Electronic Supplementary Information

Syntheses of Indolizinones From an Intramolecular One-Pot Process of *gem*-Dibromoolefins

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I. General Information

All reactions involving air sensitive reagents were carried out in pre-heated glassware under an argon atmosphere using standard Schlenk techniques. All reagents were obtained from commercial suppliers and used without further purification. Reactions were monitored using thin-layer chromatography (TLC) on commercial silica gel plates (GF254). Column chromatography was performed on silica gel (200-300 mesh). ¹H and ¹³C NMR spectra were recorded on a 400 or 500 MHz spectrometer. The ¹H NMR chemical shifts were measured relative to CDCl₃ or DMSO-d₆ as the internal reference (CDCl₃: $\delta = 7.26$; DMSO-d₆: $\delta = 2.50$). The ¹³C NMR chemical shifts were given using CDCl₃ or DMSO-d₆ as the internal standard (CDCl₃: $\delta = 77.16$; DMSO-d₆: $\delta = 39.52$). 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. High resolution mass spectra (HRMS) were obtained on an ESI-LC-MS/MS Spectrometer.

II. General procedure for the preparation of starting material 1

1. General procedure for the preparation of pyridines N-oxides (1b-1e)



To a solution of 2-(2,2-dibromovinyl)benzoic acid (1.0 equiv) in dichloromethane were added EDCI (1.1 equiv) and HOBT (1.1 equiv), then amine reagent (1.0 equiv) was added and the reaction mixture was stirred at r.t. for 1h. The reaction mixture was washed with brine and the organic layer was dried over anhydrous Na₂SO₄. Then m-CPBA (2.0 equiv) was added to the organic layer and the reaction mixture was stirred at r.t. for 5h. The reaction mixture was quenched by Na₂SO₃ and brine. The resulting mixture was extracted with dichloromethane. The combined organic extracts were dried over anhydrous Na₂SO₄ and concentrated under reduced pressure. The crude product was purified by column chromatography to give the pure product.

2. General procedure for the preparation of other starting material (1a, 1g-1t)



To a solution of 2-(2,2-dibromovinyl)benzoic acid (1.0 equiv) in dichloromethane were added EDCI (1.1 equiv) and HOBT (1.1 equiv), then amine reagent (1.0 equiv) was added and the reaction mixture was stirred at r.t. for 1h. The reaction mixture was added brine. The resulting mixture was extracted with dichloromethane. The combined organic extracts were dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by column chromatography to give the pure product.



2-(2,2-dibromovinyl)-N-(pyridin-3-ylmethyl)benzamide (1a)

Yield = 48.8%. Yed oil. ¹**H NMR** (400 MHz, CDCl₃): δ = 8.53 (s, 1H), 8.48 (s, 1H), 7.73 (d, *J* = 8 Hz, 2H), 7.53 (t, *J* = 8 Hz, 2H), 7.45 (t, *J* = 8 Hz, 1H), 7.36 (t, *J* = 8 Hz, 1H), 7.29 (t, *J* = 8 Hz, 1H), 6.69 (s, 1H), 4.59 (d, *J* = 8 Hz, 2H) ppm. ¹³**C NMR** (500 MHz, CDCl₃): δ = 168.55, 149.17, 149.00, 136.08, 135.94, 134.75, 134.26, 133.95, 130.57, 129.70, 128.69, 127.60, 123.95, 92.29, 41.62 ppm.



3-((2-(2,2-dibromovinyl)benzamido)methyl)pyridine 1-oxide (1b)

Yield = 45%. White solid. M.p. 147-148 °C. ¹H NMR (400 MHz, CDCl₃): 8.12 (s, 1H), 7.93 (d, J = 4Hz, 1H), 7.76 (s, 1H), 7.60-7.54 (m, 2H), 7.50-7.46 (m, 1H), 7.42-7.35 (m, 2H), 7.24-7.20 (m, 2H), 4.55 (d, J = 4Hz, 2H) ppm. ¹³C NMR (500 MHz, DMSO-d₆): δ = 167.71, 138.78, 137.62, 137.24, 136.60, 134.75, 133.95, 130.14,

129.06, 128.43, 127.67, 126.23, 124.24, 90.53, 40.00 ppm.



3-((2-(2,2-dibromovinyl)benzamido)methyl)-4-methylpyridine 1-oxide (1c)

Yield = 64.6%. Yellow solid. M.p. 140-141 °C. ¹**H NMR** (400 MHz, CDCl₃): 8.07 (s, 1H), 7.76-7.63 (m, 2H), 7.61 (d, J = 8Hz, 1H), 7.56 (d, J = 8Hz, 1H), 7.49-7.45 (m, 2H), 7.39 (t, J = 8Hz, 1H), 7.01 (d, J = 8Hz, 1H), 4.56 (d, J = 4Hz, 2H), 2.38 (s, 3H) ppm. ¹³C NMR (500 MHz, DMSO-d₆): δ = 167.93, 138.09, 137.12, 136.98, 136.47, 135.22, 135.14, 134.39, 130.55, 129.51, 128.86, 128.12, 127.94, 90.88, 38.78, 17.62 ppm.



3-((2-(2,2-dibromovinyl)benzamido)methyl)-5-methylpyridine 1-oxide (1d)

Yield = 48.8%. White solid. M.p. 145-146 °C. ¹H NMR (500 MHz, CDCl₃): 9.00 (s, 1H), 8.05 (s, 2H), 7.82 (s, 1H), 7.62-7.49 (m, 4H), 7.14 (s, 1H), 4.37 (d, J = 5Hz, 2H), 2.27 (s, 3H) ppm. ¹³C NMR (500 MHz, DMSO-d₆): δ = 168.15, 138.45, 137.46, 137.12, 136.80, 135.42, 135.25, 134.43, 130.56, 129.47, 128.86, 128.13, 125.65, 90.89, 39.48, 18.13 ppm.



3-(2-(2-(2,2-dibromovinyl)benzamido)ethyl)pyridine 1-oxide (1e)

Yield = 76.5%. Yellow oil. ¹**H NMR** (400 MHz, CDCl₃): 8.07 (s, 1H), 7.96 (s, 1H), 7.73 (s, 1H), 7.54 (d, J = 8Hz, 1H), 7.46-7.41 (m, 2H), 7.36-7.32 (m, 1H), 7.21 (d, J = 4Hz, 2H), 6.60 (s, 1H), 3.70 (dd, 2H), 2.92 (t, J = 8Hz, 2H) ppm. ¹³**C NMR** (500 MHz, CDCl₃): $\delta = 168.54$, 139.15, 138.25, 137.32, 136.06, 134.68, 134.14, 130.33,

129.60, 128.51, 127.33, 126.90, 125.83, 91.83, 39.97, 32.47 ppm.



N-benzyl-2-(2,2-dibromovinyl)benzamide (1g)

Yield = 54.6%. White solid. M.p. 95-97 °C. ¹H NMR (400 MHz, CDCl₃): 7.78 (s, 1H), 7.58-7.54 (m, 2H), 7.47-7.43 (m, 1H), 7.40-7.35 (m, 5H), 7.33-7.30 (m, 1H), 6.12 (s, 1H), 4.62 (d, J = 4Hz, 2H) ppm. ¹³C NMR (500 MHz, CDCl₃): δ = 168.28, 137.96, 136.18, 135.14, 134.24, 130.47, 129.77, 129.08, 128.74, 128.04, 127.88, 127.66, 92.29, 44.41 ppm.



2-(2,2-dibromovinyl)-N-(4-fluorobenzyl)benzamide (1h)

Yield = 72.3%. White solid. M.p. 91-93 °C. ¹H NMR (400 MHz, CDCl₃): 7.74 (s, 1H), 7.55 (t, J = 8Hz, 2H), 7.46 (t, J = 8Hz, 1H), 7.40-7.32 (m, 3H), 7.06 (t, J = 8Hz, 2H), 6.13 (s, 1H), 4.58 (d, J = 4Hz, 2H) ppm. ¹³C NMR (500 MHz, CDCl₃): $\delta = 168.29$, 163.45, 161.49, 136.17, 135.02, 134.22, 133.86, 133.84, 130.54, 129.78, 129.71, 128.76, 127.64, 116.01, 115.84, 92.37, 43.63 ppm.



2-(2,2-dibromovinyl)-N-(4-methylbenzyl)benzamide (1i)

Yield = 87.7%. White solid. M.p. 90-91 °C. ¹H NMR (400 MHz, CDCl₃): 7.78 (s, 1H), 7.58-7.53 (m, 2H), 7.45 (t, J = 8Hz, 1H), 7.37 (t, J = 8Hz, 1H), 7.24 (d, J = 4Hz, 2H), 7.18 (d, J = 8Hz, 2H), 6.07 (s, 1H), 4.57 (d, J = 4Hz, 2H) ppm. ¹³C NMR (500 MHz, DMSO-d₆): δ = 168.15, 138.45, 137.46, 137.12, 136.80, 135.42, 135.25, 134.43, 130.56, 129.47, 128.86, 128.13, 125.65, 90.89, 18.13 ppm.



2-(2,2-dibromovinyl)-N-(4-(trifluoromethyl)benzyl)benzamide (1j)

Yield = 84.8%. Yellow solid. M.p. 82-83 °C. ¹H NMR (400 MHz, CDCl₃): 7.74 (s, 1H), 7.63 (d, J = 8Hz, 2H), 7.57-7.55 (m, 2H), 7.49-7.45 (m, 3H), 7.39 (t, J = 8Hz, 1H), 6.27 (s, 1H), 4.67 (d, J = 8Hz, 2H) ppm. ¹³C NMR (500 MHz, CDCl₃): $\delta =$ 168.48, 142.15, 136.15, 134.81, 134.30, 130.67, 129.83, 128.79, 128.16, 127.61, 126.01, 125.98, 125.95, 92.49, 43.77 ppm.



2-(2,2-dibromovinyl)-N-(4-methoxybenzyl)benzamide (1k)

Yield = 85.3%. White solid. M.p. 92-94 °C. ¹H NMR (400 MHz, CDCl₃): 7.76 (s, 1H), 7.57-7.52 (m, 2H), 7.44 (t, J = 8Hz, 1H), 7.37 (t, J = 8Hz, 1H), 7. 28 (t, J = 8Hz, 2H), 6.90 (d, J = 8Hz, 2H), 6.07 (s, 1H), 4.54 (d, J = 4Hz, 2H), 3.80 (s, 3H) ppm. ¹³C NMR (500 MHz, CDCl₃): δ = 168.18, 159.36, 136.18, 135.21, 134.19, 130.40, 130.06, 129.73, 129.41, 128.71, 127.65, 114.46, 92.21, 55.48, 43.88 ppm.



2-(2,2-dibromovinyl)-N-(3,4,5-trimethoxybenzyl)benzamide (11)

Yield = 76.9%. Yellow solid. M.p. 153-154 °C. ¹H NMR (400 MHz, CDCl₃): 7.79 (s, 1H), 7.57 (t, J = 8Hz, 2H), 7.46 (t, J = 8Hz, 1H), 7.39 (t, J = 8Hz, 1H), 6.58 (s, 2H), 6.13 (s, 1H), 4.54 (d, J = 4Hz, 2H), 3.87 (s, 6H), 3.83 (s, 3H) ppm. ¹³C NMR (500 MHz, CDCl₃): δ = 168.01, 153.56, 137.57, 136.01, 134.79, 134.15, 133.57, 130.41, 129.70, 128.61, 127.44, 105.07, 91.99, 60.84, 56.22, 44.59 ppm.



2-(2,2-dibromovinyl)-N-(2-methylbenzyl)benzamide (1m)

Yield = 86.1%. White solid. M.p. 98-99 °C. ¹H NMR (400 MHz, CDCl₃): 7.79 (s, 1H), 7.58-7.53 (m, 2H), 7.43 (t, J = 8Hz, 1H), 7.37 (t, J = 8Hz, 1H), 7.30 (s, 1H), 7.25-7.22 (m, 3H), 5.93 (s, 1H), 4.62 (d, J = 4Hz, 2H) ppm. ¹³C NMR (500 MHz, CDCl₃): $\delta =$ 167.91, 136.49, 135.97, 135.36, 134.96, 134.09, 130.69, 130.25, 129.62, 128.67, 128.53, 127.98, 127.38, 126.40, 92.06, 42.35, 19.03 ppm.



2-(2,2-dibromovinyl)-N-(thiophen-3-ylmethyl)benzamide (1n)

Yield = 59.6%. Yellow solid. M.p. 77-78 °C. ¹H NMR (400 MHz, CDCl₃): 7.76 (s, 1H), 7.56-7.53 (m, 2H), 7.46-7.44 (m, 1H), 7.38-7.33 (m, 2H), 7.24 (m, 1H), 7.12-7.10 (m, 1H), 6.10 (s, 1H), 4.62 (d, J = 4 Hz, 2H) ppm. ¹³C NMR (500 MHz, DMSO-d₆): δ = 167.97, 140.41, 136.84, 135.65, 133.97, 130.25, 129.25, 128.79, 127.87, 127,62, 126.67, 121.72, 90.91, 38.50 ppm.



2-(2,2-dibromovinyl)-N-(thiophen-2-ylmethyl)benzamide (10)

Yield = 87.5%. Yellow solid. M.p. 87-89 °C. ¹H NMR (400 MHz, CDCl₃): 7.77 (s, 1H), 7.59-7.54 (m, 2H), 7.48-7.45 (m, 1H), 7.40-7.36 (m, 1H), 7.27 (m, 1H), 6.06-6.05 (m, 1H), 6.98-6.97 (m, 1H), 6.17 (s, 1H), 4.79 (d, J = 4 Hz, 2H) ppm. ¹³C NMR (500 MHz, CDCl₃): δ = 167.85, 140.33, 135.89, 134.63, 134.16, 130.40, 129.65, 128.56, 127.52, 127.02, 126.30, 125.49, 92.16, 38.87 ppm.



2-(2,2-dibromovinyl)-N-(furan-3-ylmethyl)benzamide (1p)

Yield = 56.9%. Brown oil. ¹H NMR (400 MHz, CDCl₃): 7.73 (s, 1H), 7.57-7.51 (m, 2H), 7.46-7.26 (m, 4H), 6.44 (s, 1H), 6.07 (s, 1H), 4.44 (d, J = 4 Hz, 2H) ppm. ¹³C NMR (500 MHz, CDCl₃): δ = 168.11, 143.65, 140.26, 135.94, 134.82, 133.99, 130.30, 129.55, 128.55, 127.49, 121.85, 110.24, 92.01, 34.98 ppm.



2-(2,2-dibromovinyl)-N-(furan-2-ylmethyl)benzamide (1q)

Yield = 87.5%. Yellow solid. M.p. 87-89 °C. ¹H NMR (400 MHz, CDCl₃): 7.74 (s, 1H), 7.59-7.54 (m, 2H), 7.47-7.45 (m, 1H), 7.40-7.36 (m, 2H), 6.36-6.34 (m, 1H), 6.32-6.31 (m, 1H), 6.17 (s, 1H), 4.61 (d, J = 4 Hz, 2H) ppm. ¹³C NMR (500 MHz, CDCl₃): δ = 167.87, 150.69, 142.45, 135.85, 134.58, 134.10, 130.38, 129.62, 128.55, 127.63, 110.52, 107.73, 92.08, 37.07 ppm.



N-((1H-indol-3-yl)methyl)-2-(2,2-dibromovinyl)benzamide (1r)

Yield = 54.7%. Yellow oil. ¹**H NMR** (400 MHz, CDCl₃): 8.52 (s, 1H), 7.73 (s, 1H), 7.67 (d, J = 8 Hz, 1H), 7.53 (d, J = 8 Hz, 1H), 7.46 (d, J = 8 Hz, 1H), 6.41-6.27 (m, 3H), 7.23-7.12 (m, 2H), 6.13 (s, 1H), 4.76 (d, J = 8 Hz, 2H) ppm. ¹³**C NMR** (500 MHz, CDCl₃): δ = 168.34, 136.64, 135.98, 135.14, 134.12, 130.29, 129.63, 128.61, 127.54, 126.54, 123.59, 122.53, 120.12, 118.81, 112.13, 111.60, 91.98, 35.89 ppm.



2-(2,2-dibromovinyl)-N-(quinolin-3-ylmethyl)benzamide (1s)

Yield = 68.4%. White oil. ¹**H** NMR (400 MHz, CDCl₃): 8.92 (s, 1H), 8.17 (s, 1H), 7.10 (d, J = 8 Hz, 1H), 7.85 (d, J = 8 Hz, 1H), 7.77 (s, 1H), 7.71 (t, J = 2 Hz, 1H), 7.59-7.55 (m, 3H), 7.47 (d, J = 8 Hz, 1H), 7.40 (d, J = 8 Hz, 1H), 6.35 (s, 1H), 4.82 (d, J = 8 Hz, 2H) ppm. ¹³C NMR (500 MHz, CDCl₃): δ = 168.47, 150.41, 135.93, 135.29, 134.88, 134.48, 134.16, 130.76, 130.52, 129.95, 129.60, 128.99, 128.58, 127.78, 127.50, 127.24, 127.03, 92.17, 41.73 ppm.



2-(2,2-dibromovinyl)-N-(naphthalen-1-ylmethyl)benzamide (1t)

Yield = 89.5%. Yellow solid. M.p. 105-106 °C. ¹H NMR (400 MHz, CDCl₃): 8.10 (d, J = 8 Hz, 1H), 7.89 (d, J = 8 Hz, 1H), 7.84 (d, J = 8 Hz, 1H), 7.72 (s, 1H), 7.61 (t, J = 8 Hz, 1H), 7.55-7.40 (m, 6H), 7.33 (t, J = 8 Hz, 1H), 6.08 (s, 1H), 5.07 (d, J = 4 Hz, 2H) ppm. ¹³C NMR (500 MHz, CDCl₃): δ = 167.95, 136.02, 135.00, 134.26, 134.20, 133.27, 131.57, 130.45, 129.75, 129.06, 129.02, 128.68, 127.69, 127.18, 127.10, 126.28, 125.60, 123.59, 92.20, 42.57 ppm.

III. General procedure for the preparation of indolizinone compounds 3



Compound **1** (1.0 equiv) was dissolved in toluene and K_2CO_3 (3.0 equiv) was added. The mixture was stirred at 70°C for 5h. Then Pd(OAc)₂ (10 mol%) and P(2-MeOPh)₃

(20 mol%) were added. The reaction mixture was stirred under an argon atmosphere at 120° C for 12 h. The resulting mixture was concentrated in vacuo and purified by column chromatography on silica gel to give the product **3**.



isoindolo[2,1-g][1,6]naphthyridin-7(5H)-one (3a)

Yield = 90.0% (from **1b**), 30.0% (from **1a**). Yellow solid. M.p. 202-204 °C. ¹H NMR (400 MHz, CDCl₃): 8.47 (d, J = 4 Hz, 1H), 7.91 (d, J = 8 Hz, 1H), 7.82 (d, J = 8 Hz, 1H), 7.67-7.63 (m, 1H), 7.60-7.56 (m, 1H), 7.49 (d, J = 8 Hz, 1H), 7.14-7.11 (m, 1H), 6.64 (s, 1H), 5.15 (s, 2H) ppm. ¹³C NMR (500 MHz, CDCl₃): δ = 166.07, 150.13, 149.10, 138.41, 134.33, 133.85, 131.91, 130.26, 129.15, 125.29, 123.31, 121.86, 120.94, 104.13, 42.64 ppm. HRMS (ESI): calcd for C₁₅H₁₁N₂O [M+H]⁺ 235.0867, found 235.0856.



isoindolo[2,1-b][2,6]naphthyridin-7(5H)-one (4)

Yield = 60.2%. Yellow solid. M.p. 208-209 °C. ¹H NMR (400 MHz, CDCl₃): 8.48-8.45 (m, 2H), 7.92 (d, J = 8 Hz, 1H), 7.79 (d, J = 8 Hz, 1H), 7.67-7.57 (m, 2H), 7.09 (d, J = 4 Hz, 1H), 6.38 (s, 1H), 5.12 (s, 2H) ppm. ¹³C NMR (500 MHz, CDCl₃): δ = 166.35, 149.80, 147.69, 138.40, 138.11, 134.31, 132.13, 130.70, 129.67, 123.80, 123.63, 120.94, 120.57, 100.37, 40.84 ppm. HRMS (ESI): calcd for C₁₅H₁₁N₂O [M+H]⁺ 235.0867, found 235.0851.



7-oxo-5,7-dihydroisoindolo[2,1-g][1,6]naphthyridine 1-oxide (3b)

Yield = 90.6%. Yellow solid. M.p. 217-219 °C. ¹H NMR (400 MHz, CDCl₃): 8.13 (t, J = 4 Hz, 1H), 7.90-7.85 (m, 2H), 7.67 (t, J = 8 Hz, 1H), 7.60 (t, J = 8 Hz, 1H), 7.33

(s, 1H), 7.06 (d, J = 4 Hz, 2H), 5.12 (s, 2H) ppm. ¹³C NMR (500 MHz, CDCl₃): δ = 165.98, 142.30, 139.80, 138.43, 134.12, 132.37, 130.83, 129.09, 128.19, 123.45, 123.02, 122.79, 121.46, 93.33, 42.01 ppm. HRMS (ESI): calcd for C₁₅H₁₁N₂O₂ [M+H]⁺ 251.0815, found 251.0821.



4-methyl-7-oxo-5,7-dihydroisoindolo[2,1-g][1,6]naphthyridine 1-oxide (3c)

Yield = 81.2%. Yellow solid. M.p. 237-329 °C. ¹H NMR (400 MHz, CDCl₃): 8.05 (d, J = 4 Hz, 1H), 7.92-7.86 (m, 2H), 7.67 (t, J = 8 Hz, 1H), 7.60 (t, J = 8 Hz, 1H), 7.36 (s, 1H), 6.90 (d, J = 4 Hz, 1H), 5.02 (s, 2H), 2.28 (s, 3H) ppm. ¹³C NMR (500 MHz, CDCl₃): δ = 165.99, 141.47, 139.10, 137.59, 134.01, 133.30, 132.32, 130.74, 129.10, 126.53, 124.57, 123.40, 121.49, 93.57, 40.86, 17.71 ppm. HRMS (ESI): calcd for C₁₆H₁₃N₂O₂ [M+H]⁺ 265.0972, found 265.1003.



3-methyl-7-oxo-5,7-dihydroisoindolo[2,1-g][1,6]naphthyridine 1-oxide (3d)

Yield = 84.2%. Yellow solid. M.p. 228-229 °C. ¹H NMR (400 MHz, CDCl₃): 8.00 (s, 1H), 7.90-7.84 (m, 2H), 7.66 (t, J = 8 Hz, 1H), 7.59 (t, J = 8 Hz, 1H), 7.31 (s, 1H), 6.91 (s, 1H), 5.08 (s, 2H), 2.30 (s, 3H) ppm. ¹³C NMR (500 MHz, CDCl₃): δ = 166.02, 139.57, 138.87, 138.20, 134.20, 133.82, 132.31, 130.63, 129.09, 127.65, 124.80, 123.41, 121.36, 93.55, 41.97, 18.28 ppm. HRMS (ESI): calcd for C₁₆H₁₃N₂O₂ [M+H]⁺ 265.0972, found 265.0986.



8-oxo-6,8-dihydro-5H-pyrido[2',3':4,5]azepino[2,1-a]isoindole 1-oxide (3e) Yield = 63.3%. Yellow solid. M.p. 216-217 °C. ¹H NMR (400 MHz, CDCl₃): 8.25-8.24 (m, 1H), 7.97 (d, J = 8 Hz, 1H), 7.85 (d, J = 8 Hz, 1H), 7.67-7.64 (m, 2H), 7.56-7.53 (m, 1H), 7.05 (s, 2H), 3.13 (s, 2H) ppm. ¹³**C NMR** (500 MHz, CDCl₃): δ = 165.93, 145.42, 139.94, 138.46, 138.04, 137.05, 132.56, 130.10, 128.23, 126.26, 123.62, 122.43, 120.62, 95.97, 40.98, 34.11 ppm. HRMS (ESI): calcd for C₁₆H₁₃N₂O₂ [M+H]⁺ 265.0972, found 265.0982.



isoindolo[2,1-b]isoquinolin-7(5H)-one (3g)

Yield = 84.6%. Yellow solid. M.p. 149-151 °C. ¹H NMR (400 MHz, CDCl₃): 7.91 (d, J = 8 Hz, 1H), 7.77 (d, J = 8 Hz, 1H), 7.61 (t, J = 8 Hz, 1H), 7.53 (t, J = 8 Hz, 1H), 7.26 (m, 4H), 6.48 (s, 1H), 5.13 (s, 2H) ppm. ¹³C NMR (500 MHz, CDCl₃): δ = 166.17, 134.57, 134.05, 131.39, 130.30, 129.34, 129.27, 127.98, 127.89, 127.30, 126.74, 123.11, 120.15, 103.44, 42.96 ppm. HRMS (ESI): calcd for C₁₆H₁₂NO [M+H]⁺ 234.0914, found 234.0979.



2-fluoroisoindolo[2,1-b]isoquinolin-7(5H)-one (3h)

Yield = 95.2%. Yellow solid. M.p. 203-205 °C. ¹H NMR (400 MHz, CDCl₃): 7.90 (d, J = 8 Hz, 1H), 7.76 (d, J = 8 Hz, 1H), 7.62 (t, J = 8 Hz, 1H), 7.54 (t, J = 8 Hz, 1H), 7.17 (t, J = 8 Hz, 1H), 6.95-6.91 (m, 2H), 6.40 (s, 1H), 5.07 (s, 2H) ppm. ¹³C NMR (500 MHz, CDCl₃): δ = 166.34, 163.39, 161.44, 135.35, 134.51, 132.63, 132.57, 131.77, 129.92, 129.53, 128.28, 128.21, 124.90, 124.88, 123.41, 120.51, 114.71, 114.53, 113.88, 113.70, 102.46, 102.44, 42.73 ppm. HRMS (ESI): calcd for C₁₆H₁₁FNO [M+H]⁺ 252.0819, found 252.0833.



2-methylisoindolo[2,1-b]isoquinolin-7(5H)-one (3i)

Yield = 92.2%. Yellow solid. M.p. 187-189 °C. ¹**H** NMR (400 MHz, CDCl₃): 7.90 (d, J = 8 Hz, 1H), 7.76 (d, J = 8 Hz, 1H), 7.60 (t, J = 8 Hz, 1H), 7.52 (t, J = 8 Hz, 1H), 7.13-7.05 (m, 3H), 6.44 (s, 1H), 5.08 (s, 2H), 2.35 (s, 3H) ppm. ¹³C NMR (500 MHz, CDCl₃): δ = 166.18, 137.54, 134.62, 134.02, 131.32, 130.12, 129.30, 129.25, 128.73, 127.96, 126.60, 126.35, 123.10, 120.11, 103.62, 42.77, 20.97 ppm. HRMS (ESI): calcd for C₁₇H₁₄NO [M+H]⁺ 248.1070, found 248.1082.



2-(trifluoromethyl)isoindolo[2,1-b]isoquinolin-7(5H)-one (3j)

Yield = 66.3%. Yellow solid. M.p. 213-214 °C. ¹**H** NMR (400 MHz, CDCl₃): 7.91 (d, J = 8 Hz, 1H), 7.78 (d, J = 8 Hz, 1H), 7.64 (t, J = 8 Hz, 1H), 7.57 (t, J = 8 Hz, 1H), 7.47 (d, J = 8 Hz, 2H), 7.32 (d, J = 8 Hz, 1H), 6.47 (s, 1H), 5.16 (s, 2H) ppm. ¹³C NMR (500 MHz, CDCl₃): δ = 166.33, 135.71, 134.48, 132.94, 131.94, 131.53, 130.13, 129.47, 127.32, 124.54, 124.51, 123.85, 123.82, 123.50, 120.62, 101.95, 43.10 ppm. HRMS (ESI): calcd for C₁₇H₁₁F₃NO [M+H]⁺ 302.0787, found 302.0793.



2-methoxyisoindolo[2,1-b]isoquinolin-7(5H)-one (3k)

Yield = 95.1%. Yellow solid. M.p. 136-137 °C. ¹H NMR (400 MHz, CDCl₃): 7.90 (d, J = 8 Hz, 1H), 7.77 (d, J = 8 Hz, 1H), 7.61 (t, J = 8 Hz, 1H), 7.53 (t, J = 8 Hz, 1H), 7.14 (d, J = 8 Hz, 1H), 6.79 (s, 2H), 6.44 (s, 1H), 5.06 (s, 2H), 3.83 (s, 3H) ppm. ¹³C NMR (500 MHz, CDCl₃): δ = 166.36, 159.34, 134.71, 134.67, 131.61, 131.57, 129.57, 129.54, 127.80, 123.31, 121.57, 120.34, 113.54, 112.75, 103.62, 55.55, 42.67 ppm. HRMS (ESI): calcd for C₁₇H₁₄NO₂ [M+H]⁺ 264.1019, found 264.1022.



1,2,3-trimethoxyisoindolo[2,1-b]isoquinolin-7(5H)-one (3l)

Yield = 85.2%. Yellow solid. M.p. 177-179 °C. ¹**H** NMR (400 MHz, CDCl₃): 7.89 (d, J = 8 Hz, 1H), 7.80 (d, J = 8 Hz, 1H), 7.60 (t, J = 8 Hz, 1H), 7.50 (t, J = 8 Hz, 1H), 6.78 (s, 1H), 6.56 (s, 1H), 5.04 (s, 2H), 3.98 (s, 3H), 3.90 (s, 6H) ppm. ¹³C NMR (500 MHz, CDCl₃): δ = 166.01, 149.46, 147.35, 137.45, 134.46, 134.36, 131.85, 131.76, 129.96, 129.08, 124.89, 123.20, 120.75, 104.20, 42.55, 18.27 ppm. HRMS (ESI): calcd for C₁₉H₁₈NO₄ [M+H]⁺ 324.1231, found 324.1249.



4-methylisoindolo[2,1-b]isoquinolin-7(5H)-one (3m)

Yield = 88.2%. Yellow solid. M.p. 200-201 °C. ¹**H NMR** (400 MHz, CDCl₃): 7.92 (d, J = 8 Hz, 1H), 7.78 (d, J = 8 Hz, 1H), 7.61 (t, J = 8 Hz, 1H), 7.53 (t, J = 8 Hz, 1H), 7.18 (t, J = 8 Hz, 1H), 7.09 (d, J = 8 Hz, 2H), 6.46 (s, 1H), 5.03 (s, 2H), 2.32 (s, 3H) ppm. ¹³C NMR (500 MHz, CDCl₃): δ = 166.32, 135.50, 134.60, 133.55, 131.50, 130.20, 130.05, 129.50, 129.42, 128.03, 127.79, 125.49, 123.29, 120.34, 104.07, 41.76, 18.85 ppm. HRMS (ESI): calcd for C₁₇H₁₄NO [M+H]⁺ 248.1070, found 248.1075.



thieno[2',3':4,5]pyrido[2,1-a]isoindol-6(4H)-one (3n)

Yield = 88.4%. Yellow solid. M.p. 187-188 °C. ¹H NMR (400 MHz, CDCl₃): 7.90 (d, J = 8 Hz, 1H), 7.72 (d, J = 8 Hz, 1H), 7.61-7.57 (m, 1H), 7.53-7.49 (m, 1H), 7.29 (d, J= 4 Hz, 1H), 6.98 (d, J = 4 Hz, 1H), 6.53 (s, 1H), 5.13 (s, 2H) ppm. ¹³C NMR (500 MHz, DMSO-d₆): δ = 165.04, 133.92, 131.81, 131.66, 130.72, 130.37, 129.18, 128.14, 126.83, 126.55, 122.42, 120.75, 98.18, 42.06 ppm. HRMS (ESI): calcd for C₁₄H₁₀NOS [M+H]⁺ 240.0478, found 240.0479.



thieno[3',2':4,5]pyrido[2,1-a]isoindol-9(11H)-one (3o)

Yield = 87.2%. Yellow solid. M.p. 120-121 °C. ¹H NMR (400 MHz, CDCl₃): 7.89 (d, J = 8 Hz, 1H), 7.73 (d, J = 8 Hz, 1H), 7.59 (t, J = 8 Hz, 1H), 7.50 (t, J = 8 Hz, 1H), 7.27-7.26 (m, 1H), 6.99 (d, J = 4 Hz, 1H), 6.52 (s, 1H), 5.23 (s, 2H) ppm. ¹³C NMR (500 MHz, DMSO-d₆): δ = 161.71, 129.91, 128.25, 127.09, 126.65, 124.85, 124.25, 123.96, 120.37, 120.01, 118.32, 115.11, 93.95, 37.10 ppm. HRMS (ESI): calcd for C₁₄H₁₀NOS [M+H]⁺ 240.0478, found 240.0468.



furo[2',3':4,5]pyrido[2,1-a]isoindol-6(4H)-one (3p)

Yield = 93.5%. Yellow solid. M.p. 172-173 °C. ¹**H** NMR (400 MHz, CDCl₃): 7.89 (d, J = 8 Hz, 1H), 7.70 (d, J = 8 Hz, 1H), 7.59 (t, J = 8 Hz, 1H), 7.50 (t, J = 8 Hz, 1H), 7.44 (s, 1H), 6.46 (s, 2H), 5.03 (s, 2H) ppm. ¹³C NMR (500 MHz, CDCl₃): δ = 166.38, 147.75, 143.67, 134.47, 133.84, 131.55, 129.22, 128.77, 123.32, 120.09, 114.71, 110.36, 94.05, 41.13 ppm. HRMS (ESI): calcd for C₁₄H₁₀NO₂ [M+H]⁺ 224.0706, found 224.0721.



furo[3',2':4,5]pyrido[2,1-a]isoindol-9(11H)-one (3q)

Yield = 69.8%. Yellow solid. M.p. 112-113 °C. ¹H NMR (400 MHz, CDCl₃): 7.90 (d, J = 8 Hz, 1H), 7.70 (d, J = 8 Hz, 1H), 7.58 (t, J = 8 Hz, 1H), 7.48 (t, J = 8 Hz, 1H), 7.42 (s, 1H), 6.44 (s, 1H), 6.37 (s, 1H), 5.08 (s, 2H) ppm. ¹³C NMR (500 MHz, CDCl₃): δ = 166.11, 146.13, 143.59, 134.81, 132.20, 131.64, 129.10, 128.79, 123.37, 119.92, 115.65, 108.11, 97.43, 41.35 ppm. HRMS (ESI): calcd for C₁₄H₁₀NO₂ [M+H]⁺ 224.0706, found 224.0730.



5H-benzo[1,2]indolizino[7,6-b]indol-11(13H)-one (3r)

Yield = 60.2%. Yellow solid. M.p. 182-184 °C. ¹**H** NMR (400 MHz, DMSO-d₆): 11.40 (s, 1H), 8.11 (d, J = 8 Hz, 1H), 7.82 (d, J = 8 Hz, 1H), 7.70 (t, J = 8 Hz, 1H), 7.59-7.52 (m, 2H), 7.39 (d, J = 8 Hz, 1H), 7.13 (t, J = 8 Hz, 1H), 7.05 (t, J = 8 Hz, 1H), 6.89 (s, 1H), 5.16 (s, 2H) ppm. ¹³C NMR (500 MHz, DMSO-d₆): δ = 165.31, 137.35, 134.21, 133.91, 131.58, 130.08, 129.09, 127.95, 125.27, 122.40, 122.15, 120.94, 119.69, 118.01, 111.55, 104.64, 96.02, 39.35 ppm. HRMS (ESI): calcd for C₁₈H₁₃N₂O [M+H]⁺ 273.1022, found 273.1023.



benzo[h]isoindolo[2,1-b][2,6]naphthyridin-12(14H)-one (3s)

Yield = 58.4%. Yellow solid. M.p. 218-219 °C. ¹H NMR (400 MHz, CDCl₃): 8.76 (s, 1H), 8.20 (d, J = 12 Hz, 1H), 8.11 (d, J = 8 Hz, 1H), 7.97-7.92 (m, 2H), 7.76-7.61 (m, 4H), 7.12 (s, 1H), 5.31 (s, 2H) ppm. ¹³C NMR (500 MHz, CDCl₃): δ = 148.49, 131.95, 130.59, 130.25, 129.38, 127.15, 123.50, 123.41, 122.16, 120.85, 120.11, 95.74, 41.56 ppm. HRMS (ESI): calcd for C₁₉H₁₃N₂O [M+H]⁺ 285.1022, found 285.1025.



benzo[h]isoindolo[2,1-b]isoquinolin-12(14H)-one (3t)

Yield = 76.7%. Yellow solid. M.p. 208-209 °C. ¹H NMR (400 MHz, CDCl₃): 7.95 (d, J = 8 Hz, 1H), 7.90 (d, J = 8 Hz, 1H), 7.85-7.78 (m, 3H), 7.63-7.58 (m, 2H), 7.57-7.51 (m, 2H), 7.39 (d, J = 8 Hz, 1H), 6.59 (s, 1H), 5.52 (s, 2H) ppm. ¹³C NMR (500 MHz, CDCl₃): δ = 166.56, 134.58, 134.21, 133.19, 131.60, 130.16, 129.55, 129.44, 128.83, 128.50, 127.64, 127.39, 126.27, 125.67, 124.26, 123.34, 122.53, 120.44, 103.73, 41.70 ppm. HRMS (ESI): calcd for C₂₀H₁₄NO [M+H]⁺ 284.1070, found 284.1097.

IV. General procedure for reduction of the pyridine N-oxides



Methanol was added to the mixture of pyridine N-oxide (1.0 equiv) and Raney Ni (10%), and the reaction mixture was stirred under H_2 for 5h. The mixture was filtered to give the product.



4-methylisoindolo[2,1-g][1,6]naphthyridin-7(5H)-one (4c)

Yield = 95.4%. Yellow solid. M.p. 247-248 °C. ¹**H** NMR (400 MHz, CDCl₃): 8.34 (d, J = 4 Hz, 1H), 7.92 (d, J = 8 Hz, 1H), 7.82 (d, J = 8 Hz, 1H), 7.67-7.64 (m, 1H), 7.58 (t, J = 8 Hz, 1H), 6.96 (d, J = 4 Hz, 1H), 6.62 (s, 1H), 5.08 (s, 2H), 2.31 (s, 3H) ppm. ¹³C NMR (500 MHz, CDCl₃): δ = 166.05, 149.45, 148.61, 143.76, 137.68, 134.23, 131.83, 130.12, 129.19, 124.38, 123.74, 123.26, 120.90, 104.45, 41.04, 18.19 ppm. HRMS (ESI): calcd for C₁₆H₁₃N₂O [M+H]⁺ 249.1022, found 249.1032.



3-methylisoindolo[2,1-g][1,6]naphthyridin-7(5H)-one (4d)

Yield = 96.3%. Yellow solid. M.p. 222-223 °C. ¹**H** NMR (400 MHz, CDCl₃): 8.31 (s, 1H), 7.90 (d, J = 8 Hz, 1H), 7.80 (d, J = 8 Hz, 1H), 7.62 (t, J = 8 Hz, 1H), 7.56 (t, J = 8 Hz, 1H), 7.31 (s, 1H), 6.63 (s, 1H), 5.11 (s, 2H), 2.34 (s, 3H) ppm. ¹³C NMR (500 MHz, CDCl₃): δ = 166.03, 149.40, 147.33, 137.48, 134.50, 134.36, 131.87, 131.77, 129.98, 129.08, 124.90, 123.21, 120.77, 104.15, 42.55, 18.27 ppm. HRMS (ESI): calcd for C₁₆H₁₃N₂O [M+H]⁺ 249.1022, found 249.1026.

V. Copies of ¹H and ¹³C NMR spectra























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S29










































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Hz
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DB
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DB
6.50

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4.772

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DE	6.50	usec
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P1	12.58	usec
PL1	0.00	dB
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SI	32768	
SF	400.1300099	MHz
WDW	no	
SSB	0	
LB	0.00	Hz
GB	0	
PC	1.00	





5.074



S55






































































NAME
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SOLVENT
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Hz
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DB
6.50

DB
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DG
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DB
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TE
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D1
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TD0
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P1
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4.772

8.522 8.522 664 77.664 77.664 77.754 77.412 77.412 77.412 77.412 77.412 77.412 77.412 77.412 77.412 77.412 77.723



















VI. Copies of 1H, 13C and 2-D NMR spectra for 2b









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