Supporting Information

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

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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. $^1$H NMR spectra were measured on a Bruker AV-400 spectrometer and reported in parts per million. $^1$H NMR spectra were recorded at 400 MHz in CDCl$_3$ were referenced internally to tetramethylsilane as a standard, and $^{13}$C 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"
CrCl₃ (10 mol %)
dppe (10 mol %)
n-BuBr (2 eq)
Grignard reagents (3.5 eq)
2-MeTHF, 65 °C, 24 h

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst</th>
<th>Grignard reagents</th>
<th>Yield of 3a (%)&lt;sup&gt;b&lt;/sup&gt;</th>
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<tr>
<td>1</td>
<td>CrCl₃</td>
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<td>6</td>
<td>CrCl₃</td>
<td>PhMgBr</td>
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<sup>a</sup>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. <sup>b</sup>Isolated yield. n.d. = Not detected by GC-MS and TLC analyses.

**Table S2.** Studying the effect of ligands<sup>a</sup>

CrCl₃ (10 mol %)
Ligand (20 mol %)
n-BuBr (4 eq)
PhMgBr (3.5 eq)
2-MeTHF, 65 °C, 24 h

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst</th>
<th>Ligand</th>
<th>Yield of 3a (%)&lt;sup&gt;b&lt;/sup&gt;</th>
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<td>6</td>
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<td>7</td>
<td>CrCl₃</td>
<td>IPr·HCl</td>
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S3
8 CrCl₃ IMesHCl 43

*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. Isolated yield. 10 mol % ligand was used.

Table S3. Studying the amount of PhMgBr

<table>
<thead>
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<th>Entry</th>
<th>PhMgBr (equiv)</th>
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<tr>
<td>4</td>
<td>5</td>
<td>52</td>
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*Conditions: 1a (0.2 mmol), CrCl₃ (10 mol %), IPr·HCl (20 mol %), 2-MeTHF (0.3 mL), 2a (0.8 mmol), PhMgBr (0.5-1.0 mmol), 65 °C, 24 h. Isolated yield.

Table S4. Studying the amount of alkyl bromide

<table>
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<tbody>
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<tr>
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<td>83</td>
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<tr>
<td>4</td>
<td>5</td>
<td>81</td>
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</tbody>
</table>

*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. Isolated yield.
Table S5. Studying the effect of temperature<sup>a</sup>

![Chemical Structure](Image)

<table>
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<tr>
<th>Entry</th>
<th>T (°C)</th>
<th>Yield of 3a (%)&lt;sup&gt;b&lt;/sup&gt;</th>
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<sup>a</sup>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. <sup>b</sup>Isolated yield.

Table S6. Studying the effect of Chromium salts<sup>a</sup>

![Chemical Structure](Image)

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst</th>
<th>Yield of 3a (%)&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
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<tbody>
<tr>
<td>1</td>
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<td>n.d.</td>
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<td>CrCl₃</td>
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<td>Cr(CO)₆</td>
<td>n.d.</td>
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<sup>a</sup>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. <sup>b</sup>Isolated yield. 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.\textsuperscript{1} Alkyl bromides 2k-2l were prepared according to the corresponding literatures.\textsuperscript{2}

**2-Methyl-N-(quinolin-8-yl)benzamide (1a):** white solid. \(^{1}\text{H} \) NMR (400 MHz, CDCl\(_3\)): \(\delta = 10.22 \text{ (s, 1H)}, 8.97 \text{ (d, } J = 7.6 \text{ Hz, 1H)}, 8.78-8.77 \text{ (m, 1H)}, 8.19-8.16 \text{ (m, 1H)}, 7.70 \text{ (d, } J = 7.6 \text{ Hz, 1H)}, 7.62-7.54 \text{ (m, 2H)}, 7.47-7.39 \text{ (m, 2H)}, 7.35-7.31 \text{ (m, 2H)}, 2.62 \text{ (s, 3H)}; \(^{13}\text{C} \) NMR (100 MHz, CDCl\(_3\)): \(\delta = 168.2, 148.2, 138.6, 136.7, 136.6, 136.3, 134.7, 131.4, 130.3, 128.0, 127.4, 127.2, 126.0, 121.7, 121.6, 116.5, 20.2.\)
2-Methoxy-N-(quinolin-8-yl)benzamide (1b): white solid. $^1$H NMR (400 MHz, CDCl$_3$): $\delta = 12.34$ (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); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta = 163.6, 157.7, 148.2, 139.2, 136.2, 135.7, 133.1, 132.3, 128.0, 127.5, 122.3, 121.4, 121.3, 121.2, 117.2, 111.5, 56.0.$

$N$-(quinolin-8-yl)-[1,1'-biphenyl]-2-carboxamide (1c): brown solid. $^1$H NMR (400 MHz, CDCl$_3$): $\delta = 9.78$ (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); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta = 167.8, 147.7, 140.2, 140.0, 138.4, 136.1, 135.9, 134.5, 130.7, 130.5, 129.2, 128.9, 128.3, 127.7, 127.6, 127.5, 127.2, 121.5, 121.4, 116.2.$

$N$-(quinolin-8-yl)-1-naphthamide (1d): brown solid. $^1$H NMR (400 MHz, CDCl$_3$): $\delta = 10.4$ (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); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta = 167.7, 148.3, 138.6, 136.3, 134.8, 134.6, 133.9, 131.1, 130.3, 128.4, 128.0, 127.4, 127.3, 126.5, 125.6, 125.5, 124.8, 121.9, 121.7, 116.7.$
2,3-Dimethyl-N-(quinolin-8-yl)benzamide (1e): white solid. $^1$H NMR (400 MHz, CDCl$_3$): $\delta = 10.1$ (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); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta = 169.0$, 148.2, 138.5, 138.1, 137.6, 136.3, 134.7, 134.6, 131.5, 127.9, 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. $^1$H NMR (400 MHz, CDCl$_3$): $\delta = 10.15$ (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); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta = 168.2$, 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. $^1$H NMR (400 MHz, CDCl$_3$): $\delta = 10.14$ (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); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta = 167.4$, 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. $^1$H NMR (400 MHz, CDCl$_3$): $\delta = 10.24$ (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); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta = 168.1$, 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.

![2,4-Dimethyl-N-(quinolin-8-yl)benzamide](image)

4-Fluoro-2-methyl-N-(quinolin-8-yl)benzamide (1i): white solid. $^1$H NMR (400 MHz, CDCl$_3$): $\delta = 10.19$ (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); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta = 167.2$, 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; $^{19}$F NMR (377 MHz, CDCl$_3$): $\delta = -110.4$.

![4-Fluoro-2-methyl-N-(quinolin-8-yl)benzamide](image)

2,5-Dimethyl-N-(quinolin-8-yl)benzamide (1j): white solid. $^1$H NMR (400 MHz, CDCl$_3$): $\delta = 10.18$ (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); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta = 168.4$, 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. $^1$H NMR (400 MHz, CDCl$_3$): $\delta = 10.19$ (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); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta = 166.8$ (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; $^{19}$F NMR (377 MHz, CDCl$_3$): $\delta = -116.6$.

1a-D: white solid. $^1$H NMR (400 MHz, CDCl$_3$): $\delta = 10.2$ (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); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta = 168.0$, 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 C$_{17}$H$_{13}$DN$_2$ONa [M+Na]$^+$ 286.1067, found 286.1065.

1-(3-Bromopropoxy)-2-chlorobenzene (2k): colorless oil. $^1$H NMR (400 MHz, CDCl$_3$): $\delta = 7.36$ (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); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta = 154.1$, 130.2, 127.7, 123.0, 121.6, 113.5, 66.3, 32.2, 30.0.
1-Bromo-2-(3-bromopropoxy)benzene (2l): colorless oil. $^1$H NMR (400 MHz, CDCl$_3$): $\delta = 7.55$-$7.52$ (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); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta = 155.0$, 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. $^1$H NMR (400 MHz, CDCl$_3$): $\delta = 6.72$ (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); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta = 154.1$, 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(sp$^2$)-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 NH$_4$Cl and extracted with ethyl acetate (3 x 10 mL). The combined organic phase was dried over anhydrous Na$_2$SO$_4$ 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, Rᵣ = 0.42) to afford the title compound as a colorless oil (53 mg, 83% yield). ¹H NMR (400 MHz, CDCl₃): δ = 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): δ = 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, Rᵣ = 0.43) to afford the title compound as a colorless oil (59 mg,
85% yield). $^1$H NMR (400 MHz, CDCl$_3$): $\delta = 9.94$ (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); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta = 168.8, 148.2, 139.4, 138.4, 137.7, 136.2, 134.4, 134.3, 128.9, 127.9, 127.6, 127.3, 126.7, 121.8, 121.6, 116.7, 33.4, 31.6, 31.5, 29.1, 22.4, 19.4, 13.9. HRMS (ESI$^+$): calcd for C$_{23}$H$_{26}$N$_2$ONa [M+Na]$^+$ 369.1943, found 369.1945.

![Compound Structure](image)

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), CrCl$_3$ (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). $^1$H NMR (400 MHz, CDCl$_3$): $\delta = 9.93$ (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); $^{13}$C NMR (100 MHz, CDCl$_3$): $\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.\textsuperscript{1e}
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 °C for 24 h. The crude product was purified by column chromatography on silica gel (EtOAc/PE = 1/20, Rf = 0.35) to afford the title compound as a pale yellow oil (67 mg, 92% yield). $^1$H 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); $^{13}$C 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.\textsuperscript{1a}

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 °C for 24 h. The crude product was purified by column chromatography on silica gel.
(EtOAc/PE = 1/20, Rₜ = 0.37) to afford the title compound as a pale yellow oil (67 mg, 88% yield). ¹H NMR (400 MHz, CDCl₃): δ = 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): δ = 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 C₂₆H₂₄N₂O₂Na [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, Rₜ = 0.28) to afford the title compound as a colorless oil (53 mg, 79% yield). ¹H NMR (400 MHz, CDCl₃): δ = 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): δ = 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), CrCl$_3$ (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 °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 (62 mg, 88% yield). $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ = 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); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ = 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 C$_{21}$H$_{21}$ClN$_2$ONa [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), CrCl$_3$ (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). $^1$H NMR (400 MHz, CDCl$_3$): $\delta = 9.92$ (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); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta =$ 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 C$_{21}$H$_{21}$BrN$_2$O$_2$Na$^+$ [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), CrCl$_3$ (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). $^1$H NMR (400 MHz, CDCl$_3$): $\delta = 9.93$ (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); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta =$ 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 C$_{22}$H$_{22}$N$_2$O$_2$Na$^+$ [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, Rₛ = 0.38) to afford the title compound as a colorless oil (45 mg, 71% yield). ¹H NMR (400 MHz, CDCl₃): δ = 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): δ = 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, Rₛ =
0.26) to afford the title compound as a pale yellow oil (55 mg, 64% yield). $^1$H NMR (400 MHz, CDCl$_3$): $\delta = 9.95$ (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); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta = 168.6$, 154.3, 148.3, 138.3, 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 C$_{26}$H$_{23}$ClN$_2$O$_2$Na [M+Na]$^+$ 453.1346, found 453.1352.

2-(3-(2-Bromophenoxy)propyl)-6-methyl-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), CrCl$_3$ (3.2 mg, 0.02 mmol), IPr·HCl (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). $^1$H NMR (400 MHz, CDCl$_3$): $\delta = 9.95$ (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); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta = 168.7$, 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 C$_{26}$H$_{25}$BrN$_2$O$_2$Na [M+Na]$^+$ 497.0841, found 497.0842.
2-(3-(Benzo[\textit{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, Rₜ = 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), 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
The crude product was purified by column chromatography on silica gel (EtOAc/PE = 1/20, Rf = 0.2) to afford the title compound as a colorless oil (53 mg, 80% yield). {superscript}1H NMR (400 MHz, CDCl₃): δ = 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); {superscript}13C NMR (100 MHz, CDCl₃): δ = 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, 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 (3o)

The general procedure was applied 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, Rf = 0.3) to afford the title compound as a pale yellow oil (40 mg, 53% yield). {superscript}1H NMR (400 MHz, CDCl₃): δ = 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); {superscript}13C NMR (100 MHz, CDCl₃): δ = 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 C₂₆H₂₄N₂O₄Na [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, Rₜ = 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), 7.37-7.34 (m, 1H), 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, Rₜ = 0.4) to afford the title compound as a pale yellow oil (42 mg,
63% yield). $^1$H NMR (400 MHz, CDCl$_3$): $\delta = 9.42$ (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); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta = 169.4, 148.2, 138.5, 138.0, 136.8, 136.2, 134.5, 134.4, 132.7, 130.3, 128.0, 127.4, 126.5, 121.8, 121.6, 116.7, 33.8, 32.9, 22.6, 19.8, 16.6, 13.8. HRMS (ESI$^+$): calcd for C$_{22}$H$_{24}$N$_2$O$_2$Na [M+Na]$^+$ 355.1786, found 355.1792.

![Chemical structure](image)

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

The general procedure was applied to 3-methoxy-2-methyl-N-(quinolin-8-yl)benzamide (1f) (58 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, $R_f = 0.29$) to afford the title compound as a pale yellow oil (35 mg, 50% yield). $^1$H NMR (400 MHz, CDCl$_3$): $\delta = 9.92$ (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); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta = 168.6, 155.8, 148.2, 138.9, 138.5, 136.3, 134.4, 131.1, 128.0, 127.4, 123.1, 121.8, 121.6, 116.7, 110.8, 55.6, 33.9, 32.5, 22.5, 13.8. 13.0. HRMS (ESI$^+$): calcd for C$_{22}$H$_{24}$N$_2$O$_2$Na [M+Na]$^+$ 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), IPr·HCl (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, Rf = 0.28) to afford the title compound as a pale yellow oil (49 mg, 69% yield). H NMR (400 MHz, CDCl₃): δ = 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); C NMR (100 MHz, CDCl₃): δ = 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 C₂₁H₂₁ClN₂O₂Na [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), IPr·HCl (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, Rf = 0.4) to afford the title compound as a pale yellow oil (47 mg, 71% yield). H NMR (400 MHz, CDCl₃): δ = 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); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \( \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\(^+\)): calcld for C\(_{22}\)H\(_{24}\)N\(_2\)O\(_3\)Na [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), 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, \( R_f = 0.38 \)) to afford the title compound as a pale yellow oil (50 mg, 74% yield). \(^1\)H NMR (400 MHz, CDCl\(_3\)): \( \delta = 9.91 \) (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); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \( \delta = 168.1, 163.9 \) (d, \( J_{CF} = 245.7 \) Hz), 148.3, 142.4 (d, \( J_{CF} = 8.0 \) Hz), 138.5, 137.4 (d, \( J_{CF} = 8.5 \) Hz), 136.3, 134.3, 134.0 (d, \( J_{CF} = 2.9 \) Hz), 128.0, 127.4, 122.0, 121.7, 116.8, 114.6 (d, \( J_{CF} = 21.2 \) Hz), 113.4 (d, \( J_{CF} = 21.0 \) Hz), 33.4, 33.1 (d, \( J_{CF} = 1.5 \) Hz), 22.5, 19.6 (d, \( J_{CF} = 1.6 \) Hz), 13.8. \(^{19}\)F NMR (377 MHz, CDCl\(_3\)): \( \delta = -112.97 \). Spectroscopic data are in accordance with those described in the literature.\(^1\)a
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): δ = 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): δ = 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). $^1$H NMR (400 MHz, CDCl$_3$): $\delta = 9.92$ (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); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta = 167.5$ (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. $^{19}$F NMR (377 MHz, CDCl$_3$): $\delta = -121.1$. HRMS (ESI$^+$): calcd for C$_{21}$H$_{21}$FN$_2$ONa [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 NH$_4$Cl and extracted with ethyl acetate (3 x 10 mL). The combined organic phase was dried over anhydrous Na$_2$SO$_4$ and concentrated under vacuum. The crude product was purified by silica gel chromatography to give the coupling product 3a (15 mg, 23%).

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A dried Schlenk tube were placed benzamide 1a (52.4 mg, 0.2 mmol), CrCl\(_3\) (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 D\(_2\)O and stirred for another 0.5 h before extracted with ethyl acetate (3 x 10 mL). The combined organic phase was dried over anhydrous Na\(_2\)SO\(_4\) 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. \(^1\)H NMR analysis showed that the D contents in the recovered amide was 29%.

78% with ortho D-content: 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-MeTHF (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-MeTHF (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, Rᵣ = 0.4) to give the coupling product an inseparable mixture (47 mg, 69%) of 7 and 8 as a clear oil which ratio (7:8 = 38:62) was detected by ¹H-NMR.
2-(Hex-5-en-1-yl)-6-methyl-N-(quinolin-8-yl)benzamide (7) and 2-(Cyclopentylmethyl)-6-methyl-N-(quinolin-8-yl)benzamide (8)

$^1$H NMR (400 MHz, CDCl$_3$): $\delta = 9.93$ (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); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta = 168.92$, 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 C$_{23}$H$_{24}$N$_2$O$_2$Na [M+Na]$^+$ 367.1786, found 367.1784.

$^1$H NMR Spectra of 7 and 8
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), 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), CrCl$_3$ (3.2 mg, 0.02 mmol), IPr·HCl (17 mg, 0.02 mmol), 1-bromobutane (0.8 mmol) and freshly distilled 2-MeTHF (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 NH$_4$Cl and extracted with ethyl acetate (3 x 10 mL). After removing the volatiles under vacuum, the crude product was analyzed by $^1$H 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), CrCl₃ (3 mg, 0.02 mmol), IPr·HCl (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).
$^1$H NMR spectra for C4-fully or partially deuterated biphenyl.

Proposed Mechanism
6. Supplementary References


7. $^1$H, $^{13}$C and $^{19}$F NMR Spectra
$^1$H and $^{13}$C NMR Spectra of 1a
$^1$H and $^{13}$C NMR Spectra of 1b
$^1$H and $^{13}$C NMR Spectra of 1c
$^1$H and $^{13}$C NMR Spectra of 1d
$^1$H and $^{13}$C NMR Spectra of 1e
1H and 13C NMR Spectra of 1f
$^1$H and $^{13}$C NMR Spectra of 1g
$^1$H and $^{13}$C NMR Spectra of 1h
$^{1}H$, $^{13}C$ and $^{19}F$ NMR Spectra of 1i
$^1$H and $^{13}$C NMR Spectra of 1j
$^1$H, $^{13}$C and $^{19}$F NMR Spectra of 1k
\[ ^1H \text{ and } ^{13}C \text{ NMR Spectra of 1a-D} \]
$^1$H and $^{13}$C NMR Spectra of 2k
$^1$H and $^{13}$C NMR Spectra of 2l
$^1$H and $^{13}$C NMR Spectra of 2m
$^1$H and $^{13}$C NMR Spectra of 3a
$^1$H and $^{13}$C NMR Spectra of 3b
$^1$H and $^{13}$C NMR Spectra of 3c
$^1$H and $^{13}$C NMR Spectra of 3d
$^{1}H$ and $^{13}C$ NMR Spectra of 3e
$^1$H and $^{13}$C NMR Spectra of 3f
$^1$H and $^{13}$C NMR Spectra of 3g
$^1$H and $^{13}$C NMR Spectra of 3h
$^1$H and $^{13}$C NMR Spectra of 3i
$^1$H and $^{13}$C NMR Spectra of 3j
$^1$H and $^{13}$C NMR Spectra of 3k
$^1$H and $^{13}$C NMR Spectra of 3l
$^1$H and $^{13}$C NMR Spectra of 3m
$^1$H and $^{13}$C NMR Spectra of 3n
$^1$H and $^{13}$C NMR Spectra of 3p
$^1$H and $^{13}$C NMR Spectra of 3q
$^1$H and $^{13}$C NMR Spectra of 3r
$^{1}\text{H}$ and $^{13}\text{C}$ NMR Spectra of 3s
$^1$H and $^{13}$C NMR Spectra of 3t
$^1\text{H}, ^{13}\text{C}$ and $^{19}\text{F}$ NMR Spectra of 3u

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\(^1\)H and \(^{13}\)C NMR Spectra of 3v
$^1$H, $^{13}$C and $^{19}$F NMR Spectra of 3w