I₂-Catalyzed Intramolecular Oxidative Amination of C(sp³)-H Bond: Efficient Access to 3-Acylimidazo[1,2-a]pyridines Under Neat Condition

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Table of contents

1. General information ...........................................................................................................2

2. Synthesis and characterization of starting materials 1a-1v ........................................2

   2.1 Synthesis of starting materials 1a-1v ..................................................................2

   2.2 Product characterization ......................................................................................4

3. General procedure and product characterization .........................................................12

   3.1 General procedure ..............................................................................................12

   3.2 Product Characterization ....................................................................................13

4. Diversification of 3-acylimidazo[1,2-a]pyridines ...................................................20

5. Contral Experiments .......................................................................................................24

6. References .........................................................................................................................24

7. Copies of 1H NMR and 13C NMR Spectra .................................................................26
1. General information

Reactions were monitored by using thin-layer chromatography (TLC) on commercial silica gel plates (GF254). Visualization of the developed plates was performed under UV lights (254 nm). Flash column chromatography was performed on silica gel (200-300 mesh). $^1$H and $^{13}$C NMR spectra were recorded on Bruker AV300, 400, 500 and 600 MHz spectrometers. Chemical shifts (δ) were reported in ppm referenced to the CDCl$_3$ residual peak (δ 7.26) or the DMSO-d$_6$ residual peak (δ 2.50) for $^1$H NMR. Chemical shifts of $^{13}$C NMR were reported relative to CDCl$_3$ (δ 77.0) or D$_6$-DMSO (δ 39.5). The following abbreviations were used to describe peak splitting patterns when appropriate: br s = broad singlet, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet. Coupling constant, $J$, was reported in Hertz unit (Hz). Melting points (mp) were taken on a MEL-TEMP® apparatus and were uncorrected. High resolution mass spectra (HRMS) were obtained on an ESI-LC-MS/MS spectrometer.

2. Synthesis and characterization of starting materials 1a-1v

2.1 Synthesis of starting materials 1a-1v

Method I: The material 1a was prepared according to the following method.

$^1$H and $^{13}$C NMR spectra were recorded on Bruker AV300, 400, 500 and 600 MHz spectrometers. Chemical shifts (δ) were reported in ppm referenced to the CDCl$_3$ residual peak (δ 7.26) or the DMSO-d$_6$ residual peak (δ 2.50) for $^1$H NMR. Chemical shifts of $^{13}$C NMR were reported relative to CDCl$_3$ (δ 77.0) or D$_6$-DMSO (δ 39.5). The following abbreviations were used to describe peak splitting patterns when appropriate: br s = broad singlet, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet. Coupling constant, $J$, was reported in Hertz unit (Hz). Melting points (mp) were taken on a MEL-TEMP® apparatus and were uncorrected. High resolution mass spectra (HRMS) were obtained on an ESI-LC-MS/MS spectrometer.

2. Synthesis and characterization of starting materials 1a-1v

2.1 Synthesis of starting materials 1a-1v

Method I: The material 1a was prepared according to the following method.

$$
\begin{align*}
\text{S1} & : \text{pyridin-2-amine} & \text{S2} & : \text{3-chloro-1-phenylpropan-1-one}
\end{align*}
$$

1-phenyl-3-(pyridin-2-ylamino)propan-1-one (1a). A sealed tube was equipped with a magnetic stir bar and was charged with pyridin-2-amine S1 (339 mg, 3.6 mmol), 3-chloro-1-phenylpropan-1-one S2 (506 mg, 3.0 mmol), triethylamine (0.6 mL, 4.2 mmol) in ethanol (2 mL). The reaction mixture was stirred under 150 W microwave irradiation at 100 ºC for 5 minutes. After the reaction was complete (as judged by TLC analysis), the solution was cooled to room temperature and extracted with EtOAc (20 mL) and washed with brine for three times. Then the combined organic layers were dried over Na$_2$SO$_4$ and removed the volatiles in vacuo. The residues were purified by column chromatography on silica gel (petroleum ether/EtOAc = 5 : 1) to afford the desired product 1-phenyl-3-(pyridin-2-ylamino)propan-1-one 1a (461 mg, 68% yield) as a white solid.

1b-1i, 1l-1n, 1r-1v were prepared according to the procedure described for 1a.
Method II: The material 1j was prepared according to the following method.

A sealed tube was equipped with a magnetic stir bar and was charged with 1-(m-tolyl)ethan-1-one S3 (402 mg, 3 mmol), paraformaldehyde (900 mg), dimethylamine hydrochloride (489 mg, 6 mmol) in ethanol (2 mL). The reaction mixture was stirred under 150 W microwave irradiation at 100 °C until the color turned out to be yellow. The solution was cooled to room temperature, to which a sat. aqueous NaHCO$_3$ was added dropwise until there was no CO$_2$ release. Then the mixture was extracted with EtOAc (20 mL) and washed with brine for three times, and the resulted organic layers were dried over Na$_2$SO$_4$ and removed the volatiles under reduced pressure to give the crude product S4.

A sealed tube was equipped with a magnetic stir bar and charged with 1-(m-tolyl)ethan-1-one S4, pyridin-2-amine (338 mg, 3.6 mmol) in ethanol (2 mL). The reaction mixture was stirred under 150 W microwave irradiation at 100 °C until the reaction was complete (as judged by TLC analysis). Then the reaction mixture was cooled to room temperature and extracted with EtOAc (20 mL) and washed with brine for three times, and the resulted organic layers were dried over Na$_2$SO$_4$ and removed the volatiles under reduced pressure. The residues were purified by column chromatography on silica gel (petroleum ether/EtOAc = 5 : 1) to give the desired product 1j (389 mg, 54% yield) as a white solid.

1k, 1o and 1q were prepared according to procedures described for 1j.

Method III: The material 1p was prepared according to the following method.

A sealed tube was equipped with a magnetic stir bar and charged with pyridin-2-amine (283 mg, 3 mmol), ethyl vinyl ketone (379 mg, 4.5 mmol) and stirred overnight at room temperature. After the reaction was complete (as determined by TLC analysis), the reaction mixture was extracted with EtOAc (20 mL) and washed with brine for three
times, and the resulted organic layers were dried over Na$_2$SO$_4$ and evaporated under reduced pressure. The residues were purified by column chromatography on silica gel (petroleum ether/EtOAc = 5 : 1) to give the desired product 1p (401 mg, 75% yield) as a white solid.

### 2.2 Product characterization

#### 1-phenyl-3-(pyridin-2-ylamino)propan-1-one (1a)

![Structure of 1a](image)

Yield: 57%. Mp 82-84 °C. White solid. $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 8.10 (d, $J = 5.1$ Hz, 1H), 8.00-7.96 (m, 2H), 7.59 (t, $J = 5.1$ Hz, 1H), 7.56-7.47 (m, 2H), 7.45-7.36 (m, 1H), 6.58-6.54 (m, 1H), 6.41 (d, $J = 8.4$ Hz, 1H), 4.97 (br s, 1H), 3.84 (t, $J = 6.0$ Hz, 2H), 3.34 (t, $J = 6.0$ Hz, 2H); $^{13}$C NMR (75 MHz, CDCl$_3$): $\delta$ 199.6, 158.3, 147.9, 137.3, 136.8, 133.3, 128.6, 128.1, 112.8, 108.0, 38.2, 36.6; HRMS (ESI): Exact mass calcd for C$_{14}$H$_{14}$N$_2$O [M+H]$^+$, 227.1179; Found: 227.1176.

#### 3-((5-methylpyridin-2-yl)amino)-1-phenylpropan-1-one (1b)

![Structure of 1b](image)

Yield: 61%. Mp 96-97 °C. White solid. $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 8.00-7.93 (m, 3H), 7.60-7.54 (m, 1H), 7.49-7.44 (m, 2H), 7.23 (d, $J = 8.7$ Hz, 1H), 6.35 (d, $J = 8.4$ Hz, 1H), 4.80 (br s, 1H), 3.80 (t, $J = 6.0$ Hz, 2H), 3.32 (t, $J = 6.0$ Hz, 2H), 2.18 (s, 3H); $^{13}$C NMR (150 MHz, CDCl$_3$): $\delta$ 199.7, 156.5, 147.4, 138.4, 136.8, 133.3, 128.6, 128.0, 121.6, 107.7, 38.2, 36.9, 17.4; HRMS (ESI): Exact mass calcd for C$_{15}$H$_{16}$N$_2$O [M+H]$^+$, 241.1335; Found: 241.1332.

#### 3-((5-fluoropyridin-2-yl)amino)-1-phenylpropan-1-one (1c)
Yield: 71%. Mp 93-94 °C. White solid. $^1$H NMR (300 MHz, CDCl$_3$): δ 8.00-7.96 (m, 2H), 7.62-7.56 (m, 1H), 7.51-7.45 (m, 2H), 6.39-6.35 (m, 1H), 4.91 (br s, 1H), 3.80 (t, $J = 12.3$ Hz, 2H), 3.32 (t, $J = 6.0$ Hz, 2H); $^{13}$C NMR (150 MHz, CDCl$_3$): δ 199.8, 155.0, 153.9, 152.6, 136.7, 134.3, 134.2, 133.4, 128.6, 128.0, 125.3, 125.2, 110.0, 108.4, 38.0, 37.1; HRMS (ESI): Exact mass calcd for C$_{14}$H$_{13}$FN$_2$O [M+H]$^+$, 245.1085; Found: 245.1087.

3-((5-chloropyridin-2-yl)amino)-1-phenylpropan-1-one (1d)

Yield: 72%. Mp 110-112 °C. Pale yellow solid. $^1$H NMR (600 MHz, CDCl$_3$): δ 8.01 (s, 1H), 7.94 (d, $J = 8.4$ Hz, 2H), 7.57-7.54 (m, 1H), 7.44 (t, $J = 7.8$ Hz, 2H), 7.29 (d, $J = 8.4$ Hz, 1H), 6.32 (d, $J = 8.4$ Hz, 1H), 5.00 (br s, 1H), 3.78 (t, $J = 6.0$ Hz, 1H), 3.29 (t, $J = 5.4$ Hz, 2H); $^{13}$C NMR (150 MHz, CDCl$_3$): δ 199.5, 156.6, 146.2, 137.0, 136.6, 133.4, 128.7, 128.0, 119.6, 108.9, 37.9, 36.7; HRMS (ESI): Exact mass calcd for C$_{14}$H$_{13}$ClN$_2$O [M+H]$^+$, 261.0789; Found: 261.0792.

3-((5-bromopyridin-2-yl)amino)-1-phenylpropan-1-one (1e)

Yield: 72%. Mp 110-112 °C. Pale yellow solid. $^1$H NMR (300 MHz, CDCl$_3$): δ 8.13 (s, 1H), 8.00-7.96 (m, 2H), 7.62-7.56 (m, 1H), 7.50-7.42 (m, 3H), 6.32 (d, $J = 9.0$ Hz, 1H), 5.04 (br s, 1H), 3.81 (t, $J = 6.0$ Hz, 2H), 3.32 (t, $J = 6.0$ Hz, 2H); $^{13}$C NMR (75 MHz,
CDCl$_3$): $\delta$ 199.5, 156.9, 148.5, 139.6, 136.7, 133.4, 128.7, 128.0, 109.6, 106.9, 38.0, 36.7; HRMS (ESI): Exact mass calcd for C$_{14}$H$_{13}$BrN$_2$O [M+H]$^+$, 305.0290; Found: 305.0287.

**phenyl-3-((5-(trifluoromethyl)pyridin-2-yl)amino)propan-1-one (1f)**

Yield: 69%. Mp 126-128 °C. White solid. $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 8.35 (s, 1H), 8.00-7.96 (m, 2H), 7.63-7.46 (m, 4H), 6.42 (d, $J$ = 8.7 Hz, 1H), 5.40 (br s, 1H), 3.90 (t, $J$ = 6.0 Hz, 2H), 3.35 (t, $J$ = 5.7 Hz, 2H); $^{13}$C NMR (150 MHz, CDCl$_3$): $\delta$ 199.3, 159.8, 145.9, 134.1, 133.5, 128.7, 128.0, 107.4, 47.4, 37.9, 36.3; HRMS (ESI): Exact mass calcd for C$_{15}$H$_{13}$F$_3$N$_2$O [M+H]$^+$, 295.1053; Found: 295.1049.

**methyl 6-((3-oxo-3-phenylpropyl)amino)nicotinate (1g)**

Yield: 48%. Mp 161-162 °C. White solid. $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 8.77 (s, 1H), 7.99-7.93 (m, 3H), 7.59 (t, $J$ = 7.5 Hz, 1H), 7.47 (t, $J$ = 7.8 Hz, 2H), 6.37 (d, $J$ = 8.7 Hz, 1H), 5.55 (br s, 1H), 3.94-3.87 (m, 5H), 3.35 (t, $J$ = 5.7 Hz, 2H); $^{13}$C NMR (150 MHz, CDCl$_3$): $\delta$ 205.3, 166.4, 160.3, 151.4, 138.1, 133.5, 128.7, 128.0, 115.0, 51.6, 38.0, 36.4; HRMS (ESI): Exact mass calcd for C$_{16}$H$_{16}$N$_2$O$_3$ [M+H]$^+$, 285.1234; Found: 285.1229.

**3-((4-methylpyridin-2-yl)amino)-1-phenylpropan-1-one (1h)**
Yield: 65%. Mp 88-89 °C. White solid. \(^1\)H NMR (300 MHz, CDCl\(_3\)): δ 8.00-7.96 (m, 3H), 7.61-7.55 (m, 1H), 7.50-7.44 (m, 2H), 6.42 (d, J = 5.1 Hz, 1H), 6.23 (s, 1H), 4.87 (br s, 1H), 3.85-3.78 (m, 2H), 3.53-3.31 (m, 2H), 2.22 (s, 3H); \(^{13}\)C NMR (150 MHz, CDCl\(_3\)): δ 199.6, 158.5, 148.2, 147.6, 136.7, 133.3, 128.6, 128.0, 114.5, 108.1, 38.2, 36.6, 21.1; HRMS (ESI): Exact mass calcd for C\(_{15}\)H\(_{16}\)N\(_2\)O \([\text{M+H}]^+\), 241.1335; Found: 241.1334.

3-((4-methoxypyridin-2-yl)amino)-1-phenylpropan-1-one (1i)

\[
\begin{array}{c}
\text{MeO} \\
\text{N} \\
\text{O}
\end{array}
\]

Yield: 63%. Mp 106-107 °C. White solid. \(^1\)H NMR (300 MHz, CDCl\(_3\)): δ 7.97-7.92 (m, 3H), 7.59-7.54 (m, 1H), 7.45 (t, J = 7.2 Hz, 2H), 6.20 (d, J = 6.0 Hz, 1H), 5.87 (s, 1H), 5.00 (br s, 1H), 3.82-3.76 (m, 5H), 3.31 (t, J = 6.0 Hz, 2H); \(^{13}\)C NMR (75 MHz, CDCl\(_3\)): δ 199.6, 167.0, 160.2, 149.1, 136.7, 133.3, 128.6, 128.0, 101.7, 91.2, 54.9, 38.2, 36.8; HRMS (ESI): Exact mass calcd for C\(_{15}\)H\(_{16}\)N\(_2\)O\(_2\) \([\text{M+H}]^+\), 257.1285; Found: 257.1283.

3-(pyridin-2-ylamino)-1-(m-tolyl)propan-1-one (1j)

\[
\begin{array}{c}
\text{N} \\
\text{O}
\end{array}
\]

Yield: 30%. Mp 87-88 °C. White solid. \(^1\)H NMR (300 MHz, CDCl\(_3\)): δ 8.11 (d, J = 5.4 Hz, 1H), 7.79-7.76 (m, 2H), 7.42-7.35 (m, 3H), 6.59-6.56 (m, 1H), 6.40 (d, J = 8.4 Hz, 1H), 4.93 (br s, 1H), 3.82 (t, J = 6.0 Hz, 2H), 3.32 (t, J = 6.0 Hz, 2H), 2.42 (s, 3H); \(^{13}\)C NMR (150 MHz, CDCl\(_3\)): δ 199.8, 147.9, 137.2, 136.7, 134.1, 128.6, 128.5, 125.2, 112.7, 108.0, 38.2, 36.6, 21.3; HRMS (ESI): Exact mass calcd for C\(_{15}\)H\(_{16}\)N\(_2\)O \([\text{M+H}]^+\), 241.1335; Found: 241.1340.

3-(pyridin-2-ylamino)-1-(p-tolyl)propan-1-one (1k)
Yield: 33%. Yellow oil. \(^1\)H NMR (600 MHz, CDCl\(_3\)): \(\delta\) 8.07 (d, \(J = 5.4\) Hz, 1H), 7.75 (t, \(J = 7.2\) Hz, 2H), 7.37-7.31 (m, 3H), 6.53 (t, \(J = 6.0\) Hz, 1H), 6.37 (d, \(J = 8.4\) Hz, 1H), 4.92 (br s, 1H), 3.78 (t, \(J = 6.0\) Hz, 2H), 3.29 (t, \(J = 6.0\) Hz, 2H), 2.39 (s, 3H); \(^{13}\)C NMR (150 MHz, CDCl\(_3\)): \(\delta\) 199.8, 158.3, 147.9, 138.4, 137.3, 136.7, 134.1, 128.6, 128.5, 125.3, 112.8, 108.0, 38.2, 36.6, 21.3; HRMS (ESI): Exact mass calcd for C\(_{15}\)H\(_{16}\)N\(_2\)O \([\text{M+H}]^+\), 241.1335; Found: 241.1340.

\textbf{1-(4-fluorophenyl)-3-(pyridin-2-ylamino)propan-1-one (II)}

Yield: 80%. Mp 85-86 °C. Pale yellow solid. \(^1\)H NMR (600 MHz, CDCl\(_3\)): \(\delta\) 8.04 (s, 1H), 7.94-7.91 (m, 2H), 7.32-7.29 (m, 1H), 7.07-7.03 (m, 2H), 6.49 (t, \(J = 7.2\) Hz, 1H), 6.34 (d, \(J = 8.4\) Hz, 1H), 5.08 (br s, 1H), 3.75 (t, \(J = 6.0\) Hz, 2H), 3.23 (t, \(J = 6.0\) Hz, 2H); \(^{13}\)C NMR (150 MHz, CDCl\(_3\)): \(\delta\) 198.0, 166.6, 164.9, 158.2, 147.9, 137.2, 133.2, 130.7, 130.6, 115.8, 115.6, 112.8, 108.0, 38.1, 36.6; HRMS (ESI): Exact mass calcd for C\(_{14}\)H\(_{13}\)FN\(_2\)O \([\text{M+H}]^+\), 245.1085; Found: 245.1087.

\textbf{1-(4-chlorophenyl)-3-(pyridin-2-ylamino)propan-1-one (1m)}
Yield: 62%. Mp 100-101 °C. White solid. \(^1\)H NMR (300 MHz, CDCl\(_3\)): \(\delta\) 8.10 (d, \(J = 6.9\) Hz, 1H), 7.95-7.90 (m, 2H), 7.47-7.36 (m, 3H), 6.59-6.55 (m, 1H), 6.40 (d, \(J = 8.4\) Hz, 1H), 4.90 (br s, 1H), 3.83 (t, \(J = 6.0\) Hz, 2H), 3.31 (t, \(J = 6.0\) Hz, 2H); \(^{13}\)C NMR (150 MHz, CDCl\(_3\)): \(\delta\) 198.4, 147.9, 139.7, 137.2, 135.0, 129.5, 128.9, 112.8, 108.1, 38.2, 36.5; HRMS (ESI): Exact mass calcd for C\(_{14}\)H\(_{13}\)ClN\(_2\)O [M+H]\(^+\), 261.0789; Found: 261.0794.

1-(4-bromophenyl)-3-(pyridin-2-ylamino)propan-1-one (1n)

Yield: 74%. Mp 96-97 °C. White solid. \(^1\)H NMR (300 MHz, CDCl\(_3\)): \(\delta\) 8.10 (d, \(J = 5.1\) Hz, 1H), 7.83 (d, \(J = 9.3\) Hz, 2H), 7.61 (d, \(J = 9.0\) Hz, 2H), 7.39 (t, \(J = 7.2\) Hz, 1H), 6.59-6.55 (m, 1H), 6.40 (d, \(J = 7.5\) Hz, 1H), 4.91 (br s, 1H), 3.82 (t, \(J = 6.3\) Hz, 2H), 3.30 (t, \(J = 6.0\) Hz, 2H); \(^{13}\)C NMR (150 MHz, CDCl\(_3\)): \(\delta\) 198.6, 158.2, 147.9, 137.2, 135.4, 131.9, 129.6, 128.5, 112.9, 108.1, 38.2, 36.5; HRMS (ESI): Exact mass calcd for C\(_{14}\)H\(_{13}\)BrN\(_2\)O [M+H]\(^+\), 305.0284; Found: 305.0289.

3-(pyridin-2-ylamino)-1-(thiophen-2-yl)propan-1-one (1o)

Yield: 62%. Mp 86-88 °C. White solid. \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 8.08 (d, \(J = 4.4\) Hz, 1H), 7.71 (d, \(J = 3.6\) Hz, 1H), 7.63 (d, \(J = 4.8\) Hz, 1H), 7.36 (t, \(J = 7.2\) Hz, 1H), 7.11 (t, \(J = 4.4\) Hz, 1H), 6.55 (t, \(J = 6.0\) Hz, 1H), 6.38 (d, \(J = 8.4\) Hz, 1H), 4.91 (br s, 1H), 3.80 (t, \(J = 6.0\) Hz, 2H), 3.26 (t, \(J = 6.0\) Hz, 2H); \(^{13}\)C NMR (75 MHz, CDCl\(_3\)): \(\delta\) 192.2, 158.0, 147.7, 144.0, 137.0, 133.6, 132.0, 127.9, 112.6, 107.9, 53.2, 38.7, 36.7; HRMS (ESI): Exact mass calcd for C\(_{12}\)H\(_{12}\)N\(_2\)OS [M+H]\(^+\), 233.0743; Found: 233.0742.

1-(pyridin-2-ylamino)pentan-3-one (1p)
Yield: 75%. Mp 78-79 °C. White solid. $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 8.09-8.07 (m, 1H), 7.38-7.35 (m, 1H), 6.57-6.53 (m, 1H), 6.36 (d, $J$ = 7.5 Hz, 1H), 4.91 (br s, 1H), 3.66-3.59 (m, 2H), 2.77-2.73 (m, 2H), 2.48-2.41 (m, 2H), 1.09-1.03 (m, 3H); $^{13}$C NMR (75 MHz, CDCl$_3$): $\delta$ 211.0, 158.4, 147.9, 137.2, 112.7, 107.7, 41.7, 36.4, 36.2, 7.6; HRMS (ESI): Exact mass calcd for C$_{10}$H$_{14}$N$_2$O [M+H]$^+$, 179.1106; Found: 179.1110.

4,4-dimethyl-1-(pyridin-2-ylamino)pentan-3-one (1q)

Yield: 43%. Colourless oil. $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 8.08-8.05 (m, 1H), 7.39-7.33 (m, 1H), 6.55-6.51 (m, 1H), 6.35 (d, $J$ = 8.4 Hz, 1H), 4.89 (br s, 1H), 3.60 (t, $J$ = 6.0 Hz, 2H), 2.81 (t, $J$ = 6.0 Hz, 2H), 1.11 (s, 9H); $^{13}$C NMR (75 MHz, CDCl$_3$): $\delta$ 215.9, 158.3, 147.9, 137.2, 112.7, 107.7, 44.2, 36.6, 36.1, 26.2; HRMS (ESI): Exact mass calcd for C$_{12}$H$_{18}$N$_2$O [M+H]$^+$, 207.1492; Found: 207.1494.

methyl 3-(pyridin-2-ylamino)propanoate (1r)

Yield: 56%. Mp 53-55 °C. White solid. $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 8.08 (d, $J$ = 3.9 Hz, 1H), 7.42-7.36 (m, 1H), 6.59-6.55 (m, 1H), 6.39 (d, $J$ = 8.4 Hz, 1H), 4.94 (br s, 1H), 3.69-3.66 (m, 5H), 2.65 (t, $J$ = 6.0 Hz, 2H); $^{13}$C NMR (75 MHz, CDCl$_3$): $\delta$ 173.0, 158.2, 148.0, 137.3, 113.0, 107.7, 51.7, 37.3, 34.0; HRMS (ESI): Exact mass calcd for C$_9$H$_{12}$N$_2$O$_2$ [M+H]$^+$, 181.0977; Found: 181.0978.

phenyl-3-(quinolin-2-ylamino)propan-1-one (1s)
Yield: 77%. Mp 127-128 °C. White solid. $^1$H NMR (300 MHz, CDCl₃): δ 8.03 (d, $J = 6.9$ Hz, 2H), 7.80-7.72 (m, 2H), 7.59-7.48 (m, 5H), 7.29-7.23 (m, 1H), 6.61 (d, $J = 8.7$ Hz, 1H), 5.27 (br s, 1H), 4.04 (d, $J = 5.7$ Hz, 2H), 3.44 (t, $J = 5.7$ Hz, 2H); $^{13}$C NMR (150 MHz, CDCl₃): δ 200.0, 156.4, 148.0, 137.1, 136.7, 133.3, 129.4, 128.6, 128.1, 127.4, 126.2, 123.4, 122.0, 112.4, 38.3, 36.3; HRMS (ESI): Exact mass calcd for C$_{18}$H$_{16}$N$_2$O [M+H]$^+$, 277.1335; Found: 277.1339.

1-phenyl-3-(pyrimidin-2-ylamino)propan-1-one (1t)

Yield: 68%. Mp 94-96 °C. Pale yellow solid. $^1$H NMR (600 MHz, CDCl₃): δ 8.25 (d, $J = 4.8$ Hz, 2H), 7.95 (d, $J = 8.4$ Hz, 2H), 7.56-7.53 (m, 1H), 7.45-7.43 (m, 2H), 6.51-6.50 (m, 1H), 5.66 (br s, 1H), 3.87 (t, $J = 6.0$ Hz, 2H), 3.31 (t, $J = 6.0$ Hz, 2H); $^{13}$C NMR (150 MHz, CDCl₃): δ 199.2, 162.1, 158.1, 136.7, 133.2, 128.6, 128.0, 110.5, 38.2, 36.3; HRMS (ESI): Exact mass calcd for C$_{13}$H$_{13}$N$_3$O [M+H]$^+$, 228.1132; Found: 228.1130.

phenyl-3-(pyridazin-3-ylamino)propan-1-one (1u)

Yield: 45%. Mp 126-127 °C. Pale yellow solid. $^1$H NMR (300 MHz, CDCl₃): δ 8.54 (d, $J = 4.5$ Hz, 1H), 8.00-7.97 (m, 2H), 7.62-7.56 (m, 1H), 7.51-7.45 (m, 2H), 7.12 (t, $J = 4.5$ Hz, 1H), 6.63 (d, $J = 9.0$ Hz, 1H), 5.16 (br s, 1H), 4.04-3.98 (m, 2H), 3.42 (t, $J = 4.5$ Hz, 1H); $^1$H NMR (600 MHz, CDCl₃): δ 8.58-8.51 (m, 2H), 7.90-7.70 (m, 2H), 7.60 (t, $J = 4.5$ Hz, 1H), 6.70 (d, $J = 9.0$ Hz, 1H), 5.10 (br s, 1H), 4.00-3.90 (m, 2H), 3.40 (t, $J = 4.5$ Hz, 1H); $^{13}$C NMR (150 MHz, CDCl₃): δ 199.0, 161.0, 156.0, 136.0, 133.0, 128.0, 128.0, 110.5, 38.2, 36.3; HRMS (ESI): Exact mass calcd for C$_{13}$H$_{13}$N$_2$O [M+H]$^+$, 228.1132; Found: 228.1130.
5.7 Hz, 2H); $^{13}$C NMR (75 MHz, CDCl$_3$): $\delta$ 199.8, 158.6, 143.6, 136.6, 133.5, 128.7, 128.1, 114.4, 37.7, 36.4; HRMS (ESI): Exact mass calcd for C$_{13}$H$_{13}$N$_3$O [M+H]$^+$, 228.1131; Found: 228.1130.

3-(benzo[d]thiazol-2-ylamino)-1-phenylpropan-1-one (1v)

Yield: 51%. Mp 137-138 °C. White solid. $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 8.01-7.97 (m, 2H), 7.63-7.56 (m, 3H), 7.51-7.45 (m, 2H), 7.33-7.28 (m, 1H), 7.09 (t, $J = 7.5$ Hz, 1H), 5.98 (br s, 1H), 3.96 (t, $J = 5.7$ Hz, 2H), 3.44 (t, $J = 5.7$ Hz, 2H); $^{13}$C NMR (75 MHz, CDCl$_3$): $\delta$ 199.2, 166.7, 152.5, 136.4, 133.6, 130.5, 128.7, 128.1, 125.9, 121.7, 120.8, 118.9, 39.8, 37.9; HRMS (ESI): Exact mass calcd for C$_{16}$H$_{14}$N$_2$OS [M+H]$^+$, 283.0900; Found:283.0899.

3. General procedure and product characterization

3.1 General procedure

Typical procedure for I$_2$-catalyzed intramolecular $\alpha$-amination of carbonyl compounds to 3-acylimidazo[1,2-a]pyridines 2a-2v.

**Procedure:** A reaction tube was equipped with a magnetic stir bar and successively charged with a mixture of 1a-1v (0.2 mmol), I$_2$ (20 mol%) and H$_2$O$_2$ (0.4 mmol, 30 wt.% in H$_2$O) and was stirred at 80 °C in air for 0.5-6 h. [**Caution:** H$_2$O$_2$ is slightly unstable, so it should be kept at 2-8 °C; H$_2$O$_2$ also has certain dangerousness to the human, so, if it touches your skin or eyes, please splash it with warm water as soon as possible.] After the reaction was complete (as determined by TLC analysis), the reaction was cooled to room temperature and excess I$_2$ was quenched with a saturated aqueous solution of Na$_2$S$_2$O$_3$. Then EtOAc (20 mL) was added to the solution and
washed with brine, dried over Na₂SO₄, concentrated under reduced pressure. The crude product was purified by column chromatography on silica gel (petroleum ether/EtOAc = 2:1) to afford the targeted product 2a-2v.

3.2 Product Characterization

imidazo[1,2-a]pyridin-3-yl(phenyl)methanone (2a)

Yield: 88%. Mp 104-105 °C. White solid. ¹H NMR (400 MHz, CDCl₃): δ 9.75 (d, J = 6.8 Hz, 1H), 8.21 (s, 1H), 7.89-7.80 (m, 3H), 7.63-7.52 (m, 4H), 7.16 (t, J = 6.8 Hz, 1H); ¹³C NMR (125 MHz, CDCl₃): δ 184.7, 149.0, 145.5, 139.2, 131.9, 129.3, 128.8, 128.7, 128.5, 123.5, 117.6, 115.0.

(6-methylimidazo[1,2-a]pyridin-3-yl)(phenyl)methanone (2b)

Yield: 81%. Mp 101-103 °C. White solid. ¹H NMR (300 MHz, CDCl₃): δ 9.58 (s, 1H), 8.17 (s, 1H), 7.88 (d, J = 8.1 Hz, 2H), 7.71 (d, J = 9.0 Hz, 1H), 7.64-7.51 (m, 3H), 7.42 (d, J = 9.0 Hz, 1H), 2.48 (s, 3H); ¹³C NMR (75 MHz, CDCl₃): δ 184.8, 148.1, 145.6, 139.4, 132.4, 131.9, 128.8, 128.6, 126.9, 125.3, 123.3, 116.9, 18.4; HRMS (ESI): Exact mass calcd for C₁₅H₁₂N₂O [M+H]⁺, 237.1022; Found: 237.1030.

(6-fluoroimidazo[1,2-a]pyridin-3-yl)(phenyl)methanone (2c)
Yield: 74%. Mp 122-124 °C. White solid. \(^1\)H NMR (300 MHz, CDCl\(_3\)): \(\delta\) 9.79-9.77 (m, 1H), 8.26 (s, 1H), 7.92-7.88 (m, 2H), 7.84-7.78 (m, 1H), 7.67-7.46 (m, 4H); \(^1^3\)C NMR (150 MHz, CDCl\(_3\)): \(\delta\) 184.9, 155.4, 153.8, 145.9, 138.9, 132.3, 128.8, 128.7, 121.0, 120.8, 118.0, 117.9, 116.3, 116.0; HRMS (ESI): Exact mass calcd for C\(_{14}\)H\(_9\)FN\(_2\)O [M+H]\(^+\), 241.0772; Found: 241.0770.

\((6\text{-chloroimidazo}[1,2-\text{a}]\text{pyridin-3-yl})(\text{phenyl})\text{methanone (2d)}\)

Yield: 67%. Mp 132-133 °C. White solid. \(^1\)H NMR (300 MHz, CDCl\(_3\)): \(\delta\) 9.86 (s, 1H), 8.23 (s, 1H), 7.88 (d, \(J = 7.8\) Hz, 2H), 7.77 (d, \(J = 9.3\) Hz, 1H), 7.67-7.52 (m, 4H); \(^1^3\)C NMR (75 MHz, CDCl\(_3\)): \(\delta\) 184.8, 145.6, 138.9, 132.3, 130.6, 128.8, 128.7, 126.9, 123.7, 123.6, 118.0; HRMS (ESI): Exact mass calcd for C\(_{14}\)H\(_9\)ClN\(_2\)O [M+H]\(^+\), 257.0476; Found: 257.0473.

\((6\text{-bromoimidazo}[1,2-\text{a}]\text{pyridin-3-yl})(\text{phenyl})\text{methanone (2e)}\)

Yield: 82%. Mp 144-145 °C. White solid. \(^1\)H NMR (300 MHz, CDCl\(_3\)): \(\delta\) 9.96 (s, 1H), 8.21 (s, 1H), 7.89 (d, \(J = 6.0\) Hz, 2H), 7.74-7.54 (m, 5H); \(^1^3\)C NMR (150 MHz, CDCl\(_3\)): \(\delta\) 184.8, 145.5, 138.8, 132.8, 132.3, 129.0, 128.8, 128.7, 118.2, 110.1.

\(\text{phenyl}(6\text{-}(\text{trifluoromethyl})\text{imidazo}[1,2-\text{a}]\text{pyridin-3-yl})\text{methanone (2f)}\)
Yield: 48%. Mp 148-149 °C. White solid. \(^1\)H NMR (300 MHz, CDCl\(_3\)): \(\delta\) 10.16 (s, 1H), 8.33 (s, 1H), 7.96-7.90 (m, 3H), 7.73-7.64 (m, 2H), 7.61-7.55 (m, 2H); \(^{13}\)C NMR (75 MHz, CDCl\(_3\)): \(\delta\) 185.0, 148.8, 146.3, 138.6, 132.6, 128.9, 128.8, 127.9, 127.8, 125.2, 125.0, 124.2, 121.4, 119.7, 119.2, 118.5, 53.4; HRMS (ESI): Exact mass calcd for C\(_{15}\)H\(_8\)F\(_3\)N\(_2\)O [M+H]\(^+\), 291.0740; Found: 291.0740.

methyl 3-benzoylimidazo[1,2-\(a\)]pyridine-6-carboxylate (2g)

Yield: 67%. Mp 126-128 °C. White solid. \(^1\)H NMR (300 MHz, CDCl\(_3\)): \(\delta\) 10.43 (s, 1H), 8.30 (s, 1H), 8.13 (d, \(J = 9.3\) Hz, 1H), 7.94-7.91 (m, 2H), 7.85 (d, \(J = 9.3\) Hz, 1H), 7.67-7.55 (m, 3H), 4.03 (s, 3H); \(^{13}\)C NMR (150 MHz, CDCl\(_3\)): \(\delta\) 184.8, 164.9, 146.6, 138.7, 132.5, 132.4, 129.1, 128.9, 128.7, 119.1, 117.2, 52.7, 29.7; HRMS (ESI): Exact mass calcd for C\(_{16}\)H\(_{12}\)N\(_2\)O \([\text{M+H}]^+\), 281.0921; Found: 281.0919.

(7-methylimidazo[1,2-\(a\)]pyridin-3-yl)(phenyl)methanone (2h)

Yield: 93%. Mp 135-136 °C. Pale yellow solid. \(^1\)H NMR (300 MHz, CDCl\(_3\)): \(\delta\) 9.62 (d, \(J = 7.2\) Hz, 1H), 8.16 (s, 1H), 7.89-7.86 (m, 2H), 7.64-7.51 (m, 4H), 7.00 (d, \(J = 5.4\) Hz, 1H), 2.53 (s, 3H); \(^{13}\)C NMR (75 MHz, CDCl\(_3\)): \(\delta\) 184.5, 149.6, 146.0, 144.1, 130.4, 131.9, 128.8, 128.0, 128.3, 117.6, 116.4, 21.6; HRMS (ESI): Exact mass calcd for C\(_{15}\)H\(_{12}\)N\(_2\)O \([\text{M+H}]^+\), 237.1022; Found: 237.1033.

(7-methoxyimidazo[1,2-\(a\)]pyridin-3-yl)(phenyl)methanone (2i)

Yield: 82%. Mp 84-86 °C. White solid. \(^1\)H NMR (300 MHz, CDCl\(_3\)): \(\delta\) 9.56 (d, \(J = 7.5\) Hz, 1H), 8.10 (s, 1H), 7.86 (d, \(J = 6.6\) Hz, 2H), 7.63-7.50 (m, 3H), 7.07 (s, 1H), 6.82 (d, \(J = 7.5\) Hz, 1H), 3.95 (s, 3H); \(^{13}\)C NMR (75 MHz, CDCl\(_3\)): \(\delta\) 184.2, 161.1, 151.4,
imidazo[1,2-a]pyridin-3-yl(m-tolyl)methanone (2j)

Yield: 91%. Mp 123-125 °C. White solid. ¹H NMR (400 MHz, CDCl₃): δ 9.75 (d, J = 6.8 Hz, 1H), 8.21 (s, 1H), 7.81 (d, J = 9.2 Hz, 1H), 7.68-7.66 (m, 2H), 7.57-7.53 (m, 1H), 7.42 (d, J = 4.8 Hz, 2H), 7.15 (t, J = 6.4 Hz, 1H), 2.46 (s, 3H); ¹³C NMR (125 MHz, CDCl₃): δ 185.1, 149.1, 145.6, 139.3, 138.5, 132.8, 129.3, 128.9, 128.4, 126.0, 117.7, 115.0, 21.4; HRMS (ESI): Exact mass calcd for C₁₅H₁₂N₂O [M+H]⁺, 253.0576; Found: 253.0580.

imidazo[1,2-a]pyridin-3-yl(p-tolyl)methanone (2k)

Yield: 89%. Mp 120-122 °C. White solid. ¹H NMR (400 MHz, CDCl₃): δ 9.73 (d, J = 6.8 Hz, 1H), 8.21 (s, 1H), 7.81 (t, J = 4.0 Hz, 3H), 7.56-7.52 (m, 1H), 7.34 (d, J = 8.0 Hz, 2H), 7.14 (t, J = 7.2 Hz, 1H), 2.47 (s, 3H); ¹³C NMR (125 MHz, CDCl₃): δ 184.6, 148.9, 145.2, 142.6, 136.5, 129.1, 128.9, 128.8, 123.5, 117.6, 114.8, 53.3; HRMS (ESI): Exact mass calcd for C₁₅H₁₂N₂O [M+H]⁺, 237.1022; Found: 237.1020.

(4-fluorophenyl)(imidazo[1,2-a]pyridin-3-yl)methanone (2l)

Yield: 93%. Mp 174-176 °C. White solid. ¹H NMR (300 MHz, CDCl₃): δ 9.74 (d, J = 6.9 Hz, 1H), 8.21 (s, 1H), 7.96-7.91 (m, 2H), 7.84 (d, J = 9.0 Hz, 1H), 7.61-7.56 (m, 1H), 7.28-7.16 (m, 3H); ¹³C NMR (150 MHz, CDCl₃): δ 183.3, 181.0, 166.8, 163.5, 157.4, 149.2, 145.4, 135.5, 131.3, 131.2, 129.5, 128.9, 123.4, 117.8, 115.9, 115.6, 115.2, 94.0; HRMS (ESI): Exact mass calcd for C₁₄H₉FN₂O [M+H]⁺, 241.0771; Found:
(4-chlorophenyl)(imidazo[1,2-a]pyridin-3-yl)methanone (2m)

\[
\begin{array}{c}
\text{N} \\
\text{O} \\
\text{Cl}
\end{array}
\]

Yield: 80%. Mp 129-130 °C. White solid. \(^1\)H NMR (300 MHz, CDCl\(_3\)): \(\delta\) 9.74 (d, \(J = 6.9 \text{ Hz}, 1\text{H}\)), 8.21 (s, 1H), 7.87-7.82 (m, 3H), 7.62-7.51 (m, 3H), 7.18 (t, \(J = 6.9 \text{ Hz}, 1\text{H}\)); \(^1^3\)C NMR (150 MHz, CDCl\(_3\)): \(\delta\) 183.4, 149.2, 145.6, 138.4, 137.5, 130.2, 129.6, 128.9, 123.3, 117.8, 115.3, 110.0; HRMS (ESI): Exact mass calcd for C\(_{14}\)H\(_9\)ClN\(_2\)O \([\text{M+H}]^+\), 257.0476; Found: 257.0471.

(4-bromophenyl)(imidazo[1,2-a]pyridin-3-yl)methanone (2n)

\[
\begin{array}{c}
\text{N} \\
\text{O} \\
\text{Br}
\end{array}
\]

Yield: 93%. Mp 175-177 °C. White solid. \(^1\)H NMR (300 MHz, CDCl\(_3\)): \(\delta\) 9.73 (d, \(J = 7.2 \text{ Hz}, 1\text{H}\)), 8.20 (s, 1H), 7.83 (d, \(J = 9.0 \text{ Hz}, 1\text{H}\)), 7.78-7.67 (m, 4H), 7.62-7.56 (m, 1H), 7.19 (t, \(J = 6.9 \text{ Hz}, 1\text{H}\)); \(^1^3\)C NMR (150 MHz, CDCl\(_3\)): \(\delta\) 183.5, 149.2, 148.6, 145.6, 138.0, 137.0, 131.9, 130.3, 129.7, 128.9, 126.9, 123.3, 122.3, 117.8, 115.3; HRMS (ESI): Exact mass calcd for C\(_{14}\)H\(_9\)BrN\(_2\)O \([\text{M+H}]^+\), 300.9971; Found: 300.9970.

imidazo[1,2-a]pyridin-3-yl(thiophen-2-yl)methanone (2o)

\[
\begin{array}{c}
\text{N} \\
\text{O} \\
\text{S}
\end{array}
\]

Yield: 83%. Mp 126-127 °C. White solid. \(^1\)H NMR (600 MHz, CDCl\(_3\)): \(\delta\) 9.63 (d, \(J = 7.2 \text{ Hz}, 1\text{H}\)), 8.49 (s, 1H), 7.87 (t, \(J = 4.8 \text{ Hz}, 1\text{H}\)), 7.79 (d, \(J = 9.0 \text{ Hz}, 1\text{H}\)), 7.69 (t, \(J = 4.8 \text{ Hz}, 1\text{H}\)), 7.54-7.51 (m, 1H), 7.25-7.20 (m, 1H), 7.11 (t, \(J = 7.2 \text{ Hz}, 1\text{H}\)); \(^1^3\)C NMR (150 MHz, CDCl\(_3\)): \(\delta\) 175.7, 149.0, 143.9, 143.7, 132.6, 131.9, 131.8, 129.4, 129.3, 128.9, 128.7, 128.1, 127.9, 123.2, 117.8, 115.2, 114.9; HRMS (ESI): Exact mass calcd for C\(_{12}\)H\(_8\)BrN\(_2\)O \([\text{M+H}]^+\), 229.0433; Found: 229.0433.

1-(imidazo[1,2-a]pyridin-3-yl)propan-1-one (2p)
Yield: 56%. Mp 127-129 °C. White solid. $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 9.69 (d, J = 6.9 Hz, 1H), 8.38 (s, 1H), 7.78 (d, J = 9.0 Hz, 1H), 7.53-7.48 (m, 1H), 7.10 (t, J = 6.9 Hz, 1H), 2.99 (t, J = 7.5 Hz, 2H), 1.31 (t, J = 7.5 Hz, 3H); $^{13}$C NMR (150 MHz, CDCl$_3$): $\delta$ 191.1, 142.5, 128.9, 128.7, 117.6, 115.0, 32.6, 9.0; HRMS (ESI): Exact mass calcd for C$_{10}$H$_{10}$N$_2$O [M+H]$^+$, 175.0866; Found: 175.0869.

1-(imidazo[1,2-a]pyridin-3-yl)-2,2-dimethylpropan-1-one (2q)

Yield: 97%. Mp 137-139 °C. White solid. $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 9.80 (d, J = 6.9 Hz, 1H), 8.51 (s, 1H), 7.78 (d, J = 8.7 Hz, 1H), 7.50 (t, J = 7.5 Hz, 1H), 7.08 (t, J = 6.9 Hz, 1H), 1.48 (s, 9H); $^{13}$C NMR (150 MHz, CDCl$_3$): $\delta$ 197.1, 142.5, 129.3, 128.7, 117.5, 114.8, 44.1, 28.7; HRMS (ESI): Exact mass calcd for C$_{12}$H$_{14}$N$_2$O [M+H]$^+$, 203.1179; Found: 203.1178.

imidazo[1,2-a]quinolin-1-yl(phenyl)methanone (2s)

Yield: 90%. Mp 157-158 °C. White solid. $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 8.46 (d, J = 8.7 Hz, 1H), 8.10 (d, J = 7.2 Hz, 2H), 8.01 (s, 1H), 7.91-7.84 (m, 2H), 7.73-7.65 (m, 3H), 7.62-7.54 (m, 3H); $^{13}$C NMR (75 MHz, CDCl$_3$): $\delta$ 184.3, 149.3, 146.5, 138.6, 133.1, 131.5, 130.1, 129.1, 129.0, 128.6, 125.8, 124.7, 119.9, 116.8, 100.0; HRMS (ESI): Exact mass calcd for C$_{18}$H$_{12}$N$_2$O [M+H]$^+$, 273.1022; Found: 273.1019.

imidazo[1,2-a]pyrimidin-3-yl(phenyl)methanone (2t)

Yield: 74%. Mp 215-216 °C. White solid. $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 10.01 (d, J =
6.9 Hz, 1H), 8.85 (d, J = 4.2 Hz, 1H), 8.43 (s, 1H), 7.94-7.90 (m, 2H), 7.70-7.55 (m, 3H), 7.28-7.23 (m, 1H); 13C NMR (75 MHz, CDCl3): δ 185.2, 153.7, 151.5, 146.4, 138.3, 136.7, 132.6, 128.9, 128.8, 121.8, 111.3; HRMS (ESI): Exact mass calcd for C13H9N3O [M+H]+, 224.0818; Found: 224.0817.

**imidazo[1,2-b]pyridazin-3-yl(phenyl)methanone (2u)**

Yield: 83%. Mp 140-142 ºC. White solid. 1H NMR (300 MHz, CDCl3): δ 8.69 (d, J = 4.5 Hz, 1H), 8.23 (s, 1H), 8.15 (d, J = 9.3 Hz, 1H), 7.96 (d, J = 6.9 Hz, 2H), 7.69-7.53 (m, 3H), 7.35 (t, J = 4.8 Hz, 1H); 13C NMR (75 MHz, CDCl3): δ 183.5, 144.6, 143.2, 142.7, 138.7, 132.7, 129.4, 128.6, 126.7, 126.2, 120.3; HRMS (ESI): Exact mass calcd for C13H9N3O [M+H]+, 224.0818; Found: 224.0816.

**benzo[d]imidazo[2,1-b]thiazol-3-yl(phenyl)methanone (2v)**

Yield: 82%. Mp 161-163 ºC. White solid. 1H NMR (300 MHz, CDCl3): δ 8.97 (d, J = 8.7 Hz, 1H), 7.99-7.95 (m, 2H), 7.86 (s, 1H), 7.77 (d, J = 8.1 Hz, 1H), 7.69-7.63 (m, 1H), 7.59-7.52 (m, 3H), 7.45 (t, J = 7.8 Hz, 1H); 13C NMR (150 MHz, CDCl3): δ 183.5, 147.1, 138.5, 132.6, 129.3, 128.6, 126.6, 124.7, 128.6; HRMS (ESI): Exact mass calcd for C16H10N3OS [M+H]+, 279.0587; Found: 279.0591.

### 4. Diversification of 3-acylimidazo[1,2-a]pyridines

**3-benzylimidazo[1,2-a]pyridine (3)**

| 2a | 1) N₂H₄, toluene, uW | 2) KOH, uW | 3 |

A mixture of 2a (0.2 mmol) and 80% hydrazine hydrate (2 equiv.) in toluene (1 mL)
was taken in a flame-dried Schlenk tube and placed in a commercial microwave oven operating at 2450 MHz frequency. After irradiation of the mixture for 20 mins., (monitored by TLC) it was cooled to room temperature, extracted with chloroform and dried over anhydrous Na$_2$SO$_4$. Removal of solvent gave the hydrazone. Then a mixture of the obtained hydrazone and KOH (1.4 mmol) were taken in a flame-dried Schlenk tube and placed in a microwave oven. After the reaction was complete (as determined by TLC analysis), the reaction was cooled to room temperature and EtOAc (20 mL) was added to the solution and washed with brine, dried over Na$_2$SO$_4$, concentrated under reduced pressure. The crude product was purified by column chromatography on silica gel (petroleum ether/EtOAc = 2:1) to afford the targeted product 3. Yield: 77%. White semisolid. $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 7.78 (d, $J = 6.9$ Hz, 1H), 7.64 (d, $J = 9.0$ Hz, 1H), 7.48 (s, 1H), 7.32-7.26 (m, 3H), 7.22-7.16 (m, 3H), 6.74 (t, $J = 6.9$ Hz, 1H), 4.27 (s, 2H); $^{13}$C NMR (75 MHz, CDCl$_3$): $\delta$ 145.8, 136.6, 132.6, 128.8, 128.3, 126.9, 123.6, 123.2, 122.5, 117.9, 112.1, 30.3; HRMS (ESI): Exact mass calcd for C$_{14}$H$_{12}$N$_2$ [M+H$^+$], 209.1079; Found: 209.1082.

2-bromo-1-(imidazo[1,2-a]pyridin-3-yl)propan-1-one (4)$^3$

$^N$-bromosuccinimide (NBS, 1.2 equiv.) and $p$-toluenesulfonic acid (T$_3$OH.H$_2$O, 0.2 equiv.) was added to a solution of 2p (0.2 mmol) in anhydrous CH$_3$CN (1 mL) at room temperature. After the addition, the reaction mixture was warmed to 60 $^\circ$C and stirred for 4 h. After the reaction was complete (as determined by TLC analysis), the reaction was cooled to room temperature and EtOAc (20 mL) was added to the solution and washed successively with H$_2$O, saturated NaHCO$_3$ solution, brine, dried over Na$_2$SO$_4$, concentrated under reduced pressure. The crude product was purified by column chromatography on silica gel (petroleum ether/EtOAc = 2:1) to afford the targeted product 4. Yield: 86%. Mp 185-187 $^\circ$C. White solid. 1H NMR (300 MHz, CDCl$_3$): $\delta$ 9.65 (d, $J = 6.9$ Hz, 1H), 8.50 (s, 1H), 7.82 (d, $J = 9.0$ Hz, 1H), 7.57 (t, $J = 6.9$ Hz, 1H), 7.17 (t, $J = 6.9$ Hz, 1H), 5.24 (t, $J = 6.9$ Hz, 1H), 1.96 (d, $J = 6.6$ Hz, 3H); $^{13}$C NMR (75 MHz, CDCl$_3$): $\delta$ 183.7, 149.5, 143.6, 129.8, 129.0, 121.1, 117.9, 115.6, 42.9, 20.5; HRMS (ESI): Exact mass calcd for C$_{10}$H$_9$BrN$_2$O [M+H$^+$], 252.9977; Found: 252.9974.
1-(imidazo[1,2-a]pyridin-3-yl)-2-phenylpropan-1-one (5)

To a flame-dried Schlenk flask were added KOtBu (5.0 equiv.) and 2p (2.0 equiv.). The flask was evacuated and backfilled with argon 3 times, then iodobenzene (0.1 mmol) was dissolved in dry DMF (1 mL) then was added by syringe, and the mixture was allowed to stir for 10 minutes at room temperature. The reaction mixture was stirred and heated at 60 °C for 13 h. After allowing the reaction to cool to room temperature, 1N HCl (2 mL) was added and the mixture was allowed to stir for 10 minutes at room temperature. After the reaction was complete (as determined by TLC analysis), the reaction was cooled to room temperature and EtOAc (20 mL) was added to the solution and washed with brine, dried over Na₂SO₄, concentrated under reduced pressure. The crude product was purified by column chromatography on silica gel (petroleum ether/EtOAc = 2:1) to afford the targeted product 5. Yield: 54%. Mp 169-171 °C. White solid. 1H NMR (300 MHz, CDCl₃): δ 9.70 (d, J = 6.9 Hz, 1H), 8.40 (s, 1H), 7.74 (d, J = 9.0 Hz, 1H), 7.49 (t, J = 7.8 Hz, 1H), 7.41 (d, J = 7.5 Hz, 2H), 7.36-7.21 (m, 3H), 7.08 (t, J = 6.6 Hz, 1H), 4.58 (t, J = 6.9 Hz, 1H), 1.63 (d, J = 6.9 Hz, 3H); 13C NMR (75 MHz, CDCl₃): δ 190.6, 148.8, 143.3, 141.6, 138.6, 129.1, 128.9, 127.6, 127.1, 123.2, 117.7, 115.0, 49.1, 18.7; HRMS (ESI): Exact mass calcd for C₁₆H₁₄N₂O [M+H]⁺, 251.1184; Found: 251.1187.

1-(imidazo[1,2-a]pyridin-3-yl)-2-methylprop-2-en-1-one (6)

In a Schlenk tube of 25 mL, DABCO (0.5 equiv.) and 2p (0.2 mmol) were dissolved in DMSO (1.0 mL) and stirred at room temperature for 1 minutes. Then K₂S₂O₈ (2 equiv.) were added. The mixture was stirred at 120 °C for 20 h under Ar atmosphere. After the reaction was complete (as determined by TLC analysis), the reaction was cooled to
room temperature and EtOAc (20 mL) was added to the solution and washed with brine, dried over Na$_2$SO$_4$, concentrated under reduced pressure. The crude product was purified by column chromatography on silica gel (petroleum ether/EtOAc = 2:1) to afford the targeted product 6. Yield: 74%. Mp 165-167 °C. Pale yellow solid. 1H NMR (300 MHz, CDCl$_3$): δ 9.63 (d, $J = 6.9$ Hz, 1H), 8.28 (s, 1H), 7.79 (d, $J = 9.0$ Hz, 1H), 7.53 (t, $J = 7.8$ Hz, 1H), 7.12 (t, $J = 6.9$ Hz, 1H), 5.77 (s, 2H), 2.13 (s, 3H); 13C NMR (75 MHz, CDCl$_3$): δ 186.7, 149.3, 144.9, 129.2, 128.8, 123.1, 122.7, 117.7, 115.0, 18.8; HRMS (ESI): Exact mass calcd for C$_{11}$H$_{10}$N$_2$O [M+H]$^+$, 187.0871; Found: 187.0868.

1-(imidazo[1,2-a]pyridin-3-yl)-2-morpholinopropan-1-one (7)$^3$

\[
\begin{array}{c}
\text{N-bromosuccinimide (NBS, 1.2 equiv.) and and } p\text{-toluenesulfonic acid (TsOH.H}_2\text{O, 0.2 equiv.) was added to a solution of } 2p (0.2 \text{ mmol) in anhydrous CH}_3\text{CN (1 mL) at room temperature. After the addition, the reaction mixture was warmed to 60 °C and stirred for 4 h. After the reaction was complete (as determined by TLC analysis), the reaction was cooled to room temperature and EtOAc (20 mL) was added to the solution and washed successively with H}_2\text{O, saturated NaHCO}_3 \text{ solution, brine, dried over Na}_2\text{SO}_4, concentrated under reduced pressure to give 4, which was used for the next step without purification. Then to the mixture of K}_2\text{CO}_3 (2.5 equiv.) and morpholine (3.0 equiv.) in CH}_3\text{CN (0.5 mL), 4 in CH}_3\text{CN (0.3 mL) was added slowly. After the addition, the reaction mixture was stirred until the reaction was completed at room temperature. EtOAc (20 mL) was added to the solution and washed with brine, dried over Na}_2\text{SO}_4, concentrated under reduced pressure. The crude product was purified by column chromatography on silica gel (petroleum ether/EtOAc = 2:1) to afford the targeted product 7. Yield: 72%. Mp 178-180 °C. White solid. 1H NMR (300 MHz, CDCl$_3$): δ 9.70 (d, $J = 6.9$ Hz, 1H), 8.76 (s, 1H), 7.78 (d, $J = 9.0$ Hz, 1H), 7.51 (t, $J = 6.9$ Hz, 1H), 7.10 (t, $J = 6.9$ Hz, 1H), 3.78 (t, $J = 6.6$ Hz, 1H), 3.74-3.70 (m, 4H), 2.72-2.65 (m, 2H), 2.61-2.54 (m, 2H), 1.38 (d, $J = 6.9$ Hz, 3H); 13C NMR (75 MHz, CDCl$_3$): δ 191.2, 148.7, 143.9, 129.3, 128.9, 122.8, 117.7, 115.2, 67.4, 67.1, 50.7, 13.7; HRMS (ESI): Exact mass calcd for C$_{14}$H$_{17}$N$_3$O$_2$ [M+H]$^+$, 260.1399; Found: 260.1393.
\end{array}
\]
N-bromosuccinimide (NBS, 1.2 equiv.) and p-toluenesulfonic acid (TsOH.H2O, 0.2 equiv.) was added to a solution of 2p (0.2 mmol) in anhydrous CH3CN (1 mL) at room temperature. After the addition, the reaction mixture was warmed to 60 °C and stirred for 4 h. After the reaction was complete (as determined by TLC analysis), the reaction was cooled to room temperature and EtOAc (20 mL) was added to the solution and washed successively with H2O, saturated NaHCO3 solution, brine, dried over Na2SO4, concentrated under reduced pressure to give 4, which was used for the next step without purification. A solution of sodium iodide (1.1 equiv.) in anhydrous acetone (0.5 mL) was added to a solution of 4 in the same solvent (0.5 mL). The formation of sodium bromide precipitate is observed instantly. The reaction was stirred at rt for 10 min and, then, filtered. Removal of the solvent under reduced pressure afforded the expected product 8. No further purification was needed. Yield: 76%. Mp 195-197 °C. White solid. 1H NMR (300 MHz, CDCl3): δ 9.63 (d, J = 6.9 Hz, 1H), 8.47 (s, 1H), 7.80 (d, J = 7.5 Hz, 1H), 7.59-7.50 (m, 1H), 7.18-7.12 (m, 1H), 5.45 (t, J = 6.9 Hz, 1H), 2.10 (d, J = 6.9 Hz, 3H); 13C NMR (75 MHz, CDCl3): δ 185.3, 149.4, 143.6, 143.1, 129.8, 129.6, 129.0, 120.1, 117.9, 115.6, 115.5, 43.0, 18.7; HRMS (ESI): Exact mass calcd for C10H9IN2O [M+H]+, 300.9769; Found: 300.9765.
5. Contral Experiments

\[ \text{Ph}(\text{OAc})_2 \text{ (2 equiv)} \text{ or } \text{Bu}_2\text{NIO}_3 \text{ (2 equiv)} \text{ or } \text{Bu}_2\text{NIO}_4 \text{ (2 equiv)} \text{ neat, } 80 \text{ °C, air} \]

\[ \begin{align*}
\text{Ph} \rightleftharpoons \text{N} \rightleftharpoons \text{H} &\rightarrow \text{Ph} \text{N} \text{O} \\
\text{I}_2 \text{ (2 equiv)} \text{ neat, } 80 \text{ °C, air} &\rightarrow \text{messy} \\
\text{I}_2 \text{ (20 mol\%)} \text{ H}_2\text{O}_2 \text{ (2 equiv)} \text{ TEMPO (2 equiv)} \text{ neat, } 80 \text{ °C, air} &\rightarrow \text{Ph} \text{N} \text{O} \end{align*} \]

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7. Copies of 1H NMR and 13C NMR Spectra
