Supporting Information

N-Heterocyclic Carbene-Chromium-Catalyzed Alkylative Cross-Coupling of Benzamide Derivatives with Aliphatic Bromides

Jinghua Tang,^{†,‡} Pei Liu,^{†,‡} and Xiaoming Zeng^{*,†,‡}

[†]*Frontier Institute of Science and Technology, Xi'an Jiaotong University, Xi'an*

710054, China

[‡]Key Laboratory of Green Chemistry & Technology, Ministry of Education, College

of Chemistry, Sichuan University, Chengdu 610064, China

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1. Materials and Methods

General. All reactions dealing with air- or moisture-sensitive compounds were carried out in a flame-dried, sealed Schlenk reaction tube under an atmosphere of nitrogen. Analytical thin-layer chromatography was performed on glass plates coated with 0.25 mm 230–400 mesh silica gel containing a fluorescent indicator (Merck). Flash silica gel column chromatography was performed on silica gel 60N (spherical and neutral, 140–325 mesh) as described by Still. ¹H NMR spectra were measured on a Bruker AV-400 spectrometer and reported in parts per million. ¹H NMR spectra were recorded at 400 MHz in CDCl₃ were referenced internally to tetramethylsilane as a standard, and ¹³C NMR spectra were recorded at 100 MHz and referenced to the solvent resonance. Analytical gas chromatography (GC) was carried out on a Thermo Trace 1300 gas chromatograph, equipped with a flame ionization detector. Mass spectra (GC-MS) were taken at Thermo Trace 1300 gas chromatograph mass spectrometer. High resolution mass spectra (HRMS) were recorded on the Exactive Mass Spectrometer (Thermo Scientific, USA) equipped with ESI ionization source. Melting points were determined with a Hanon MP-300.

Materials. Unless otherwise noted, materials were purchased from Tokyo Chemical Industry Co., Aldrich Inc., Alfa Aesar, Adamas-beta and other commercial suppliers and used as received. Solvents were dried over sodium (for THF, 2-MeTHF and ether) by refluxing for overnight and freshly distilled prior to use. Grignard reagents were purchased from commercial suppliers or prepared by the reaction between related organic halides and magnesium turnings and titrated prior to use.

2. Optimizing Reaction Parameters

Table S1. Studying the effect of Grignard reagents^{*a*}



Entry	Catalyst	Grignard reagents	Yield of 3a (%) ^b
1	CrCl ₃		n.d.
2	CrCl ₃	TMSCH ₂ MgCl	trace
3	CrCl ₃	CyMgBr	n.d.
4	CrCl ₃	EtMgBr	20
5	CrCl ₃	MeMgCl	13
6	CrCl ₃	PhMgBr	23

^{*a*}Conditions: **1a** (0.2 mmol), CrCl₃ (10 mol %), dppe (10 mol %), 2-MeTHF (0.3 mL), **2a** (0.4 mmol), Grignard reagents (0.7 mmol), 65 °C, 24 h. ^{*b*}Isolated yied. n.d. = Not detected by GC-MS and TLC analyses.

Table S2. Studying the effect of ligands^a





Entry	Catalyst	Ligand	Yield of $3a (\%)^b$
1	CrCl ₃		22
2	CrCl ₃	PCy ₃	40
3	CrCl ₃	dppe ^c	37
4	CrCl ₃	$dppbz^{c}$	25
5	CrCl ₃	$\mathbf{b}\mathbf{p}\mathbf{y}^{c}$	29
6	CrCl ₃	1,10-phen	35
7	CrCl ₃	IPr·HCl	47

8 CrCl₃ IMes'HCl 43

^{*a*}Conditions: **1a** (0.2 mmol), CrCl₃ (10 mol %), ligand (20 mol %), 2-MeTHF (0.3 mL), **2a** (0.8 mmol), PhMgBr (0.7 mmol), 65 °C, 24 h. ^{*b*}Isolated yied. ^{*c*}10 mol % ligand was used.

Table S3. Studying the amount of PhMgBr^a



Entry	PhMgBr (equiv)	Yield of 3a (%) ["]
1	3	47
2	3.5	53
3	4	55
4	5	52

^{*a*}Conditions: **1a** (0.2 mmol), CrCl₃ (10 mol %), IPr·HCl (20 mol %), 2-MeTHF (0.3 mL), **2a** (0.4 mmol), PhMgBr (0.5-1.0 mmol), 65 °C, 24 h. ^{*b*}Isolated yied.

Table S4. Studying the amount of alkyl bromide^a



Entry	ⁿ⁻ BuBr (equiv)	Yield of 3a (%) ^b
1	2	63
2	3	79
3	4	83
4	5	81

^{*a*}Conditions: **1a** (0.2 mmol), Chromium salt (10 mol %), IPr·HCl (20 mol %), 2-MeTHF (0.3 mL), **2a** (0.4-0.8 mmol), PhMgBr (0.7 mmol), 40 °C, 24 h. ^{*b*}Isolated yied.

Table S5. Studying the effect of temperature^{*a*}



^{*a*}Conditions: **1a** (0.2 mmol), CrCl₃ (10 mol %), IPr·HCl (20 mol %), 2-MeTHF (0.3 mL), **2a** (0.8 mmol), PhMgBr (0.7 mmol), 24 h. ^{*b*}Isolated yied.

Table S6. Studying the effect of Chromium salts^a



Entry	Catalyst	Yield of 3a (%) ^b
1		n.d.
2	CrCl ₃	83
3	CrCl ₂	70
4	$Cr(acac)_3$	59
5	Cr(CO) ₆	n.d.

^{*a*}Conditions: **1** (0.2 mmol), Chromium salt (10 mol %), IPr·HCl (20 mol %), 2-MeTHF (0.3 mL), **2a** (0.8 mmol), PhMgBr (0.7 mmol), 40 °C, 24 h. ^{*b*}Isolated yied. n.d. = Not detected by GC-MS and TLC analyses.

3. Preparation of Substrates

Figure S1. Representative benzamides and alkyl bromides that did not undergo catalytic alkylation.



Figure S2. Representative benzamides and alkyl bromides that were used in this transformation.



8-Aminoquinoline-bearing carboxamides 1a-1k were prepared from the reaction of 8-amino- quinolines with carboxylic acids or chlorides according to the literatures.¹ Alkyl bromides 2k-2l were prepared according to the corresponding literatures.²



2-Methyl-*N***-(quinolin-8-yl)benzamide (1a):** white solid. ¹H NMR (400 MHz, CDCl₃): $\delta = 10.22$ (s, 1H), 8.97 (d, J = 7.6 Hz, 1H), 8.78-8,77 (m, 1H), 8.19-8.16 (m, 1H), 7.70 (d, J = 7.6 Hz, 1H), 7.62-7.54 (m, 2H), 7.47-7.39 (m, 2H), 7.35-7.31 (m, 2H), 2.62 (s, 3H); ¹³C NMR (100 MHz, CDCl₃): $\delta = 168.2$, 148.2, 138.6, 136.7, 136.6, 136.3, 134.7, 131.4, 130.3, 128.0, 127.4, 127.2, 126.0, 121.7, 121.6, 116.5, 20.2.



2-Methoxy-*N***-(quinolin-8-yl)benzamide (1b):** white solid. ¹H NMR (400 MHz, CDCl₃): $\delta = 12.34$ (s, 1H), 9.05-9.03 (m, 1H), 8.85-8.84 (m, 1H), 8.37-8.35 (m, 1H), 8.16-8.13 (m, 1H), 7.60-7.55 (m,1H), 7.51-7.47 (m, 2H), 7.45-7.41 (m, 1H), 7.15-7.11 (m, 1H), 7.08-7.04 (m, 1H), 4.18 (s, 3H); ¹³C NMR (100 MHz, CDCl₃): $\delta = 163.6$, 157.7, 148.2, 139.2, 136.2, 135.7, 133.1, 132.3, 128.0, 127.5, 122.3, 121.4, 121.3, 121.2, 117.2, 111.5, 56.0.



N-(quinolin-8-yl)-[1,1'-biphenyl]-2-carboxamide (1c): brown solid. ¹H NMR (400 MHz, CDCl₃): δ = 9,78 (s, 1H), 8.82-8.80 (m, 1H), 8.52-8.51(m, 1H), 8.07-8.04 (m, 1H), 7.92-7.90 (m, 1H), 7.58-7.43 (m, 7H), 7.34-7.31 (m, 1H), 7.29-7.25 (m, 2H), 7.17-7.14 (m, 1H); ¹³C NMR (100 MHz, CDCl₃): δ = 167.8, 147.7, 140.2, 140.0, 138.4, 136.1, 135.9, 134.5, 130.7, 130.5, 129.2, 128.9, 128.3, 127.7, 127.6, 127.5, 127.2, 121.5, 121.4, 116.2.



N-(quinolin-8-yl)-1-naphthamide (1d): brown solid. ¹H NMR (400 MHz, CDCl₃): δ = 10.4 (s,1H), 9.08-9.06 (m, 1H), 8.76-8.76 (m, 1H), 8.56-8.54 (m, 1H), 8.20 (dd, *J* = 8.4, 1.6 Hz, 1H), 8.02 (d, *J* = 8.0 Hz, 1H), 7.94-7.92 (m, 2H), 7.67-7.54 (m, 5H), 7.46-7.43 (m, 1H); ¹³C NMR (100 MHz, CDCl₃): δ = 167.7, 148.3, 138.6, 136.3, 134.8, 134.6, 133.9, 131.1, 130.3, 128.4, 128.0, 127.4, 127.3, 126.5, 125.6, 125.5, 124.8, 121.9, 121.7, 116.7.



2,3-Dimethyl-*N***-(quinolin-8-yl)benzamide (1e):** white solid. ¹H NMR (400 MHz, CDCl₃): $\delta = 10.1$ (s, 1H), 8.97 (d, J = 7.6 Hz, 1H), 8.75 (dd, J = 4.4, 1.6 Hz, 1H), 8.17 (dd, J = 8.4, 1.6 Hz, 1H), 7.61-7.52 (m, 2H), 7.48-7.41 (m, 2H), 7.29-7.19 (m, 2H), 2.45 (s, 3H), 2.35 (s, 3H); ¹³C NMR (100 MHz, CDCl₃): $\delta = 169.0$, 148.2, 138.5, 138.1, 137.6, 136.3, 134.7, 134.6, 131.5, 127.9, 127.4, 125.7, 124.7, 121.7, 121.6, 116.5, 20.3, 16.4.



3-Methoxy-2-methyl-*N***-(quinolin-8-yl)benzamide (1f):** white solid. ¹H NMR (400 MHz, CDCl₃): $\delta = 10.15$ (s, 1H), 8,96 (dd, J = 7.2, 1.2 Hz, 1H), 8.77 (dd, J = 4.4, 1.6 Hz, 1H), 8.19 (dd, J = 8.4, 1.6 Hz, 1H), 7.62-7.53 (m, 2H), 7.46-7.43 (m, 1H), 7.31-7.24 (m, 2H), 6.99 (dd, J = 8.0, 1.2 Hz, 1H), 3.89 (s, 3H), 2.43 (s, 3H); ¹³C NMR (100 MHz, CDCl₃): $\delta = 168.2$, 158.2, 148.2, 138.6, 138.4, 136.3, 134.7, 128.0, 127.4, 126.8, 125.1, 121.7, 121.6, 119.1, 116.5, 111.7, 55.7, 12.8.



3-Chloro-2-methyl-*N***-(quinolin-8-yl)benzamide (1g):** white solid. ¹H NMR (400 MHz, CDCl₃): δ = 10.14 (s, 1H), 8.94 (dd, *J* = 7.2, 1.6 Hz, 1H), 8.78 (dd, *J* = 4.4, 1.6 Hz, 1H), 8.20 (dd, *J* = 8.4, 1.6 Hz, 1H), 7.62-7.55 (m, 2H), 7.54-7.49 (m, 2H), 7.47-7.44 (m, 1H), 7.28-7.24 (m, 1H), 2.59 (s, 3H); ¹³C NMR (100 MHz, CDCl₃): δ = 167.4, 148.3, 139.0, 138.5, 136.4, 136.0, 134.4, 134.3, 130.9, 128.0, 127.4, 127.0, 125.4, 122.1, 121.7, 116.6, 17.2.



2,4-Dimethyl-*N***-(quinolin-8-yl)benzamide (1h):** white solid. ¹H NMR (400 MHz, CDCl₃): $\delta = 10.24$ (s, 1H), 8.96 (d, J = 7.6 Hz, 1H), 8.78 (dd, J = 4.4, 1.6 Hz, 1H), 8.17-8.15 (m, 1H), 7.63-7.57 (m, 2H), 7.54-7.52 (m, 1H), 7.45-7.42 (m, 1H), 7.14-7.13 (m, 2H), 2.60 (s, 3H), 2.39 (s, 3H); ¹³C NMR (100 MHz, CDCl₃): $\delta = 168.1$, 148.1, 140.4, 138.5, 136.8, 136.2, 134.8, 133.6, 132.1, 127.9, 127.4, 126.6, 121.6, 121.5, 116.3, 21.3, 20.2.



4-Fluoro-2-methyl-*N***-(quinolin-8-yl)benzamide (1i):** white solid. ¹H NMR (400 MHz, CDCl₃): $\delta = 10.19$ (s, 1H), 8.92 (dd, J = 7.2, 1.2 Hz, 1H), 8.80 (dd, J = 4.0, 1.6 Hz, 1H), 8.20 (dd, J = 8.4, 1.6 Hz, 1H), 7.71-7.67 (m, 1H), 7.62-7.55 (m, 2H), 7.49-7.45 (m, 1H), 7.03-6.99 (m, 1H), 2.61 (s, 3H); ¹³C NMR (100 MHz, CDCl₃): $\delta = 167.2$, 164.8, 162.3, 148.3, 140.1 (d, $J_{C-F} = 8.5$ Hz), 138.6, 136.4, 134.6, 132.8 (d, $J_{C-F} = 3.1$ Hz), 129.5 (d, $J_{C-F} = 8.9$ Hz), 128.0, 127,4, 121.9 (d, $J_{C-F} = 15.9$ Hz), 118.3 (d, $J_{C-F} = 21.2$ Hz), 116.5, 113.0 (d, $J_{C-F} = 21.4$ Hz), 20.4; ¹⁹F NMR (377 MHz, CDCl₃): $\delta = -110.4$.



2,5-Dimethyl-*N***-(quinolin-8-yl)benzamide (1j):** white solid. ¹H NMR (400 MHz, CDCl₃): $\delta = 10.18$ (s, 1H), 8.95 (d, J = 7.2 Hz, 1H), 8.78 (dd, J = 4.4, 1.6 Hz, 1H), 8.18 (dd, J = 8.4, 1.2 Hz, 1H), 7.61-7.53 (m, 2H), 7,48-7.43 (m, 2H), 7.22-7.18 (m, 2H), 2.56 (s, 3H), 2.39 (s, 3H); ¹³C NMR (100 MHz, CDCl₃): $\delta = 168.4$, 148.2, 138.6, 136.5, 136.3, 135.6, 134.7, 133.3, 131.2, 131.0, 128.0, 127.8, 127.4, 121.7, 121.6, 116.5, 20.9, 19.7.



5-Fluoro-2-methyl-*N***-(quinolin-8-yl)benzamide (1k):** white solid. ¹H NMR (400 MHz, CDCl₃): $\delta = 10.19$ (s, 1H), 8.92 (dd, J = 7.2, 1.6 Hz, 1H), 8.80 (dd, J = 4.4, 1.6 Hz, 1H), 8.20 (dd, J = 8.4, 1.6 Hz, 1H), 7.62-7.56 (m, 2H), 7,48-7.45 (m, 1H), 7.40-7.38 (m, J = 8.8, 2.8 Hz, 1H), 7.29-7.25 (m, 1H), 7.12-7.08 (m, 1H), 2.56 (s, 3H); ¹³C NMR (100 MHz, CDCl₃): $\delta = 166.8$ (d, $J_{C-F} = 2.1$ Hz), 162.0, 159.6, 148.4, 138.6, 137.9 (d, $J_{C-F} = 6.2$ Hz), 136.4, 134.4, 132.9 (d, $J_{C-F} = 7.4$ Hz), 132.2 (d, $J_{C-F} = 3.4$ Hz), 128.0, 127.4, 122.1 (d, $J_{C-F} = 29.1$ Hz), 117.3 (d, $J_{C-F} = 20.7$ Hz), 116.7, 114.4 (d, $J_{C-F} = 22.6$ Hz), 19.5; ¹⁹F NMR (377 MHz, CDCl₃): $\delta = -116.6$.



1a-D: white solid. ¹H NMR (400 MHz, CDCl₃): $\delta = 10.2$ (s, 1H), 8.96 (d, J = 7.6 Hz, 1H), 8.75-8.73 (m, 1H), 8.14-8.11 (m, 1H), 7.59-7.55 (m, 1H), 7.51-7.49 (m,1H), 7.42-7.36 (m, 2H), 7.31-7.28 (m, 2H), 2.60 (s, 3H); ¹³C NMR (100 MHz, CDCl₃): $\delta = 168.0$, 148.1, 138.4, 136.6, 136.4, 136.2, 134.6, 131.3, 130.2, 127.8, 127.3, 125.8, 121.7, 121.5, 116.3, 20.1. HRMS (ESI⁺): calcd for C₁₇H₁₃DN₂ONa [M+Na]⁺286.1067, found 286.1065.



1-(3-Bromopropoxy)-2-chlorobenzene (2k): colorless oil. ¹H NMR (400 MHz, CDCl₃): δ = 7.36 (dd, J = 7.6, 1.6 Hz, 1H), 7.24-7.18 (m, 1H), 6.95-6.88 (m, 2H), 4.15 (t, J = 6.0 Hz, 2H), 3.67 (t, J = 6.4 Hz, 2H), 2.38-2.32 (m, 2H); ¹³C NMR (100 MHz, CDCl₃): δ = 154.1, 130.2, 127.7, 123.0, 121.6, 113.5, 66.3, 32.2, 30.0.



1-Bromo-2-(3-bromopropoxy)benzene (21): colorless oil. ¹H NMR (400 MHz, CDCl₃): δ = 7.55-7.52 (m, 1H), 7.28-7.24 (m, 1H), 6.92-6.90 (d, *J* = 8.0 Hz, 1H), 6.87-6.83 (m, 1H), 4.17-4.13 (m, 2H), 3.68 (t, *J* = 6.4 Hz, 2H), 2.39-2.32 (m, 2H); ¹³C NMR (100 MHz, CDCl₃): δ = 155.0, 133.3, 128.5, 122.1, 113.3, 112.3, 66.3, 32.3, 30.2.



5-(3-Bromopropoxy)benzo[*d*][1,3]dioxole (2m): white solid. ¹H NMR (400 MHz, CDCl₃): $\delta = 6.72$ (d, J = 8.4 Hz, 1H), 6.50 (d, J = 2.4 Hz, 1H), 6.34 (dd, J = 8.4, 2.4 Hz, 1H), 5.92 (s, 2H), 4.03 (t, J = 5.6 Hz, 2H), 3.59 (t, J = 6.4 Hz, 2H), 2.31-2.25 (m, 2H); ¹³C NMR (100 MHz, CDCl₃): $\delta = 154.1$, 148.2, 141.8, 107.9, 105.7, 101.1, 98.1, 66.2, 32.3, 30.1.

4. General Procedure for Chromium-Catalyzed Direct Alkylation of C(sp²)-H bonds in Benzamides with Primary Alkyl Electrophiles



A dried Schlenk tube were placed benzamide **1** (0.2 mmol), $CrCl_3$ (3.2 mg, 0.02 mmol), IPrHCl (17 mg, 0.02 mmol), alkyl bromide **2** (0.8 mmol) and freshly distilled 2-Me THF (0.3 mL). Phenylmagnesium bromide (0.7 mmol) was added dropwise by syringe at 40 °C over 10 min. After stirring for 24 h at 40 °C, the resulting mixture was quenched by an aqueous solution of NH₄Cl and extracted with ethyl acetate (3 x 10 mL). The combined organic phase was dried over anhydrous Na₂SO₄ and concentrated under vacuum. The crude product was purified by silica gel chromatography to give the desired coupling product **3**.



2-Butyl-6-methyl-N-(quinolin-8-yl)benzamide (3a)

The general procedure was applied to 2-methyl-*N*-(quinolin-8-yl)benzamide **1a** (52 mg, 0.2 mmol), CrCl₃ (3.2 mg, 0.02 mmol), IPrHCl (17 mg, 0.02 mmol), 1-bromobutane (0.8 mmol) and phenylmagnesium bromide (0.7 mmol) at 40 °C for 24 h. The crude product was purified by column chromatography on silica gel (EtOAc/PE = 1/20, $R_f = 0.42$) to afford the title compound as a colorless oil (53 mg, 83% yield). ¹H NMR (400 MHz, CDCl₃): $\delta = 9.93$ (s, 1H), 9.00 (dd, J = 7.6, 1.2 Hz, 1H), 8.73 (dd, J = 4.0, 1.6 Hz, 1H), 8.18 (dd, J = 8.4, 1.6 Hz, 1H), 7.62-7,54 (m, 2H), 7.44-7.41 (m, 1H), 7.29-7.25 (m, 1H), 7.15-7.10 (m, 2H), 2.74-2.70 (m, 2H), 2.43 (s, 3H), 1.72-1.62 (m, 2H), 1.34-1.24 (m, 2H), 0.82 (t, J = 7.2 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃): $\delta = 168.9$, 148.2, 139.4, 138.4, 137.7, 136.3, 134.5, 134.4, 128.9, 127.9, 127.6, 127.4, 126.7, 121.8, 121.6, 116.7, 33.8, 33.1, 22.6, 19.5, 13.8. Spectroscopic data are in accordance with those described in the literature.^{1a}



2-Hexyl-6-methyl-N-(quinolin-8-yl)benzamide (3b)

The general procedure was applied to 2-methyl-*N*-(quinolin-8-yl)benzamide **1a** (52 mg, 0.2 mmol), CrCl₃ (3.2 mg, 0.02 mmol), IPrHCl (17 mg, 0.02 mmol), 1-bromohexane (0.8 mmol) and phenylmagnesium bromide (0.7 mmol) at 40 °C for 24 h. The crude product was purified by column chromatography on silica gel (EtOAc/PE = 1/20, $R_f = 0.43$) to afford the title compound as a colorless oil (59 mg,

85% yield). ¹H NMR (400 MHz, CDCl₃): $\delta = 9.94$ (s, 1H), 9.02 (dd, J = 7.6, 1.2 Hz, 1H), 8.73 (dd, J = 4.4, 1.6 Hz, 1H), 8.17 (dd, J = 8.4, 1.6 Hz, 1H), 7.63-7,54 (m, 2H), 7.44-7.41 (m, 1H), 7.29-7.24 (m, 1H), 7.15-7.10 (m, 2H), 2.73-2.69 (m, 2H), 2.43 (s, 3H), 1.71-1.63 (m, 2H), 1.28-1.22 (m, 2H), 1.17-1.13 (m, 4H), 0.73-0.69 (m, 3H); ¹³C NMR (100 MHz, CDCl₃): $\delta = 168.8$, 148.2, 139.4, 138.4, 137.7, 136.2, 134.4, 134.3, 128.9, 127.9, 127.6, 127.3, 126.7, 121.8, 121.6, 116.7, 33.4, 31.6, 31.5, 29.1, 22.4, 19.4, 13.9. HRMS (ESI⁺): calcd for C₂₃H₂₆N₂ONa [M+Na]⁺ 369.1943, found 369.1945.



2-Methyl-6-pentyl-*N*-(quinolin-8-yl)benzamide (3c)

The general procedure was applied to 2-methyl-*N*-(quinolin-8-yl)benzamide **1a** (52 mg, 0.2 mmol), CrCl₃ (3.2 mg, 0.02 mmol), IPrHCl (17 mg, 0.02 mmol), 1-Iodopentane (0.8 mmol) and phenylmagnesium bromide (0.7 mmol) at 40 °C for 24 h. The crude product was purified by column chromatography on silica gel (EtOAc/PE = 1/20, $R_f = 0.42$) to afford the title compound as a colorless oil (28 mg, 42% yield). ¹H NMR (400 MHz, CDCl₃): $\delta = 9.93$ (s, 1H), 9.00 (dd, J = 7.6, 0.8 Hz, 1H), 8.73 (dd, J = 4.0, 1.6 Hz, 1H), 8.19 (dd, J = 8.4, 1.6 Hz, 1H), 7.63-7,55 (m, 2H), 7.45-7.42 (m, 1H), 7.30-7.25 (m, 1H), 7.15-7.10 (m, 2H), 2.73-2.69 (m, 2H), 2.43 (s, 3H), 1.71-1.64 (m, 2H), 1.27-1.19 (m, 4H), 0.77-0.74 (m, 3H); ¹³C NMR (100 MHz, CDCl₃): $\delta = 168.9$, 148.2, 139.5, 138.5, 137.7, 136.3, 134.5, 134.4, 128.9, 128.0, 127.7, 127.4, 126.7, 121.9, 121.6, 116.7, 33.4, 31.7, 31.3, 22.4, 19.5, 13.9. Spectroscopic data are in accordance with those described in the literature.^{1e}



2-Methyl-6-phenethyl-N-(quinolin-8-yl)benzamide (3d)

The general procedure was applied to 2-methyl-*N*-(quinolin-8-yl)benzamide **1a** (52 mg, 0.2 mmol), CrCl₃ (3.2 mg, 0.02 mmol), IPrHCl (17 mg, 0.02 mmol), (2-bromoethyl)benzene (0.8 mmol) and phenylmagnesium bromide (0.7 mmol) at 40 ^oC for 24 h. The crude product was purified by column chromatography on silica gel (EtOAc/PE = 1/20, $R_f = 0.35$) to afford the title compound as a pale yellow oil (67 mg, 92% yield). ¹H NMR (400 MHz, CDCl₃): $\delta = 9.94$ (s, 1H), 9.03 (dd, J = 7.6, 1.2 Hz, 1H), 8.72 (dd, J = 4.0, 1.6 Hz, 1H), 8.17 (dd, J = 8.4, 1.6 Hz, 1H), 7.64-7,55 (m, 2H), 7.44-7.40 (m, 1H), 7.29-7.23 (m, 1H), 7.15-7.12 (m, 4H), 7.08-7.07 (m, 3H), 3.04-2.97 (m, 4H), 2.45 (s, 3H); ¹³C NMR (100 MHz, CDCl₃): $\delta = 168.7$, 148.3, 141.6, 138.45, 138.41, 137.8, 136.3, 134.6, 134.3, 129.0, 128.4, 128.2, 128.1, 128.0, 127.4, 126.9, 125.8, 122.0, 121.6, 116.8, 38.1, 35.8, 19.5. Spectroscopic data are in accordance with those described in the literature.^{1a}



2-Methyl-6-(3-phenylpropyl)-N-(quinolin-8-yl)benzamide (3e)

The general procedure was applied to 2-methyl-*N*-(quinolin-8-yl)benzamide **1a** (52 mg, 0.2 mmol), CrCl₃ (3.2 mg, 0.02 mmol), IPrHCl (17 mg, 0.02 mmol), (3-bromopropyl)benzene (0.8 mmol) and phenylmagnesium bromide (0.7 mmol) at 40 $^{\circ}$ C for 24 h. The crude product was purified by column chromatography on silica gel

(EtOAc/PE = 1/20, $R_f = 0.37$) to afford the title compound as a pale yellow oil (67 mg, 88% yield). ¹H NMR (400 MHz, CDCl₃): $\delta = 9.92$ (s, 1H), 8.98 (dd, J = 7.2, 1.2 Hz, 1H), 8.68 (dd, J = 4.0, 1.6 Hz, 1H), 8.17 (dd, J = 8.4, 1.6 Hz, 1H), 7.63-7,54 (m, 2H), 7.42-7.39 (m, 1H), 7.28-7.25 (m, 1H), 7.14-7.10 (m, 2H), 7.05-6.99 (m, 5H), 2.77-2.73 (m, 2H), 2.60-2.56 (m, 2H), 2.43 (s, 3H), 2.06-1.98 (m, 2H); ¹³C NMR (100 MHz, CDCl₃): $\delta = 168.7$, 148.2, 141.9, 138.9, 138.4, 137.7, 136.2, 134.5, 134.3, 129.0, 128.2, 128.0, 127.9, 127.8, 127.4, 126.7, 125.4, 121.9, 121.6, 116.7, 35.7, 33.15, 33.09, 19.4. HRMS (ESI⁺): calcd for C₂₆H₂₄N₂ONa [M+Na]⁺ 403.1786, found 403.1784.



2-(3-Methoxypropyl)-6-methyl-N-(quinolin-8-yl)benzamide (3f)

The general procedure was applied to 2-methyl-*N*-(quinolin-8-yl)benzamide **1a** (52 mg, 0.2 mmol), CrCl₃ (3.2 mg, 0.02 mmol), IPrHCl (17 mg, 0.02 mmol), 1-bromo-3-methoxypropane (0.8 mmol) and phenylmagnesium bromide (0.7 mmol) at 40 °C for 24 h. The crude product was purified by column chromatography on silica gel (EtOAc/PE = 1/20, $R_f = 0.28$) to afford the title compound as a colorless oil (53 mg, 79% yield). ¹H NMR (400 MHz, CDCl₃): $\delta = 9.93$ (s, 1H), 9.00 (d, J = 7.6 Hz, 1H), 8.73 (dd, J = 4.4, 1.2 Hz, 1H), 8.19 (d, J = 8.0 Hz, 1H), 7.63-7,56 (m, 2H), 7.46-7.42 (m, 1H), 7.31-7.26 (m, 1H), 7.18-7.12 (m, 2H), 3.35-3.32 (m, 2H), 3.22 (s, 3H), 2.82-2.78 (m, 2H), 2.43 (s, 3H), 1.99-1.92 (m, 2H); ¹³C NMR (100 MHz, CDCl₃): $\delta = 168.7$, 148.3, 138.6, 138.5, 137.8, 136.3, 134.6, 134.4, 129.0, 128.0, 127.9, 127.4, 126.9, 121.9, 121.6, 116.8, 71.9, 58.3, 31.2, 29.9, 19.5. HRMS (ESI⁺): calcd for C₂₁H₂₂N₂O₂Na [M+Na]⁺ 357.1579, found 357.1575.



2-(4-Chlorobutyl)-6-methyl-*N*-(quinolin-8-yl)benzamide (3g)

The general procedure was applied to 2-methyl-*N*-(quinolin-8-yl)benzamide **1a** (52 mg, 0.2 mmol), CrCl₃ (3.2 mg, 0.02 mmol), IPrHCl (17 mg, 0.02 mmol), 1-bromo-4-chlorobutane (0.8 mmol) and phenylmagnesium bromide (0.7 mmol) at 40 ^oC for 24 h. The crude product was purified by column chromatography on silica gel (EtOAc/PE = 1/20, $R_f = 0.4$) to afford the title compound as a pale yellow oil (62 mg, 88% yield). ¹H NMR (400 MHz, CDCl₃): $\delta = 9.93$ (s, 1H), 8.99 (dd, J = 7.2 1.6 Hz, 1H), 8.74 (dd, J = 4.0, 1.6 Hz, 1H), 8.20 (dd, J = 8.4 1.6 Hz, 1H), 7.64-7,57 (m, 2H), 7.47-7.44 (m, 1H), 7.30 (t, J = 7.6 Hz, 1H), 7.16-7.13 (m, 2H), 3.45 (t, J = 6.8 Hz, 2H), 2.75 (t, J = 7.2 Hz, 2H), 2.44 (s, 3H), 1.88-1.72 (m, 4H); ¹³C NMR (100 MHz, CDCl₃): $\delta = 168.7$, 148.3, 138.49, 138.48, 137.8, 136.3, 134.6, 134.3, 129.1, 128.03, 128.01, 127.4, 126.7, 122.0, 121.7, 116.8, 44.7, 32.6, 32.2, 28.7, 19.5. HRMS (ESI⁺): calcd for C₂₁H₂₁ClN₂ONa [M+Na]⁺ 375.1240, found 375.1243.



2-(4-Bromobutyl)-6-methyl-N-(quinolin-8-yl)benzamide (3h)

The general procedure was applied to 2-methyl-*N*-(quinolin-8-yl)benzamide **1a** (52 mg, 0.2 mmol), CrCl₃ (3.2 mg, 0.02 mmol), IPrHCl (17 mg, 0.02 mmol), 1,4-dibromobutane (0.8 mmol) and phenylmagnesium bromide (0.7 mmol) at 40 °C for 24 h. The crude product was purified by column chromatography on silica gel (EtOAc/PE = 1/20, $R_f = 0.42$) to afford the title compound as a pale yellow oil (51 mg,

67% yield). ¹H NMR (400 MHz, CDCl₃): δ = 9.92 (s, 1H), 8.99 (dd, *J* = 7.6, 1.6 Hz, 1H), 8.75 (dd, *J* = 4.4, 1.6 Hz, 1H), 8.20 (dd, *J* = 8.4, 1.6 Hz, 1H), 7.64-7,57 (m, 2H), 7.47-7.44 (m, 1H), 7.30 (t, *J* = 7.6 Hz, 1H), 7.16-7.13 (m, 2H), 3.33-3.30 (m, 2H), 2.77-2.73 (m, 2H), 2.44 (s, 3H), 1.85-1.82 (m, 4H); ¹³C NMR (100 MHz, CDCl₃): δ = 168.7, 148.3, 138.5, 138.4, 137.8, 136.4, 134.6, 134.3, 129.1, 128.1, 128.0, 127.4, 126.7, 122.0, 121.7, 116.8, 33.5, 32.5, 32.4, 30.0, 19.5. HRMS (ESI⁺): calcd for C₂₁H₂₁BrN₂ONa [M+Na]⁺ 419.0735, found 419.0730.



2-Methyl-6-(pent-4-en-1-yl)-N-(quinolin-8-yl)benzamide (3i)

The general procedure was applied to 2-methyl-*N*-(quinolin-8-yl)benzamide **1a** (52 mg, 0.2 mmol), CrCl₃ (3.2 mg, 0.02 mmol), IPrHCl (17 mg, 0.02 mmol), 5-bromopent-1-ene (0.8 mmol) and phenylmagnesium bromide (0.7 mmol) at 40 °C for 24 h. The crude product was purified by column chromatography on silica gel (EtOAc/PE = 1/20, $R_f = 0.44$) to afford the title compound as a pale yellow oil (36 mg, 55% yield). ¹H NMR (400 MHz, CDCl₃): $\delta = 9.93$ (s, 1H), 9.00 (dd, J = 7.6, 1.2 Hz, 1H), 8.73 (dd, J = 4.4, 1.6 Hz, 1H), 8.18 (dd, J = 8.4, 1.6 Hz, 1H), 7.63-7,56 (m, 2H), 7.45-7.42 (m, 1H), 7.30-7.25 (m, 1H), 7.15-7.11 (m, 2H), 5.74-5.64 (m, 1H), 4.91-4.79 (m, 2H), 2.75-2.71 (m, 2H), 2.43 (s, 3H), 2.06-2.00 (m, 2H), 1.82-1.75 (m, 2H); ¹³C NMR (100 MHz, CDCl₃): $\delta = 168.8, 148.2, 139.1, 138.5, 138.3, 137.8, 136.3, 134.5, 134.3, 129.0, 127.9, 127.8, 127.4, 126.8, 121.9, 121.6, 116.7, 114.6, 33.5, 32.9, 30.8, 19.5. HRMS (ESI⁺): calcd for C₂₂H₂₂N₂ONa [M+Na]⁺ 353.1630, found 353.1628.$



2-Isobutyl-6-methyl-N-(quinolin-8-yl)benzamide (3j)

The general procedure was applied to 2-methyl-*N*-(quinolin-8-yl)benzamide **1a** (52 mg, 0.2 mmol), CrCl₃ (3.2 mg, 0.02 mmol), IPrHCl (17 mg, 0.02 mmol), 1-bromo-2-methylpropane (0.8 mmol) and phenylmagnesium bromide (0.7 mmol) at 40 °C for 24 h. The crude product was purified by column chromatography on silica gel (EtOAc/PE = 1/20, $R_f = 0.38$) to afford the title compound as a colorless oil (45 mg, 71% yield). ¹H NMR (400 MHz, CDCl₃): $\delta = 9.91$ (s, 1H), 9.01 (dd, J = 7.6, 1.2 Hz, 1H), 8.73 (dd, J = 4.4, 1.6 Hz, 1H), 8.18 (dd, J = 8.4, 1.6 Hz, 1H), 7.63-7,55 (m, 2H), 7.45-7.42 (m, 1H), 7.27 (t, J = 7.6 Hz, 1H), 7.13 (d, J = 8.0 Hz, 2H), 2.62 (d, J = 7.2 Hz, 2H), 2.43 (s, 3H), 2.04-1.98 (m, 1H), 0.88 (d, J = 6.4 Hz, 6H); ¹³C NMR (100 MHz, CDCl₃): $\delta = 168.9$, 148.2, 138.5, 138.3, 138.1, 136.3, 134.43, 134.38, 128.7, 128.0, 127.7, 127.4, 121.8, 121.6, 116.7, 45.5, 29.9, 22.6, 19.5. Spectroscopic data are in accordance with those described in the literature.^{1a}



2-(3-(2-Chlorophenoxy)propyl)-6-methyl-N-(quinolin-8-yl)benzamide (3k)

The general procedure was applied to 2-methyl-*N*-(quinolin-8-yl)benzamide **1a** (52 mg, 0.2 mmol), CrCl₃ (3.2 mg, 0.02 mmol), IPrHCl (17 mg, 0.02 mmol), **2k** (0.8 mmol) and phenylmagnesium bromide (0.7 mmol) at 40 °C for 24 h. The crude product was purified by column chromatography on silica gel (EtOAc/PE = 1/20, R_f =

0.26) to afford the title compound as a pale yellow oil (55 mg, 64% yield). ¹H NMR (400 MHz, CDCl₃): δ = 9.95 (s, 1H), 8.99 (dd, *J* = 7.2, 1.6 Hz, 1H), 8.71 (dd, *J* = 4.4, 1.6 Hz, 1H), 8.18 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.63-7,56 (m, 2H), 7.44-7.41 (m, 1H), 7.31-7.20 (m, 3H), 7.16 (d, *J* = 7.6 Hz, 1H), 7.09-7.05 (m, 1H), 6.80-6.76 (m, 2H), 3.99 (t, *J* = 6.4 Hz, 2H), 2.99 (t, *J* = 7.2 Hz, 2H), 2.46 (s, 3H), 2.27-2.20 (m, 2H); ¹³C NMR (100 MHz, CDCl₃): δ = 168.6, 154.3, 148.3, 138.5, 138.1, 137.9, 136.3, 134.6, 134.3, 130.0, 129.1, 128.1, 128.0, 127.4, 127.3, 127.1, 122.8, 122.0, 121.6, 120.9, 116.8, 113.2, 67.9, 30.9, 29.7, 19.5. HRMS (ESI⁺): calcd for C₂₆H₂₃ClN₂O₂Na [M+Na]⁺ 453.1346, found 453.1352.



2-(3-(2-Bromophenoxy)propyl)-6-methyl-*N*-(quinolin-8-yl)benzamide (31)

The general procedure was applied to 2-methyl-*N*-(quinolin-8-yl)benzamide **1a** (52 mg, 0.2 mmol), CrCl₃ (3.2 mg, 0.02 mmol), IPrHCl (17 mg, 0.02 mmol), **2l** (0.8 mmol) and phenylmagnesium bromide (0.7 mmol) at 40 °C for 24 h. The crude product was purified by column chromatography on silica gel (EtOAc/PE = 1/20, R_f = 0.26) to afford the title compound as a pale yellow oil (61 mg, 64% yield). ¹H NMR (400 MHz, CDCl₃): δ = 9.95 (s, 1H), 8.98 (dd, *J* = 7.6, 1.2 Hz, 1H), 8.71 (dd, *J* = 4.4, 1.6 Hz, 1H), 8.18 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.62-7,55 (m, 2H), 7.44-7.39 (m, 2H), 7.31-7.25 (m, 1H), 7.21 (d, *J* = 7.6 Hz, 1H), 7.15-7.09 (m, 2H), 6.76-6.70 (m, 2H), 3.97 (t, *J* = 6.0 Hz, 2H), 2.99 (t, *J* = 7.6 Hz, 2H), 2.44 (s, 3H), 2.26-2.17 (m, 2H); ¹³C NMR (100 MHz, CDCl₃): δ = 168.7, 155.1, 148.3, 138.5, 138.1, 137.9, 136.3, 134.7, 134.3, 133.1, 129.1, 128.2, 128.1, 128.0, 127.4, 127.1, 122.0, 121.6, 121.4, 116.8, 112.9, 112.1, 67.9, 30.9, 29.8, 19.5. HRMS (ESI⁺): calcd for C₂₆H₂₃BrN₂O₂Na [M+Na]⁺ 497.0841, found 497.0842.



2-(3-(Benzo[*d*][1,3]dioxol-5-yloxy)propyl)-6-methyl-*N*-(quinolin-8-yl)benzamide (3m)

The general procedure was applied to 2-methyl-*N*-(quinolin-8-yl)benzamide **1a** (52 mg, 0.2 mmol), CrCl₃ (3.2 mg, 0.02 mmol), IPrHCl (17 mg, 0.02 mmol), **2m** (0.8 mmol) and phenylmagnesium bromide (0.7 mmol) at 40 °C for 24 h. The crude product was purified by column chromatography on silica gel (EtOAc/PE = 1/20, R_f = 0.2) to afford the title compound as a pale yellow oil (55 mg, 63% yield). ¹H NMR (400 MHz, CDCl₃): δ = 9.94 (s, 1H), 8.99 (dd, *J* = 7.2, 1.2 Hz, 1H), 8.70 (dd, *J* = 4.0, 1.6 Hz, 1H), 8.17 (dd, *J* = 8.4, 1.6 Hz, 1H), 7.62-7,55 (m, 2H), 7.43-7.40 (m, 1H), 7.30-7.24 (m, 1H), 7.18-7.13 (m, 2H), 6.54 (d, *J* = 8.4 Hz, 1H), 6.29 (d, *J* = 2.8 Hz, 1H), 6.15 (dd, *J* = 8.4, 2.4 Hz, 1H), 5.83 (s, 2H), 3.81 (t, *J* = 6.2 Hz, 2H), 2.91 (t, *J* = 7.6 Hz, 2H), 2.44 (s, 3H), 2.16-2.09 (m, 2H); ¹³C NMR (100 MHz, CDCl₃): δ = 168.7, 154.3, 148.2, 147.9, 141.2, 138.4, 138.2, 137.9, 136.3, 134.6, 134.2, 129.1, 128.1, 128.0, 127.3, 126.9, 122.0, 121.6, 116.8, 107.6, 105.4, 100.9, 97.9, 67.7, 30.9, 29.7, 19.5. HRMS (ESI⁺): calcd for C₂₇H₂₄N₂O₄Na [M+Na]⁺ 463.1634, found 463.1638.



2-Butyl-6-methoxy-N-(quinolin-8-yl)benzamide (3n)

The general procedure was applied to 2-methoxy-*N*-(quinolin-8-yl)benzamide (**1b**) (56 mg, 0.2 mmol), $CrCl_3$ (3.2 mg, 0.02 mmol), IPrHCl (17 mg, 0.02 mmol), 1-bromobutane (0.8 mmol) and phenylmagnesium bromide (0.7 mmol) at 40 °C for 24

h. The crude product was purified by column chromatography on silica gel (EtOAc/PE = 1/20, $R_f = 0.2$) to afford the title compound as a colorless oil (53 mg, 80% yield). ¹H NMR (400 MHz, CDCl₃): $\delta = 10.04$ (s, 1H), 9.02 (dd, J = 7.2, 0.9 Hz, 1H), 8.74 (dd, J = 4.0, 1.6 Hz, 1H), 8.16 (dd, J = 8.4, 1.6 Hz, 1H), 7.59 (t, J = 7.8 Hz, 1H), 7.54-7.52 (m, 1H), 7.43-7.40 (m, 1H), 7.32 (t, J = 7.8 Hz, 1H), 6.92 (d, J = 7.6 Hz, 1H), 6.84 (d, J = 8.0 Hz, 1H), 3.82 (s, 3H), 2.73 (t, J = 7.8 Hz, 2H), 1.69-1.62 (m, 2H), 1.33-1.26 (m, 2H), 0.81 (t, J = 7.4 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃): $\delta = 166.5$, 156.3, 148.1, 142.0, 138.5, 136.2, 134.7, 130.0, 127.9, 127.4, 126.9, 121.8, 121.6, 121.5, 116.7, 108.4, 55.7, 33.6, 32.9, 22.6, 13.8. HRMS (ESI⁺): calcd for C₂₁H₂₂N₂O₂Na [M+Na]⁺ 357.1579, found 357.1538.



3-Butyl-*N*-(quinolin-8-yl)-[1,1'-biphenyl]-2-carboxamide (30)

The general procedure applied was to N-(quinolin-8-yl)-[1,1'-biphenyl]-2-carboxamide (1c) (63 mg, 0.2 mmol), CrCl₃ (3.2 mg, 0.02 mmol), IPrHCl (17 mg, 0.02 mmol), 1-bromobutane (0.8 mmol) and phenylmagnesium bromide (0.7 mmol) at 40 °C for 24 h. The crude product was purified by column chromatography on silica gel (EtOAc/PE = 1/20, $R_f = 0.3$) to afford the title compound as a pale yellow oil (40 mg, 53% yield). ¹H NMR (400 MHz, CDCl₃): $\delta = 9.62$ (s, 1H), 8.75 (d, J = 7.2 Hz, 1H), 8.60 (d, J = 4.0 Hz, 1H), 8.07-8.05 (m, 1H), 7.53-7.47 (m, 3H), 7.45-7.42 (m, 2H), 7.36-7.29 (m, 3H), 7.20 (t, J = 7.6 Hz, 2H), 7.07 (t, J = 7.4 Hz, 1H), 2.83 (t, J = 7.8 Hz, 2H), 1.75-1.67 (m, 2H), 1.39-1.29 (m, 2H), 0.83 (t, J = 7.4 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃): $\delta = 168.2$, 147.9, 140.7, 140.5, 139.7, 138.3, 136.6, 136.0, 134.4, 129.1, 128.7, 128.6, 128.1, 127.7, 127.6, 127.2, 127.1, 121.6, 121.4, 116.4, 33.8, 33.2, 22.7, 13.9. HRMS (ESI⁺): calcd for C₂₆H₂₄N₂ONa [M+Na]⁺ 403.1786, found 403.1786.



2-Butyl-N-(quinolin-8-yl)-1-naphthamide (3p)

The general procedure was applied to *N*-(quinolin-8-yl)-1-naphthamide (1d) (60 mg, 0.2 mmol), CrCl₃ (3.2 mg, 0.02 mmol), IPrHCl (17 mg, 0.02 mmol), 1-bromobutane (0.8 mmol) and phenylmagnesium bromide (0.7 mmol) at 40 °C for 24 h. The crude product was purified by column chromatography on silica gel (EtOAc/PE = 1/20, R_f = 0.3) to afford the title compound as a pale yellow oil (44 mg, 62% yield). ¹H NMR (400 MHz, CDCl₃): δ = 10.14 (s, 1H), 9.14 (dd, *J* = 7.2, 0.9 Hz, 1H), 8.67 (dd, *J* = 4.0, 1.6 Hz, 1H), 8.19 (dd, *J* = 8.4, 1.6 Hz, 1H), 8.00-7.98 (m, 1H), 7.89-7.85 (m, 2H), 7.66 (t, *J* = 8.0 Hz, 1H), 7.61-7.58 (m, 1H), 7.48-7.40 (m, 4H), 2.89 (t, *J* = 7.8 Hz, 2H), 1.80-1.72 (m, 2H), 1.39-1.29 (m, 2H), 0.82 (t, *J* = 7.2 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃): δ = 168.4, 148.2, 138.5, 137.2, 136.3, 134.5, 133.9, 131.8, 130.3, 129.2, 128.0, 127.9, 127.5, 127.4, 126.9, 125.6, 124.9, 122.0, 121.7, 116.8, 33.8, 33.6, 22.7, 13.9. Spectroscopic data are in accordance with those described in the literature.^{1a}



6-Butyl-2,3-dimethyl-N-(quinolin-8-yl)benzamide (3q)

The general procedure was applied to 2,3-dimethyl-*N*-(quinolin-8-yl)benzamide (**1e**) (55 mg, 0.2 mmol), CrCl₃ (3.2 mg, 0.02 mmol), IPrHCl (17 mg, 0.02 mmol), 1-bromobutane (0.8 mmol) and phenylmagnesium bromide (0.7 mmol) at 40 °C for 24 h. The crude product was purified by column chromatography on silica gel (EtOAc/PE = 1/20, $R_f = 0.4$) to afford the title compound as a pale yellow oil (42 mg,

63% yield). ¹H NMR (400 MHz, CDCl₃): δ = 9.42 (s, 1H), 9.04 (d, *J* = 7.6 Hz, 1H), 8.74 (d, *J* = 3.6 Hz, 1H), 8.19 (d, *J* = 8.4 Hz, 1H), 7.64-7.56 (m, 2H), 7.46-7.42 (m, 1H), 7.19 (d, *J* = 7.6 Hz, 1H), 7.08 (d, *J* = 7.6 Hz, 1H), 2.69 (t, *J* = 7.8 Hz, 2H), 2.33 (s, 3H), 2.31 (s, 3H), 1.70-1.62 (m, 2H), 1.34-1.25 (m, 2H), 0.80 (t, *J* = 7.4 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃): δ = 169.4, 148.2, 138.5, 138.0, 136.8, 136.2, 134.5, 134.4, 132.7, 130.3, 128.0, 127.4, 126.5, 121.8, 121.6, 116.7, 33.8, 32.9, 22.6, 19.8, 16.6, 13.8. HRMS (ESI⁺): calcd for C₂₂H₂₄N₂ONa [M+Na]⁺ 355.1786, found 355.1792.



6-Butyl-3-methoxy-2-methyl-N-(quinolin-8-yl)benzamide (3r)

The general procedure applied was to 3-methoxy-2-methyl-N-(quinolin-8-yl)benzamide (1f) (58 mg, 0.2 mmol), CrCl₃ (3.2 mg, 0.02 mmol), IPrHCl (17 mg, 0.02 mmol), 1-bromobutane (0.8 mmol) and phenylmagnesium bromide (0.7 mmol) at 40 °C for 24 h. The crude product was purified by column chromatography on silica gel (EtOAc/PE = 1/20, $R_f = 0.29$) to afford the title compound as a pale yellow oil (35 mg, 50% yield). ¹H NMR (400 MHz, CDCl₃): $\delta = 9.92$ (s, 1H), 9.00 (d, J = 7.6 Hz, 1H), 8.73 (m, 1H), 8.18 (d, J =8.4 Hz, 1H), 7.63-7.55 (m, 2H), 7.45-7.42 (m, 1H), 7.13 (d, J = 8.4 Hz, 1H), 6.89 (d, J= 8.4 Hz, 1H), 3.86 (s, 3H), 2.66 (t, J = 7.8 Hz, 2H), 2.29 (s, 3H), 1.67-1.60 (m, 2H), 1.31-1.24 (m, 2H), 0.80 (t, J = 7.4 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃): $\delta = 168.6$, 155.8, 148.2, 138.9, 138.5, 136.3, 134.4, 131.1, 128.0, 127.4, 123.1, 121.8, 121.6, 116.7, 110.8, 55.6, 33.9, 32.5, 22.5, 13.8, 13.0. HRMS (ESI⁺): calcd for $C_{22}H_{24}N_2O_2Na [M+Na]^+ 371.1735$, found 371.1735.



6-Butyl-3-chloro-2-methyl-N-(quinolin-8-yl)benzamide (3s)

The general procedure was applied to 3-chloro-2-methyl-*N*-(quinolin-8-yl)benzamide (**1g**) (59 mg, 0.2 mmol), CrCl₃ (3.2 mg, 0.02 mmol), IPrHCl (17 mg, 0.02 mmol), 1-bromobutane (0.8 mmol) and phenylmagnesium bromide (0.7 mmol) at 40 °C for 24 h. The crude product was purified by column chromatography on silica gel (EtOAc/PE = 1/20, $R_f = 0.28$) to afford the title compound as a pale yellow oil (49 mg, 69% yield). ¹H NMR (400 MHz, CDCl₃): $\delta = 9.93$ (s, 1H), 8.98 (dd, J = 7.2, 1.6 Hz, 1H), 8.76 (dd, J = 4.4, 1.6 Hz, 1H), 8.20 (dd, J = 8.4, 1.6 Hz, 1H), 7.64-7.57 (m, 2H), 7.47-7.44 (m, 1H), 7.38 (d, J = 8.0 Hz, 1H), 7.11 (d, J = 8.4 Hz, 1H), 2.67 (t, J = 7.8 Hz, 2H), 2.45 (s, 3H), 1.67-1.60 (m, 2H), 1.33-1.23 (m, 2H), 0.80 (t, J = 7.4 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃): $\delta = 167.8$, 148.3, 139.3, 138.4, 138.1, 136.3, 134.1, 132.4, 132.3, 130.0, 128.03, 127.98, 127.4, 122.2, 121.7, 116.8, 33.6, 32.8, 22.5, 17.3, 13.8. HRMS (ESI⁺): calcd for C₂₁H₂₁ClN₂ONa [M+Na]⁺ 375.1240, found 375.1238.



2-Butyl-4,6-dimethyl-N-(quinolin-8-yl)benzamide (3t)

The general procedure was applied to 2,4-dimethyl-*N*-(quinolin-8-yl)benzamide (**1h**) (55 mg, 0.2 mmol), CrCl₃ (3.2 mg, 0.02 mmol), IPrHCl (17 mg, 0.02 mmol), 1-bromobutane (0.8 mmol) and phenylmagnesium bromide (0.7 mmol) at 40 °C for 24 h. The crude product was purified by column chromatography on silica gel (EtOAc/PE = 1/20, $R_f = 0.4$) to afford the title compound as a pale yellow oil (47 mg, 71% yield). ¹H NMR (400 MHz, CDCl₃): $\delta = 9.94$ (s, 1H), 9.02 (d, J = 7.2 Hz, 1H),

8.73 (d, J = 4.0 Hz, 1H), 8.18 (d, J = 8.4 Hz, 1H), 7.64-7.55 (m, 2H), 7.45-7.42 (m, 1H), 6.97 (d, J = 10.4 Hz, 2H), 2.70 (t, J = 8.0 Hz, 2H), 2.41 (s, 3H), 2.36 (s, 3H), 1.71-1.63 (m, 2H), 1.35-1.26 (m, 2H), 0.82 (t, J = 7.4 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃): $\delta = 169.1$, 148.1, 139.5, 138.6, 138.5, 136.2, 135.1, 134.5, 134.4, 128.4, 128.0, 127.4, 121.8, 121.6, 116.6, 33.8, 33.1, 22.6, 21.2, 19.4, 13.8. HRMS (ESI⁺): calcd for C₂₂H₂₄N₂ONa [M+Na]⁺ 355.1786, found 355.1787.



2-Butyl-4-fluoro-6-methyl-N-(quinolin-8-yl)benzamide (1i)

The general procedure was applied to 4-fluoro-2-methyl-*N*-(quinolin-8-yl)benzamide (**S9**) (56 mg, 0.2 mmol), CrCl₃ (3.2 mg, 0.02 mmol), IPrHCl (17 mg, 0.02 mmol), 1-bromobutane (0.8 mmol) and phenylmagnesium bromide (0.7 mmol) at 40 °C for 24 h. The crude product was purified by column chromatography on silica gel (EtOAc/PE = 1/20, $R_f = 0.38$) to afford the title compound as a pale yellow oil (50 mg, 74% yield). ¹H NMR (400 MHz, CDCl₃): $\delta = 9.91$ (s, 1H), 8.98 (dd, J = 7.2 1.6 Hz, 1H), 8.75 (dd, J = 4.0 1.6 Hz, 1H), 8.20 (dd, J = 8.4 1.6 Hz, 1H), 7.64-7.56 (m, 2H), 7.47-7.44 (m, 1H), 6.86-6.80 (m, 2H), 2.71 (t, J = 8.0 Hz, 2H), 2.43 (s, 3H), 1.69-1.62 (m, 2H), 1.34-1.25 (m, 2H), 0.81 (t, J = 7.2 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃): $\delta = 168.1$, 163.9 (d, $J_{C-F} = 245.7$ Hz), 148.3, 142.4 (d, $J_{C-F} = 8.0$ Hz), 138.5, 137.4 (d, $J_{C-F} = 8.5$ Hz), 136.3, 134.3, 134.0 (d, $J_{C-F} = 2.9$ Hz), 128.0, 127.4, 122.0, 121.7, 116.8, 114.6 (d, $J_{C-F} = 1.6$ Hz), 13.8. ¹⁹F NMR (377 MHz, CDCl₃): $\delta = -112.97$. Spectroscopic data are in accordance with those described in the literature.^{1a}



2-Butyl-3,6-dimethyl-*N*-(quinolin-8-yl)benzamide (3v)

The general procedure was applied to 2,5-dimethyl-*N*-(quinolin-8-yl)benzamide (**1j**) (55 mg, 0.2 mmol), CrCl₃ (3.2 mg, 0.02 mmol), IPrHCl (17 mg, 0.02 mmol), 1-bromobutane (0.8 mmol) and phenylmagnesium bromide (0.7 mmol) at 40 °C for 24 h. The crude product was purified by column chromatography on silica gel (EtOAc/PE = 1/20, $R_f = 0.4$) to afford the title compound as a pale yellow oil (59 mg, 75% yield). ¹H NMR (400 MHz, CDCl₃): $\delta = 9.93$ (s, 1H), 9.02 (d, J = 7.2 Hz, 1H), 8.74 (d, J = 4.0 Hz, 1H), 8.19 (d, J = 8.4 Hz, 1H), 7.64-7.56 (m, 2H), 7.46-7.42 (m, 1H), 7.15 (d, J = 7.6 Hz, 1H), 7.04 (d, J = 8.0 Hz, 1H), 2.69 (t, J = 8.4 Hz, 2H), 2.39 (s, 3H), 2.36 (s, 3H), 1.66-1.59 (m, 2H), 1.33-1.27 (m, 2H), 0.79 (t, J = 7.4 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃): $\delta = 169.4$, 148.2, 138.5, 138.2, 137.6, 136.3, 134.4, 134.0, 131.9, 130.9, 128.0, 127.6, 127.4, 121.8, 121.6, 116.7, 32.8, 30.9, 23.2, 19.2, 19.1, 13.7. HRMS (ESI⁺): calcd for C₂₂H₂₄N₂ONa [M+Na]⁺ 355.1786, found 355.1785.



2-Butyl-3-fluoro-6-methyl-N-(quinolin-8-yl)benzamide (3w)

The general procedure was applied to 5-fluoro-2-methyl-*N*-(quinolin-8-yl)benzamide (**1k**) (56 mg, 0.2 mmol), CrCl₃ (3.2 mg, 0.02 mmol), IPrHCl (17 mg, 0.02 mmol), 1-bromobutane (0.8 mmol) and phenylmagnesium bromide (0.7 mmol) at 40 °C for 24 h. The crude product was purified by column chromatography on silica gel (EtOAc/PE = 1/20, $R_f = 0.35$) to afford the title compound as a pale yellow oil (36 mg,

54% yield). ¹H NMR (400 MHz, CDCl₃): $\delta = 9.92$ (s, 1H), 8.98 (dd, J = 7.2, 1.6 Hz, 1H), 8.76 (dd, J = 4.0, 1.6 Hz, 1H), 8.21 (dd, J = 8.4, 1.6 Hz, 1H), 7.64-7.57 (m, 2H), 7.48-7.44 (m, 1H), 7.09-6.99 (m, 2H), 2.73-2.69 (m, 2H), 2.39 (s, 3H), 1.69-1.61 (m, 2H), 1.33-1.24 (m, 2H), 0.78 (t, J = 7.4 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃): $\delta = 167.5$ (d, $J_{C-F} = 3.2$ Hz), 160.8, 158.4, 148.3, 139.2 (d, $J_{C-F} = 4.1$ Hz), 138.5, 136.4, 134.2, 130.1 (d, $J_{C-F} = 3.7$ Hz), 129.1 (d, $J_{C-F} = 8.0$ Hz), 128.0, 127.4, 127.0 (d, $J_{C-F} = 7.5$ Hz), 122.1 (d, $J_{C-F} = 39.5$ Hz), 116.8, 115.8 (d, $J_{C-F} = 22.6$ Hz), 32.9 (d, $J_{C-F} = 0.9$ Hz), 27.0 (d, $J_{C-F} = 2.1$ Hz), 22.8, 18.9, 13.7. ¹⁹F NMR (377 MHz, CDCl₃): $\delta = -121.1$. HRMS (ESI⁺): calcd for C₂₁H₂₁FN₂ONa [M+Na]⁺ 359.1536, found 359.1540.

5. Mechanistic Studies



A dried Schlenk tube were placed $CrCl_3$ (3.2 mg, 0.02 mmol), IPrHCl (17 mg, 0.02 mmol) and freshly distilled 2-Me THF (0.1 mL). Phenylmagnesium bromide (0.1 mmol) was added dropwise by syringe at 40 °C. After stirring for 2 h at 40 °C, **1a** (52.4 mg, 0.2 mmol) and **2a** (0.8 mmol) was added in glovebox followed by dropwise addition of Phenylmagnesium bromide (0.6 mmol). The resulting mixture was stirred for another 22 h at 40 °C. After that, the mixture was quenched by an aqueous solution of NH₄Cl and extracted with ethyl acetate (3 x 10 mL). The combined organic phase was dried over anhydrous Na₂SO₄ and concentrated under vacuum. The crude product was purified by silica gel chromatography to give the coupling product **3a** (15 mg, 23%).



A dried Schlenk tube were placed benzamide **1a** (52.4 mg, 0.2 mmol), CrCl₃ (15.8 mg, 0.1 mmol), IPrHCl (170 mg, 0.2 mmol) and freshly distilled 2-Me THF (0.3 mL). Phenylmagnesium bromide (0.7 mmol) was added dropwise by syringe at 40 °C over 10 min. After stirring for 6 h at 40 °C, the resulting mixture was quenched by D₂O and stirred for another 0.5 h before extracted with ethyl acetate (3 x 10 mL). The combined organic phase was dried over anhydrous Na₂SO₄ and concentrated under vacuum. The crude product was purified by silica gel chromatography to give the mixture of **1a** and **1a-D** in 78% recovery. ¹H NMR analysis showed that the D contents in the recovered amide was 29%.





A dried Schlenk tube were placed benzamide **1a** (52.4 mg, 0.2 mmol), CrCl₃ (3.2 mg, 0.02 mmol), IPrHCl (17 mg, 0.02 mmol), hex-1-ene or styrene (0.8 mmol) and freshly distilled 2-Me THF (0.3 mL). Phenylmagnesium bromide (0.7 mmol) was added dropwise by syringe at 40 °C over 10 min. After stirring for 24 h at 40 °C, the resulting mixture was quenched by an aqueous solution of NH₄Cl. Product **3b** or **3d** was not detected by TLC and GC-MS analysis.



A dried Schlenk tube were placed benzamide **1a** (52.4 mg, 0.2 mmol), CrCl₃ (3.2 mg, 0.02 mmol), IPrHCl (17 mg, 0.02 mmol), 6-bromohex-1-ene (0.8 mmol) and freshly distilled 2-Me THF (0.3 mL). Phenylmagnesium bromide (0.7 mmol) was added dropwise by syringe at 40 °C over 10 min. After stirring for 24 h at 40 °C, the resulting mixture was quenched by an aqueous solution of NH₄Cl and extracted with ethyl acetate (3 x 10 mL). The combined organic phase was dried over anhydrous Na₂SO₄ and concentrated under vacuum. The crude product was purified by silica gel chromatography (EtOAc/PE = 1/20, $R_f = 0.4$) to give the coupling product an inseparable mixture (47 mg, 69%) of 7 and 8 as a clear oil which rario (7:8 = 38:62) was detected by ¹H-NMR.



2-(Hex-5-en-1-yl)-6-methyl-N-(quinolin-8-yl)benzamide(7)and2-(Cyclopentylmethyl)-6-methyl-N-(quinolin-8-yl)benzamide(8)

¹H NMR (400 MHz, CDCl₃): $\delta = 9.93$ (s), 9,92 (s), 8.98 (d, J = 7.2 Hz), 8.73-8.71 (m), 8.16 (d, J = 8.4 Hz), 7.63-7.55 (m), 7.44-7.41 (m), 7.29-7.25 (m), 7.17-7.10 (m), 5.72-5.62 (m), 4.88-4.77 (m), 2.75-2.70 (m), 2.43 (s), 2.27-2.16 (m), 1.99-1.93 (m), 1.71-1.64 (m), 1.55-1.35 (m), 1.20-1.11 (m); ¹³C NMR (100 MHz, CDCl₃): $\delta = 168.92$, 168.83, 148.23, 148.20, 139.25, 138.88, 138.71, 138.51, 138.49, 137.92, 137.75, 136.28, 134.50, 134.43, 134.41, 134.39, 128.96, 128.75, 127.98, 127.75, 127.67, 127.40, 127.08, 126.73, 121.89, 121.85, 121.62, 116.74, 114.20, 41.59, 39.10, 33.46, 33.26, 32.61, 31.07, 28.72, 24.75, 19.52, 19.47. HRMS (ESI⁺): calcd for C₂₃H₂₄N₂ONa [M+Na]⁺ 367.1786, found 367.1784.



¹H NMR Spectra of 7 and 8



A dried Schlenk tube were placed benzamide **1a** (52.4 mg, 0.2 mmol), $CrCl_3$ (3.2 mg, 0.02 mmol), IPrHCl (17 mg, 0.02 mmol), 1-bromobutane (0.8 mmol), TEMPO (0.2 mmol) and freshly distilled 2-Me THF (0.3 mL). Phenylmagnesium bromide (0.7 mmol) was added dropwise by syringe at 40 °C over 10 min. After stirring for 24 h at 40 °C, the resulting mixture was quenched by an aqueous solution of NH₄Cl. Product **3a** was not detected by TLC and GC-MS analysis.

KIE experiment



A dried Schlenk tube were placed benzamide **1a** or **1a-D** (0.2 mmol), CrCl₃ (3.2 mg, 0.02 mmol), IPrHCl (17 mg, 0.02 mmol), 1-bromobutane (0.8 mmol) and freshly distilled 2-Me THF (0.3 mL). Phenylmagnesium bromide (0.7 mmol) was added dropwise by syringe at 40 °C over 10 min. After stirring for designated time (30 min, 60 min, 90 min, 120 min, and 150 min) at 40 °C, the resulting mixture was quenched by an aqueous solution of NH₄Cl and extracted with ethyl acetate (3 x 10 mL). After removing the volatiles under vacuum, the crude product was analyzed by ¹H NMR using 1,3,5-trimethoxybenzene as an internal standard. A KIE value of $K_H/K_D = 1.42$ was obtained.



KIE = 0.001/0.0007 = 1.4

Deuterium experiment by alkylation with ortho-D-containing benzamide (1a-D)



A dried Schlenk tube were placed benzamide **1a-D** (0.2 mmol), $CrCl_3$ (3 mg, 0.02 mmol), IPrHCl (17 mg, 0.02 mmol), 1-bromobutane (0.8 mmol) and freshly distilled 2-MeTHF (0.3 mL). 4-Biphenylmagnesium bromide (0.7 mmol) was added dropwise by syringe at 40 °C over 10 min. After stirring for designated time 16 h at 40 °C, the resulting mixture was quenched by an aqueous solution of NH₄Cl and extracted with ethyl acetate (3 x 10 mL). After removing the volatiles under vacuum, the crude product was analyzed by GC-MS and GC analysis using tridecane as internal standard. The crude products were then purified by silican gel chromatography to give the alkylated compound **3a** in 53% yield combined with 177% of biphenyl (yield was based on **1a-D**). ¹H NMR analysis of biphenyl found that nearly 16% D was incorporated into the C4 position of biphenyl (please see the following Figures for details).



¹H NMR spectra for C4-fully or partially deuterated biphenyl.

Proposed Mechanism



6. Supplementary References

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- Sheng, C.; Wang, W.; Che, X.; Dong, G.; Wang, S.; Ji, S.; Miao, Z.; Yao, J.; Zhang, W. *ChemMedChem* 2010, *5*, 390.

7. ¹H, ¹³C and ¹⁹F NMR Spectra


¹H and ¹³C NMR Spectra of 1a





9,780 9,780 9,798 8,817 8,817 8,817 8,816 8,817 1,757 1,



¹H and ¹³C NMR Spectra of 1c























----0.000



¹H, ¹³C and ¹⁹F NMR Spectra of 1i





---0.000



¹H, ¹³C and ¹⁹F NMR Spectra of 1k



¹H and ¹³C NMR Spectra of 1a-D



C 2 384 C 2 369 2 354 2 339 2 339 2 339











¹H and ¹³C NMR Spectra of 2m







¹H and ¹³C NMR Spectra of 3b



¹H and ¹³C NMR Spectra of 3c











 $\begin{array}{c} 3.351 \\ 3.319 \\ 3.319 \\ 2.777 \\ 2.777 \\ 2.777 \\ 2.777 \\ 1.991 \\ 1.915 \\ 1.955 \\ 1.955 \\ 1.955 \\ 1.937 \\ 1.920 \end{array}$























¹⁸⁰ 170 160 150 140 130 120 110 100 90 80 ¹H and ¹³C NMR Spectra of 31



¹H and ¹³C NMR Spectra of 3m



¹H and ¹³C NMR Spectra of 3n

S65





¹H and ¹³C NMR Spectra of 30





S67

¹H and ¹³C NMR Spectra of 3p











 $\begin{array}{c} \int 2 & 691 \\ 2 & 672 \\ -2 & 652 \\ -2 & 449 \\ -2 & 449 \\ -1 & 674 \\ -1 & 678 \\ -1 & -1 & 270 \\ -1 & 270 \\ -1 & 270 \\ -1 & 777 \\ -1 & 770$

¹H and ¹³C NMR Spectra of 3s

 $\begin{array}{c} -9.925 \\ -9.925 \\ \hline 8.865 \\ 8.865 \\ -8.740 \\ -8.740 \\ -8.740 \\ -8.730 \\ \hline 8.128 \\ \hline 8.128 \\ -8.233 \\ -7.363 \\ -7.$

S70



 $\begin{array}{c} \int & 2722 \\ \int & 2702 \\ 2682 \\ \hline & 2682 \\ \hline & 2614 \\ 1.634 \\ 1.634 \\ \hline & 1.634 \\ 1.634 \\ \hline & 0.818 \\ \hline & 0.0818 \\ \hline & 0.0818 \\ \hline \end{array}$

¹H and ¹³C NMR Spectra of 3t

 $\sum_{k=1}^{9,018} \sum_{k=1}^{9,018} \sum_{k=1}^{9,018} \sum_{k=1}^{9,000} \sum_{j=1}^{9,010} \sum_{j=1}^{9,010} \sum_{k=1}^{9,010} \sum_{j=1}^{9,010} \sum_{k=1}^{9,010} \sum_{k=1}^{9,0$

S71



¹H, ¹³C and ¹⁹F NMR Spectra of 3u






¹H, ¹³C and ¹⁹F NMR Spectra of 3w