Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

Supporting Information

Cobalt-catalyzed C-H Activation and Regioselective Intermolecular Annulation with Allenes

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Materials and Methods

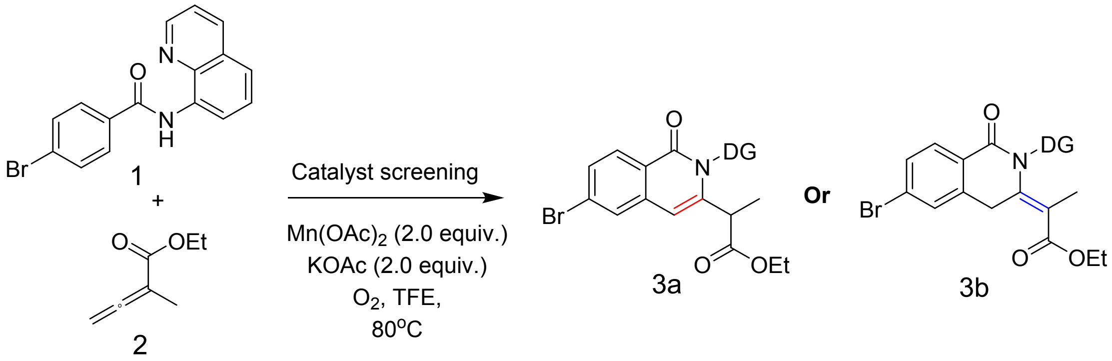
All commercial materials (Alfa Aesar, Aladdin, J&K Chemical LTD.) were used without further purification. All solvents were analytical grade. The potassium persulfate were ground to powder. The ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker AVANCE^{III} 400 MHz spectrometer in $CDCl_3$ using TMS or solvent peak as a standard. All ^{13}C NMR spectra were recorded with complete proton decoupling. Low-resolution mass spectral analyses were performed with a Waters AQUITY UPLC^{TM}/MS. All reactions were carried out in sealed tube with Teflon cap. Analytical TLC was performed on Yantai Chemical Industry Research Institute silica gel 60 F254 plates and flash column chromatography was performed on Qingdao Haiyang Chemical Co. Ltd silica gel 60 (200-300mesh). The rotavapor was BUCHI's Rotavapor R-3.

1. Optimization of cobalt-catalyzed sp^2 C-H functionalization

1.1 Catalyst screening:

General procedure:

A sealed tube with a screw cap (PTFE) was charged with 4-bromo-N-(quinolin-8-yl) benzamide (32.6 mg, 0.1 mmol), $Mn(OAc)_2$ (34.7 mg, 0.2 mmol, 2 equiv.), KOAc (19.8 mg, 0.2 mmol, 2 equiv.), Catalysts (0.02 mmol, 20 mol%), CF_3CH_2OH (1.0 mL), and ethyl 2-methylbuta-2,3-dienoate (37.8 mg, 0.3 mmol, 3.0 equiv.) under oxygen atmosphere. Resulting mixture was heated at corresponding temperature for 12 – 18 h, cooled to room temperature and analyzed by TLC (Petroleum ether:Ethyl acetate 4:1, Petroleum ether:Ethyl acetate = 1:1) and 1H-NMR spectroscopy.



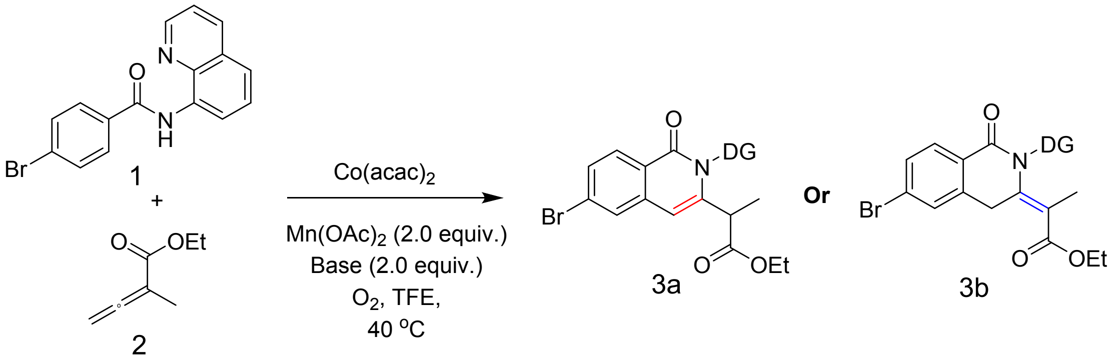
entry	catalyst	**3a** yield[a] (%)	**3b** yield[a] (%)
1	$Pd(acac)_2$	N.O.	N.O.
2	(1,5-Cyclooctadiene)(methoxy)iridium (I)	N.O.	N.O.
3	$Fe(acac)_3$	N.O.	N.O.
4	$Ni(acac)_2$	N.O.	N.O.
5	$[Cp^*RhCl_2]_2$	N.O.	N.O.
6	Without catalyst	N.O.	N.O.

Note: **a)** the reaction conversion was monitored by ^{1}H-NMR; **b)** N.O. means no observation in this reaction.

1.2 Bases screening:

General procedure:

A sealed tube with a screw cap (PTFE) was charged with 4-bromo-N-(quinolin-8-yl) benzamide (32.6 mg, 0.1 mmol), $Mn(OAc)_2$ (34.7 mg, 0.2 mmol, 2 equiv.), Base (0.2 mmol, 2 equiv.), $Co(acac)_2$ (5.7 mg, 0.02 mmol, 20 mol%), CF_3CH_2OH (1.0 mL), and ethyl 2-methylbuta-2,3-dienoate (37.8 mg, 0.3 mmol, 3.0 equiv.) under oxygen atmosphere. Resulting mixture was heated at corresponding temperature for 12 – 18 h, cooled to room temperature and analyzed by TLC (Petroleum ether:Ethyl acetate 4:1, Petroleum ether:Ethyl acetate = 1:1) and 1H-NMR spectroscopy.

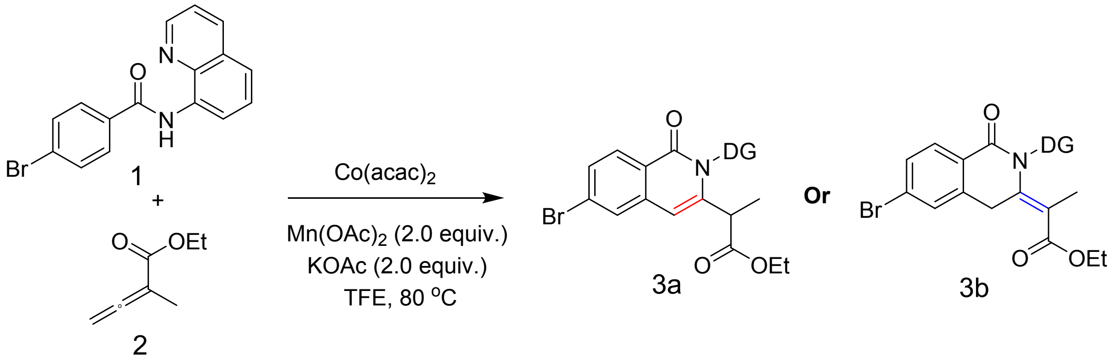


Entry	Base	Temperature (°C)	time (h)	3a yield (%)	3b yield (%)
1	Pyridine	80	15	N.O.	N.O.
2	DMAP	80	15	N.O.	N.O.
3	CsOPiv	40	9	11	47
4	KOTf	30	20	<5	26
5	KOTf	40	9	<5	71
6	KOTf	50	4	<15	25
7	KOTf	60	4	<25	27
8	NaOPiv	80	3	43	<5
9	NaOAc	80	4	51	<5
10	KOAc	80	3	82	<5
11	KOAc	40	9	43	13
12	$NaOCOCF_3$	40	12	<30	<15
13	Sodium benzoate	40	12	<30	<15
14	K_2CO_3	40	12	<25	<15

Note: **a)** the reaction conversion was monitored by ^{1}H-NMR; **b)** N.O. means no observation in this reaction.

1.3 Oxidant screening:

A sealed tube with a screw cap (PTFE) was charged with 4-bromo-N-(quinolin-8-yl) benzamide (32.6 mg, 0.1 mmol), Oxidant (0.2 mmol, 2 equiv.), KOAc (19.8 mg, 0.2 mmol, 2 equiv.), $Co(acac)_2$ (5.7 mg, 0.02 mmol, 20 mol%), CF_3CH_2OH (1.0 mL), and ethyl 2-methylbuta-2,3-dienoate (37.8 mg, 0.3 mmol, 3.0 equiv.) under oxygen atmosphere. Resulting mixture was heated at corresponding temperature for 12 – 18 h, cooled to room temperature and analyzed by TLC (Petroleum ether:Ethyl acetate 4:1, Petroleum ether:Ethyl acetate = 1:1) and 1H-NMR spectroscopy.

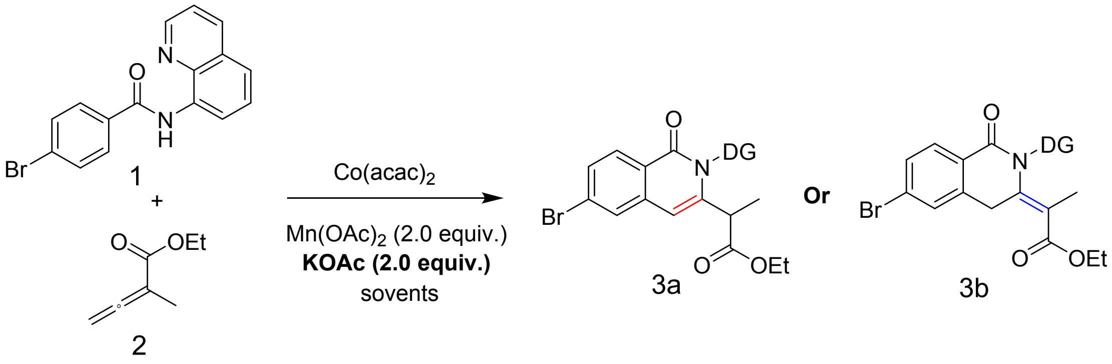


entry	Oxidant	**3a** yield[a] (%)	**3b** yield[a] (%)
1	$K_2S_2O_8$	23	< 5
2	$Cu(OAc)_2$	N.O.	N.O.
3	$Cu(OAc)_2 + O_2$	N.O.	N.O.
4	$Ph(OAc)_2I$	N.O.	N.O.
5	mCPBA	N.O.	N.O.
6	$Fe(OAc)_2$(II)	N.O.	N.O.
7	$Fe(OAc)_2$(II) + O_2	N.O.	N.O.
8	AgOAc	37	< 5
9	$Mn(OAc)_2$	13	< 5
10	$Mn(OAc)_2 + O_2$	82	< 5
11	$Mn(OAc)_2$ + air	35	< 5
12	O_2	41	< 5

Note: **a)** the reaction conversion was monitored by ^{1}H-NMR; **b)** N.O. means no observation in this reaction.

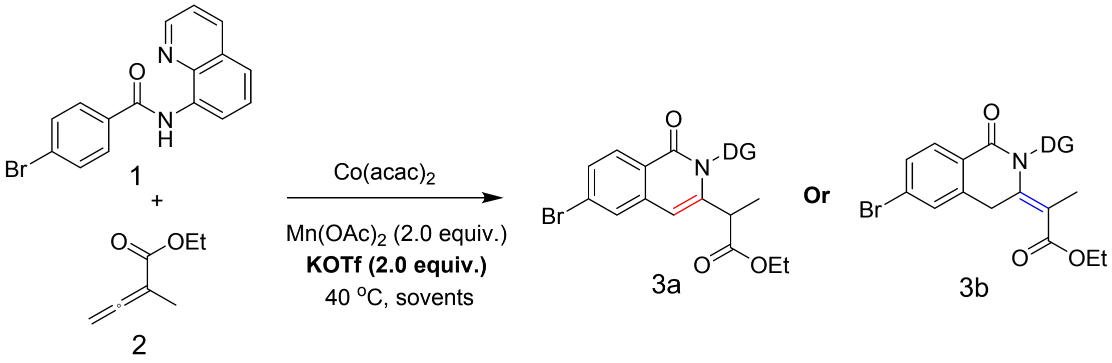
1.4 Solvents screening:

A sealed tube with a screw cap (PTFE) was charged with 4-bromo-N-(quinolin-8-yl) benzamide (32.6 mg, 0.1 mmol), Oxidant (0.2 mmol, 2 equiv.), KOAc (19.8 mg, 0.2 mmol, 2 equiv.) or KOTf (37.8 mg, 0.2 mmol, 2 equiv.), $Co(acac)_2$ (5.7 mg, 0.02 mmol, 20 mol%), CF_3CH_2OH (1.0 mL), and ethyl 2-methylbuta-2,3-dienoate (37.8 mg, 0.3 mmol, 3.0 equiv) under oxygen atmosphere. Resulting mixture was heated at corresponding temperature for 12 – 18 h, cooled to room temperature and analyzed by TLC (Petroleum ether:Ethyl acetate 4:1, Petroleum ether:Ethyl acetate = 1:1) and 1H-NMR spectroscopy.



Entry	Base	Temperature (°C)	time (h)	3a yield (%)	3b yield (%)
1	MeOH	80	4	27[a]	< 5
2	EtOH	80	4	35[a]	8
3	TFE	80	3	68[a]	< 5
4	n-butyl alcohol	80	12	<10[b]	N.O.
5	Trifluoromethylbenzene	80	9	<10[b]	N.O.
6	Chlorobenzene	80	12	N.O.	N.O.
7	DCE	80	12	< 5[b]	N.O.
8	Dioxane	80	12	<10[b]	N.O.
9	HFIP	80	5	<20[b,c]	N.O.

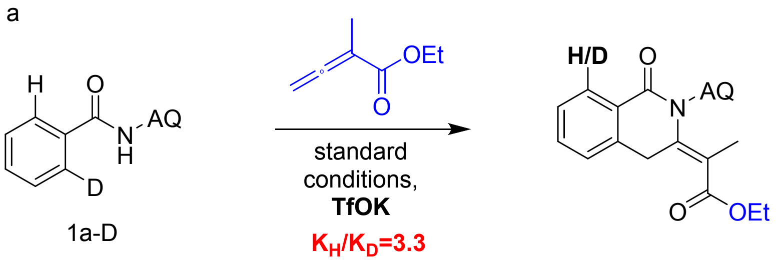
Note: 1) the reaction conversion was monitored by ^{1}H-NMR; 2) N.O. means no observation in this reaction; a) Isolated yields; b) reaction conversion after 12 h; c) the main product is the dimer.



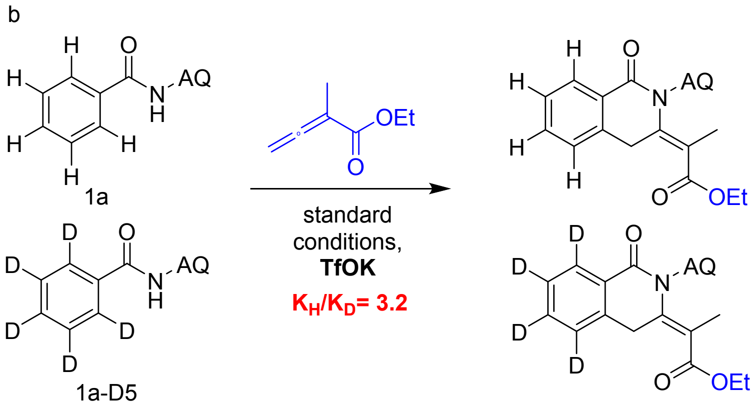
Entry	Base	Temperature (°C)	time (h)	3a yield (%)	3b yield (%)
1	MeOH	40	12	< 5	31[a]
2	EtOH	40	18	14	25[a]
3	TFE	40	13	15	63[a]
4	n-butyl alcohol	40	12	<10	<10[b]
5	Trifluoromethylbenzene	40	12	<15	<15[b]
6	Chlorobenzene	40	12	<15	<15[b]
7	DCE	40	12	<15	<15[b]
8	Dioxane	40	12	<10	<20[b]

Note: **1)** the reaction conversion was monitored by ^{1}H-NMR; **2)** N.O. means no observation in this reaction;a) Isolated yields; b) reaction converstion.

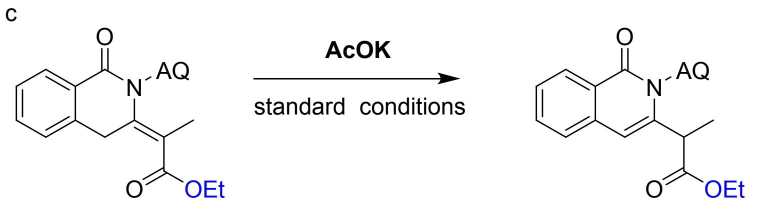
1.5 Deuteration experiments and KIE study:



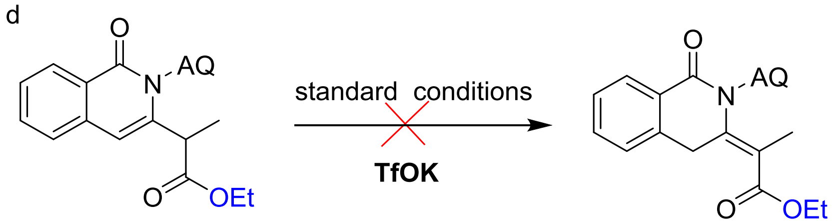
A sealed tube with a screw cap (PTFE) was charged with *N*-(quinolin-8-yl)benzamide-2-d (24.9 mg, 0.1 mmol), Mn(OAc)$_2$ (0.2 mmol, 2 equiv.), KOTf (37 mg, 0.2 mmol, 2 equiv.), Co(acac)$_2$ (5.7 mg, 0.02 mmol, 20 mol%), CF$_3$CH$_2$OH (1.0 mL), and ethyl 2-methylbuta-2,3-dienoate (37.8 mg, 0.3 mmol, 3.0 equiv) under oxygen atmosphere. Resulting mixture was heated at 40 °C for 45 min, cooled to room temperature and analyzed by TLC (Petroleum ether:Ethyl acetate 10:1, Petroleum ether:Ethyl acetate = 4:1) and 1H-NMR spectroscopy.



A sealed tube with a screw cap (PTFE) was charged with *N*-(quinolin-8-yl)benzamide (12.4 mg, 0.05 mmol) and *N*-(quinolin-8-yl)benzamide-2,3,4,5,6-d5 (12.7 mg, 0.05 mmol), Mn(OAc)$_2$ (0.2 mmol, 2 equiv.), KOTf (37.8 mg, 0.2 mmol, 2 equiv.), Co(acac)$_2$ (5.7 mg, 0.02 mmol, 20 mol%), CF$_3$CH$_2$OH (1.0 mL), and ethyl 2-methylbuta-2,3-dienoate (37.8 mg, 0.3 mmol, 3.0 equiv) under oxygen atmosphere. Resulting mixture was heated at corresponding temperature for 45 min, cooled to room temperature and analyzed by TLC (Petroleum ether:Ethyl acetate 10:1, Petroleum ether:Ethyl acetate = 4:1) and 1H-NMR spectroscopy.

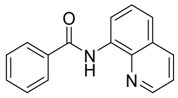
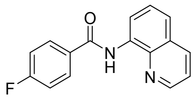
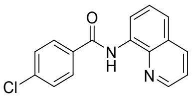
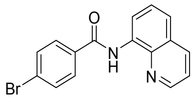
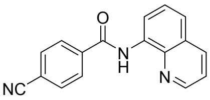
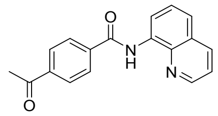
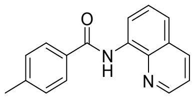
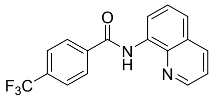
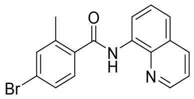
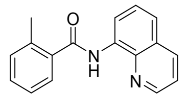
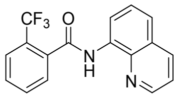
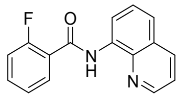
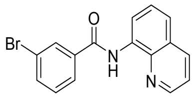
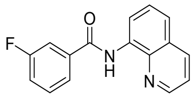
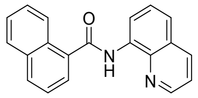
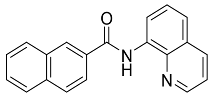


A sealed tube with a screw cap (PTFE) was charged with ethyl (*E*)-2-(1-oxo-2-(quinolin-8-yl)-1,4-dihydroisoquinolin-3(2*H*)-ylidene)propanoate (37 mg, 0.1 mmol), Mn(OAc)$_2$ (0.2 mmol, 2 equiv.), KOAc (20 mg, 0.2 mmol, 2 equiv.), Co(acac)$_2$ (5.7 mg, 0.02 mmol, 20 mol%), and CF$_3$CH$_2$OH (1.0 mL) under oxygen atmosphere, then the reaction mixture was stirred at 80 °C until the complete consumption as monitored by TLC analysis. The reaction mixture was then diluted with EtOAc (10 mL) and washed with saturated bine. The aqueous phase was extracted with EtOAc again. The organic layer was combined, washed with brine and dried over Na_2SO_4. The mixture was purified by flash column chromatography on silica with an appropriate solvent to afford the desired product.

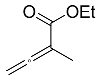
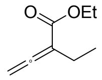
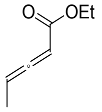
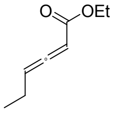
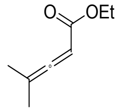
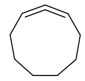
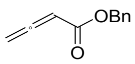
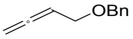
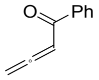


A sealed tube with a screw cap (PTFE) was charged with ethyl ethyl 2-(1-oxo-2-(quinolin-8-yl)-1,2-dihydroisoquinolin-3-yl)propanoate (37 mg, 0.1 mmol), $Mn(OAc)_2$ (0.2 mmol, 2 equiv.), KOAc (20 mg, 0.2 mmol, 2 equiv.), $Co(acac)_2$ (5.7 mg, 0.02 mmol, 20 mol%), and CF_3CH_2OH (1.0 mL) under oxygen atmosphere, then the reaction mixture was stirred at 80 °C until the complete consumption as monitored by TLC analysis. The reaction mixture was then diluted with EtOAc (10 mL) and washed with saturated bine. The aqueous phase was extracted with EtOAc again. The organic layer was combined, washed with brine and dried over Na_2SO_4. The mixture was purified by flash column chromatography on silica with an appropriate solvent to afford the starting material.

Synthesis of N-(quinolin-8-yl)benzamide analogues

 1	 1a	 1b	 1c	 1d
 1e	 1f	 1g	 1h	 1i
 1j	 1k	 1l	 1m	 1n
 1o				

Synthesis of Allenes

 2	 2a	 2b	 2c	 2d
 2e	 2f	 2g	 2h	

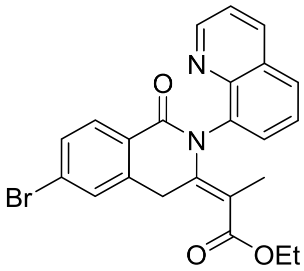
I. General Procedure for the *exo*- Synthesis:

The Co(acac)$_2$ (20 mol%), Mn(OAc)$_2$ (2.0 equiv.), KOTf (2.0 equiv.) and benzamide substrate 1 (1.0 equiv.) was dissolved in 2,2,2-trifluoroethanol (1.0 mL) in a sealed tube. Allene (3.0 equiv.) was subsequently slowly added at room temperature. Resulting solution was purged with O_2 ballon for 0.5 min, then the reaction mixture was stirred at 40 ^{o}C until the complete consumption of 2 as monitored by TLC analysis. The reaction mixture was then diluted with EtOAc (10 mL) and washed with saturated bine. The aqueous phase was extracted with EtOAc again. The organic layer was combined, washed with brine and dried over Na_2SO_4. The mixture was purified by flash column chromatography on silica with an appropriate solvent to afford the pure product.

II. General Procedure for the *endo*- Synthesis:

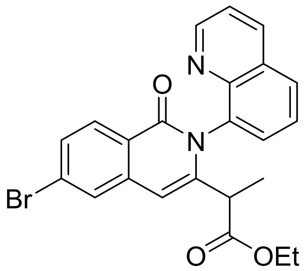
The Co(acac)$_2$ (20 mol%), Mn(OAc)$_2$ (2.0 equiv.), KOAc (2.0 equiv.) and benzamide substrate 1 (1.0 equiv.) was dissolved in 2,2,2-trifluoroethanol (1.0 mL) in a sealed tube. Allene (3.0 equiv.) was subsequently slowly added at room temperature. Resulting solution was purged with O_2 ballon for 0.5 min, then the reaction mixture was stirred at 80 ^{o}C until the complete consumption of 1 as monitored by TLC analysis. The reaction mixture was then diluted with EtOAc (10 mL) and washed with saturated brine. The aqueous phase was extracted with EtOAc again. The organic layer was combined, washed with brine and dried over Na_2SO_4. The mixture was purified by flash column chromatography on silica with an appropriate solvent to afford the pure product.

III. Data of Products



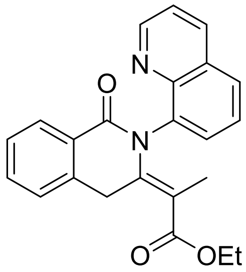
Ethyl (*E*)-2-(6-bromo-1-oxo-2-(quinolin-8-yl)-1,4-dihydroisoquinolin-3(*2H*)-ylidene)propanoate (3a)

Following the general procedure I, 4-bromo-*N*-(quinolin-8-yl)benzamide (33 mg, 0.1 mmol), ethyl 2-methylbuta-2,3-dienoate (38 mg, 0.3 mmol), Co(acac)$_2$ (5.4 mg, 0.02 mmol), Mn(OAc)$_2$ (35 mg, 0.2 mmol), KOTf (37 mg, 0.2 mmol), and TFE 2.0 ml were used. Resulting solution was purged with O_2 ballon for 0.5 min, then the reaction mixture was stirred at 40 ^{o}C for 5 h. After completion of the reaction, the reaction mixture was diluted with EtOAc and washed once with saturated aqueous $NaHCO_3$. Then organic layer was dried over Na_2SO_4 and concentrated on rotavapor under reduced pressure. Finally, the residue was purified by silica gel column chromatography (Petroleum ether:Ethyl acetate = 4:1) to **3** (32 mg) in 71% yield. ^{1}H-NMR (400 MHz, $CDCl_3$) δ (ppm) 8.87 (d, *J* = 2.0 Hz, 1H), 8.17 (d, *J* = 8.0 Hz, 1H), 7.94 (m, 2H), 7.81 (d, *J* = 8.4 Hz, 1H), 7.63 (t, *J* = 7.6 Hz, 1H), 7.51 (m, 2H), 7.41 (m, 1H), 4.83 (d, *J* = 13.6 Hz, 1H), 4.45 (d, *J* = 13.6 Hz, 1H), 4.14 (m, 2H), 1.25 (t, *J* = 7.2 Hz, 3H), 1.24 (m, 6H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ (ppm) 169.0, 163.8, 150.1, 147.7, 143.4, 139.6, 138.1, 136.3, 131.1, 130.5, 130.4, 129.8, 129.2, 127.7, 127.6, 127.5, 125.8, 121.6, 116.9, 60.7, 34.5, 15.8, 14.3; MS (ESI) calcd for $C_{23}H_{19}BrN_2O_3$ $[M+H]^+$: 451.06, found: 451.02.



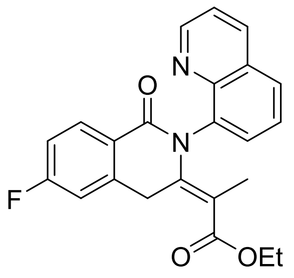
Ethyl 2-(6-bromo-1-oxo-2-(quinolin-8-yl)-1,2-dihydroisoquinolin-3-yl)propanoate (3b)

Following the general procedure II, 4-bromo-*N*-(quinolin-8-yl)benzamide (32.6 mg, 0.1 mmol), ethyl 2-methylbuta-2,3-dienoate (37.8 mg, 0.3 mmol), Co(acac)$_2$ (5.4 mg, 0.02 mmol), Mn(OAc)$_2$ (35 mg, 0.2 mmol), KOAc (19.8 mg, 0.2 mmol), and TFE 1.0 ml were used. Resulting solution was purged with O_2 ballon for 0.5 min, then the reaction mixture was stirred at 40 ^{o}C for 9.0 h. After completion of the reaction, the reaction mixture was diluted with EtOAc and washed once with saturated brine. Then organic layer was dried over Na_2SO_4 and concentrated on rotavapor under reduced pressure. Finally, the residue was purified by silica gel column chromatography (Petroleum ether:Ethyl acetate = 1:1) to **3b** (including two fraction 1F and 2F**)** (37 mg) in 82% yield. **3b-1F** ^{1}H-NMR (400 MHz, $CDCl_3$) δ (ppm) 8.85 (m, 1H), 8.25 (d, *J* = 8.4 Hz, 1H), 8.22 (d, *J* = 8.8 Hz, 1H), 8.00 (dd, *J* = 1.6 Hz, *J* = 8.0 Hz, 1H)， 7.78 (s, 1H), 7.68-7.66 (m, 2H), 7.56 (dd, *J* = 1.6 Hz, *J* = 8.8 Hz, 1H)， 7.47 (q, *J* = 4.0 Hz, 1H), 6.57 (s, 1H), 3.97 (m, 2H), 3.12 (q, *J* = 7.2 Hz, 1H), 1.37 (d, *J* = 7.2 Hz, 3H), 1.11 (t, *J* = 7.2 Hz, 3H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ (ppm) 172.9, 163.2, 151.6, 144.6, 144.2, 138.7, 136.6, 135.5, 131.6, 130.2, 130.0, 129.8, 129.5, 128.7, 127.8, 126.4, 124.2, 122.2, 103.6, 61.4, 42.7, 17.2, 14.1; MS (ESI) calcd for $C_{23}H_{19}BrN_2O_3$ $[M+H]^+$: 451.06, found: 450.92. **3b-2F** ^{1}H-NMR (400 MHz, $CDCl_3$) δ (ppm) 8.85 (d, *J* = 2.8 Hz, 1H), 8.23 (m 2H), 8.00 (d, *J* = 4.8 Hz, 1H)， 7.75 (s, 1H), 7.70 (m, 2H), 7.54 (d, *J* = 8.8 Hz, 1H)， 7.44 (q, *J* = 4.0 Hz, 1H), 6.64 (s, 1H), 3.84-3.76 (m, 1H), 3.68-3.61 (m, 1H), 3.22 (q, *J* = 7.2 Hz, 1H), 1.36 (d, *J* = 7.2 Hz, 3H), 0.95 (t, *J* = 7.2 Hz, 3H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ (ppm) 172.1, 163.2, 151.3, 144.7, 144.5, 138.7, 136.2, 136.0, 130.2, 130.0, 129.9, 129.6, 128.7, 127.8, 126.4, 124.1, 122.1, 103.7, 61.1, 42.6, 18.7, 13.8; MS (ESI) calcd for $C_{23}H_{19}BrN_2O_3$ $[M+H]^+$: 451.06, found: 450.92.



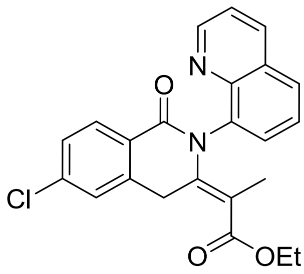
Ethyl(*E*)-2-(1-oxo-2-(quinolin-8-yl)-1,4-dihydroisoquinolin-3(2*H*) ylidene)propan–oate (4a)

Following the general procedure I, *N*-(quinolin-8-yl)benzamide (24.8 mg, 0.1 mmol), ethyl 2-methylbuta-2,3-dienoate (37.8 mg, 0.3 mmol), $Co(acac)_2$ (5.4 mg, 0.02 mmol), $Mn(OAc)_2$ (35 mg, 0.2 mmol), KOTf (39.8 mg, 0.2 mmol), and TFE 1.0 ml were used. Resulting solution was purged with O_2 ballon for 0.5 min, then the reaction mixture was stirred at 40 °C for 9.0 h. After completion of the reaction, the reaction mixture was diluted with EtOAc and washed once with saturated brine. Then organic layer was dried over Na_2SO_4 and concentrated on rotavapor under reduced pressure. Finally, the residue was purified by silica gel column chromatography (Petroleum ether:Ethyl acetate = 4:1) to **4a** (24 mg) in 65% yield. ^{1}H-NMR (400 MHz, $CDCl_3$) δ (ppm) 8.88 (d, *J* = 2.4 Hz, 1H), 8.16 (d, *J*= 8.4 Hz, 1H), 8.10 (d, *J* = 7.6 Hz, 1H), 7.94 (d, *J*= 7.2 Hz, 1H), 7.81 (d, *J* = 8.0 Hz, 1H), 7.63 (t, *J* = 8.0 Hz, 1H), 7.50 (t, *J* = 7.2 Hz, 1H), 7.41-7.36 (m, 2H), 7.33 (d, *J* = 7.6 Hz, 1H), 4.85 (d, *J* = 15.6 Hz, 1H), 4.67 (d, *J* = 15.6 Hz, 1H), 4.17-4.12 (m, 2H), 1.28-1.22 (m, 6H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ (ppm) 169.3, 164.5, 150.2, 148.7, 143.6, 148.5, 137.7, 136.3, 132.7, 131.2, 129.2, 128.8, 128.7, 127.7, 127.1, 126.8, 126.0, 121.6, 60.7, 34.9, 15.9, 14.0; MS (ESI) calcd for MS (ESI) calcd for $C_{23}H_{20}N_2O_3$ $[M+H]^+$: 373.15, found: 373.19.



Ethyl (*E*) -2-(6-fluoro-1-oxo-2-(quinolin-8-yl)-1,4-dihydroisoquinolin-3 (2*H*)-ylidene) propanoate (4b)

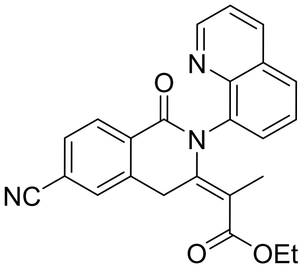
Following the general procedure I, 4-fluoro-*N*-(quinolin-8-yl)benzamide (26.6 mg, 0.1 mmol), ethyl 2-methylbuta-2,3-dienoate (37.8 mg, 0.3 mmol), Co(acac)$_2$ (5.4 mg, 0.02 mmol), Mn(OAc)$_2$ (35 mg, 0.2 mmol), KOTf (39.8 mg, 0.2 mmol), and TFE 1.0 ml were used. Resulting solution was purged with O$_2$ ballon for 0.5 min, then the reaction mixture was stirred at 40 °C for 9.0 h. After completion of the reaction, the reaction mixture was diluted with EtOAc and washed once with saturated brine. Then organic layer was dried over Na$_2$SO$_4$ and concentrated on rotavapor under reduced pressure. Finally, the residue was purified by silica gel column chromatography (Petroleum ether:Ethyl acetate = 4:1) to **4b** (23 mg) in 59% yield. ^{1}H-NMR (400 MHz, CDCl$_3$) δ (ppm) 8.87 (dd, *J* = 8.4 Hz, *J* = 1.6 Hz, 1H), 8.17 (dd, *J* = 8.4 Hz, *J* = 1.6 Hz, 1H), 8.11 (dd, *J* = 8.4 Hz, *J* = 6.0 Hz, 1H), 7.94 (d, *J* = 7.2 Hz, 1H), 7.81 (d, *J* = 7.2 Hz, 1H), 7.63 (t, *J* = 8.0 Hz, 1H), 7.40 (t, *J* = 8.0 Hz, 1H), 7.08-7.02 (m, *2*H), 4.87 (d, *J* = 15.6 Hz, 1H), 4.66 (d, *J* = 16.0 Hz, 1H), 4.17-4.10 (m, 2H), 1.26 (t, *J* = 7.2 Hz, 6H). ^{13}C-NMR (100 MHz, CDCl$_3$) δ (ppm) 169.1, 166.7, 163.7, 150.2, 148.0, 143.5, 140.8, 140.7, 138.2, 136.3, 131.7, 131.6, 131.3, 129.2, 127.7, 125.8, 125.0, 121.6, 116.7, 114.6, 114.4, 113.8, 113.6, 60.8, 34.8, 15.9, 14.3; MS (ESI) calcd for $C_{23}H_{19}FN_2O_3$ [M+H]$^+$: 391.14, found 391.06.



Ethyl(*E*)-2-(6-chloro-1-oxo-2-(quinolin-8-yl)-1,4-dihydroisoquinolin-3(*2H*)-ylidene)propanoate (4c)

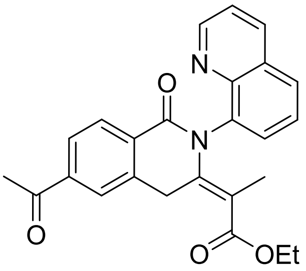
Following the general procedure I, 4-chloro-N-(quinolin-8-yl)benzamide (29 mg, 0.1 mmol), ethyl 2-methylbuta-2,3-dienoate (39 mg, 0.3 mmol), Co(acac)$_2$ (2.7 mg, 0.02 mmol), Mn(OAc)$_2$ (35 mg, 0.2 mmol), KOTf (37 mg, 0.2 mmol), and TFE 1.5 ml were used. Resulting solution was purged with O$_2$ ballon for 0.5 min, then the reaction mixture was stirred at 40 °C for 13 h. After completion of the reaction, the reaction mixture was diluted with EtOAc and washed once with saturated aqueous NaHCO$_3$. Then organic layer was dried over Na$_2$SO$_4$ and concentrated on rotavapor under reduced pressure. Finally, the residue was purified by silica gel column chromatography

(Petroleum ether:Ethyl acetate = 4:1) to **4c** (24.4 mg) in 61% yield. ^{1}H-NMR (400 MHz, $CDCl_3$) δ (ppm) 8.89-8.87 (m, 1H), 8.18 (dd, *J* = 8.4 Hz, *J* = 1.2 Hz, 2H), 8.03 (d, *J* = 8.4 Hz, 1H), 7.93 (d, *J* = 7.6 Hz, 1H), 7.82 (d, *J* = 8.0 Hz, 1H), 7.63 (t, *J* = 8.0 Hz, 1H), 7.42-7.39 (m, 1H), 7.36-7.34 (m, 2H), 4.87-4.83 (m, 1H), 4.66-4.62 (m, 1H), 4.17-4.11 (m, 2H), 1.28-1.23 (m, 6H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ (ppm) 169.1, 163.7, 150.2, 147.8, 143.4, 139.5, 138.8, 138.1, 136.3, 131.1, 130.3, 129.2, 127.8, 127.5, 127.2, 126.9, 125.8, 121.6, 116.9, 60.8, 34.5, 15.9, 14.3; MS (ESI) calcd for $C_{23}H_{19}ClN_2O_3$ $[M+H]^+$: 406.11, found 407.05.



Ethyl(*E*)-2-(6-cyano-1-oxo-2-(quinolin-8-yl)-1,4-dihydroisoquinolin-3(*2H*)-ylidene)propanoate (4d)

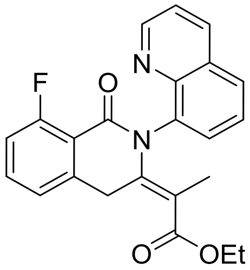
Following the general procedure I, 4-cyano-*N*-(quinolin-8-yl)benzamide (14 mg, 0.05 mmol), ethyl 2-methylbuta-2,3-dienoate (19 mg, 0.15 mmol), $Co(acac)_2$ (2.7 mg, 0.01 mmol), $Mn(OAc)_2$ (18 mg, 0.1 mmol), KOTf (19 mg, 0.1 mmol), and TFE 1.5 ml were used. Resulting solution was purged with O_2 ballon for 0.5 min, then the reaction mixture was stirred at 30 °C for 13 h. After completion of the reaction, the reaction mixture was diluted with EtOAc and washed once with saturated aqueous $NaHCO_3$. Then organic layer was dried over Na_2SO_4 and concentrated on rotavapor under reduced pressure. Finally, the residue was purified by silica gel column chromatography (Petroleum ether:Ethyl acetate = 4:1) to **4d** (15 mg) in 70% yield. ^{1}H-NMR (400 MHz, $CDCl_3$) δ (ppm) 8.88 (d, *J* = 2.0 Hz, 1H), 8.19 (d, *J* = 8.0 Hz, 2H), 7.94 (d, *J* = 7.2 Hz, 1H), 7.84 (d, *J* = 8.0 Hz, 1H), 7.68-7.63 (m, 3H), 7.44-7.41 (m, 1H),4.90 (d, *J* = 14.8 Hz, 1H), 4.72 (d, *J* = 14.8 Hz, 1H), 4.16-4.11 (m, 2H), 1.27-1.23 (m, 6H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ (ppm) 168.9, 163.0, 150.3, 146.6, 143.3, 138.9, 137.8, 136.4, 132.5, 131.0, 130.7, 130.5, 129.5, 129.3, 128.0, 125.9, 121.8, 118.3, 117.8, 116.0, 61.0, 34.4, 15.9, 14.3; MS (ESI) calcd for $C_{24}H_{19}N_3O_3$ $[M+H]^+$:398.14, found: 398.37.



Ethyl (*E*)-2-(6-acetyl-1-oxo-2-(quinolin-8-yl)-1,4-dihydroisoquinolin-3(*2H*)-ylidene)propanoate (4e)

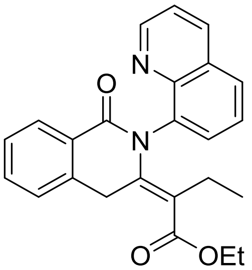
Following the general procedure I, 4-acetyl-N-(quinolin-8-yl)benzamide (29 mg, 0.1

mmol), ethyl 2-methylbuta-2,3-dienoate (38 mg, 0.3 mmol), Co(acac)$_2$ (5.4 mg, 0.02 mmol), Mn(OAc)$_2$ (35 mg, 0.2 mmol), KOTf (25 mg, 0.13 mmol), KOAc (10 mg, 0.1 mmol), and TFE 1.5 ml were used. Resulting solution was purged with O$_2$ ballon for 0.5 min, then the reaction mixture was stirred at 40 °C for 6.5 h. After completion of the reaction, the reaction mixture was diluted with EtOAc and washed once with saturated aqueous NaHCO$_3$. Then organic layer was dried over Na$_2$SO$_4$ and concentrated on rotavapor under reduced pressure. Finally, the residue was purified by silica gel column chromatography (Petroleum ether:Ethyl acetate = 4:1) to **4e** (25 mg) in 61% yield. ^{1}H-NMR (400 MHz, CDCl$_3$) δ (ppm) 8.90-8.88 (m, 1H), 8.19 (d, *J* = 8.0 Hz, 2H), 7.95-7.92 (m, 3H), 7.83 (d, *J* = 7.6 Hz, 1H), 7.64 (t, *J* = 7.6 Hz, 1H), 7.43-7.40 (m, 1H), 4.93-4.89 (m, 1H), 4.73-4.69 (m, 1H), 4.18-4.10 (m, 2H), 2.66 (s, 3H), 1.28-1.24 (m, 6H); ^{13}C-NMR (100 MHz, CDCl$_3$) δ (ppm) 197.8, 169.1, 163.4, 150.3, 147.6, 143.4, 140.0, 138.11, 138.08, 136.4, 132.4, 130.9, 129.2, 129.1, 127.9, 126.9, 126.7, 125.9, 121.6, 117.1, 60.9, 34.8, 27.1, 15.9, 14.3; MS (ESI) calcd for $C_{25}H_{22}N_2O_4$ $[M+H]^+$: 414.16, found 415.09.



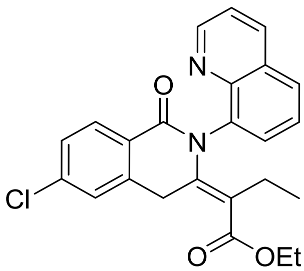
Ethyl (*E*)-2-(8-fluoro-1-oxo-2-(quinolin-8-yl)-1,4-dihydroisoquinolin-3(*2H*)-ylidene)propanoate (4f)

Following the general procedure I, 2-fluoro-N-(quinolin-8-yl)benzamide (27 mg, 0.1 mmol), ethyl 2-methylbuta-2,3-dienoate (38 mg, 0.3 mmol), Co(acac)$_2$ (5.4 mg, 0.02 mmol), Mn(OAc)$_2$ (35 mg, 0.2 mmol), KOTf (19 mg, 0.1 mmol), KOAc (10 mg, 0.1 mmol), and TFE 1.5 ml were used. Resulting solution was purged with O$_2$ ballon for 0.5 min, then the reaction mixture was stirred at 40 °C for 10 h. After completion of the reaction, the reaction mixture was diluted with EtOAc and washed once with saturated aqueous NaHCO$_3$. Then organic layer was dried over Na$_2$SO$_4$ and concentrated on rotavapor under reduced pressure. Finally, the residue was purified by silica gel column chromatography (Petroleum ether:Ethyl acetate = 4:1) to **4f** (21 mg) in 54% yield. ^{1}H-NMR (400 MHz, CDCl$_3$) δ (ppm) 8.87 (d, *J* = 2.0 Hz, 1H), 8.16 (d, *J* = 8.0 Hz, 1H), 7.92 (d, *J* = 7.2 Hz, 1H), 7.80 (d, *J* = 8.0 Hz, 1H), 7.62 (t, *J* = 7.6 Hz, 1H), 7.41 (m, 2H), 7.12 (d, *J* = 7.6 Hz, 1H), 7.06 (t, *J* = 9.6 Hz, 1H), 4.88 (d, *J* = 15.2 Hz, 1H), 4.13 (d, *J* = 15.2 Hz, 1H), 4.12 (m, 2H), 1.29 (m, 3H), 1.24 (t, *J* = 7.2 Hz, 6H). ^{13}C-NMR (100 MHz, CDCl$_3$) δ (ppm) 169.1, 162.4 (d, *J* = 221.0 Hz, 1C), 160.9, 150.2, 148.0, 143.5, 140.3, 137.9, 136.3, 133.8 (d, *J* = 9.0 Hz, 1C), 131.3, 129.3, 127.7, 125.9, 122.5 (d, *J* = 3.0 Hz, 1C), 121.6, 117.2, 116.6, 115.5 (d, *J* = 22.0 Hz, 1C), 60.7, 35.3, 15.8, 14.3; MS (ESI) calcd for $C_{23}H_{19}FN_2O_3$ $[M+H]^+$: 391.14, found: 391.06.



Ethyl (*E*)-2-(1-oxo-2-(quinolin-8-yl)-1,4-dihydroisoquinolin-3(2*H*)-ylidene)butanoate (4g)

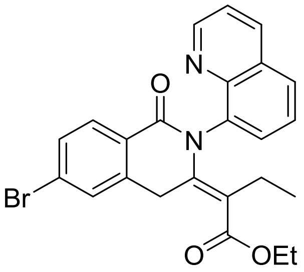
Following the general procedure I, *N*-(quinolin-8-yl)benzamide (24.8 mg, 0.1 mmol), ethyl 2-ethylbuta-2,3-dienoate (42 mg, 0.3 mmol), Co(acac)$_2$ (5.4 mg, 0.02 mmol), Mn(OAc)$_2$ (35 mg, 0.2 mmol), KOTf (39.8 mg, 0.2 mmol), and TFE 1.0 ml were used. Resulting solution was purged with O_2 ballon for 0.5 min, then the reaction mixture was stirred at 40 °C for 9.0 h. After completion of the reaction, the reaction mixture was diluted with EtOAc and washed once with saturated brine. Then organic layer was dried over Na_2SO_4 and concentrated on rotavapor under reduced pressure. Finally, the residue was purified by silica gel column chromatography (Petroleum ether:Ethyl acetate = 1:1) to **4g** (24 mg) in 62% yield. ^{1}H-NMR (400 MHz, CDCl$_3$) δ (ppm) 8.91 (d, *J* = 2.4 Hz, 1H), 8.16 (d, *J*= 8.0 Hz, 1H), 8.10 (d, *J* = 7.6 Hz, 1H), 8.01 (d, *J*= 7.2 Hz, 1H), 7.83 (d, *J* = 8.0 Hz, 1H), 7.64 (t, *J* = 8.0 Hz, 1H), 7.50 (t, *J* = 7.6 Hz, 1H), 7.41-7.36 (m, 2H), 7.30 (d, *J* = 7.6 Hz, 1H), 4.84 (d, *J* = 15.6 Hz, 1H), 4.47 (d, *J* = 16.0 Hz, 1H), 4.18 (dd, *J* = 14.0 Hz, *J* = 6.8 Hz, 2H), 2.14-1.90 (m, 2H), 1.26 (t, *J* = 7.2 Hz, 3H), -0.12 (t, *J* = 7.2 Hz, 3H). ^{13}C-NMR (100 MHz, CDCl$_3$) δ (ppm) 169.2, 164.5, 150.3, 146.9, 143.7, 139.1, 138.0, 136.1, 132.7, 131.1, 129.3, 128.8, 127.7, 127.1, 126.7, 126.0, 123.5, 121.5, 60.6, 35.3, 22.6, 14.3, 10.5; MS (ESI) calcd for $C_{24}H_{22}N_2O_3$ $[M+H]^+$: 387.16, found: 387.11.



Ethyl (*E*)-2-(6-chloro-1-oxo-2-(quinolin-8-yl)-1,4-dihydroisoquinolin-3(*2H*)-ylidene)butanoate (4h)

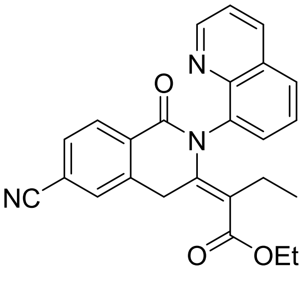
Following the general procedure I, 4-chloro-N-(quinolin-8-yl)benzamide (29 mg, 0.1 mmol), ethyl 2-ethylbuta-2,3-dienoate (42 mg, 0.3 mmol), Co(acac)$_2$ (5.4 mg, 0.02 mmol), Mn(OAc)$_2$ (35 mg, 0.2 mmol), KOTf (37 mg, 0.2 mmol), and TFE 2.0 ml were used. Resulting solution was purged with O_2 ballon for 0.5 min, then the reaction mixture was stirred at 40 °C for 13 h. After completion of the reaction, the reaction mixture was diluted with EtOAc and washed once with saturated aqueous $NaHCO_3$. Then organic layer was dried over Na_2SO_4 and concentrated on rotavapor under reduced pressure. Finally, the residue was purified by silica gel column chromatography

(Petroleum ether:Ethyl acetate = 4:1) to **4h** (28 mg) in 60% yield. ^{1}H-NMR (400 MHz, CDCl$_3$) δ (ppm) 8.91-8.90 (m, 1H), 8.17 (d, *J* = 8.0 Hz, 1H), 8.02 (t, *J* = 8.4 Hz, 2H), 7.83 (d, *J* = 8.0 Hz, 1H), 7.64 (t, *J* = 7.6 Hz, 1H), 7.42-7.39 (m, 1H), 7.34 (d, *J* = 8.4 Hz, 1H), 7.31 (s, 1H), 4.85-4.81 (m, 1H), 4.48-4.44 (m, 1H), 4.20-4.15 (m, 2H), 2.13-2.02 (m, 2H), 1.26 (t, *J* = 7.2 Hz, 3H), -0.11 (t, *J* = 7.2 Hz, 3H); ^{13}C-NMR (100 MHz, CDCl$_3$) δ (ppm) 169.0, 163.7, 150.3, 146.0, 143.6, 139.8, 138.82, 138.80, 136.2, 131.1, 130.4, 129.4, 127.8, 127.5, 127.2, 126.8, 126.0, 124.2, 121.6, 60.7, 35.1, 22.6, 14.3, 10.5; MS (ESI) calcd for $C_{24}H_{21}ClN_2O_3$ [M+H]$^+$: 420.12, found 421.04.



Ethyl (*E*)-2-(6-bromo-1-oxo-2-(quinolin-8-yl)-1,4-dihydroisoquinolin-3(2*H*)-ylidene)butanoate (4i)

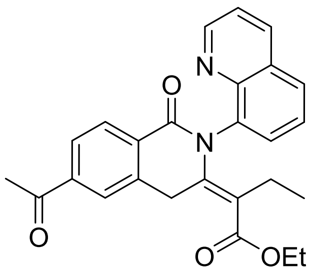
Following the general procedure I, 4-bromo-*N*-(quinolin-8-yl)benzamide (32.6 mg, 0.1 mmol), ethyl 2-ethylbuta-2,3-dienoate (42 mg, 0.3 mmol), Co(acac)$_2$ (5.4 mg, 0.02 mmol), Mn(OAc)$_2$ (35 mg, 0.2 mmol), KOTf (39.8 mg, 0.2 mmol), and TFE 1.0 ml were used. Resulting solution was purged with O$_2$ ballon for 0.5 min, then the reaction mixture was stirred at 40 ^{o}C for 9.0 h. After completion of the reaction, the reaction mixture was diluted with EtOAc and washed once with saturated brine. Then organic layer was dried over Na$_2$SO$_4$ and concentrated on rotavapor under reduced pressure. Finally, the residue was purified by silica gel column chromatography (Petroleum ether:Ethyl acetate = 4:1) to **4i** (41 mg) in 88% yield. ^{1}H-NMR (400 MHz, CDCl$_3$) δ (ppm) 8.90 (dd, *J* = 8.0 Hz, *J* = 1.6 Hz, 1H), 8.16 (dd, *J* = 8.4 Hz, *J* = 1.6 Hz, 1H), 8.00 (d, *J* = 7.2 Hz, 1H), 7.95 (d, *J* = 8.0 Hz, 1H), 7.83 (d, *J* = 8.0 Hz, 1H), 7.64 (t, *J* = 7.6 Hz, 1H), 7.50 (t, *J* = 8.4 Hz, 1H), 7.48 (s, 1H), 7.40 (dd, *J* = 8.0 Hz, *J* = 4.0 Hz, 1H), 4.83 (d, *J* = 16.4 Hz, 1H), 4.45 (d, *J* = 16.4 Hz, 1H), 4.17 (dd, *J* = 14.0 Hz, *J* = 6.8 Hz, 2H), 2.20-1.90 (m, 2H), 1.25 (t, *J* = 7.2 Hz, 3H), -0.12 (t, *J* = 7.2 Hz, 3H). ^{13}C-NMR (100 MHz, CDCl$_3$) δ (ppm) 168.9, 163.8, 150.3, 145.9, 143.5, 139.9, 138.7, 136.2, 131.0, 130.5, 130.4, 129.7, 129.3, 127.8, 127.6, 127.4, 125.9, 124.2, 121.6, 60.7, 35.0, 22.6, 14.3, 10.5; MS (ESI) calcd for $C_{24}H_{21}BrN_2O_3$ [M+H]$^+$: 465.07, found: 464.96.



Ethyl (*E*)-2-(6-cyano-1-oxo-2-(quinolin-8-yl)-1,4-dihydroisoquinolin-3(2*H*)-ylide-

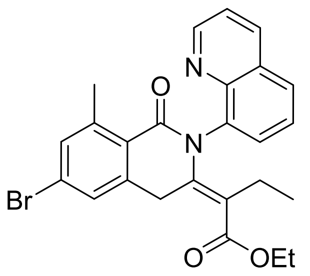
ne)butanoate (4j)

Following the general procedure I, 4-cyano-*N*-(quinolin-8-yl)benzamide (27 mg, 0.1 mmol), ethyl 2-ethylbuta-2,3-dienoate (42 mg, 0.3 mmol), Co(acac)$_2$ (5.4 mg, 0.02 mmol), Mn(OAc)$_2$ (35 mg, 0.2 mmol), KOTf (39.8 mg, 0.2 mmol), and TFE 1.0 ml were used. Resulting solution was purged with O_2 ballon for 0.5 min, then the reaction mixture was stirred at 40 ^{o}C for 9.0 h. After completion of the reaction, the reaction mixture was diluted with EtOAc and washed once with saturated brine. Then organic layer was dried over Na_2SO_4 and concentrated on rotavapor under reduced pressure. Finally, the residue was purified by silica gel column chromatography (Petroleum ether:Ethyl acetate = 4:1) to **4j** (26 mg) in 63% yield. ^{1}H-NMR (400 MHz, $CDCl_3$) δ (ppm) 8.90 (m, 1H), 8.20-8.17 (m, 2H), 8.00 (d, *J* = 8.4 Hz, 1H), 7.85 (d, *J* = 8.4 Hz, 1H), 7.70-7.62 (m, 3H), 7.41 (q, *J* = 4.0 Hz, 1H), 4.88 (d, *J* = 15.6 Hz, 1H), 4.53 (d, *J* = 15.6 Hz, 1H), 4.16 (m, 2H), 2.11 (m, 1H), 2.01 (m, 1H), 1.26 (t, *J* = 7.2 Hz, 3H), -0.10 (t, *J* = 7.2 Hz, 3H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ (ppm) 168.7, 163.0, 150.4, 144.8, 143.3, 139.1, 138.4, 136.3, 132.5, 130.8, 130.7, 130.4, 129.5, 129.4, 128.0, 125.9, 125.0, 121.7, 118.2, 115.9, 60.9, 34.8, 22.6, 14.3, 10.4. MS (ESI) calcd for $C_{25}H_{21}N_3O_3$ $[M+H]^+$: 412.16, found: 412.46.



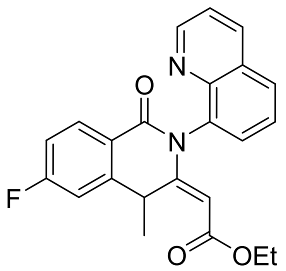
Ethyl (*E*)-2-(6-acetyl-1-oxo-2-(quinolin-8-yl)-1,4-dihydroisoquinolin-3(*2H*)-ylidene)butanoate (4k)

Following the general procedure I, 4-acetyl-N-(quinolin-8-yl)benzamide (29 mg, 0.1 mmol), ethyl 2-ethylbuta-2,3-dienoate (42 mg, 0.3 mmol), Co(acac)$_2$ (5.4 mg, 0.02 mmol), Mn(OAc)$_2$ (35 mg, 0.2 mmol), KOTf (37 mg, 0.2 mmol), and TFE 2.0 ml were used. Resulting solution was purged with O_2 ballon for 0.5 min, then the reaction mixture was stirred at 40 ^{o}C for 13 h. After completion of the reaction, the reaction mixture was diluted with EtOAc and washed once with saturated aqueous $NaHCO_3$. Then organic layer was dried over Na_2SO_4 and concentrated on rotavapor under reduced pressure. Finally, the residue was purified by silica gel column chromatography (Petroleum ether:Ethyl acetate = 4:1) to **4k** (27 mg) in 63% yield. ^{1}H-NMR (400 MHz, $CDCl_3$) δ (ppm) 8.92-8.91 (m, 1H), 8.18 (d, *J* = 7.2 Hz, 2H), 8.01 (d, *J* = 7.2 Hz, 1H), 7.93 (d, *J* = 8.4 Hz, 1H), 7.89 (s, 1H), 7.85 (d, *J* = 8.0 Hz, 1H), 7.65 (d, *J* = 8.0 Hz, 1H), 7.43-7.40 (m, 1H), 4.90-4.86 (m, 1H), 4.55-4.51 (m, 1H), 4.22-4.16 (m, 2H), 2.66 (s, 3H), 2.13-2.04 (m, 2H), 1.26 (t, *J* = 7.2 Hz, 3H), -0.11 (t, *J* = 7.2 Hz, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ (ppm) 197.8, 169.0, 163.7, 150.4, 145.8, 143.5, 140.0, 138.8, 138.5, 136.2, 132.5, 130.9, 129.4, 129.2, 127.9, 126.9, 126.6, 126.0, 124.4, 121.7, 60.8, 35.3, 27.1, 22.6, 14.3, 10.5; MS (ESI) calcd for $C_{26}H_{24}N_2O_4$ $[M+H]^+$: 428.17, found 429.08.



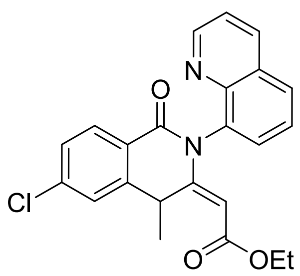
Ethyl (*E*)-2-(6-bromo-8-methyl-1-oxo-2-(quinolin-8-yl)-1,4-dihydroisoquinolin-3(*2H*)-ylidene)butanoate (4l)

Following the general procedure I, 4-bromo-2-methyl-*N*-(quinolin-8-yl)benzamide (34 mg, 0.1 mmol), ethyl 2-ethylbuta-2,3-dienoate (42 mg, 0.3 mmol), Co(acac)$_2$ (5.4 mg, 0.02 mmol), Mn(OAc)$_2$ (35 mg, 0.2 mmol), KOTf (37 mg, 0.2 mmol), and TFE 2.0 ml were used. Resulting solution was purged with O_2 ballon for 0.5 min, then the reaction mixture was stirred at 40 °C for 12 h. After completion of the reaction, the reaction mixture was diluted with EtOAc and washed once with saturated aqueous $NaHCO_3$. Then organic layer was dried over Na_2SO_4 and concentrated on rotavapor under reduced pressure. Finally, the residue was purified by silica gel column chromatography (Petroleum ether:Ethyl acetate = 4:1) to **4l** (30 mg) in 64% yield. ^{1}H-NMR (400 MHz, $CDCl_3$) δ (ppm) 8.91-8.90 (m, 1H), 8.17 (d, *J* = 8.4 Hz, *J* = 1.2 Hz, 1H), 7.90 (d, *J* = 7.2 Hz, *J* = 0.8 Hz, 1H), 7.83 (d, *J* = 8.0 Hz, 1H), 7.63 (t, *J* = 7.6 Hz, 1H), 7.42-7.39 (m, 1H), 7.32 (d, *J* = 9.6 Hz, 2H), 4.83-4.79 (m, 1H), 4.40-4.36 (m, 1H), 4.18 (q, *J* = 7.2 Hz, 2H), 2.66 (s, 3H), 2.16-2.09 (m, 1H), 2.05-1.98 (m, 1H), 1.26 (t, *J* = 7.2 Hz, 3H), -0.12 (t, *J* = 7.6 Hz, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ (ppm) 168.9, 164.5, 150.4, 146.2, 143.8, 143.1, 140.2, 139.4, 136.3, 133.4, 130.9, 129.4, 127.9, 127.5, 126.2, 126.1, 123.2, 121.7, 60.7, 36.0, 22.6, 21.6, 14.3, 10.5; MS (ESI) calcd for $C_{25}H_{23}BrN_2O_3$ $[M+H]^+$: 478.09, found 478.95.



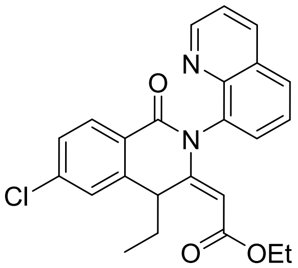
Ethyl (*E*)-2-(6-fluoro-4-methyl-1-oxo-2-(quinolin-8-yl)-1,4-dihydroisoquinolin-3(*2H*)-ylidene)acetate (4m)

Following the general procedure I, 4-flouro-*N*-(quinolin-8-yl)benzamide (34 mg, 0.1 mmol), ethyl penta-2,3-dienoate (38 mg, 0.3 mmol), Co(acac)$_2$ (5.4 mg, 0.02 mmol), Mn(OAc)$_2$ (35 mg, 0.2 mmol), KOTf (37 mg, 0.2 mmol), and TFE 2.0 ml were used. Resulting solution was purged with O_2 ballon for 0.5 min, then the reaction mixture was stirred at 40 °C for 11 h. After completion of the reaction, the reaction mixture was diluted with EtOAc and washed once with saturated aqueous $NaHCO_3$. Then organic layer was dried over Na_2SO_4 and concentrated on rotavapor under reduced pressure. Finally, the residue was purified by silica gel column chromatography (Petroleum ether:Ethyl acetate = 4:1) to **4m** (28 mg) (including two fraction 1F and 2F**)** in 72% yield. **4m-1F** ^{1}H-NMR (400 MHz, $CDCl_3$) δ (ppm) 8.87 (dd, *J* = 4.0 Hz, *J* = 1.2 Hz, 1H), 8.25 (dd, *J* = 8.4 Hz, *J* = 1.6 Hz, 1H), 8.16-8.12 (m, 1H), 7.96 (d, *J* = 7.8 Hz, 1H), 7.70-7.66 (m, 1H), 7.61 (d, *J* = 6.8 Hz, 1H), 7.46 (dd, *J* = 8.4 Hz, *J* = 4.4 Hz, 1H), 7.10-7.06 (m, 2H), 5.53-5.47 (m, 1H), 4.61 (s, 1H), 4.10-3.99 (m, 2H), 1.91 (d, *J* = 7.2 Hz, 3H), 1.15-1.12 (m, 3H). **4m-2F** ^{1}H-NMR (400 MHz, $CDCl_3$) δ (ppm) 8.83 (dd, *J* = 4.0 Hz, *J* = 1.2 Hz, 0.6H), 8.21 (dd, *J* = 4.0 Hz, *J* = 1.2 Hz, 0.6H), 8.16-8.12 (m, 0.6H), 7.95 (d, *J* = 9.6 Hz, 0.6H), 7.70-7.66 (m, 1.2H), 7.43 (dd, *J* = 8.4 Hz, *J* = 4.4 Hz, 0.6H), 7.10-7.06 (m, 1.2H), 5.53-5.47 (m, 0.6H), 4.81 (s, 0.6H), 4.10-3.99 (m, 1.2H), 1.91 (d, *J* = 7.2 Hz, 1.8H), 1.15-1.12 (m, 1.8H); MS (ESI) calcd for $C_{23}H_{19}FN_2O_3$ $[M+H]^+$: 391.14, found 391.07.



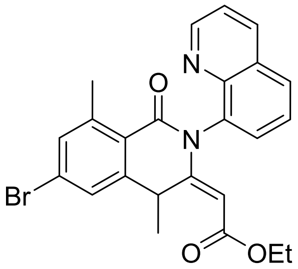
Ethyl (*E*)-2-(6-chloro-4-methyl-1-oxo-2-(quinolin-8-yl)-1,4-dihydroisoquinolin-3(*2H*)-ylidene)acetate (4n)

Following the general procedure I, 4-chloro-*N*-(quinolin-8-yl)benzamide (28.2 mg, 0.1 mmol), ethyl penta-2,3-dienoate (38 mg, 0.3 mmol), $Co(acac)_2$ (5.4 mg, 0.02 mmol), $Mn(OAc)_2$ (35 mg, 0.2 mmol), KOTf (37 mg, 0.2 mmol), and TFE 2.0 ml were used. Resulting solution was purged with O_2 ballon for 0.5 min, then the reaction mixture was stirred at 40 ^oC for 12 h. After completion of the reaction, the reaction mixture was diluted with EtOAc and washed once with saturated aqueous $NaHCO_3$. Then organic layer was dried over Na_2SO_4 and concentrated on rotavapor under reduced pressure. Finally, the residue was purified by silica gel column chromatography (Petroleum ether:Ethyl acetate = 4:1) to **4n** (28.8 mg) (including two fraction 1F and 2F**)** in 71% yield. **4n-1F** ^{1}H-NMR (400 MHz, $CDCl_3$) δ (ppm) 8.85 (d, *J* = 4.0 Hz, 1H), 8.23 (d, *J* = 8.0 Hz, 1H), 8.05 (d, *J* = 8.4 Hz, 1H), 7.96-7.93 (m, 1H), 7.69-7.65 (m, 1H), 7.60 (d, *J* = 7.2 Hz, 1H), 7.46-7.35 (m, 3H), 5.51-5.44 (m, 1H), 4.60 (s, 1H), 4.09-3.97 (m, 2H), 1.74 (d, *J* = 7.2 Hz, 3H), 1.14-1.10 (m, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ (ppm) 166.57, 162.4, 161.1, 151.6, 144.5, 144.4, 139.8, 136.6, 136.2, 129.6, 129.3, 127.8, 127.11, 127.0, 126.2, 124.4, 122.2, 101.2, 59.9, 35.0, 26.7, 14.3. **4n-2F** ^{1}H-NMR (400 MHz, $CDCl_3$) δ (ppm) 8.82 (d, *J* = 4.0 Hz, 0.7H), 8.20 (d, *J* = 8.0 Hz, 0.7H), 8.05 (d, *J* = 8.4 Hz, 0.7H), 7.96-7.93 (m, 0.7H), 7.69-7.65 (m, 1.4H), 7.46-7.35 (m, 2.1H), 5.51-5.44 (m, 0.7H), 4.81 (s, 0.7H), 4.09-3.97 (m, 1.4H), 1.90 (d, *J* = 7.2 Hz, 2.1H), 1.14-1.10 (m, 2.1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ (ppm) 166.64, 162.4, 160.7, 151.1, 144.8, 143.8, 139.7, 136.9, 135.2, 129.53, 129.45, 127.7, 127.09, 127.0, 126.2, 124.5, 122.1, 100.5, 59.8, 35.3, 27.2, 14.3; MS (ESI) calcd for $C_{23}H_{19}ClN_2O_3$ $[M+H]^+$: 407.11, found 407.15.



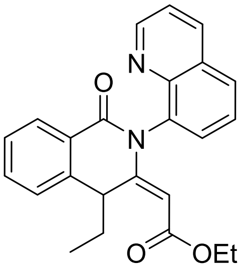
Ethyl (*E*)-2-(6-chloro-4-ethyl-1-oxo-2-(quinolin-8-yl)-1,4-dihydroisoquinolin-3(*2H*)-ylidene)acetate (4o)

Following the general procedure I, 4-chloro-*N*-(quinolin-8-yl)benzamide (28 mg, 0.1 mmol), ethyl hexa-2,3-dienoate (42 mg, 0.3 mmol), Co(acac)$_2$ (5.4 mg, 0.02 mmol), Mn(OAc)$_2$ (35 mg, 0.2 mmol), KOTf (37 mg, 0.2 mmol), and TFE 1.5 ml were used. Resulting solution was purged with O_2 ballon for 0.5 min, then the reaction mixture was stirred at 40 °C for 8.5 h. After completion of the reaction, the reaction mixture was diluted with EtOAc and washed once with saturated aqueous $NaHCO_3$. Then organic layer was dried over Na_2SO_4 and concentrated on rotavapor under reduced pressure. Finally, the residue was purified by silica gel column chromatography (Petroleum ether:Ethyl acetate = 4:1) to **4o** (30 mg) (including two fraction 1F and 2F**)** in 74% yield. **4o-1F** ^{1}H-NMR (400 MHz, $CDCl_3$) δ (ppm) 8.85 (br, 1H), 8.22 (t, *J* = 8.0 Hz, 1H), 8.07 (d, *J* = 8.4 Hz, 1H), 7.95 (d, *J* = 8.0 Hz, 1H), 7.70-7.61 (m, 2H), 7.45-7.38 (m, 3H), 5.46-5.43 (m, 1H), 4.67 (s, 1H), 4.13-3.95 (m, 2H), 2.15-2.05 (m, 2H), 1.17-1.01 (m, 6H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ (ppm) 166.7, 162.8, 160.1, 151.6, 144.3, 142.6, 139.3, 136.5, 136.2, 131.0, 130.4, 129.6, 129.3, 127.7, 127.0, 126.3, 125.3, 122.2, 101.9, 59.84, 40.7, 33.7, 14.3, 11.0. **4o-2F** ^{1}H-NMR (400 MHz, $CDCl_3$) δ (ppm) 8.85 (br, 0.6H), 8.22 (t, *J* = 8.0 Hz, 0.6H), 8.07 (d, *J* = 8.4 Hz, 0.6H), 7.95 (d, *J* = 8.0 Hz, 0.6H), 7.70-7.61 (m, 1.2H), 7.45-7.38 (m, 1.8H), 5.41-5.38 (m, 0.6H), 4.86 (s, 0.6H), 4.13-3.95 (m, 1.2H), 2.39-2.34 (m, 0.6H), 2.28-2.22 (m, 0.6H), 1.17-1.01 (m, 3.6H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ (ppm) 166.8, 162.7, 159.7, 151.0, 143.9, 143.0, 139.1, 137.0, 135.2, 130.3, 130.0, 129.4, 129.3, 127.8, 127.0, 126.3, 125.4, 122.0, 101.4, 59.80, 41.4, 34.3, 14.3, 11.4; MS (ESI) calcd for $C_{24}H_{21}ClN_2O_3$ $[M+H]^+$: 420.13, found 421.04.



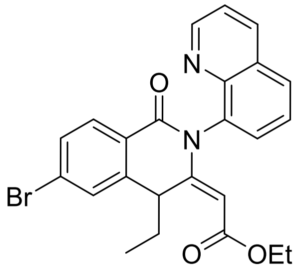
Ethyl (*E*)-2-(6-bromo-4,8-dimethyl-1-oxo-2-(quinolin-8-yl)-1,4 dihydroisoquinolin-3(*2H*)-ylidene)acetate (4p)

Following the general procedure I, 4-bromo-2-methyl-*N*-(quinolin-8-yl)benzamide (34 mg, 0.1 mmol), ethyl penta-2,3-dienoate (38 mg, 0.3 mmol), Co(acac)$_2$ (5.4 mg, 0.02 mmol), Mn(OAc)$_2$ (35 mg, 0.2 mmol), KOTf (37 mg, 0.2 mmol), and TFE 2.0 ml were used. Resulting solution was purged with O_2 ballon for 0.5 min, then the reaction mixture was stirred at 40 °C for 10 h. After completion of the reaction, the reaction mixture was diluted with EtOAc and washed once with saturated aqueous $NaHCO_3$. Then organic layer was dried over Na_2SO_4 and concentrated on rotavapor under reduced pressure. Finally, the residue was purified by silica gel column chromatography (Petroleum ether:Ethyl acetate = 4:1) to **4p** (25 mg) (including two fraction 1F and 2F) in 55% yield. **4p-1F** ^{1}H-NMR (400 MHz, $CDCl_3$) δ (ppm) 8.85 (d, *J* = 4.0 Hz, 1H), 8.25 (d, *J* = 1.6 Hz, 1H), 7.94 (d, *J* = 8.0 Hz, 1H), 7.68-7.63 (m, 2H), 7.46-7.41 (m, 2H), 7.36 (s, 1H), 5.47-5.41 (m, 1H), 4.58 (s, 1H), 4.09-3.96 (m, 2H), 2.59 (s, 3H), 1.75 (d, *J* = 7.2 Hz, 3H), 1.16-1.12 (m, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ (ppm) 166.79, 163.5, 161.1, 151.4, 145.3, 144.2, 144.0, 136.6, 136.2, 133.8, 130.7, 129.6, 129.3, 128.2, 127.06, 126.98, 126.3, 123.5, 122.2, 100.0, 59.8, 36.0, 27.2, 22.7, 14.3. **4p-2F** ^{1}H-NMR (400 MHz, $CDCl_3$) δ (ppm) 8.85 (d, *J* = 4.0 Hz, 0.8H), 8.23 (dd, *J* = 1.6 Hz, 0.8H), 7.94 (d, *J* = 8.0 Hz, 0.8H), 7.68-7.63 (m, 1.6H), 7.36 (s, 1H), 5.47-5.41 (m, 0.8H), 4.74 (s, 0.8H), 4.09-3.96 (m, 1.6H), 2.59 (s, 2.4H), 1.92 (d, *J* = 7.2 Hz, 2.4H), 1.16-1.12 (m, 2.4H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ (ppm) 166.75, 163.2, 160.7, 151.1, 145.9, 144.3, 143.9, 137.5, 135.8, 133.7, 130.7, 129.9, 129.4, 128.3, 127.06, 126.98, 126.3, 123.2, 122.0, 99.2, 59.7, 35.6, 26.3, 22.5, 14.3; MS (ESI) calcd for $C_{24}H_{21}BrNO_3$ $[M+H]^+$: 464.07, found 464.96.



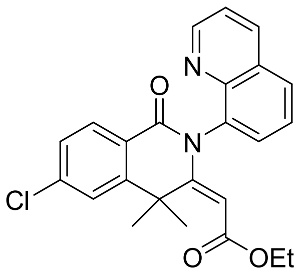
Ethyl (*E*)-2-(4-ethyl-1-oxo-2-(quinolin-8-yl)-1,4-dihydroisoquinolin-3(*2H*)-ylidene)acetate (4q)

Following the general procedure I, *N*-(quinolin-8-yl)benzamide (24.8 mg, 0.1 mmol), ethyl hexa-2,3-dienoate (42 mg, 0.3 mmol), $Co(acac)_2$ (5.4 mg, 0.02 mmol), $Mn(OAc)_2$ (35 mg, 0.2 mmol), KOTf (37 mg, 0.2 mmol), and TFE 1.5 ml were used. Resulting solution was purged with O_2 ballon for 0.5 min, then the reaction mixture was stirred at 40 °C for 8.5 h. After completion of the reaction, the reaction mixture was diluted with EtOAc and washed once with saturated aqueous $NaHCO_3$. Then organic layer was dried over Na_2SO_4 and concentrated on rotavapor under reduced pressure. Finally, the residue was purified by silica gel column chromatography (Petroleum ether:Ethyl acetate = 4:1) to **4q** (26 mg) (including two fraction 1F and 2F) in 67% yield. **4q-1F** ^{1}H-NMR (400 MHz, $CDCl_3$) δ (ppm) 8.86-8.84 (m, 1H), 8.23 (d, *J* = 8.4 Hz, 1H), 8.13 (d, *J* = 8.0 Hz, 1H), 7.96-7.94 (m, 1H), 7.70-7.62 (m, 2H), 7.58 (t, *J* = 8.0 Hz, 1H), 7.45-7.36 (m, 3H), 5.47-5.39 (m, 1H), 4.67 (s, 1H), 4.15-3.97 (m, 2H), 2.15-2.08 (m, 2H), 1.16-1.06 (m, 6H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ (ppm) 166.9, 163.6, 161.2, 151.6, 144.5, 140.9, 136.5, 136.2, 133.0, 131.0, 129.5, 129.4, 128.8, 127.8, 127.4, 127.1, 126.3, 122.2, 101.4, 59.8, 41.6, 34.5, 14.4, 11.4. **4q-2F** ^{1}H-NMR (400 MHz, $CDCl_3$) δ (ppm) 8.86-8.84 (m, 0.55H), 8.21 (d, *J* = 8.0 Hz, 0.55H), 8.13 (d, *J* = 8.0 Hz, 0.55H), 7.96-7.94 (m, 0.55H), 7.70-7.62 (m, 1.1H), 7.58 (t, *J* = 8.0 Hz, 0.55H), 7.45-7.36 (m, 1.65H), 5.47-5.39 (m, 0.55H), 4.84 (s, 0.55H), 4.15-3.97 (m, 1.1H), 2.35-2.23 (m, 1.1H), 1.16-1.06 (m, 3.3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ (ppm) 167.0, 163.6, 160.7, 151.0, 144.1, 141.3, 137.3, 135.7, 132.9, 131.0, 129.6, 129.3, 128.6, 127.8, 127.2, 126.7, 126.3, 122.0, 100.8, 59.7, 41.0, 33.8, 14.3, 11.1; MS (ESI) calcd for $C_{24}H_{22}N_2O_3$ $[M+H]^+$: 387.16, found 387.11.



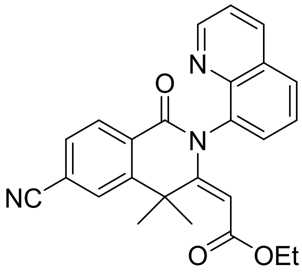
Ethyl (*E*)-2-(6-bromo-4-ethyl-1-oxo-2-(quinolin-8-yl)-1,4-dihydroisoquinolin-3(*2H*)-ylidene)acetate (4r)

Following the general procedure I, 4-bromo-N-(quinolin-8-yl)benzamide (33 mg, 0.1 mmol), ethyl hexa-2,3-dienoate (42 mg, 0.3 mmol), $Co(acac)_2$ (5.4 mg, 0.02 mmol), $Mn(OAc)_2$ (35 mg, 0.2 mmol), KOTf (37 mg, 0.2 mmol), and TFE 1.5 ml were used. Resulting solution was purged with O_2 ballon for 0.5 min, then the reaction mixture was stirred at 40 °C for 9 h. After completion of the reaction, the reaction mixture was diluted with EtOAc and washed once with saturated aqueous $NaHCO_3$. Then organic layer was dried over Na_2SO_4 and concentrated on rotavapor under reduced pressure. Finally, the residue was purified by silica gel column chromatography (Petroleum ether:Ethyl acetate = 4:1) to **4r** (28 mg) (including two fraction 1F and 2F**)** in 60% yield. **4r-1F** ^{1}H-NMR (400 MHz, $CDCl_3$) δ (ppm) 8.84 (s, 1H), 8.23 (t, *J* = 9.0 Hz, 1H), 7.99-7.94 (m, 2H), 7.70-7.61 (m, 2H), 7.55 (d, *J* = 5.4 Hz, 2H), 7.45-7.43 (m, 1H), 5.45-5.41 (m, 1H), 4.66 (s, 1H), 4.09-3.95 (m, 2H), 2.14-2.07 (m, 2H), 1.16-1.07 (m, 6H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ (ppm) 166.7, 162.9, 160.0, 151.6, 144.3, 142.7, 136.5, 136.2, 130.7, 130.6, 130.3, 129.6, 129.5, 129.2, 127.9, 126.3, 125.68, 122.2, 101.9, 59.82, 40.6, 33.7, 14.3, 10.9. **4r-2F** ^{1}H-NMR (400 MHz, $CDCl_3$) δ (ppm) 8.84 (s, 0.55H), 8.23 (t, *J* = 9.0 Hz, 0.55H), 7.99-7.94 (m, 1.1H), 7.70-7.61 (m, 1.1H), 7.55 (d, *J* = 5.4 Hz, 1.1H), 7.45-7.43 (m, 0.55H), 5.40-5.36 (m, 0.55H), 4.86 (s, 0.55H), 4.09-3.95 (m, 1.1H), 2.38-2.20 (m, 1.1H), 1.16-1.07 (m, 3.3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ (ppm) 166.8, 162.9, 159.6, 151.0, 143.8, 143.1, 136.9, 135.2, 130.9, 130.5, 129.9, 129.4, 129.2, 127.8, 126.3, 125.72, 122.0, 101.4, 59.78, 41.2, 34.3, 14.3, 11.3; MS (ESI) calcd for $C_{24}H_{21}BrN_2O_3$ $[M+H]^+$: 465.07, found: 465.01.



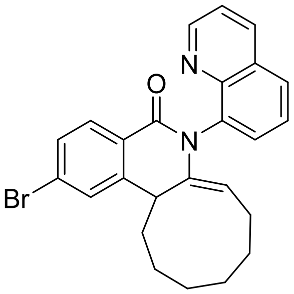
Ethyl (*E*)-2-(6-chloro-4,4-dimethyl-1-oxo-2-(quinolin-8-yl)-1,4-dihydroisoquinolin -3(2*H*)-ylidene)propanoate (4s)

Following the general procedure I, 4-chloro-*N*-(quinolin-8-yl)benzamide (27.3 mg, 0.1 mmol), ethyl 4-methylpenta-2,3-dienoate (42 mg, 0.3 mmol), Co(acac)$_2$ (5.4 mg, 0.02 mmol), Mn(OAc)$_2$ (35 mg, 0.2 mmol), KOTf (39.8 mg, 0.2 mmol), and TFE 1.0 ml were used. Resulting solution was purged with O_2 ballon for 0.5 min, then the reaction mixture was stirred at 40 °C for 9.5 h. After completion of the reaction, the reaction mixture was diluted with EtOAc and washed once with saturated brine. Then organic layer was dried over Na_2SO_4 and concentrated on rotavapor under reduced pressure. Finally, the residue was purified by silica gel column chromatography (Petroleum ether:Ethyl acetate = 1:1) to **4s** (29 mg) in 67% yield. ^{1}H-NMR (400 MHz, CDCl$_3$) δ (ppm) 8.91 (dd, *J* = 1.6 Hz, *J* = 4.0 Hz, 1H), 8.24 (d, *J* = 8.0 Hz, 1H), 8.17 (d, *J* = 8.0 Hz, 1H), 7.83 (d, *J* = 2.0 Hz, 1H), 7.75-7.71 (m, 3H), 7.60 (t, *J* = 8.0 Hz, 1H), 7.43 (q, *J* = 4.0 Hz, 1H), 5.48 (s, 1H), 3.23 (m, 1H), 2.98 (m, 1H), 1.87 (s, 3H), 1.78 (s, 3H), 0.70 (t, *J* = 7.2 Hz, 1H). ^{13}C-NMR (100 MHz, CDCl$_3$) δ (ppm) 165.5, 162.5, 153.6, 150.0, 146.7, 144.2, 139.2, 137.4, 136.1, 131.0, 130.1, 129.0, 128.3, 127.6, 126.7, 125.8, 123.0, 121.5, 103.8, 60.0, 41.2 (2C), 13.7; MS (ESI) calcd for $C_{24}H_{21}ClN_2O_3$ $[M+H]^+$: 421.12, found: 421.04.



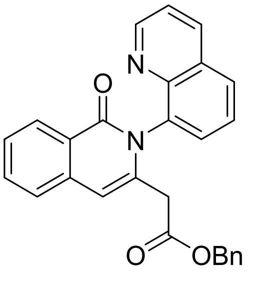
Ethyl (*E*)-2-(6-cyano-4,4-dimethyl-1-oxo-2-(quinolin-8-yl)-1,4-dihydroisoquinolin -3(2*H*)-ylidene)propanoate (4t)

Following the general procedure I, 4-cyano-*N*-(quinolin-8-yl)benzamide (27.3 mg, 0.1 mmol), ethyl 4-methylpenta-2,3-dienoate (42 mg, 0.3 mmol), Co(acac)$_2$ (5.4 mg, 0.02 mmol), Mn(OAc)$_2$ (35 mg, 0.2 mmol), KOTf (39.8 mg, 0.2 mmol), and TFE 1.0 ml were used. Resulting solution was purged with O_2 ballon for 0.5 min, then the reaction mixture was stirred at 40 °C for 9.0 h. After completion of the reaction, the reaction mixture was diluted with EtOAc and washed once with saturated brine. Then organic layer was dried over Na_2SO_4 and concentrated on rotavapor under reduced pressure. Finally, the residue was purified by silica gel column chromatography (Petroleum ether:Ethyl acetate = 1:1) to **4t** (30 mg) in 71% yield. ^{1}H-NMR (400 MHz, CDCl$_3$) δ (ppm) 8.91 (dd, *J* = 1.6 Hz, *J* = 4.0 Hz, 1H), 8.23 (dd, *J* = 7.6 Hz, 1H), 8.19 (dd, *J* = 1.6 Hz, *J* = 7.6 Hz, 1H), 7.85 (dd, *J* = 2.0 Hz, *J* = 8.0 Hz, 1H)，7.74-7.70 (m, 3H), 7.59 (t, *J* = 8.0 Hz, 1H), 7.43 (q, *J* = 4.0 Hz, 1H), 5.48 (s, 1H), 3.23 (m, 1H), 2.98 (m, 1H), 1.87 (s, 3H), 1.78 (s, 3H), 0.70 (t, *J* = 7.2 Hz, 1H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ (ppm) 165.3, 161.7, 152.6, 150.1, 145.9, 137.0, 136.2, 132.0, 131.0, 130.1, 129.9, 129.1, 128.6, 126.6, 125.8, 121.7, 116.3, 104.7, 60.2, 41.2, 13.7; MS (ESI) calcd for $C_{25}H_{21}N_3O_3$ $[M+H]^+$: 412.16, found: 412.12.



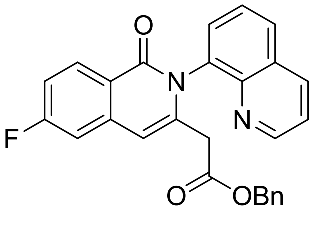
(*E*)-2-bromo-6-(quinolin-8-yl)-6,8,9,10,11,12,13,13a-octahydro-5*H*-cyclonona[c] isoquinolin-5-one (4u)

Following the general procedure I, 4-bromo-*N*-(quinolin-8-yl)benzamide (32.6 mg, 0.1 mmol), cyclonona-1,2-diene (36.6 mg, 0.3 mmol), $Co(acac)_2$ (5.4 mg, 0.02 mmol), $Mn(OAc)_2$ (35 mg, 0.2 mmol), KOTf (39.8 mg, 0.2 mmol), and TFE 1.0 ml were used. Resulting solution was purged with O_2 ballon for 0.5 min, then the reaction mixture was stirred at 80 °C for 10.0 h. After completion of the reaction, the reaction mixture was diluted with EtOAc and washed once with saturated brine. Then organic layer was dried over Na_2SO_4 and concentrated on rotavapor under reduced pressure. Finally, the residue was purified by silica gel column chromatography (Petroleum ether:Ethyl acetate = 6:1) to **4u** (15.4 mg) in 34% yield. ^{1}H-NMR (400 MHz, $CDCl_3$) δ (ppm) 8.91 (dd, *J* = 1.2 Hz, *J* = 4.0 Hz,, 1H), 8.21 (dd, *J* = 1.2 Hz, *J* = 8.0 Hz, 1H), 8.04 (d, *J* = 8.4 Hz, 1H), 7.87-7.82 (m, 1H), 7.88 (d, *J* =1.6 Hz, 3H), 7.77 (s, 1H), 7.64-7.61 (m, 1H), 7.51 (dd, *J* = 1.6 Hz, *J* = 8.4 Hz, 1H), 7.42 (q, *J* = 4.0 Hz, 1H), 6.48 (t, *J* = 8.4 Hz, 1H), 5.32 (m, 2H), 2.54 (m, 1H), 2.34-2.18 (m, 2H), 2.06-1.12 (m, 20H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ (ppm) 162.6, 150.6, 138.5, 136.7, 131.3, 131.1, 130.9, 130.6, 129.9, 128.1, 127.1, 126.8, 126.5, 126.3, 121.5, 33.0, 27.8, 26.7, 25.6, 22.6. MS (ESI) calcd for $C_{25}H_{23}BrN_2O$ $[M+H]^+$: 447.10, found: 447.02.



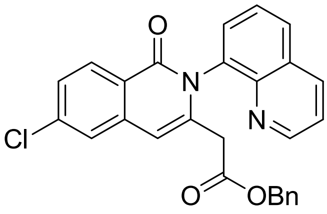
Benzyl 2-(1-oxo-2-(quinolin-8-yl)-1,2-dihydroisoquinolin-3-yl)acetate (5a)

Following the general procedure II, *N*-(quinolin-8-yl)benzamide (24.8 mg, 0.1 mmol), benzyl buta-2,3-dienoate (53 mg, 0.3 mmol), Co(acac)$_2$ (5.4 mg, 0.02 mmol), Mn(OAc)$_2$ (35 mg, 0.2 mmol), KOAc (39.8 mg, 0.2 mmol), and TFE 1.0 ml were used. Resulting solution was purged with O$_2$ ballon for 0.5 min, then the reaction mixture was stirred at 80 °C for 3.5 h. After completion of the reaction, the reaction mixture was diluted with EtOAc and washed once with saturated brine. Then organic layer was dried over Na$_2$SO$_4$ and concentrated on rotavapor under reduced pressure. Finally, the residue was purified by silica gel column chromatography (Petroleum ether:Ethyl acetate = 1:1) to **5a** (25 mg) in 59% yield. ^{1}H-NMR (400 MHz, CDCl$_3$) δ (ppm) 8.85 (dd, *J* = 1.6 Hz, *J* = 4.0 Hz,, 1H), 8.39 (d, *J* = 7.6 Hz, 2H), 8.22 (dd, *J* =1.6 Hz, *J* = 8.4 Hz, 1H), 7.90 (dd, *J* = 1.2 Hz, *J* = 8.0 Hz, 1H), 7.66 (m, 1H), 7.60 (dd, *J* = 1.2 Hz, *J* = 7.2 Hz, 1H), 7.55 (d, *J* = 7.6 Hz, 1H), 7.48 (m, 1H), 7.49-7.47 (m, 3H), 7.17 (dd, *J* = 2.0 Hz, *J* = 6.0 Hz, 2H), 6.63 (s, 1H), 4.90 (d, *J* = 16.4 Hz, 1H), 4.89 (d, *J* = 16.4 Hz, 1H), 3.41 (d, *J* = 17.2 Hz, 1H), 3.12 (d, *J* = 17.2 Hz, 1H). ^{13}C-NMR (100 MHz, CDCl$_3$) δ (ppm) 169.2, 163.5, 151.4, 144.3, 137.0, 136.3, 135.5, 135.0, 132.5, 131.2, 129.5, 129.3, 128.48, 128.47, 128.4, 128.2, 126.7, 126.2, 125.9, 125.5, 121.8, 107.9, 66.8, 40.0.



Benzyl 2-(6-fluoro-1-oxo-2-(quinolin-8-yl)-1,2-dihydroisoquinolin-3-yl)acetate (5b)

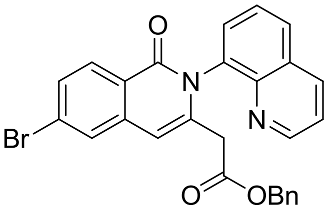
Following the general procedure II, 4-flouro-*N*-(quinolin-8-yl)benzamide (26.6 mg, 0.1 mmol), benzyl buta-2,3-dienoate (53 mg, 0.3 mmol), Co(acac)$_2$ (5.4 mg, 0.02 mmol), Mn(OAc)$_2$ (35 mg, 0.2 mmol), KOAc (39.8 mg, 0.2 mmol), and TFE 1.0 ml were used. Resulting solution was purged with O$_2$ ballon for 0.5 min, then the reaction mixture was stirred at 80 °C for 3.0 h. After completion of the reaction, the reaction mixture was diluted with EtOAc and washed once with saturated brine. Then organic layer was dried over Na$_2$SO$_4$ and concentrated on rotavapor under reduced pressure. Finally, the residue was purified by silica gel column chromatography (Petroleum ether:Ethyl acetate = 1:1) to **5b** (32.9 mg) in 75% yield. ^{1}H-NMR (400 MHz, CDCl$_3$) δ (ppm) 8.85 (dd, *J* = 4.0, 1.6 Hz, 1H), 8.40 (m, 1H), 8.22 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.91 (dd, *J* = 8.4, 1.6 Hz, 1H), 7.59 (dd, *J* = 7.2, 1.2 Hz, 1H), 7.48-7.42 (m, 2H), 7.34-7.31 (m, 3H), 7.19-7.17 (m, 5H), 6.57 (s, 1H), 4.90-4.89 (m, 2H), 3.40 (d, *J* = 17.2 Hz, 1H), 3.10 (d, *J* = 16.8 Hz, 1H);^{13}C-NMR (100 MHz, CDCl$_3$) δ (ppm) 169.1, 165.5 (d, $J_{C\text{-}F}$ = 251 Hz), 163.0, 144.4, 139.4 (d, $J_{C\text{-}F}$ = 10.6 Hz), 138.1, 136.5, 135.4, 135.1, 131.7 (d, $J_{C\text{-}F}$ = 10 Hz), 131.4, 129.8, 129.4, 128.7, 128.6, 126.3, 122.3, 122.1, 115.4 (d, $J_{C\text{-}F}$ = 23.3 Hz), 110.8 (d, $J_{C\text{-}F}$ = 21.8 Hz), 107.4 (d, $J_{C\text{-}F}$ = 3 Hz), 67.1, 40.1; MS (ESI) calcd for $C_{27}H_{19}FN_2O_3$ [M+H]$^+$: 438.14, found 439.12.



Benzyl 2-(6-chloro-1-oxo-2-(quinolin-8-yl)-1,2-dihydroisoquinolin-3-yl)acetate (5c)

Following the general procedure II, 4-chloro-*N*-(quinolin-8-yl)benzamide (28.2 mg, 0.1 mmol), benzyl buta-2,3-dienoate (53 mg, 0.3 mmol), Co(acac)$_2$ (5.4 mg, 0.02 mmol), Mn(OAc)$_2$ (35 mg, 0.2 mmol), KOAc (39.8 mg, 0.2 mmol), and TFE 1.0 ml were used. Resulting solution was purged with O$_2$ ballon for 0.5 min, then the reaction mixture was stirred at 80 °C for 3.0 h. After completion of the reaction, the reaction mixture was diluted with EtOAc and washed once with saturated brine. Then organic layer was dried over Na$_2$SO$_4$ and concentrated on rotavapor under reduced pressure. Finally, the residue was purified by silica gel column chromatography (Petroleum ether:Ethyl acetate = 1:1) to **5c** (30 mg) in 67% yield.

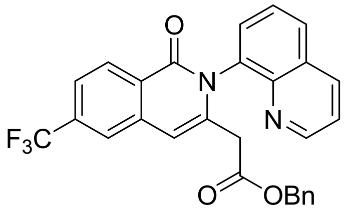
^{1}H-NMR (400 MHz, CDCl$_3$) δ (ppm) 8.84 (d, *J* = 2.8 Hz, 1H), 8.31 (d, *J* = 8.4 Hz, 1H), 8.22 (d, *J* = 8.0 Hz, 1H), 7.91 (d, *J* = 8.0 Hz, 1H), 7.58 (d, *J* = 6.8 Hz, 1H), 7.53 (s, 1H), 7.49-7.40 (m, 3H), 7.35-7.28 (m, 3H), 7.17 (d, *J* = 4.0 Hz, 2H), 4.95-4.89 (m, 2H), 3.39 (d, *J* = 16.8 Hz, 1H), 3.10 (d, *J* = 16.8 Hz, 1H);^{13}C-NMR (100 MHz, CDCl$_3$) δ (ppm) 169.1, 163.1, 151.7, 144.4, 139.2, 138.4, 138.2, 136.5, 135.4, 135.2, 131.3, 130.3, 129.8, 129.5, 128.7, 128.7, 128.7, 127.3, 126.3, 125.3, 124.0, 122.1, 107.0, 67.1, 40.2; MS (ESI) calcd for $C_{27}H_{19}ClN_2O_3$ [M+H]$^+$: 454.12, found 455.02.



Benzyl 2-(6-bromo-1-oxo-2-(quinolin-8-yl)-1,2-dihydroisoquinolin-3-yl)acetate (5d)

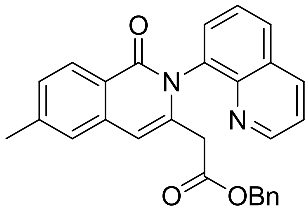
Following the general procedure II, 4-bromo-*N*-(quinolin-8-yl)benzamide (33 mg, 0.1 mmol), benzyl buta-2,3-dienoate (53 mg, 0.3 mmol), Co(acac)$_2$ (5.4 mg, 0.02 mmol), Mn(OAc)$_2$ (35 mg, 0.2 mmol), KOAc (20 mg, 0.2 mmol), and TFE 1.0 ml were used. Resulting solution was purged with O$_2$ ballon for 0.5 min, then the reaction mixture was stirred at 80 °C for 3.0 h. After completion of the reaction, the reaction mixture was diluted with EtOAc and washed once with H$_2$O. Then organic layer was dried over Na$_2$SO$_4$ and concentrated on rotavapor under reduced pressure. Finally, the residue was purified by silica gel column chromatography (Petroleum ether:Ethyl acetate = 1:1) to **5d** (36 mg) in 72% yield. ^{1}H-NMR (400 MHz, CDCl$_3$) δ (ppm) 8.83 (m, 1H), 8.22 (t, *J* = 8.8 Hz, 2H), 7.90 (d, *J* = 8.0 Hz, 1H), 7.70 (s, 1H), 7.57 (t, *J* = 8.4 Hz, 2H), 7.48-7.40 (m, 2H), 7.34-7.32 (m, 3H), 7.18-7.16 (m, 2H), 6.52 (s, 1H), 4.90-4.89 (m, 2H), 3.40

(d, *J* = 16.8 Hz, 1H), 3.10 (d, *J* = 16.8 Hz, 1H);^{13}C-NMR (100 MHz, $CDCl_3$) δ (ppm) 169.2, 163.0, 151.6, 144.3, 138.6, 138.2, 136.5, 135.4, 135.1, 131.3, 130.3, 130.0, 129.8, 129.4, 128.7, 128.7, 128.6, 128.6, 128.4, 127.8, 126.3, 124.3, 122.1, 106.8, 67.1, 40.1; MS (ESI) calcd for $C_{27}H_{19}BrN_2O_3$ $[M+H]^+$:498.06, found 498.99.



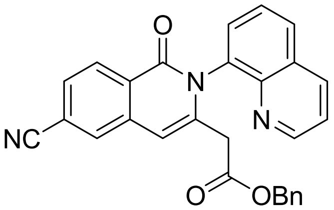
Benzyl 2-(1-oxo-2-(quinolin-8-yl)-6-(trifluoromethyl)-1,2-dihydroisoquinolin-3-yl) acetate (5e)

Following the general procedure II, *N*-(quinolin-8-yl)-4-(trifluoromethyl)benzamide (32 mg, 0.1 mmol), benzyl buta-2,3-dienoate (53 mg, 0.3 mmol), $Co(acac)_2$ (5.4 mg, 0.02 mmol), $Mn(OAc)_2$ (35 mg, 0.2 mmol), KOAc (20 mg, 0.2 mmol), and TFE 1.0 ml were used. Resulting solution was purged with O_2 ballon for 0.5 min, then the reaction mixture was stirred at 80 °C for 3.0 h. After completion of the reaction, the reaction mixture was diluted with EtOAc and washed once with H_2O. Then organic layer was dried over Na_2SO_4 and concentrated on rotavapor under reduced pressure. Finally, the residue was purified by silica gel column chromatography (Petroleum ether:Ethyl acetate = 1:1) to **5e** (34 mg) in 70% yield. ^{1}H-NMR (400 MHz, $CDCl_3$) δ (ppm) 8.83 (dd, *J* = 4.0, 1.6 Hz, 1H), 8.49 (d, *J* = 8.4 Hz, 1H), 8.23 (dd, *J* = 8.4, 1.6 Hz, 1H), 7.92 (dd, *J* = 8.4, 1.2 Hz, 1H), 7.83 (s, 1H), 7.67 (d, *J* = 8.4 Hz, 1H), 7.59 (dd, *J* = 7.2, 1.2 Hz, 1H), 7.49-7.42 (m, 2H), 7.34-7.31 (m, 3H), 7.19-7.17 (m, 2H), 4.95-4.87 (m, 1H), 3.42 (d, *J* = 16.8 Hz, 1H), 3.11 (d, *J* = 16.8 Hz, 1H); MS (ESI) calcd for $C_{28}H_{19}F_3N_2O_3$ $[M+H]^+$: 488.13, found 489.04.

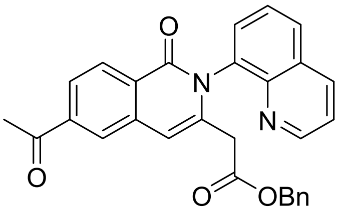


Benzyl-2-(6-methyl-1-oxo-2-(quinolin-8-yl)-1,2-dihydroisoquinolin-3-yl)acetate (5f)

Following the general procedure II, 4-methyl-*N*-(quinolin-8-yl)benzamide (26.2 mg, 0.1 mmol), benzyl buta-2,3-dienoate (53 mg, 0.3 mmol), $Co(acac)_2$ (5.4 mg, 0.02 mmol), $Mn(OAc)_2$ (35 mg, 0.2 mmol), KOAc (20 mg, 0.2 mmol), and TFE 1.0 ml were used. Resulting solution was purged with O_2 ballon for 0.5 min, then the reaction mixture was stirred at 80 °C for 3.0 h. After completion of the reaction, the reaction mixture was diluted with EtOAc and washed once with H_2O. Then organic layer was dried over Na_2SO_4 and concentrated on rotavapor under reduced pressure. Finally, the residue was purified by silica gel column chromatography (Petroleum ether:Ethyl acetate = 1:1) to **5f** (25 mg) in 57% yield. ^{1}H-NMR (400 MHz, $CDCl_3$) δ (ppm) 8.84 (dd, *J* = 4.4, 1.6 Hz, 1H), 8.27 (d, *J* = 8.0 Hz, 1H), 8.21 (dd, *J* = 8.4, 1.6 Hz, 1H), 7.89 (dd, *J* = 8.4, 1.2 Hz, 1H), 7.58 (dd, *J* = 7.2, 1.2 Hz, 1H), 7.48-7.40 (m, 2H), 7.34-7.28 (m, 5H), 7.18-7.15 (m, 2H), 6.56 (s, 1H), 4.90-4.88 (m, 2H), 3.39 (d, *J* = 16.8 Hz, 1H), 3.10 (d, *J* = 16.8 Hz, 1H), 2.50 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ (ppm) 169.4, 163.7, 151.6, 144.7, 143.3, 137.4, 136.5, 136.5, 135.9, 135.3, 131.6, 129.7, 129.5, 128.7, 128.7, 128.6, 128.5, 128.5, 126.4, 125.9, 123.6, 122.0, 108.0, 67.0, 40.2, 22.1; MS (ESI) calcd for $C_{27}H_{19}BrN_2O_3$ $[M+H]^+$: 434.16, found 435.18.

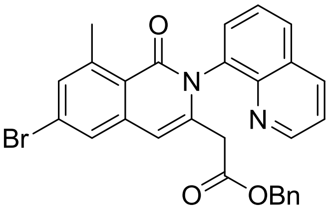


Benzyl 2-(6-cyano-1-oxo-2-(quinolin-8-yl)-1,2-dihydroisoquinolin-3-yl)acetate (5g)
Following the general procedure I, 4-cyano-*N*-(quinolin-8-yl)benzamide (27 mg, 0.1 mmol), benzyl buta-2,3-dienoate (53 mg, 0.3 mmol), $Co(acac)_2$ (5.4 mg, 0.02 mmol), $Mn(OAc)_2$ (35 mg, 0.2 mmol), KOAc (20 mg, 0.2 mmol), and TFE 1.0 ml were used. Resulting solution was purged with O_2 ballon for 0.5 min, then the reaction mixture was stirred at 80 °C for 3.0 h. After completion of the reaction, the reaction mixture was diluted with EtOAc and washed once with H_2O. Then organic layer was dried over Na_2SO_4 and concentrated on rotavapor under reduced pressure. Finally, the residue was purified by silica gel column chromatography (Petroleum ether:Ethyl acetate = 1:1) to **5g** (37 mg) in 80% yield. ^{1}H-NMR (400 MHz, $CDCl_3$) δ (ppm) 8.83 (d, *J* = 2.8 Hz, 1H), 8.46 (d, *J* = 8.4 Hz, 1H), 8.23 (d, *J* = 8.0 Hz, 1H), 7.92 (d, *J* = 8.0 Hz, 1H), 7.87 (s, 1H), 7.65 (d, *J* = 8.0 Hz, 1H), 7.58 (d, *J* = 7.2 Hz, 1H), 7.49-7.43 (m, 2H), 7.34-7.33 (m, 3H), 7.17 (d, *J* = 4.0 Hz, 2H), 6.62 (s, 1H), 4.95-4.89 (m, 2H), 3.42 (d, *J* = 17.2 Hz, 1H), 3.11 (d, *J* = 16.8 Hz, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ (ppm) 168.9, 162.6, 151.8, 144.1, 139.1, 137.2, 136.6, 135.0, 135.0, 131.1, 130.7, 130.1, 129.6, 129.5, 128.7, 128.7, 128.7 128.6, 128.0, 126.4, 122.3, 118.4, 116.2, 106.8, 67.3, 40.1; MS (ESI) calcd for $C_{28}H_{19}N_3O_3$ $[M+H]^+$: 445.14, found 446.09.



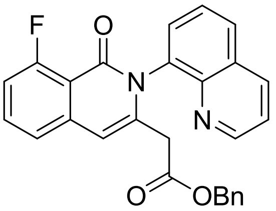
Benzyl 2-(6-acetyl-1-oxo-2-(quinolin-8-yl)-1,2-dihydroisoquinolin-3-yl)acetate (5h)
Following the general procedure I, 4-acetyl-*N*-(quinolin-8-yl)benzamide (29 mg, 0.1 mmol), benzyl buta-2,3-dienoate (53 mg, 0.3 mmol), $Co(acac)_2$ (5.4 mg, 0.02 mmol), $Mn(OAc)_2$ (35 mg, 0.2 mmol), KOAc (20 mg, 0.2 mmol), and TFE 1.0 ml were used. Resulting solution was purged with O_2 ballon for 0.5 min, then the reaction mixture

was stirred at 80 °C for 3.0 h. After completion of the reaction, the reaction mixture was diluted with EtOAc and washed once with H_2O. Then organic layer was dried over Na_2SO_4 and concentrated on rotavapor under reduced pressure. Finally, the residue was purified by silica gel column chromatography (Petroleum ether:Ethyl acetate = 1:1) to **5h** (38 mg) in 83% yield. ^{1}H-NMR (400 MHz, $CDCl_3$) δ (ppm) 8.83 (dd, J = 4.0, 1.2 Hz, 1H), 8.46 (d, J = 8.4 Hz, 1H), 8.23 (dd, J = 8.4, 1.2 Hz, 1H), 8.13 (d, J = 0.8 Hz, 1H), 8.00 (dd, J = 8.4, 1.2 Hz, 1H), 7.92 (d, J = 7.6 Hz, 1H), 7.59 (d, J = 7.2 Hz, 1H), 7.49-7.42 (m, 2H), 7.34-7.32 (m, 3H), 7.18-7.17(m, 2H), 6.70 (s, 1H), 4.95-4.90 (m, 1H), 3.43 (d, J = 16.8 Hz, 1H), 3.12 (d, J = 16.8 Hz, 1H), 2.72 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ (ppm) 198.0, 169.1, 163.1, 151.7, 144.3, 140.1, 137.7, 137.1, 136.5, 135.4, 135.2, 131.3, 129.9, 129.5, 129.1, 128.7, 128.6, 128.6, 128.4, 126.6, 126.4, 125.5, 122.1, 108.0, 67.1, 40.1, 27.2; MS (ESI) calcd for $C_{29}H_{22}N_2O_4$ $[M+H]^+$: 462.16, found 463.11.



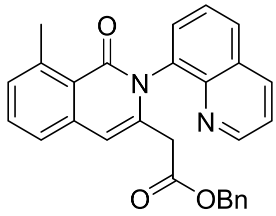
Benzyl 2-(6-bromo-8-methyl-1-oxo-2-(quinolin-8-yl)-1,2-dihydroisoquinolin-3-yl)acetate (5i)

Following the general procedure I, 4-bromo-2-methyl-N-(quinolin-8-yl)benzamide (34 mg, 0.1 mmol), benzyl buta-2,3-dienoate (53 mg, 0.3 mmol), $Co(acac)_2$ (5.4 mg, 0.02 mmol), $Mn(OAc)_2$ (35 mg, 0.2 mmol), KOAc (20 mg, 0.2 mmol), and TFE 1.0 ml were used. Resulting solution was purged with O_2 ballon for 0.5 min, then the reaction mixture was stirred at 80 °C for 3.0 h. After completion of the reaction, the reaction mixture was diluted with EtOAc and washed once with H_2O. Then organic layer was dried over Na_2SO_4 and concentrated on rotavapor under reduced pressure. Finally, the residue was purified by silica gel column chromatography (Petroleum ether:Ethyl acetate = 1:1) to **5i** (35 mg) in 68% yield. ^{1}H-NMR (400 MHz, $CDCl_3$) δ (ppm) 8.85 (dd, J = 4.0, 1.6 Hz, 1H), 8.21 (dd, J = 8.4, 2.0 Hz, 1H), 7.89 (dd, J = 8.0, 1.2 Hz, 1H), 7.58 (d, J = 1.2 Hz, 1H), 7.56 (d, J = 1.2 Hz, 1H), 7.52 (d, J = 2.0 Hz, 1H), 7.48-7.41 (m, 2H), 7.35-7.31(m, 3H), 7.18-7.15 (m, 2H), 6.45 (s, 1H), 4.95-4.89 (m, 2H), 3.34 (d, J = 16.8 Hz, 1H), 3.04 (d, J = 16.8 Hz, 1H), 2.79 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ (ppm) 169.1, 164.0, 151.7, 144.8, 144.4, 140.2, 137.7, 136.6, 135.8, 135.2, 132.6, 131.4, 129.7, 129.5, 128.7, 128.7, 128.6, 126.7, 126.7, 126.4, 122.8, 122.1, 107.3, 67.1, 40.0, 23.7; MS (ESI) calcd for $C_{28}H_{21}BrN_2O_3$ $[M+H]^+$: 512.07, found 512.93.



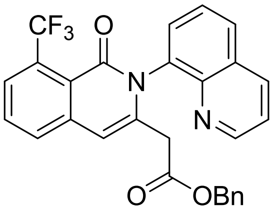
Benzyl 2-(8-fluoro-1-oxo-2-(quinolin-8-yl)-1,2-dihydroisoquinolin-3-yl)acetate (5j)

Following the general procedure I, 4-bromo-2-methyl-N-(quinolin-8-yl)benzamide (34 mg, 0.1 mmol), benzyl buta-2,3-dienoate (53 mg, 0.3 mmol), Co(acac)$_2$ (5.4 mg, 0.02 mmol), Mn(OAc)$_2$ (35 mg, 0.2 mmol), KOAc (20 mg, 0.2 mmol), and TFE 1.0 ml were used. Resulting solution was purged with O_2 ballon for 0.5 min, then the reaction mixture was stirred at 80 °C for 3.0 h. After completion of the reaction, the reaction mixture was diluted with EtOAc and washed once with H_2O. Then organic layer was dried over Na_2SO_4 and concentrated on rotavapor under reduced pressure. Finally, the residue was purified by silica gel column chromatography (Petroleum ether:Ethyl acetate = 1:1) to **5j** (34 mg) in 78% yield. ^{1}H-NMR (400 MHz, $CDCl_3$) δ (ppm) 8.84 (dd, J = 4.4, 1.6 Hz, 1H), 8.20 (dd, J = 8.4, 1.6 Hz, 1H), 7.89 (dd, J = 8.0, 1.2 Hz, 1H), 7.61-7.56 (m, 2H), 7.48-7.41 (m, 2H), 7.35-7.29 (m, 4H), 7.18-7.15 (m, 2H), 7.13-7.08 (m, 1H), 6.58 (d, J = 1.6 Hz, 1H), 4.94-4.86 (m, 2H), 3.38 (d, J = 17.2 Hz, 1H), 3.10 (d, J = 16.8 Hz, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ (ppm) 169.1, 162.9 (d, $J_{C\text{-}F}$ = 263 Hz), 160.8 (d, $J_{C\text{-}F}$ = 4.8 Hz), 144.5, 139.9, 137.8, 136.5, 135.2 (d, $J_{C\text{-}F}$ = 12 Hz), 133.6 (d, $J_{C\text{-}F}$ = 12 Hz), 131.6, 129.7, 129.4, 128.7, 128.6 (d, $J_{C\text{-}F}$ = 3.7 Hz), 126.3, 122.0, 121.9 (d, $J_{C\text{-}F}$ = 4.3 Hz), 114.8 (d, $J_{C\text{-}F}$ = 5.7 Hz), 113.7 (d, $J_{C\text{-}F}$ = 3.7 Hz), 107.3 (d, $J_{C\text{-}F}$ = 4.0 Hz), 67.1, 40.1; MS (ESI) calcd for $C_{27}H_{19}FN_2O_3$ $[M+H]^+$: 438.14, found 439.07.



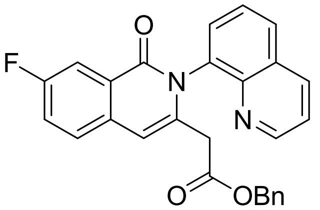
Benzyl 2-(8-methyl-1-oxo-2-(quinolin-8-yl)-1,2-dihydroisoquinolin-3-yl)acetate (5k)

Following the general procedure I, 2-methyl-N-(quinolin-8-yl)benzamide (27 mg, 0.1 mmol), benzyl buta-2,3-dienoate (53 mg, 0.3 mmol), Co(acac)$_2$ (5.4 mg, 0.02 mmol), Mn(OAc)$_2$ (35 mg, 0.2 mmol), KOAc (20 mg, 0.2 mmol), and TFE 1.0 ml were used. Resulting solution was purged with O_2 ballon for 0.5 min, then the reaction mixture was stirred at 80 °C for 3.0 h. After completion of the reaction, the reaction mixture was diluted with EtOAc and washed once with saturated aqueous $NaHCO_3$. Then organic layer was dried over Na_2SO_4 and concentrated on rotavapor under reduced pressure. Finally, the residue was purified by silica gel column chromatography (Petroleum ether:Ethyl acetate = 1:1) to **5k** (26 mg) in 60% yield. ^{1}H-NMR (400 MHz, $CDCl_3$) δ (ppm) 8.87-8.86 (m, 1H), 8.21 (dd, J = 8.0 Hz, J = 1.2 Hz, 1H), 7.89 (d, J = 8.4 Hz, 1H), 7.60 (d, J = 6.4 Hz, 1H), 7.52-7.45 (m, 2H), 7.44-7.41 (m, 1H), 7.38-7.32 (m, 5H), 7.23 (d, J = 7.2 Hz, 1H), 7.18-7.16 (m, 2H), 6.57 (s, 1H), 4.93-4.86 (m, 2H), 3.37 (d, J = 16.8 Hz, 1H), 3.06 (d, J = 16.8 Hz, 1H), 2.85 (s, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ (ppm) 169.4, 164.5, 151.6, 144.6, 142.4, 138.9, 136.5, 136.2, 135.2, 132.0, 131.6, 130.0, 129.5, 128.7, 126.4, 124.5, 124.1, 122.0, 108.5, 67.0, 40.0, 23.9; MS (ESI) calcd for $C_{28}H_{22}N_2O_3$ $[M+H]^+$: 435.16, found 435.08.



Benzyl 2-(1-oxo-2-(quinolin-8-yl)-8-(trifluoromethyl)-1,2-dihydroisoquinolin-3-yl) acetate (5l)

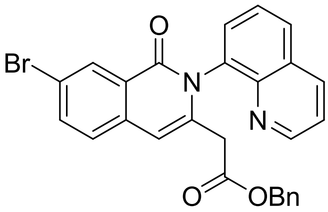
Following the general procedure I, N-(quinolin-8-yl)-2-(trifluoromethyl)benzamide (32 mg, 0.1 mmol), benzyl buta-2,3-dienoate (53 mg, 0.3 mmol), Co(acac)$_2$ (5.4 mg, 0.02 mmol), Mn(OAc)$_2$ (35 mg, 0.2 mmol), KOAc (20 mg, 0.2 mmol), and TFE 1.0 ml were used. Resulting solution was purged with O_2 ballon for 0.5 min, then the reaction mixture was stirred at 80 °C for 3.0 h. After completion of the reaction, the reaction mixture was diluted with EtOAc and washed once with H_2O. Then organic layer was dried over Na_2SO_4 and concentrated on rotavapor under reduced pressure. Finally, the residue was purified by silica gel column chromatography (Petroleum ether:Ethyl acetate = 1:1) to **5l** (36.5 mg) in 75% yield. ^{1}H-NMR (400 MHz, CDCl$_3$) δ (ppm) 8.83 (dd, *J* = 4.0, 1.2 Hz, 1H), 8.20 (dd, *J* = 8.4, 1.2 Hz, 1H), 7.90-7.87 (m, 2H), 7.72-7.69 (m, 2H), 7.61 (d, *J* = 7.2 Hz, 1H), 7.48-7.40 (m, 2H), 7.34-7.32 (m, 3H), 7.17-7.15 (m, 2H), 6.62 (s, 1H), 4.94-4.89 (m, 2H), 3.39 (d, *J* = 16.8 Hz, 1H), 3.10 (d, *J* = 16.8 Hz, 1H); MS (ESI) calcd for $C_{28}H_{19}F_3N_2O_3$ [M+H]$^+$: 489.13, found 489.04.

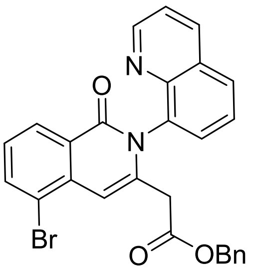


Benzyl-2-(7-fluoro-1-oxo-2-(quinolin-8-yl)-1,2-dihydroisoquinolin-3-yl)acetate (5m)

Following the general procedure I, *N*-(quinolin-8-yl)-2-(trifluoromethyl)benzamide (26.6 mg, 0.1 mmol), benzyl buta-2,3-dienoate (53 mg, 0.3 mmol), Co(acac)$_2$ (5.4 mg, 0.02 mmol), Mn(OAc)$_2$ (35 mg, 0.2 mmol), KOAc (20 mg, 0.2 mmol), and TFE 1.0 ml were used. Resulting solution was purged with O_2 ballon for 0.5 min, then the reaction mixture was stirred at 80 °C for 3.0 h. After completion of the reaction, the reaction mixture was diluted with EtOAc and washed once with H_2O. Then organic layer was dried over Na_2SO_4 and concentrated on rotavapor under reduced pressure. Finally, the residue was purified by silica gel column chromatography (Petroleum ether:Ethyl acetate = 1:1) to **5m** (28.9 mg) in 66% yield. ^{1}H-NMR (400 MHz, CDCl$_3$) δ (ppm) 8.84 (dd, *J* = 4.4, 1.6 Hz, 1H), 8.22 (dd, *J* = 8.4, 1.6 Hz, 1H), 8.17 (d, *J* = 7.6 Hz, 1H), 7.91 (dd, *J* = 8.4, 1.2 Hz, 1H), 7.58 (dd, *J* = 7.6, 1.6 Hz, 1H), 7.48-7.35 (m, 4H), 7.34-7.31 (m, 3H), 7.18-7.15 (m, 2H), 6.86 (s, 1H), 4.90-4.89 (m, 2H), 3.45 (d, *J* = 17.2 Hz, 1H), 3.11 (d, *J* = 17.2 Hz, 1H); MS (ESI) calcd for $C_{27}H_{19}FN_2O_3$ [M+H]$^+$: 439.14, found

439.03.

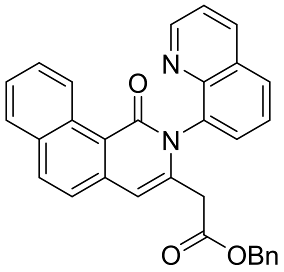




Benzyl-2-(7-bromo-1-oxo-2-(quinolin-8-yl)-1,2-dihydroisoquinolin-3-yl)acetate (5n)

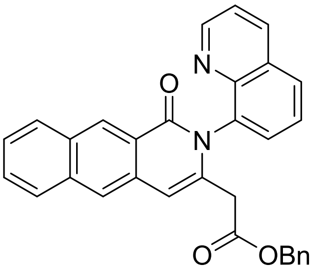
Benzyl-2-(5-bromo-1-oxo-2-(quinolin-8-yl)-1,2-dihydroisoquinolin-3-yl)acetate (5n’)

Following the general procedure I, 3-bromo-N-(quinolin-8-yl)benzamide (33 mg, 0.1 mmol), benzyl buta-2,3-dienoate (53 mg, 0.3 mmol), Co(acac)$_2$ (5.4 mg, 0.02 mmol), Mn(OAc)$_2$ (35 mg, 0.2 mmol), KOAc (20 mg, 0.2 mmol), and TFE 1.0 ml were used. Resulting solution was purged with O_2 ballon for 0.5 min, then the reaction mixture was stirred at 80 ^{o}C for 3.0 h. After completion of the reaction, the reaction mixture was diluted with EtOAc and washed once with H_2O. Then organic layer was dried over Na_2SO_4 and concentrated on rotavapor under reduced pressure. Finally, the residue was purified by silica gel column chromatography (Petroleum ether:Ethyl acetate = 1:1) to **5n** (22 mg) in 42% yield and **5n’** (15 mg) in 28% yield. For **5n**, ^{1}H-NMR (400 MHz, $CDCl_3$) δ (ppm) 8.83 (dd, *J* = 4.4, 2.0 Hz, 1H), 8.51 (d, *J* = 2.0 Hz, 1H), 8.22 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.91 (dd, *J* = 8.4, 1.6 Hz, 1H), 7.76 (d, *J* = 8.4, 2.0 Hz, 1H), 7.58 (d, *J* = 7.2, 1.2 Hz, 1H), 7.49-7.41 (m, 3H), 7.34-7.31 (m, 3H), 7.18-7.15 (m, 2H), 6.59 (s, 1H), 4.93-4.86 (m, 2H), 3.39 (d, *J* = 17.2 Hz, 1H), 3.08 (d, *J* = 17.2 Hz, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ (ppm) 169.1, 162.5, 151.7, 144.4, 137.3, 136.5, 135.9, 135.9, 135.5, 135.2, 131.3, 131.1, 129.9, 129.5, 128.7, 128.7, 128.7, 127.8, 127.1, 126.4, 122.1, 120.6, 107.4, 67.1, 40.2; MS (ESI) calcd for $C_{27}H_{19}BrN_2O_3$ $[M+H]^+$: 498.06, found 498.94. For **5n’**, ^{1}H-NMR (400 MHz, $CDCl_3$) δ (ppm) 8.84 (dd, *J* = 4.4, 1.6 Hz, 1H), 8.36 (d, *J* = 8.0 Hz, 1H), 8.22 (dd, *J* = 8.4, 1.6 Hz, 1H), 7.94-7.90 (m, 2H), 7.58 (dd, *J* = 7.2, 1.2 Hz, 1H), 7.48-7.42 (m, 2H), 7.35-7.30 (m,4H), 7.18-7.16 (m, 2H), 7.00 (s, 1H), 4.94-4.86 (m, 2H), 3.49 (d, *J* = 17.2 Hz, 1H), 3.13 (d, *J* = 17.2 Hz, 1H), ^{13}C-NMR (100 MHz, $CDCl_3$) δ (ppm) 169.1, 163.0, 151.7, 144.3, 138.0, 136.5, 136.5, 135.4, 135.2, 131.4, 129.9, 129.5, 128.7, 128.7, 128.7, 128.6, 128.2, 127.4, 127.3, 126.4, 122.2, 120.8, 106.7, 67.1, 40.5; MS (ESI) calcd for $C_{27}H_{19}BrN_2O_3$ $[M+H]^+$: 498.06, found 498.89.



Benzyl-2-(1-oxo-2-(quinolin-8-yl)-1,2-dihydrobenzo[*H*]isoquinolin-3-yl)acetate (5o)

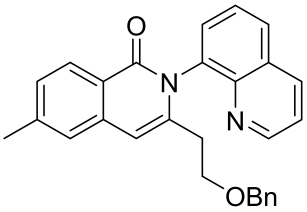
Following the general procedure II, *N*-(quinolin-8-yl)-1-naphthamide (29.8 mg, 0.1 mmol), benzyl buta-2,3-dienoate (53 mg, 0.3 mmol), Co(acac)$_2$ (5.4 mg, 0.02 mmol), Mn(OAc)$_2$ (35 mg, 0.2 mmol), KOAc (39.8 mg, 0.2 mmol), and TFE 1.0 ml were used. Resulting solution was purged with O$_2$ ballon for 0.5 min, then the reaction mixture was stirred at 80 °C for 3.5 h. After completion of the reaction, the reaction mixture was diluted with EtOAc and washed once with saturated brine. Then organic layer was dried over Na$_2$SO$_4$ and concentrated on rotavapor under reduced pressure. Finally, the residue was purified by silica gel column chromatography (Petroleum ether:Ethyl acetate = 1:1) to **5o** (25 mg) in 53% yield. ^{1}H-NMR (400 MHz, CDCl$_3$) δ (ppm) 10.03 (d, *J* = 8.8 Hz, 1H), 8.84 (d, *J*= 4.0 Hz, 1H), 8.24 (d, *J* = 8.4 Hz, 1H), 8.07 (d, *J*= 8.4 Hz, 1H), 7.94 (d, *J* = 8.4 Hz, 1H), 7.90 (d, *J* = 7.2 Hz, 1H), 7.67-7.53 (m, 4H), 7.52 (t, *J* = 8.0 Hz, 1H), 7.44 (dd, *J* = 8.0 Hz, *J* = 4.0 Hz, 1H), 7.34-7.32 (m, 3H), 7.20-7.17 (m, 2H), 6.79 (s, 1H), 4.93 (dd, *J* = 8.0 Hz, *J* = 17.6 Hz, 2H), 3.50 (d, *J* = 16.8 Hz, 1H), 3.19 (d, *J* = 16.8 Hz, 1H). ^{13}C-NMR (100 MHz, CDCl$_3$) δ (ppm) 169.2, 164.2, 151.8, 144.5, 139.2, 138.0, 136.6, 136.3, 135.2, 134.4, 132.6, 132.3, 131.3, 129.7, 129.6, 128.8, 128.7, 128.5, 128.4, 127.5, 126.5, 126.4, 124.9, 122.2, 119.0, 108.8, 67.2, 40.2; MS (ESI) calcd for C$_{31}$H$_{22}$N$_2$O$_3$ [M+H]$^+$: 471.16, found 471.06.



Benzyl 2-(1-oxo-2-(quinolin-8-yl)-1,2-dihydrobenzo[g]isoquinolin-3-yl)acetate (5p)

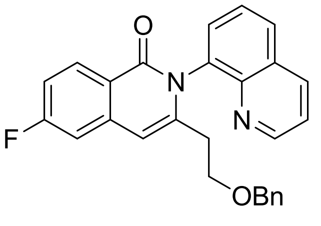
Following the general procedure II, *N*-(quinolin-8-yl)-2-naphthamide (29.8 mg, 0.1 mmol), benzyl buta-2,3-dienoate (53 mg, 0.3 mmol), Co(acac)$_2$ (5.4 mg, 0.02 mmol), Mn(OAc)$_2$ (35 mg, 0.2 mmol), KOAc (19.8 mg, 0.2 mmol), and TFE 1.0 ml were used. Resulting solution was purged with O$_2$ ballon for 0.5 min, then the reaction mixture was stirred at 80 °C for 3.0 h. After completion of the reaction, the reaction mixture was diluted with EtOAc and washed once with saturated brine. Then organic layer was dried over Na$_2$SO$_4$ and concentrated on rotavapor under reduced pressure. Finally, the residue was purified by silica gel column chromatography (Petroleum ether:Ethyl acetate = 1:1) to **5p** (31 mg) in 67% yield. ^{1}H-NMR (400 MHz, CDCl$_3$) δ (ppm) 9.01

(s, 1H), 8.85 (dd, J = 1.6 Hz, J = 4.0 Hz,, 1H), 8.22 (dd, J = 1.6 Hz, J = 8.4 Hz, 1H), 8.03 (d, J = 8.4 Hz, 1H), 8.02 (s, 1H)，7.95 (d, J = 8.4 Hz, 1H), 7.91 (dd, J = 1.2 Hz, J = 8.4 Hz, 1H), 7.6m (dd, J = 1.6 Hz, J = 7.6 Hz, 1H), 7.59 (m, 1H), 7.49 (m, 2H), 7.43 (q, J = 4.0 Hz, 1H), 7.32 (m, 3H), 7.17 (m, 1H), 6.74 (s, 1H), 4.91 (d, J = 12.0 Hz, 1H), 4.87 (d, J = 12.0 Hz, 1H), 3.43 (d, J = 17.2 Hz, 1H), 3.12 (d, J = 17.2 Hz, 1H). ^{13}C-NMR (100 MHz, CDCl$_3$) δ (ppm) 169.5, 164.1, 151.6, 144.7, 137.0, 136.5, 135.8, 135.4, 135.3, 133.0, 132.0, 131.6, 129.8, 129.8, 129.7, 129.4, 128.7, 128.6, 128.57, 128.2, 127.7, 126.3, 125.9, 124.2, 124.1, 122.0, 108.2, 67.0, 40.3; MS (ESI) calcd for $C_{31}H_{22}N_2O_3$ [M+H]$^+$: 471.16, found 471.09.



3-(2-(benzyloxy)ethyl)-6-methyl-2-(quinolin-8-yl)isoquinolin-1(2*H*)-one (5q)

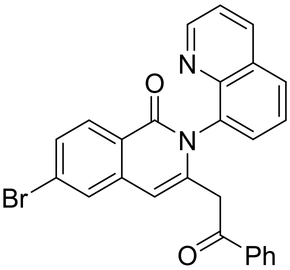
Following the general procedure II, 4-methyl-*N*-(quinolin-8-yl)benzamide (26.2 mg, 0.1 mmol), benzyl buta-2,3-dienoate (53 mg, 0.3 mmol), Co(acac)$_2$ (5.4 mg, 0.02 mmol), Mn(OAc)$_2$ (35 mg, 0.2 mmol), KOAc (39.8 mg, 0.2 mmol), and TFE 1.0 ml were used. Resulting solution was purged with O$_2$ ballon for 0.5 min, then the reaction mixture was stirred at 80 °C for 2.5 h. After completion of the reaction, the reaction mixture was diluted with EtOAc and washed once with saturated brine. Then organic layer was dried over Na$_2$SO$_4$ and concentrated on rotavapor under reduced pressure. Finally, the residue was purified by silica gel column chromatography (Petroleum ether:Ethyl acetate = 1:1) to **5q** (26 mg) in 62% yield. ^{1}H-NMR (400 MHz, CDCl$_3$) δ (ppm) 8.83 (d, J= 2.8 Hz, 1H), 8.27 (d, J = 8.4 Hz, 1H), 8.21 (d, J= 8.4 Hz, 1H), 7.94 (m, 1H), 7.63 (d, J = 4.8 Hz, 1H), 7.40 (q, J= 4.4 Hz, 4H), 7.32-7.25 (m, 5H), 7.19 (d, J = 7.2 Hz, 2H), 6.48 (s, 1H), 4.35 (m, 2H), 3.57 (m, 1H), 3.50 (m, 1H), 2.50 (s, 3H). ^{13}C-NMR (100 MHz, CDCl$_3$) δ (ppm) 163.8, 151.5, 144.8, 143.1, 140.9, 138.0, 137.6, 137.59, 136.4, 130.6, 129.5, 129.3, 128.5, 128.3, 127.9, 127.8, 126.4, 125.5, 123.0, 121.9, 105.1, 73.1, 68.2, 33.6, 22.0; MS (ESI) calcd for $C_{28}H_{24}N_2O_2$ [M+H]$^+$: 421.18, found 421.19.



3-(2-(benzyloxy)ethyl)-6-fluoro-2-(quinolin-8-yl)isoquinolin-1(2*H*)-one (5r)

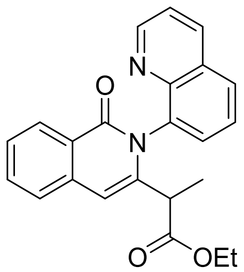
Following the general procedure II, 4-flouro-*N*-(quinolin-8-yl)benzamide (26.2 mg, 0.1 mmol), benzyl buta-2,3-dienoate (53 mg, 0.3 mmol), Co(acac)$_2$ (5.4 mg, 0.02 mmol),

$Mn(OAc)_2$ (35 mg, 0.2 mmol), KOAc (39.8 mg, 0.2 mmol), and TFE 1.0 ml were used. Resulting solution was purged with O_2 ballon for 0.5 min, then the reaction mixture was stirred at 80 °C for 2.5 h. After completion of the reaction, the reaction mixture was diluted with EtOAc and washed once with saturated brine. Then organic layer was dried over Na_2SO_4 and concentrated on rotavapor under reduced pressure. Finally, the residue was purified by silica gel column chromatography (Petroleum ether:Ethyl acetate = 1:1) to **5r** (32 mg) in 75% yield. ^{1}H-NMR (400 MHz, $CDCl_3$) δ (ppm) 8.84 (dd, *J* = 4.0, 1.6 Hz, 1H), 8.39-8.35 (m, 1H), 8.23 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.96 (dd, *J* = 6.8, 2.4 Hz, 1H), 7.67-7.61 (m, 2H), 7.44-7.41 (m, 1H), 7.32-7.27 (m, 3H), 7.21-7.19 (m, 2H), 7.16-7.11 (m, 2H), 6.48 (s, 1H), 4.37-4.36 (m, 2H), 3.61-3.46 (m, 2H), 2.47 (t, *J* = 6.8 Hz, 2H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ (ppm) 165.52 (d, $J_{C\text{-}F}$ = 250.52 Hz, 1C), 163.0, 151.5, 144.5, 142.5, 139.62 (d, $J_{C\text{-}F}$ = 10.68 Hz, 1C), 137.74, 136.22 (d, $J_{C\text{-}F}$ = 10.04 Hz, 1C), 130.38, 129.44, 128.55, 128.44, 127.99, 127.82, 127.78, 126.33, 121.92, 121.70, 114.7 (d, $J_{C\text{-}F}$ = 23.33 Hz, 1C), 110.4 (d, $J_{C\text{-}F}$ = 21.68 Hz, 1C), 104.5 (d, $J_{C\text{-}F}$ = 3.08 Hz, 1C), 73.0, 67.7, 33.5; MS (ESI) calcd for $C_{27}H_{21}FN_2O_2$ $[M+H]^+$: 424.16, found 425.08.



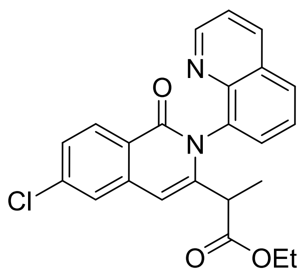
3-(2-oxo-2-phenylethyl)-2-(quinolin-8-yl)isoquinolin-1(2*H*)-one (5s)

Following the general procedure II, 4-bromo-*N*-(quinolin-8-yl)benzamide (32.6 mg, 0.1 mmol), 1-phenylbuta-2,3-dien-1-one (43.2 mg, 0.3 mmol), $Co(acac)_2$ (5.4 mg, 0.02 mmol), $Mn(OAc)_2$ (35 mg, 0.2 mmol), KOAc (39.8 mg, 0.2 mmol), and TFE 1.0 ml were used. Resulting solution was purged with O_2 ballon for 0.5 min, then the reaction mixture was stirred at 80 °C for 2.5 h. After completion of the reaction, the reaction mixture was diluted with EtOAc and washed once with saturated brine. Then organic layer was dried over Na_2SO_4 and concentrated on rotavapor under reduced pressure. Finally, the residue was purified by silica gel column chromatography (Petroleum ether:Ethyl acetate = 1:1) to **5s** (28.5 mg) in 61% yield. ^{1}H-NMR (400 MHz, $CDCl_3$) δ (ppm) 8.67 (d, *J*= 2.8 Hz, 1H), 8.16 (d, *J* = 8.4 Hz, 1H), 8.07 (d, *J*= 8.4 Hz, 1H), 7.76 (d, *J* = 8.0 Hz, 1H), 7.75 (s, 1H), 7.62 (d, *J* = 8.0 Hz, 1H), 7.55 (d, *J* = 8.0 Hz, 1H), 7.51(m, 4H), 7.26 (m, 3H), 7.10 (s, 1H), 4.09 (d, *J* = 8.0 Hz, 2H), 4.07 (d, *J* = 8.0 Hz, 1H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ (ppm) 162.2, 160.4, 151.0, 144.2, 136.6, 136.4, 136.2, 133.8, 133.0, 130.7, 130.4, 130.3, 131.1, 129.6, 129.2, 129.1, 128.4, 128.3, 126.9, 126.2, 121.8, 112.0, 61.2; MS (ESI) calcd for $C_{26}H_{17}BrN_2O_2$ $[M+H]^+$: 469.05, found 469.04.



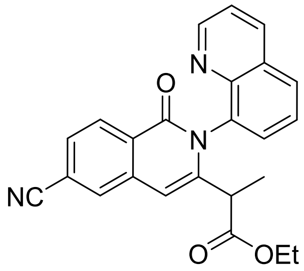
Ethyl 2-(1-oxo-2-(quinolin-8-yl)-1,2-dihydroisoquinolin-3-yl)propanoate (5t)

Following the general procedure II, *N*-(quinolin-8-yl)benzamide (24.8 mg, 0.1 mmol), ethyl 2-methylbuta-2,3-dienoate (37.8 mg, 0.3 mmol), Co(acac)$_2$ (5.4 mg, 0.02 mmol), Mn(OAc)$_2$ (35 mg, 0.2 mmol), KOAc (19.6 mg, 0.2 mmol), and TFE 1.0 ml were used. Resulting solution was purged with O$_2$ ballon for 0.5 min, then the reaction mixture was stirred at 80 °C for 3.5 h. After completion of the reaction, the reaction mixture was diluted with EtOAc and washed once with saturated brine. Then organic layer was dried over Na$_2$SO$_4$ and concentrated on rotavapor under reduced pressure. Finally, the residue was purified by silica gel column chromatography (Petroleum ether:Ethyl acetate = 1:1) to **5t** (25 mg) (including two fraction 1F and 2F**)** in 67% yield. ^{1}H-NMR (400 MHz, CDCl$_3$) δ (ppm) 8.87 (d, *J*= 4.0 Hz, 1H), 8.40 (m, *J*= 8.0 Hz, 1H), 8.27 (d, *J* = 8.4 Hz, 1H), 8.00 (d, *J*= 8.0 Hz, 1H), 7.73-7.67 (m, 3H), 7.61 (d, *J* = 8.4 Hz, 1H), 7.90 (d, *J* = 7.2 Hz, 1H), 7.67-7.53 (m, 4H), 7.52 (t, *J* = 8.0 Hz, 1H), 7.44 (dd, *J* = 8.0 Hz, *J* = 4.0 Hz, 1H), 7.34-7.32 (m, 3H), 6.69 (s, 1H), 4.01 (m, 2H), 3.50 (d, *J* = 7.2 Hz, 1H), 1.41 (d, *J* = 7.2 Hz, 3H), 1.08 (t, *J* = 7.2 Hz, 3H). ^{13}C-NMR (100 MHz, CDCl$_3$) δ (ppm) 173.1, 163.6, 151.8, 142.7, 137.2, 136.5, 136.1, 135.9, 132.7, 131.7, 129.6, 129.5, 128.3, 126.7, 126.3, 126.2, 125.6, 122.0, 104.6, 61.2, 42.6, 18.7, 17.2; MS (ESI) calcd for $C_{23}H_{20}N_2O_3[M+H]^+$: 273.15, found 273.08.



Ethyl 2-(6-chloro-1-oxo-2-(quinolin-8-yl)-1,2-dihydroisoquinolin-3-yl)propanoate (5u)

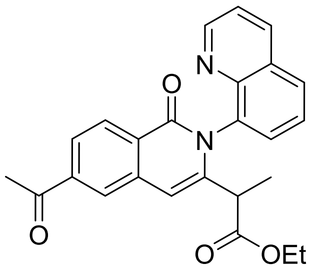
Following the general procedure II, 4-chloro-*N*-(quinolin-8-yl)benzamide (29 mg, 0.1 mmol), ethyl 2-methylbuta-2,3-dienoate (38 mg, 0.3 mmol), Co(acac)$_2$ (5.4 mg, 0.02 mmol), Mn(OAc)$_2$ (35 mg, 0.2 mmol), KOAc (20 mg, 0.2 mmol), and TFE 1.0 ml were used. Resulting solution was purged with O$_2$ ballon for 0.5 min, then the reaction mixture was stirred at 80 °C for 12 h. After completion of the reaction, the reaction mixture was diluted with EtOAc and washed once with saturated aqueous NaHCO$_3$. Then organic layer was dried over Na$_2$SO$_4$ and concentrated on rotavapor under reduced pressure. Finally, the residue was purified by silica gel column chromatography (Petroleum ether:Ethyl acetate = 1:1) to **5u** (28 mg) (including two fraction 1F and 2F**)** in 70% yield. ^{1}H-NMR (400 MHz, $CDCl_3$) δ (ppm) 8.85 (s, 1H), 8.31-8.25 (m, 2H), 8.00 (br, 1H), 7.69-7.58 (m, 3H), 7.44-7.39 (m, 2H), 6.65 (s, 1H), 3.79-3.64 (m, 2H), 3.23-3.21 (m, 1H), 1.38 (br, 3H), 0.95 (br, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ (ppm) 172.0, 163.0, 151.3, 144.7, 144.4, 139.09, 138.4, 136.5, 136.2, 131.6, 130.19, 129.9, 129.53, 127.2, 126.3, 125.5, 123.78, 122.10, 103.8, 61.4, 42.7, 18.7, 17.2, 13.8; ^{1}H-NMR (400 MHz, $CDCl_3$) δ (ppm) 8.85 (s, 0.6H), 8.31-8.25 (m, 1.2H), 8.00 (br, 0.6H), 7.69-7.58 (m, 1.8H), 7.44-7.39 (m, 1.2H), 6.59 (s, 1H), 4.00-3.95 (m, 1.2H), 3.12-3.11 (m, 0.6H), 1.38 (br, 1.8H), 1.11 (br, 1.8fH); ^{13}C-NMR (100 MHz, $CDCl_3$) δ (ppm) 172.9, 163.0, 151.6, 144.6, 144.3, 139.07, 138.4, 135.5, 135.9, 131.6, 130.16, 129.8, 129.48, 127.2, 126.3, 125.5, 123.85, 122.12, 103.6, 61.1, 42.6, 18.7, 17.2, 14.1; MS (ESI) calcd for $C_{23}H_{19}ClN_2O_3$ $[M+H]^+$: 407.11, found 407.05.



Ethyl 2-(6-cyano-1-oxo-2-(quinolin-8-yl)-1,2-dihydroisoquinolin-3-yl)propanoate (5v)

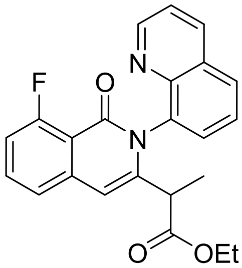
Following the general procedure II, 4-cyano-*N*-(quinolin-8-yl)benzamide (28 mg, 0.1 mmol), ethyl 2-methylbuta-2,3-dienoate (38 mg, 0.3 mmol), $Co(acac)_2$ (5.4 mg, 0.02 mmol), $Mn(OAc)_2$ (35 mg, 0.2 mmol), KOAc (20 mg, 0.2 mmol), KOTf (4 mg, 0.04 mmol), and TFE 1.0 ml were used. Resulting solution was purged with O_2 ballon for 0.5 min, then the reaction mixture was stirred at 80 °C for 3 h. After completion of the reaction, the reaction mixture was diluted with EtOAc and washed once with saturated aqueous $NaHCO_3$. Then organic layer was dried over Na_2SO_4 and concentrated on rotavapor under reduced pressure. Finally, the residue was purified by silica gel column chromatography (Petroleum ether:Ethyl acetate = 1:1) to **5v** (32 mg) in 80% (including two fraction 1F and 2F**)** yield. **5v-2F** ^{1}H-NMR (400 MHz, $CDCl_3$) δ (ppm) 8.84 (m, 1H), 8.46 (dd, *J* = 2.8 Hz, *J* = 8.0 Hz, 1H), 8.27 (dd, *J* = 1.2 Hz, *J* = 8.4 Hz, 1H), 8.02 (dd, *J* = 3.6 Hz, *J* = 6.0 Hz, 1H)，7.94 (s, 1H), 7.69-7.64 (m, 3H), 7.48 (q, *J* = 4.0 Hz, 1H), 6.67 (s, 1H), 3.99 (m, 2H), 3.13 (q, *J* = 6.8 Hz, 1H), 1.40 (d, *J* = 7.2 Hz, 1H), 1.10 (d, *J* = 7.2 Hz, 1H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ (ppm) 172.7, 162.5, 151.7, 145.2, 144.3, 137.2, 136.6, 135.1, 131.4, 130.95, 130.0, 129.5, 128.4, 127.9, 126.4, 122.3, 118.4, 116.1, 103.5, 61.5, 42.7, 17.1, 14.0. **5v-2F** ^{1}H-NMR (400 MHz, $CDCl_3$) δ (ppm) 8.85 (dd, *J* = 1.6 Hz, *J* = 8.4 Hz, 1H), 8.45 (d, *J* = 8.4Hz, 1H), 8.26 (dd, *J* = 1.6 Hz, *J* = 8.4 Hz, 1H), 8.03 (dd, *J* = 2.4 Hz, *J* = 6.8 Hz, 1H)，7.93 (s, 1H), 7.73-7.71 (m, 2H), 7.64 (d, *J* = 1.6 Hz, *J* = 8.4 Hz, 1H), 7.46-7.45 (m, 2H), 6.74 (s, 1H), 3.80 (m, 1H), 3.64 (m, 1H), 3.25 (m, 1H), 1.39 (d, *J* = 7.2 Hz, 1H), 0.95 (d, *J* = 7.2 Hz, 1H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ (ppm) 171.8, 162.6, 151.4, 145.5, 144.6, 137.3, 136.3, 135.6, 131.0, 130.1, 130.08, 129.6, 129.5, 128.4, 128.0, 127.8, 126.4, 122.3, 118.4, 116.2, 103.7, 61.2, 42.7, 18.7, 13. MS (ESI) calcd for $C_{24}H_{19}N_3O_3$ $[M+H]^+$: 398.14, found:

398.06.



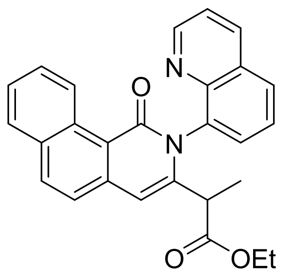
Ethyl 2-(6-acetyl-1-oxo-2-(quinolin-8-yl)-1,2-dihydroisoquinolin-3-yl)propanoate (5w)

Following the general procedure II, 4-acetyl-N-(quinolin-8-yl)benzamide (30 mg, 0.1 mmol), ethyl 2-methylbuta-2,3-dienoate (38 mg, 0.3 mmol), Co(acac)$_2$ (5.4 mg, 0.02 mmol), Mn(OAc)$_2$ (35 mg, 0.2 mmol), KOAc (20 mg, 0.2 mmol), and TFE 1.0 ml were used. Resulting solution was purged with O$_2$ ballon for 0.5 min, then the reaction mixture was stirred at 80 °C for 12 h. After completion of the reaction, the reaction mixture was diluted with EtOAc and washed once with saturated aqueous NaHCO$_3$. Then organic layer was dried over Na$_2$SO$_4$ and concentrated on rotavapor under reduced pressure. Finally, the residue was purified by silica gel column chromatography (Petroleum ether:Ethyl acetate = 1:1) to **5w** (28 mg) (including two fraction 1F and 2F**)** in 68% yield. **5w-1F** ^{1}H-NMR (400 MHz, CDCl$_3$) δ (ppm) 8.85-8.84 (m, 1H), 8.45 (d, *J* = 8.4 Hz, 1H), 8.27 (dd, *J* = 8.4 Hz, *J* = 1.2 Hz, 1H), 8.19 (s, 1H), 8.01-7.97 (m, 2H), 7.72-7.65 (m, 2H), 7.48-7.45 (m, 1H), 6.76 (s, 1H), 4.04-3.93 (m, 2H), 3.17-3.12 (m, 1H), 2.72 (s, 3H), 1.40 (d, *J* = 7.2 Hz, 3H), 1.12 (t, *J* = 7.2 Hz, 3H); ^{13}C-NMR (100 MHz, CDCl$_3$) δ (ppm)198.1, 173.0, 163.1, 151.7, 144.6, 143.9, 140.1, 137.2, 136.6, 135.6, 131.6, 130.0, 129.5, 129.0, 128.3, 127.0, 126.4, 125.4, 122.2, 104.8, 61.4, 42.7, 27.2, 17.2, 14.1; **5w-2F** ^{1}H-NMR (400 MHz, CDCl$_3$) δ (ppm) 8.86-8.84 (m, 1H), 8.45 (d, *J* = 8.4 Hz, 1H), 8.26 (dd, *J* = 8.4 Hz, *J* = 1.2 Hz, 1H), 8.17 (d, *J* = 0.8 Hz, 1H), 8.03-7.97 (m, 2H), 7.72-7.71 (m, 2H), 7.46-7.44 (m, 1H), 6.82 (s, 1H), 3.83-3.76 (m, 1H), 3.67-3.59 (m, 1H), 3.28-3.22 (m, 1H), 2.72 (s, 3H), 1.39 (d, *J* = 7.2 Hz, 3H), 0.95 (t, *J* = 7.2 Hz, 3H); ^{13}C-NMR (100 MHz, CDCl$_3$) δ (ppm) 198.1, 172.1, 163.1, 151.4, 144.8, 144.1, 140.1, 137.2, 136.2, 136.0, 130.2, 129.9, 129.6, 129.0, 128.2, 127.0, 126.4, 125.4, 122.2, 104.9, 61.1, 42.6, 27.2, 18.7, 13.8; MS (ESI) calcd for $C_{25}H_{22}N_2O_4$ $[M+H]^+$:415.16, found 415.05.



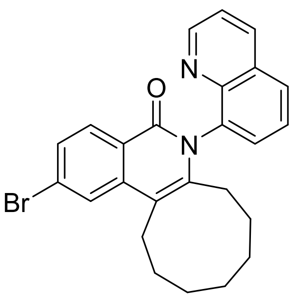
Ethyl 2-(8-fluoro-1-oxo-2-(quinolin-8-yl)-1,2-dihydroisoquinolin-3-yl)propanoate (5x)

Following the general procedure II, 2-flouro-*N*-(quinolin-8-yl)benzamide (26.6 mg, 0.1 mmol), ethyl 2-methylbuta-2,3-dienoate (38 mg, 0.3 mmol), Co(acac)$_2$ (5.4 mg, 0.02 mmol), Mn(OAc)$_2$ (35 mg, 0.2 mmol), KOAc (20 mg, 0.2 mmol), and TFE 1.0 ml were used. Resulting solution was purged with O$_2$ ballon for 0.5 min, then the reaction mixture was stirred at 80 ^{o}C for 9 h. After completion of the reaction, the reaction mixture was diluted with EtOAc and washed once with saturated aqueous NaHCO$_3$. Then organic layer was dried over Na$_2$SO$_4$ and concentrated on rotavapor under reduced pressure. Finally, the residue was purified by silica gel column chromatography (Petroleum ether:Ethyl acetate = 1:1) to **5x** (30 mg) (including two fraction 1F and 2F**)** in 77% yield. **5x-1F** ^{1}H-NMR (400 MHz, CDCl$_3$) δ (ppm) 8.87-8.85 (m, 1H), 8.25 (dd, *J* = 8.0 Hz, *J* = 1.6 Hz, 1H), 7.97 (dd, *J* = 7.6 Hz, *J* = 1.6 Hz, 1H), 7.70-7.63 (m, 2H), 7.62-7.56 (m, 2H), 7.46-7.43 (m, 1H), 7.35 (d, *J* = 8.0 Hz, 1H), 7.10-7.05 (m, 1H), 6.62 (d, *J* = 1.6 Hz, 1H), 4.04-3.92 (m, 2H), 3.15-3.10 (m, 1H), 1.38 (d, *J* = 7.2 Hz, 3H), 1.12 (t, *J* = 7.2 Hz, 3H); ^{13}C-NMR (100 MHz, CDCl$_3$) δ (ppm) 173.0, 162.9 (d, $J_{\text{C-F}}$ = 263.2 Hz), 160.8 (d, $J_{\text{C-F}}$ = 4.7 Hz), 151.6, 144.8, 143.9, 140.0, 136.4 (d, $J_{\text{C-F}}$ = 17 Hz), 135.5, 133.5 (d, $J_{\text{C-F}}$ = 10 Hz), 131.9, 129.8, 129.6 (d, $J_{\text{C-F}}$ = 18 Hz), 126.3, 122.14 (d, $J_{\text{C-F}}$ = 4.5 Hz), 122.08, 114.7 (d, $J_{\text{C-F}}$ = 5.2 Hz), 113.5 (d, $J_{\text{C-F}}$ = 17 Hz), 104.0 (d, $J_{\text{C-F}}$ = 2.6 Hz), 61.4, 42.7, 17.1, 14.1; **5x-2F** ^{1}H-NMR (400 MHz, CDCl$_3$) δ (ppm) 8.86-8.85 (m, 1H), 8.23 (d, *J* = 8.0 Hz, 1H), 8.00-7.97 (m, 1H), 7.70-7.68 (m, 2H), 7.61-7.56 (m, 1H), 7.45-7.42 (m, 2H), 7.34 (d, *J* = 8.0 Hz, 1H), 7.10-7.05 (m, 1H), 6.68 (s, 1H), 3.86-3.78 (m, 1H), 3.68-3.60 (m, 1H), 3.24-3.19 (m, 1H), 1.37 (d, *J* = 6.8 Hz, 3H), 0.95 (t, *J* = 7.2 Hz, 3H); ^{13}C-NMR (100 MHz, CDCl$_3$) δ (ppm) 172.2, 162.9 (d, $J_{\text{C-F}}$ = 263.0 Hz), 160.7 (d, $J_{\text{C-F}}$ = 5.0 Hz), 151.3, 144.9, 144.1, 140.0, 136.2, 135.9, 133.5 (d, $J_{\text{C-F}}$ = 10 Hz), 130.5, 129.8, 129.5, 126.3, 122.12 (d, $J_{\text{C-F}}$ = 4.5 Hz), 122.07, 114.6 (d, $J_{\text{C-F}}$ = 5.2 Hz), 113.5 (d, $J_{\text{C-F}}$ = 21 Hz), 104.8 (d, $J_{\text{C-F}}$ = 2.4 Hz), 61.1, 42.6, 18.7, 13.8; MS (ESI) calcd for C$_{23}$H$_{19}$FN$_2$O$_3$ [M+H]$^+$: 391.14, found 391.66.



Ethyl 2-(1-oxo-2-(quinolin-8-yl)-1,2-dihydrobenzo[h]isoquinolin-3-yl)propanoate (5y)

Following the general procedure II, *N*-(quinolin-8-yl)-1-naphthamide (29.8 mg, 0.1 mmol), ethyl 2-methylbuta-2,3-dienoate (37.8 mg, 0.3 mmol), Co(acac)$_2$ (5.4 mg, 0.02 mmol), Mn(OAc)$_2$ (35 mg, 0.2 mmol), KOAc (39.8 mg, 0.2 mmol), and TFE 1.0 ml were used. Resulting solution was purged with O$_2$ ballon for 0.5 min, then the reaction mixture was stirred at 80 ^{o}C for 3.5 h. After completion of the reaction, the reaction mixture was diluted with EtOAc and washed once with saturated brine. Then organic layer was dried over Na$_2$SO$_4$ and concentrated on rotavapor under reduced pressure. Finally, the residue was purified by silica gel column chromatography (Petroleum ether:Ethyl acetate = 1:1) to **5y** (29 mg) (including two fraction 1F and 2F) in 69% yield. **5y-1F** ^{1}H-NMR (400 MHz, $CDCl_3$) δ (ppm) 10.04 (m, 1H), 8.84 (s, 1H), 8.26 (d, *J* = 8.0 Hz, 1H), 8.07-8.01 (m, 2H), 7.89 (d, *J* = 8.4 Hz, 1H), 7.78-7.13 (m, 2H), 7.62-7.53 (m, 4H), 7.52 (t, *J* = 8.0 Hz, 1H), 7.44 (dd, *J* = 8.0 Hz, *J* = 4.0 Hz, 1H), 7.62-7.54 (m, 4H), 7.46-7.42 (m, 2H), 6.89 (s, 1H), 3.32-3.26 (m, 1H), 3.24-3.19 (m, 1H), 1.44 (m, 3H), 0.98 (t, *J* = 7.2 Hz, 3H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ (ppm) 173.0, 172.2, 164.0, 151.3, 144.9, 144.3, 139.2, 136.9, 136.5, 134.3, 132.5, 132.2, 131.6, 130.1, 129.7, 129.6, 128.4, 128.2, 127.5, 126.5, 126.4, 125.1, 122.1, 108.7, 105.5, 61.1, 42.8, 17.2, 13.8. **5y-2F** ^{1}H-NMR (400 MHz, $CDCl_3$) δ (ppm) 10.04 (m, 1H), 8.84 (s, 1H), 8.26 (d, *J* = 8.0 Hz, 1H), 8.07-8.01 (m, 2H), 7.89 (d, *J* = 8.4 Hz, 1H), 7.78-7.13 (m, 2H), 7.62-7.53 (m, 4H), 7.52 (t, *J* = 8.0 Hz, 1H), 7.44 (dd, *J* = 8.0 Hz, *J* = 4.0 Hz, 1H), 7.62-7.54 (m, 4H), 7.46-7.42 (m, 2H), 6.82 (s, 1H), 4.01 (m, 2H), 1.44 (m, 3H), 1.11 (t, *J* = 7.2 Hz, 3H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ (ppm) 172.2, 171.6, 164.0, 151.7, 144.7, 144.1, 139.2, 136.5, 136.2, 134.3, 132.5, 132.2, 131.6, 130.1, 129.6, 129.56, 128.3, 128.2, 127.5, 126.4, 125.1, 122.1, 108.6, 105.4, 61.3, 42.8, 21.2, 17.2; MS (ESI) calcd for $C_{27}H_{22}N_2O_3$ $[M+H]^+$: 423.16, found 423.09.



2-bromo-6-(quinolin-8-yl)-6,7,8,9,10,11,12,13-octahydro-5*H*-cyclonona[*c*] isoquinolin-5-one (5z)

Following the general procedure II, 4-bromo-*N*-(quinolin-8-yl)benzamide (32.6 mg, 0.1 mmol), cyclonona-1,2-diene (36.6 mg, 0.3 mmol), $Co(acac)_2$ (5.4 mg, 0.02 mmol), $Mn(OAc)_2$ (35 mg, 0.2 mmol), KOAc (19.6 mg, 0.2 mmol), and TFE 1.0 ml were used. Resulting solution was purged with O_2 ballon for 0.5 min, then the reaction mixture was stirred at 80 °C for 6.0 h. After completion of the reaction, the reaction mixture was diluted with EtOAc and washed once with saturated brine. Then organic layer was dried over Na_2SO_4 and concentrated on rotavapor under reduced pressure. Finally, the residue was purified by silica gel column chromatography (Petroleum ether:Ethyl acetate = 5:1) to **5z** (18.3 mg) (including two fraction 1F and 2F) in 41% yield. ^{1}H-NMR (400 MHz, $CDCl_3$) δ (ppm) 8.85 (dd, *J* = 1.2 Hz, *J* = 4.0 Hz,, 1H), 8.30 (d, *J* = 8.4 Hz, 1H), 8.24 (dd, *J* =1.2 Hz, *J* = 8.4 Hz, 1H), 7.95 (dd, *J* = 2.0 Hz, *J* = 7.2 Hz, 1H), 7.88 (d, *J* =1.6 Hz, 1H), 7.68 (m, 1H), 7.54 (d, *J* = 1.6 Hz, *J* = 8.8 Hz, 1H), 7.42 (q, *J* = 4.0 Hz, 1H), 3.02 (m, 1H), 2.93 (m, 1H), 2.64 (m, 1H), 2.22-2.15 (m, 1H), 1.82 (m, 2H), 1.62-1.21 (m , 14H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ (ppm) 151.4, 144.7, 143.2, 138.9, 137.2, 136.3, 130.6, 130.5, 129.3, 129.2, 128.9, 127.9, 126.2, 126.0, 124.3, 121.9, 112.7, 29.6, 26.8, 26.7, 26.4, 25.8, 25.1, 22.7; MS (ESI) calcd for $C_{25}H_{23}BrN_2O$ $[M+H]^+$: 447.10, found: 447.06.