

One-pot synthesis of pyrrolo[1,2-*a*]quinoxaline derivatives via a copper-catalyzed aerobic oxidative domino reaction

Huanhuan Liu,^a Tiantian Duan^a, Zeyuan Zhang^a, Caixia Xie^a and Chen Ma^{*ab}

^a*School of Chemistry and Chemical Engineering, Shandong University, Jinan 250100, P. R. China*

^b*State Key Laboratory of Natural and Biomimetic Drugs, Peking University, Beijing, 100191, P. R. China*

Email: chenma@sdu.edu.cn (C. Ma); Tel.: +86 531 8836 4464; Fax: +86 531 8856 4464;

Table of Contents

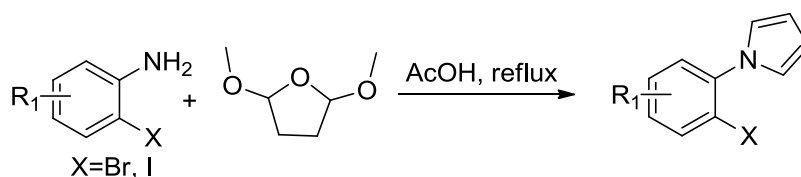
1. General information.....	S2
2. Preparation of starting materials.....	S2
3. General experimental procedures for the synthesis of 3.....	S2
4. UV–vis absorption and emission spectra of 3q, 3r, 3s, and 3t.....	S3
5. Spectra data.....	S5
6. References.....	S14
7. ¹H NMR and ¹³C NMR spectra.....	S15

1. General information

1-(2-halophenyl)-1*H*-pyrroles¹, 1-(2-halophenyl)-1*H*-indoles² were prepared according to literature procedures. DMSO was distilled from calcium hydride prior to use. Other reagents were commercially available and were used without further purification. All reactions were monitored by thin-layer chromatography (TLC). ¹H NMR and ¹³C NMR spectra were recorded on a Bruker Avance 400 (400 MHz) or 300 (300 MHz) spectrometer, using CDCl₃ or DMSO as solvent and tetramethylsilane (TMS) as internal standard. HRMS spectra were determined on a Q-TOF6510 spectrograph (Agilent).

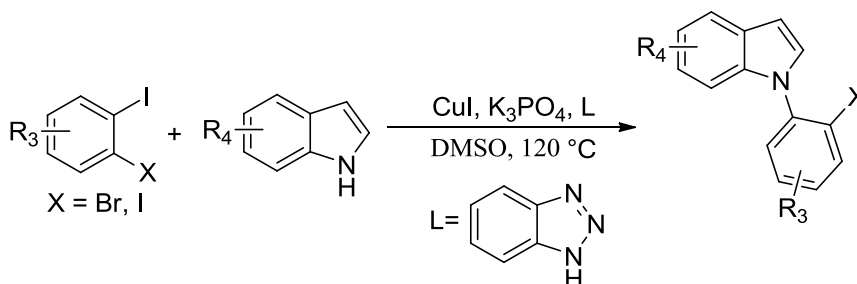
2. Preparation of starting materials

2.1 General procedure for preparation of 1-(2-halophenyl)-1*H*-pyrroles



A mixture of substituted 2-haloaniline (0.07 mol) and 2,5-dimethoxytetrahydrofuran (0.07 mol) in acetic acid (100 mL) was refluxed for 1 h with vigorous stirring. After cooling, the reaction mixture was poured into water (300 mL) and extracted with ethyl acetate twice (2×50 mL). The combined organic layers were dried with MgSO₄ and the solvent was removed in vacuo to afford a residue. The residue was purified by column chromatography on silica gel using petroleum ether/ethyl acetate as eluent to provide the desired product.

2.2 General procedure for preparation of 1-(2-halophenyl)-1*H*-indoles



CuI (10 mol %) and benzotriazole (20 mol %) ligand were added to a 5 mL round bottom flask containing the aryl halide (0.5 mmol), nitrogen heterocycles (1.1 equiv), and K₃PO₄ (2 equiv) in 2.0 mL of DMSO. The flask was sealed with a cap containing a PTFE septum. The mixture was then heated at 120 °C until the aryl halides were consumed, as determined by TLC. The reaction mixture was washed with ethyl acetate and water. The organic layer was then washed with brine and dried over Na₂SO₄. The solvent was removed in vacuo and the crude residue was purified by column chromatography on silica gel using hexanes or a mixture of hexane and ethylacetate as eluent.

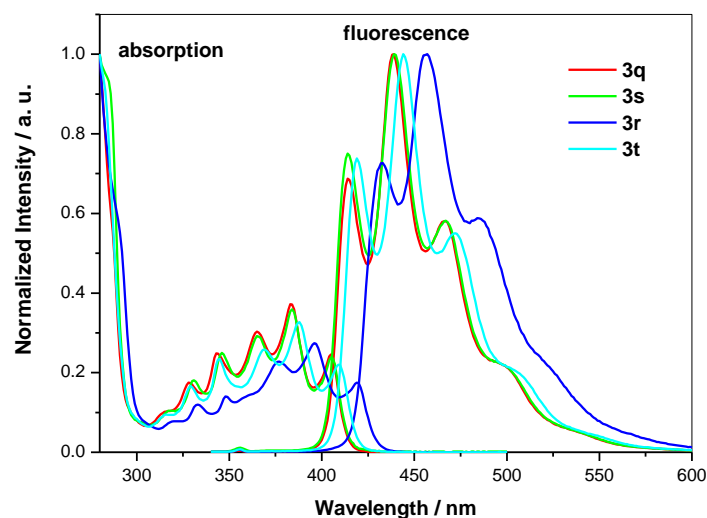
3. General experimental procedures for the synthesis of 3

A 25 mL flask equipped with a magnetic stirring bar was charged with substituted 1-(2-halophenyl)-1*H*-pyrrole **1** (0.3 mmol), α -amino acid **2** (1.2 mmol), K₃PO₄ (1.5 mmol), and Cu(OAc)₂ (0.06 mmol) in DMSO (3 mL). The mixture was allowed to stir under air at 130 °C, 3 h. After that, the reaction was cooled to room temperature, filtered through a short silica gel column eluting with ethyl acetate. The filtrate was diluted with brine (60 mL) and extracted with ethyl acetate

twice (2×30 mL). The combined organic layers were dried with MgSO₄ and the solvent was removed in vacuo to afford a residue. The residue was purified by column chromatography on silica gel using petroleum ether/ethyl acetate as eluent to provide the desired product.

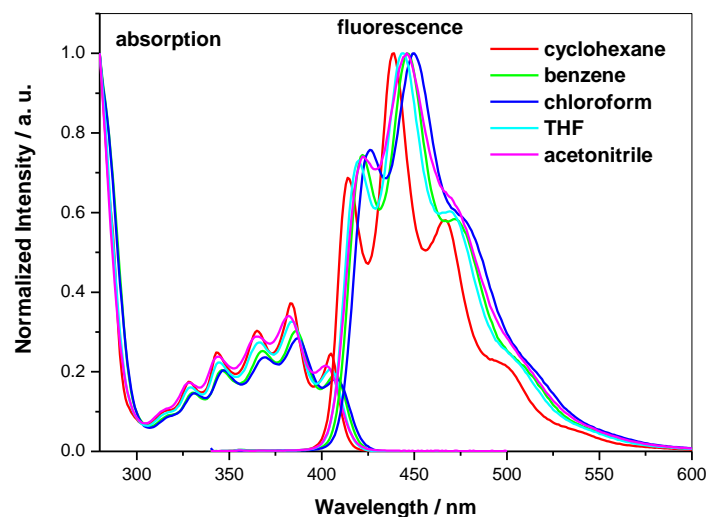
4. UV-vis absorption and emission spectra of 3q, 3r, 3s, and 3t

4.1 Absorption spectra and fluorescence spectra of 3q, 3r, 3s, and 3t in cyclohexane

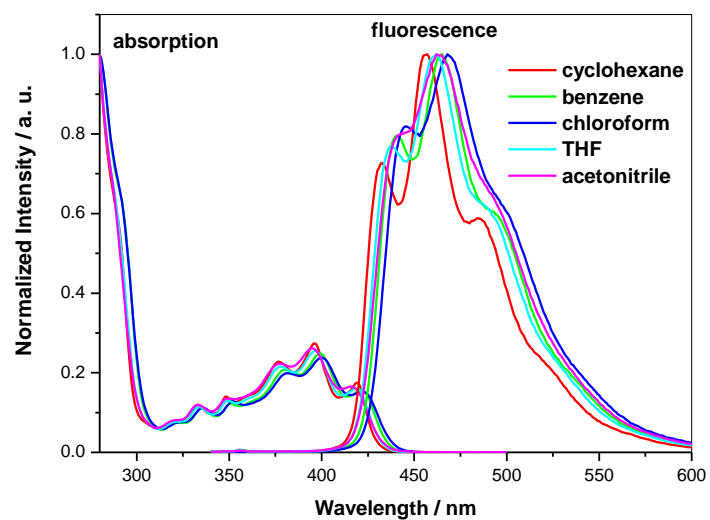


In cyclohexane, **3q** and **3s** showed similar absorption and emission spectra. The emission of **3t** has a small red shift compared with **3q** and **3s**. The emission of **3r** has a relatively bigger red shift compared with **3q** and **3s**. We can find that substituents at different positions of the compounds have impacts on their emission spectra.

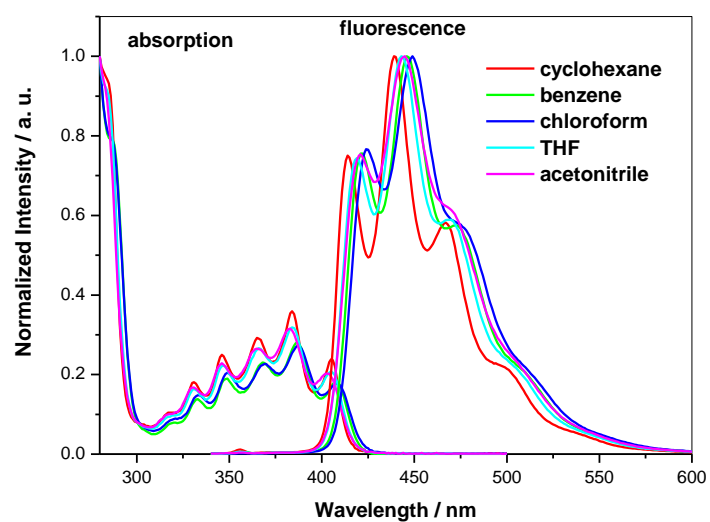
4.2 Absorption spectra and fluorescence spectra of 3q in different solvents



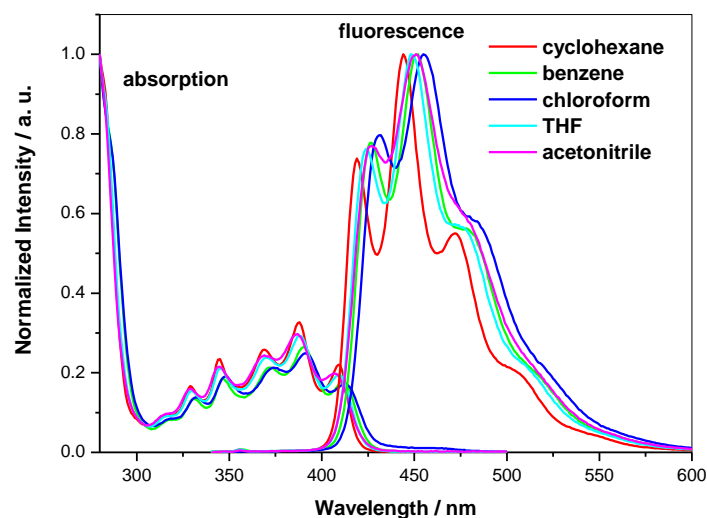
4.3 Absorption spectra and fluorescence spectra of 3r in different solvents



4.4 Absorption spectra and fluorescence spectra of 3s in different solvents

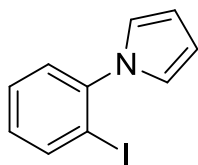


4.5 Absorption spectra and fluorescence spectra of 3t in different solvents

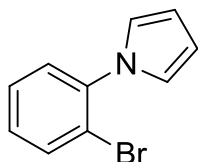


In different solvents, the Stokes shifts values of **3q**, **3r**, **3s** and **3t** are all small, which are reasonable for their rigid and planar structures.

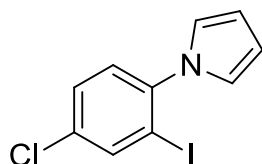
5. Spectra data



1-(2-iodophenyl)-1H-pyrrole 1a^{2,3}: colorless oil. ¹H NMR (CDCl₃, 300 MHz, ppm): δ 7.95 (d, *J*=7.8 Hz, 1H), 7.43-7.38 (m, 1H), 7.31 (dd, *J*₁=7.8 Hz, *J*₂=1.5 Hz, 1H), 7.12 (td, *J*₁=7.6 Hz, *J*₂=1.4 Hz, 1H), 6.82 (t, *J*=2.1 Hz, 2H), 6.34 (t, *J*=2.1 Hz, 2H); ¹³C NMR (CDCl₃, 75 MHz, ppm): δ 144.0, 139.9, 129.3, 128.9, 128.0, 122.1, 109.1, 95.8; HRMS called for: C₁₀H₉IN [M+H]⁺ 269.9774, found 269.9786.

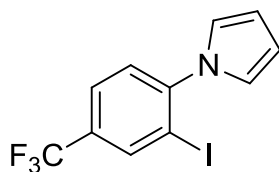


1-(2-bromophenyl)-1H-pyrrole 1b²: colorless oil. ¹H NMR (CDCl₃, 300 MHz, ppm): δ 7.70 (dd, *J*₁=8.1 Hz, *J*₂=1.2 Hz, 1H), 7.4-7.31 (m, 2H), 7.25-7.20 (m, 1H), 6.88 (t, *J*=2.1 Hz, 2H), 6.34 (t, *J*=2.1 Hz, 2H); ¹³C NMR (CDCl₃, 75 MHz, ppm): δ 140.4, 133.8, 128.8, 128.3, 128.1, 122.2, 119.9, 109.2; HRMS called for: C₁₀H₉BrN [M+H]⁺ 221.9913, found 221.9919.

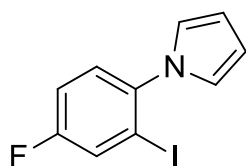


1-(4-chloro-2-iodophenyl)-1H-pyrrole 1c³: white solid. Mp = 64-65 °C. ¹H NMR (CDCl₃, 300 MHz, ppm): δ 7.92 (d, *J*=2.4 Hz, 1H), 7.40 (dd, *J*₁=8.4 Hz, *J*₂=2.4 Hz, 1H), 7.22 (d, *J*=8.4 Hz, 1H), 6.78 (t, *J*=2.3 Hz, 2H), 6.34 (d, *J*=2.3 Hz, 2H); ¹³C NMR (CDCl₃, 75 MHz, ppm): δ 142.8, 139.2, 134.2, 129.1,

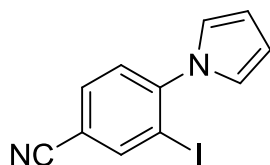
128.4, 122.1, 109.5, 96.0; HRMS called for: C₁₀H₈ClIN [M+H]⁺ 303.9385, found 303.9396.



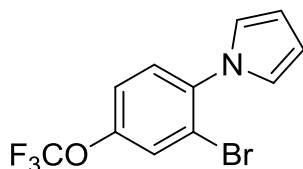
1-(2-iodo-4-(trifluoromethyl)phenyl)-1H-pyrrole 1d: white solid. Mp = 67-69 °C; IR (neat, cm⁻¹): 3130, 3102, 1924, 1604, 1507, 1322, 1335, 1160, 1130, 1069, 725, 707, 616; ¹H NMR (CDCl₃, 300 MHz, ppm): δ 8.20 (d, *J*=1.2 Hz, 1H), 7.69 (dd, *J*₁=8.1 Hz, *J*₂=1.5 Hz, 1H), 7.39 (d, *J*=8.4 Hz, 1H), 6.85 (t, *J*=2.1 Hz, 2H), 6.37 (t, *J*=2.1 Hz, 2H); ¹³C NMR (CDCl₃, 75 MHz, ppm): δ 147.0, 137.3 (q, *J*=3.8 Hz, 1C), 131.4, 130.9, 128.0, 126.2 (q, *J*=3.8 Hz, 1C), 124.5, 121.9, 120.9, 110.0, 95.0; HRMS called for: C₁₁H₈F₃IN [M+H]⁺ 337.9648, found 337.9664.



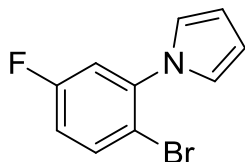
1-(4-fluoro-2-iodophenyl)-1H-pyrrole 1e³: white solid. Mp = 55-56 °C. ¹H NMR (CDCl₃, 300 MHz, ppm): δ 7.66 (dd, *J*₁=7.8 Hz, *J*₂=2.7 Hz, 1H), 7.30-7.25 (m, 1H), 7.16 (td, *J*₁=8.1 Hz, *J*₂=2.7 Hz, 1H), 6.77 (t, *J*=2.0 Hz, 2H), 6.34 (t, *J*=2.1 Hz, 2H); ¹³C NMR (CDCl₃, 75 MHz, ppm): δ 162.9 (d, *J*=252 Hz, 1C), 140.6, 128.7 (d, *J*=8.3 Hz, 1C), 126.7 (d, *J*=24.8 Hz, 1C), 122.3, 116.0 (d, *J*=1.5 Hz, 1C), 115.7 (d, *J*=1.5 Hz, 1C), 109.3, 96.0 (d, *J*=3.8 Hz, 1C), 95.9 (d, *J*=3.8 Hz, 1C); HRMS called for: C₁₀H₈FIN [M+H]⁺ 287.9680, found 287.9718.



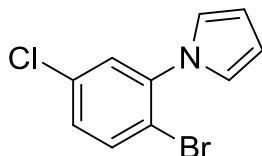
3-iodo-4-(1H-pyrrol-1-yl)benzotrile 1f: white solid. Mp = 129-130 °C; IR (neat, cm⁻¹): 3132, 3049, 2271, 2226, 1925, 1581, 1496, 1323, 1068, 844, 740, 617, 595; ¹H NMR (CDCl₃, 300 MHz, ppm): δ 8.24 (d, *J*=1.8 Hz, 1H), 7.72 (dd, *J*₁=8.1 Hz, *J*₂=1.8 Hz, 1H), 7.37 (d, *J*=8.4 Hz, 1H), 6.86 (t, *J*=2.1 Hz, 2H), 6.39 (t, *J*=2.1 Hz, 2H); ¹³C NMR (CDCl₃, 75 MHz, ppm): δ 147.7, 143.7, 132.7, 128.1, 121.8, 116.6, 112.9, 110.4, 94.7; HRMS called for: C₁₁H₈IN₂ [M+H]⁺ 294.9727, found 294.9767.



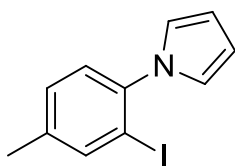
1-(2-bromo-4-(trifluoromethoxy)phenyl)-1H-pyrrole 1g: yellow oil; IR (neat, cm⁻¹): 3106, 2925, 2855, 1718, 1576, 1505, 1395, 1262, 1218, 1173, 1072, 826, 728, 621; ¹H NMR (CDCl₃, 300 MHz, ppm): δ 7.57 (d, *J*=1.8 Hz, 1H), 7.35 (d, *J*=8.7 Hz, 1H), 7.25-7.21 (m, 1H), 6.84 (t, *J*=2.1 Hz, 2H), 6.34 (t, *J*=2.1 Hz, 2H); ¹³C NMR (CDCl₃, 75 MHz, ppm): δ 148.1 (d, *J*=2.3 Hz, 1C), 139.3, 129.0, 126.3, 125.5, 122.2 (d, *J*=9.0 Hz, 1C), 120.6 (d, *J*=10.5 Hz, 1C), 118.7, 115.2 109.7; HRMS called for: C₁₁H₈BrF₃NO [M+H]⁺ 305.9736, found 305.9792.



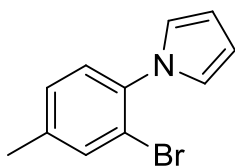
1-(2-bromo-5-fluorophenyl)-1H-pyrrole 1h⁴: colorless oil. ¹H NMR (CDCl₃, 300 MHz, ppm): δ 7.65-7.58 (m, 1H), 7.09 (dd, *J*₁=8.7 Hz, *J*₂=3.0 Hz, 1H), 7.00-6.93 (m, 1H), 6.88 (t, *J*=2.1 Hz, 2H), 6.34 (t, *J*=2.1 Hz, 2H); ¹³C NMR (CDCl₃, 75 MHz, ppm): δ 163.5 (d, *J*=247.5 Hz, 1C), 141.5 (d, *J*=9.8 Hz, 1C), 134.8 (d, *J*=8.3 Hz, 1C), 122.1, 116.1 (d, *J*=21.8 Hz, 1C), 115.9 (d, *J*=24.0 Hz, 1C), 113.9 (d, *J*=3.8 Hz, 1C), 109.8; HRMS called for: C₁₀H₈BrFN [M+H]⁺ 239.9819, found 239.9857.



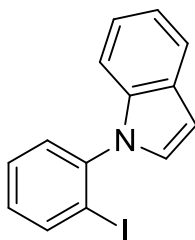
1-(2-bromo-5-chlorophenyl)-1H-pyrrole 1i: colorless oil; IR (neat, cm⁻¹): 3395, 3097, 2926, 2855, 1721, 1579, 1492, 1465, 1409, 1317, 1096, 1070, 1018, 813, 728, 624; ¹H NMR (CDCl₃, 300 MHz, ppm): δ 7.62 (d, *J*=8.7 Hz, 1H), 7.34 (d, *J*=2.7 Hz, 1H), 7.23 (dd, *J*₁=8.7 Hz, *J*₂=2.4 Hz, 1H), 6.88 (t, *J*=2.1 Hz, 2H), 6.35 (t, *J*=2.1 Hz, 2H); ¹³C NMR (CDCl₃, 75 MHz, ppm): δ 141.3, 134.6, 133.8, 128.7, 128.3, 122.0, 117.6, 109.7; HRMS called for: C₁₀H₈BrClN [M+H]⁺ 255.9352, found 255.9372.



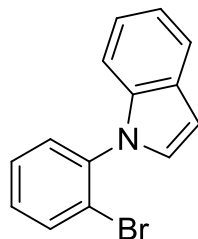
1-(2-iodo-4-methylphenyl)-1H-pyrrole 1j³: colorless oil. ¹H NMR (CDCl₃, 300 MHz, ppm): δ 7.76 (s, 1H), 7.18 (t, *J*=3.9 Hz, 2H), 6.78 (t, *J*=2.1 Hz, 2H), 6.32 (t, *J*=2.1 Hz, 2H), 2.36 (s, 3H); ¹³C NMR (CDCl₃, 75 MHz, ppm): δ 141.6, 140.2, 139.7, 129.6, 127.6, 122.2, 109.0, 95.8, 20.5; HRMS called for: C₁₁H₁₁IN [M+H]⁺ 283.9931, found 283.9890.



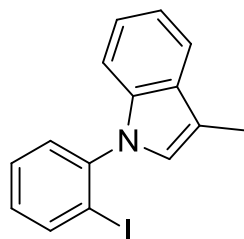
1-(2-bromo-4-methylphenyl)-1H-pyrrole 1k⁵: colorless oil. ¹H NMR (CDCl₃, 300 MHz, ppm): δ 7.50 (d, *J*=0.6 Hz, 1H), 7.22 (d, *J*=7.8 Hz, 1H), 7.17 (dd, *J*₁=7.8 Hz, *J*₂=1.2 Hz, 1H), 6.84 (t, *J*=2.1 Hz, 2H), 6.32 (t, *J*=2.1 Hz, 2H), 2.38 (s, 3H); ¹³C NMR (CDCl₃, 75 MHz, ppm): δ 139.2, 137.9, 134.0, 128.8, 127.9, 122.3, 119.6, 109.0, 20.7; HRMS called for: C₁₁H₁₁BrN [M+H]⁺ 236.0069, found 236.0056.



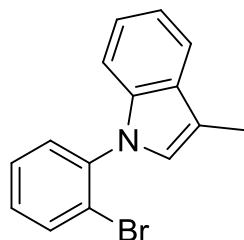
1-(2-iodophenyl)-1*H*-indole 1l²: colorless oil. ¹H NMR (CDCl₃, 300 MHz, ppm): δ 8.02 (dd, *J*₁=8.1 Hz, *J*₂=1.2 Hz, 1H), 7.71-7.66 (m, 1H), 7.48 (td, *J*₁=7.5 Hz, *J*₂=1.2 Hz, 1H), 7.37 (dd, *J*₁=7.8 Hz, *J*₂=1.8 Hz, 1H), 7.21-7.12 (m, 4H), 7.06-7.02 (m, 1H), 6.69 (d, *J*=3.0 Hz, 1H); ¹³C NMR (CDCl₃, 75 MHz, ppm): δ 142.1, 140.2, 136.7, 129.9, 129.4, 129.2, 128.6, 128.4, 122.3, 121.0, 120.3, 110.7, 103.2, 97.7; HRMS called for: C₁₄H₁₁IN [M+H]⁺ 319.9931, found 319.9901.



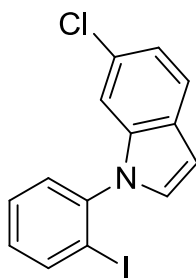
1-(2-bromophenyl)-1*H*-indole 1m²: colorless oil. ¹H NMR (CDCl₃, 400 MHz, ppm): δ 7.78-7.76 (m, 1H), 7.70-7.68 (m, 1H), 7.44-7.42 (m, 2H), 7.33-7.29 (m, 1H), 7.23 (t, *J*=1.6 Hz, 1H), 7.19-7.16 (m, 2H), 7.11-7.09 (m, 1H), 6.70 (d, *J*=3.2 Hz, 1H); ¹³C NMR (CDCl₃, 100 MHz, ppm): δ 138.5, 136.8, 134.0, 129.8, 129.5, 128.7, 128.4, 128.3, 122.3, 122.0, 121.0, 120.3, 110.6, 103.2; HRMS called for: C₁₄H₁₁BrN [M+H]⁺ 272.0069, found 272.0061.



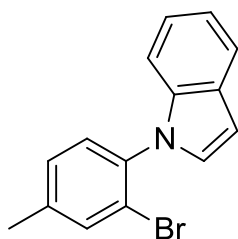
1-(2-iodophenyl)-3-methyl-1*H*-indole 1n²: colorless oil. ¹H NMR (CDCl₃, 300 MHz, ppm): δ 8.01 (d, *J*=8.1 Hz, 1H), 7.64 (t, *J*=4.5 Hz, 1H), 7.47 (t, *J*=7.5 Hz, 1H), 7.34 (d, *J*=4.8 Hz, 1H), 7.20-7.11 (m, 3H), 7.04-6.97 (m, 2H), 2.40 (s, 3H); ¹³C NMR (CDCl₃, 75 MHz, ppm): δ 142.3, 140.2, 137.0, 129.6, 129.4, 129.2, 128.9, 126.1, 122.2, 119.6, 119.1, 112.4, 110.7, 97.5, 9.7; HRMS called for: C₁₅H₁₃IN [M+H]⁺ 334.0087, found 333.9993.



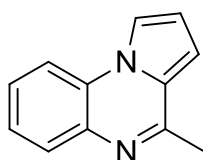
1-(2-bromophenyl)-3-methyl-1*H*-indole 1o²: colorless oil. ¹H NMR (CDCl₃, 300 MHz, ppm): δ 7.76-7.73 (m, 1H), 7.64-7.61 (m, 1H), 7.44-7.37 (m, 2H), 7.30-7.24 (m, 1H), 7.19-7.15 (m, 2H), 7.10-7.05 (m, 1H), 7.01 (d, *J*=1.2 Hz, 1H), 2.39 (s, 3H); ¹³C NMR (CDCl₃, 75 MHz, ppm): δ 138.8, 137.0, 134.0, 129.7, 129.1, 129.0, 128.3, 126.2, 122.2, 121.8, 119.7, 119.1, 112.4, 110.6, 9.7; HRMS called for: C₁₅H₁₃BrN [M+H]⁺ 286.0226, found 286.0202.



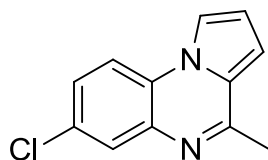
6-chloro-1-(2-iodophenyl)-1H-indole 1p: yellow oil; IR (neat, cm^{-1}): 3785, 3698, 3662, 3634, 3057, 1668, 1607, 1580, 1506, 1478, 1329, 1232, 1207, 1142, 901, 803, 759, 717; ^1H NMR (CDCl_3 , 400 MHz, ppm): δ 8.03 (dd, $J_1=8.0$ Hz, $J_2=1.2$ Hz, 1H), 7.59 (d, $J=8.4$ Hz, 1H), 7.50 (td, $J_1=7.6$ Hz, $J_2=1.3$ Hz, 1H), 7.37 (dd, $J_1=7.8$ Hz, $J_2=1.6$ Hz, 1H), 7.21-7.11 (m, 3H), 7.01 (t, $J=0.6$ Hz, 1H), 6.66 (dd, $J_1=3.2$ Hz, $J_2=0.5$ Hz, 1H); ^{13}C NMR (CDCl_3 , 100 MHz, ppm): δ 141.5, 140.3, 137.1, 130.2, 129.4, 129.3, 128.4, 126.9, 121.8, 121.0, 110.6, 103.2, 97.5; HRMS called for: $\text{C}_{14}\text{H}_{10}\text{ClIN}$ $[\text{M}+\text{H}]^+$ 353.9541, found 353.9617.



1-(2-bromo-4-methylphenyl)-1H-indole 1q: colorless oil; IR (neat, cm^{-1}): 3052, 2921, 1604, 1504, 1456, 1332, 1307, 1234, 1211, 1136, 824, 741; ^1H NMR (CDCl_3 , 300 MHz, ppm): δ 7.70-7.67 (m, 1H), 7.59 (d, $J=0.6$ Hz, 1H), 7.31 (d, $J=8.1$ Hz, 1H), 7.22-7.15 (m, 4H), 7.10-7.07 (m, 1H), 6.68 (d, $J=3.3$ Hz, 1H), 2.43 (s, 3H); ^{13}C NMR (CDCl_3 , 75 MHz, ppm): δ 139.9, 136.9, 135.8, 134.2, 129.3, 129.0, 128.8, 128.3, 122.1, 121.7, 120.9, 120.1, 110.6, 102.9, 20.9; HRMS called for: $\text{C}_{15}\text{H}_{13}\text{BrN}$ $[\text{M}+\text{H}]^+$ 286.0226, found 286.0221.

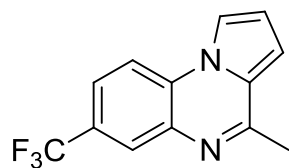


4-Methylpyrrolo[1,2-*a*]quinoxaline 3a⁶: yellow solid (X = I, 36.5 mg, 67%; X = Br, 29.5 mg, 54%). Mp = 132-133 °C. ^1H NMR (300 MHz, DMSO): δ 8.43 (t, $J=1.2$ Hz, 1H), 8.26 (dd, $J_1=8.1$ Hz, $J_2=0.9$ Hz, 1H), 7.83 (dd, $J_1=8.1$ Hz, $J_2=1.5$ Hz, 1H), 7.57 (td, $J_1=7.2$ Hz, $J_2=1.5$ Hz, 1H), 7.48-7.43 (m, 1H), 7.03 (dd, $J_1=3.9$ Hz, $J_2=0.9$ Hz, 1H), 6.92 (dd, $J_1=3.9$ Hz, $J_2=3.0$ Hz, 1H), 2.65 (s, 3H); ^{13}C NMR (DMSO, 100 MHz, ppm): δ 153.6, 135.8, 129.1, 127.5, 127.3, 125.9, 125.6, 116.3, 115.1, 114.0, 107.2, 22.0; HRMS called for: $\text{C}_{12}\text{H}_{11}\text{N}_2$ $[\text{M}+\text{H}]^+$ 183.0917, found 183.0916.

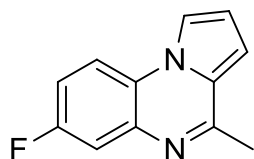


7-chloro-4-methylpyrrolo[1,2-*a*]quinoxaline 3b⁶: yellow solid (50.5 mg, 78%). Mp = 175-176 °C. ^1H NMR (CDCl_3 , 300 MHz, ppm): δ 7.89-7.86 (m, 2H), 7.76 (d, $J=8.7$ Hz, 1H), 7.44 (dd, $J_1=9.0$ Hz, $J_2=2.4$ Hz, 1H), 6.92 (dd, $J_1=3.9$ Hz, $J_2=1.2$ Hz, 1H), 6.87 (dd, $J_1=3.9$ Hz, $J_2=3.0$ Hz, 1H), 2.72 (s, 3H); ^{13}C NMR (CDCl_3 , 75 MHz, ppm): δ 154.9, 136.9, 130.2, 128.7, 127.0, 126.2, 126.0, 114.8, 114.6,

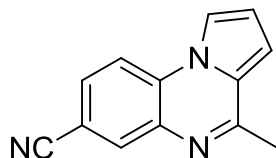
113.9, 107.2, 22.0; HRMS called for: C₁₂H₁₀ClN₂ [M+H]⁺ 217.0527, found 217.0537.



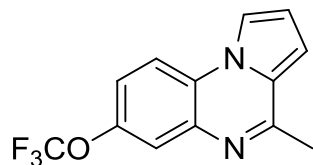
4-methyl-7-(trifluoromethyl)pyrrolo[1,2-a]quinoxaline 3c: yellow solid (60.7 mg, 81%). Mp = 125-127 °C; IR (neat, cm⁻¹): 3465, 3150, 3092, 2923, 2853, 1877, 1774, 1626, 1536, 1501, 1457, 1426, 1327, 1172, 1100, 899, 811, 721; ¹H NMR (CDCl₃, 400 MHz, ppm): δ 8.19 (s, 1H), 7.93-7.92 (m, 1H), 7.90 (d, *J*=8.6 Hz, 1H), 7.70 (dd, *J*₁=8.6 Hz, *J*₂=1.6 Hz, 1H), 6.96 (dd, *J*₁=4.0 Hz, *J*₂=1.0 Hz, 1H), 6.91-6.90 (m, 1H), 2.74 (s, 3H); ¹³C NMR (CDCl₃, 100 MHz, ppm): δ 155.2, 135.6, 129.4, 127.4 (d, *J*=33.0 Hz, 1C), 126.9 (q, *J*=4.0 Hz, 1C), 126.4, 125.3 (d, *J*=271.0 Hz, 1C), 123.4 (q, *J*=4.0 Hz, 1C), 114.9, 114.5, 114.3, 107.6, 22.0; HRMS called for: C₁₃H₁₀F₃N₂ [M+H]⁺ 251.0791, found 251.0795.



7-fluoro-4-methylpyrrolo[1,2-a]quinoxaline 3d: yellow solid (42.6 mg, 71%). Mp = 167-168 °C; IR (neat, cm⁻¹): 3099, 3036, 2930, 2845, 1585, 1485, 1412, 1375, 1288, 1244, 1143, 810, 739; ¹H NMR (CDCl₃, 400 MHz, ppm): δ 7.86 (d, *J*=1.3 Hz, 1H), 7.80-7.76 (m, 1H), 7.59 (dd, *J*₁=9.6 Hz, *J*₂=2.8 Hz, 1H), 7.23 (td, *J*₁=8.4 Hz, *J*₂=2.8 Hz, 1H), 6.91 (d, *J*=3.1 Hz, 1H), 6.86 (t, *J*=3.3 Hz, 1H), 2.73 (s, 3H); ¹³C NMR (CDCl₃, 100 MHz, ppm): δ 161.0 (d, *J*=242.0 Hz, 1C), 155.0, 137.2, 137.1, 126.0, 124.0, 114.8 (d, *J*=8.0 Hz, 1C), 114.7 (d, *J*=20.0 Hz, 1C), 114.5, 113.7, 106.9, 22.0; HRMS called for: C₁₂H₁₀FN₂ [M+H]⁺ 201.0823, found 201.0865.

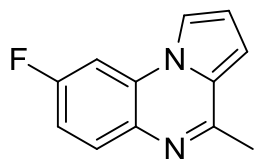


4-methylpyrrolo[1,2-a]quinoxaline-7-carbonitrile 3e: yellow solid (48.4 mg, 78%). Mp = 232-234 °C; IR (neat, cm⁻¹): 3439, 3110, 3030, 2920, 2851, 1924, 1614, 1528, 1493, 1423, 1365, 1311, 1041, 884, 831, 736; ¹H NMR (CDCl₃, 300 MHz, ppm): δ 8.19 (s, 1H), 7.93 (t, *J*=9.3 Hz, 2H), 7.72 (d, *J*=8.4 Hz, 1H), 6.98-6.93 (m, 2H), 2.74 (s, 3H); ¹³C NMR (CDCl₃, 75 MHz, ppm): δ 155.8, 136.0, 133.9, 130.3, 129.6, 126.4, 118.5, 115.2, 115.0, 114.8, 108.5, 108.1, 22.0; HRMS called for: C₁₃H₁₀N₃ [M+H]⁺ 208.0869, found 208.0806.

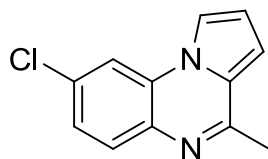


4-methyl-7-(trifluoromethoxy)pyrrolo[1,2-a]quinoxaline 3f: yellow solid (66.2 mg, 83%). Mp = 77-78 °C; IR (neat, cm⁻¹): 3320, 3097, 2924, 1590, 1490, 1419, 1355, 1270, 1213, 1160, 954, 876, 743, 716; ¹H NMR (CDCl₃, 300 MHz, ppm): δ 7.88 (q, *J*=1.2 Hz, 1H), 7.83 (s, 1H), 7.80-7.78 (m, 1H), 7.34 (dd, *J*₁=8.7 Hz, *J*₂=2.1 Hz, 1H), 6.93-6.85 (m, 2H), 2.73 (s, 3H); ¹³C NMR (CDCl₃, 75 MHz, ppm): δ 155.2, 146.0, 136.8, 126.2, 125.9, 122.3, 121.1, 119.9, 118.9, 114.7, 114.0, 107.3, 22.0; HRMS called for:

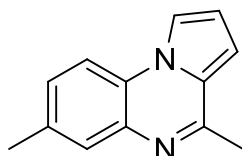
C₁₃H₁₀F₃N₂O [M+H]⁺ 267.0740, found 267.0797.



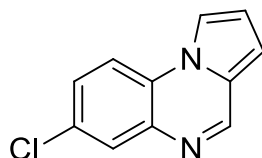
8-fluoro-4-methylpyrrolo[1,2-*a*]quinoxaline 3g: yellow solid (35.4 mg, 59%). Mp = 150-151 °C; IR (neat, cm⁻¹): 3097, 3036, 2943, 1621, 1533, 1482, 1419, 1358, 1230, 1198, 867, 816, 731; ¹H NMR (CDCl₃, 400 MHz, ppm): δ 7.89-7.85 (m, 1H), 7.78 (s, 1H), 7.49 (dd, *J*₁=9.2 Hz, *J*₂=2.3 Hz, 1H), 7.16 (td, *J*₁=8.5 Hz, *J*₂=2.3 Hz, 1H), 6.88-6.87 (m, 2H), 2.71 (s, 3H); ¹³C NMR (CDCl₃, 100 MHz, ppm): δ 162.2 (d, *J* = 246.0 Hz, 1C), 152.8, 132.5, 131.0 (d, *J* = 10.0 Hz, 1C), 128.0 (d, *J* = 11.0 Hz, 1C), 126.0, 114.4, 114.0, 113.1 (d, *J* = 23.0 Hz, 1C), 106.76, 100.6 (d, *J* = 26.0 Hz, 1C), 21.9; HRMS called for: C₁₂H₁₀FN₂ [M+H]⁺ 201.0823, found 201.0830.



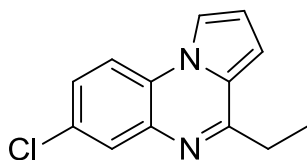
8-chloro-4-methylpyrrolo[1,2-*a*]quinoxaline 3h: yellow solid (40.2 mg, 62%). Mp = 139-140 °C; IR (neat, cm⁻¹): 3468, 3100, 2924, 2851, 1877, 1609, 1530, 1481, 1421, 1380, 1353, 1124, 1087, 1036, 846, 815, 743; ¹H NMR (CDCl₃, 300 MHz, ppm): δ 7.82-7.78 (m, 3H), 7.38 (dd, *J*₁=8.7 Hz, *J*₂=2.4 Hz, 1H), 6.90-6.85 (m, 2H), 2.71 (s, 3H); ¹³C NMR (CDCl₃, 75 MHz, ppm): δ 153.9, 134.5, 132.2, 130.4, 127.9, 126.1, 125.5, 114.5, 114.1, 113.8, 107.0, 22.0; HRMS called for: C₁₂H₁₀ClN₂ [M+H]⁺ 217.0527, found 217.0553.



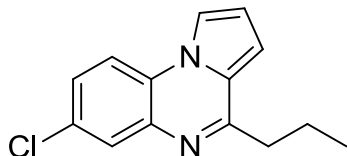
4,7-dimethylpyrrolo[1,2-*a*]quinoxaline 3i: yellow solid (X = I, 27.6 mg, 47%; X = Br, 22.3 mg, 38%). Mp = 128-129 °C; IR (neat, cm⁻¹): 3470, 3100, 3039, 2921, 2856, 1901, 1740, 1589, 1528, 1493, 1455, 1417, 1381, 1308, 1088, 1035, 810, 732; ¹H NMR (CDCl₃, 400 MHz, ppm): δ 7.87 (d, *J*=1.2 Hz, 1H), 7.72 (t, *J*=4.1 Hz, 2H), 7.30-7.26 (m, 1H), 6.88-6.82 (m, 2H), 2.73 (s, 3H), 2.49 (s, 3H); ¹³C NMR (CDCl₃, 100 MHz, ppm): δ 153.5, 134.9, 129.0, 128.1, 126.2, 125.1, 114.1, 113.4, 113.3, 106.4, 21.9, 21.1; HRMS called for: C₁₃H₁₃N₂ [M+H]⁺ 197.1073, found 197.1076.



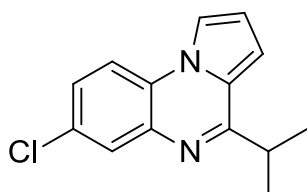
7-chloropyrrolo[1,2-*a*]quinoxaline 3j⁶: yellow solid (43.6 mg, 72%). Mp = 174-175 °C. ¹H NMR (CDCl₃, 300 MHz, ppm): δ 8.80 (s, 1H), 7.94 (d, *J*=2.1 Hz, 1H), 7.89 (s, 1H), 7.80 (d, *J*=9.0 Hz, 1H), 7.49 (dd, *J*₁=9.0 Hz, *J*₂=2.4 Hz, 1H), 6.928-6.880 (m, 2H); ¹³C NMR (CDCl₃, 75 MHz, ppm): δ 146.8, 136.8, 130.4, 129.5, 127.8, 126.7, 126.4, 115.0, 114.5, 114.4, 108.0; HRMS called for: C₁₁H₈ClN₂ [M+H]⁺ 203.0371, found 203.0411.



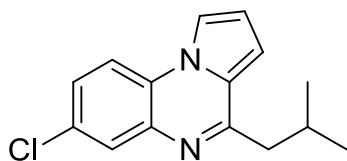
7-chloro-4-ethylpyrrolo[1,2-*a*]quinoxaline 3k⁶: yellow solid (51.7 mg, 75%). Mp = 112-113 °C. ¹H NMR (CDCl₃, 400 MHz, ppm): δ 7.95 (s, 1H), 7.88 (d, *J*=1.3 Hz, 1H), 7.77 (d, *J*=8.8 Hz, 1H), 7.44 (dd, *J*₁=8.7 Hz, *J*₂=2.3 Hz, 1H), 6.95 (d, *J*=2.8 Hz, 1H), 6.88 (t, *J*=3.3 Hz, 1H), 3.09 (q, *J*=7.6 Hz, 2H), 1.47 (t, *J*=7.6 Hz, 3H); ¹³C NMR (CDCl₃, 100 MHz, ppm): δ 159.5, 130.3, 128.9, 127.0, 125.9, 125.6, 114.8, 113.9, 107.0, 28.7, 12.4; HRMS called for: C₁₃H₁₂ClN₂ [M+H]⁺ 231.0684, found 231.0687.



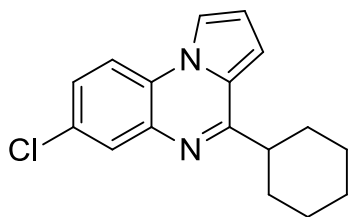
7-chloro-4-propylpyrrolo[1,2-*a*]quinoxaline 3l⁶: yellow solid (50.5 mg, 69%). Mp = 71-73 °C. ¹H NMR (CDCl₃, 400 MHz, ppm): δ 7.92 (d, *J*=1.7 Hz, 1H), 7.86 (d, *J*=1.4 Hz, 1H), 7.75 (d, *J*=8.7 Hz, 1H), 7.42 (dd, *J*₁=8.8 Hz, *J*₂=2.3 Hz, 1H), 6.93 (d, *J*=3.4 Hz, 1H), 6.86 (t, *J*=3.3 Hz, 1H), 3.00 (t, *J*=7.7 Hz, 2H), 1.96-1.90 (m, 2H), 1.09 (t, *J*=7.4 Hz, 3H); ¹³C NMR (CDCl₃, 100 MHz, ppm): δ 158.6, 130.2, 128.9, 126.9, 126.0, 125.9, 114.8, 114.5, 113.9, 106.9, 37.7, 21.8, 14.3; HRMS called for: C₁₄H₁₄ClN₂ [M+H]⁺ 245.0840, found 245.0847.



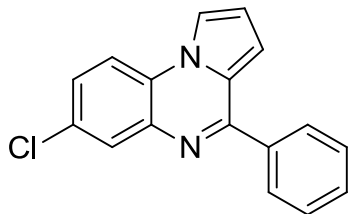
7-chloro-4-isopropylpyrrolo[1,2-*a*]quinoxaline 3m: yellow solid (33.7 mg, 46%). Mp = 68-69 °C; IR (neat, cm⁻¹): 3742, 3679, 3649, 3622, 3143, 2965, 2924, 1741, 1694, 1517, 1480, 1423, 1362, 1313, 1205, 957, 914, 720; ¹H NMR (CDCl₃, 400 MHz, ppm): δ 7.95 (s, 1H), 7.87 (s, 1H), 7.75 (d, *J*=8.7 Hz, 1H), 7.42 (dd, *J*₁=8.7 Hz, *J*₂=1.7 Hz, 1H), 6.94 (s, 1H), 6.85 (s, 1H), 3.50-3.44 (m, 1H), 1.45 (d, *J*=6.8 Hz, 6H); ¹³C NMR (CDCl₃, 100 MHz, ppm): δ 162.9, 130.1, 129.1, 126.8, 125.9, 125.3, 114.6, 114.3, 113.7, 106.4, 33.2, 21.0; HRMS called for: C₁₄H₁₄ClN₂ [M+H]⁺ 245.0840, found 245.0895.



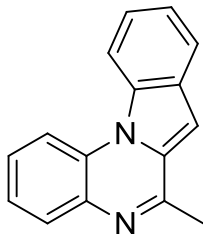
7-chloro-4-isobutylpyrrolo[1,2-*a*]quinoxaline 3n: yellow solid (51.9 mg, 67%). Mp = 68-69 °C; IR (neat, cm⁻¹): 3785, 3703, 3662, 3634, 3103, 3016, 2958, 2926, 2865, 1730, 1581, 1526, 1478, 1420, 1375, 1292, 1202, 1099, 809, 731; ¹H NMR (CDCl₃, 400 MHz, ppm): δ 7.94 (s, 1H), 7.87 (d, *J*=1.5 Hz, 1H), 7.76 (d, *J*=8.8 Hz, 1H), 7.43 (dd, *J*₁=8.8 Hz, *J*₂=2.3 Hz, 1H), 6.93 (d, *J*=3.5 Hz, 1H), 6.86 (t, *J*=3.3 Hz, 1H), 2.89 (d, *J*=7.3 Hz, 1H), 2.44-2.34 (m, 1H), 1.04 (d, *J*=6.6 Hz, 6H); ¹³C NMR (CDCl₃, 100 MHz, ppm): δ 158.1, 130.2, 128.9, 126.9, 126.5, 125.8, 114.8, 114.6, 113.9, 107.3, 44.5, 28.5, 22.9; HRMS called for: C₁₅H₁₆ClN₂ [M+H]⁺ 259.1000, found 259.1025.



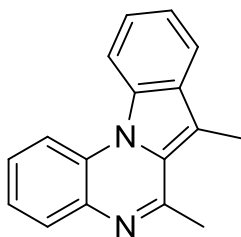
7-chloro-4-cyclohexylpyrrolo[1,2-*a*]quinoxaline 3o: yellow solid (29.8 mg, 35%). Mp = 74-75 °C; IR (neat, cm⁻¹): 3785, 3698, 3662, 3634, 3094, 2925, 2851, 1730, 1668, 1583, 1524, 1482, 1423, 1351, 1299, 794, 739, 711; ¹H NMR (CDCl₃, 400 MHz, ppm): δ 7.93 (d, *J*=2.3 Hz, 1H), 7.85 (dd, *J*₁=2.7 Hz, *J*₂=1.1 Hz, 1H), 7.73 (d, *J*=8.8 Hz, 1H), 7.40 (dd, *J*₁=8.7 Hz, *J*₂=2.3 Hz, 1H), 6.94 (dd, *J*₁=4.0 Hz, *J*₂=1.0 Hz, 1H), 6.84-6.82 (m, 1H), 3.11-3.08 (m, 1H), 2.02-2.01 (m, 2H), 1.98-1.91 (m, 2H), 1.84-1.78 (m, 3H), 1.50-1.39 (m, 3H); ¹³C NMR (CDCl₃, 100 MHz, ppm): δ 162.3, 137.2, 130.0, 129.1, 126.7, 125.8, 125.5, 114.6, 114.3, 113.6, 106.3, 43.5, 31.2, 26.5, 26.1; HRMS called for: C₁₇H₁₈ClN₂ [M+H]⁺ 285.1153, found 285.1198.



7-chloro-4-cyclohexylpyrrolo[1,2-*a*]quinoxaline 3p⁶: yellow solid (10.0 mg, 12%). Mp = 154-155 °C. ¹H NMR (CDCl₃, 300 MHz, ppm): δ 8.05 (s, 1H), 8.01-7.97 (m, 3H), 7.81 (d, *J*=8.7 Hz, 1H), 7.59-7.53 (m, 3H), 7.48 (dd, *J*₁=8.7 Hz, *J*₂=2.1 Hz, 1H), 7.03 (d, *J*=3.6 Hz, 1H), 6.92 (t, *J*=3.2 Hz, 1H); ¹³C NMR (CDCl₃, 75 MHz, ppm): δ 155.4, 137.1, 130.5, 130.2, 129.5, 128.7, 127.5, 125.8, 125.2, 115.1, 114.8, 114.5, 109.5; HRMS called for: C₁₇H₁₂ClN₂ [M+H]⁺ 279.0684, found 279.0695.

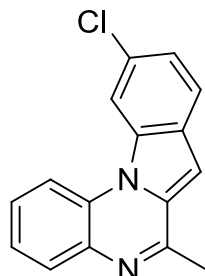


6-methylindolo[1,2-*a*]quinoxaline 3q: yellow solid (X = I, 51.5 mg, 74%; X = Br, 43.8 mg, 63%). Mp = 104-105 °C; IR (neat, cm⁻¹): 3042, 2919, 1531, 1473, 1445, 1396, 1363, 1300, 1204, 933, 842, 788, 745; ¹H NMR (CDCl₃, 400 MHz, ppm): δ 8.41(t, *J*=8.8 Hz, 2H), 7.90 (d, *J*=8.0 Hz, 2H), 7.53-7.45 (m, 2H), 7.39-7.33 (m, 2H), 7.11 (s, 1H), 2.75 (s, 3H); ¹³C NMR (CDCl₃, 100 MHz, ppm): δ 155.3, 135.8, 133.0, 130.3, 129.8, 129.6, 129.1, 127.8, 124.3, 124.1, 122.7, 122.6, 114.63, 114.58, 100.1, 22.3; HRMS called for: C₁₆H₁₃N₂ [M+H]⁺ 233.1073, found 233.1070.

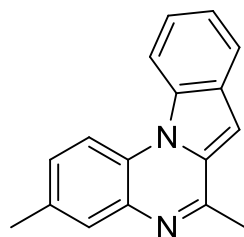


6,7-dimethylindolo[1,2-*a*]quinoxaline 3r: yellow solid (X = I, 62.0 mg, 84%; X = Br, 48.0 mg, 65%).

Mp = 125-126 °C; IR (neat, cm⁻¹): 3050, 2920, 2854, 1607, 1537, 1479, 1443, 1402, 1363, 1330, 1302, 1207, 743; ¹H NMR (CDCl₃, 400 MHz, ppm): δ 8.37 (d, *J*=8.8 Hz, 2H), 7.91 (d, *J*=8.0 Hz, 1H), 7.86 (dd, *J*₁=7.8 Hz, *J*₂=0.9 Hz, 1H), 7.53-7.47 (m, 2H), 7.45 (d, *J*=7.5 Hz, 1H), 7.36-7.32 (m, 1H), 2.91 (s, 3H), 2.80 (s, 3H); ¹³C NMR (CDCl₃, 100 MHz, ppm): δ 155.9, 131.7, 130.5, 130.0, 129.1, 127.6, 126.7, 124.5, 123.6, 121.9, 120.5, 114.4, 114.3, 25.7, 11.2; HRMS called for: C₁₇H₁₅N₂ [M+H]⁺ 247.1230, found 247.1233.



10-chloro-6-methylindolo[1,2-*a*]quinoxaline 3s: yellow solid (44.7 mg, 56%). Mp = 146-147 °C; IR (neat, cm⁻¹): 3742, 3678, 3649, 3622, 3018, 2923, 2852, 1740, 1694, 1530, 1469, 1430, 1393, 1359, 1296, 1201, 938, 810, 738; ¹H NMR (CDCl₃, 400 MHz, ppm): δ 8.35 (s, 1H), 8.27 (d, *J*=7.7 Hz, 1H), 7.94 (dd, *J*₁=7.9 Hz, *J*₂=1.2 Hz, 1H), 7.83 (d, *J*=8.6 Hz, 1H), 7.59-7.54 (m, 1H), 7.44-7.37 (m, 2H), 7.06 (s, 1H), 2.76 (s, 3H); ¹³C NMR (CDCl₃, 100 MHz, ppm): δ 155.1, 135.7, 132.8, 130.2, 129.9, 129.70, 129.67, 128.0, 127.3, 124.5, 123.4, 123.3, 114.41, 114.39, 100.0, 22.3; HRMS called for: C₁₆H₁₂ClN₂ [M+H]⁺ 267.0684, found 267.0682.



3,6-dimethylindolo[1,2-*a*]quinoxaline 3t: yellow solid (35.4 mg, 48%). Mp = 100-101 °C; IR (neat, cm⁻¹): 3784, 3701, 3662, 3633, 3047, 2918, 2849, 1720, 1589, 1529, 1485, 1442, 1369, 1355, 1298, 1205, 1112, 873, 790, 733, 680; ¹H NMR (CDCl₃, 400 MHz, ppm): δ 8.41 (d, *J*=8.6 Hz, 1H), 8.33 (d, *J*=8.4 Hz, 1H), 7.95 (d, *J*=8.0 Hz, 1H), 7.75 (s, 1H), 7.53 (t, *J*=7.6 Hz, 1H), 7.44 (t, *J*=7.4 Hz, 1H), 7.38 (d, *J*=8.2 Hz, 1H), 7.13 (s, 1H), 2.79 (s, 3H), 2.50 (s, 3H); ¹³C NMR (CDCl₃, 100 MHz, ppm): δ 155.2, 133.8, 132.9, 129.6, 128.9, 128.7, 128.0, 124.1, 122.7, 122.5, 114.5, 114.3, 99.9, 22.2, 20.9; HRMS called for: C₁₇H₁₅N₂ [M+H]⁺ 247.1230, found 247.1237.

6. References

- (1) Guillon, J.; Grellier, P.; Labaied, M.; Sonnet, P.; Léger, J. M.; Déprez-Poulain, R.; Forfar-Bares, I.; Dallemagne, P.; Lemaître, N.; Péhourcq, F.; Rochette, J.; Sergheraert, C.; Jarry, C. *J. Med. Chem.* **2004**, *47*, 1997.
- (2) Verma, A. K.; Singh, J.; Larock, R. C. *Tetrahedron.* **2009**, *65*, 8434.
- (3) Chai, D. I.; Thansandote, P.; Lautens, M. *Chem. - Eur. J.* **2011**, *17*, 8175-8188.
- (4) Panteleev, J.; Geyer, K.; Aguilar-Aguilar, A.; Wang, L.; Lautens, M. *Org. Lett.* **2010**, *12*, 5092-5095.
- (5) Hulcoop, D. G.; Lautens, M. *Org. Lett.* **2007**, *9*, 1761-1764.
- (6) Pereira, M. d. F.; Thiery, V. *Org. Lett.* **2012**, *14*, 4754-4757.

7. ¹H NMR and ¹³C NMR spectra

