Electronic Supplementary Information (ESI)

I₂-Catalyzed Intramolecular Dehydrogenative Aminooxygenation of Alkynes to Acylated Imidazo[1,2a]pyridines and Indolizines

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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). ¹H and ¹³C NMR spectra were recorded on a Bruker AV300, 400 or 500 spectrometer. Chemical shifts (δ) were reported in ppm referenced to the CDCl₃ residual peak (δ 7.26) or the DMSO-d₆ residual peak (δ 2.50) for ¹H NMR. Chemical shifts of ¹³C NMR were reported relative to CDCl₃ (δ 77.0) or D₆-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. General procedure and product characterization

2.1 General procedure

Typical procedure for I_2 -catalyzed intramolecular dehydrogenative aminooxygenation of alkynes to 3-acylimidazo[1,2-a]pyridines **2a-2t** and 3-acylindolizines **4a-4d**.



A 15 mL schlenk tube was equipped with a rubber septum and magnetic stir bar and was charged with a mixture of **1a-1t** or **3a-3d** (0.2 mmol), I_2 (10 mol%) and TBHP (0.4 mmol) in toluene (1.0 mL) and was stirred at 50 °C 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 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-2t** or **4a-4d**.

2.2 Product Characterization

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



Yield: 85%. Mp 104-105 °C. White solid. ¹H NMR (400 MHz, CDCl₃): δ 9.75 (d, *J* = 6.8 Hz, 1H), 8.21 (s, 1H), 7.88 (d, *J* = 7.2 Hz, 2H), 7.81 (d, *J* = 8.8 Hz, 1H), 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.

imidazo[1,2-a]pyridin-3-yl(m-tolyl)methanone (2b)¹



Yield: 77%. Mp 123-125 °C. Pale yellow 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), 7.55 (t, J = 8.4 Hz, 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]⁺, 237.1022; Found: 237.1020.

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



Yield: 74%. Mp 120-122 °C. White solid. ¹H NMR (400 MHz, CDCl₃): δ 9.74 (d, *J* = 6.8 Hz, 1H), 8.21 (s, 1H), 7.81-7.79 (m, 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, 21.4; HRMS (ESI): Exact

mass calcd for $C_{15}H_{12}N_2O$ [M+H]⁺, 237.1022; Found: 237.1021. (3,5-dimethylphenyl)(imidazo[1,2-a]pyridin-3-yl)methanone (2d)



Yield: 62%. Mp 100-102 °C. White solid. ¹H NMR (400 MHz, CDCl₃): δ 9.74 (d, *J* = 6.8 Hz, 1H), 8.21 (s, 1H), 7.81 (d, *J* = 8.8 Hz, 1H), 7.54 (t, *J* = 7.6 Hz, 1H), 7.48 (s, 2H), 7.25 (d, *J* = 7.6 Hz, 1H), 7.15 (t, *J* = 7.2 Hz, 1H), 2.42 (s, 6H); ¹³C NMR (125 MHz, CDCl₃): δ 185.2, 149.0, 145.5, 139.3, 138.2, 133.6, 129.2, 128.8, 123.6, 117.6, 114.9, 21.4; HRMS (ESI): Exact mass calcd for C₁₆H₁₄N₂O [M+H]⁺, 251.1179; Found: 251.1177.

[1,1'-biphenyl]-4-yl(imidazo[1,2-a]pyridin-3-yl)methanone (2e)¹



Yield: 76%. Mp 189-190 °C. White solid. ¹H NMR (400 MHz, CDCl₃): δ 9.77 (d, *J* = 6.8 Hz, 1H), 8.28 (s, 1H), 7.98 (d, *J* = 8.0 Hz, 2H), 7.83 (d, *J* = 8.8 Hz, 1H), 7.77 (d, *J* = 8.0 Hz, 2H), 7.67 (t, *J* = 7.2 Hz, 2H), 7.56 (t, *J* = 7.2 Hz, 1H), 7.50 (t, *J* = 7.2 Hz, 2H), 7.42 (t, *J* = 7.2 Hz, 1H), 7.17 (t, *J* = 7.2 Hz, 1H); ¹³C NMR (125 MHz, CDCl₃): δ 184.4, 149.1, 145.5, 145.0, 140.0, 138.0, 129.5, 129.4, 129.0, 128.9, 128.1, 127.3, 123.7, 117.8, 115.1; HRMS (ESI): Exact mass calcd for C₂₀H₁₄N₂O [M+H]⁺, 299.1179; Found: 299.1180.

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



Yield: 75%. Mp 135-137 °C. White solid. ¹H NMR (400 MHz, CDCl₃): δ 9.72 (d, *J* = 7.2 Hz, 1H), 8.19 (s, 1H), 7.82 (d, *J* = 9.2 Hz, 1H), 7.75 (d, *J* = 6.8 Hz, 2H), 7.68 (t, *J* = 6.8 Hz, 2H), 7.59-7.55 (m, 1H), 7.19-7.15 (m, 1H); ¹³C NMR (125 MHz, CDCl₃): δ

183.5, 149.3, 145.6, 138.0, 131.9, 130.3, 129.6, 128.9, 126.9, 123.3, 117.8, 115.3; HRMS (ESI): Exact mass calcd for C₁₄H₉FN₂O [M+H]⁺, 241.0772; Found: 241.0773. (4-chlorophenyl)(imidazo[1,2-a]pyridin-3-yl)methanone (2g)¹



Yield: 88%. Mp 129-131 °C. Pale yellow solid. ¹H NMR (400 MHz, CDCl₃): δ 9.72 (d, J = 6.8 Hz, 1H), 8.19 (s, 1H), 7.84-7.81 (m, 3H), 7.59-7.51 (m, 3H), 7.17 (t, J = 6.4 Hz, 1H); ¹³C NMR (125 MHz, CDCl₃): δ 183.3, 149.2, 145.5, 138.4, 137.5, 130.1, 129.5, 128.9, 128.8, 123.3, 117.8, 115.2; HRMS (ESI): Exact mass calcd for C₁₄H₉ClN₂O [M+H]⁺, 257.0476; Found: 257.0471.

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



Yield: 65%. Mp 175-177 °C. White solid. ¹H NMR (400 MHz, CDCl₃): δ 9.72 (d, *J* = 6.8 Hz, 1H), 8.19 (s, 1H), 7.93-7.89 (m, 2H), 7.82 (d, *J* = 8.8 Hz, 1H), 7.58-7.54 (m, 1H), 7.26-7.14 (m, 3H); ¹³C NMR (125 MHz, CDCl₃): δ 183.1, 166.0, 164.0, 149.0, 145.3, 135.4, 131.1, 131.0, 129.3, 128.7, 123.2, 117.7, 115.7, 115.5 115.0; HRMS (ESI): Exact mass calcd for C₁₄H₉BrN₂O [M+H]⁺, 300.9971; Found: 300.9970. **imidazo[1,2-a]pyridin-3-yl(4-(trifluoromethyl)phenyl)methanone (2i)**¹



Yield: 76%. Mp 128-130 °C. White solid. ¹H NMR (300 MHz, CDCl₃): δ 9.72 (d, J = 3.6 Hz, 1H), 8.17 (s, 1H), 7.95 (d, J = 3.9 Hz, 2H), 7.83-7.78 (m, 3H), 7.59-7.57 (m, 1H), 7.18 (t, J = 3.3 Hz, 1H); ¹³C NMR (75 MHz, CDCl₃): δ 183.3, 149.4, 146.0, 142.3, 133.9, 133.6, 133.4, 133.1, 130.1, 129.9, 129.1, 128.9, 124.6, 123.3, 122.7, 118.0, 117.8, 115.7, 115.4; HRMS (ESI): Exact mass calcd for C₁₅H₉F₃N₂O [M+H]⁺,

291.0745; Found: 291.0744.

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



Yield: 72%. Yellow oil. ¹H NMR (300 MHz, CDCl₃): δ 9.94 (d, *J* = 6.9 Hz, 1H), 8.23 (d, *J* = 7.2 Hz, 1H), 8.05 (d, *J* = 8.1 Hz, 1H), 8.00 (s, 1H), 7.97-7.94 (m, 1H), 7.88-7.85 (m, 1H), 7.79-7.76 (m, 1H), 7.65-7.54 (m, 4H), 7.28-7.24 (m, 1H); ¹³C NMR (75 MHz, CDCl₃): δ 186.0, 149.4, 146.5, 136.7, 133.8, 131.2, 130.7, 129.7, 129.1, 128.4, 127.3, 127.1, 126.6, 125.3, 125.0, 124.4, 117.9, 115.4; HRMS (ESI): Exact mass calcd for C₁₈H₁₂N₂O [M+H]⁺, 273.1028; Found: 273.1028.

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



Yield: 56%. Mp 223-224 °C. Purple solid. ¹H NMR (300 MHz, CDCl₃): δ 9.76 (d, *J* = 6.9 Hz, 1H), 9.12 (s, 1H), 8.87-8.84 (m, 1H), 8.24 (s, 1H), 8.18 (d, *J* = 7.8 Hz, 1H), 7.86 (d, *J* = 9.0 Hz, 1H), 7.62 (t, *J* = 7.8 Hz, 1H), 7.54-7.49 (m, 1H), 7.22 (t, *J* = 6.9 Hz, 1H); ¹³C NMR (75 MHz, CDCl₃): δ 182.3, 152.6, 149.6, 149.4, 145.9, 136.2, 134.9, 130.1, 128.9, 123.6, 123.4, 117.9, 115.6; HRMS (ESI): Exact mass calcd for C₁₃H₉N₃O [M+H]⁺, 224.0824; Found: 224.0822.

(3,5-dimethylisoxazol-4-yl)(imidazo[1,2-a]pyridin-3-yl)methanone (2l)



Yield: 51%. mp 241-242 °C. Yellow solid. ¹H NMR (300 MHz, CDCl₃): δ 9.63 (d, J = 3.6 Hz, 1H), 8.07 (s, 1H), 7.82 (d, J = 4.5 Hz, 1H), 7.61-7.58 (m, 1H), 7.18 (t, J = 3.6 Hz, 1H), 2.51 (s, 3H), 2.37 (s, 3H); ¹³C NMR (75 MHz, CDCl₃): δ 177.0, 169.7, 159.0, 149.5, 145.4, 130.1, 128.7, 124.2, 118.0, 117.1, 115.6, 13.0, 10.9; HRMS (ESI): Exact

mass calcd for C₁₃H₁₁N₃O₂ [M+H]⁺, 242.0930; Found: 242.0926.

1-(imidazo[1,2-a]pyridin-3-yl)ethan-1-one (2m)¹



Yield: 81%. Mp 91-93 °C. Pale yellow solid. ¹H NMR (300 MHz, CDCl₃): δ 9.61 (d, *J* = 6.9 Hz, 1H), 8.32 (s, 1H), 7.74 (d, *J* = 9.0 Hz, 1H), 7.50-7.44 (m, 1H), 7.06 (t, *J* = 6.9 Hz, 1H), 2.59 (s, 3H); ¹³C NMR (75 MHz, CDCl₃): δ 187.2, 148.7, 143.4, 129.0, 128.7, 123.9, 117.6, 115.0, 27.1; HRMS (ESI): Exact mass calcd for C₉H₈N₂O [M+H]⁺, 161.0715; Found: 161.0712.

imidazo[1,2-a]pyridine-3-carbaldehyde (2n)¹



Yield: 65%. Mp 118-120 °C. White solid. ¹H NMR (300 MHz, CDCl₃): δ 9.96 (s, 1H), 9.51 (d, J = 6.9 Hz, 1H), 8.34 (s, 1H), 7.82 (d, J = 9.0 Hz, 1H), 7.61-7.55 (m, 1H), 7.15 (t, J = 6.9 Hz, 1H); ¹³C NMR (75 MHz, CDCl₃): δ 177.8, 149.4, 146.8, 130.1, 128.7, 125.0, 117.9, 115.5; HRMS (ESI): Exact mass calcd for C₈H₆N₂O [M+H]⁺, 147.0558; Found: 147.0566.

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



Yield: 97%. Mp 105-106 °C. Pale yellow solid. ¹H NMR (400 MHz, CDCl₃): δ 9.61 (d, J = 7.2 Hz, 1H), 8.15 (s, 1H), 7.86 (t, J = 7.2 Hz, 2H), 7.60-7.51 (m, 4H), 6.98 (d, J = 6.8 Hz, 1H), 2.51 (s, 3H); ¹³C NMR (125 MHz, CDCl₃): δ 184.6, 149.7, 146.0, 141.2, 139.5, 131.9, 128.8, 128.6, 128.1, 123.4, 117.6, 116.5, 21.6; HRMS (ESI): Exact mass calcd for C₁₅H₁₂N₂O [M+H], 237.1023; Found: 237.1025.

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



Yield: 83%. Mp 103-105 °C. White solid. ¹H NMR (400 MHz, CDCl₃): δ 9.57 (s, 1H), 8.15 (s, 1H), 7.86 (d, J = 8.0 Hz, 2H), 7.70 (d, J = 8.8 Hz, 1H), 7.61-7.50 (m, 3H), 7.39 (d, J = 8.8 Hz, 1H), 2.46 (s, 3H); ¹³C NMR (125 MHz, CDCl₃): δ 184.7, 148.0, 145.5,

139.4, 132.2, 131.8, 128.7, 128.4, 126.8, 125.1, 123.2, 116.8, 18.3; HRMS (ESI): Exact mass calcd for $C_{15}H_{12}N_2O$ [M+H]⁺, 237.1022; Found: 237.1021.

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



Yield: 75%. Mp 161-163 °C. White solid. ¹H NMR (400 MHz, CDCl₃): δ 9.55 (d, J = 7.6 Hz, 1H), 8.09 (s, 1H), 7.85 (t, J = 6.8 Hz, 2H), 7.61-7.50 (m, 3H), 7.06 (s, 1H), 6.81 (d, J = 7.6 Hz, 1H), 3.94 (s, 3H); ¹³C NMR (125 MHz, CDCl₃): δ 183.9, 160.8, 151.1, 146.1, 139.2, 131.5, 129.2, 128.4, 128.2, 122.9, 108.8, 95.5, 55.5; HRMS (ESI): Exact mass calcd for C₁₅H₁₂N₂O₂ [M+H]⁺, 253.0972; Found: 253.0970.

(6-bromoimidazo[1,2-a]pyridin-3-yl)(phenyl)methanone (2r)¹



Yield: 62%. Mp 144-146 °C. White solid. ¹H NMR (400 MHz, CDCl₃): δ 9.94 (s, 1H), 8.19 (s, 1H), 7.87 (t, *J* = 7.2 Hz, 2H), 7.71 (d, *J* = 8.8 Hz, 1H), 7.63-7.61 (m, 2H), 7.55 (t, *J* = 8.0 Hz, 2H); ¹³C NMR (125 MHz, CDCl₃): δ 184.7, 147.3, 145.3, 138.8, 132.6, 132.2, 128.9, 128.7, 128.6, 123.5, 118.1, 110.0; HRMS (ESI): Exact mass calcd for C₁₄H₉BrN₂O [M+H]⁺, 300.9971; Found: 300.9969.

methyl 3-benzoylimidazo[1,2-a]pyridine-7-carboxylate (2s)¹



Yield: 50%. Mp 202-204 °C. White solid. ¹H NMR (400 MHz, CDCl₃): δ 9.76 (d, *J* = 7.2 Hz, 1H), 8.49 (s, 1H), 8.30 (s, 1H), 7.88 (t, *J* = 7.2 Hz, 2H), 7.72 (d, *J* = 7.2 Hz, 1H), 7.64 (t, *J* = 7.6 Hz, 1H), 7.55 (t, *J* = 8.0 Hz, 2H), 4.02 (s, 3H); ¹³C NMR (125 MHz, CDCl₃): δ 184.7, 164.6, 147.8, 146.0, 138.5, 132.1, 130.1, 128.6, 128.4, 128.1, 123.9, 119.5, 113.9, 52.5; HRMS (ESI): Exact mass calcd for C₁₆H₁₂N₂O₃ [M+H]⁺, 281.0921; Found: 281.0919.

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



Yield: 85%. Mp 157-158 °C. White solid. ¹H NMR (300 MHz, CDCl₃): δ 8.45 (d, J = 8.7 Hz, 1H), 8.11 (d, J = 6.0 Hz, 2H), 8.01 (s, 1H), 7.90-7.83 (m, 2H), 7.73-7.65 (m, 3H), 7.61-7.53 (m, 3H); ¹³C NMR (75 MHz, CDCl₃): δ 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 C₁₈H₁₂N₂O [M+H]⁺, 273.1028; Found: 273.1032.

1-(4-methoxyphenyl)-3-(pyridin-2-ylamino)propan-1-one (2u)



Yield: 90%. Mp 108-110 °C. White solid. ¹H NMR (400 MHz, CDCl₃): δ 8.08 (d, J = 4.4 Hz, 1H), 7.94 (d, J = 8.8 Hz, 2H), 7.36 (t, J = 6.8 Hz, 1H), 6.92 (t, J = 8.8 Hz, 2H), 6.54 (t, J = 5.6 Hz, 1H), 6.38 (d, J = 8.8 Hz, 1H), 4.94 (br s, 1H), 3.86 (s, 3H), 3.80 (t, J = 6.0 Hz, 2H), 3.26 (t, J = 6.0 Hz, 2H); ¹³C NMR (125 MHz, CDCl₃): δ 198.2, 163.8, 158.5, 148.1, 137.3, 130.5, 130.1, 113.9, 112.9, 108.1, 55.6, 53.5, 38.0, 37.0; HRMS (ESI): Exact mass calcd for C₁₅H₁₆N₂O₂ [M+H]⁺, 257.1285; Found: 257.1282.

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



Yield: 88%. Mp 86-88 °C. White solid. ¹H NMR (400 MHz, CDCl₃): δ 8.08 (d, *J* = 4.4 Hz, 1H), 7.72 (d, *J* = 3.6 Hz, 1H), 7.63 (t, *J* = 4.8 Hz, 1H), 7.37 (t, *J* = 7.2 Hz, 1H), 7.11 (t, *J* = 4.4 Hz, 1H), 6.55 (t, *J* = 6.0 Hz, 1H), 6.38 (t, *J* = 8.4 Hz, 1H), 4.91 (br s, 1H), 3.81 (t, *J* = 6.0 Hz, 2H), 3.26 (t, *J* = 6.0 Hz, 2H); ¹³C NMR (125 MHz, CDCl₃): δ 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 C₁₂H₁₂N₂OS [M+H]⁺, 233.0743; Found: 233.0742.

ethyl 3-benzoylindolizine-1-carboxylate (4a)²



Yield: 78%. Mp 78-80 °C. White solid. ¹H NMR (300 MHz, CDCl₃): δ 9.99 (d, *J* = 7.2 Hz, 1H), 8.41 (d, *J* = 9.0 Hz, 1H), 7.84 (t, *J* = 4.2 Hz, 3H), 7.62-7.44 (m, 4H), 7.11 (t, *J* = 6.9 Hz, 1H), 4.40 (t, *J* = 7.2 Hz, 2H), 1.41 (t, *J* = 7.2 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃): δ 185.6, 164.1, 139.9, 131.5, 129.2, 129.1, 129.0, 128.4, 127.7, 122.5, 119.5, 115.3, 106.3, 60.1, 14.6; HRMS (ESI): Exact mass calcd for C₁₈H₁₅NO₃ [M+H]⁺, 294.1256; Found: 294.1257.

ethyl 3-(4-(trifluoromethyl)benzoyl)indolizine-1-carboxylate (4b)²



Yield: 71%. Mp 103-105 °C. Yellow solid. ¹H NMR (300 MHz, CDCl₃): δ 10.00 (d, *J* = 7.2 Hz, 1H), 8.44 (t, *J* = 9.0 Hz, 1H), 7.93 (d, *J* = 8.1 Hz, 2H), 7.80 (t, *J* = 8.1 Hz, 3H), 7.53 (t, *J* = 7.8 Hz, 1H), 7.16 (t, *J* = 6.9 Hz, 1H), 4.40 (t, *J* = 7.2 Hz, 2H), 1.42 (t, *J* = 6.9 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃): δ 184.0, 163.9, 143.1, 140.2, 133.6, 132.8, 132.2, 129.3, 129.2, 128.3, 125.5, 122.1, 119.6, 115.7, 106.9, 60.3, 14.6; HRMS (ESI): Exact mass calcd for C₁₉H₁₄F₃NO₃ [M+H]⁺, 362.1004; Found: 362.1001.

ethyl 3-(thiophene-2-carbonyl)indolizine-1-carboxylate (4c)²



Yield: 37%. Mp 91-93 °C. Yellow solid. ¹H NMR (300 MHz, CDCl₃): δ 9.87 (d, *J* = 6.9 Hz, 1H), 8.42 (d, *J* = 9.0 Hz, 1H), 8.17 (s, 1H), 7.85 (d, *J* = 3.6 Hz, 1H), 7.69 (d, *J* = 5.1 Hz, 1H), 7.46 (t, *J* = 7.8 Hz, 1H), 7.23 (t, *J* = 4.5 Hz, 1H), 7.08 (t, *J* = 7.2 Hz, 1H), 4.43 (t, *J* = 7.2 Hz, 2H), 1.45 (t, *J* = 7.2 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃): δ 176.5, 164.1, 144.3, 139.9, 132.1, 132.0, 129.1, 127.8, 127.6, 127.3, 122.2, 119.6, 115.2, 106.4, 60.2, 14.6; HRMS (ESI): Exact mass calcd for C₁₆H₁₃NO₃S [M+H]⁺, 300.0804; Found: 300.0802.

ethyl 3-formylindolizine-1-carboxylate (4d)²



Yield: 56%. Mp 91-93 °C. White solid. ¹H NMR (300 MHz, CDCl₃): δ 9.74 (s, 1H), 9.68 (d, *J* = 6.9 Hz, 1H), 8.33 (d, *J* = 8.7 Hz, 1H), 7.90 (s, 1H), 7.44 (t, *J* = 7.2 Hz, 1H), 7.05 (t, *J* = 6.9 Hz, 1H), 4.38 (t, *J* = 7.2 Hz, 2H), 1.42 (t, *J* = 7.2 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃): δ 178.5, 163.7, 140.0, 129.4, 128.8, 128.3, 123.8, 119.6, 115.6, 107.4, 60.2, 14.5; HRMS (ESI): Exact mass calcd for C₁₂H₁₁NO₃ [M+H]⁺, 218.0736; Found: 218.0740.

3. Mechanistic studies

3.1 Discovery of intermediate C

A 15 mL schlenk tube was equipped with a rubber septum and magnetic stir bar and was charged with a mixture of **1u-1v** (0.2 mmol), I₂ (10 mol%) and TBHP (0.4 mmol) in toluene (1.0 mL) and was stirred at 50 °C 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 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 **2u-2v** in 90% and 88% yield, respectively.



The Preperation of Intermediate C

A 25 mL glass vial 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 °C for 15 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 Na₂SO₄ 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 **C** (461 mg, 68% yield) as a white solid.



The characterization of intermediate C³



Yield: 68%. Mp 82-84 °C. White solid. ¹H NMR (300 MHz, CDCl₃): δ 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); ¹³C NMR (75 MHz, CDCl₃): δ 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 C₁₄H₁₄N₂O [M+H]⁺, 227.1179; Found: 227.1176.



A 15 mL schlenk tube was equipped with a rubber septum and magnetic stir bar and was charged with a mixture of C (0.2 mmol), I_2 (10 mol%) and TBHP (0.4 mmol) in

toluene (1.0 mL) and was stirred at 50 °C 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 with brine, dried over Na_2SO_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 **2a** in 75% yield.

3.2 Free-Radical inhibition experiment



A 15 mL schlenk tube was equipped with a rubber septum and magnetic stir bar and was charged with a mixture of **1a** (0.2 mmol), I_2 (10 mol%), TBHP (0.4 mmol) and TEMPO (0.4 mmol) in toluene (1.0 mL) and was stirred at 50 °C 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 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** in 73% yield.

3.3 The effect of water on the reaction

To explore the source of water as well as the effect of the amount of water on the reaction, we conducted the following experiments. The reaction initially proceeded in distilled toluene without the addition of water in air, and **2a** was obtained in 44% yield (entry 1). The yield of **2a** was sharply decreased in Ar (entry 2). Gradually adding the amount of water from 1 equiv to 5 equiv (entries 3-7), the yield was accordingly increased, however, further adding the amount of water (entries 8, 9), the yield wasn't further improved. These results implied that 5 equiv amount of water might be suitable for this reaction and the source of water might be the air or the solvent or the reagents (it had still 17% yield of **2a** in the reaction conditions of distilled toluene as well as Ar (entry 2)).

H N Pf 1a , 0.2 mmo	Ph O		
entry ^a	H ₂ O (equiv)	atmosphere	yield ^b
1	0	air	44%
2	0	Ar	17%
3	1	Ar	61%
4	2	Ar	69%
5	3	Ar	78%
6	4	Ar	83%
7	5	Ar	86%
8	6	Ar	85%
9	10	Ar	81%

^{*a*} Reaction conditions: **1a** (0.2 mmol), catalyst (10 mol%), oxidant (0.4 mmol) in solvent (1 mL). ^{*b*} Determined by NMR analysis using 4-iodoanisole as internal standard. ^{*c*} TBHP (5.0 - 6.0 M in decane).

4. References

- (a) N. Chernyak, V. Gevorgyan, Angew. Chem., Int. Ed., 2010, 49, 2743; (b) H. G. Wang, Y. Wang, D. D. Liang, L. Y. Liu, J. C. Zhang, Q. Zhu, Angew. Chem., Int. Ed., 2011, 50, 5677; (c) L. J. Ma, X. P. Wang, W. Yu, B. Han, Chem. Commun., 2011, 47, 11333; (d) D. Chandra Mohan, S. N. Rao, S. Adimurthy, J. Org. Chem., 2013, 78, 1266; (e) H. Cao, X. Liu, J. Liao, J. Huang, H. Qiu, Q. Chen, Y. Chen, J. Org. Chem., 2014, 79, 11209; (f) H. Zhan, L. Zhao, J. Liao, N. Li, Q. Chen, S. Qiu, H. Cao, Adv. Synth. Catal., 2015, 357, 46; (g) K. R. Reddy, A. P. Gupta, P. Das, Asian J. Org. Chem., 2016, 5, 900.
- 2. I. Kim, S. G. Kim, J. Y. Kim, G. H. Lee, Tetrahedron Lett., 2007, 48, 8976.
- 3. X. Jie, Y. Shang, X. Zhang, W. Su, J. Am. Chem. Soc., 2016, 138, 5623.

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

















220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 fl (ppm)

