Microwave Assisted Flexible Synthesis of 7-Azaindoles

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EXPERIMENTAL

Unless otherwise noted, all materials were obtained from commercial suppliers and used without further purification. Flash chromatography was done on silica gel 60 (0.063–0.200 mm) from Merck KgaA, Darmstadt, Germany. Preparative HPLC chromatography was done on a 250 mm x 30 mm column packed with YMC gel ODS-AQ S-5 / 15 μ M, with acetonitril / water as eluent and UV-detection. All ^1H NMR and ^{13}C NMR spectra were recorded in DMSO- d_6 or CDCl_3 . Spin multiplicities are given as s (singlet), d (doublet), t (triplet), q (quartet), and m (multiplet) as well as br (broad).

Microwave equipment.

All microwave irradiation experiments were carried out using the EmrysTM optimizer microwave from Biotage. The reactions were performed in Biotage microwave vials (for 0.5–2 mL and 2–5 mL, respectively) sealed with a septum. The power range was up to 300 W at 2.45 GHz. The temperature-, pressure-, and power curve for a typical experiment is given below:

Reaction 1

Temperature: 200°C
Time: 1200 s
Fixed Hold Time: Off
Absorption Level: Normal
Pre-stirring: 0 s
Status: OK
Date: 27-January-2006 at 08:42
Included in: Experiment 139 by phsir
Vialtype: 0.5-2 or 2-5 ml

Graphs

Synthesis of 7-azaindoles. General procedure.

Method A: The epoxide and the amine (1–2 eq.) were dissolved in 1-butanol (1 mL / mmol epoxide), and the mixture was heated for the given reaction time to 110 °C (higher temperatures were achieved in sealed pressure tubes). The solvent was evaporated and the residue was treated with ethanol (3 mL / mmol epoxide) and conc. hydrochloric acid (1 mL) was added. The reaction was stirred overnight, then diluted with water, basified with diluted NaOH solution and extracted with ethyl acetate. The organic layer was dried over sodium sulfate, and the solvent was evaporated. The crude product was purified by column chromatography on silica gel or by HPLC.

Method B: The reaction was run similar to method A, but microwave heating to the given temperature for the given time was used. Distinct from method A, the reaction was not treated with acid.

6-Chloro-1-(4-methoxybenzyl)-3-methyl-1H-pyrrolo[2,3-b]pyridine (1b).

The title compound was synthesized following method A (115 °C, 4 h) in 21% yield. Following method B (200 °C, 30 min) it was isolated in 69% yield. ¹H NMR (400 MHz, DMSO-*d*₆): δ = 2.23 (s, 3H), 3.70 (s, 3H), 5.28 (s, 2H), 6.87 (d, *J* = 8.6 Hz, 2H), 7.12 (d, *J* = 8.1 Hz, 1H), 7.17 (d, *J* = 8.6 Hz, 2H), 7.34 (s, 1H), 7.99 (d, *J* = 8.1 Hz, 1H). ¹³C NMR (125 MHz, DMSO-*d*₆): δ = 9.36, 46.4, 54.9, 108.7, 113.9, 114.6, 119.2, 126.6, 128.7, 129.8, 130.1, 143.0, 145.9, 158.5. HRMS calcd for C₁₆H₁₅ClN₂O, 286.0873; found, 286.0876.

1-Allyl-6-chloro-3-methyl-1H-pyrrolo[2,3-b]pyridine (1d).

The title compound was synthesized following method A (95 °C, 2 h) in 47% yield. Following method B (150 °C, 30 min) it was isolated in 67% yield. ¹H NMR (300 MHz, DMSO-*d*₆): δ = 2.26 (s, 3H), 4.78 (d, *J* = 5.3 Hz, 2H), 4.98 (d, *J* = 17.0 Hz, 1H), 5.14 (d, *J* = 10.2 Hz, 1H), 6.02 (ddt, *J* = 17.0, 10.2, 5.3 Hz, 1H), 7.11 (d, *J* = 8.1 Hz, 1H), 7.28 (s, 1H), 7.99 (d, *J* = 8.1 Hz, 1H). ¹³C NMR (125 MHz, DMSO-*d*₆): δ = 9.36, 45.7, 108.6, 114.5, 116.7, 119.2, 126.7, 130.1, 134.1, 143.0, 145.8. HRMS calcd for C₁₁H₁₁ClN₂ + [H⁺]: 207.0684; found, 207.0683.

1-Butyl-6-chloro-3-phenyl-1H-pyrrolo[2,3-b]pyridine (1e).

The title compound was synthesized following method A (110 °C, 8 h) in 95% yield. Following method B (200 °C, 8 min) it was isolated in 95% yield. ¹H NMR (400 MHz, DMSO-*d*₆): δ = 0.91 (t, *J* = 7.4 Hz, 3H), 1.28 (tq, *J* = 7.5, 7.4 Hz, 2H), 1.83 (tt, *J* = 7.5, 7.1 Hz, 2H), 4.26 (t, *J* = 7.1 Hz, 2H), 7.22 (d, *J* = 8.3 Hz, 1H), 7.28 (t, *J* = 7.4 Hz, 1H), 7.45 (dd, *J* = 7.4, 7.2 Hz, 2H), 7.70 (d, *J* = 7.2 Hz, 2H), 8.03 (s, 1H), 8.34 (d, *J* = 8.3 Hz, 1H). ¹³C NMR (125 MHz, DMSO-*d*₆): δ = 13.4, 19.3, 31.5, 43.7, 113.8, 115.8, 116.4, 126.0, 126.2, 127.0, 128.9, 131.0, 134.0, 143.2, 146.5. HRMS calcd for C₁₇H₁₇ClN₂: 284.1080; found, 284.1086.

6-Chloro-1-cyclopentyl-3-phenyl-1H-pyrrolo[2,3-b]pyridine (1f).

The title compound was synthesized following method A (110 °C, 16 h) in 86% yield. Following method B (200 °C, 30 min) it was isolated in 95% yield. ¹H NMR (400 MHz, DMSO-*d*₆): δ = 1.67–1.80 (m, 2H), 1.86–2.00 (m, 4H), 2.11–2.22 (m, 2H), 5.16 (quint., *J* = 7.4 Hz, 1H), 7.22 (d, *J* = 8.3 Hz, 1H), 7.28 (t, *J* = 7.3 Hz, 1H), 7.45 (t, *J* = 7.3 Hz, 2H), 7.73 (d, *J* = 7.3 Hz, 2H), 8.08 (s, 1H), 8.33 (d, *J* = 8.3 Hz, 1H). ¹³C NMR (125 MHz, DMSO-*d*₆): δ = 23.6, 32.1, 54.7, 114.3, 115.9, 116.5, 124.3, 126.0, 126.3, 128.8, 131.0, 134.0, 143.1, 146.5. HRMS calcd for C₁₈H₁₇ClN₂: 296.1080; found, 296.1069.

1-Butyl-6-chloro-3-methyl-1H-pyrrolo[2,3-b]pyridine (1h).

The title compound was synthesized following method A (95 °C, 2 h) in 86% yield. ¹H NMR (300 MHz, DMSO-*d*₆): δ = 0.88 (t, *J* = 7.4 Hz, 3H), 1.22 (tq, *J* = 7.4, 7.4 Hz, 2H), 1.73 (tt, *J* = 7.4, 7.0 Hz, 2H), 2.25 (s, 3H), 4.14 (t, *J* = 7.0 Hz, 2H), 7.08 (d, *J* = 8.1 Hz, 1H), 7.34 (s, 1H), 7.96 (d, *J* = 8.1 Hz, 1H). ¹³C NMR (125 MHz, DMSO-*d*₆): δ = 9.46, 13.5, 19.4, 31.7, 43.2, 108.2, 114.3, 119.2, 126.8, 130.0, 142.9, 146.0. HRMS calcd for C₁₂H₁₅ClN₂ + [H⁺]: 223.0997; found, 223.0996.

6-Chloro-1-(4-chlorobenzyl)-3-methyl-1H-pyrrolo[2,3-b]pyridine (1i).

The title compound was synthesized following method A (115 °C, 4 h) in 63% yield. ¹H NMR (400 MHz, DMSO-*d*₆): δ = 2.25 (s, 3H), 5.37 (s, 2H), 7.14 (d, *J* = 8.2 Hz, 1H), 7.21 (d, *J* = 8.4 Hz, 1H), 7.37–7.39 (m, 3H), 8.01 (d, *J* = 8.2 Hz, 1H). ¹³C NMR (125 MHz, DMSO-*d*₆): δ = 9.38, 46.19, 109.0, 114.8, 119.3, 126.8, 128.5, 128.9, 130.2, 131.9, 137.0, 143.2, 145.9. HRMS calcd for C₁₅H₁₂Cl₂N₂, 290.0378; found, 290.0385.

6-Chloro-3-methyl-1-(1-phenylethyl)-1H-pyrrolo[2,3-b]pyridine (1j).

The title compound was synthesized following method B (150 °C, 1.5 h) in 82% yield. ¹H NMR (400 MHz, DMSO-*d*₆): δ = 1.84 (d, *J* = 7.2 Hz, 3H), 2.26 (s, 3H), 6.02 (q, *J* = 7.2 Hz, 1H), 7.11 (d, *J* = 8.1 Hz, 1H), 7.21–7.34 (m, 5H), 7.52 (s, 1H), 7.98 (d, *J* = 8.1 Hz, 1H). ¹³C NMR (125 MHz, DMSO-*d*₆): δ = 9.51, 20.5, 51.8, 109.0, 114.8, 119.3, 124.0, 126.0, 127.2, 128.4, 130.1, 142.4, 142.9, 145.7. HRMS calcd for C₁₆H₁₅ClN₂ + [H⁺], 271.0997; found, 271.0988.

6-Chloro-1-cyclopropyl-3-methyl-1H-pyrrolo[2,3-b]pyridine (1k).

The title compound was synthesized following method B (150 °C, 1.5 h) in 63% yield. ¹H NMR (400 MHz, DMSO-*d*₆): δ = 0.93–1.05 (m, 4H), 2.22 (s, 3H), 3.49 (tt, *J* = 7.1, 3.9 Hz, 1H), 7.12 (d, *J* = 8.1 Hz, 1H), 7.26 (s, 1H), 7.96 (d, *J* = 8.1 Hz, 1H). ¹³C NMR (125 MHz, DMSO-*d*₆): δ = 5.97, 9.40, 26.2, 108.2, 114.9, 119.9, 126.3, 130.0, 143.1, 147.3. HRMS calcd for C₁₁H₁₁ClN₂, 206.0611; found, 206.0609.

6-Chloro-1-cyclobutyl-3-methyl-1H-pyrrolo[2,3-b]pyridine (1l).

The title compound was synthesized following method B (150 °C, 1.5 h) in 79% yield. ¹H NMR (400 MHz, DMSO-*d*₆): δ = 1.77–1.86 (m, 2H), 2.26 (s, 3H), 2.35–2.49 (m, 4H), 5.16 (tt, *J* = 8.9, 8.3 Hz, 1H), 7.10 (d, *J* = 8.1 Hz, 1H), 7.62 (s, 3H), 7.97 (d, *J* = 8.1 Hz, 1H). ¹³C NMR (125 MHz,

DMSO-*d*₆): δ = 9.49, 14.3, 30.3, 47.2, 108.9, 114.6, 119.3, 124.1, 130.0, 142.8, 145.6. HRMS calcd for C₁₂H₁₃ClN₂, 220.0767; found, 220.0774.

6-Chloro-3-methyl-1-(3-morpholin-4-ylpropyl)-1H-pyrrolo[2,3-*b*]pyridine (1m).

The title compound was synthesized following method B (150 °C, 30 min) in 79% yield. ¹H NMR (400 MHz, DMSO-*d*₆): δ = 1.90 (quint., *J* = 7.0 Hz, 2H), 2.22 (t, *J* = 7.0 Hz, 2H), 2.25 (s, 3H), 2.26–2.33 (m, 4H), 3.54 (dd, *J* = 5.9, 3.2 Hz, 4H), 4.18 (t, *J* = 7.0 Hz, 2H), 7.09 (d, *J* = 8.1 Hz, 1H), 7.35 (s, 1H), 7.97 (d, *J* = 8.1 Hz, 1H). ¹³C NMR (125 MHz, DMSO-*d*₆): δ = 9.38, 26.4, 41.7, 53.1, 55.1, 66.1, 108.1, 114.2, 119.2, 126.9, 129.9, 142.8, 145.9. HRMS calcd for C₁₅H₂₀ClN₃O, 293.1295; found, 293.1298.

3-(6-Chloro-3-methyl-1H-pyrrolo[2,3-*b*]pyridin-1-yl)propan-1-amine (1n).

The title compound was synthesized following method B (150 °C, 30 min) with 5 eq. 1,3-diaminopropane in 28% yield. ¹H NMR (400 MHz, DMSO-*d*₆): δ = 1.58 (br. s, 2H), 1.80 (tt, *J* = 7.0, 6.7 Hz, 2H), 2.25 (s, 3H), 2.45 (t, *J* = 6.7 Hz, 2H), 4.19 (t, *J* = 7.0 Hz, 2H), 7.09 (d, *J* = 8.2 Hz, 1H), 7.34 (s, 1H), 7.97 (d, *J* = 8.2 Hz, 1H). ¹³C NMR (125 MHz, DMSO-*d*₆): δ = 9.37, 32.9, 38.4, 41.2, 108.2, 114.3, 119.1, 126.9, 130.0, 142.8, 145.9. HRMS calcd for C₁₁H₁₄ClN₃, 223.0876; found, 223.0882.

trans-4-(6-Chloro-3-methyl-1H-pyrrolo[2,3-b]pyridin-1-yl)cyclohexanol (1o).

The title compound was synthesized following method B (150 °C, 1 h) in 71% yield. ¹H NMR (300 MHz, DMSO-*d*₆): δ = 1.33–1.48 (m, 2H), 1.80–2.00 (m, 6H), 2.24 (d, *J* = 0.9 Hz, 3H), 3.47–3.60 (m, 1H), 4.44–4.56 (m, 1H), 4.65 (d, *J* = 4.5 Hz, 1H), 7.08 (d, *J* = 8.1 Hz, 1H), 7.42 (q, *J* = 0.9 Hz, 1H), 7.95 (d, *J* = 8.1 Hz, 1H). ¹³C NMR (125 MHz, DMSO-*d*₆): δ = 9.62, 30.6, 34.5, 51.9, 68.1, 108.6, 114.6, 119.4, 123.9, 130.1, 142.8, 145.6. HRMS calcd for C₁₄H₁₇ClN₂O, 264.1029; found, 264.1025.

4-[2-(6-Chloro-3-methyl-1H-pyrrolo[2,3-b]pyridin-1-yl)ethyl]phenol (1p).

The title compound was synthesized following method B (150 °C, 30 min) in 52% yield. ¹H NMR (400 MHz, DMSO-*d*₆): δ = 2.22 (s, 3H), 2.95 (t, *J* = 7.4 Hz, 2H), 4.30 (t, *J* = 7.4 Hz, 2H), 6.64 (d, *J* = 8.3 Hz, 2H), 6.97 (d, *J* = 8.3 Hz, 2H), 7.08 (d, *J* = 8.1 Hz, 1H), 7.25 (s, 1H), 7.95 (d, *J* = 8.1 Hz, 1H), 9.18 (s, 1H). ¹³C NMR (125 MHz, DMSO-*d*₆): δ = 9.38, 34.7, 45.2, 108.0, 114.3, 115.0, 119.2, 126.8, 128.4, 129.4, 129.9, 142.8, 145.8, 155.7. HRMS calcd for C₁₆H₁₅ClN₂O, 286.0873; found, 286.0874.

Methyl 3-(6-chloro-3-methyl-1H-pyrrolo[2,3-b]pyridin-1-yl)propanoate (1q).

The title compound was synthesized following method B (150 °C, 30 min) in methanol instead of butanol to prevent transesterification. The title compound was isolated in 35% yield. ¹H NMR (300 MHz, DMSO-*d*₆): δ = 2.23 (d, *J* = 0.9 Hz, 3H), 2.86 (t, *J* = 6.9 Hz, 2H), 3.58 (s, 3H), 4.39 (t, *J* = 6.9 Hz, 2H), 7.11 (d, *J* = 8.1 Hz, 1H), 7.32 (q, *J* = 0.9 Hz, 1H), 7.97 (d, *J* = 8.1 Hz, 1H). ¹³C NMR (125 MHz, DMSO-*d*₆): δ = 9.35, 33.9, 39.6, 51.4, 108.4, 114.6, 119.3, 126.8, 130.1, 142.9, 145.8, 171.2. HRMS calcd for C₁₂H₁₃ClN₂O₂, 252.0666; found, 252.0658.

3-(6-Chloro-3-methyl-1H-pyrrolo[2,3-b]pyridin-1-yl)propanoic acid (1r).

The title compound was synthesized following method B (1N NaOH solution was added until dissolution of the amino acid) (150 °C, 30 min). The solution was acidified with diluted hydrochloric acid previous to extraction, and the title compound was isolated after purification by HPLC in 57% yield. ¹H NMR (300 MHz, DMSO-*d*₆): δ = 2.23 (d, *J* = 1.0 Hz, 3H), 2.77 (t, *J* = 7.0 Hz, 2H), 4.35 (t, *J* = 7.0 Hz, 2H), 7.11 (d, *J* = 8.1 Hz, 1H), 7.32 (q, *J* = 1.0 Hz, 1H), 7.97 (d, *J* = 8.1 Hz, 1H), 12.4 (br. s, 1H). ¹³C NMR (125 MHz, DMSO-*d*₆): δ = 9.46, 34.4, 40.0, 108.3, 114.6, 119.4, 127.0, 130.1, 142.9, 145.9, 172.4. HRMS calcd for C₁₁H₁₁ClN₂O₂, 238.0509; found, 238.0508.

1-Benzyl-6-chloro-3-phenyl-1H-pyrrolo[2,3-b]pyridine (1s).

The title compound was synthesized following method A (110 °C, 3 h) in 66% yield. ¹H NMR (400 MHz, DMSO-*d*₆): δ = 5.49 (s, 2H), 7.26 (d, *J* = 8.3 Hz, 1H), 7.26–7.36 (m, 6H), 7.49 (t, *J* = 7.7 Hz, 2H), 7.70 (d, *J* = 7.2 Hz, 2H), 8.09 (s, 1H), 8.38 (d, *J* = 8.3 Hz, 1H). ¹³C-NMR (125 MHz, DMSO-*d*₆): δ = 114.4, 116.2, 116.5, 126.17, 126.20, 127.1, 127.2, 127.5, 128.6, 128.9, 131.3, 133.8, 137.6, 143.5, 146.4. HRMS calcd for C₂₀H₁₅ClN₂, 318.0924; found, 318.0931.

6-Chloro-1-(1,1-dimethylpropyl)-3-phenyl-1H-pyrrolo[2,3-b]pyridine (1t).

The title compound was synthesized following method A (110 °C, 48 h) in 78% yield. ¹H NMR (400 MHz, DMSO-*d*₆): δ = 0.61 (t, *J* = 7.4 Hz, 3H), 1.78 (s, 6H), 2.26 (q, *J* = 7.4 Hz, 2H), 7.24 (d, *J* = 8.3 Hz, 7.30 (t, *J* = 7.4 Hz, 1H), 7.47 (t, *J* = 7.4 Hz, 2H), 7.74 (d, *J* = 7.4 Hz, 2H), 7.93 (s, 1H), 8.35 (d, *J* = 8.3 Hz, 1H). ¹³C NMR (125 MHz, DMSO-*d*₆): δ = 8.14, 26.7, 31.9, 59.9, 112.7, 115.6, 117.7, 125.8, 125.9, 126.4, 128.8, 130.7, 134.1, 141.7, 146.3. HRMS calcd for C₁₈H₁₉ClN₂: 298.1237; found, 298.1245.

2-(6-Chloro-3-phenyl-1H-pyrrolo[2,3-b]pyridin-1-yl)ethanol (1u).

The title compound was synthesized following method A (110 °C, 12 h) in 74% yield. ¹H NMR (300 MHz, DMSO-*d*₆): δ = 3.81 (dt, *J* = 5.8, 5.4 Hz, 2H), 4.32 (t, *J* = 5.8 Hz, 2H), 4.94 (t, *J* = 5.4 Hz, 1H), 7.22 (d, *J* = 8.3 Hz, 1H), 7.28 (tt, *J* = 7.4, 1.1 Hz, 1H), 7.45 (m, 2H), 7.97 (s, 1H), 8.34 (d, *J* = 8.3 Hz, 1H). ¹³C NMR (125 MHz, DMSO-*d*₆): δ = 46.7, 59.5, 113.6, 115.8, 116.5, 126.0, 126.1, 127.6, 128.9, 130.9, 134.0, 143.1, 146.6. HRMS calcd for C₁₅H₁₃ClN₂O, 272.0716; found, 272.0723.

1-(4-Chlorobenzyl)-3-methyl-1H-pyrrolo[2,3-b]pyridine (1v).

The title compound was synthesized following method A (120 °C, 18 h) in 64% yield. ¹H NMR (500 MHz, DMSO-*d*₆): δ = 2.26 (s, 3H), 5.41 (s, 2H), 7.08 (dd, *J* = 7.7, 4.6 Hz, 1H), 7.23 (d, *J* = 8.2 Hz, 2H), 7.36 (d, *J* = 8.2 Hz, 2H), 7.37 (s, 1H), 7.94 (d, *J* = 7.7 Hz, 1H), 8.23 (d, *J* = 4.6 Hz, 1H). ¹³C NMR (125 MHz, DMSO-*d*₆): δ = 9.41, 46.0, 108.3, 115.0, 120.3, 126.1, 126.9, 128.4, 129.0, 131.7, 137.6, 142.4, 147.0. HRMS calcd for C₁₅H₁₃ClN₂, 256.0767; found, 256.0761.

1-(2-Bromobenzyl)-3-methyl-1H-pyrrolo[2,3-*b*]pyridine (1w).

The title compound was synthesized following method A (120 °C, 18 h) in 52% yield. ¹H NMR (400 MHz, DMSO-*d*₆): δ = 2.29 (s, 3H), 5.47 (s, 2H), 6.60 (dd, *J* = 7.0, 2.0 Hz, 1H), 7.10 (dd, *J* = 7.8, 4.7 Hz, 1H), 7.19–7.27 (m, 2H), 7.33 (s, 1H), 7.67 (dd, *J* = 7.3, 1.7 Hz, 1H), 7.98 (dd, 7.8, 1.3 Hz, 1H), 8.21 (dd, *J* = 4.7, 1.3 Hz, 1H). ¹³C NMR (125 MHz, DMSO-*d*₆): δ = 9.46, 47.0, 108.4, 115.2, 120.3, 121.6, 126.2, 127.0, 127.9, 128.1, 129.2, 132.5, 137.3, 142.5, 147.2. HRMS calcd for C₁₅H₁₃BrN₂, 300.0262; found, 300.0254.

1-[2-(4-Bromophenyl)ethyl]-3-methyl-1H-pyrrolo[2,3-*b*]pyridine (1x).

The title compound was synthesized following method B (200 °C, 40 min) in 78% yield. ¹H NMR (500 MHz, DMSO-*d*₆): δ = 2.23 (s, 3H), 3.08 (t, *J* = 7.3 Hz, 2H), 4.41 (t, *J* = 7.3 Hz, 2H), 7.04 (dd, *J* = 7.7, 4.6 Hz, 1H), 7.14 (d, *J* = 8.0 Hz, 2H), 7.25 (s, 1H), 7.43 (d, *J* = 8.0 Hz, 2H), 7.89 (d, *J* = 7.7 Hz, 1H), 8.21 (d, *J* = 4.6 Hz, 1H). ¹³C NMR (125 MHz, DMSO-*d*₆): δ = 9.41, 35.0, 44.4, 107.4, 114.7, 119.3, 120.3, 126.0, 126.6, 130.8, 131.0, 138.1, 142.1, 147.0. HRMS calcd for C₁₆H₁₅BrN₂, 314.0419; found, 314.0419.

3-Methyl-1-[2-(4-nitrophenyl)ethyl]-1H-pyrrolo[2,3-b]pyridine (1y).

The title compound was synthesized following method B (200 °C, 20 min) in 53% yield. ¹H NMR (400 MHz, DMSO-*d*₆): δ = 2.23 (s, 3H), 3.26 (t, *J* = 7.2 Hz, 2H), 4.50 (t, *J* = 7.2 Hz, 2H), 7.04 (dd, *J* = 7.8, 4.7 Hz, 1H), 7.27 (s, 1H), 7.45 (d, *J* = 8.6 Hz, 2H), 7.89 (dd, *J* = 7.8, 1.5 Hz, 1H), 8.11 (d, *J* = 8.6 Hz, 2H), 8.20 (dd, *J* = 4.7, 1.5 Hz, 1H). ¹³C NMR (125 MHz, DMSO-*d*₆): δ = 9.41, 35.4, 44.0, 107.6, 114.8, 120.3, 123.3, 125.9, 126.7, 129.9, 142.1, 146.0, 147.07, 147.10. HRMS calcd for C₁₆H₁₅N₃O₂ + [H⁺], 282.1238; found, 282.1246.

1-(3,3-Diphenylpropyl)-3-methyl-1H-pyrrolo[2,3-b]pyridine (1z).

The title compound was synthesized following method B (200 °C, 10 min) in 74% yield. ¹H NMR (400 MHz, DMSO-*d*₆): δ = 2.25 (s, 3H), 2.58 (dt, *J* = 7.7, 7.5 Hz, 2H), 3.97 (t, *J* = 7.7 Hz, 1H), 4.10 (dd, *J* = 7.5, 7.5 Hz, 2H), 7.03 (dd, *J* = 7.8, 4.5 Hz, 1H), 7.17 (dt, *J* = 7.0, 1.6 Hz, 2H), 7.24–7.36 (m, 9H), 7.89 (dd, *J* = 4.8, 1.5 Hz, 1H), 8.18 (dd, *J* = 4.5, 1.5 Hz, 1H). ¹³C NMR (125 MHz, DMSO-*d*₆): δ = 9.41, 34.9, 42.3, 48.1, 107.5, 114.7, 120.3, 125.9, 126.1, 126.6, 127.4, 128.4, 142.0, 144.3, 147.0. HRMS calcd for C₂₃H₂₂N₂, 326.1783; found, 326.1774.

1-Cycloheptyl-3-methyl-1H-pyrrolo[2,3-b]pyridine (1aa).

The title compound was synthesized following method B (200 °C, 40 min) in 83% yield. ¹H NMR (300 MHz, DMSO-*d*₆): δ = 1.50–1.72 (m, 6H), 1.72–1.80 (m, 2H), 1.88–2.00 (m, 4H), 2.26 (s, 3H), 4.84 (tt, *J* = 9.2, 5.3 Hz, 1H), 7.03 (dd, *J* = 7.8, 4.7 Hz, 1H), 7.38 (s, 1H), 7.88 (d, *J* = 7.8, 1.5 Hz, 1H), 8.20 (dd, *J* = 4.4, 1.5 Hz, 1H). ¹³C NMR (125 MHz, DMSO-*d*₆): δ = 9.62, 24.3, 27.2, 34.9, 54.3, 107.7, 114.7, 120.3, 123.3, 126.6, 141.9, 146.4. HRMS calcd for C₁₅H₂₀N₂, 228.1626; found, 228.1621.

1-(1-Adamantyl)-3-methyl-1H-pyrrolo[2,3-b]pyridine (1bb).

The title compound was synthesized following method B (200 °C, 3 h) in 61% yield. ¹H NMR (300 MHz, DMSO-*d*₆): δ = 1.68–1.83 (m, 6H), 2.16–2.22 (m, 3H), 2.23 (s, 3H), 2.42–2.45 (d, *J* = 2.7 Hz, 6H), 7.02 (dd, *J* = 7.8, 4.6 Hz, 1H), 7.34 (s, 1H), 7.87 (dd, *J* = 7.8, 1.7 Hz, 1H), 8.20 (dd, *J* = 4.6, 1.7 Hz, 1H). ¹³C NMR (125 MHz, DMSO-*d*₆): δ = 9.50, 29.2, 35.9, 41.1, 56.2, 106.5, 114.4, 121.8, 123.1, 126.6, 141.0, 147.4. HRMS calcd for C₁₈H₂₂N₂ + [H⁺], 267.1856; found, 267.1855.

3-Methyl-1-(tetrahydrofuran-2-ylmethyl)-1H-pyrrolo[2,3-b]pyridine (1cc).

The title compound was synthesized following method B (200 °C, 30 min) in 58% yield. ¹H NMR (400 MHz, DMSO-*d*₆): δ = 1.49–1.59 (m, 1H), 1.75 (tt, *J* = 7.1, 6.8 Hz, 2H), 1.83–1.92 (m, 1H), 2.26 (s, 3H), 3.61 (dt, *J* = 8.1, 6.9 Hz, 1H), 3.77 (dt, *J* = 8.1, 6.8 Hz, 1H), 4.13–4.29 (m, 3H), 7.05 (dd, *J* = 7.8, 4.6 Hz, 1H), 7.29 (s, 1H), 7.90 (dd, *J* = 7.8, 1.5 Hz, 1H), 8.21 (dd, *J* = 4.6, 1.5 Hz, 1H). ¹³C NMR (125 MHz, DMSO-*d*₆): δ = 9.39, 24.9, 28.3, 47.0, 67.1, 77.3, 107.3, 114.7, 120.1, 126.6, 126.8, 142.0, 147.3. HRMS calcd for C₁₃H₁₆N₂O, 216.1263; found, 216.1254.

2-(3-Methyl-1H-pyrrolo[2,3-b]pyridin-1-yl)-1-phenylethanol (1dd).

The title compound was synthesized following method B (200 °C, 30 min) in 67% yield. ¹H NMR (400 MHz, DMSO-*d*₆): δ = 2.24 (s, 3H), 4.23 (dd, *J* = 13.8, 8.3 Hz, 1H), 4.39 (dd, *J* = 13.8, 4.2 Hz, 1H), 4.96 (ddd, *J* = 8.3, 4.7, 4.2 Hz, 1H), 5.65 (d, *J* = 4.7 Hz, 1H), 7.05 (dd, *J* = 7.7, 4.7 Hz, 1H), 7.21–7.39 (m, 6H), 7.90 (dd, *J* = 7.7, 1.5 Hz, 1H), 8.21 (dd, *J* = 4.7, 1.5 Hz, 1H). ¹³C NMR (125 MHz, DMSO-*d*₆): δ = 9.39, 51.2, 71.6, 106.8, 114.6, 120.3, 125.9, 126.5, 127.1, 127.2, 128.0, 141.9, 143.1, 147.2. HRMS calcd for C₁₆H₁₆N₂O, 252.1263; found, 252.1263.

3-Methyl-1-(2,2,6,6-tetramethylpiperidin-4-yl)-1H-pyrrolo[2,3-b]pyridine (1ee).

The title compound was synthesized following method B (200 °C, 20 min) in 55% yield. ¹H NMR (300 MHz, DMSO-*d*₆): δ = 1.10 (s, 6H), 1.27 (s, 6H), 1.59–1.78 (m, 4H), 2.26 (s, 3H), 5.18 (tt, *J* = 12.3, 3.8 Hz, 1H), 7.05 (dd, *J* = 7.5, 4.5 Hz, 1H), 7.38 (s, 1H), 7.90 (dd, *J* = 7.7, 1.5 Hz, 1H), 8.23 (dd, *J* = 4.5, 1.5 Hz, 1H). ¹³C NMR (125 MHz, DMSO-*d*₆): δ = 9.51, 28.4, 34.4, 44.2,

45.9, 50.8, 107.7, 114.8, 120.4, 123.1, 126.6, 141.8, 146.7. HRMS calcd for C₁₇H₂₅N₃, 271.2048; found, 271.2043.

tert-Butyl [3-(3-methyl-1H-pyrrolo[2,3-b]pyridin-1-yl)propyl]carbamate (1ff).

The title compound was synthesized following method B (200 °C, 10 min) in 44% yield. ¹H NMR (300 MHz, DMSO-*d*₆): δ = 1.37 (s, 9H), 1.85 (tt, *J* = 7.0, 6.9 Hz, 2H), 2.25 (s, 3H), 2.89 (dt, *J* = 7.0, 5.4 Hz, 2H), 4.18 (t, *J* = 6.9 Hz, 2H), 6.90 (br. t, *J* = 5.4 Hz, 1H), 7.05 (dd, *J* = 7.9, 4.6 Hz, 1H), 7.32 (s, 1H), 7.91 (dd, *J* = 7.9, 1.5 Hz, 1H), 8.21 (dd, *J* = 4.6, 1.5 Hz, 1H). ¹³C NMR (125 MHz, DMSO-*d*₆): δ = 9.50, 28.2, 30.3, 37.5, 41.2, 77.5, 107.4, 114.7, 120.3, 126.3, 126.7, 142.1, 147.1, 155.5. HRMS calcd for C₁₆H₂₃N₃O₂, 289.1790; found 289.1782.

4-[2-(3-Methyl-1H-pyrrolo[2,3-b]pyridin-1-yl)ethyl]aniline (1gg).

The title compound was synthesized following method B (200 °C, 30 min) in 55% yield. ¹H NMR (300 MHz, DMSO-*d*₆): δ = 2.23 (s, 3H), 2.88 (dd, *J* = 7.7, 7.4 Hz, 2H), 4.31 (dd, *J* = 7.7, 7.4 Hz, 2H), 4.88 (br. s, 2H), 6.47 (d, *J* = 8.1 Hz, 2H), 6.86 (d, *J* = 8.1 Hz, 2H), 7.04 (dd, *J* = 7.7, 4.5 Hz, 1H), 7.23 (s, 1H), 7.89 (dd, *J* = 7.7, 1.5 Hz, 1H), 8.23 (dd, *J* = 4.5, 1.5 Hz, 1H). ¹³C NMR (125 MHz, DMSO-*d*₆): δ = 9.42, 35.1, 45.2, 107.1, 113.8, 114.6, 120.2, 125.3, 126.1, 126.6, 128.9, 142.0, 146.8, 147.0. HRMS calcd for C₁₆H₁₇N₃, 275.1422; found, 275.1424.

Suzuki-Miyaura reactions with 6-chloro-7-azaindoles. General procedure. A degassed mixture of dimethoxyethane and water (3.5 : 1, 4 mL/mmol azaindole) was added under argon to 6-chloro-7-azaindole, boronic acid (2 eq.), PdCl₂(dppf)×CH₂Cl₂ (0.05 eq.) and sodium bicarbonate (3 eq.). The mixture was heated in a sealed pressure tube to 115 °C for 3 h. Subsequently, the layers were separated and the organic layer was evaporated. The residue was separated by HPLC to yield the coupling product.

1-Benzyl-6-(4-methoxyphenyl)-3-methyl-1H-pyrrolo[2,3-b]pyridine (11a).

The title compound was prepared from **1a** following the general procedure in 84% yield. ¹H NMR (300 MHz, DMSO-*d*₆): δ = 2.26 (s, 3H), 3.81 (s, 3H), 5.46 (s, 2H), 7.04 (m, 2H), 7.20–7.30 (m, 2H), 7.31 (m, 4H), 7.61 (d, *J* = 8.1 Hz, 1H), 7.95 (d, *J* = 8.1 Hz, 1H), 8.10 (m, 1H). ¹³C NMR (125 MHz, DMSO-*d*₆): δ = 9.51, 46.7, 55.1, 108.2, 111.2, 114.0, 118.8, 126.3, 127.2, 127.4, 127.57, 127.63, 128.4, 132.1, 138.6, 147.1, 149.1, 159.4. HRMS calcd for C₂₂H₂₀N₂O: 328.1576; found, 328.1571.

[4-(1-Benzyl-3-methyl-1H-pyrrolo[2,3-b]pyridin-6-yl)phenyl]methanol (11b).

The title compound was prepared from **1a** following the general procedure in 95% yield. ¹H NMR (300 MHz, DMSO-*d*₆): δ = 2.27 (s, 3H), 4.55 (d, *J* = 5.7 Hz, 2H), 5.18 (t, *J* = 5.7 Hz, 1H), 5.48 (s, 2H), 7.20–7.36 (m, 6H), 7.42 (d, *J* = 8.3 Hz, 2H), 7.67 (d, *J* = 8.3 Hz, 1H), 7.99 (d, *J* = 8.3 Hz, 1H), 8.11 (d, *J* = 8.3 Hz, 2H). ¹³C NMR (125 MHz, DMSO-*d*₆): δ = 9.50, 46.7, 62.6,

108.2, 111.7, 119.3, 126.0, 126.61, 126.64, 127.2, 127.4, 127.6, 128.4, 138.0, 138.6, 142.5, 147.1, 149.2. HRMS calcd for C₂₂H₂₀N₂O, 328.1576; found, 328.1566.

1-Benzyl-6-(2-fluoro-6-methylpyridin-3-yl)-3-methyl-1H-pyrrolo[2,3-b]pyridine (11d).

The title compound was prepared from **1a** following the general procedure in 96% yield. ¹H NMR (300 MHz, DMSO-*d*₆): δ = 2.28 (d, *J* = 0.9 Hz, 3H), 2.49 (s, 3H), 5.47 (s, 2H), 7.21–7.32 (m, 5H), 7.37 (dd, *J* = 7.7, 1.9 Hz, 1H), 7.44 (q, *J* = 0.9 Hz, 1H), 7.58 (dd, *J* = 8.1, 2.1 Hz, 1H), 8.05 (d, *J* = 8.1 Hz, 1H), 8.47 (dd, *J* = 10.6, 8.1 Hz, 1H). ¹³C NMR (125 MHz, DMSO-*d*₆): δ = 9.44, 23.0, 46.8, 108.3, 115.0 (d, ⁴*J*_{C,F} = 9.6 Hz), 119.3 (d, ²*J*_{C,F} = 26.6 Hz), 119.8, 121.7 (d, ⁴*J*_{C,F} = 4.1 Hz), 127.2, 127.4, 127.5, 128.4, 138.4, 141.5 (d, ³*J*_{C,F} = 3.6 Hz), 143.7 (d, ³*J*_{C,F} = 7.2 Hz), 147.0, 156.4 (d, ³*J*_{C,F} = 14.7 Hz), 159.1 (d, ¹*J*_{C,F} = 238 Hz). HRMS calcd for C₂₁H₁₈FN₃: 331.1485; found, 331.1471.

1-Benzyl-6-(3-furyl)-3-methyl-1H-pyrrolo[2,3-b]pyridine (11e).

The title compound was prepared from **1a** following the general procedure in 89% yield. ¹H NMR (300 MHz, DMSO-*d*₆): δ = 2.25 (d, *J* = 0.8 Hz, 3H), 5.42 (s, 2H), 7.09 (dd, *J* = 1.7, 0.8 Hz, 1H), 7.20–7.32 (m, 6H), 7.43 (d, *J* = 8.1 Hz, 1H), 7.74 (t, *J* = 1.7 Hz, 1H), 7.92 (d, *J* = 8.1 Hz, 1H), 8.31 (dd, *J* = 1.7, 0.8 Hz, 1H). ¹³C NMR (125 MHz, DMSO-*d*₆): δ = 9.48, 46.6, 108.4, 108.9, 112.1, 119.0, 126.1, 127.2, 127.45, 127.54, 127.7, 128.4, 138.6, 140.8, 144.0, 144.1, 146.9. HRMS calcd for C₁₉H₁₆N₂O: 288.1263; found, 288.1252.

1-Butyl-6-(2-methoxyphenyl)-3-phenyl-1H-pyrrolo[2,3-b]pyridine (11f).

The title compound was prepared from **1** following the general procedure in 90% yield. ^1H NMR (400 MHz, $\text{DMSO-}d_6$): δ = 0.92 (t, J = 7.3 Hz, 3H), 1.30 (tq, J = 7.5, 7.3 Hz, 2H), 1.88 (tt, J = 7.5, 6.8 Hz, 2H), 3.85 (s, 3H), 4.35 (t, J = 6.8 Hz, 2H), 7.10 (t, J = 7.4 Hz, 1H), 7.17 (d, J = 8.2 Hz, 1H), 7.26 (t, J = 7.5 Hz, 1H), 7.40 (m, 1H), 7.45 (t, J = 7.5 Hz, 2H), 7.66 (d, J = 8.3 Hz, 1H), 7.74 (d, J = 7.5 Hz, 2H), 7.80 (dd, J = 7.4, 1.4 Hz, 1H), 8.00 (s, 1H), 8.30 (d, J = 8.3 Hz, 1H). ^{13}C NMR (125 MHz, $\text{DMSO-}d_6$): δ = 13.4, 19.4, 31.7, 43.3, 55.5, 111.9, 113.1, 115.8, 117.6, 120.6, 125.5, 125.9, 126.8, 127.3, 128.8, 129.2, 129.4, 130.7, 134.8, 147.5, 148.6, 156.7. HRMS calcd for $\text{C}_{24}\text{H}_{24}\text{N}_2\text{O}$: 356.1889; found, 356.1899.

2-(6-Dibenzo[*b,d*]furan-1-yl-3-phenyl-1H-pyrrolo[2,3-*b*]pyridin-1-yl)ethanol (11h).

The title compound was prepared from **11** following the general procedure in 97% yield. ^1H NMR (300 MHz, $\text{DMSO-}d_6$): δ = 1.76–1.88 (m, 2H), 2.31 (s, 3H), 2.36–2.58 (m, 4H), 4.62 (d, J = 5.8 Hz, 2H), 5.15–5.25 (m, 1H), 5.28 (t, J = 5.8 Hz, 1H), 7.29 (d, J = 8.1 Hz, 1H), 7.33–7.45 (m, 2H), 7.50 (dd, J = 7.2, 1.7 Hz, 1H), 7.60 (d, J = 0.8 Hz, 1H), 7.63 (dd, J = 7.2, 1.3 Hz, 1H), 8.00 (d, J = 8.1 Hz, 1H). ^{13}C NMR (125 MHz, $\text{DMSO-}d_6$): δ = 9.56, 14.4, 30.3, 47.4, 61.4, 108.1, 115.5, 119.2, 124.1, 126.6, 127.4, 127.6, 127.7, 129.6, 139.4, 140.3, 146.1, 151.1. HRMS calcd for $\text{C}_{19}\text{H}_{20}\text{N}_2\text{O} + [\text{H}^+]$, 293.1649; found, 293.1657.

1-(1,1-Dimethylpropyl)-6-(3-methoxyphenyl)-3-phenyl-1H-pyrrolo[2,3-*b*]pyridine (11i).

The title compound was prepared from **1t** following the general procedure in 96% yield. ^1H NMR (400 MHz, $\text{DMSO-}d_6$): δ = 0.61 (t, J = 7.3 Hz, 3H), 1.84 (s, 6H), 2.39 (q, J = 7.3 Hz, 2H), 3.86 (s, 3H), 7.00 (dd, J = 8.1, 2.2 Hz, 1H), 7.26 (m, 1H), 7.41–7.47 (m, 3H), 7.70–7.78 (m, 4H), 7.79 (d, J = 8.3 Hz, 1H), 7.92 (s, 1H), 8.34 (d, J = 8.3 Hz, 1H). ^{13}C NMR (125 MHz, $\text{DMSO-}d_6$): δ = 8.22, 27.0, 32.2, 54.9, 59.5, 111.8, 112.3, 112.7, 113.5, 117.9, 118.5, 125.6, 126.2, 128.3, 128.8, 129.8, 134.7, 140.9, 147.7, 148.0, 159.6. HRMS calcd for $\text{C}_{25}\text{H}_{26}\text{N}_2\text{O}$, 370.2045; found, 370.2056.

2-(6-Dibenzo[*b,d*]furan-1-yl-3-phenyl-1H-pyrrolo[2,3-*b*]pyridin-1-yl)ethanol (11j).

The title compound was prepared from **1u** following the general procedure in 91% yield. ^1H NMR (300 MHz, $\text{DMSO-}d_6$): δ = 3.94 (dt, J = 5.6, 5.4 Hz, 2H), 4.50 (t, J = 5.6 Hz, 2H), 5.03 (t, J = 5.4 Hz, 1H), 7.29 (tt, J = 7.4, 1.2 Hz, 1H), 7.44–7.52 (m, 3H), 7.56–7.62 (m, 2H), 7.76–7.83 (m, 3H), 8.05 (s, 1H), 8.20–8.25 (m, 2H), 8.29 (d, J = 8.3 Hz, 1H), 8.40 (dd, J = 7.7, 1.1 Hz, 1H), 8.53 (d, J = 8.3 Hz, 1H). HRMS calcd for $\text{C}_{27}\text{H}_{20}\text{N}_2\text{O}_2$, 404.1525; found, 404.1526.