127.9, 127.8, 127.5, 126.2, 121.6, 121.3, 116.4, 45.6, 36.9, 36.2, 32.3, 29.8, 22.8, 14.0.

HRMS (ESI): Calcd for $C_{23}H_{26}N_2O$ $[M+H]^+$: 347.2123, Found: 347.2122.

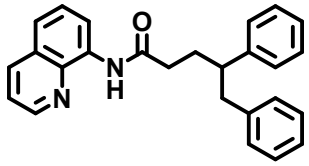


4-Phenyl-*N*-(quinolin-8-yl)nonanamide (P86) . According to the general procedure A. The reaction mixture was stirred at 130°C for 18h. The product was purified by flash chromatography (1:40 EA/PE) as yellow oil (95 mg, 88%).

^{1}H NMR (400 MHz, $CDCl_3$): δ 9.65 (s, 1H), 8.77-8.76 (m, 2H), 8.14 (dd, *J* = 8.3Hz, 1.6Hz, 1H), 7.54-7.41 (m, 3H), 7.33-7.19 (m, 5H), 2.66-2.56 (m, 1H), 2.39-2.21 (m, 3H), 2.04-1.95 (m, 1H), 1.73-1.57 (m, 2H), 1.34-1.10 (m, 6H), 0.82 (t, *J* = 6.5Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 171.8, 148.1, 145.0, 138.3, 136.4, 134.5, 128.5, 127.9, 127.8, 127.4, 126.2, 121.6, 121.4, 116.4, 45.6, 37.2, 36.2, 32.3, 31.9, 27.3, 22.6, 14.1.

HRMS (ESI): Calcd for $C_{24}H_{28}N_2O$ $[M+H]^+$: 361.2280, Found: 361.2287.

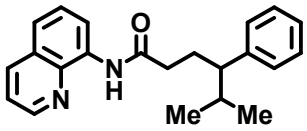


4,5-Diphenyl-*N*-(quinolin-8-yl)pentanamide (P87). According to the general procedure A. The reaction mixture was stirred at 130°C for 18 hours. The product was purified by flash chromatography (1:50 EA/PE) as yellow oil (107 mg, 94%).

^{1}H NMR (400 MHz, $CDCl_3$): δ 9.61 (s, 1H), 8.74-8.73 (m, 2H), 8.11 (dd, *J* = 8.3Hz, 1.6Hz, 1H), 7.52-7.39 (m, 3H), 7.31-7.02 (m, 10H), 2.98-2.88 (m, 3H), 2.43-2.25 (m, 3H), 2.15-2.05 (m, 1H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 171.5, 148.1, 143.9, 140.2, 138.3, 136.4, 134.5, 129.2, 128.5, 128.1, 127.9, 127.4, 126.5, 125.9, 121.6, 121.4, 116.4, 47.6, 44.1, 36.1, 31.1.

HRMS (ESI): Calcd for $C_{26}H_{24}N_2O$ $[M+H]^+$: 381.1967, Found: 381.1960.

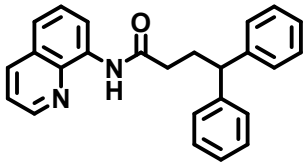


5-Methyl-4-phenyl-*N*-(quinolin-8-yl)hexanamide (P88). According to the general procedure A. The reaction mixture was stirred at 130°C for 18h. The product was purified by flash chromatography (1:40 EA/PE) as yellow oil (75 mg, 75%).

^{1}H NMR (400 MHz, $CDCl_3$): δ 9.52 (s, 1H), 8.68-8.64 (m, 2H), 8.01 (dd, *J* = 8.2Hz, 1.5Hz, 1H), 7.43-7.29 (m, 3H), 7.22-7.19 (m, 2H), 7.13-7.07 (m, 3H), 2.34-2.13 (m, 4H), 1.98-1.87 (m, 1H), 1.81-1.71 (m, 1H), 0.92 (d, *J* = 6.6Hz, 3H), 0.64 (d, *J* = 6.7Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 171.9, 148.0, 143.6, 138.2, 136.4, 134.5, 128.6, 128.3, 127.9, 127.5, 126.2, 121.6, 121.3, 116.45, 52.6, 36.4, 33.8, 28.7, 21.0, 20.9.

HRMS (ESI): Calcd for $C_{22}H_{24}N_2O$ $[M+H]^+$: 333.1967, Found: 333.1965.

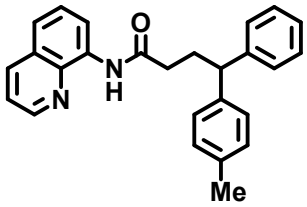


4,4-Diphenyl-*N*-(quinolin-8-yl)butanamide (P89). According to the general procedure A. The reaction mixture was stirred at 130°C for 18h. The product was purified by flash chromatography (1:50 EA/PE) as yellow oil (100 mg, 91%).

^{1}H NMR (400 MHz, $CDCl_3$): δ 9.69 (s, 1H), 8.78-8.76 (m, 2H), 8.13 (dd, *J* = 8.3Hz, 1.4Hz, 1H), 7.55-7.41 (m, 3H), 7.36-7.16 (m, 10H), 4.06 (t, *J* = 7.5Hz, 1H), 2.61-2.50 (m, 4H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 171.3, 148.1, 144.3, 138.3, 136.4, 134.5, 128.6, 128.0, 127.5, 126.4, 121.6, 121.4, 116.5, 50.6, 36.3, 31.0.

HRMS (ESI): Calcd for $C_{25}H_{22}N_2O$ $[M+H]^+$: 367.1810, Found: 367.1808.

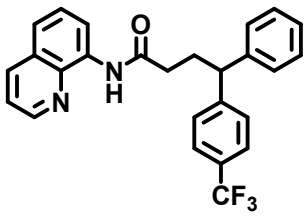


4-Phenyl-*N*-(quinolin-8-yl)-4-(p-tolyl)butanamide (P90). According to the general procedure A. The reaction mixture was stirred at 130°C for 18h. The product was purified by flash chromatography (1:20 EA/PE) as yellow oil (96 mg, 84%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.69 (s, 1H), 8.78-8.76 (m, 2H), 8.14 (dd, *J* = 8.2Hz, 1.7Hz, 1H), 7.55-7.42 (m, 3H), 7.29-7.08 (m, 9H), 4.01 (t, *J* = 7.4Hz, 1H), 2.60-2.49 (m, 4H), 2.29 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 171.4, 148.1, 144.6, 141.3, 138.3, 136.4, 135.9, 134.5, 129.3, 128.6, 128.0, 127.9, 127.8, 127.5, 126.3, 121.6, 121.4, 116.5, 50.2, 36.4, 31.1, 21.0.

HRMS (ESI): Calcd for $C_{26}H_{24}N_2O$ $[M+H]^+$: 381.1967, Found: 381.1967.



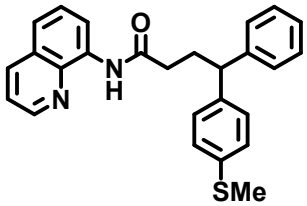
4-Phenyl-*N*-(quinolin-8-yl)-4-(4-(trifluoromethyl)phenyl)butanamide (P91). According to the general procedure A. The reaction mixture was stirred at 130°C for 18h. The product was purified by flash chromatography (1:20 EA/PE) as yellow oil (119 mg, 91%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.69 (s, 1H), 8.78-8.75 (m, 2H), 8.14 (dd, *J* = 8.3Hz, 1H), 7.55-7.48 (m, 4H), 7.45-7.40 (m, 3H), 7.33-7.19 (m, 5H), 4.13 (t, *J* = 7.6Hz, 1H), 2.62-2.50 (m, 4H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 171.0, 148.5, 148.1, 143.2, 138.3, 136.4, 134.4, 128.8, 128.3, 128.0 (d, *J* = 1.9Hz), 127.4, 126.8, 125.6 (q, *J* = 3.4Hz), 121.6 (d, *J* = 9.8Hz), 116.5, 50.3, 36.0, 30.8.

^{19}F NMR (376 MHz, $CDCl_3$) δ - 62.31.

HRMS (ESI): Calcd for $C_{26}H_{21}F_3N_2O$ $[M+H]^+$: 435.1684, Found: 435.1682.

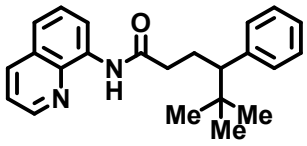


4-(4-(Methylthio)phenyl)-4-phenyl-*N*-(quinolin-8-yl)butanamide (P92). According to the general procedure A. The reaction mixture was stirred at 130 °C for 18h. The product was purified by flash chromatography (1:20 EA/PE) as yellow oil (101 mg, 82%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.69 (s, 1H), 8.77-8.76 (m, 2H), 8.14 (d, *J* = 8.3, 1H), 7.55-7.42 (m, 3H), 7.31-7.17 (m, 9H), 4.01 (t, *J* = 7.4 Hz, 1H), 2.56-2.46 (m, 4H), 2.44 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 171.3, 148.1, 144.2, 141.3, 138.3, 136.4, 136.1, 134.5, 128.6, 128.5, 128.0, 127.9, 127.5, 127.1, 126.4, 121.6, 121.5, 116.5, 50.0, 36.3, 31.0, 16.1.

HRMS (ESI): Calcd for $C_{26}H_{24}N_2OS$ $[M+H]^+$: 413.1688, Found: 413.1685.

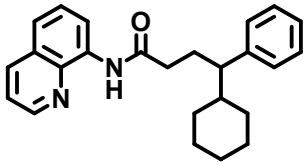


5,5-Dimethyl-4-phenyl-*N*-(quinolin-8-yl)hexanamide (P93). According to the general procedure A. The reaction mixture was stirred at 130°C for 18h. The product was purified by flash chromatography (1:20 EA/PE) as yellow oil (84 mg, 81%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.58 (s, 1H), 8.77-8.74 (m, 2H), 8.15-8.13 (m, 1H), 7.45-7.42 (m, 3H), 7.31-7.20 (m, 5H), 2.46-2.11 (m, 5H), 0.92 (s, 9H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 172.0, 148.0, 142.1, 138.3, 136.3, 134.6, 127.9, 127.4, 126.3, 121.6, 121.3, 116.4, 56.2, 36.9, 34.0, 29.5, 29.4, 28.3, 25.2.

HRMS (ESI): Calcd for $C_{23}H_{26}N_2O$ $[M+H]^+$: 347.2123, Found: 347.2122.

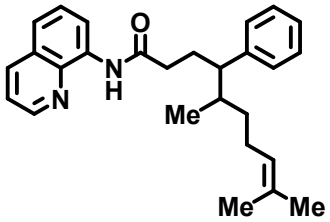


4-Cyclohexyl-4-phenyl-*N*-(quinolin-8-yl)butanamide (P94). According to the general procedure A. The title compound was prepared from alkene S14 (Z/E = 1.6:1). The reaction mixture was stirred at 130°C for 18h. The product was purified by flash chromatography (1:20 EA/PE) as yellow solid (101 mg, 90%). Mp: 95.2-97.0 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.60 (s, 1H), 8.77-8.75 (m, 2H), 8.14 (dd, *J* = 8.2Hz, 1.7Hz, 1H), 7.54-7.41 (m, 3H), 7.32-7.16 (m, 5H), 2.43-2.25 (m, 4H), 2.01-1.97 (m, 2H), 1.76-1.41 (m, 4H), 1.25-1.22 (m, 2H), 1.13-0.96 (m, 3H), 0.83-0.79 (m, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 171.9, 148.0, 143.7, 138.3, 136.3, 134.6, 128.6, 128.3, 127.9, 127.5, 126.1, 121.6, 121.3, 116.4, 51.7, 43.4, 36.4, 31.3, 31.2, 28.3, 26.6, 26.5.

HRMS (ESI): Calcd for $C_{25}H_{28}N_2O$ $[M+H]^+$: 373.2280, Found: 373.2286.

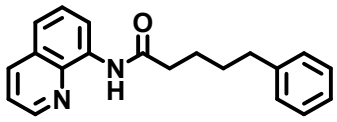


5,9-Dimethyl-4-phenyl-*N*-(quinolin-8-yl)dec-8-enamide (P95). According to the general procedure A. The reaction mixture was stirred at 130°C for 18h. The product was purified by flash chromatography (1:20 EA/PE) as yellow oil (90 mg, 75%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.54 (s, 1H), 8.69-8.68 (m, 2H), 8.06 (dd, *J* = 8.3Hz, 1.7Hz, 1H), 7.47-7.34 (m, 3H), 7.25-7.10 (m, 5H), 5.03-4.88 (m, 1H), 2.49-2.41 (m, 1H), 2.32-2.17 (m, 3H), 2.04-1.76 (m, 3H), 1.68-1.64 (m, 1H), 1.60-1.45 (m, 6H), 1.28-1.24 (m, 1H), 1.06-1.03 (m, 1H), 0.91 (d, *J* = 6.7Hz, 2H), 0.69 (d, *J* = 6.8Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 171.9, 171.8, 148.0, 143.7, 143.0, 138.3, 136.3, 134.5, 131.3, 131.2, 128.9, 128.6, 128.3, 128.2, 127.9, 127.4, 126.2, 126.1, 124.7, 121.6, 121.3, 116.4, 51.0, 50.7, 38.3, 38.1, 36.5, 36.4, 34.8, 34.4, 28.8, 27.7, 25.8, 25.7, 25.6, 25.5, 17.7, 17.6, 17.0, 16.8.

HRMS (ESI): Calcd for $C_{27}H_{32}N_2O$ $[M+H]^+$: 401.2593, Found: 401.2596.

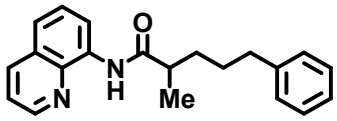


***N*-(Naphthalen-1-yl)-5-phenylpentanamide (P96).** According to the general procedure B. The reaction mixture was stirred at 130°C for 18h. The product was purified by flash chromatography (1:50 EA/PE) as yellow solid (78 mg, 85%). Without addition of $NCCH_2COOH$, the product was only afforded in 12% yield. Mp: 53.6-55.0 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ 9.80 (s, 1H), 8.79-8.77 (m, 2H), 8.13 (dd, *J* = 8.3Hz, 1.6Hz, 1H), 7.54-7.41 (m, 3H), 7.28- 7.15 (m, 5H), 2.69 (t, *J* = 7.6Hz, 2H), 2.57 (t, *J* = 7.4Hz, 2H), 1.91-1.83 (m, 2H). 1.81-1.72 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 171.7, 148.1, 142.2, 138.3, 136.4, 134.5, 128.5, 128.4, 128.0, 127.5, 125.8, 121.6, 121.4, 116.4, 38.1, 35.8, 31.1, 25.4.

HRMS (ESI): Calcd for $C_{20}H_{20}N_2O$ $[M+H]^+$: 305.1654, Found: 305.1656.

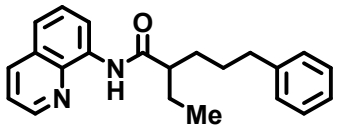


2-Methyl-*N*-(naphthalen-1-yl)-5-phenylpentanamide (P97). According to the general procedure B. The reaction mixture was stirred at 130°C for 18h. The product was purified by flash chromatography (1:50 EA/PE) as yellow oil (76 mg, 80%). Without addition of $NCCH_2COOH$, the product was only afforded in 56% yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ 9.86 (s, 1H), 8.82-8.80 (m, 2H), 8.17-8.14 (m, 1H), 7.56-7.43 (m, 3H), 7.26-7.13 (m, 5H), 2.68-2.59 (m, 3H), 1.95-1.86 (m, 1H), 1.78-1.56 (m, 3H), 1.32 (d, J = 6.6Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 175.3, 148.2, 142.2, 138.5, 136.4, 134.5, 128.4, 128.3, 128.0, 127.5, 125.7, 121.6, 121.4, 116.5, 43.0, 36.0, 34.1, 29.4, 18.1.

HRMS (ESI): Calcd for $C_{21}H_{22}N_2O$ $[M+H]^+$: 319.1810, Found: 319.1812.

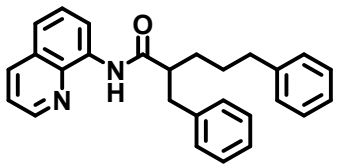


2-Ethyl-*N*-(naphthalen-1-yl)-5-phenylpentanamide (P98). According to the general procedure B. The title compound was prepared by using 5 equiv NaH instead of Cs_2CO_3 and without H_2O. The reaction mixture was stirred at 130°C for 18h. The product was purified by flash chromatography (1:50 EA/PE) as yellow oil (58 mg, 58%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.85 (s, 1H), 8.85-8.79 (m, 2H), 8.14 (dd, J = 8.3Hz, 1.7Hz, 1H), 7.55-7.42 (m, 3H), 7.25-7.11 (m, 5H), 2.65 (t, J = 7.6Hz, 2H), 2.44-2.37 (m, 1H), 1.89-1.60 (m, 6H), 0.99 (t, J = 7.4Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 174.7, 148.2, 142.3, 138.4, 136.4, 134.5, 128.4, 128.3, 128.0, 127.5, 125.7, 121.6, 121.4, 116.5, 50.9, 36.0, 32.6, 29.5, 26.3, 12.2.

HRMS (ESI): Calcd for $C_{22}H_{24}N_2O$ $[M+H]^+$: 333.1967, Found: 333.1969.

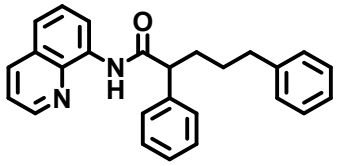


2-Benzyl-*N*-(naphthalen-1-yl)-5-phenylpentanamide (P99). According to the general procedure B. The reaction mixture was stirred at 130°C for 18h. The product was purified by flash chromatography (1:50 EA/PE) as yellow oil (80 mg, 68%).

^{1}H NMR (400 MHz, $CDCl_3$): δ 9.67 (s, 1H), 8.79-8.71 (m, 2H), 8.10 (dd, *J* = 8.2Hz, 1.6Hz, 1H), 7.53-7.38 (m, 3H), 7.28-7.11 (m, 10H), 3.16-3.11 (m, 1H), 2.88-2.72 (m, 2H), 2.63 (t, *J* = 7.5Hz, 2H), 1.98-1.88 (m, 1H), 1.84-1.63 (m, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 173.8, 148.1, 142.1, 139.6, 138.4, 136.3, 134.3, 129.0, 128.4, 128.3, 127.9, 127.4, 126.3, 125.8, 121.6, 121.5, 116.5, 51.2, 39.3, 36.0, 32.4, 29.4.

HRMS (ESI): Calcd for $C_{27}H_{26}N_2O$ $[M+H]^+$: 395.2123, Found: 395.2131.

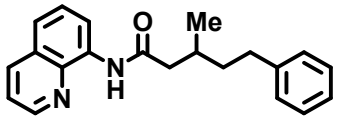


2,5-Diphenyl-*N*-(quinolin-8-yl)pentanamide (P100). According to the general procedure B. The title compound was prepared by using 5 equiv NaH instead of Cs_2CO_3 and without H_2O. The reaction mixture was stirred at 130°C for 18h. The product was purified by flash chromatography (1:50 EA/PE) as yellow oil (78 mg, 68%)

^{1}H NMR (400 MHz, $CDCl_3$): δ 9.89 (s, 1H), 8.77-8.69 (m, 2H), 8.07 (dd, *J* = 8.2Hz, 1.6Hz, 1H), 7.49-7.41 (m, 4H), 7.38-7.33 (m, 3H), 7.29-7.21 (m, 3H), 7.15-7.12 (m, 3H), 3.71 (t, *J* = 7.6Hz, 1H), 2.74-2.60 (m, 2H), 2.40-2.31 (m, 1H), 2.03-1.94 (m, 1H), 1.80-1.58 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 172.1, 148.2, 142.2, 139.8, 138.4, 136.3, 134.5, 128.9, 128.5, 128.3, 128.1, 127.9, 127.4, 127.3, 125.8, 121.6, 121.5, 116.4, 54.9, 35.9, 33.1, 29.7.

HRMS (ESI): Calcd for $C_{26}H_{24}N_2O$ $[M+H]^+$: 381.1967, Found: 381.1969.

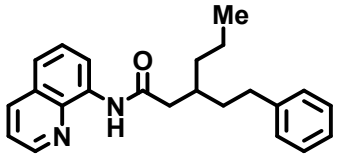


3-Methyl-*N*-(naphthalen-1-yl)-5-phenylpentanamide (P101). According to the general procedure B. The title compound was prepared by using 5 equiv NaH instead of Cs_2CO_3 and without H_2O. The reaction mixture was stirred at 130°C for 18h. The product was purified by flash chromatography (1:50 EA/PE) as yellow oil (84 mg, 88%).

^{1}H NMR (400 MHz, $CDCl_3$): δ 9.80 (s, 1H), 8.81-8.78 (m, 2H), 8.15 (dd, *J* = 8.3Hz, 1.6Hz, 1H), 7.55-7.43 (m, 3H), 7.28-7.14 (m, 5H), 2.78-2.59 (m, 3H), 2.43-2.37 (m, 1H), 2.29-2.20 (m, 1H), 1.85-1.76 (m, 1H), 1.66-1.56 (m, 1H), 1.12 (d, *J* = 6.6Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 171.2, 148.2, 142.5, 138.3, 136.4, 134.5, 128.4, 128.3, 128.0, 127.5, 125.7, 121.6, 121.4, 116.4, 45.9, 38.8, 33.5, 30.8, 19.8.

HRMS (ESI): Calcd for $C_{21}H_{22}N_2O$ $[M+H]^+$: 319.1810, Found: 319.1812.

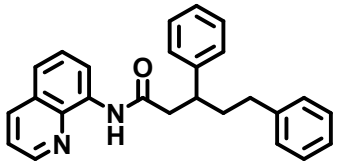


***N*-(Naphthalen-1-yl)-3-phenethylhexanamide (P102).** According to the general procedure B. The reaction mixture was stirred at 130°C for 18h. The product was purified by flash chromatography (1:50 EA/PE) as yellow oil (52 mg, 50 %).

^{1}H NMR (400 MHz, $CDCl_3$): δ 9.82 (s, 1H), 8.81-8.79 (m, 2H), 8.16 (dd, *J* = 8.0Hz, 1.6Hz, 1H), 7.54-7.44 (m, 3H), 7.26-7.14 (m, 5H), 2.72-2.68 (m, 2H), 2.57-2.56 (m, 2H), 2.21-2.15 (m, 1H), 1.78-1.73 (m, 2H), 1.47-1.42 (m, 4H), 0.92 (t, *J* = 6.9Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 171.3, 148.1, 142.6, 138.3, 136.3, 134.5, 128.4, 128.3, 127.9, 127.4, 125.6, 121.6, 121.3, 116.4, 43.1, 36.1, 35.9, 35.2, 33.1, 19.7, 14.3.

HRMS (ESI): Calcd for $C_{23}H_{26}N_2O$ $[M+H]^+$: 347.2123, Found: 347.2128.

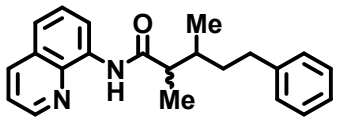


***N*-(Naphthalen-1-yl)-3,5-diphenylpentanamide (P103).** According to the general procedure B. The reaction mixture was stirred at 130^{o}C for 18h. The product was purified by flash chromatography (1:50 EA/PE) as yellow oil (74 mg, 65 %).

^{1}H NMR (400 MHz, $CDCl_3$): δ 9.65(s, 1H), 8.72-8.70 (m, 2H), 8.08 (dd, *J* = 8.2Hz, 1.2Hz, 1H), 7.49-7.37 (m, 3H), 7.32-7.29 (m, 4H), 7.23-7.09 (m, 6H), 3.38-3.35 (m, 1H), 2.86 (d, *J* = 7.4Hz, 2H), 2.53-2.48 (m, 2H), 2.17-2.14 (m, 1H), 2.03-2.00 (m, 1H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 170.2, 148.1, 143.8, 142.1, 138.3, 136.3, 134.4, 128.7, 128.6, 128.4, 128.3, 127.9, 127.7, 127.4, 126.7, 125.8, 121.6, 121.5, 116.5, 45.9, 42.4, 38.0, 33.8.

HRMS (ESI): Calcd for $C_{26}H_{24}N_2O$ $[M+H]^+$: 381.1967, Found: 381.1962.

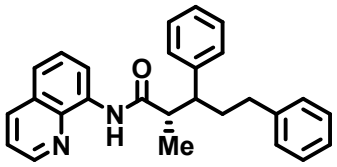


2,3-Dimethyl-*N*-(naphthalen-1-yl)-5-phenylpentanamide (P104). According to the general procedure B. The title compound was prepared from alkene S27 (*dr* = 1.2:1). The reaction mixture was stirred at 130^{o}C for 18h. The product was purified by flash chromatography (1:50 EA/PE) as yellow oil (78 mg, 78%). The *dr* value is 1.4:1 analysis by GCMS. Without addition of $NCCH_2COOH$, the product was only afforded in 71% yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ 9.86 (s, 1H), 8.82-8.78 (m, 2H), 8.18-8.15 (m, 1H), 7.53-7.42 (m, 3H), 7.25-7.12 (m, 5H), 2.80-2.71 (m, 1H), 2.65-2.47 (m, 2H), 2.07-1.75 (m, 2H), 1.62-1.52(m, 1H), 1.33-1.28 (m, 3H), 1.12-1.05 (m, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 174.9, 174.8, 148.2, 142.5, 142.4, 138.5, 136.5, 134.6, 134.5, 128.3, 128.0, 127.5, 125.8, 125.7, 121.6, 121.4, 121.3, 116.5, 116.4, 48.2, 47.8, 36.9, 36.4, 36.0, 35.4, 33.7, 33.3, 17.5, 16.0, 15.0, 13.7.

HRMS (ESI): Calcd for $C_{22}H_{24}N_2O$ $[M+H]^+$: 333.1967, Found: 333.1969.

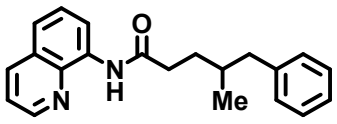


***anti*-2-Methyl-3,5-diphenyl-*N*-(quinolin-8-yl)pentanamide (P105).** According to the general procedure B. The title compound was prepared from *anti*-alkene S28. The reaction mixture was stirred at 130°C for 18h. The product was purified by flash chromatography (1:50 EA/PE) as yellow oil (96 mg, 81%).

^{1}H NMR (400 MHz, $CDCl_3$): δ 9.52 (s, 1H), 8.72 (dd, *J* = 4.2Hz, 1.7Hz, 1H), 8.61 (dd, *J* = 7.1Hz, 2.3Hz, 1H), 8.10 (dd, *J* = 8.5Hz, 1.7Hz, 1H), 7.44-7.39 (m, 3H), 7.30-7.29 (m, 2H), 7.16-7.03 (m, 8H), 3.06-3.02 (m, 1H), 2.86-2.82 (m, 1H), 2.46-2.39 (m, 2H), 2.29-2.21 (m, 1H), 2.06-1.96 (m, 1H), 1.40 (d, *J* = 6.8Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 174.0, 148.0, 142.8, 142.4, 136.4, 134.4, 128.5, 128.4(6), 128.4, 128.3, 127.9, 127.4, 126.6, 125.8, 121.5, 121.3, 49.6, 48.9, 33.8, 33.7, 15.7.

HRMS (ESI): Calcd for $C_{27}H_{26}N_2O$ $[M+H]^+$: 395.2123, Found: 395.2122.



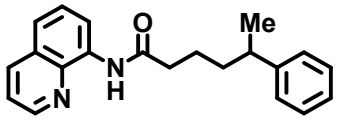
4-Methyl-5-phenyl-*N*-(quinolin-8-yl)pentanamide (P106). According to the general procedure B. The title compound was prepared by using NaO^{t}Bu (5 equiv) and H_2O (50 equiv). The reaction mixture was stirred at 130°C for 18h. The product was

purified by flash chromatography (1:20 EA/PE) as yellow oil (73 mg, 76%).

^{1}H NMR (401 MHz, $CDCl_3$) δ 9.80 (s, 1H), 8.81-8.77 (m, 2H), 8.17 (d, *J* = 8.6Hz, 1H), 7.56-7.44 (m, 3H), 7.28 (d, *J* = 8.1Hz, 2H), 7.18 (d, *J* = 7.7Hz, 3H), 2.77-2.43 (m, 4H), 1.97-1.82 (m, 2H), 1.75-1.67 (m, 1H), 0.95 (d, *J* = 8.2Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 172.0, 148.2, 141.1, 138.4, 136.5, 134.7, 129.3, 128.3, 128.1, 127.6, 125.9, 121.7, 121.5, 116.5, 43.6, 36.2, 34.9, 32.5, 19.3.

HRMS (ESI): Calcd for $C_{21}H_{22}N_2O$ $[M+H]^+$: 319.1810, Found: 319.1811.

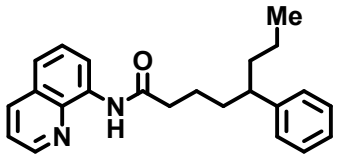


5-Phenyl-*N*-(quinolin-8-yl)hexanamide (P107). According to the general procedure B. The title compound was prepared from PhBr (3 equiv). The reaction mixture was stirred at 130°C for 18h. The product was purified by flash chromatography (1:50 EA/PE) as yellow oil (76 mg, 80%). Without addition of $NCCH_2COOH$, the product was only afforded in 23% yield.

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.76 (s, 1H), 8.79-8.76 (m, 2H), 8.14 (dd, *J* = 8.2Hz, 1.7Hz, 1H), 7.54-7.42 (m, 3H), 7.30-7.25 (m, 2H), 7.21-7.15 (m, 3H), 2.76 (q, *J* = 6.9Hz, 1H), 2.51 (t, *J* = 7.1Hz, 2H), 1.83-1.65 (m, 4H), 1.27 (d, *J* = 7.0Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 171.7, 148.1, 147.3, 138.3, 136.4, 134.5, 128.4, 127.9, 127.5, 127.0, 126.0, 121.6, 121.4, 116.4, 39.9, 38.2, 37.9, 23.9, 22.3.

HRMS (ESI): Calcd for $C_{21}H_{22}N_2O$ $[M+H]^+$: 319.1810, Found: 319.1812.

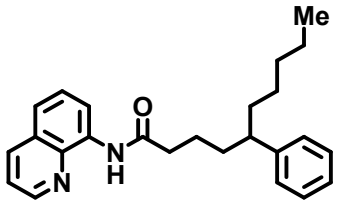


5-Phenyl-*N*-(quinolin-8-yl)octanamide (P108). According to the general procedure B. The title compound was prepared from PhBr (3 equiv). The reaction mixture was stirred at 130°C for 18h. The product was purified by flash chromatography (1:20 EA/PE) as yellow oil (91 mg, 88%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.67 (s, 1H), 8.69-8.68 (m, 2H), 8.05 (dd, *J* = 8.3Hz, 1.7Hz, 1H), 7.43-7.37 (m, 2H), 7.36-7.33 (m, 1H), 7.20-7.16 (m, 2H), 7.09-7.06 (m, 3H), 2.42-2.39 (m, 3H), 1.66-1.48 (m, 6H), 1.09-1.07 (m, 2H), 0.74 (t, *J* = 7.3Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 171.8, 148.0, 145.7, 138.2, 136.6, 134.5, 128.3, 128.0, 127.7, 127.5, 126.0, 121.6, 121.4, 116.6, 45.7, 39.1, 38.2, 36.5, 23.9, 20.7, 14.2.

HRMS (ESI): Calcd for $C_{23}H_{26}N_2O$ $[M+H]^+$: 347.2123, Found: 347.2128.

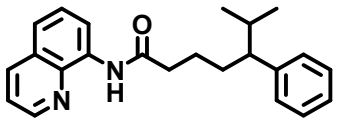


5-Phenyl-*N*-(quinolin-8-yl)decanamide (P109). According to the general procedure B. The title compound was prepared from PhBr (3 equiv). The reaction mixture was stirred at 130^{o}C for 18h. The product was purified by flash chromatography (1:20 EA/PE) as yellow oil (103 mg, 92%).

1H NMR (400 MHz, $CDCl_3$) δ 9.74 (s, 1H), 8.77-8.75 (m, 2H), 8.11 (d, *J* = 1.7Hz, 1H), 7.53-7.40 (m, 3H), 7.29-7.15 (m, 5H), 2.55-2.46 (m, 3H), 1.78-1.58 (m, 6H), 1.20-1.14 (m, 6H), 0.83-0.79 (m, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 171.7, 148.1, 145.7, 138.3, 136.4, 134.5, 128.3, 127.9, 127.7, 127.5, 126.0, 121.6, 121.4, 116.4, 46.0, 38.3, 36.8, 36.5, 32.0, 27.3, 23.9, 22.6, 14.1.

HRMS (ESI): Calcd for $C_{25}H_{30}N_2O$ $[M+H]^+$: 375.2436, Found: 375.2429.

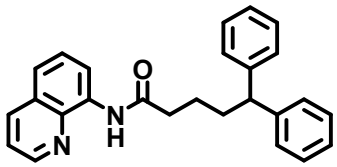


6-Methyl-5-phenyl-*N*-(quinolin-8-yl)heptanamide (P110). According to the general procedure B. The title compound was prepared from PhBr (3 equiv). The reaction mixture was stirred at 130^{o}C for 18h. The product was purified by flash chromatography (1:20 EA/PE) as yellow oil (60 mg, 58%).

1H NMR (400 MHz, $CDCl_3$) δ 9.72(s, 1H), 8.78-8.73 (m, 2H), 8.15-8.13 (m, 1H) , 7.53-7.42 (m, 3H), 7.27-7.23 (m, 2H), 7.18-7.12 (m, 3H), 2.50-2.45 (m, 2H), 2.32-2.31 (m, 1H), 1.89 -1.57 (m, 5H), 0.94 (d, *J* =4.0Hz, 3H), 0.71 (d, *J* =4.0Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 171.8, 148.1, 144.2, 138.4, 136.4, 134.6, 128.9, 128.6, 128.1, 128.0, 127.5, 126.0, 121.6, 121.4, 116.5, 53.1, 38.4, 33.5, 32.6, 24.2, 21.1, 20.8.

HRMS (ESI): Calcd for $C_{23}H_{26}N_2O$ $[M+H]^+$: 347.2123, Found: 347.2122.

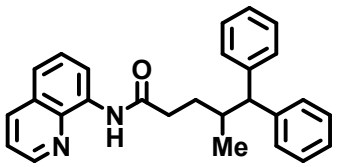


5,5-Diphenyl-*N*-(quinolin-8-yl)pentanamide (P111). According to the general procedure B. The title compound was prepared from PhBr (3 equiv). The reaction mixture was stirred at 130°C for 18h. The product was purified by flash chromatography (1:20 EA/PE) as yellow oil (78 mg, 68%). Without addition of $NCCH_2COOH$, the product was only afforded in 28% yield.

^1H NMR (400 MHz, $CDCl_3$) δ 9.63 (s, 1H), 8.65-8.61 (m, 2H), 8.01-8.00 (m, 1H), 7.40-7.28 (m, 3H), 7.13-7.11 (m, 8H), 7.04-7.00 (m, 2H), 3.83 (t, *J* = 7.8Hz, 1H), 2.44 (t, *J* = 7.4Hz, 2H), 2.08-2.02 (m, 2H), 1.70-1.62 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 171.5, 148.1, 144.8, 138.3, 136.4, 134.5, 128.5, 128.0, 127.9, 127.5, 126.2, 121.6, 121.4, 116.5, 51.3, 38.1, 35.2, 24.3.

HRMS (ESI): Calcd for $C_{26}H_{24}N_2O$ $[M+H]^+$: 381.1967, Found: 381.1963.



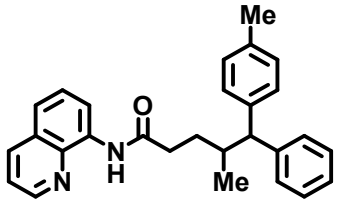
4-Methyl-5,5-diphenyl-*N*-(quinolin-8-yl)pentanamide (P112). According to the

general procedure B. The title compound was prepared from PhBr (3 equiv) and Na_2CO_3 (5 equiv). The reaction mixture was stirred at 130°C for 18h. The product was purified by flash chromatography (1:20 EA/PE) as yellow oil (103 mg, 87%).

1H NMR (400 MHz, $CDCl_3$) δ 9.71 (s, 1H), 8.79-8.74 (m, 2H), 8.16-8.14 (m, 1H), 7.54-7.43 (m, 3H), 7.33-7.08 (m, 10H), 3.58 (d, *J* = 10.8 Hz, 1H), 2.63-2.48(m, 3H), 2.07-1.99 (m, 1H), 1.55-1.52 (m, 1H), 0.94 (d, *J* = 6.5Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 171.7, 148.1, 144.5, 144.1, 138.3, 136.4, 134.5, 128.6, 128.5, 128.1, 128.0, 127.9, 127.5, 126.2, 126.1, 121.6, 121.3, 116.4, 59.4, 36.0, 35.8, 30.9, 18.2.

HRMS (ESI): Calcd for $C_{27}H_{26}N_2O$ $[M+H]^+$: 395.2123, Found: 395.2122.

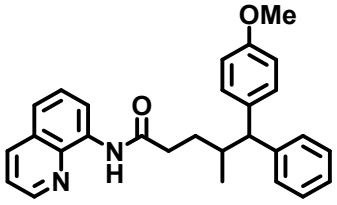


4-Methyl-5-phenyl-*N*-(quinolin-8-yl)-5-(*p*-tolyl)pentanamide (P113). According to the general procedure B. The title compound was prepared from PhBr (3 equiv) and Na_2CO_3 (5 equiv). The reaction mixture was stirred at 130°C for 18h. The product was purified by flash chromatography (1:20 EA/PE) as yellow oil (65 mg, 53%). The *dr* value is 2.2:1 analysis by GCMS.

^1H NMR (400 MHz, $CDCl_3$) δ 9.71 (s, 1H), 8.78-8.73 (m, 2H), 8.15 (d, *J* = 8.2Hz, 1H), 7.52-7.44 (m, 3H), 7.22-7.05 (m, 9H), 3.55 (d, *J* = 10.8Hz, 1H), 2.68-2.46 (m, 3H), 2.24 (d, *J* = 19.7Hz, 2H), 2.02-1.91 (m, 1H), 1.58-1.44 (m, 1H), 1.03-0.80 (m, 1H), 0.94(d, *J* = 6.2Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 171.9, 148.2, 144.5, 141.6, 138.4, 136.5, 135.6, 134.6, 129.7, 129.4, 129.3, 128.7, 128.6, 128.5, 128.4, 128.1, 128.0(2), 128.0, 127.9, 127.8, 127.6, 127.5, 127.4, 126.6, 126.2, 121.7, 121.4, 116.4, 59.0, 36.1, 35.9, 31.0, 21.1, 18.2.

HRMS (ESI): Calcd for $C_{28}H_{28}N_2O$ $[M+H]^+$: 409.2280, Found: 409.2282.

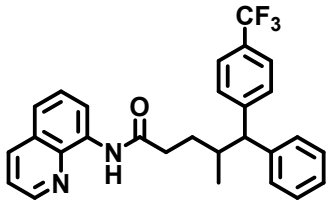


5-(4-Methoxyphenyl)-4-methyl-5-phenyl-*N*-(quinolin-8-yl)pentanamide (P114). According to the general procedure B. The title compound was prepared from PhBr (3 equiv) and Na_2CO_3 (5 equiv). The reaction mixture was stirred at 130°C for 18h. The product was purified by flash chromatography (1:20 EA/PE) as yellow oil (87 mg, 68%). The *dr* value is 2.9:1 analysis by GC.

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.63 (s, 1H), 8.70-8.65 (m, 2H), 8.06-8.04 (m, 1H), 7.45-7.33 (m, 3H), 7.24-7.00 (m, 7H), 6.72-6.66 (m, 2H), 3.65-3.47 (m, 3H), 3.45 (dd, *J* = 10.7Hz, 3.4Hz, 1H), 2.57-2.35 (m, 3H), 1.94-1.84 (m, 1H), 1.48-1.39 (m, 1H), 0.87-0.84 (m, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 171.8, 157.9, 157.8, 148.1, 144.9, 144.5, 138.3, 136.7, 136.4, 134.6, 129.0, 128.9, 128.6, 128.5, 128.0, 127.9, 127.5, 126.1, 126.0, 121.6, 121.3, 116.4, 114.0, 113.9, 58.5, 58.4, 55.2, 55.1, 36.2, 35.8, 30.9, 18.2, 18.1.

HRMS (ESI): Calcd for $C_{28}H_{28}N_2O_2$ $[M+H]^+$: 425.2229, Found: 425.2227.



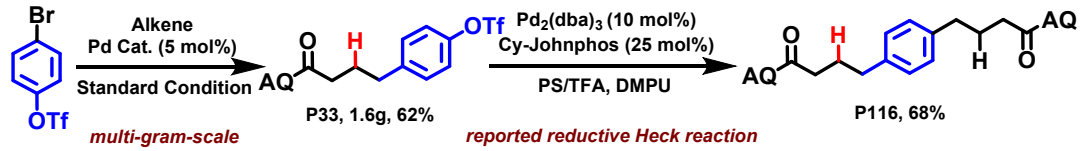
4-Methyl-5-phenyl-*N*-(quinolin-8-yl)-5-(4-(trifluoromethyl)phenyl)pentanamide (P115). According to the general procedure B. The title compound was prepared from PhBr (3 equiv) and Na_2CO_3 (5 equiv). The reaction mixture was stirred at 130°C for 18h. The product was purified by flash chromatography (1:20 EA/PE) as yellow oil (83 mg, 60%). The *dr* value is 2.5:1 analysis by GC.

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.65 (s, 1H), 8.83-8.47 (m, 2H), 8.09 (dd, *J* = 8.3Hz, 1.7Hz, 1H), 7.48-7.32 (m, 7H), 7.24-7.14 (m, 4H), 7.07-7.03 (m, 1H), 3.58 (d, *J* = 10.8Hz, 1H), 2.56-2.43 (m, 3H), 2.01-1.85 (m, 1H), 1.53-1.45 (m, 1H), 0.86 (d, *J* = 6.5Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 171.6, 148.7, 148.2, 143.1, 138.4, 136.5, 134.5, 128.5, 128.9, 128.1, 128.0, 127.5, 126.7, 125.7, 125.6(3), 125.6 125.5, 125.4, 121.7, 121.5, 116.5, 59.3, 35.9, 35.7, 30.7, 18.1.

HRMS (ESI): Calcd for $C_{28}H_{25}F_3N_2O$ $[M+H]^+$: 463,1997, Found: 463.1995.

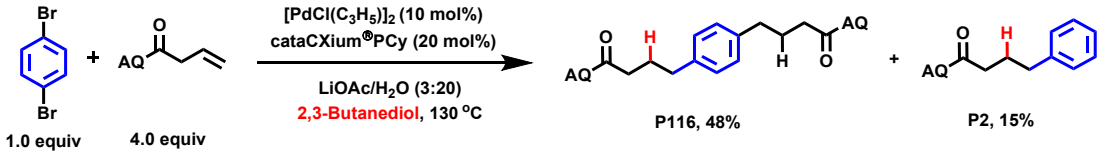
VI. Amplification reaction and drug synthesis



Scheme S1.

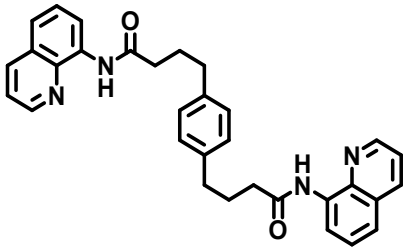
General Procedure: In an argon atmosphere, a dry 500-mL Schlenk tube containing a magnetic stirbar was charged with $[PdCl(C_3H_5)]_2$ (5 mol%, 0.114 g, 0.3 mmol), cataCXium@PCy (10 mol%, 0.204 g, 0.6 mmol), alkenes S2 (1 equiv, 1.27 g, 6 mmol), LiOAc(3 equiv, 18 mmol, 1.2 g), 4-bromophenyl triflate (1.5 equiv, 9 mmol, 2.74 g), dry 2,3-butanediol (100 mL) , cyanoacetic acid (3 equiv, 18 mmol, 1.536 g) and H_2O (20 equiv, 1.2 mmol, 2.2 mL). The tube was capped tightly and the mixture was vigorously stirred in a *pre*-warmed 130°C oil bath. After alkenes was almost fully consumed (monitored by GCMS), the reaction mixture was concentrated on a rotary evaporator and then distilled under vacuum and the resulting residue was directly subjected to silica gel flash chromatography (1:20 EA/PE), **P33** was obtained as yellow oil (1.62 g, 62%).

In an argon atmosphere, a dry 25-mL Schlenk tube containing a magnetic stirbar was charged with $Pd_2(dba)_3$ (10 mol%, 27.6 mg, 0.03 mmol), Cy-Johnphos (25 mol%, 29.3 mg, 0.075 mmol), alkenes S2 (1 equiv, 0.3 mmol, 63.6 mg), Proton Sponge (3 equiv, 0.9 mmol, 193 mg)， **P33** (1.5 equiv, 0.45 mmol, 197.2 mg), dry DMPU (6 mL) and trifluoroacetic acid (3 equiv, 0.9 mmol, 75 uL). The tube was capped tightly and the mixture was vigorously stirred in a *pre*-warmed 130°C oil bath. After alkenes was almost fully consumed (monitored by GCMS), the reaction mixture was concentrated on a rotary evaporator and then distilled under vacuum, the resulting residue was directly subjected to preparative TLC (15:1 PE/EtOAc), **P116** was got as yellow oil (103 mg, 68%).



Scheme S2.

General Procedure A : In an argon atmosphere, a dry 25-mL Schlenk tube containing a magnetic stirbar was charged with $[PdCl(C_3H_5)]_2$ (10 mol%, 11.4 mg, 0.03 mmol), cataCXium@PCy (20 mol%, 20.4 mg, 0.02 mmol), alkenes S2 (4 equiv, 1.2 mmol), LiOAc (3 equiv, 0.9 mmol, 60 mg)， 1,4-dibromobenzene (1.0 equiv, 0.3 mmol), dry 2,3-butanediol (3 mL) and H_2O (20 equiv, 6 mmol, 108 uL). The tube was capped tightly and the mixture was vigorously stirred in a *pre*-warmed 130°C oil bath. After alkenes was almost fully consumed (monitored by GCMS), the reaction mixture was concentrated on a rotary evaporator and then distilled under vacuum, the resulting residue was directly subjected to preparative TLC (15:1 PE/EtOAc), **P116** was got in 48% yield, 15% yield of byproduct **P2** was also observed due to the debromination.

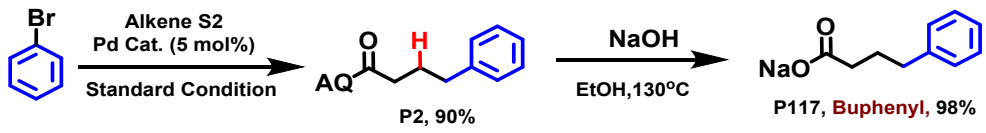


4,4'-(1,4-Phenylene)bis(*N*-(quinolin-8-yl)butanamide) (P116)

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.79 (s, 2H), 9.03-8.75 (m, 4H), 8.15 (dd, *J* = 8.2Hz, 1.7Hz, 2H), 7.55-7.48 (m, 4H), 7.45-7.42 (m, 2H), 7.18 (s, 4H), 2.74 (t, *J* = 7.5Hz, 4H), 2.58 (t, *J* = 7.4Hz, 4H), 2.19-2.11 (m, 4H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 171.5, 148.1, 139.1, 138.3, 136.4, 134.5, 128.7, 127.9, 127.4, 121.6, 121.4, 116.4, 37.4, 34.8, 27.1.

HRMS (ESI): Calcd for $C_{32}H_{30}N_4O_2$ $[M+H]^+$: 503.4427 , Found: 503.4426.

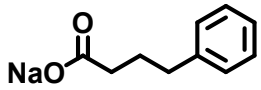


Scheme S3.

General Procedure: In an argon atmosphere, a dry 50-mL Schlenk tube containing a magnetic stirbar was charged with $[PdCl(C_3H_5)]_2$ (5 mol%, 19 mg, 0.05 mmol),

cataCXium@PCy (10 mol%, 34 mg, 0.1 mmol), alkenes (1 equiv, 1 mmol, 212 mg), LiOAc (3 equiv, 3 mmol, 200 mg)，bromobenzene (1.5 equiv, 1.5 mmol, 170 uL), dry 2,3-butanediol (10 mL) and H_2O (20 equiv, 20 mmol, 0.36 mL). The tube was capped tightly and the mixture was vigorously stirred in a *pre*-warmed 130°C oil bath. After alkenes was almost fully consumed (monitored by GCMS), the reaction mixture was concentrated on a rotary evaporator and then distilled under vacuum, the resulting residue was directly subjected to preparative TLC (30:1 PE/EtOAc), **P2** was got in 90% yield (261 mg).

The 8-aminoquinoline directing group was removed by adapting a literature procedure.[2] **P2** (261 mg, 0.9 mmol, 1 equiv) and NaOH (0.54 g, 13.5 mmol, 2 equiv) were suspended in EtOH (10 mL) in a capped vial and heated at 130 °C for 14h. The reaction mixture was then transferred to a separation funnel and diluted with 1 M aqueous NaOH (1.5 mL) and CH_2Cl_2 (3 mL). The aqueous alkaline layer was collected, and the organic layer was extracted with 1 M aqueous NaOH (3 × 2 mL). **P117** was got in 98% yield (164 mg).

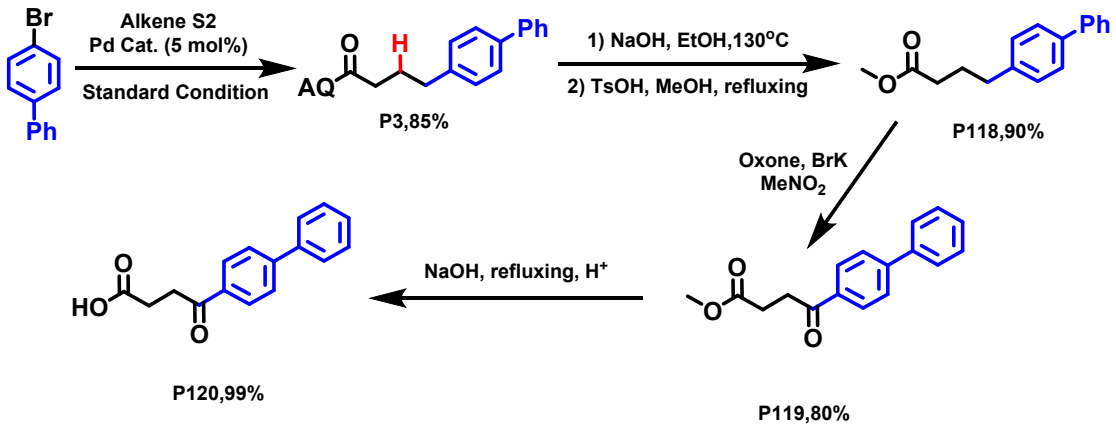


Sodium 4-phenylbutanoate (P117)

^{1}H NMR (400 MHz, DMSO-d_6) δ 7.66-6.75 (m, 5H), 2.79-2.36 (m, 2H), 2.06 (t, J = 7.4Hz, 2H), 1.75-1.71 (m, 2H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 142.8, 128.7, 128.6, 126.0, 36.34, 35.5, 28.0.

HRMS (ESI): Calcd for $C_{10}H_{11}NaO_2$ $[M+H]^+$: 187.0735, Found: 187.0759.



Scheme S4.

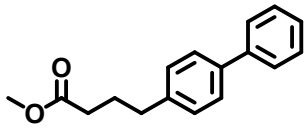
General Procedure: In an argon atmosphere, a dry 50-mL Schlenk tube containing a magnetic stirbar was charged with $[PdCl(C_3H_5)]_2$ (5 mol%, 19 mg, 0.05 mmol), cat aCXium@PCy (10 mol%, 34 mg, 0.1 mmol), alkenes S2 (1 equiv.1 mmol, 212 mg), LiOAc (3 equiv, 3 mmol, 200 mg)，4-bromobiphenyl (1.5 equiv, 1.5 mmol, 0.35 g), dry 2,3-butanediol (10 mL) and H_2O (20 equiv, 20 mmol, 0.36 mL). The tube was capped tightly and the mixture was vigorously stirred in a *pre*-warmed 130°C oil bath. After alkenes was almost fully consumed (monitored by GCMS), the reaction mixture was concentrated on a rotary evaporator and then distilled under vacuum, the resulting residue was directly subjected to preparative TLC (30:1 PE/EtOAc), **P3** was obtained in 85% yield (311mg).

The 8-aminoquinoline directing group was removed by adapting a literature procedure.[2] **P3** (311 mg, 0.85 mmol, 1 equiv) and NaOH (0.51 g, 12.75 mmol, 2 equiv) were suspended in EtOH (9.5 mL) in a capped vial and heated at 130°C for 14h. The reaction was then transferred to a separation funnel and diluted with 1 M aqueous NaOH (1.3 mL) and CH_2Cl_2 (3 mL). The aqueous alkaline layer was collected, and the organic layer was extracted with 1 M aqueous NaOH (3 × 2 mL). Product was got in 96% yield. A mixture of product and TsOH (42 mg, 0.24 mmol, 3 mol%) was heated to reflux in MeOH (10 mL) for 6h. The reaction mixture was concentrated on a rotary evaporator and then distilled under reduced pressure to afford the product **P118** in 90% yield.

The oxidation of esters is based on the reported literature.[3] To the solution of **P118**

(76.3 mg, 0.3 mmol) and Oxone (553.3 mg, 0.9 mmol) in $MeNO_2$ (4.5 mL) was added KBr (17.9 mg, 0.15 mmol) at room temperature, then stirred at 50°C for 24h. Saturated Na_2SO_3 aqueous solution (10 mL) was added to the reaction mixture, then extracted with EtOAc (15 mL × 3). The combined extracts were washed by brine (10 mL) and dried over Na_2SO_4. The organic phase was concentrated under reduced pressure and the crude product was purified by silica gel column chromatography (hexane/EtOAc = 20/1), **P119** was obtained as yellow oil (64 mg, 80%).

P119 (54mg, 0.2mmol, 1equiv) and NaOH (0.16 g, 4 mmol, 20 equiv) were suspended in H_2O (10 mL) in a capped vial and heated at 100°C for 2h. The reaction mixture was then transferred to a separation funnel and diluted with 1 M aqueous HCl (1.3 mL) and extracted with CH_2Cl_2 (3 × 2 mL) to afford **P120** (51 mg, 99%).

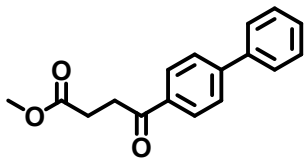


Methyl 4-([1,1'-biphenyl]-4-yl)butanoate (P118)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50-7.47 (m, 2H), 7.43-7.41 (m, 2H), 7.35-7.31 (m, 2H), 7.26-7.23 (m, 1H), 7.16-7.14 (m, 2H), 3.57 (s, 3H), 2.59 (t, *J* = 7.6Hz, 2H), 2.27 (t, *J* = 7.5Hz, 2H), 1.90 (p, *J* = 7.6Hz, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 174.0, 141.1, 140.5, 139.0, 129.0, 128.8, 127.2, 127.1, 127.0, 51.6, 34.8, 33.4, 26.5.

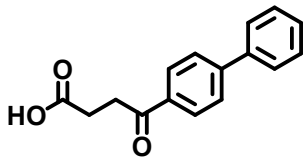
HRMS (ESI): Calcd for $C_{17}H_{18}O_2$ $[M+H]^+$: 255.1385, Found: 255.1384.



Methyl 4-([1,1'-biphenyl]-4-yl)-4-oxobutanoate (P119)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06-8.04 (m, 2H), 7.70-7.61 (m, 4H), 7.49-7.46 (m, 2H), 7.40-7.38 (m, 1H), 3.71 (s, 3H), 3.35-3.32 (m, 2H), 2.81-2.77 (m, 2H).

HRMS (ESI): Calcd for $C_{17}H_{16}O_3$ $[M+H]^+$: 269.1178, Found: 269.1181.



4-([1,1'-Biphenyl]-4-yl)-4-oxobutanoic acid (P120).

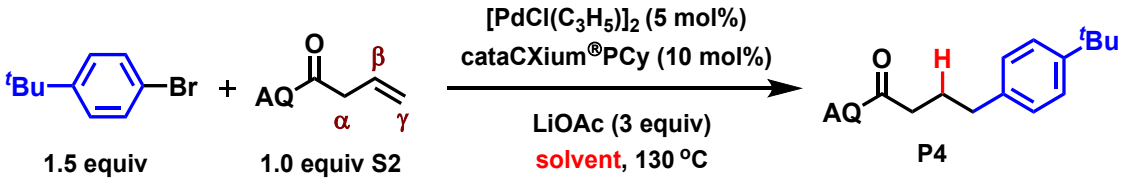
^{1}H NMR (400 MHz, DMSO-d_6) δ 8.07 (d, J = 8.2 Hz, 2H), 7.84 (d, J = 8.2 Hz, 2H), 7.76 (d, J = 7.7Hz, 2H), 7.52 (t, J = 7.5Hz, 2H), 7.44 (t, J = 7.3Hz, 1H), 3.30-3.28 (m, 2H), 2.62-2.51 (m, 2H).

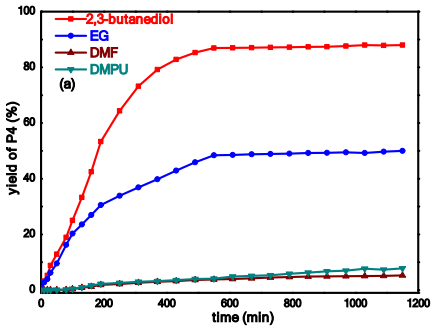
^{13}C NMR (100 MHz, DMSO-d_6) δ 198.6, 174.3, 145.0, 139.4, 135.7, 129.6, 129.1, 128.9, 127.5, 127.4, 33.6, 28.4.

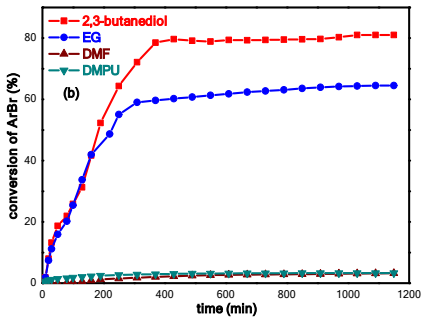
HRMS (ESI): Calcd for $C_{16}H_{14}O_3$ $[M+H]^+$: 255.1021, Found: 255.1021.

VII. Mechanistic Study

Figure S3. Monitoring of Reaction Progress for Reductive Heck Reaction. (a) Comparison of Reaction Rates for the Formation of **P4** in Different Solvents. (b) Comparison of Conversion Rates of 4-^{t}BuPhBr in Different Solvents, Which Based on 1.5 equiv of ArBr.



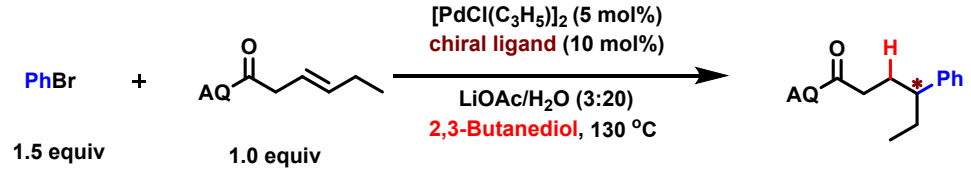


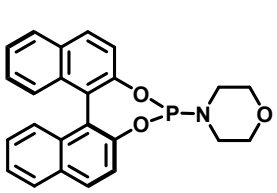


Comment: In order to gain more insight into the possible mechanism, we firstly detected the progress of reductive Heck reaction of 4-^{t}BuPhBr with alkene **S2** by GC analysis. Monitoring of the reaction with 2,3-butanediol, ethylene glycol (EG), 1,3-dimethyl-propyleneurea (DMPU) and DMF as solvent respectively demonstrated that the diol solvent dramatically increased the rates of the reductive Heck reaction, while almost no desired reaction occurred in *nonprotic* solvents (DMPU and DMF)

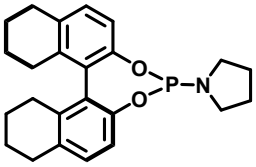
(Figure S3a). Despite that EG acting as hydrogen-bond donor has already been proved to efficiently promote halide dissociation from neutral arylpalladium complexes to access cationic reductive Heck-type pathways, homologous 2,3-butanediol exhibited higher activity in our catalytic system, which indirectly supported 2,3-butanediol might play the role of halide abstracter via hydrogen-bonding effect. Moreover, EG has previously been demonstrated to facilitate oxidative addition in cationic Heck-type reactions of aryl halides, we wonder whether homologous 2,3-butanediol could also performed similarly in our proposed cationic reductive Heck reaction. Comparison of the conversion rates of 4-^{t}BuPhBr in different solvents revealed that parallel reactivity of aryl bromide was presented in EG and 2,3-butanediol solvent, but no or little oxidative addition took place in *nonprotic* solvents (DMPU and DMF) (Figure S3b). Thus, by comparing the activity of 2,3-butanediol with the known halide abstracter EG, we gained indirect evidence suggesting that 2,3-butanediol was likely acted as hydrogen-bond donor to promote the oxidative addition and halide dissociation steps for accessing cationic reductive Heck pathways.

Table S9 Ligand Effect on Asymmetric Intermolecular Reductive Heck Reaction.

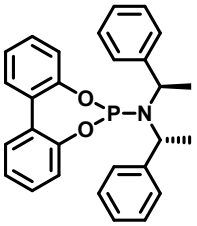




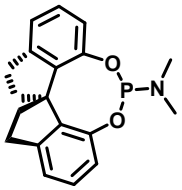
L1
(S)-MorfPhos



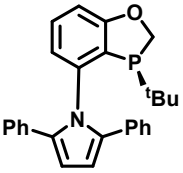
L2



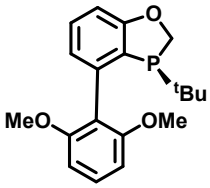
L3
(R)-BIPOL-A1



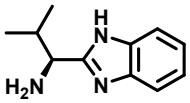
L4
(S)-SIPHOS



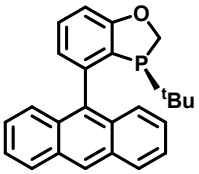
L5



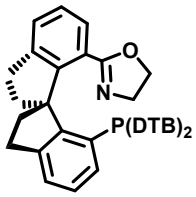
L6
(S)-BI-DIME



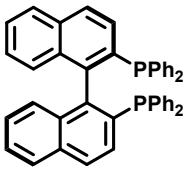
L7
(R)-i-Pr-BIMAH



L8
(S)-AntPhos



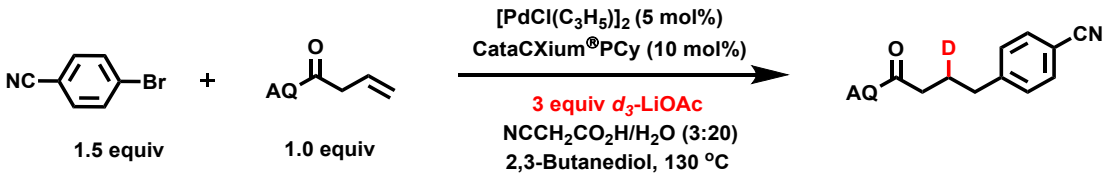
L9
(S)-DTB-SIPHOX



L10
(R)-BINAP

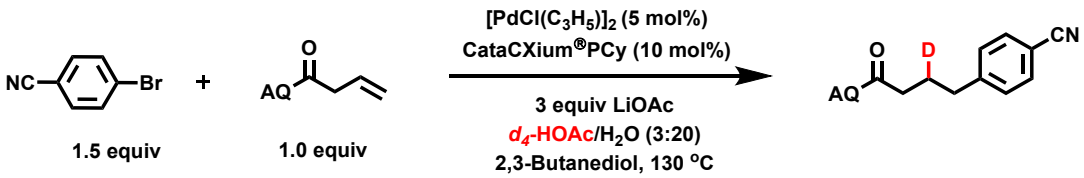
Entry	ligand	ArBr/Conversion (%)	Alkene/Conversion (%)	Yield (%)	ee%
1	L1	100	92	80	0
2	L2	99	78	65	0
3	L3	99	90	76	0
4	L4	98	90	69	0
5	L5	93	87	62	0
6	L6	98	98	55	0
7	L7	100	98	42	0
8	L8	96	100	75	0
9	L9	99	98	70	0
10	L10	95	68	16	0

Study on Generation of Hydride Species:



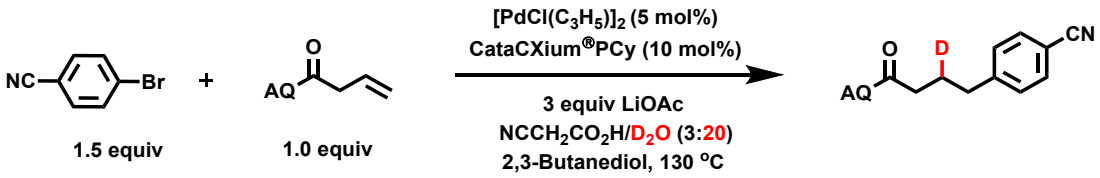
Scheme S5.

General Procedure: In an argon atmosphere, a dry 10-mL Schlenk tube containing a magnetic stirbar was charged with $[PdCl(C_3H_5)]_2$ (5 mol%, 1.9 mg, 0.005 mmol), cataCXium@PCy (10 mol%, 3.4 mg, 0.01 mmol), alkenes S2 (1 equiv, 0.1 mmol, 21.2 mg), d_3-LiOAc (3 equiv, 0.3 mmol, 20 mg)， 4-bromobenzonitrile (1.5 equiv, 0.15 mmol, 27 mg), dry 2,3-butanediol (1.0 mL), cyanoacetic acid (3 equiv, 0.3 mmol, 25.6 mg) and H_2O (20 equiv, 2 mmol, 36 uL). The tube was capped tightly and the mixture was vigorously stirred in a *pre*-warmed 130°C oil bath. After alkenes was almost fully consumed (monitored by GCMS), the reaction mixture was concentrated on a rotary evaporator and then distilled under vaccum, the resulting residue was directly subjected to preparative TLC (10:1 PE/EtOAc), no D-product was got in 72% yield.



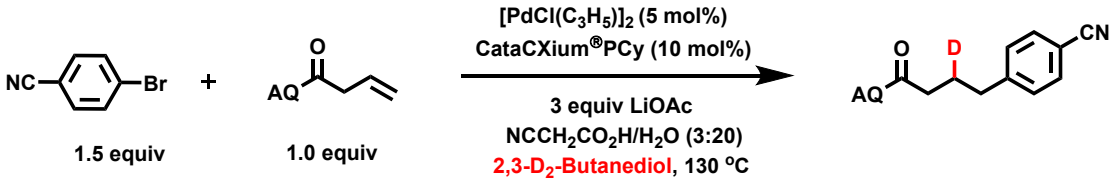
Scheme S6.

General Procedure: In an argon atmosphere, a dry 10-mL Schlenk tube containing a magnetic stirbar was charged with $[PdCl(C_3H_5)]_2$ (5 mol%, 1.9 mg, 0.005 mmol), cataCXium@PCy (10 mol%, 3.4 mg, 0.01 mmol), alkenes S2 (1 equiv, 0.1 mmol , 21.2 mg), LiOAc (3 equiv, 0.3 mmol, 20 mg)， 4-bromobenzonitrile (1.5 equiv, 0.15 mmol, 27 mg), dry 2,3-butanediol (1.0 mL), d_4-HOAc (3 equiv, 0.3 mmol, 18 uL) and H_2O (20 equiv, 2 mmol, 36 uL). The tube was capped tightly and the mixture was vigorously stirred in a *pre*-warmed 130°C oil bath. After alkenes was almost fully consumed (monitored by GCMS), the reaction mixture was concentrated on a rotary evaporator and then distilled under vacuum, the resulting residue was directly subjected to preparative TLC (10:1 PE/EA), no D-product was got in 80% yield.



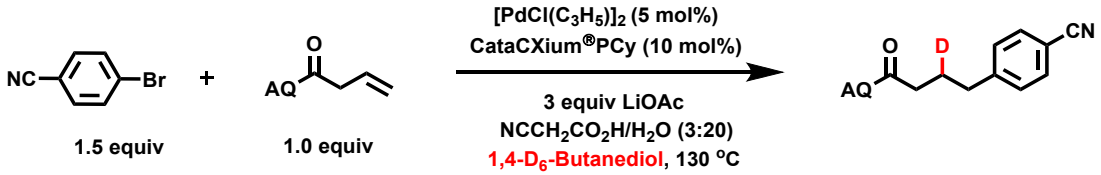
Scheme S7.

General Procedure: In an argon atmosphere, a dry 10-mL Schlenk tube containing a magnetic stirbar was charged with $[PdCl(C_3H_5)]_2$ (5 mol%, 1.9 mg, 0.005 mmol), cataCXium@PCy (10 mol%, 3.4 mg, 0.01 mmol), alkenes S2 (1 equiv, 0.1 mmol, 21.2 mg), LiOAc (3 equiv, 0.3 mmol, 20 mg)，4-bromobenzonitrile (1.5 equiv, 0.15 mmol, 27 mg), dry 2,3-butanediol (1.0 mL), cyanoacetic acid (3 equiv, 0.3 mmol, 25.6 mg) and D_2O (20 equiv, 2 mmol, 36 uL). The tube was capped tightly and the mixture was vigorously stirred in a *pre*-warmed 130°C oil bath. After 12h, 10 uL dodecane was added in the tube. After alkenes was almost fully consumed (monitored by GCMS), the reaction mixture was concentrated on a rotary evaporator and then distilled under reduced pressure, the resulting residue was directly subjected to preparative TLC (10:1 PE/EA), no D-product was got in 73% yield.



Scheme S8.

General Procedure: In an argon atmosphere, a dry 10-mL Schlenk tube containing a magnetic stirbar was charged with $[PdCl(C_3H_5)]_2$ (5 mol%, 1.9 mg, 0.005 mmol), cataCXium@PCy (10 mol%, 3.4 mg, 0.01 mmol), alkenes S2 (1 equiv, 0.1 mmol, 21.2 mg), LiOAc (3 equiv, 0.3 mmol, 20 mg), 4-bromobenzonitrile (1.5 equiv, 0.15 mmol, 27 mg), dry 2,3-D_2-2,3-Butanediol[4] (1.0 mL), cyanoacetic acid (3 equiv, 0.3 mmol, 25.6 mg) and H_2O (20 equiv, 2 mmol, 36 uL). The tube was capped tightly and the mixture was vigorously stirred in a *pre*-warmed 130°C oil bath. After alkenes was almost fully consumed (monitored by GCMS), the reaction mixture was concentrated on a rotary evaporator and then distilled under vaccum, the resulting residue was directly subjected to preparative TLC (10:1 PE/EA), D-product was got in 42% yield.



Scheme S9.

General Procedure: In an argon atmosphere, a dry 10-mL Schlenk tube containing a magnetic stirbar was charged with $[PdCl(C_3H_5)]_2$ (5 mol%, 1.9 mg, 0.005 mmol), cataCXium@PCy (10 mol%, 3.4 mg, 0.01 mmol), alkenes S2 (1 equiv, 0.1 mmol, 21.2 mg), LiOAc (3 equiv, 0.3 mmol, 20 mg), 4-bromobenzonitrile (1.5 equiv, 0.15 mmol, 27 mg), dry 1,4-D_6-2,3-butanediol[4] (1.0 mL), cyanoacetic acid (3 equiv, 0.3 mmol, 25.6 mg) and H_2O (20 equiv, 2 mmol, 36 uL). The tube was capped tightly and the mixture was vigorously stirred in a *pre*-warmed 130°C oil bath. After alkenes was almost fully consumed (monitored by GCMS), the reaction mixture was concentrated on a rotary evaporator and then distilled under vacuum, the resulting residue was directly subjected to preparative TLC (10:1 PE/EA), no D-product was got in 25% yield.

VIII. Reference

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