

Silver triflate-catalyzed tandem reaction of *N'*-(2-alkynylbenzylidene)hydrazide with pyridyne

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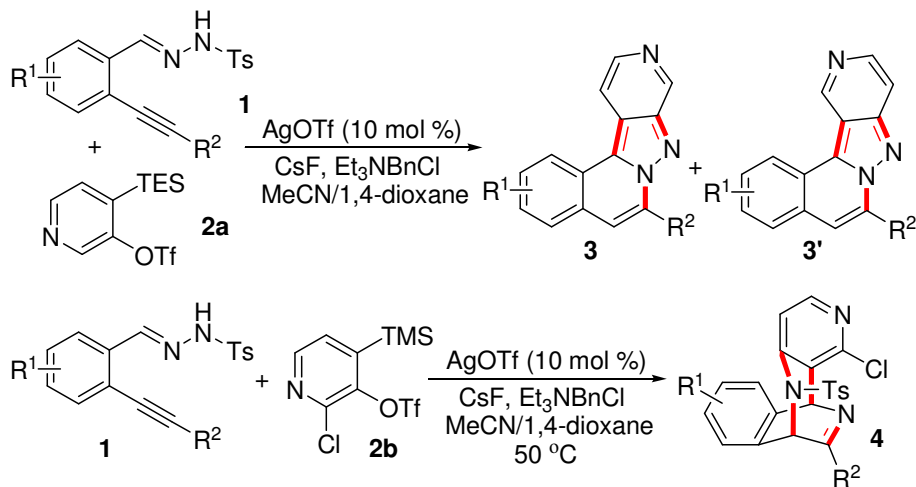
Supporting Information

1. General experimental method (S2)
2. Experimental procedure and characterization data (S2-S12)
3. ¹H and ¹³C NMR spectra of compounds **3** and **4** (S13-S60)

General experimental methods:

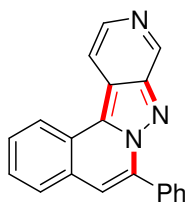
Unless otherwise stated, all commercial reagents were used as received. All solvents were dried and distilled according to standard procedures. Flash column chromatography was performed using silica gel (60-Å pore size, 32–63µm, standard grade). Analytical thin-layer chromatography was performed using glass plates pre-coated with 0.25 mm 230–400 mesh silica gel impregnated with a fluorescent indicator (254 nm). Thin layer chromatography plates were visualized by exposure to ultraviolet light. Organic solutions were concentrated on rotary evaporators at ~20 Torr at 25–35°C. Nuclear magnetic resonance (NMR) spectra are recorded in parts per million from internal tetramethylsilane on the δ scale. ^1H and ^{13}C NMR spectra were recorded in CDCl_3 on a Bruker DRX-400 spectrometer operating at 400 MHz and 100 MHz, respectively. All chemical shift values are quoted in ppm and coupling constants quoted in Hz. High resolution mass spectrometry (HRMS) spectra were obtained on a micrOTOF II Instrument.

General experimental procedure for the silver triflate-catalyzed tandem reaction of N' -(2-alkynylbenzylidene)hydrazide with pyridyne.

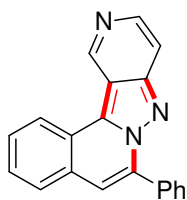


A mixture of N' -(2-alkynylbenzylidene)hydrazide **1** (0.3 mmol) and AgOTf (10 mol %) in 1,4-dioxane (2.0 mL) was heated at 70 °C with vigorous stirring for 1 hour. Then, pyridyne precursor **2** (0.45 mmol, 1.5 equiv), CsF (0.9 mmol, 3.0 equiv), TEAC (0.075 mmol, 0.25 equiv), and MeCN (2.0 mL) were added. The reaction mixture was

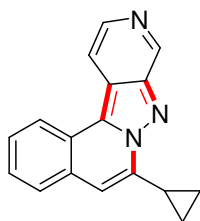
stirred at room temperature or 50 °C until completion of the reaction. The reaction mixture was diluted with ethyl acetate (5.0 mL), and quenched with water (5.0 mL). The organic layer was washed with brine, dried over Na₂SO₄ and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel to provide the desired product.



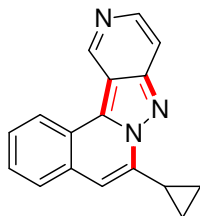
6-Phenylpyrido[3',4':3,4]pyrazolo[5,1-*a*]isoquinoline **3a**. ¹H NMR (400 MHz, CDCl₃) δ 7.57-7.61 (m, 4H), 7.66 (t, *J* = 7.6 Hz, 1H), 7.79 (t, *J* = 7.6 Hz, 1H), 7.92 (d, *J* = 8.2 Hz, 1H), 7.98 (d, *J* = 6.4 Hz, 2H), 8.26 (d, *J* = 6.0 Hz, 1H), 8.43 (d, *J* = 6.0 Hz, 1H), 8.64 (d, *J* = 7.8 Hz, 1H), 9.50 (s, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 114.5, 118.9, 119.0, 122.7, 125.8, 127.9, 128.0, 128.6, 128.8, 129.8, 129.9, 131.4, 133.3, 137.8, 138.7, 144.3, 144.8; HRMS calcd for C₂₀H₁₄N₃ (M⁺+H): 296.1188, found: 296.1180.



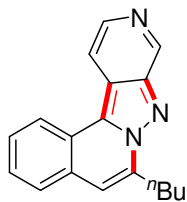
6-Phenylpyrido[4',3':3,4]pyrazolo[5,1-*a*]isoquinoline **3a'**. ¹H NMR (400 MHz, CDCl₃) δ 7.58-7.64 (m, 4H), 7.73-7.77 (m, 2H), 7.85 (t, *J* = 7.6 Hz, 1H), 7.95-8.00 (m, 3H), 8.47 (d, *J* = 6.4 Hz, 1H), 8.76 (d, *J* = 8.2 Hz, 1H), 9.97 (s, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 111.3, 114.9, 118.7, 123.6, 124.6, 128.0, 128.7, 129.1, 129.2, 129.6, 129.8, 130.0, 133.2, 138.7, 142.1, 146.1, 150.1; HRMS calcd for C₂₀H₁₄N₃ (M⁺+H): 296.1188, found: 296.1181.



6-Cyclopropylpyrido[3',4':3,4]pyrazolo[5,1-*a*]isoquinoline **3b**. ^1H NMR (400 MHz, CDCl_3) δ 0.99-1.03 (m, 2H), 1.32-1.36 (m, 2H), 2.87-2.95 (m, 1H), 7.17 (s, 1H), 7.61 (t, $J = 7.3$ Hz, 1H), 7.71 (t, $J = 7.3$ Hz, 1H), 7.81 (d, $J = 7.8$ Hz, 1H), 8.22 (d, $J = 6.0$ Hz, 1H), 8.42 (d, $J = 5.5$ Hz, 1H), 8.55 (d, $J = 7.8$ Hz, 1H), 9.58 (s, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 7.6, 11.9, 113.1, 114.6, 119.2, 122.6, 124.9, 127.2, 127.8, 128.0, 128.5, 130.9, 137.6, 141.2, 143.9, 144.9; HRMS calcd for $\text{C}_{17}\text{H}_{13}\text{N}_3$ ($\text{M}^+\text{+H}$): 260.1188, found: 260.1181.

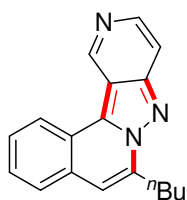


6-Cyclopropylpyrido[4',3':3,4]pyrazolo[5,1-*a*]isoquinoline **3b'**. ^1H NMR (400 MHz, CDCl_3) δ 0.99-1.04 (m, 2H), 1.32-1.36 (m, 2H), 2.90-2.97 (m, 1H), 7.18 (s, 1H), 7.67 (t, $J = 7.3$ Hz, 1H), 7.75 (t, $J = 7.3$ Hz, 1H), 7.81-7.85 (m, 2H), 8.51 (d, $J = 6.0$ Hz, 1H), 8.66 (d, $J = 7.8$ Hz, 1H), 9.88 (s, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 7.8, 12.0, 110.8, 112.6, 115.1, 123.4, 123.9, 127.3, 128.2, 128.6, 129.4, 132.5, 141.2, 143.1, 146.6, 150.1; HRMS calcd for $\text{C}_{17}\text{H}_{13}\text{N}_3$ ($\text{M}^+\text{+H}$): 260.1188, found: 260.1170.

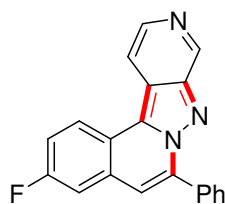


6-Butylpyrido[3',4':3,4]pyrazolo[5,1-*a*]isoquinoline **3c**. ^1H NMR (400 MHz, CDCl_3) δ 1.04 (t, $J = 7.3$ Hz, 3H), 1.56-1.60 (m, 2H), 1.91-1.99 (m, 2H), 3.32-3.36 (m, 2H), 7.32 (s, 1H), 7.61 (t, $J = 7.3$ Hz, 1H), 7.70 (t, $J = 7.6$ Hz, 1H), 7.83 (d, $J = 7.8$ Hz, 1H), 8.17 (d, $J = 5.5$ Hz, 1H), 8.40 (d, $J = 5.5$ Hz, 1H), 8.51 (d, $J = 7.8$ Hz, 1H), 9.52 (s, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 14.0, 22.6, 28.8, 31.0, 114.6, 115.7, 119.0, 122.5,

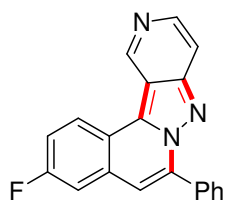
125.1, 127.2, 127.7, 127.9, 128.4, 130.8, 137.6, 139.8, 143.9, 144.8; HRMS calcd for $C_{18}H_{18}N_3$ ($M^+ + H$): 276.1501, found: 276.1485.



6-Butylpyrido[4',3':3,4]pyrazolo[5,1-*a*]isoquinoline **3c**. 1H NMR (400 MHz, $CDCl_3$) δ 1.03 (t, $J = 6.8$ Hz, 3H), 1.53-1.58 (m, 2H), 1.91-1.95 (m, 2H), 3.30-3.34 (m, 2H), 7.31 (s, 1H), 7.64-7.76 (m, 3H), 7.83 (d, $J = 7.8$ Hz, 1H), 8.49 (d, $J = 6.0$ Hz, 1H), 8.57 (d, $J = 7.8$ Hz, 1H), 9.81 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.0, 22.6, 28.8, 31.1, 110.8, 114.9, 115.3, 123.3, 123.9, 127.2, 128.1, 128.6, 129.3, 132.4, 139.8, 142.8, 146.4, 149.9; HRMS calcd for $C_{18}H_{18}N_3$ ($M^+ + H$): 276.1501, found: 276.1483.

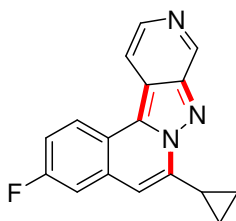


3-Fluoro-6-phenylpyrido[3',4':3,4]pyrazolo[5,1-*a*]isoquinoline **3d**. 1H NMR (400 MHz, $CDCl_3$) δ 7.51-7.60 (m, 6H), 7.95-7.97 (m, 2H), 8.19 (d, $J = 5.5$ Hz, 1H), 8.42 (d, $J = 5.5$ Hz, 1H), 8.60-8.64 (m, 1H), 9.49 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 112.6 (d, $^2J_{CF} = 22$ Hz), 114.2, 117.8 (d, $^2J_{CF} = 24$ Hz), 117.9, 118.5, 122.5, 125.1 (d, $^3J_{CF} = 9$ Hz), 128.7, 129.7, 130.2, 130.3, 131.2, 132.9, 137.9, 139.8, 144.4, 144.9, 161.8 (d, $^1J_{CF} = 248$ Hz); HRMS calcd for $C_{20}H_{13}FN_3$ ($M^+ + H$): 314.1094, found: 314.1071.

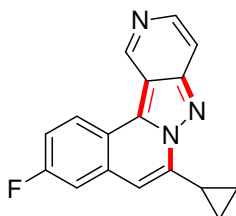


3-Fluoro-6-phenylpyrido[4',3':3,4]pyrazolo[5,1-*a*]isoquinoline **3d'**. 1H NMR (400 MHz, $CDCl_3$) δ 7.55-7.63 (m, 6H), 7.74 (d, $J = 6.0$ Hz, 1H), 7.95-7.97 (m, 2H), 8.48-8.49 (m, 1H), 8.75-8.77 (m, 1H), 9.92 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ

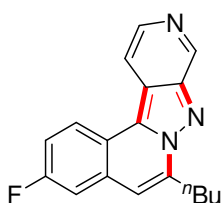
111.2, 112.6 (d, $^2J_{CF} = 21$ Hz), 114.6, 117.6, 117.7, 118.4 (d, $^2J_{CF} = 24$ Hz), 121.5, 126.1 (d, $^3J_{CF} = 9$ Hz), 128.7, 129.8, 130.2, 131.3 (d, $^3J_{CF} = 9$ Hz), 133.0, 139.7, 143.0, 146.4, 150.2, 162.3 (d, $^1J_{CF} = 251$ Hz); HRMS calcd for $C_{20}H_{13}FN_3$ ($M^+ + H$): 314.1094, found: 314.1097.



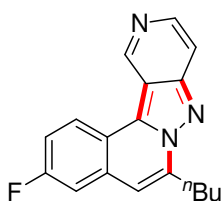
6-Cyclopropyl-3-fluoropyrido[3',4':3,4]pyrazolo[5,1-*a*]isoquinoline **3e**. 1H NMR (400 MHz, $CDCl_3$) δ 1.01-1.05 (m, 2H), 1.34-1.39 (m, 2H), 2.91-2.98 (m, 1H), 7.13 (s, 1H), 7.46-7.50 (m, 2H), 8.19 (d, $J = 6.0$ Hz, 1H), 8.41-8.43 (m, 1H), 8.56-8.59 (m, 1H), 9.57 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 7.9, 11.9, 112.0 (d, $^2J_{CF} = 22$ Hz), 112.2, 114.5, 117.1 (d, $^2J_{CF} = 24$ Hz), 118.8, 121.7, 125.0 (d, $^3J_{CF} = 9$ Hz), 126.5, 129.7, 130.3 (d, $^3J_{CF} = 9$ Hz), 137.4, 142.5, 143.9, 161.7 (d, $^1J_{CF} = 248$ Hz); HRMS calcd for $C_{17}H_{13}FN_3$ ($M^+ + H$): 278.1094, found: 278.1088.



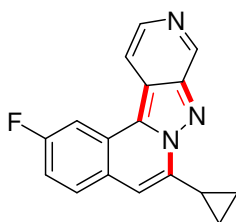
6-Cyclopropyl-3-fluoropyrido[4',3':3,4]pyrazolo[5,1-*a*]isoquinoline **3e'**. 1H NMR (400 MHz, $CDCl_3$) δ 1.01-1.05 (m, 2H), 1.34-1.39 (m, 2H), 2.93-3.00 (m, 1H), 7.13 (s, 1H), 7.50-7.52 (m, 2H), 7.82 (d, $J = 6.0$ Hz, 1H), 8.51-8.53 (m, 1H), 8.66-8.70 (m, 1H), 9.86 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 8.0, 12.0, 110.9, 111.7, 111.9 (d, $^2J_{CF} = 22$ Hz), 114.8, 117.6 (d, $^2J_{CF} = 25$ Hz), 120.7, 125.9 (d, $^3J_{CF} = 10$ Hz), 131.3 (d, $^3J_{CF} = 10$ Hz), 132.4, 142.5, 143.2, 146.5, 150.2, 162.2 (d, $^1J_{CF} = 249$ Hz); HRMS calcd for $C_{17}H_{13}FN_3$ ($M^+ + H$): 278.1094, found: 278.1085.



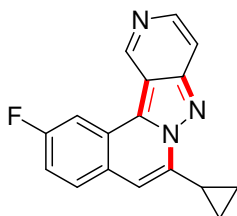
6-Butyl-3-fluoropyrido[3',4':3,4]pyrazolo[5,1-*a*]isoquinoline **3f**. ^1H NMR (400 MHz, CDCl_3) δ 1.04 (t, $J = 7.3$ Hz, 3H), 1.53-1.60 (m, 2H), 1.92-2.00 (m, 2H), 3.35-3.39 (m, 2H), 7.30 (s, 1H), 7.46-7.52 (m, 2H), 8.15 (d, $J = 5.5$ Hz, 1H), 8.42 (d, $J = 5.5$ Hz, 1H), 8.53-8.56 (m, 1H), 9.54 (s, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 14.0, 22.6, 28.7, 31.1, 111.9 (d, $^2J_{\text{CF}} = 22$ Hz), 114.3, 114.9, 117.1 (d, $^2J_{\text{CF}} = 24$ Hz), 118.6, 121.9, 124.9 (d, $^3J_{\text{CF}} = 9$ Hz), 130.2 (d, $^3J_{\text{CF}} = 10$ Hz), 130.6, 137.7, 141.1, 144.1, 144.9, 161.6 (d, $^1J_{\text{CF}} = 248$ Hz); HRMS calcd for $\text{C}_{18}\text{H}_{17}\text{FN}_3$ ($\text{M}^+\text{+H}$): 294.1407, found: 294.1379.



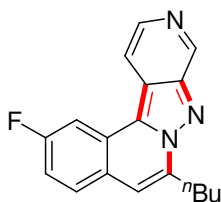
6-Butyl-3-fluoropyrido[4',3':3,4]pyrazolo[5,1-*a*]isoquinoline **3f'**. ^1H NMR (400 MHz, CDCl_3) δ 1.04 (t, $J = 7.3$ Hz, 3H), 1.54-1.59 (m, 2H), 1.92-1.96 (m, 2H), 3.33-3.37 (m, 2H), 7.29 (s, 1H), 7.48-7.52 (m, 2H), 7.76 (d, $J = 4.2$ Hz, 1H), 8.51 (s, 1H), 8.61-8.64 (m, 1H), 9.81 (s, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 14.0, 22.6, 28.8, 31.2, 110.7, 111.9 (d, $^2J_{\text{CF}} = 22$ Hz), 114.4, 117.5 (d, $^2J_{\text{CF}} = 23$ Hz), 120.8, 125.8 (d, $^3J_{\text{CF}} = 9$ Hz), 131.1 (d, $^3J_{\text{CF}} = 9$ Hz), 132.1, 141.0, 143.4, 146.5, 150.0, 162.1 (d, $^1J_{\text{CF}} = 249$ Hz); HRMS calcd for $\text{C}_{18}\text{H}_{17}\text{FN}_3$ ($\text{M}^+\text{+H}$): 294.1407, found: 294.1428.



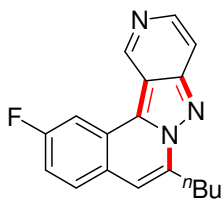
6-Cyclopropyl-2-fluoropyrido[3',4':3,4]pyrazolo[5,1-*a*]isoquinoline **3g**. ^1H NMR (400 MHz, CDCl_3) δ 1.01-1.05 (m, 2H), 1.34-1.39 (m, 2H), 2.94-2.96 (m, 1H), 7.13 (s, 1H), 7.46-7.50 (m, 2H), 8.19 (d, $J = 6.0$ Hz, 1H), 8.42 (d, $J = 5.5$ Hz, 1H), 8.56-8.60 (m, 1H), 9.58 (s, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 7.9, 11.9, 112.0 (d, $^2J_{\text{CF}} = 22$ Hz), 112.2, 114.4, 117.1 (d, $^2J_{\text{CF}} = 24$ Hz), 118.8, 121.7, 125.0 (d, $^3J_{\text{CF}} = 9$ Hz), 130.3 (d, $^3J_{\text{CF}} = 9$ Hz), 130.7, 137.6, 142.6, 144.1, 144.9, 161.7 (d, $^1J_{\text{CF}} = 248$ Hz); HRMS calcd for $\text{C}_{17}\text{H}_{13}\text{FN}_3$ ($\text{M}^+\text{+H}$): 278.1094, found: 278.1107.



6-Cyclopropyl-2-fluoropyrido[4',3':3,4]pyrazolo[5,1-a]isoquinoline **3g'**. ^1H NMR (400 MHz, CDCl_3) δ 1.01-1.05 (m, 2H), 1.33-1.39 (m, 2H), 2.94-2.99 (m, 1H), 7.14 (s, 1H), 7.45-7.54 (m, 2H), 7.81 (d, $J = 6.0$ Hz, 1H), 8.52 (d, $J = 6.0$ Hz, 1H), 8.67-8.71 (m, 1H), 9.87 (s, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 8.1, 12.0, 110.9, 111.6, 111.9 (d, $^2J_{\text{CF}} = 22$ Hz), 114.7, 117.6 (d, $^2J_{\text{CF}} = 24$ Hz), 120.7, 125.9 (d, $^3J_{\text{CF}} = 10$ Hz), 131.3 (d, $^3J_{\text{CF}} = 10$ Hz), 132.4, 142.5, 143.2, 146.5, 150.2, 162.2 (d, $^1J_{\text{CF}} = 249$ Hz); HRMS calcd for $\text{C}_{17}\text{H}_{13}\text{FN}_3$ ($\text{M}^+\text{+H}$): 278.1094, found: 278.1102.

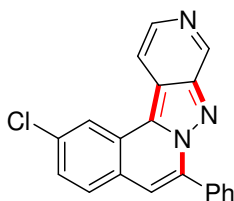


6-Butyl-2-fluoropyrido[3',4':3,4]pyrazolo[5,1-a]isoquinoline **3h**. ^1H NMR (400 MHz, CDCl_3) δ 1.04 (t, $J = 7.3$ Hz, 3H), 1.54-1.60 (m, 2H), 1.90-1.98 (m, 2H), 3.31-3.34 (m, 2H), 7.30-7.37 (m, 2H), 7.80-7.84 (m, 1H), 8.09-8.10 (m, 2H), 8.42-8.43 (m, 1H), 9.53 (s, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 14.0, 22.6, 28.7, 30.9, 107.7 (d, $^2J_{\text{CF}} = 24$ Hz), 114.1, 115.1, 116.7 (d, $^2J_{\text{CF}} = 24$ Hz), 119.2, 124.9, 126.1 (d, $^3J_{\text{CF}} = 10$ Hz), 129.5 (d, $^3J_{\text{CF}} = 9$ Hz), 129.9, 138.0, 139.2, 143.9, 144.7, 161.9 (d, $^1J_{\text{CF}} = 247$ Hz); HRMS calcd for $\text{C}_{18}\text{H}_{17}\text{FN}_3$ ($\text{M}^+\text{+H}$): 294.1407, found: 294.1410.

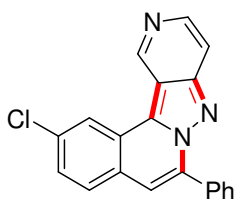


6-Butyl-2-fluoropyrido[4',3':3,4]pyrazolo[5,1-a]isoquinoline **3h'**. ^1H NMR (400 MHz, CDCl_3) δ 1.04 (t, $J = 7.3$ Hz, 3H), 1.53-1.60 (m, 2H), 1.94-2.01 (m, 2H), 3.38-3.42 (m, 2H), 7.41 (s, 1H), 7.44-7.48 (m, 1H), 7.81 (d, $J = 6.0$ Hz, 1H), 7.91-7.94 (m, 1H), 8.31 (d, $J = 7.3$ Hz, 1H), 8.55 (d, $J = 5.0$ Hz, 1H), 9.86 (s, 1H); ^{13}C NMR (100 MHz,

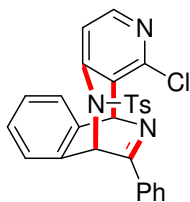
CDCl_3) δ 14.0, 22.6, 28.8, 31.1, 108.5 (d, $^2J_{\text{CF}} = 24$ Hz), 110.9, 114.8, 117.9 (d, $^2J_{\text{CF}} = 24$ Hz), 125.1 (d, $^3J_{\text{CF}} = 9$ Hz), 126.1, 129.8 (d, $^3J_{\text{CF}} = 9$ Hz), 131.7, 139.4, 143.4, 145.1, 146.2, 150.1, 162.0 (d, $^1J_{\text{CF}} = 247$ Hz); HRMS calcd for $\text{C}_{18}\text{H}_{17}\text{FN}_3$ ($\text{M}^+\text{+H}$): 294.1407, found: 294.1412.



2-Chloro-6-phenylpyrido[3',4':3,4]pyrazolo[5,1-*a*]isoquinoline **3i**. ^1H NMR (400 MHz, CDCl_3) δ 7.54-7.62 (m, 5H), 7.86 (d, $J = 8.7$ Hz, 1H), 7.96-7.97 (m, 2H), 8.23 (d, $J = 5.5$ Hz, 1H), 8.46 (s, 1H), 8.57 (s, 1H), 9.51 (s, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 114.1, 118.1, 119.0, 122.1, 126.6, 126.8, 128.5, 128.7, 129.3, 129.7, 130.1, 130.3, 133.0, 134.8, 138.3, 139.0, 144.5, 145.1; HRMS calcd for $\text{C}_{20}\text{H}_{13}\text{ClN}_3$ ($\text{M}^+\text{+H}$): 330.0798, found: 330.0796.

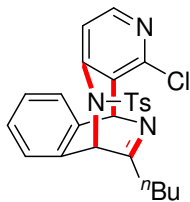


2-Chloro-6-phenylpyrido[4',3':3,4]pyrazolo[5,1-*a*]isoquinoline **3i'**. ^1H NMR (400 MHz, CDCl_3) δ 7.32-7.35 (m, 1H), 7.59-7.62 (m, 3H), 7.69 (d, $J = 8.3$ Hz, 1H), 7.73-7.77 (m, 1H), 7.84 (d, $J = 7.3$ Hz, 1H), 7.92-7.97 (m, 2H), 8.53 (s, 1H), 8.72 (s, 1H), 9.94 (s, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 117.7, 120.5, 122.9, 127.9, 128.2, 128.7, 129.4, 129.8, 130.1, 130.2, 130.3, 133.1, 135.1, 139.0, 143.4, 146.3, 151.2; HRMS calcd for $\text{C}_{20}\text{H}_{13}\text{ClN}_3$ ($\text{M}^+\text{+H}$): 330.0798, found: 330.0792.

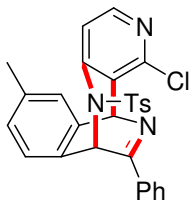


1-Chloro-13-phenyl-5-tosyl-6,11-dihydro-5*H*-11,6-(azeno)thieno[2,3-*b*]pyridine,

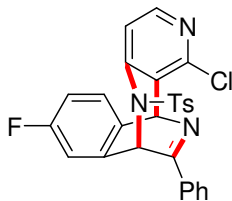
3-*b*]azepine **4a**. ^1H NMR (400 MHz, CDCl_3) δ 2.27 (s, 3H), 6.76 (s, 1H), 7.01 (d, $J = 8.3$ Hz, 2H), 7.08 (s, 1H), 7.19 (d, $J = 8.2$ Hz, 2H), 7.24 (d, $J = 6.0$ Hz, 1H), 7.40-7.57 (m, 6H), 7.72 (d, $J = 6.9$ Hz, 1H), 7.80 (d, $J = 6.0$ Hz, 1H), 8.08-8.10 (m, 2H); ^{13}C NMR (100 MHz, CDCl_3) δ 21.5, 53.2, 62.0, 114.7, 120.5, 125.0, 127.4, 127.5, 127.6, 128.6, 129.1, 129.3, 129.9, 131.6, 131.9, 134.5, 135.5, 141.9, 145.1, 145.5, 147.9, 150.9, 167.0; HRMS calcd for $\text{C}_{27}\text{H}_{21}\text{ClN}_3\text{O}_2\text{S}$ ($\text{M}^+\text{+H}$): 486.1043, found: 486.1043.



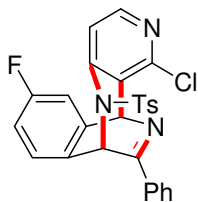
13-Butyl-1-chloro-5-tosyl-6,11-dihydro-5*H*-11,6-(azenometheno)benzo[*e*]pyrido[4,3-*b*]azepine **4b**. ^1H NMR (400 MHz, CDCl_3) δ 0.91 (t, $J = 7.2$ Hz, 3H), 1.28-1.37 (m, 2H), 1.65-1.72 (m, 2H), 2.29 (s, 3H), 2.61-2.79 (m, 2H), 6.19 (s, 1H), 6.49 (s, 1H), 7.07 (d, $J = 7.8$ Hz, 2H), 7.21 (t, $J = 7.3$ Hz, 3H), 7.37-7.45 (m, 2H), 7.49 (d, $J = 6.9$ Hz, 1H), 7.62 (d, $J = 7.3$ Hz, 1H), 7.81 (d, $J = 5.5$ Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 13.8, 21.5, 22.4, 27.7, 37.9, 55.6, 61.4, 114.7, 121.0, 124.9, 127.3, 127.5, 128.4, 129.2, 129.9, 131.7, 134.7, 142.3, 145.1, 145.4, 147.8, 150.7, 172.7; HRMS calcd for $\text{C}_{25}\text{H}_{25}\text{ClN}_3\text{O}_2\text{S}$ ($\text{M}^+\text{+H}$): 466.1356, found: 466.1345.



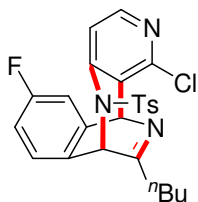
1-Chloro-9-methyl-13-phenyl-5-tosyl-6,11-dihydro-5*H*-11,6-(azenometheno)benzo[*e*]pyrido[4,3-*b*]azepine **4c**. ^1H NMR (400 MHz, CDCl_3) δ 2.28 (s, 3H), 2.42 (s, 3H), 6.70 (s, 1H), 7.02-7.05 (m, 3H), 7.22-7.26 (m, 4H), 7.37 (s, 1H), 7.48-7.50 (m, 3H), 7.59 (d, $J = 7.8$ Hz, 1H), 7.79 (d, $J = 6.0$ Hz, 1H), 8.07-8.09 (m, 2H); ^{13}C NMR (100 MHz, CDCl_3) δ 21.5, 53.1, 62.0, 114.6, 120.6, 125.6, 127.4, 127.6, 128.8, 129.0, 129.1, 129.9, 131.5, 134.6, 135.6, 139.5, 142.0, 145.0, 145.5, 147.8, 150.9, 167.3; HRMS calcd for $\text{C}_{28}\text{H}_{23}\text{ClN}_3\text{O}_2\text{S}$ ($\text{M}^+\text{+H}$): 500.1200, found: 500.1218.



1-Chloro-8-fluoro-13-phenyl-5-tosyl-6,11-dihydro-5H-11,6-(azeno)benzo[e]pyrido[4,3-b]azepine **4d**. ^1H NMR (400 MHz, CDCl_3) δ 2.30 (s, 3H), 6.75 (s, 1H), 7.03-7.13 (m, 4H), 7.23-7.26 (m, 3H), 7.42-7.54 (m, 5H), 7.83 (d, $J = 5.5$ Hz, 1H), 8.06 (d, $J = 6.4$ Hz, 2H); ^{13}C NMR (100 MHz, CDCl_3) δ 21.5, 52.9, 61.4, 114.8 (d, $^2J_{\text{CF}} = 23$ Hz), 114.9, 116.0 (d, $^2J_{\text{CF}} = 22$ Hz), 120.5, 126.7 (d, $^3J_{\text{CF}} = 8$ Hz), 127.4, 127.5, 129.1, 130.0, 131.7, 133.9 (d, $^3J_{\text{CF}} = 8$ Hz), 134.5, 135.3, 137.7, 145.3, 145.5, 148.0, 150.8, 162.8 (d, $^1J_{\text{CF}} = 247$ Hz), 166.4; HRMS calcd for $\text{C}_{27}\text{H}_{20}\text{ClFN}_3\text{O}_2\text{S}$ ($\text{M}^+\text{+H}$): 504.0949, found: 504.0968.



1-Chloro-9-fluoro-13-phenyl-5-tosyl-6,11-dihydro-5H-11,6-(azeno)benzo[e]pyrido[4,3-b]azepine **4e**. ^1H NMR (400 MHz, CDCl_3) δ 2.30 (s, 3H), 6.75 (s, 1H), 7.03-7.13 (m, 4H), 7.23-7.26 (m, 3H), 7.42-7.54 (m, 5H), 7.83 (d, $J = 6.0$ Hz, 1H), 8.06 (d, $J = 7.3$ Hz, 2H); ^{13}C NMR (100 MHz, CDCl_3) δ 21.5, 52.9, 61.4, 114.8 (d, $^2J_{\text{CF}} = 23$ Hz), 114.9, 116.0 (d, $^2J_{\text{CF}} = 21$ Hz), 126.7 (d, $^3J_{\text{CF}} = 8$ Hz), 127.4, 127.5, 129.0, 129.1, 130.0, 131.7, 133.9 (d, $^3J_{\text{CF}} = 8$ Hz), 134.5, 135.3, 137.7, 145.3, 145.5, 148.0, 150.8, 162.8 (d, $^1J_{\text{CF}} = 247$ Hz), 166.4; HRMS calcd for $\text{C}_{27}\text{H}_{20}\text{ClFN}_3\text{O}_2\text{S}$ ($\text{M}^+\text{+H}$): 504.0949, found: 504.0974.



13-Butyl-1-chloro-9-fluoro-5-tosyl-6,11-dihydro-5H-11,6-(azeno)benzo[e]pyrido[4,3-b]azepine **4f**. ^1H NMR (400 MHz, CDCl_3) δ 0.91 (t, $J = 7.3$ Hz, 3H),

1.28-1.37 (m, 2H), 1.64-1.71 (m, 2H), 2.32 (s, 3H), 2.61-2.79 (m, 2H), 6.17 (s, 1H), 6.46 (s, 1H), 7.11-7.13 (m, 3H), 7.20-7.28 (m, 4H), 7.57-7.60 (m, 1H), 7.83 (d, $J = 6.0$ Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 13.8, 21.5, 22.3, 27.6, 37.8, 54.9, 61.2, 112.5 (d, $^2J_{\text{CF}} = 22$ Hz), 114.7, 115.3 (d, $^2J_{\text{CF}} = 22$ Hz), 120.4, 127.4, 129.1 (d, $^3J_{\text{CF}} = 8$ Hz), 130.1, 134.7, 144.6 (d, $^3J_{\text{CF}} = 8$ Hz), 145.3, 145.4, 148.0, 150.8, 162.9 (d, $^1J_{\text{CF}} = 250$ Hz), 172.9; HRMS calcd for $\text{C}_{25}\text{H}_{24}\text{ClFN}_3\text{O}_2\text{S}$ ($\text{M}^+\text{+H}$): 484.1262, found: 484.1252.

