KI-Catalyzed Imidation of sp$^3$ C–H Bonds Adjacent to an Amide Nitrogen Atom

Supporting information

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(A) General Remarks

All the reagents were provided by commercial suppliers without further purification. The products were purified by column chromatography that was performed on silica gel (230-400 mesh, Merck). $^1$H NMR and $^{13}$C NMR spectra were recorded on Bruker AM-400 spectrometer in CDCl$_3$ solution. $^1$H NMR chemical shifts (in ppm) were referenced to the hydrogen signal in tetramethylsilane (δ = 0 ppm) in the deuterated solvent. $^{13}$C NMR spectra were referenced to the CDCl$_3$ triplet signal (δ = 77.0 ppm). The following abbreviations were used to describe splitting patterns: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet. A Bruker APEX IV mass spectrometer was used to obtain the HR-ESI-MS.

(B) General Experimental Procedure

(a) Imidation of Amide

A reaction vessel was charged with imide (1 mmol), KI (0.2 mmol) and amide (1mL, about 9mmol). After the quick addition of TBHP (4 mmol, 70% aqueous solution), the mixture was stirred at 90 °C for proper time until imide was fully consumed. The reaction mixture was washed with saturated NaSO$_3$ solution (20 mL) until colorless. After extracting the water phase with CH$_2$Cl$_2$ (20 mL), combined organic phases were dried over NaSO$_4$. The crude mixture was purified by column chromatography (silica gel, petroleum ether: acetone= 3:1 to 6:1).

(b) Imidation of N,N-Dimethylaniline

A reaction vessel was charged with imide (1 mmol), KI (0.1 mmol) and N,N-dimethylaniline (1 mL, about 9 mmol). After the quick addition of TBHP (1.5 mmol, 70% aqueous solution), the mixture was stirred at 90 °C for proper time until imide was fully consumed. The reaction mixture was washed with saturated NaSO$_3$ solution (20 mL) until colorless. After extracting the water phase with CH$_2$Cl$_2$ (20 mL), combined organic phases were dried over NaSO$_4$. The crude mixture was purified by column chromatography (silica gel, petroleum ether: acetone= 3:1 to 6:1).
Analytical Data for 3a-3q

Note: The rotamers\(^1\) lead to obvious duplication (3a-3j, 3l, 3m, 3o, 3x) or triple copy (3k, 3n) in spectra. Considering the difference between 3a and 3p in spectra (3a has duplication while 3p doesn’t have), it is plausible that the nitrogen atom which originally belongs to amide may be responsible for the duplication. In order to explain the \(^{13}\)C NMR definitly, we discuss the duplication of each peak in detail.

\[ \text{White solid; } ^1\text{H NMR (400 MHz, CDCl}_3\text{): } \delta 7.79-7.65 (m, 4H), 5.22, 5.14 (2xs, 2H), 3.02, 2.86 (2xs, 3H), 2.36, 1.99 (2xs, 3H); } ^{13}\text{C NMR (100 MHz, CDCl}_3\text{): } \delta 170.8 (1C), 167.5, 167.3 (2C), 134.3-123.2 (6C), 52.4, 49.1 (1C), 35.5, 32.2 (1C), 21.5, 21.1 (1C). \]

\[ \text{Slightly yellow solid; } ^1\text{H NMR (400 MHz, CDCl}_3\text{): } \delta 8.73-8.08 (m, 3H), \]

\[ \text{N-[(1,3-dihydro-1,3-dioxo-2H-isoindol-2-yl)methyl]-N-methyl-acetamide (3a) }^2\]

\[ \text{N-[(4-nitro-1,3-dihydro-1,3-dioxo-2H-isoindol-2-yl)methyl]-N-methyl-acetamide (3b) }\]
5.36, 5.31 (2×s, 2H), 3.20, 3.00 (s×2, 2H), 2.48, 2.11 (s×2, 2H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 170.9, 170.7 (1C), 165.2-162.3 (2C), 144.9-123.0 (6C), 53.1, 50.3 (1C), 36.2, 32.3 (1C), 21.5, 21.1 (1C). HRMS (ESI): calcd for C$_{12}$H$_{12}$N$_3$O$_5$ [M+H]$^+$ 278.07715, found 278.07702.

![Structure 3c](image)

$N$-[(5-nitro-1,3-dihydro-1,3-dioxo-2H-isoindol-2-yl)methyl]-$N$-methyl-acetamide (3c)

Yellow solid; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 8.20-7.93 (m, 3H), 5.33, 5.29 (2×s, 2H), 3.19, 2.98 (2×s, 3H), 2.46, 2.10 (2×s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 171.5, 170.9 (1C), 163.6-163.1 (2C), 139.5-120.6 (6C), 54.2, 51.6 (1C), 35.4, 31.4 (1C), 22.0, 21.4 (1C). HRMS (ESI): calcd for C$_{12}$H$_{12}$N$_3$O$_5$ [M+H]$^+$ 278.07715, found 278.07709.

![Structure 3d](image)

$N$-[(5-methyl-1,3-dihydro-1,3-dioxo-2H-isoindol-2-yl)methyl]-$N$-methyl-acetamide (3d)

White solid; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.78-7.54 (m, 3H), 5.32, 5.21 (2×s, 2H), 3.10, 2.97 (2×s, 3H), 2.54, 2.52 (2×s, 3H), 2.47, 2.09 (2×s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 171.1, 170.9 (1C), 167.9, 167.8 (2C), 146.0-123.4 (6C), 52.5, 49.2 (1C), 35.6, 32.4 (1C), 21.9, 21.9 (1C), 21.8,

\[
\begin{align*}
\text{(3e)} \\
\end{align*}
\]

**N-[(1,8-naphthalimidol-N-yl)methyl]-N-methyl-acetamide (3e)**

White solid; \(^1\)H NMR (400 MHz, CDCl\(_3\)): \( \delta \) 8.59-7.74 (m, 6H); 5.84, 5.75 (2×s, 2H), 3.07, 2.92 (2×s, 3H), 2.53, 2.08 (2×s, 3H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \( \delta \) 171.6 (1C), 164.2 (2C), 131.7-122.0 (10C), 54.2, 51.5 (1C), 31.4, 29.6 (1C), 22.0, 21.5 (1C). HRMS (ESI): calcd for \( \text{C}_{16}\text{H}_{15}\text{N}_{2}\text{O}_{3} \) [M+H]\(^+\) 283.10772, found 283.10778.

\[
\begin{align*}
\text{(3f)} \\
\end{align*}
\]

**N-[(4-chlorine-1,8-naphthalimidol-N-yl)methyl]-N-methyl-acetamide (3f)**

White solid; \(^1\)H NMR (400 MHz, CDCl\(_3\)): \( \delta \) 8.67-7.85 (m, 5H), 5.85, 5.78 (2×s, 2H), 3.12, 2.94 (2×s, 3H), 2.55, 2.11 (2×s, 3H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \( \delta \) 171.2, 171.0 (1C), 165.5, 165.3 (2C), 152.0-118.9 (10C), 53.2, 50.6 (1C), 32.7, 29.6 (1C), 21.8, 21.4 (1C). HRMS (ESI): calcd for \( \text{C}_{16}\text{H}_{14}\text{ClN}_{2}\text{O}_{3} \) [M+H]\(^+\) 317.06875, found 317.06886.
N-[(2,5-dioxo-1-pyrrolidinyl)methyl]-N-methyl-acetamide (3g)<sup>3,4</sup>

White solid; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 5.06, 5.00 (2×s, 2H), 3.05, 2.87 (2×s, 3H), 2.74, 2.69 (2×s, 4H), 2.34, 2.03 (2×s, 3H), <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ 176.7, 176.4 (1C), 171.2, 171.0 (2C); 53.1, 50.5 (1C); 36.3, 32.6 (1C), 28.0 (2C), 21.7, 21.3 (1C).

![Chemical Structure](3h)

N-[(2,6-dioxo-1-piperidinyl)methyl]-N-methyl-acetamide (3h)

White solid; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 5.34, 5.33 (2×s, 2H), 2.98, 2.70 (2×s, 3H), 2.70-2.63 (m, 4H), 2.33, 2.02 (2×s, 3H), 1.98-1.89 (m, 2H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ 172.5, 172.2 (1C), 171.5 (2C), 53.2, 51.4 (1C), 32.8 (2C), 31.4 (1C), 22.0, 21.2 (1C), 16.9, 16.8 (1C). HRMS (ESI): calcd for C<sub>9</sub>H<sub>15</sub>N<sub>2</sub>O<sub>3</sub> [M+H]<sup>+</sup> 199.10772, found 199.10752.

![Chemical Structure](3i)

N-[(3,3-dimethyl-2,6-dioxo-1-piperidinyl)methyl]-N-methyl-acetamide (3i)

White solid; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 5.33, 5.32 (2×s, 2H), 2.99, 2.80 (2×s, 3H), 2.53, 2.50 (2×s, 4H), 2.34, 2.02 (2×s, 3H), 1.07, 1.05 (2×s, 6H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ 171.9, 171.6 (1C), 171.4 (2C); 53.2, 51.3 (1C), 46.3 (2C), 31.5 (1C), 29.5, 28.9 (1C), 27.6 (2C), 25.4, 21.2
HRMS (ESI): calcd for C\textsubscript{11}H\textsubscript{19}N\textsubscript{2}O\textsubscript{3} [M+H]\textsuperscript{+} 227.13902, found 277.13893.

\[ \text{N-}[\text{(N-tosyl-1-isobutylaminyl)methyl}-\text{N-methyl-acetamide} (3j)] \]

White solid; \textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}): \( \delta \) 7.63, 7.61, 7.27, 7.25 (m, 4H), 4.81, 4.72 (2\times s, 2H), 3.04, 2.72 (2\times s, 3H), 2.91, 2.89, 2.87, 2.85 (2\times d, 2H), 2.38 (s, 3H), 2.14, 2.03 (2\times s, 3H), 1.92-1.83 (m, 1H), 0.85, 0.83, 0.76, 0.74 (2\times d, 6H); \textsuperscript{13}C NMR (100 MHz, CDCl\textsubscript{3}): \( \delta \) 171.8 (1C), 143.4-126.8 (6C), 60.0 (1C), 56.1 (1C), 34.2 (1C), 27.2 (1C), 22.0 (1C), 20.0 (1C), 19.8 (2C). HRMS (ESI): calcd for C\textsubscript{15}H\textsubscript{25}N\textsubscript{2}O\textsubscript{3}S [M+H]\textsuperscript{+} 313.15804, found 313.15827.

\[ \text{3k} \]

N-[(1,3-dihydro-1,3-dioxo-2\textit{H}-isoindol-2-yl)methyl]-N-methyl-formamide (3k)

White solid; \textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}): \( \delta \) 8.45 (s, 1H), 7.86-7.75 (m, 4H), 5.28, 5.28, 5.12 (3\times s, 2H), 3.00, 2.90, 2.88 (3\times s, 3H), \textsuperscript{13}C NMR (100MHz, CDCl\textsubscript{3}): \( \delta \) 167.5 (1C), 163.6 (2C), 134.6-123.6 (6C), 51.4 (1C), 29.5 (1C). HRMS (ESI): calcd for C\textsubscript{11}H\textsubscript{11}N\textsubscript{2}O\textsubscript{3} [M+H]\textsuperscript{+} 219.07642, found 219.07625.
N-methyl-(1,3-dihydro-1,3-dioxo-2H isoindol-2-yl)methyl]-N-methyl-propionamide (3l)

White solid; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.85-7.68 (m, 4H), 5.28, 5.20 (2×s, 2H), 3.08, 2.93 (2×s, 3H), 2.81-2.75, 2.31-2.26 (2×q, 2H), 1.18, 1.16, 1.14, 1.10, 1.08, 1.07 (2×t, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 174.2 (1C), 167.8, 167.6 (2C), 134.5-123.4 (6C), 51.6, 50.0 (1C), 35.0, 32.7 (1C), 26.7, 25.9 (1C), 9.3, 8.7 (1C). HRMS (ESI): calcd for C$_{13}$H$_{15}$N$_2$O$_3$ [M+H]$^+$ 247.10772, found 247.10757.

N-methyl-5-[(1,3-dihydro-1,3-dioxo-2H isoindol-2-yl)methyl]-2-pyrrolidone (3m)

White solid; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.87-7.75 (m, 4H), 5.81-5.79 (m, 1H), 3.04-2.96 (m, 1H), 2.82, 2.72 (2×s, 3H), 2.60-2.40 (m, 2H), 2.31-2.25 (m, 1H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 175.3 (1C), 167.4 (2C), 134.5-131.4 (6C), 65.6 (1C), 29.6 (1C), 27.0 (1C), 23.2 (1C). HRMS (ESI): calcd for C$_{13}$H$_{12}$N$_2$NaO$_3$ [M+Na]$^+$ 267.07401, found 267.07389.
N-[(1,3-dihydro-1,3-dioxo-2H-isoindol-2-yl)methyl]-N-methyl-isobutyramide (3n)

White solid; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.89-7.74 (m, 4H), 5.64-5.26 (m, 2H), 3.18-2.95 (m, 3H), 3.61-3.55, 2.84-2.74 (2×m, 1H), 1.26-1.11 (m, 6H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 178.7-177.3 (1C), 167.7-167.4 (2C), 138.0-123.2 (6C), 53.1-50.3 (1C), 36.2-33.0 (1C), 30.5-29.7 (1C), 19.7-18.8 (2C). HRMS (ESI): calcd for C$_{14}$H$_{17}$N$_2$O$_3$ [M+H]$^+$ 261.12337, found 261.12321.

N-[(1,3-dihydro-1,3-dioxo-2H-isoindol-2-yl)methyl]-N-methyl-n-butyramide (3o)

White solid; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.81-7.66 (m, 4H), 5.26, 5.18 (2×s, 2H), 3.06, 2.90 (2×s, 3H), 2.27, 2.71, 2.69, 2.24, 2.22, 2.20 (2×t, 2H), 1.68-1.56 (m, 2H), 0.96-0.85 (2×m, 3H). $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 173.4, 173.3 (1C), 167.7, 167.5 (2C), 134.5-123.4 (6C), 51.7, 49.8 (1C), 35.3, 34.5 (1C), 32.5, 29.5 (1C), 18.6, 17.9 (1C), 13.8, 13.7 (1C). HRMS (ESI): calcd for C$_{14}$H$_{17}$N$_2$O$_3$Na [M+Na]$^+$ 283.10517, found 283.10531.
2-[(methylphenylamino)methyl]-1H-isooindole-1,3(2H)-dione (3p)

White solid; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.82-7.24 (m, 4H), 7.06-6.77 (m, 5H), 5.27 (s, 2H), 3.16 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 168.8 (2C), 147.3-113.6 (12C), 56.5 (1C), 39.1 (1C).

1-[(methylphenylamino)methyl]-2,5-pyrrolidinedione (3q)

White solid; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.30-6.81 (m, 5H), 5.10 (s, 2H), 3.15 (s, 3H), 2.68 (s, 4H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 177.5 (2C), 147.1-113.2 (6C), 57.2 (1C), 39.4 (1C), 28.1 (2C).

N-[(2,2,6,6-tetramethylpiperidinoxy-O-yl)methyl]-N-methyl-acetamide (3x)

Slight yellow solid; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 4.96, 4.91 (2×s, 2H), 3.10, 3.04 (2×s, 3H), 2.22, 2.10 (2×s, 3H), 1.48-1.44 (m, 4H), 1.59-1.52, 1.36-1.31 (2×m, 2H), 1.25- 1.10 (m, 12H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 171.6 (1C), 85.4, 81.4 (1C), 59.9, 59.7 (2C), 39.8 (4C), 34.0, 33.1 (1C).
22.0, 21.5 (1C), 20.0 (2C), 17.0, 16.9 (1C). HRMS (ESI): calcd for C_{13}H_{27}N_{2}O_{2} [M+H]^+ 243.20670, found 243.20658.

(D) Reference


(E) $^1$H NMR and $^{13}$C NMR Spectra

$^1$H NMR Spectra of Compound 3a (400 MHz, CDCl$_3$)

$^{13}$C NMR Spectra of Compound 3a (100 MHz, CDCl$_3$)
$^1$H NMR Spectra of Compound 3b (400 MHz, CDCl$_3$)

$^{13}$C NMR Spectra of Compound 3b (100 MHz, CDCl$_3$)
$^1$H NMR Spectra of Compound 3c (400 MHz, CDCl$_3$)

$^{13}$C NMR Spectra of Compound 3c (100 MHz, CDCl$_3$)
$^1$H NMR Spectra of Compound 3e (400 MHz, CDCl$_3$)

$^{13}$C NMR Spectra of Compound 3e (100 MHz, CDCl$_3$)
\(^1\)H NMR Spectra of Compound \(3f\) (400 MHz, CDCl\(_3\))

\[^{13}\text{C}\) NMR Spectra of Compound \(3f\) (100 MHz, CDCl\(_3\))
$^1$H NMR Spectra of Compound 3g (400 MHz, CDCl$_3$)

$^{13}$C NMR Spectra of Compound 3g (100 MHz, CDCl$_3$)
$^1$H NMR Spectra of Compound 3h (400 MHz, CDCl$_3$)

$^{13}$C NMR Spectra of Compound 3h (100 MHz, CDCl$_3$)
$^1$H NMR Spectra of Compound 3i (400 MHz, CDCl$_3$)

$^{13}$C NMR Spectra of Compound 3i (100 MHz, CDCl$_3$)
$^1$H NMR Spectra of Compound 3j (400 MHz, CDCl$_3$)

$^{13}$C NMR Spectra of Compound 3j (100 MHz, CDCl$_3$)
$^1$H NMR Spectra of Compound 3k (400 MHz, CDCl$_3$)

$^{13}$C NMR Spectra of Compound 3k (100 MHz, CDCl$_3$)
$^1$H NMR Spectra of Compound 3I (400 MHz, CDCl$_3$)

$^{13}$C NMR Spectra of Compound 3I (100 MHz, CDCl$_3$)
$^{1}$H NMR Spectra of Compound 3m (400 MHz, CDCl$_3$)

$^{13}$C NMR Spectra of Compound 3m (100 MHz, CDCl$_3$)
$^1$H NMR Spectra of Compound 3n (400 MHz, CDCl$_3$)

$^{13}$C NMR Spectra of Compound 3n (100 MHz, CDCl$_3$)
$^1$H NMR Spectra of Compound 3o (400 MHz, CDCl$_3$)

$^{13}$C NMR Spectra of Compound 3o (100 MHz, CDCl$_3$)
$^1$H NMR Spectra of Compound 3p (400 MHz, CDCl$_3$)

$^{13}$C NMR Spectra of Compound 3p (100 MHz, CDCl$_3$)
$^1$H NMR Spectra of Compound 3q (400 MHz, CDCl$_3$)

$^{13}$C NMR Spectra of Compound 3q (100 MHz, CDCl$_3$)
$^1$H NMR Spectra of Compound $3x$ (400 MHz, CDCl$_3$)

$^{13}$C NMR Spectra of Compound $3x$ (100 MHz, CDCl$_3$)