Rapid synthesis of bis(hetero)aryls by one-pot Masuda borylation – Suzuki coupling sequence and its application to concise total syntheses of meridianins A and G **

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Supporting Information

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1. General Considerations

All cross coupling reactions were carried out in oven-dried Schlenk glassware using septa and syringes under nitrogen or argon atmosphere. THF and 1,4-dioxane were dried using *M*Br*au*n system MB-SPS-800, and triethylamine was refluxed under argon atmosphere over ketyl sodium, distilled and stored in a Schlenk flask over potassium hydroxide pellets under argon atmosphere. Dry methanol was purchased from *Sigma-Aldrich Chemie GmbH*. 4,4,5,5-Tetramethyl-1,3,2-dioxaborolane (pinacolborane) was purchased from *Sigma-Aldrich Chemie GmbH* and used as supplied. Tetrakis(triphenylphosphane)-palladium(0) and cesium carbonate were purchased from *Merck Serono KGaA*. Commercial grade reagents were used as supplied without further purification and were purchased from Acros Organics, *Sigma-Aldrich Chemie GmbH*, *Fluka AG*, ABCR GmbH & Co. KG, Alfa Aesar GmbH & Co. KG, Aces Pharma Inc., Interchim Inc., Synthonix Inc., Synchem OHG and *Merck Serono KGaA*.

Compounds 1h-1i, 1k-1n and 3a-3q are commercially available (see Table 1). Compounds 1a-1c,[1] 1d-1g,[2] and 1j[3] were prepared according to the literature procedures.

The purification of products was performed on silica gel 60 (0.015-0.040 mm) from *Merck Serono KGaA* Darmstadt using flash technique and under pressure of 2 bar. The crude mixtures were adsorbed on Celite® 545 (0.02-0.10 mm) from *Merck Serono KGaA* Darmstadt before chromatographic purification. The reaction progress was monitored qualitatively using TLC Silica gel 60 F254 5 x 7.5 cm aluminium sheets obtained by *Merck Serono KGaA* Darmstadt. The spots were detected with UV light at 254 nm and using aqueous potassium permanganate solution.
\(^1\)H, \(^{13}\)C, and 135-DEPT NMR spectra were recorded on Bruker DRX 500 spectrometer. Acetone-d\(_6\), CDCl\(_3\) and DMSO-d\(_6\) were used as deuterated solvents. TMS was used as reference (\(\delta = 0.0\)) or the resonances of the solvents were locked as internal standards (acetone-d\(_6\): \(^1\)H \(\delta\) 2.05, \(^{13}\)C \(\delta\) 30.8; CDCl\(_3\): \(^1\)H \(\delta\) 7.26, \(^{13}\)C \(\delta\) 77.0; DMSO-d\(_6\): \(^1\)H \(\delta\) 2.50, \(^{13}\)C \(\delta\) 39.4). The multiplicities of signals were abbreviated as follows: s: singlet; d: doublet; t: triplet; dd: doublet of doublets, ddd: doublet of doublets of doublets, dt: doublet of triplets, td: triplet of doublets, tt: triplet of triplets, q: quartet, quint: quintet, sext: sextet, m: multiplet and br: broad signal. The type of carbon atoms was determined on the basis of 135-DEPT NMR spectra.

EI mass spectra were measured on Finnigan MAT 8200 spectrometer. IR spectra were obtained on Bruker Vector 22 FT-IR. The solids were measured as KBr pellets and oils as films on KBr plates. The intensity of signals is abbreviated as follows: s (strong), m (medium) and w (weak). The melting points (uncorrected) were measured on Reichert-Jung Thermovar. Combustion analyses were carried out on Perkin Elmer Series II Analyser 2400 in the microanalytical laboratory of Institut für Pharmazeutische und Medizinische Chemie der Heinrich-Heine-Universität Düsseldorf.
2. Preparation of Starting Materials 1a, 1c, 1f and 1j

2.1. Preparation of tert-butyl 3-iodo-1H-pyrrolo[2,3-b]pyridine-1-carboxylate (1a)[1]

\[
\text{I}_2 \quad \text{I} \quad \text{Boc}_2\text{O} \quad \text{1a}
\]

A solution of iodine (25.7 g, 101 mmol) in 180 mL DMF was dropped to the solution of 7-azaindole (12.1 g, 100 mmol) and potassium hydroxide (16.5 g, 250 mmol) in 180 mL DMF at room temperature and the mixture was stirred for 45 min. The reaction mixture was then poured on 1 L ice water containing 1 % ammonia and 0.2 % sodium disulfite. The precipitate was filtered, washed with ice water and dried in vacuo to obtain 23.7 g (97.2 mmol, 97 % yield) of a yellow solid.

The obtained solid was used without further purification for the next step. It was suspended in 180 mL dichloromethane, 4-dimethylaminopyridine (1.21 g, 9.72 mmol) was added and di-tert-butyl dicarbonate (32.8 g, 146 mmol), dissolved in 180 mL dichloromethane, was added dropwise for 30 min. The mixture was stirred for 30 min. at room temperature, washed with 200 mL 0.1 N HCl, and the aqueous phase was extracted with dichloromethane (2 x 100 mL). The combined organic layers were dried with sodium sulphate, the solvents were removed under reduced pressure and the residue was adsorbed onto Celite® and purified chromatographically on silica gel with petroleum ether (boiling range 40-60 °C)/ethyl acetate (PE-EtOAc = 5:1, \( R_f \) (PE-EtOAc = 20:1): 0.14) to give 31.6 g (91.8 mmol, 94 % yield; 92 % total yield over two steps) of 1a as an orange oil, which solidifies upon storage in refrigerator.

**tert-Butyl 3-iodo-1H-pyrrolo[2,3-b]pyridine-1-carboxylate (1a)**

\[
\text{C}_{12}\text{H}_{13}\text{IN}_{2}\text{O}_{2}
\]

31.6 g (91.8 mmol, 92 % yield over two steps) as a yellow oil (solidified upon storage in refrigerator). Mp 79 °C. \(^1\)H NMR (acetone-\(d_6\), 300 MHz): \(\delta 1.67\) (s, 9 H), 7.36 (dd, \(J = 8.1\) Hz, \(J = 4.8\) Hz, 1 H), 7.75 (dd, \(J = 8.1\) Hz, \(J = 1.5\) Hz, 1 H), 7.99 (s, 1 H), 8.44 (dd, \(J = 4.8\) Hz, \(J = 1.5\) Hz, 1 H). \(^{13}\)C NMR (acetone-\(d_6\), 75 MHz): \(\delta 28.1\) (CH\(_3\)), 61.9 (C\(_{\text{quat}}\)), 84.8 (C\(_{\text{quat}}\)), 120.1 (CH), 125.8 (C\(_{\text{quat}}\)), 130.1 (CH), 132.1 (CH), 146.6 (CH), 147.8 (C\(_{\text{quat}}\)), 147.9 (C\(_{\text{quat}}\)). EI + MS (m/z (%)): 344 (M\(^+\), 7), 271 ((M-C\(_5\)H\(_9\)O\(^+\))\(^+\), 3), 245 (10), 244 ((M-C\(_{5}\)H\(_9\)O\(_2\))\(^+\), 100), 217 ((M-I\(^+\)), 5), 162 (C\(_8\)H\(_8\)N\(_2\)O\(_2\))\(^+\), 13), 144 (C\(_8\)H\(_4\)N\(_2\)O\(^+\), 1), 127 (I\(^+\)), 2), 117 (C\(_7\)H\(_5\)N\(_2\))\(^+\), 14), 116 (C\(_7\)H\(_4\)N\(_2\))\(^+\), 8), 57 (C\(_4\)H\(_9\))\(^+\), 22).

Data reported in the literature:


\(^1\)H NMR (CDCl\(_3\)): \(\delta 1.70\) (s, 9 H), 7.28 (dd, \(J = 8.5\) Hz, 1 H), 7.72 (dd, \(J = 8.1\) Hz, 1 H), 7.80 (s, 1 H), 8.49 (dd, \(J = 5.1\) Hz, 1 H).
2.2. Preparation of tert-butyl 3-iodo-4-methoxy-1H-indole-1-carboxylate (1c)[1]

A solution of iodine (2.57 g, 10.1 mmol) in 15 mL DMF was dropped to the solution of 4-methoxy-1H-indole (1.50 g, 10.0 mmol) and potassium hydroxide (1.65 g, 25.0 mmol) in 15 mL DMF at room temperature and the mixture was stirred for 45 min. The reaction mixture was then poured on 200 mL ice water containing 1 % ammonia and 0.2 % sodium disulfite. The precipitate was filtered, washed with ice water and dried in vacuo to obtain 3.34 g (8.58 mmol, 86 % yield) of a gray solid.

The obtained solid was used without further purification for the next step. It was suspended in 15 mL dichloromethane, 4-dimethylaminopyridine (106 mg, 0.86 mmol) was added and di-tert-butyl dicarbonate (2.90 g, 12.9 mmol), dissolved in 15 mL dichloromethane, was added dropwise for 25 min. The mixture was stirred for 30 min at room temperature, washed with 15 mL 0.1 N HCl, and the aqueous phase was extracted with dichloromethane (4 x 15 mL, monitored by TLC). The combined organic layers were dried with sodium sulphate, the solvents were removed under reduced pressure and the residue was adsorbed onto Celite® and purified chromatographically on silica gel with petroleum ether (boiling range 40-60 °C)/ethyl acetate (PE-EtOAc = 100:1 → 50:1 (stepwise gradient), $R_f$ (PE-EtOAc = 50:1): 0.21) to give 3.08 g (8.24 mmol, 96 % yield; 82 % total yield over two steps) of 1c as a pale yellow oil, which solidifies upon storage in refrigerator to a pale yellow amorphous solid.

tert-Butyl 3-iodo-4-methoxy-1H-indole-1-carboxylate (1c)

3.08 g (8.24 mmol, 82 % yield over two steps) as a pale yellow oil (solidified upon storage in refrigerator). Mp 68 °C. $^1$H NMR (CDCl$_3$, 500 MHz): $\delta$ 1.64 (s, 9 H), 3.92 (s, 3 H), 6.67 (d, $J = 8.2$ Hz, 1 H), 7.24 (t, $J = 8.2$ Hz, 1 H), 7.61 (s, 1 H), 7.80 (d, $J = 8.2$ Hz, 1 H). $^{13}$C NMR (CDCl$_3$, 125 MHz): $\delta$ 28.1 (CH$_3$), 55.4 (CH$_3$), 57.6 (C$_{quat}$), 84.2 (C$_{quat}$), 104.0 (CH), 108.0 (CH), 119.6 (C$_{quat}$), 125.9 (CH), 130.0 (CH), 136.5 (C$_{quat}$), 148.5 (C$_{quat}$), 153.2 (C$_{quat}$). EI + MS (m/z (%)): 373 (M$^+$, 33), 317 ((M-C$_4$H$_9$+H)$^+$, 100), 273 ((M-C$_4$H$_9$+H-CO$_2$)$^+$, 56), 258 ((M-C$_4$H$_9$+H-CO$_2$-CH$_3$)$^+$, 23), 57 (C$_4$H$_9^+$, 83). IR (film): $\tilde{\nu}$ 3151 (w) cm$^{-1}$, 2979 (s), 2937 (m), 2837 (w), 1732 (s), 1606 (m), 1586 (s), 1494 (s), 1427 (s), 1394 (m), 1370 (s), 1339 (s), 1286 (s), 1153 (s), 1124 (s), 1046 (s), 955 (w), 903 (w), 852 (m), 819 (w), 775 (m), 735 (m), 696 (w), 668 (w), 597 (w). Anal. calcd for C$_{14}$H$_{16}$INO$_3$ (373.2): C 45.06, H 4.32, N 3.75. Found: C 45.07, H 4.11, N 3.56.
2.3. Preparation of tert-butyl 4-iodo-2-(4-methoxyphenyl)-1H-pyrrole-1-carboxylate (1f)[2]

PdCl₂(PPh₃)₂ (425 mg, 0.60 mmol, 2 mol %) and CuI (233 mg, 1.20 mmol, 4 mol %) were placed under argon atmosphere in a screw-cap vessel, which was then dried with a heat gun and cooled to room temperature (water bath). Then, 150 mL of dry THF were added and the mixture was degassed with argon. Dry triethylamine (4.16 mL, 30.0 mmol), 4-methoxybenzoyl chloride (5.28 g, 30.0 mmol), and tert-butyl prop-2-ynylcarbamate (4.66 g, 30.0 mmol) were successively added to the mixture which was stirred at room temperature for 1 h (monitored by TLC). Then, sodium iodide (22.7 g, 150 mmol), toluene-4-sulfonic acid monohydrate (11.6 g, 60.0 mmol) and 30 ml of tert-butanol were successively added to the mixture which was stirred at room temperature for 1 h (monitored by TLC). The reaction mixture was diluted with 300 mL brine, the phases were separated and the aqueous phase was extracted with dichloromethane (3 x 150 mL). The combined organic layers were dried with anhydrous sodium sulfate. After removal of the solvents in vacuo the residue was absorbed onto Celite® and purified chromatographically on silica gel with petroleum ether (boiling range 40-60 °C)/ethyl acetate (PE-EtOAc = 100:1) to give 9.23 g (23.1 mmol, 77 % yield) of the desired product (1f) as a colorless solid.

2.4. Preparation of 2-ethyl-3-iodo-5-(thiophen-2-yl)furan (1j)[3]

PdCl$_2$(PPh$_3$)$_2$ (142 mg, 0.20 mmol, 2 mol %) and Cu I (78 mg, 0.40 mmol, 4 mol %) were placed under argon atmosphere in a screw-cap vessel, which was then dried with a heat gun and cooled to room temperature (water bath). Then, 50 mL of dry THF were added and the mixture was degassed with argon. Dry triethylamine (1.39 mL, 10.0 mmol), thiophene-2-carbonyl chloride (1.50 g, 10.0 mmol), and tetrahydro-2-(pent-1-yn-3-yloxy)-2H-pyran (4.66 g, 10.0 mmol) were successively added to the mixture which was stirred at room temperature for 2 h (monitored by TLC). Then, sodium iodide (7.57 g, 50.0 mmol), toluene-4-sulfonic acid monohydrate (2.14 g, 11.0 mmol) and 30 ml of methanol were successively added to the mixture which was stirred at room temperature for 2 h (monitored by TLC). After removal of the solvents in vacuo the residue was absorbed onto Celite® and purified chromatographically on silica gel with petroleum ether (boiling range 40-60 °C)/ethyl acetate (PE-EtOAc = 10:1) to give 2.72 g (8.93 mmol, 89 % yield) of 1j as an orange oil.


3. Preparation of tert-butyl 3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrrolo[2,3-b]pyridine-1-carboxylate (2a)

Tetrakis(triphenylphosphane)-palladium(0) (35 mg, 0.03 mmol, 3 mol %) and tert-butyl 3-iodo-1H-pyrrolo[2,3-b]pyridine-1-carboxylate (1a) (344 mg, 1.00 mmol) were placed under argon atmosphere in a dry screw-cap vessel with septum. Then, 5 mL of dry dioxane were added and the mixture was degassed with argon. Dry triethylamine (1.39 mL, 10.0 mmol, 10.0 equiv), and 4,4,5,5-tetramethyl-1,3,2-dioxaborolane (0.22 mL, 1.50 mmol, 1.50 equiv) were successively added to the mixture which was stirred at 80 °C (preheated oil bath) for 3 h (monitored by TLC). Then, after cooling to room temperature (water bath), the solvent was removed in vacuo and the residue was absorbed onto Celite® and purified chromatographically* on silica gel with petroleum ether (boiling range 40-60 °C)/ethyl acetate (PE-EtOAc = 5:1) to give 291 mg (0.85 mmol, 85 % yield) of 2a as a yellow solid. Recrystallization from n-pentane gave colorless crystals.

*The purification was performed on Biotage SP-1 system using a 50 g silica gel SNAP cartridge.
**tert-Butyl 3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrrolo[2,3-b]pyridine-1-carboxylate (2a)**

![Chemical Structure](image)

C_{18}H_{25}BN_{2}O_{4}

344.21

291 mg (0.85 mmol, 85 % yield) as a yellow solid. R_{f} (PE-EtOAc = 5:1): 0.30. Mp 97-98 °C. \(^{1}\)H NMR (acetone-d\(_{6}\), 500 MHz): \(\delta 1.37\) (s, 12 H), 1.68 (s, 9 H), 7.28 (dd, \(J = 7.6\) Hz, \(J = 4.7\) Hz, 1 H), 8.05 (s, 1 H), 8.21 (dd, \(J = 7.9\) Hz, \(J = 1.9\) Hz, 1 H), 8.40 (dd, \(J = 4.7\) Hz, \(J = 1.6\) Hz, 1 H). \(^{13}\)C NMR (acetone-d\(_{6}\), 125 MHz): \(\delta 26.2\) (CH\(_{3}\)), 29.2 (CH\(_{3}\)), 85.3 (C\(_{quat}\)), 85.6 (C\(_{quat}\)), 120.7 (CH), 127.7 (C\(_{quat}\)), 132.2 (CH), 137.6 (CH), 146.5 (CH), 149.5 (C\(_{quat}\)), 150.8 (C\(_{quat}\)), 207.1 (C\(_{quat}\)). EI + MS (m/z (%)): 344 (M\(^{+}\), 10), 244 (100), 229 (28), 185 (10), 171 (9), 158 (37), 144 (62), 118 (12), 57 (13).

Data reported in the literature:


White solid. Mp 115-117 °C. \(^{1}\)H NMR (CDCl\(_{3}\), 500 MHz): \(\delta 1.33\) (br s, 12 H), 1.62 (br s, 9 H), 7.16-7.18 (dd, \(J = 7.8\) Hz, \(J = 4.6\) Hz, 1 H), 8.01 (br s, 1 H), 8.20-8.22 (dd, \(J = 7.8\) Hz, \(J = 1.7\) Hz, 1 H), 8.45-8.46 (dd, \(J = 4.9\) Hz, \(J = 1.7\) Hz, 1 H). \(^{13}\)C NMR (CDCl\(_{3}\), 125 MHz): \(\delta 24.8\) (CH\(_{3}\)), 28.1 (CH\(_{3}\)), 83.5 (C\(_{quat}\)), 84.3 (C\(_{quat}\)), 118.8 (CH), 126.1 (C\(_{quat}\)), 130.9 (CH), 135.4 (CH), 145.1 (CH), 147.6 (C\(_{quat}\)), 149.3 (C\(_{quat}\)), 207.1 (C\(_{quat}\)). GCMS (EI) (m/z (%)): 244 (100), 229 (38), 187 (35), 158 (37), 144 (46), 117 (11). \(^{11}\)B NMR (CDCl\(_{3}\), 96 MHz): \(\delta 30.2\). Anal. calcd for C\(_{18}H_{25}BN_{2}O_{4}\) (344.2): C 62.81, H 7.32, N 8.14. Found: C 62.75, H 7.39, N 8.10.

Found: C 62.75, H 7.39, N 8.10.
4. Preparation of Compounds 4a-u by the *Masuda* Borylation – *Suzuki* Coupling Sequence

4.1. *General Procedure*

Tetrakis(triphenylphosphane)-palladium(0) (35 mg, 0.03 mmol, 3 mol %) and tert-butyl 3-iodo-1H-pyrrolo[2,3-b]pyridine-1-carboxylate (1a) (344 mg, 1.00 mmol) were placed under argon atmosphere in a dry screw-cap vessel with septum. Then, 5 mL of dry dioxane were added and the mixture was degassed with argon. Dry triethylamine (1.39 mL, 10.0 mmol, 10.0 equiv), and 4,4,5,5-tetramethyl-1,3,2-dioxaborolane (0.22 mL, 1.50 mmol, 1.50 equiv)* were successively added to the mixture which was stirred at 80 °C (preheated oil bath) for 3 h (monitored by TLC). Then, after cooling to room temperature (water bath), 5 mL of dry methanol, 1.00 mmol of (hetero)aryl halide 3 and cesium carbonate (823 mg, 2.50 mmol, 2.50 equiv) were successively added and the mixture was stirred at 100 °C overnight (preheated oil bath; for exact reaction times, see *Table 2*). Then, after cooling to room temperature (water bath) the solvents were removed in vacuo and the residue was absorbed onto Celite® and purified chromatographically on silica gel with dichloromethane-methanol-aqueous ammonia (isocratic or stepwise gradient). The obtained bis(hetero)aryls 4 can be further purified by suspending in dichloromethane, sonication in ultrasound bath for 0.5-1.0 h, filtration and drying in vacuo overnight.

*For the preparation of compounds 4r-4t, 3.00 equiv (0.44 mL, 3.00 mmol) of 4,4,5,5-tetramethyl-1,3,2-dioxaborolane (pinacolborane) were used.

The experimental details are given in *Table 1*. 

\[ 
\text{1} \xrightarrow{\text{H-B(OH)}_2} \text{2} \xrightarrow{\text{(Hetero)Aryl-Hal}} \text{4} 
\]
Table 1. Experimental details for the synthesis of bis(hetero)aryls 4.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Substrate 1</th>
<th>(Hetero)aryl halide 3</th>
<th>Bis(hetero)aryl 4 (isolated yield %)</th>
<th>Chromatographic purification (eluent) UV purity</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>tert-Butyl 3-iodo-1H-pyrrolo[2,3-b]pyridine-1-carboxylate</td>
<td>4-Chloropyrimidin-2-amine (Synchem)</td>
<td>Pale yellow solid 134 mg (0.63 mmol, 63 %)</td>
<td>DCM-MeOH-NH₃ = 100:1:1 → 100:2:1 → 100:3:1 → 100:4:1 → 100:5:1 → 100:6:1</td>
</tr>
<tr>
<td></td>
<td>344 mg (1.00 mmol) 1a</td>
<td>134 mg (1.00 mmol) 3a</td>
<td></td>
<td>HT-LC-MS: 100 %</td>
</tr>
<tr>
<td>2</td>
<td>344 mg (1.00 mmol) 1a</td>
<td>6-Chloropyrazin-2-amine (Synthonix)</td>
<td>Green-brown solid 112 mg (0.53 mmol, 53 %)</td>
<td>DCM-MeOH-NH₃ = 100:1:1 → 100:2:1 → 100:3:1 → 100:4:1 → 100:5:1 → 100:6:1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>132 mg (1.00 mmol) 3b</td>
<td></td>
<td>HT-LC-MS: 100 %</td>
</tr>
<tr>
<td>3</td>
<td>344 mg (1.00 mmol) 1a</td>
<td>5-Iodopyrimidin-2-amine (Alfa Aesar)</td>
<td>Pale yellow solid 139 mg (0.66 mmol, 66 %)</td>
<td>DCM-MeOH-NH₃ = 100:1:1 → 100:2:1 → 100:3:1 → 100:4:1 → 100:5:1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>228 mg (1.00 mmol) 3c</td>
<td></td>
<td>HT-LC-MS: 100 %</td>
</tr>
<tr>
<td>4</td>
<td>344 mg (1.00 mmol) 1a</td>
<td>2-Chloropyrimidin-4-amine (Aldrich)</td>
<td>Beige solid 79 mg (0.37 mmol, 37 %)</td>
<td>DCM-MeOH-NH₃ = 100:1:1 → 100:2:1 → 100:3:1 → 100:4:1 → 100:5:1 → 100:6:1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>134 mg (1.00 mmol) 3d</td>
<td></td>
<td>HT-LC-MS: 98.1 %</td>
</tr>
</tbody>
</table>
Table 1 (continuation). Experimental details for the synthesis of bis(hetero)aryls 4.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Substrate 1</th>
<th>(Hetero)aryl halide 3</th>
<th>Bis(hetero)aryl 4 (isolated yield %)</th>
<th>Chromatographic purification (eluent)</th>
<th>UV purity</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>tert-Butyl 3-iodo-1H-pyrrolo[2,3-b]pyridine-1-carboxylate</td>
<td>6-Bromo-pyrrolo[2,3-b]pyridin-2-amine (ABCR)</td>
<td>344 mg (1.00 mmol)</td>
<td>Pale yellow solid 170 mg (0.81 mmol, 81 %)</td>
<td>DCM-MeOH-NH$_3$ = 100:1:1 → 100:2:1 → 100:3:1 → 100:4:1 → 100:5:1 → 100:6:1</td>
</tr>
<tr>
<td>6</td>
<td>344 mg (1.00 mmol)</td>
<td>4-Bromo-pyrrolo[2,3-b]pyridin-2-amine (Interchim)</td>
<td>173 mg (1.00 mmol)</td>
<td>Yellow solid 135 mg (0.64 mmol, 64 %)</td>
<td>DCM-MeOH-NH$_3$ = 100:1:1 → 100:2:1 → 100:3:1 → 100:4:1 → 100:5:1 → 100:6:1 → 100:7:1</td>
</tr>
<tr>
<td>7</td>
<td>344 mg (1.00 mmol)</td>
<td>2-Iodo-benzen-amine (Merck)</td>
<td>221 mg (1.00 mmol)</td>
<td>Pale yellow solid 154 mg (0.74 mmol, 74 %)</td>
<td>DCM-MeOH-NH$_3$ = 100:1:1</td>
</tr>
<tr>
<td>8</td>
<td>344 mg (1.00 mmol)</td>
<td>4-Iodo-phenol (Alfa Aesar)</td>
<td>222 mg (1.00 mmol)</td>
<td>Beige solid 120 mg (0.57 mmol, 57 %)</td>
<td>DCM-MeOH-NH$_3$ = 100:1:1 → 100:2:1 → 100:3:1 → 100:4:1 → 100:5:1 → 100:6:1</td>
</tr>
</tbody>
</table>
Table 1 (continuation). Experimental details for the synthesis of bis(hetero)aryls 4.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Substrate 1</th>
<th>(Hetero)aryl halide 3</th>
<th>Bis(hetero)aryl 4 (isolated yield %)</th>
<th>Chromatographic purification (eluent)</th>
<th>UV purity</th>
</tr>
</thead>
<tbody>
<tr>
<td>9</td>
<td>tert-Butyl 3-iodo-1H-indole-1-carboxylate</td>
<td>4-Chloropyrimidin-2-amine (Synchem)</td>
<td>Pale yellow solid 154 mg (0.73 mmol, 73 %)</td>
<td>DCM-MeOH-NH₃ = 100:1:1 → 100:2:1 → 100:3:1 → 100:4:1 → 100:5:1</td>
<td>HT-LC-MS: 99.6 %</td>
</tr>
<tr>
<td></td>
<td>343 mg (1.00 mmol) 1b</td>
<td>134 mg (1.00 mmol) 3a</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>tert-Butyl 3-iodo-4-methoxy-1H-indole-1-carboxylate</td>
<td></td>
<td>Colorless solid 185 mg (0.77 mmol, 77 %)</td>
<td>DCM-MeOH-NH₃ = 100:1:1 → 100:2:1 → 100:3:1 → 100:4:1 → 100:5:1 → 100:6:1</td>
<td>HT-LC-MS: 100 %</td>
</tr>
<tr>
<td></td>
<td>373 mg (1.00 mmol) 1c</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>134 mg (1.00 mmol) 3a</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>tert-Butyl 4-iodo-2-phenyl-1H-pyrrole-1-carboxylate</td>
<td></td>
<td>Rosa solid 190 mg (0.80 mmol, 80 %)</td>
<td>DCM-MeOH-NH₃ = 100:1:1 → 100:2:1</td>
<td>HT-LC-MS: 98.2 %</td>
</tr>
<tr>
<td></td>
<td>369 mg (1.00 mmol) 1d[a]</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>134 mg (1.00 mmol) 3a</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 1 (continuation). Experimental details for the synthesis of bis(hetero)aryls 4.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Substrate 1</th>
<th>(Hetero)aryl halide 3</th>
<th>Bis(hetero)aryl 4 (isolated yield %)</th>
<th>Chromatographic purification (eluent)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>tert-Butyl 2-(4-chloro-phenyl)-4-iodo-1H-pyrrole-1-carboxylate</td>
<td>5-Iodo-1,3-dimethyl-pyrimidine-2,4(1H,3H)-dione (5-Iodo-1,3-dimethyl-uracil) (Aldrich)</td>
<td>Rosa solid 202 mg (0.64 mmol, 64 %)</td>
<td>PE-EtOAc = 2:1 → 1:1 Rf (PE-EtOAc = 1:1): 0.32 HT-LC-MS: 100 %</td>
</tr>
<tr>
<td>12</td>
<td>1e[a]</td>
<td></td>
<td>3i</td>
<td></td>
</tr>
<tr>
<td></td>
<td>tert-Butyl 4-iodo-2-(4-methoxy-phenyl)-1H-pyrrole-1-carboxylate</td>
<td>4-Iodo-pyridine (ABCR)</td>
<td>Beige solid 151 mg (0.60 mmol, 60 %)</td>
<td>DCM-MeOH-NH₃ = 100:1:1 → 100:2:1 → 100:3:1 HT-LC-MS: 100 %</td>
</tr>
<tr>
<td>13</td>
<td>1f[a]</td>
<td></td>
<td>3j</td>
<td></td>
</tr>
<tr>
<td></td>
<td>tert-Butyl 4-iodo-2-(thiophen-2-yl)-1H-pyrrole-1-carboxylate</td>
<td>1-Fluoro-4-iodobenzene (ABCR)</td>
<td>Pale gray solid 170 mg (0.70 mmol, 70 %)</td>
<td>PE-EtOAc = 10:1 Rf (PE-EtOAc = 10:1): 0.21 HT-LC-MS: 100 %</td>
</tr>
<tr>
<td>14</td>
<td>1g[a]</td>
<td></td>
<td>3k</td>
<td></td>
</tr>
</tbody>
</table>

\textit{Table 1 (continuation).} Experimental details for the synthesis of bis(hetero)aryls 4.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Substrate 1</th>
<th>(Hetero)aryl halide 3</th>
<th>Bis(hetero)aryl 4 (isolated yield %)</th>
<th>Chromatographic purification (eluent)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>R\textsubscript{f} (eluent) UV purity</td>
</tr>
<tr>
<td>15</td>
<td>1-Benzyl-4-iodo-1\textsubscript{H}-pyrazole (\textit{ABCR})</td>
<td>1-(Trifluoromethyl)-4-iodobenzene (\textit{Alfa Aesar})</td>
<td>Colorless solid 106 mg (0.35 mmol, 35 %)</td>
<td>PE-EtOAc = 7:1 R\textsubscript{f} (PE-EtOAc = 7:1): 0.17 HT-LC-MS: 100 %</td>
</tr>
<tr>
<td></td>
<td>284 mg (1.00 mmol)</td>
<td>278 mg (1.00 mmol)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>1h</td>
<td>3l</td>
<td></td>
<td></td>
</tr>
<tr>
<td>16</td>
<td>3-Iodo-thiophene (\textit{Alfa Aesar})</td>
<td>1-Iodo-isoquinoline (\textit{Aldrich})</td>
<td>Colorless solid 161 mg (0.76 mmol, 76 %)</td>
<td>PE-EtOAc = 5:1 R\textsubscript{f} (PE-EtOAc = 5:1): 0.35 HT-LC-MS: 100 %</td>
</tr>
<tr>
<td></td>
<td>219 mg (1.00 mmol)</td>
<td>263 mg (1.00 mmol)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>1i</td>
<td>3m</td>
<td></td>
<td></td>
</tr>
<tr>
<td>17</td>
<td>2-Ethyl-3-iodo-5-(thiophen-2-yl)furan\textsuperscript{[b]}</td>
<td>4-Iodo-benzonitrile (\textit{ABCR})</td>
<td>Pale yellow solid 221 mg (0.79 mmol, 79 %)</td>
<td>PE-EtOAc = 20:1 R\textsubscript{f} (PE-EtOAc = 20:1): 0.36 Crystallization by suspension in \textit{n}-pentane, sonication in ultrasound bath, filtration and drying in vacuo overnight HT-LC-MS: 100 %</td>
</tr>
<tr>
<td></td>
<td>304 mg (1.00 mmol)</td>
<td>234 mg (1.00 mmol)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>1j</td>
<td>3n</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>


Table 1 (continuation). Experimental details for the synthesis of bis(hetero)aryls 4.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Substrate 1</th>
<th>(Hetero)aryl halide 3</th>
<th>Bis(hetero)aryl 4 (isolated yield %)</th>
<th>Chromatographic purification (eluent) UV purity</th>
</tr>
</thead>
<tbody>
<tr>
<td>18</td>
<td>5-iodo-pyridin-2-amine (Alfa Aesar) 227 mg (1.00 mmol) 1k</td>
<td>1-iodo-4-(trifluoroethoxy)benzene (Alfa Aesar) 294 mg (1.00 mmol) 3o</td>
<td>Colorless solid 233 mg (0.92 mmol, 92 %)[c]</td>
<td>DCM-MeOH-NH$_3$ = 100:1:1 HT-LC-MS: 100 %</td>
</tr>
<tr>
<td>19</td>
<td>5-iodopyrimidin-2-amine (Alfa Aesar) 228 mg (1.00 mmol) 1l</td>
<td>1-(Trifluoromethyl)-4-iodobenzene (Alfa Aesar) 278 mg (1.00 mmol) 3l</td>
<td>Colorless solid 105 mg (0.44 mmol, 44 %)[c]</td>
<td>DCM-MeOH-NH$_3$ = 100:1:1 HT-LC-MS: 100 %</td>
</tr>
<tr>
<td>20</td>
<td>4-Iodophenol (Alfa Aesar) 225 mg (1.00 mmol) 1m</td>
<td>4-Bromopyridazine hydrochloride[d] (Aces Pharma) 212 mg (1.00 mmol) 3p</td>
<td>Rosa solid 121 mg (0.70 mmol, 70 %)[c]</td>
<td>DCM-MeOH-NH$_3$ = 100:1:1 (\rightarrow) 100:3:1 (\rightarrow) 100:4:1 (\rightarrow) 100:6:1 (\rightarrow) 100:7:1 HT-LC-MS: 100 %</td>
</tr>
</tbody>
</table>

[c] 3.00 equiv of HBpin have been used in the Masuda borylation step.
[d] Since the bromide 3p was used as a hydrochloride, 3.00 equiv of Cs$_2$CO$_3$ were applied in the Suzuki coupling step.
Table 1 (continuation). Experimental details for the synthesis of bis(hetero)aryls 4.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Substrate 1</th>
<th>(Hetero)aryl halide 3</th>
<th>Bis(hetero)aryl 4 (isolated yield %)</th>
<th>Chromatographic purification (eluent) UV purity</th>
</tr>
</thead>
<tbody>
<tr>
<td>21</td>
<td>5-Iodo-1,2,3-trimethoxybenzene (Alfa Aesar)</td>
<td>4-Bromopyridine-2,6-diamine (ABCR)</td>
<td>Orange solid 136 mg (0.44 mmol, 44 %)[e]</td>
<td>DCM-MeOH-NH₃ = 100:1:1 → 100:2:1 → 100:3:1 → 100:4:1</td>
</tr>
<tr>
<td></td>
<td>300 mg (1.00 mmol)</td>
<td>192 mg (1.00 mmol)</td>
<td></td>
<td>Purified by dissolving in 1.25 M HCl in EtOH (Fluka), precipitation with n-pentane, filtration and drying in vacuo overnight at 70 °C</td>
</tr>
<tr>
<td></td>
<td><strong>1n</strong></td>
<td><strong>3q</strong></td>
<td></td>
<td>HT-LC-MS: 98.5 %</td>
</tr>
</tbody>
</table>

[e] The yield was determined after formation of the hydrochloride with solution of HCl in EtOH.
Table 2. Reaction times\(^{[a]}\) in the synthesis of bis(hetero)aryls 4.

<table>
<thead>
<tr>
<th>Bis(hetero)aryl</th>
<th>Masuda borylation step</th>
<th>Suzuki coupling step</th>
<th>Bis(hetero)aryl</th>
<th>Masuda borylation step</th>
<th>Suzuki coupling step</th>
</tr>
</thead>
<tbody>
<tr>
<td>4a</td>
<td>3 h</td>
<td>49 h</td>
<td>4l</td>
<td>4 h</td>
<td>23 h</td>
</tr>
<tr>
<td>4b</td>
<td>3 h</td>
<td>24 h</td>
<td>4m</td>
<td>4 h</td>
<td>19 h</td>
</tr>
<tr>
<td>4c</td>
<td>3 h</td>
<td>24 h</td>
<td>4n</td>
<td>4 h</td>
<td>19 h</td>
</tr>
<tr>
<td>4d</td>
<td>3 h</td>
<td>67 h</td>
<td>4o</td>
<td>4 h</td>
<td>18 h</td>
</tr>
<tr>
<td>4e</td>
<td>3 h</td>
<td>20 h</td>
<td>4p</td>
<td>4 h</td>
<td>17 h</td>
</tr>
<tr>
<td>4f</td>
<td>3 h</td>
<td>24 h</td>
<td>4q</td>
<td>4 h</td>
<td>23 h</td>
</tr>
<tr>
<td>4g</td>
<td>3 h</td>
<td>24 h</td>
<td>4r</td>
<td>4 h</td>
<td>17 h</td>
</tr>
<tr>
<td>4h</td>
<td>3 h</td>
<td>24 h</td>
<td>4s</td>
<td>4 h</td>
<td>18 h</td>
</tr>
<tr>
<td>4i</td>
<td>3 h</td>
<td>24 h</td>
<td>4t</td>
<td>3 h</td>
<td>19 h</td>
</tr>
<tr>
<td>4j</td>
<td>3 h</td>
<td>15 h</td>
<td>4u</td>
<td>4 h</td>
<td>18 h</td>
</tr>
<tr>
<td>4k</td>
<td>4 h</td>
<td>17 h</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

\(^{[a]}\) The reaction times for the Suzuki coupling step are not optimized. The actual reaction times might be much shorter than indicated. The actual reaction times of the Masuda borylation step may also be shorter in some cases.
4.2. Spectroscopic Data of the Compounds 4a-u

4.2.1. 4-(1H-Pyrrolo[2,3-b]pyridin-3-yl)pyrimidin-2-amine (Meriolin 1, 4a)

\[
\begin{align*}
\text{C}_{11}	ext{H}_{9}	ext{N}_{5} \\
211.22
\end{align*}
\]

134 mg (0.63 mmol, 63 % yield) as a pale yellow solid. Mp 258-271 °C. \(^1\)H NMR (DMSO-\(d_6\), 500 MHz): \(\delta\) 6.50 (s, 2 H, NH\(_2\)), 7.06 (d, \(J = 5.4\) Hz, 1 H), 7.19 (dd, \(J = 7.9\) Hz, \(J = 4.7\) Hz, 1 H), 8.14 (d, \(J = 5.4\) Hz, 1 H), 8.29 (dd, \(J = 4.7\) Hz, \(J = 1.6\) Hz, 1 H), 8.35 (d, \(J = 2.8\) Hz, 1 H), 8.93 (dd, \(J = 7.9\) Hz, \(J = 1.6\) Hz, 1 H), 12.2 (br, 1 H, NH). \(^{13}\)C NMR (DMSO-\(d_6\), 125 MHz): \(\delta\) 104.9 (CH), 112.4 (C\(_{quat}\)), 116.6 (CH), 117.7 (C\(_{quat}\)), 128.3 (CH), 130.7 (CH), 143.3 (CH), 149.1 (C\(_{quat}\)), 157.2 (CH), 162.0 (C\(_{quat}\)), 163.5 (C\(_{quat}\)). EI + MS (m/z (%)): 212 (16), 211 (M\(^+\), 100), 210 ((M-H\(^+\), 38), 195 ((M-NH\(_2\))\(^+\), 2), 170 (14).

Data reported in the literature:


Yellow prisms. Mp 286-289 °C. \(^1\)H NMR (DMSO-\(d_6\), 300 MHz): \(\delta\) 6.47 (s, 2 H, NH\(_2\)), 7.05 (d, \(J = 5.13\) Hz, 1 H, H-5\(´\)), 7.13 (dd, \(J = 8.12\) Hz, \(J = 4.7\) Hz, 1 H, H-5), 8.14 (d, \(J = 5.13\) Hz, 1 H, H-6\(´\)), 8.28 (dd, \(J = 8.12\) Hz, \(J = 1.28\) Hz, 1 H, H-6), 8.33 (s, 1 H, H-2), 8.92 (dd, \(J = 4.7\) Hz, \(J = 1.28\) Hz, 1 H, H-4), 12.17 (s, 1 H, NH). \(^{13}\)C NMR (DMSO-\(d_6\), 75 MHz): \(\delta\) 105.0 (C-5\(´\)), 112.5 (C-3), 116.6 (C-5), 117.8 (C-3a), 128.3 (C-2), 130.6 (C-6), 143.4 (C-4), 143.4 (C-7a), 157.2 (C-6\(´\)), 162.0 (C-4\(´\)), 163.5 (C-2\(´\)). EI + MS (m/z (%)): 212 (M\(^++1\), 35), 211 (M\(^+\), 100), 210 (68), 195 (11), 170 (48), 142 (31). IR (nujol): \(\nu\) 3473 (m) cm\(^{-1}\), 3294 (m), 3133 (m), 1670 (s), 1565 (s), 1223 (m). Anal. calcd for C\(_{11}\)H\(_9\)N\(_5\) (211.2): C 62.55, H 4.29, N 33.16. Found: C 62.73, H 4.45, N 33.22.
4.2.2. 6-(1H-Pyrrolo[2,3-b]pyridin-3-yl)pyrazin-2-amine (4b)

\[
\begin{align*}
\text{C}_{11}\text{H}_9\text{N}_5 & \\
211.22
\end{align*}
\]

112 mg (0.53 mmol, 53 % yield) as a green-brown solid. Mp 241-243 °C. \textsuperscript{1}H NMR (DMSO-d\textsubscript{6}, 500 MHz): \(\delta\) 6.36 (s, 2 H, NH\textsubscript{2}), 7.17 (dd, \(J = 7.9\) Hz, \(J = 4.7\) Hz, 1 H), 7.67 (s, 1 H), 8.22 (d, \(J = 2.5\) Hz, 1 H), 8.27-8.30 (m, 2 H), 8.82 (dd, \(J = 7.9\) Hz, \(J = 1.6\) Hz, 1 H), 12.1 (br, 1 H, NH). \textsuperscript{13}C NMR (DMSO-d\textsubscript{6}, 125 MHz): \(\delta\) 111.6 (C\textsubscript{quat}), 116.3 (CH), 117.8 (C\textsubscript{quat}), 125.8 (CH), 127.6 (CH), 127.9 (CH), 130.1 (CH), 143.2 (CH), 147.7 (C\textsubscript{quat}), 149.0 (C\textsubscript{quat}), 155.0 (C\textsubscript{quat}). EI + MS (m/z (%)): 211 (M\textsuperscript{+}, 100), 184 (C\textsubscript{10}H\textsubscript{8}N\textsubscript{4}\textsuperscript{+}, 23), 58 (13), 43 (32), 41 (10). IR (KBr): \(\tilde{\nu}\) 3317 (s) cm\textsuperscript{-1}, 3146 (s), 1645 (m), 1575 (w), 1541 (s), 1522 (m), 1495 (m), 1470 (m), 1434 (s), 1366 (w), 1323 (w), 1295 (m), 1280 (w), 1245 (w), 1218 (w), 1139 (w), 1121 (w), 1030 (w), 1001 (w), 886 (w), 825 (w), 796 (w), 772 (w), 697 (w), 633 (w), 586 (w), 528 (w). Anal. calcd for C\textsubscript{11}H\textsubscript{9}N\textsubscript{5} (211.2): C 62.55, H 4.29, N 33.16. Found: C 62.47, H 4.38, N 32.92.
4.2.3. 5-(1H-Pyrrolo[2,3-b]pyridin-3-yl)pyrimidin-2-amine (4c)

\[
\begin{align*}
&\text{C}_{11}\text{H}_{9}\text{N}_{5} \\
&211.22
\end{align*}
\]

139 mg (0.66 mmol, 66 % yield) as a pale yellow solid. Mp 272 °C. \(^1\)H NMR (DMSO-d\(_6\), 500 MHz): \(\delta\) 6.61 (s, 2 H, NH\(_2\)), 7.13 (dd, \(J = 7.9\) Hz, \(J = 4.7\) Hz, 1 H), 7.80 (d, \(J = 2.5\) Hz, 1 H), 8.20 (dd, \(J = 7.9\) Hz, \(J = 1.3\) Hz, 1 H), 8.27 (dd, \(J = 4.7\) Hz, \(J = 1.6\) Hz, 1 H), 8.60 (s, 2 H), 11.9 (br, 1 H, NH). \(^{13}\)C NMR (DMSO-d\(_6\), 125 MHz): \(\delta\) 108.9 (C\(_{\text{quat}}\)), 115.7 (CH), 117.0 (C\(_{\text{quat}}\)), 117.6 (C\(_{\text{quat}}\)), 122.3 (CH), 127.3 (CH), 142.8 (CH), 148.7 (C\(_{\text{quat}}\)), 155.4 (CH), 161.9 (C\(_{\text{quat}}\)). EI + MS (\(m/z\) (%)): 211 (M\(^+\), 100), 184 (10), 170 (12), 156 (13), 142 (22). IR (KBr): \(\tilde{\nu}\) 3136 (s) cm\(^{-1}\), 1670 (m), 1618 (m), 1534 (s), 1492 (s), 1423 (w), 1335 (w), 1293 (w), 1272 (w), 1219 (w), 1132 (w), 961 (w), 895 (w), 797 (w), 770 (m), 609 (w). Anal. calcd for C\(_{11}\)H\(_9\)N\(_5\) (211.2): C 62.55, H 4.29, N 33.16. Found: C 62.73, H 4.13, N 32.99.
4.2.4. 2-(1H-Pyrrolo[2,3-b]pyridin-3-yl)pyrimidin-4-amine (4d)

![Chemical Structure]

C_{11}H_{9}N_{5}

211.22

79 mg (0.37 mmol, 37 % yield) as a beige solid. Mp 239 °C. \(^1\)H NMR (DMSO-d\(_6\), 500 MHz): \(\delta\) 6.23 (d, \(J = 6.0\) Hz, 1 H), 6.7 (br, 2 H, NH\(_2\)), 7.16 (dd, \(J = 7.9\) Hz, \(J = 4.4\) Hz, 1 H), 8.08-8.11 (m, 2 H), 8.25 (dd, \(J = 4.4\) Hz, \(J = 1.6\) Hz, 1 H), 8.87 (dd, \(J = 7.9\) Hz, \(J = 1.6\) Hz, 1 H), 12.0 (br, 1 H, NH). \(^1\)^C NMR (DMSO-d\(_6\), 125 MHz): \(\delta\) 101.4 (CH), 114.2 (C\(_{\text{quat}}\)), 116.3 (CH), 118.2 (C\(_{\text{quat}}\)), 128.0 (CH), 130.4 (CH), 142.9 (CH), 149.0 (C\(_{\text{quat}}\)), 155.0 (CH), 162.4 (C\(_{\text{quat}}\)), 163.1 (C\(_{\text{quat}}\)). El + MS (m/z (%)): 211 (M\(^+\), 100), 210 ((M-H\(^+\), 11), 195 ((M-NH\(_2\))\(^+\), 4), 144 (19), 58 (25), 43 (49). IR (KBr): \(\tilde{\nu}\) 3418 (m) cm\(^{-1}\), 3316 (m), 3210 (m), 1632 (m), 1579 (s), 1557 (m), 1533 (s), 1467 (s), 1435 (m), 1398 (w), 1369 (m), 1340 (w), 1297 (w), 1238 (w), 1124 (w), 1050 (w), 1019 (w), 984 (w), 901 (w), 828 (m), 803 (w), 777 (w), 671 (w), 599 (w), 530 (w). Anal. calcd for C\(_{11}\)H\(_9\)N\(_5\) (211.2): C 62.55, H 4.29, N 33.16. Found: C 62.48, H 4.37, N 32.99.
4.2.5. 6-(1H-Pyrrolo[2,3-b]pyridin-3-yl)-pyridin-2-amine (4e)

![Chemical structure](Diagram)

C\textsubscript{12}H\textsubscript{10}N\textsubscript{4}  
210.24

170 mg (0.81 mmol, 81 % yield) as a pale yellow solid. Mp 157-158 °C. \textsuperscript{1}H NMR (DMSO-d\textsubscript{6}, 500 MHz): δ 5.87 (s, 2 H, NH\textsubscript{2}), 6.26 (dd, J = 8.2 Hz, J = 0.6 Hz, 1 H), 7.00 (dd, J = 7.6 Hz, J = 0.6 Hz, 1 H), 7.12 (dd, J = 7.9 Hz, J = 4.7 Hz, 1 H), 7.36 (t, J = 7.9 Hz, 1 H), 8.04 (d, J = 2.5 Hz, 1 H), 8.24 (dd, J = 4.4 Hz, J = 1.6 Hz, 1 H), 8.86 (dd, J = 7.9 Hz, J = 1.6 Hz, 1 H), 11.9 (br, 1 H, NH). \textsuperscript{13}C NMR (DMSO-d\textsubscript{6}, 125 MHz): δ 104.2 (CH), 107.3 (CH), 114.6 (C\textsubscript{quat}), 115.9 (CH), 117.8 (C\textsubscript{quat}), 125.0 (CH), 130.3 (CH), 137.3 (CH), 142.7 (CH), 149.0 (C\textsubscript{quat}), 152.8 (C\textsubscript{quat}), 159.1 (C\textsubscript{quat}). EI + MS (m/z (%)): 210 (M\textsuperscript{+}, 100), 209 ((M-H)+, 15), 194 ((M-NH\textsubscript{2})\textsuperscript{+}, 5), 183 (26), 182 (15), 155 (16), 39 (11). IR (KBr): ν 3139 (m) cm\textsuperscript{-1}, 2892 (m), 1633 (m), 1595 (m), 1578 (s), 1528 (s), 1493 (w), 1469 (s), 1454 (s), 1412 (w), 1369 (w), 1339 (w), 1311 (w), 1295 (m), 1273 (w), 1186 (w), 1157 (w), 1129 (w), 895 (w), 819 (w), 800 (s), 771 (m), 733 (w), 675 (w), 630 (w), 582 (w), 525 (w). Anal. calcd for C\textsubscript{12}H\textsubscript{10}N\textsubscript{4} (210.2): C 68.56, H 4.79, N 26.65. Found: C 68.32, H 4.87, N 26.86.
4.2.6. 4-(1H-Pyrrolo[2,3-b]pyridin-3-yl)-pyridin-2-amine (4f)

\[ \text{H}_2\text{N} \]
\[ \begin{array}{c}
\text{N} \\
\text{C}_12\text{H}_{10}\text{N}_4 \\
210.24
\end{array} \]

135 mg (0.64 mmol, 64 % yield) as a yellow solid. Mp 263-270 °C. $^1$H NMR (DMSO-d$_6$, 500 MHz): $\delta$ 5.85 (s, 2 H, NH$_2$), 6.87 (dd, $J = 5.4$ Hz, $J = 1.6$ Hz, 1 H), 6.89 (s, 1 H), 7.20 (dd, $J = 7.9$ Hz, $J = 4.7$ Hz, 1 H), 7.90 (d, $J = 5.4$ Hz, 1 H), 8.00 (d, $J = 2.5$ Hz, 1 H), 8.30 (dd, $J = 4.7$ Hz, $J = 1.6$ Hz, 1 H), 8.33 (dd, $J = 8.2$ Hz, $J = 1.6$ Hz, 1 H), 12.1 (br, 1 H, NH). $^{13}$C NMR (DMSO-d$_6$, 125 MHz): $\delta$ 104.0 (CH), 109.6 (CH), 112.3 (C$_{quat}$), 116.2 (CH), 117.0 (C$_{quat}$), 125.2 (CH), 127.6 (CH), 143.0 (C$_{quat}$), 143.0 (CH), 147.9 (CH), 149.1 (C$_{quat}$), 160.3 (C$_{quat}$). EI + MS (m/z (%)): 210 (M$^+$, 100), 210 ((M-H)$^+$, 25), 183 (33), 182 (20), 170 (32), 155 (25), 142 (10), 63 (11), 41 (10), 39 (10). IR (KBr): $\tilde{\nu}$ 3314 (m) cm$^{-1}$, 3191 (m), 1639 (m), 1607 (s), 1538 (m), 1525 (m), 1507 (w), 1421 (s), 1365 (w), 1323 (w), 1289 (s), 1243 (w), 1174 (w), 1146 (w), 1071 (w), 992 (w), 881 (w), 835 (w), 802 (m), 778 (m), 627 (w), 579 (w). Anal. calcd for C$_{12}$H$_{10}$N$_4$ (210.2): C 68.56, H 4.79, N 26.65. Found: C 68.36, H 4.82, N 26.89.
4.2.7. 2-(1H-Pyrrolo[2,3-b]pyridin-3-yl)-benzenamine (4g)

![Chemical Structure Image]

C₁₃H₁₁N₃
209.25

154 mg (0.74 mmol, 74 % yield) as a pale yellow solid. Mp 147 °C. \(^1\)H NMR (DMSO-d₆, 500 MHz): \(\delta\) 4.77 (s, 2 H, NH₂), 6.64 (td, \(J = 7.6\) Hz, \(J = 1.3\) Hz, 1 H), 6.80 (dd, \(J = 8.2\) Hz, \(J = 1.3\) Hz, 1 H), 7.01-7.05 (m, 1 H), 7.08 (dd, \(J = 7.9\) Hz, \(J = 4.7\) Hz, 1 H), 7.16 (dd, \(J = 7.6\) Hz, \(J = 1.6\) Hz, 1 H), 7.58 (d, \(J = 2.5\) Hz, 1 H), 7.87 (dd, \(J = 7.9\) Hz, \(J = 1.6\) Hz, 1 H), 8.26 (dd, \(J = 4.7\) Hz, \(J = 1.6\) Hz, 1 H), 11.8 (br, 1 H, NH). \(^{13}\)C NMR (DMSO-d₆, 125 MHz): \(\delta\) 111.9 (Cquat), 115.0 (CH), 115.4 (CH), 116.4 (CH), 118.3 (Cquat), 118.8 (Cquat), 124.1 (CH), 127.3 (CH), 127.7 (CH), 130.2 (CH), 142.7 (CH), 145.7 (Cquat), 148.6 (Cquat). EI + MS (m/z (%)): 209 (M⁺, 100), 208 ((M-H)+, 93), 193 (C₁₃H₁₀N₂⁺, 12), 181 (39), 154 (33), 128 (22), 127 (35), 117 (C₇H₅N₂⁺, 11), 77 (20). IR (KBr): \(\tilde{\nu}\) 3364 (m) cm⁻¹, 3142 (s), 3029 (m), 2913 (m), 1614 (s), 1581 (m), 1536 (m), 1490 (m), 1448 (m), 1418 (m), 1339 (w), 1290 (m), 1265 (m), 1152 (w), 1107 (w), 963 (m), 937 (w), 896 (w), 797 (m), 774 (s), 750 (s), 645 (w), 621 (m), 590 (w), 514 (w).

4.2.8. 4-(1H-Pyrrolo[2,3-b]pyridin-3-yl)phenol (4h)

![Chemical structure]

C_{13}H_{10}N_{2}O

210.23

120 mg (0.57 mmol, 57 % yield) as a beige solid. Mp 244 °C. $^1$H NMR (DMSO-d$_6$, 500 MHz): $\delta$ 6.85-6.89 (m, 2 H), 7.12 (dd, $J = 7.9$ Hz, $J = 4.7$ Hz, 1 H), 7.50-7.54 (m, 2 H), 7.69 (d, $J = 2.2$ Hz, 1 H), 8.21 (dd, $J = 8.2$ Hz, $J = 1.3$ Hz, 1 H), 8.26 (dd, $J = 4.7$ Hz, $J = 1.6$ Hz, 1 H), 9.39 (s, 1 H, OH), 11.76 (s, 1 H, NH). $^{13}$C NMR (DMSO-d$_6$, 125 MHz): $\delta$ 114.5 (C$_{quat}$), 115.6 (CH), 115.6 (CH), 117.3 (C$_{quat}$), 122.2 (CH), 125.8 (C$_{quat}$), 127.3 (CH), 127.4 (CH), 142.6 (CH), 148.9 (C$_{quat}$), 155.5 (C$_{quat}$). EI + MS (m/z (%)): 210 (M$^+$, 100), 209 ((M-H)$^+$, 10), 182 (14), 181 (12), 154 (13), 127 (10), 105 (14), 97 (10), 71 (11), 57 (11). IR (KBr): $\tilde{\nu}$ 3387 (m) cm$^{-1}$, 3000 (m), 2673 (m), 1604 (m), 1583 (m), 1548 (s), 1504 (m), 1488 (m), 1461 (s), 1438 (s), 1386 (w), 1340 (w), 1324 (m), 1299 (w), 1256 (s), 1169 (m), 1142 (m), 1097 (s), 1043 (w), 964 (m), 836 (s), 817 (m), 797 (m), 774 (m), 578 (m), 540 (m), 503 (w). Anal. calcd for C$_{13}$H$_{10}$N$_{2}$O (210.2): C 74.27, H 4.79, N 13.33. Found: C 74.04, H 4.86, N 13.62.
4.2.9. 4-(1H-Indol-3-yl)-pyrimidin-2-amine (*Meridianin G, 4i*)

![Chemical structure of 4-(1H-Indol-3-yl)-pyrimidin-2-amine](attachment:image.png)

C\(_{12}\)H\(_{10}\)N\(_4\)

210.23

154 mg (0.73 mmol, 73 % yield) as a pale yellow solid. Mp 195-197 °C. \(^1\)H NMR (DMSO-d\(_6\), 500 MHz): \(\delta\) 6.42 (s, 2 H, NH\(_2\)), 7.02 (dd, \(J = 5.4\) Hz, \(J = 0.6\) Hz, 1 H), 7.10-7.15 (m, 1 H), 7.15-7.20 (m, 1 H), 7.43-7.46 (m, 1 H), 8.10 (d, \(J = 5.4\) Hz, 1 H), 8.20 (d, \(J = 2.5\) Hz, 1 H), 8.59 (d, \(J = 7.9\) Hz, 1 H), 11.7 (br, 1 H, NH). \(^{13}\)C NMR (DMSO-d\(_6\), 125 MHz): \(\delta\) 105.2 (CH), 111.7 (CH), 113.6 (C\(_{quat}\)), 120.1 (CH), 121.8 (CH), 122.3 (CH), 125.2 (C\(_{quat}\)), 128.1 (CH), 136.9 (C\(_{quat}\)), 156.9 (CH), 162.6 (C\(_{quat}\)), 163.4 (C\(_{quat}\)). EI + MS (m/z (%)): 211 (15), 210 (M\(^+\), 100), 209 ((M-H\(^+\), 34), 169 (60), 141 (10), 140 (14), 105 (12), 97 (12), 85 (10), 83 (10), 71 (12), 57 (14).
Data reported in the literature:


Mp 262.2-264.3 °C (EtOAc/MeOH). $^1$H NMR (DMSO-$d_6$, 300 MHz): $\delta$ 6.39 (br s, 2 H), 7.02 (d, $J = 5.3$ Hz, 1 H), 7.15 (m, 2 H), 7.45 (d, $J = 7.9$ Hz, 1 H), 8.11 (d, $J = 5.3$ Hz, 1 H), 8.19 (s, 1 H), 8.59 (d, $J = 7.4$ Hz, 1 H), 11.65 (br s, 1 H). $^{13}$C NMR (DMSO-$d_6$, 75 MHz): $\delta$ 105.2, 111.7, 113.6, 120.2, 121.9, 122.3, 125.3, 128.1, 136.9, 156.9, 162.6, 163.4. El + MS ($m/z$ (%)): 210 (M$^+$, 100), 209 (35), 169 (48), 155 (4), 140 (9), 114 (8), 89 (4). IR (KBr): $\tilde{\nu}$ 3408 cm$^{-1}$, 3329, 3174; 1661, 1568, 1453, 1414, 1246, 1119. HRMS calcd for C$_{12}$H$_{10}$N$_4$: 210.0923. Found: 210.0914.


Mp 263-265 °C. $^1$H NMR (DMSO-$d_6$, 270 MHz): $\delta$ 6.4 (br s, 2 H, NH$_2$), 7.03 (d, 1 H, H-5´), 7.15 (m, 2 H, H-5, H-6), 7.44-7.46 (d, 1 H, H-7), 8.11 (d, 1 H, H-6´), 8.19 (s, 1 H, H-2), 8.58-8.61 (d, 1 H, H-4), 11.65 (br s, 1 H, NH). $^{13}$C NMR (DMSO-$d_6$, 300 MHz): $\delta$ 105.2 (C-5´), 111.71 (C-7), 113.70 (C-3), 120.21 (C-3a), 121.85 (C-6), 122.32 (C-5), 125.30 (C-4), 128.10 (C-2), 136.90 (C-7a), 156.91 (C-6´), 162.62 (C-4´), 163.40 (C-2´). El + MS ($m/z$ (%)): 210 (M$^+$, 100), 209 (36), 169 (49), 155 (4), 140 (10), 114 (8). IR (KBr): $\tilde{\nu}$ 3409 (NH$_2$) cm$^{-1}$, 3329 (NH$_2$), 3172 (NH), 1659, 1569, 1520, 1454, 1416, 1241, 1129, 808, 741, 684. Anal. calcd for C$_{12}$H$_{10}$N$_4$: 210.2: C 68.56, H 4.79, N 26.65. Found: C 68.72, H 4.76, N 26.47.


Yellow powder. Mp 183-185 °C. $^1$H NMR (acetone-$d_6$): $\delta$ 5.91 (br s, NH$_2$), 7.04 (d, $J = 5.3$ Hz, 1 H, H-5´), 7.10-7.22 (m, 2 H, H-5, H-6), 7.46 (d, $J = 7.3$ Hz, 1 H, H-7), 8.12 (m, 2 H, H-6´, H-2), 8.58 (d, $J = 7.7$ Hz, 1 H, H-4), 10.86 (br s, NH). $^{13}$C NMR (acetone-$d_6$): $\delta$ 111.5 (C-5´), 117.2 (C-7), 120.2 (C-3), 126.0/127.7/128.0 (C-4/C-5/C-6), 131.4 (C-3a), 133.0 (C-2), 143.0 (C-7a), 162.7 (C-6´), 168.7/169.5 (C-2´/C-4´). IR (KBr): $\tilde{\nu}$ 3408 cm$^{-1}$, 3329, 3173, 1660, 1568, 1520, 1452, 1413, 1246, 751, 735. Anal. calcd for C$_{12}$H$_{10}$N$_4$: 210.2: C 68.56, H 4.79. Found: C 68.45, H 4.78.


Beige powder.

Dark-brown solid. Mp 183 °C. $^1$H NMR (DMSO-d$_6$, 400 MHz): $\delta$ 6.40 (br, 2H), 7.01 (d, $J = 5.3$ Hz, 1 H), 7.18-7.19 (m, 2 H), 7.42 (d, $J = 7.9$ Hz, 1 H), 8.08 (d, $J = 5.3$ Hz, 1 H), 8.18 (d, $J = 2.9$ Hz, 1 H), 8.56 (d, $J = 7.9$ Hz, 1 H), 11.64 (br, 1H). MS (Cl): $m/z$ 211 (M+1). Anal. calcd for C$_{12}$H$_{10}$N$_4$: C 68.56, H 4.79, N 26.65. Found: C 68.47, H 4.81, N 26.72.


$^1$H NMR (DMSO-d$_6$, 600 MHz): $\delta$ 6.38 (s, NH$_2$), 7.00 (d, $J = 5.3$ Hz, 1 H, H-5’), 7.10 (t, $J = 6.8$ Hz, 1 H, H-6), 7.16 (t, $J = 6.8$ Hz, 1 H, H-5), 7.42 (d, $J = 7.9$ Hz, 1 H, H-7), 8.08 (d, $J = 5.3$ Hz, 1 H, H-6’), 8.17 (d, $J = 2.4$ Hz, 1 H, H-2), 8.56 (d, $J = 7.8$ Hz, 1 H, H-4), 11.93 (br s, 1 H, NH). $^{13}$C NMR (DMSO-d$_6$, 300 MHz): $\delta$ 105.3 (d, C-5’), 111.8 (d, C-7), 113.2 (s, C-3), 120.2 (d, C-6), 121.9 (d, C-4), 122.4 (d, C-5), 125.2 (s, C-7a), 128.2 (d, C-2), 137.0 (s, C-3a), 157.0 (d, C-6’).

The NMR spectra are in good agreement with those reported in the literature. However, the melting point deviates immensely from the melting point reported by Jiang and Radwan.
4.2.10. 4-(4-Methoxy-1H-indol-3-yl)pyrimidin-2-amine (4j)

\[
\begin{align*}
\text{NH} & \\
\text{OMe} & \\
\text{C}_{13}\text{H}_{12}\text{N}_{4}\text{O} & \quad 240.26
\end{align*}
\]

185 mg (0.77 mmol, 77 % yield) as a colorless solid. Mp 221-222 °C. \(^1\)H NMR (DMSO-d\(_6\), 500 MHz): \(\delta\) 3.87 (s, 3 H), 6.27 (s, 2 H, \text{NH}_2), 6.63 (d, \text{J} = 6.9 \text{ Hz}, 1 \text{ H}), 7.06-7.12 (m, 2 H), 7.26 (dd, \text{J} = 5.4 \text{ Hz}, \text{J} = 0.9 \text{ Hz}, 1 \text{ H}), 7.85 (d, \text{J} = 2.5 \text{ Hz}, 1 \text{ H}), 8.15 (d, \text{J} = 5.4 \text{ Hz}, 1 \text{ H}), 11.6 (\text{br}, 1 \text{ H, NH}). \(^{13}\)C NMR (DMSO-d\(_6\), 125 MHz): \(\delta\) 55.0 (CH\(_3\)), 101.2 (CH), 105.5 (CH), 109.7 (CH), 114.4 (C\(_{\text{quat}}\)), 115.4 (C\(_{\text{quat}}\)), 122.7 (CH), 127.5 (CH), 138.8 (C\(_{\text{quat}}\)), 153.2 (C\(_{\text{quat}}\)), 157.0 (CH), 161.8 (C\(_{\text{quat}}\)), 163.2 (C\(_{\text{quat}}\)). EI + MS (m/z (%)): 240 (M\(^+\), 50), 239 (M-H\(^+\), 21), 211 ((M-CH\(_3\)O+H\(^+\), 20), 202 ((M-C\(_2\)H\(_2\)N+2H\(^+\), 11), 58 (CH\(_4\)N\(_3\)\(^+\), 41), 43 (C\(_2\)H\(_3\)O\(^+\), 100). IR (KBr): \(\tilde{\nu}\) 3465 (m), 3313 (m), 1664 (m), 1624 (m), 1575 (s), 1555 (s), 1506 (s), 1459 (s), 1414 (m), 1359 (w), 1320 (m), 1275 (w), 1245 (m), 1212 (w), 1168 (w), 1130 (w), 1088 (m), 970 (w), 884 (w), 815 (w), 778 (w), 733 (m), 706 (w), 630 (w). Anal. calcd for C\(_{13}\)H\(_{12}\)N\(_4\)O: C 64.99, H 5.03, N 23.32. Found: C 64.86, H 4.85, N 23.25.
4.2.11. 4-(5-Phenyl-1H-pyrrol-3-yl)pyrimidin-2-amine (4k)

190 mg (0.80 mmol, 80 % yield) as a rosa solid. Mp 257 °C. $^1$H NMR (DMSO-d$_6$, 500 MHz): $\delta$ 6.35 (s, 2 H, NH$_2$), 6.87 (d, $J = 5.0$ Hz, 1 H), 7.06-7.08 (m, 1 H), 7.18-7.23 (m, 1 H), 7.37-7.41 (m, 2 H), 7.58-7.60 (m, 1 H), 7.66-7.70 (m, 2 H), 8.12 (d, $J = 5.0$ Hz, 1 H), 11.7 (br, 1 H, NH). $^{13}$C NMR (DMSO-d$_6$, 125 MHz): $\delta$ 104.0 (CH), 104.9 (CH), 120.7 (CH), 123.5 (CH), 123.9 (C$_{quat}$), 126.0 (CH), 128.7 (CH), 132.1 (C$_{quat}$), 132.4 (C$_{quat}$), 157.5 (CH), 161.2 (C$_{quat}$), 163.5 (C$_{quat}$). EI + MS (m/z (%)): 237 (16), 236 (M$^+$, 100), 235 ((M-H)$^+$, 22), 195 (35), 133 (13). IR (KBr): $\tilde{\nu}$ 3408 (m) cm$^{-1}$, 3141 (w), 1631 (m), 1567 (s), 1543 (s), 1509 (w), 1455 (s), 1416 (m), 1369 (w), 1281 (w), 1203 (m), 1156 (w), 1110 (w), 1071 (w), 1031 (w), 990 (w), 926 (w), 900 (w), 874 (w), 815 (m), 793 (w), 751 (s), 694 (m), 593 (w), 528 (w). Anal. calcd for C$_{14}$H$_{12}$N$_4$ (236.3): C 71.17, H 5.12, N 23.71. Found: C 71.30, H 5.30, N 23.98.
4.2.12. 5-(5-(4-Chlorophenyl)-1H-pyrrol-3-yl)-1,3-dimethylpyrimidine-2,4(1H,3H)-dione (4l)

202 mg (0.64 mmol, 64% yield) as a rosa solid. Mp 256 °C. $^1$H NMR (DMSO-d$_6$, 500 MHz): $\delta$ 3.25 (s, 3 H), 3.38 (s, 3 H), 6.93 (dd, $J = 2.5$ Hz, $J = 1.6$ Hz, 1 H), 7.41-7.45 (m, 2 H), 7.49 (dd, $J = 2.5$ Hz, $J = 1.6$ Hz, 1 H), 7.61-7.64 (m, 2 H), 8.04 (s, 1 H), 11.4 (br, 1 H, NH). $^{13}$C NMR (DMSO-d$_6$, 125 MHz): $\delta$ 27.6 (CH$_3$), 36.3 (CH$_3$), 103.3 (CH), 107.3 (C$_{quat}$), 116.7 (C$_{quat}$), 118.7 (CH), 124.8 (CH), 128.7 (CH), 129.8 (C$_{quat}$), 131.4 (C$_{quat}$), 137.8 (CH), 150.5 (C$_{quat}$), 161.5 (C$_{quat}$). El + MS ($m/z$ (%)): 317 ((M$^{37}$Cl$^+$, 36), 316 (20), 315 (M$^{35}$Cl$^+$, 100), 258 (22), 229 (11), 217 (27), 203 (13), 201 (28), 189 (18), 154 (13), 140 (14), 116 (10). IR (KBr): $\tilde{\nu}$ 3378 (m) cm$^{-1}$, 1694 (s), 1653 (s), 1627 (s), 1565 (w), 1515 (w), 1443 (m), 1404 (w), 1357 (w), 1231 (w), 1130 (m), 1048 (w), 928 (w), 828 (w), 800 (w), 754 (w), 726 (w), 608 (w), 540 (w). Anal. calcd for C$_{16}$H$_{14}$ClN$_{3}$O$_2$ (315.8): C 60.86, H 4.47, N 13.31. Found: C 60.93, H 4.71, N 13.11.
4.2.13. 4-(5-(4-Methoxyphenyl)-1H-pyrrol-3-yl)pyridine (4m)

![Chemical structure of 4-(5-(4-Methoxyphenyl)-1H-pyrrol-3-yl)pyridine (4m)]

C<sub>16</sub>H<sub>14</sub>N<sub>2</sub>O

250.30

151 mg (0.60 mmol, 60 % yield) as a beige solid. Mp 181-183 °C. <sup>1</sup>H NMR (DMSO-d<sub>6</sub>, 500 MHz): δ 3.77 (s, 3 H), 6.93-7.00 (m, 3 H), 7.53-7.59 (m, 3 H), 7.60-7.65 (m, 2 H), 8.40-8.45 (m, 2 H), 11.6 (br, 1 H, NH). <sup>13</sup>C NMR (DMSO-d<sub>6</sub>, 125 MHz): δ 55.0 (CH<sub>3</sub>), 102.0 (CH), 114.1 (CH), 118.2 (CH), 118.8 (CH), 121.8 (C<sub>quat</sub>), 124.9 (CH), 125.1 (C<sub>quat</sub>), 133.0 (C<sub>quat</sub>), 142.9 (C<sub>quat</sub>), 149.6 (CH), 157.7 (C<sub>quat</sub>). EI + MS (m/z (%)): 251 (21), 250 (M<sup>+</sup>, 100), 236 (13), 235 ((M-CH<sub>3</sub>)<sup>+</sup>, 89), 207 (39), 206 (20), 205 (15), 180 (11), 179 (11), 178 (13), 153 (11), 152 (35), 151 (18), 128 (11), 127 (15), 126 (12), 125 (11), 102 (10), 89 (13), 77 (19), 76 (12), 63 (15), 51 (15). IR (KBr): ν 3114 (m) cm<sup>-1</sup>, 3065 (m), 2991 (m), 2893 (m), 2834 (m), 1602 (s), 1543 (m), 1533 (w), 1505 (s), 1464 (m), 1440 (w), 1429 (m), 1376 (w), 1306 (w), 1287 (m), 1251 (s), 1216 (m), 1180 (m), 1165 (w), 1111 (w), 1094 (w), 1066 (w), 1038 (m), 1001 (m), 935 (w), 834 (m), 795 (s), 750 (w), 738 (w), 691 (m), 667 (w), 638 (w), 610 (w), 525 (m). Anal. calcd for C<sub>16</sub>H<sub>14</sub>N<sub>2</sub>O (250.3): C 76.78, H 5.64, N 11.19. Found: C 76.51, H 5.80, N 11.20.
4.2.14. 4-(4-Fluorophenyl)-2-(thiophen-2-yl)-1H-pyrrole (4n)

\[ \text{C}_{14}\text{H}_{10}\text{FNS} \]

243.30

170 mg (0.70 mmol, 70 % yield) as a pale gray solid. Mp 163 °C. \(^1\)H NMR (DMSO-d\(_6\), 500 MHz): \(\delta\) 6.67-6.69 (m, 1 H), 7.05 (dd, \(J = 5.0\) Hz, \(J = 3.8\) Hz, 1 H), 7.11-7.16 (m, 2 H), 7.26 (dd, \(J = 3.5\) Hz, \(J = 0.9\) Hz, 1 H), 7.29 (dd, \(J = 2.5\) Hz, \(J = 1.9\) Hz, 1 H), 7.35 (dd, \(J = 5.0\) Hz, \(J = 0.9\) Hz, 1 H), 7.58-7.64 (m, 2 H), 11.48 (s, 1 H, NH). \(^13\)C NMR (DMSO-d\(_6\), 125 MHz): \(\delta\) 103.3 (CH), 115.2 (d, \(J = 21.1\) Hz, CH), 116.1 (CH), 120.9 (CH), 122.7 (CH), 123.5 (C\text{quat}), 126.0 (d, \(J = 8.2\) Hz, CH), 127.1 (C\text{quat}), 127.7 (CH), 131.9 (d, \(J = 2.7\) Hz, C\text{quat}), 135.9 (C\text{quat}), 160.2 (d, \(J = 241.9\) Hz, C\text{quat}). EI + MS (m/z (%)): 244 (18), 243 (M\(^+\), 100), 242 ((M-H\(^+\), 14), 215 (14), 183 (11), 133 (18), 122 (19). IR (KBr): \(\tilde{\nu}\) 3412 (s) cm\(^{-1}\), 3123 (w), 1655 (w), 1578 (w), 1535 (w), 1501 (m), 1420 (w), 1300 (w), 1224 (m), 1161 (w), 1130 (m), 1098 (w), 1047 (w), 1010 (w), 924 (w), 840 (s), 811 (w), 793 (s), 770 (m), 685 (s), 662 (m), 597 (w), 577 (w), 538 (m), 515 (s). Anal. calcd for C\(_{14}\)H\(_{10}\)FNS: C 69.11, H 4.14, N 5.76. Found: C 69.29, H 4.35, N 5.68.
4.2.15. 1-Benzyl-4-(4-(trifluoromethyl)phenyl)-1H-pyrazole (4o)

\[
\begin{align*}
\text{C}_{17}\text{H}_{13}\text{F}_{3}\text{N}_{2} \\
302.29
\end{align*}
\]

106 mg (0.35 mmol, 35 % yield) as a colorless solid. Mp 106 °C. \(^1\)H NMR (CDCl\(_3\), 500 MHz): \(\delta\) 5.35 (s, 2 H), 7.26-7.30 (m, 2 H), 7.31-7.40 (m, 3 H), 7.52-7.56 (m, 2 H), 7.56-7.60 (m, 2 H), 7.67 (s, 1 H), 7.86 (s, 1 H). \(^{13}\)C NMR (CDCl\(_3\), 125 MHz): \(\delta\) 56.3 (CH\(_2\)), 122.2, 124.2 (q, \(J = 272.2\) Hz, C\(_{\text{quat}}\)), 125.4, 125.8 (q, \(J = 3.7\) Hz, CH), 126.6, 127.8, 128.2 (q, \(J = 33.0\) Hz, C\(_{\text{quat}}\)), 128.3, 128.9, 136.0, 136.1 (q, \(J = 1.8\) Hz, CH), 137.1. El + MS (m/z (%)): 303 (10), 302 (M\(^+\), 49), 301 ((M-H\(^+\)), 51), 91 (C\(_7\)H\(_7\)^+\), 100), 65 (C\(_5\)H\(_5\)^+\), 11). IR (KBr): \(\tilde{\nu}\) 3106 (w) cm\(^{-1}\), 2925 (w), 2852 (w), 1620 (m), 1456 (w), 1432 (w), 1337 (s), 1229 (w), 1158 (s), 1113 (s), 1080 (m), 1062 (m), 1000 (w), 953 (w), 842 (m), 729 (m), 693 (w), 597 (w), 510 (w), 453 (w). Anal. calcd for C\(_{17}\)H\(_{13}\)F\(_3\)N\(_2\) (302.3): C 67.54, H 4.33, N 9.27. Found: C 67.70, H 4.31, N 9.02.
4.2.16. 1-(Thiophen-3-yl)isoquinoline (4p)

\[
\begin{align*}
\text{C}_{13}\text{H}_{9}\text{NS} & \\
161 \text{ mg (0.76 mmol, 76 % yield) as a colorless solid. } Mp 91-92 \, ^{\circ}\text{C.} \\
\text{H NMR (CDCl}_3, 500 \text{ MHz): } \delta & = 7.49 \text{ (dd, } J = 5.0 \text{ Hz, } J = 2.8 \text{ Hz, 1 H)}, 7.54 \text{ (dd, } J = 5.0 \text{ Hz, } J = 1.3 \text{ Hz, 1 H)}, 7.55-7.59 \text{ (m, 1 H)}, 7.61 \text{ (d, } J = 5.7 \text{ Hz, 1 H}), 7.67-7.71 \text{ (m, 1 H)}, 7.72 \text{ (dd, } J = 2.8 \text{ Hz, } J = 1.3 \text{ Hz, 1 H)}, 7.87 \text{ (d, } J = 8.2 \text{ Hz, 1 H)}, 8.28 \text{ (d, } J = 8.5 \text{ Hz, 1 H)}, 8.57 \text{ (d, } J = 5.7 \text{ Hz, 1 H}). \\
\text{C NMR (CDCl}_3, 125 \text{ MHz): } \delta & = 119.9 \text{ (CH), 125.7 (CH), 126.1 (CH), 126.9 (C}_{\text{quat}}, 127.0 \text{ (CH), 127.2 (CH), 127.3 (CH), 129.2 (CH), 130.0 (CH), 136.8 (C}_{\text{quat}}, 140.7 \text{ (C}_{\text{quat}}, 142.2 \text{ (CH), 155.9 (C}_{\text{quat}}).} \\
\text{Ei + MS (m/z (%)): 212 (12), 211 (M}^+, 57), 210 ((M-H})^+, 100), 166 \text{ (C}_{12}\text{H}_{8}\text{N}^+, 13), 139 \text{ (9), 128 (C}_{9}\text{H}_{6}\text{N}^+, 3), 84 \text{ (C}_{4}\text{H}_{4}\text{S}^+, 10), 83 \text{ (C}_{3}\text{H}_{5}\text{S}^+, 4).} \\
\text{IR (KBr): } \tilde{\nu} & = 3047 \text{ (w) cm}^{-1}, 1614 \text{ (w), 1579 (w), 1552 (m), 1524 (w), 1494 (w), 1452 (w), 1415 (m), 1333 (m), 1306 (m), 1215 (w), 1192 (w), 1138 (w), 1061 (w), 1018 (w), 988 (w), 963 (w), 901 (m), 867 (m), 833 (m), 810 (s), 792 (m), 774 (m), 753 (s), 708 (w), 683 (s), 661 (w), 639 (w), 612 (w), 567 (w), 514 (w).} \\
\text{Anal. calcd for C}_{13}\text{H}_{9}\text{NS (211.3): C 73.90, H 4.29, N 6.63. Found: C 73.72, H 4.22, N 6.62.}
\end{align*}
\]

Data reported in the literature:


Yellow solid. Mp 74-75 \, ^{\circ}\text{C.} \text{H NMR (CDCl}_3, 300 \text{ MHz): } \delta = 7.49 \text{ (ddd, } J = 6 \text{ Hz, } J = 3 \text{ Hz, } J = 1 \text{ Hz, 1 H), 7.55 (dt, } J = 1.6 \text{ Hz, 1 H), 7.57 (dt, } J = 1.8 \text{ Hz, 1 H), 7.62 (d, } J = 6 \text{ Hz, 1 H), 7.69 (dt, } J = 1.8 \text{ Hz, 1 H), 7.72 (dt, } J = 1.3 \text{ Hz, 1 H), 7.87 (d, } J = 8 \text{ Hz, 1 H), 8.29 (d, } J = 8 \text{ Hz, 1 H), 8.58 (d, } J = 6 \text{ Hz, 1 H).} \\
\text{C NMR (CDCl}_3, 75 \text{ MHz): } \delta = 119.8, 125.6, 126.0, 126.9, 127.1, 127.3, 129.1, 130.0, 130.5, 136.7, 140.6, 142.1, 155.8. \text{IR (neat): } \tilde{\nu} = 3105 \text{ cm}^{-1}, 3049, 1620, 1582, 1555, 1498, 1418, 1337, 1309. \text{Anal. calcd for C}_{13}\text{H}_{9}\text{NS (211.3): C 73.90, H 4.29. Found: C 73.79, H 4.25.}
4.2.17. 4-(2-Ethyl-5-(thiophen-2-yl)furan-3-yl)benzonitrile (4q)

![Chemical Structure](image)

C_{17}H_{13}NOS

279.36

221 mg (0.79 mmol, 79 % yield) as a pale yellow solid (after crystallization by suspension in n-pentane, sonication in ultrasound bath, filtration and drying in vacuo overnight). Mp 108 °C. \(^1^H\) NMR (CDCl\(_3\), 500 MHz): \(\delta\) 1.34 (t, \(J = 7.6\) Hz, 3 H), 2.85 (q, \(J = 7.6\) Hz, 2 H), 6.60 (s, 1 H), 7.05 (dd, \(J = 5.0\) Hz, \(J = 3.8\) Hz, 1 H), 7.24 (dd, \(J = 5.0\) Hz, \(J = 0.9\) Hz, 1 H), 7.27 (dd, \(J = 3.5\) Hz, \(J = 0.9\) Hz, 1 H), 7.47-7.51 (m, 2 H), 7.66-7.70 (m, 2 H). \(^1^C\) NMR (CDCl\(_3\), 125 MHz): \(\delta\) 12.8 (CH\(_3\)), 20.6 (CH\(_2\)), 105.6 (CH), 110.0 (C\(_{\text{quat}}\)), 119.0 (C\(_{\text{quat}}\)), 121.0 (C\(_{\text{quat}}\)), 122.6 (CH), 124.2 (CH), 127.7 (CH), 128.0 (CH), 132.4 (CH), 133.2 (C\(_{\text{quat}}\)), 138.7 (C\(_{\text{quat}}\)), 147.9 (C\(_{\text{quat}}\)), 153.5 (C\(_{\text{quat}}\)). EI + MS (m/z (%)): 280 (12), 279 (M\(^+\), 59), 265 (18), 264 ((M-CH\(_3\))\(^+\), 100), 166 (22), 164 (17), 131 (13), 129 (13), 111 (23). IR (KBr): \(\tilde{\nu}\) 2975 (w) cm\(^{-1}\), 2222 (s), 1606 (s), 1503 (w), 1203 (w), 1177 (w), 1133 (w), 1060 (m), 983 (m), 947 (w), 840 (m), 799 (m), 707 (s), 567 (m), 549 (m). Anal. calcd for C\(_{17}\)H\(_{13}\)NOS (279.4): C 73.09, H 4.69, N 5.01. Found: C 72.99, H 4.43, N 4.91.
4.2.18. 5-(4-(Trifluoromethoxy)phenyl)pyridin-2-amine (4r)

\[
\text{\[OCF_3\]}
\]
\[
\text{H}_2\text{N}
\]
\[
\text{C}_{12}\text{H}_{9}\text{F}_3\text{N}_2\text{O}
\]
\[
254.21
\]

233 mg (0.92 mmol, 92 % yield) as a colorless solid. Mp 98-101 °C. \(^1\)H NMR (DMSO-d\(_6\), 500 MHz): \(\delta\) 6.12 (s, 2 H, NH\(_2\)), 6.54 (d, \(J = 8.5\) Hz, 1 H), 7.34-7.38 (m, 2 H), 7.65-7.68 (m, 2 H), 7.70 (dd, \(J = 8.5\) Hz, \(J = 2.5\) Hz, 1 H), 8.24 (d, \(J = 2.5\) Hz, 1 H). \(^{13}\)C NMR (DMSO-d\(_6\), 125 MHz): \(\delta\) 108.1 (CH), 120.2 (q, \(J = 255.7\) Hz, C\(_{\text{quat}}\)), 121.6 (CH), 122.6 (C\(_{\text{quat}}\)), 127.1 (CH), 135.6 (CH), 137.6 (C\(_{\text{quat}}\)), 146.0 (CH), 147.0 (q, \(J = 1.8\) Hz, C\(_{\text{quat}}\)), 159.5 (C\(_{\text{quat}}\)). EI + MS (m/z (%)): 255 (13), 254 (M\(^+\), 100), 185 ((M-CF\(_3\))\(^+\), 30), 158 (12). IR (KBr): \(\tilde{\nu}\) 3490 (w), 3466 (w), 3298 (w), 3150 (w), 1638 (s), 1634 (s), 1603 (m), 1562 (w), 1494 (s), 1423 (w), 1389 (m), 1249 (s), 1147 (s), 1017 (w), 997 (w), 857 (w), 827 (w), 806 (w), 671 (w), 537 (w), 509 (w). Anal. calcd for C\(_{12}\)H\(_9\)F\(_3\)N\(_2\)O (254.2): C 56.70, H 3.57, N 11.02. Found: C 56.64, H 3.57, N 10.75.
4.2.19. 5-(4-(Trifluoromethyl)phenyl)pyrimidin-2-amine (4s)

\[
\text{C}_{11}\text{H}_8\text{F}_3\text{N}_3
\]

\[
\begin{array}{c}
\text{N} \\
\text{CF}_3 \\
\text{N} \\
\end{array}
\]

105 mg (0.44 mmol, 44 % yield) as a colorless solid. Mp < 176 °C (subl.)*. \(^1\)H NMR (DMSO-d\textsubscript{6}, 500 MHz): \(\delta\) 6.93 (s, 2 H, NH\textsubscript{2}), 7.73-7.76 (m, 2 H), 7.82-7.86 (m, 2 H), 8.65 (s, 2 H). \(^{13}\)C NMR (DMSO-d\textsubscript{6}, 125 MHz): \(\delta\) 120.6 (C\textsubscript{quat}), 124.5 (q, \(J = 272.2\) Hz, C\textsubscript{quat}), 125.8 (CH), 125.9 (q, \(J = 3.7\) Hz, CH), 127.3 (q, \(J = 32.1\) Hz, C\textsubscript{quat}), 139.5 (C\textsubscript{quat}), 156.5 (CH), 163.3 (C\textsubscript{quat}). El + MS (\(m/z\) (%)): 240 (13), 239 (M\textsuperscript{+}, 100), 238 ((M-H)^{+}, 26), 211 (10), 198 (13), 170 (28), 169 (12), 151 (12), 120 (17). IR (KBr): \(\tilde{\nu}\) 3478 (w) cm\textsuperscript{-1}, 3321 (w), 3165 (w), 1661 (m), 1638 (m), 1599 (m), 1550 (w), 1528 (w), 1482 (m), 1424 (w), 1382 (w), 1324 (s), 1300 (m), 1224 (w), 1174 (m), 1133 (m), 1112 (m), 1071 (m), 1013 (w), 838 (m), 799 (w), 721 (w), 664 (w), 639 (w), 599 (w), 517 (w). Anal. calcd for C\textsubscript{11}H\textsubscript{8}F\textsubscript{3}N\textsubscript{3} (239.2): C 55.23, H 3.37, N 17.57. Found: C 55.23, H 3.44, N 17.46.

*Slow sublimation with not clearly detectable sublimation point.
4.2.20. 4-(Pyridazin-4-yl)phenol (4t)

\[
\text{\begin{tikzpicture}
  \node[draw, shape=circle] (a) at (0,0) {N};
  \node[draw, shape=circle] (b) at (-1,-1) {N};
  \node[draw, shape=circle] (c) at (0,-2) {\text{HO}};
  \node[draw, shape=circle] (d) at (1,-2) {\text{C}};
  \node[draw, shape=circle] (e) at (1,0) {\text{C}};
  \node[draw, shape=circle] (f) at (0,1) {\text{C}};
  \node[draw, shape=circle] (g) at (-1,1) {\text{C}};
  \draw (a) -- (b) -- (c) -- (d) -- (e) -- (f) -- (g) -- (a);
\end{tikzpicture}}
\]

C_{10}H_{8}N_{2}O

172.18

121 mg (0.70 mmol, 70 % yield) as a rosa solid. Mp 242 °C. \(^1\)H NMR (DMSO-d\(_6\), 500 MHz): \(\delta\) 6.91-6.95 (m, 2 H), 7.76-7.80 (m, 2 H), 7.88 (dd, J = 5.4 Hz, J = 2.5 Hz, 1 H), 9.14 (dd, J = 5.4 Hz, J = 1.3 Hz, 1 H), 9.55 (dd, J = 2.5 Hz, J = 1.3 Hz, 1 H), 10.2 (br, 1 H, OH). \(^{13}\)C NMR (DMSO-d\(_6\), 125 MHz): \(\delta\) 116.4 (CH), 122.0 (CH), 124.2 (C\text{quat}), 128.7 (CH), 137.2 (C\text{quat}), 149.0 (CH), 151.5 (CH), 159.6 (C\text{quat}). EI + MS (m/z (%)): 173 (13), 172 (M\(^+\), 100), 118 (41), 115 (30), 91 (10), 89 (16). IR (KBr): \(\tilde{\nu}\) 3448 (w) cm\(^{-1}\), 3073 (w), 1615 (w), 1574 (s), 1515 (m), 1444 (w), 1390 (w), 1360 (w), 1285 (s), 1242 (w), 1177 (m), 1111 (w), 1046 (w), 979 (w), 839 (w), 812 (m), 789 (w), 745 (w), 665 (w), 571 (w). Anal. calcd for C\(_{10}\)H\(_8\)N\(_2\)O (172.2): C 69.76, H 4.68, N 16.27. Found: C 69.49, H 4.91, N 16.10.

Data reported in the literature:


4.2.21. 4-(3,4,5-Trimethoxyphenyl)pyridine-2,6-diamine hydrochloride (4u)

\[
\begin{align*}
\text{H}_2\text{N} & \quad \text{HCl} \\
\text{N} & \quad \text{NH}_2 \\
\text{MeO} & \\
\text{MeO} & \quad \text{OMe} \\
\text{H}_2\text{N} &
\end{align*}
\]

C\textsubscript{14}H\textsubscript{18}ClN\textsubscript{3}O\textsubscript{3}  
311.76

136 mg (0.44 mmol, 44 % yield) as an orange solid (after crystallization with n-pentane from 1.25 \( M \) HCl in EtOH, filtration, washing with n-pentane, and drying in vacuo overnight at 70 °C). Mp 128-135 °C. \(^1\text{H} \text{NMR} \) (DMSO-\textsubscript{d}\textsubscript{6}, 500 MHz): \( \delta \) 1.34 (t, \( J = 7.6 \text{ Hz}, 3 \text{ H} \)), 2.85 (q, \( J = 7.6 \text{ Hz}, 2 \text{ H} \)), 6.60 (s, 1 H), 7.05 (dd, \( J = 5.0 \text{ Hz}, J = 3.8 \text{ Hz}, 1 \text{ H} \)), 7.24 (dd, \( J = 5.0 \text{ Hz}, J = 0.9 \text{ Hz}, 1 \text{ H} \)), 7.27 (dd, \( J = 3.5 \text{ Hz}, J = 0.9 \text{ Hz}, 1 \text{ H} \)), 7.47-7.51 (m, 2 H), 7.66-7.70 (m, 2 H). \(^{13}\text{C} \text{NMR} \) (DMSO-\textsubscript{d}\textsubscript{6}, 125 MHz): \( \delta \) 12.8 (CH\textsubscript{3}), 20.6 (CH\textsubscript{2}), 105.6 (CH), 110.0 (C\textsubscript{quat}), 119.0 (C\textsubscript{quat}), 121.0 (C\textsubscript{quat}), 122.6 (CH), 124.2 (CH), 127.7 (CH), 128.0 (CH), 132.4 (CH), 133.2 (C\textsubscript{quat}), 138.7 (C\textsubscript{quat}), 147.9 (C\textsubscript{quat}), 153.5 (C\textsubscript{quat}). EI + MS (m/z (%)): 276 (17), 275 ((M-HCl)\textsuperscript{+}, 100), 260 ((M-HCl-CH\textsubscript{3})\textsuperscript{+}, 17), 217 (C\textsubscript{11}H\textsubscript{11}N\textsubscript{3}O\textsubscript{2}\textsuperscript{+}, 20), 108 (C\textsubscript{6}H\textsubscript{5}N\textsubscript{3}\textsuperscript{+}, 5). IR (KBr): \( \tilde{\nu} \) 3410 (m), 3334 (m), 3207 (m), 2941 (w), 2837 (w), 2741 (w), 1645 (s), 1588 (m), 1518 (w), 1492 (w), 1463 (w), 1413 (w), 1378 (m), 1325 (m), 1267 (w), 1245 (w), 1169 (w), 1127 (s), 999 (m), 965 (w), 831 (w), 807 (w), 757 (w), 720 (w), 562 (w), 524 (w). Anal. calcd for C\textsubscript{14}H\textsubscript{18}ClN\textsubscript{3}O\textsubscript{3} (311.8): C 53.93, H 5.82, N 13.48. Found: C 53.73, H 6.03, N 13.35.
4.3. Synthesis of Meridianin A (5)

Synthesis of 3-(2-aminopyrimidin-4-yl)-1H-indol-4-ol (Meridianin A, 5)

Pyridinium hydrochloride (1.18 g, 10.0 mmol) was placed in a dry screw-cap vessel under argon atmosphere. Then, 4-(4-methoxy-1H-indol-3-yl)pyrimidin-2-amine (4j) (120 mg, 0.50 mmol) was added and the mixture was heated to 210 °C (preheated oil bath). After 30 min, the mixture was cooled to 50 °C (preheated oil bath) and methanol was added to dissolve the residue. The reaction mixture was monitored by TLC. The mixture was adsorbed on Celite® and the solvents were removed under reduced pressure. The residue was purified chromatographically on silica gel with dichloromethane-methanol-aqueous ammonia DCM-MeOH-NH₃ = 100:1:1 → 100:2:1 → 100:3:1 → 100:4:1 (stepwise gradient). After drying in vacuo, meridianin A (5) was obtained as a bright yellow fine crystalline solid.
Spectroscopic data of 3-(2-aminopyrimidin-4-yl)-1H-indol-4-ol (Meridianin A, 5)

\[
\begin{align*}
\text{C}_{12}\text{H}_{10}\text{N}_4\text{O} & \\
226.23
\end{align*}
\]

96 mg (0.43 mmol, 85 % yield) as a bright yellow fine crystalline solid. Mp 264-276 °C. (Lit.: 164-168 °C). \(^1\)H NMR (DMSO-d\(_6\), 500 MHz): \(\delta\) 6.39 (dd, \(J = 7.9\) Hz, \(J = 0.9\) Hz, 1 H), 6.76 (s, 2 H, NH\(_2\)), 6.82 (dd, \(J = 8.2\) Hz, \(J = 0.9\) Hz, 1 H), 7.00 (t, \(J = 7.9\) Hz, 1 H), 7.14 (d, \(J = 5.4\) Hz, 1 H), 8.14 (d, \(J = 5.4\) Hz, 1 H), 8.25 (d, \(J = 3.2\) Hz, 1 H), 8.27 (br s, 1 H, OH). \(^{13}\)C NMR (DMSO-d\(_6\), 125 MHz): \(\delta\) 102.3 (CH), 104.3 (CH), 105.5 (CH), 113.7 (C \_quat), 114.3 (C \_quat), 124.4 (CH), 128.4 (CH), 139.2 (C \_quat), 152.0 (C \_quat), 158.4 (CH), 160.4 (C \_quat), 161.7 (C \_quat). EI + MS (m/z (%)): 226 (M\(^+\), 100), 225 ((M-H)\(^+\), 13), 209 ((M-OH)\(^+\), 2), 197 ((M-COH)\(^+\), 6), 185 ((M-CH\(_2\)N\(_2\)+H)\(^+\), 18), 158 ((M-C\(_3\)H\(_4\)N\(_2\))\(^+\), 6). IR (KBr): \(\tilde{\nu}\) 3429 (m) cm\(^{-1}\), 3342 (m), 1638 (m), 1593 (s), 1562 (m), 1532 (m), 1469 (m), 1444 (m), 1401 (m), 1321 (m), 1272 (w), 1227 (m), 1194 (w), 1167 (w), 820 (w), 802 (w), 775 (w), 719 (m), 617 (w). Anal. calcd for C\(_{12}\)H\(_{10}\)N\(_4\)O (226.2): C 63.71, H 4.46, N 24.76. Found: C 63.48, H 4.61, N 24.72.


\(^1\)H NMR (DMSO-d\(_6\), 400 MHz): \(\delta\) 6.38 (dd, \(J = 0.7\) Hz, \(J = 0.7\) Hz, 1 H), 6.68 (br s, 2 H, NH\(_2\)), 6.81 (dd, \(J = 7.7\) Hz, \(J = 0.7\) Hz, 1 H), 6.98 (dd, \(J = 7.7\) Hz, \(J = 7.7\) Hz, 1 H), 7.12 (d, \(J = 5.4\) Hz, 1 H), 8.12 (br d, \(J = 5.4\) Hz, 1 H), 8.22 (d, \(J = 2.5\) Hz, 1 H), 11.75 (br s, 1 H, NH), 13.55 (s, 1 H, OH). \(^{13}\)C NMR (DMSO-d\(_6\), 100 MHz): \(\delta\) 102.3, 104.3, 105.4, 113.7, 114.3, 124.3, 128.3, 139.2, 152.0, 158.3, 160.7, 161.7.
Data reported in the literature:


Yellow needles (MeOH-H₂O). Mp 164-168 °C. ¹H NMR (DMSO-d₆, 200 MHz): δ 6.36 (dd, J = 7.1 Hz, J = 0.7 Hz, H-5), 6.69 (s, NH₂), 6.78 (dd, J = 7.5 Hz, J = 0.7 Hz, H-7), 6.96 (dd, J = 7.5 Hz, J = 7.1 Hz, H-6), 7.09 (d, J = 5.4 Hz, H-5’), 8.10 (d, J = 5.4 Hz, H-6’), 8.20 (d, J = 1.2 Hz, H-2), 11.71 (brs, NH), 13.55 (s, OH). ¹³C NMR (DMSO-d₆, 50 MHz): δ 102.4 (C-7), 104.5 (C-5’), 105.6 (C-5), 113.8 (C-3), 114.5 (C-3a), 124.4 (C-6), 128.5 (C-2), 139.4 (C-7a), 152.1 (C-4), 158.5 (C-6’), 160.6 (C-4’), 161.9 (C-2’). HREIMS calcd for C₁₂H₁₀N₄O: 226.0855. Found: 226.0857. IR (KBr): ʋ 3437 cm⁻¹, 3351, 3200, 2924, 1647, 1605, 1533, 1469, 1326, 820, 721. UV (CH₃Cl) Ɣ max (logε) 248 (3.68), 356 (3.58) nm.

NMR spectra of *meridianin A* are in good agreement with those given by Palermo.


Yellow prisms (EtOH-hexane). Mp 164-168 °C. ¹H NMR (DMSO-d₆, 300 MHz): δ 7.13 (dd, J = 7.8 Hz, J = 0.9 Hz, 1 H, H-5), 7.48 (brs, 2 H, NH₂), 7.57 (dd, J = 8.1 Hz, J = 0.9 Hz, 1 H), 7.74 (dd, J = 7.8 Hz, 1 H, H-6), 7.88 (d, J = 5.7 Hz, 1 H, H-5’), 9.0 (s, 1 H, H-2), 11.8 (s, 1 H, NH), 13.9 (s, 1 H, OH). ¹³C NMR (DMSO-d₆, 75 MHz): δ 102.3 (C-7), 104.4 (C-5’), 105.4 (C-5), 113.7 (C-3), 114.4 (C-3a), 124.4 (C-6), 128.4 (C-2), 139.2 (C-7a), 152.0 (C-4), 158.4 (C-6’), 160.5 (C-4’), 161.7 (C-2’). IR (nujol): ʋ 3456 (m) cm⁻¹, 3416 (m), 3340 (m), 3181 (m), 1627 (m), 1586 (s), 1532 (s), 1270 (s), 1124 (s), 1072 (s). EI + MS (m/z (%)): 226 (M⁺, 100), 185 (26), 167 (16), 149 (59). Anal. calcd for C₁₂H₁₀N₄O (226.2): C 63.71, H 4.46, N 24.76. Found: C 63.57, H 4.31, N 24.93.

The ¹³C NMR values are in good agreement with those given by Fresneda and Molina, but the ¹H NMR values deviate considerably.

However, the melting point deviates immensely from the melting point reported both by Palermo as well as Fresneda and Molina.
5. $^1$H and $^{13}$C NMR Spectra of Compounds 4a-u and 5

$^1$H NMR of 4a (15 mg) in 0.7 mL DMSO-$d_6$ at 297 K ($\delta$ in ppm). *Impurities from residual solvents.
$^{13}$C NMR of 4a (15 mg) in 0.7 mL DMSO-$_6$ at 297 K ($\delta$ in ppm).

$^{13}$C DEPT 135-NMR of 4a (15 mg) in 0.7 mL DMSO-$_6$ at 297 K ($\delta$ in ppm).
$^1$H NMR of 4b (15 mg) in 0.7 mL DMSO-d$_6$ at 296 K (δ in ppm). *Impurities from residual solvents.
$^{13}$C NMR of 4b (15 mg) in 0.7 mL DMSO-d$_6$ at 296 K ($\delta$ in ppm).

$^{13}$C DEPT 135-NMR of 4b (15 mg) in 0.7 mL DMSO-d$_6$ at 296 K ($\delta$ in ppm).
$^1$H NMR of 4c (15 mg) in 0.7 mL DMSO-$d_6$ at 299 K ($\delta$ in ppm).
\(^{13}\text{C}\) NMR of 4c (15 mg) in 0.7 mL DMSO-\(d_6\) at 299 K (\(\delta\) in ppm).

\(^{13}\text{C}\) DEPT 135-NMR of 4c (15 mg) in 0.7 mL DMSO-\(d_6\) at 299 K (\(\delta\) in ppm).
$^1$H NMR of 4d (15 mg) in 0.7 mL DMSO-d$_6$ at 297 K ($\delta$ in ppm).
$^{13}$C NMR of 4d (15 mg) in 0.7 mL DMSO-$d_6$ at 297 K (δ in ppm).

$^{13}$C DEPT 135-NMR of 4d (15 mg) in 0.7 mL DMSO-$d_6$ at 297 K (δ in ppm).
$^1$H NMR of 4e (15 mg) in 0.7 mL DMSO-d$_6$ at 299 K (δ in ppm).
$^{13}$C NMR of 4e (15 mg) in 0.7 mL DMSO-d$_6$ at 299 K ($\delta$ in ppm).

$^{13}$C DEPT 135-NMR of 4e (15 mg) in 0.7 mL DMSO-d$_6$ at 299 K ($\delta$ in ppm).
$^1$H NMR of 4f (15 mg) in 0.7 mL DMSO-d$_6$ at 298 K ($\delta$ in ppm). *Impurities from residual solvents.
$^{13}$C NMR of $4f$ (15 mg) in 0.7 mL DMSO-d$_6$ at 298 K (δ in ppm).

$^{13}$C DEPT 135-NMR of $4f$ (15 mg) in 0.7 mL DMSO-d$_6$ at 298 K (δ in ppm).
$^1$H NMR of 4g (15 mg) in 0.7 mL DMSO-d$_6$ at 298 K ($\delta$ in ppm). *Impurities from residual solvents.
$^{13}$C NMR of 4g (15 mg) in 0.7 mL DMSO-\textsubscript{d$_6$} at 297 K (\(\delta\) in ppm).

$^{13}$C DEPT 135-NMR of 4g (15 mg) in 0.7 mL DMSO-\textsubscript{d$_6$} at 298 K (\(\delta\) in ppm).
$^1$H NMR of 4h (30 mg) in 0.7 mL DMSO-d$_6$ at 296 K ($\delta$ in ppm).
$^{13}$C NMR of 4h (30 mg) in 0.7 mL DMSO-$d_6$ at 296 K ($\delta$ in ppm).

$^{13}$C DEPT 135-NMR of 4h (30 mg) in 0.7 mL DMSO-$d_6$ at 295 K ($\delta$ in ppm).
$^1$H NMR of 4i (15 mg) in 0.7 mL DMSO-d$_6$ at 296 K (δ in ppm).
$^{13}$C NMR of 4i (15 mg) in 0.7 mL DMSO-d$_6$ at 296 K ($\delta$ in ppm).

$^{13}$C DEPT 135-NMR of 4i (15 mg) in 0.7 mL DMSO-d$_6$ at 296 K ($\delta$ in ppm).
$^1$H NMR of 4j (30 mg) in 0.7 mL DMSO-d$_6$ at 297 K (δ in ppm).
$^{13}$C NMR of 4j (30 mg) in 0.7 mL DMSO-$d_6$ at 298 K (δ in ppm).

$^{13}$C DEPT 135-NMR of 4j (30 mg) in 0.7 mL DMSO-$d_6$ at 297 K (δ in ppm).
\(^1\)H NMR of 4k (20 mg) in 0.7 mL DMSO-d\(_6\) at 296 K (\(\delta\) in ppm).
$^{13}$C NMR of 4k (20 mg) in 0.7 mL DMSO-d$_6$ at 296 K ($\delta$ in ppm).

$^{13}$C DEPT 135-NMR of 4k (20 mg) in 0.7 mL DMSO-d$_6$ at 296 K ($\delta$ in ppm).
$^1$H NMR of 4I (20 mg) in 0.7 mL DMSO-$d_6$ at 298 K ($\delta$ in ppm).
$^{13}$C NMR of 4I (20 mg) in 0.7 mL DMSO-$d_6$ at 298 K ($\delta$ in ppm).

$^{13}$C DEPT 135-NMR of 4I (20 mg) in 0.7 mL DMSO-$d_6$ at 298 K ($\delta$ in ppm).
$^1$H NMR of 4m (15 mg) in 0.7 mL DMSO-$d_6$ at 297 K (δ in ppm). *Impurities from residual solvents.
$^{13}$C NMR of 4m (15 mg) in 0.7 mL DMSO-d$_6$ at 297 K ($\delta$ in ppm). *Impurities from residual solvents.

$^{13}$C DEPT 135-NMR of 4m (15 mg) in 0.7 mL DMSO-d$_6$ at 297 K ($\delta$ in ppm). *Impurities from residual solvents.
$^1$H NMR of 4n (20 mg) in 0.7 mL DMSO-$_d$$_6$ at 298 K ($\delta$ in ppm).
$^{13}$C NMR of 4n (20 mg) in 0.7 mL DMSO-$d_6$ at 299 K ($\delta$ in ppm).

$^{13}$C DEPT 135-NMR of 4n (20 mg) in 0.7 mL DMSO-$d_6$ at 298 K ($\delta$ in ppm).
$^1$H NMR of 40 (50 mg) in 0.7 mL CDCl$_3$ at 297 K ($\delta$ in ppm). *Impurities from residual solvents.
$^{13}$C NMR of 4o (50 mg) in 0.7 mL CDCl$_3$ at 298 K ($\delta$ in ppm). *Impurities from residual solvents.

$^{13}$C DEPT 135-NMR of 4o (50 mg) in 0.7 mL CDCl$_3$ at 297K ($\delta$ in ppm). *Impurities from residual solvents.
$^1$H NMR of 4p (20 mg) in 0.7 mL CDCl$_3$ at 296 K ($\delta$ in ppm). *Impurities from residual solvents.
$^{13}$C NMR of 4p (20 mg) in 0.7 mL CDCl$_3$ at 296 K ($\delta$ in ppm).

$^{13}$C DEPT 135-NMR of 4p (20 mg) in 0.7 mL CDCl$_3$ at 296 K ($\delta$ in ppm).
$^1$H NMR of 4q (20 mg) in 0.7 mL CDCl$_3$ at 298 K (δ in ppm). *Impurities from residual solvents.
$^{13}$C NMR of 4q (20 mg) in 0.7 mL CDCl$_3$ at 298 K ($\delta$ in ppm).

$^{13}$C DEPT 135-NMR of 4q (20 mg) in 0.7 mL CDCl$_3$ at 298 K ($\delta$ in ppm).
\(^1\)H NMR of 4r (30 mg) in 0.7 mL CDCl\(_3\) at 296 K (\(\delta\) in ppm).
$^{13}$C NMR of 4r (30 mg) in 0.7 mL CDCl$_3$ at 296 K ($\delta$ in ppm).

$^{13}$C DEPT 135-NMR of 4r (30 mg) in 0.7 mL CDCl$_3$ at 296 K ($\delta$ in ppm).
$^1$H NMR of 4s (15 mg) in 0.7 mL CDCl$_3$ at 297 K ($\delta$ in ppm).
$^{13}$C NMR of 4s (15 mg) in 0.7 mL CDCl$_3$ at 297 K ($\delta$ in ppm).

$^{13}$C DEPT 135-NMR of 4s (15 mg) in 0.7 mL CDCl$_3$ at 297 K ($\delta$ in ppm).
$^1$H NMR of 4t (20 mg) in 0.7 mL DMSO-d$_6$ at 297 K ($\delta$ in ppm). *Impurities from residual solvents.
$^{13}$C NMR of 4t (20 mg) in 0.7 mL DMSO-d$_6$ at 297 K ($\delta$ in ppm).

$^{13}$C DEPT 135-NMR of 4t (20 mg) in 0.7 mL DMSO-d$_6$ at 297 K ($\delta$ in ppm).
\(^1\)H NMR of 4u (20 mg) in 0.7 mL DMSO-d\(_6\) at 296 K (\(\delta\) in ppm).
$^{13}$C NMR of 4u (20 mg) in 0.7 mL DMSO-d$_6$ at 296 K ($\delta$ in ppm).

$^{13}$C DEPT 135-NMR of 4u (20 mg) in 0.7 mL DMSO-d$_6$ at 296 K ($\delta$ in ppm).
$^1$H NMR of 5 (30 mg) in 0.7 mL DMSO-$d_6$ at 298 K ($\delta$ in ppm). *Impurities from residual solvents.
$^{13}$C NMR of 5 (30 mg) in 0.7 mL DMSO-$d_6$ at 298 K (δ in ppm).

$^{13}$C DEPT 135-NMR of 5 (30 mg) in 0.7 mL DMSO-$d_6$ at 297 K (δ in ppm).
6. Appendix

6.1. UV Purity of Compounds 4a-u and 5

HT-LC-MS Spectrum (SOP 2200) of 4a. UV purity: 100 %
HT-LC-MS Spectrum (SOP 2200) of 4b. UV purity: 100%
HT-LC-MS Spectrum (SOP 2200) of 4c. UV purity: 100 %
HT-LC-MS Spectrum (SOP 2200) of 4d. UV purity: 98.1 %
HT-LC-MS Spectrum (SOP 2200) of 4e. UV purity: 100 %

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HT-LC-MS Spectrum (SOP 2200) of 4f. UV purity: 100 %
HT-LC-MS Spectrum (SOP 2222) of 4g. UV purity: 100 %
HT-LC-MS Spectrum (SOP 2200) of 4h. UV purity: 97.5 %
HT-LC-MS Spectrum (SOP 2200) of 4i. UV purity: 99.6 %
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<th>Compound</th>
<th>Time</th>
<th>Mass Found</th>
</tr>
</thead>
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<tr>
<td>2</td>
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<td>211.1 [MS ES+] 8.7e+006</td>
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</tbody>
</table>

<table>
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<th>Compound</th>
<th>Time</th>
<th>Mass Found</th>
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<td></td>
</tr>
<tr>
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<td>(Time: 1.77) Combine</td>
<td>367:371</td>
<td>212.1 [MS ES-] 1.0e+006</td>
</tr>
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</table>

| Mass | 216.9 | 248.9 | 240.6 | 243.1 | 355.0 | 220.9 | 529.0 | 650.9 | 667.2 | 787.1 | 828.6 | 923.2 | 953.6 |

m/z
HT-LC-MS Spectrum (SOP 2200) of 4j. UV purity: 100 %
HT-LC-MS Spectrum (SOP 2200) of 4k. UV purity: 98.2 %

3: UV Detector: 254 Smooth (Mn, 2x3)  

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1: MS ES+ +DPI Smooth (SG, 2x4)

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1: MS ES+ :237.11+259.11 Smooth (SG, 2x4)

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1: MS ES+ :473.22+495.22 Smooth (SG, 2x4)

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1: MS ES+ - DPT Smooth (SG, 2x4)

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HT-LC-MS Spectrum (SOP 2200) of 4l. UV purity: 100 %

3: UV Detector: 254 Smooth (N, 2x3)

Peak Number Compound Time AreaAbs Area %Total Width Height Mass Found
1 100% 315.1 (63%) 3.56

1: MS ES+ iBPI Smooth (SG, 2x4)

Peak Number Compound Time AreaAbs Area %Total Width Height Mass Found
1 100% 315.1 (63%) 3.56

2: MS ES+ 631.16+653.16 Smooth (SG, 2x4)

Peak Number Compound Time AreaAbs Area %Total Width Height Mass Found
2 100% 3.00

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HT-LC-MS Spectrum (SOP 2222) of 4m. UV purity: 100 %
HT-LC-MS Spectrum (SOP 2200) of 4n. UV purity: 100 %
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<td>244.0 245.1</td>
<td>210.9</td>
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**Supplementary Material (ESI) for Organic & Biomolecular Chemistry**

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HT-LC-MS Spectrum (SOP 2200) of 4o. UV purity: 100 %

3: UV Detector: 254 Smooth (Ms, 2x3)

1: MS ES+ iRFI Smooth (SG, 2x4)
### HT-LC-MS Spectrum (SOP 2200) of 4p. UV purity: 100%

3: UV Detector: 254 Smooth (Nt, 2x3)  

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1: MS ES+ rBPI Smooth (SG, 2x4)  

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1: MS ES+ rBPI Smooth (SG, 2x4)  

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1: MS ES+ rBPI Smooth (SG, 2x4)  

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2: MS ES- rBPI Smooth (SG, 2x4)  

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<tr>
<td>7</td>
<td>Compound</td>
<td>1.71</td>
<td>249.0, 394.9</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Supplementary Material (ESI) for Organic & Biomolecular Chemistry*
HT-LC-MS Spectrum (SOP 2200) of 4q. UV purity: 100 %

<table>
<thead>
<tr>
<th>Peak Number</th>
<th>Compound</th>
<th>Time</th>
<th>AreaAbs</th>
<th>Area %Total</th>
<th>Width</th>
<th>Height</th>
<th>Mass Found</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>MS ES+ 1BFI Smooth (SG, 2x4)</td>
<td>3.906e-1</td>
<td>1.2e+06</td>
<td>2.9e+06</td>
<td>1.5e+04</td>
<td>1.6e+05</td>
<td></td>
</tr>
</tbody>
</table>
HT-LC-MS Spectrum (SOP 2200) of 4r. UV purity: 100 %
HP-LC-MS Spectrum (SOP 2200) of 4s. UV purity: 100 %
HP-LC-MS Spectrum (SOP 2200) of 4t. UV purity: 100 %
HT-LC-MS Spectrum (SOP 2200) of 4u. UV purity: 98.5 %
<table>
<thead>
<tr>
<th>Peak ID</th>
<th>Compound</th>
<th>Time</th>
<th>Mass Found</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>103</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1: (Time: 1.03) Combine (213:216)</td>
<td>2: N5 ES-</td>
<td>2.8e+004</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>103</td>
<td>275.13</td>
<td></td>
</tr>
<tr>
<td>2: (Time: 1.93) Combine (401:405)</td>
<td>1: N5 ES+</td>
<td>1.0e+007</td>
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</tr>
<tr>
<td>3</td>
<td>198</td>
<td>275.13</td>
<td></td>
</tr>
<tr>
<td>3: (Time: 1.98) Combine (412:416)</td>
<td>1: N5 ES+</td>
<td>5.4e+005</td>
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</tr>
</tbody>
</table>
HT-LC-MS Spectrum (SOP 2200) of 5 (meridianin A). UV purity: 99.5 %
<table>
<thead>
<tr>
<th>Peak ID</th>
<th>Compound</th>
<th>Time (s)</th>
<th>Mass Found</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>(Time: 1.67)</td>
<td>1.67</td>
<td>394.2</td>
</tr>
<tr>
<td></td>
<td>237.0</td>
<td>272.9</td>
<td>394.2</td>
</tr>
<tr>
<td></td>
<td>385.6</td>
<td>431.2</td>
<td>510.8</td>
</tr>
<tr>
<td></td>
<td>617.3</td>
<td>674.5</td>
<td>777.3</td>
</tr>
<tr>
<td></td>
<td>860.7</td>
<td>894.5</td>
<td>960.1</td>
</tr>
<tr>
<td></td>
<td>981.0</td>
<td>1000.0</td>
<td>1000.0</td>
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</tbody>
</table>

**MS ES+**
3.3e+004

<table>
<thead>
<tr>
<th>Peak ID</th>
<th>Compound</th>
<th>Time (s)</th>
<th>Mass Found</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>(Time: 1.67)</td>
<td>1.67</td>
<td>227.1</td>
</tr>
<tr>
<td></td>
<td>249.1</td>
<td>394.2</td>
<td>741.0</td>
</tr>
<tr>
<td></td>
<td>508.0</td>
<td>531.0</td>
<td>657.2</td>
</tr>
<tr>
<td></td>
<td>771.2</td>
<td>839.2</td>
<td>615.0</td>
</tr>
<tr>
<td></td>
<td>992.4</td>
<td>1000.0</td>
<td>1000.0</td>
</tr>
</tbody>
</table>

**MS ES-**
1.3e+005

<table>
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<th>Compound</th>
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<th>Mass Found</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
<td>(Time: 1.75)</td>
<td>1.75</td>
<td>394.2</td>
</tr>
<tr>
<td></td>
<td>245.1</td>
<td>273.0</td>
<td>395.3</td>
</tr>
<tr>
<td></td>
<td>635.0</td>
<td>635.0</td>
<td>635.0</td>
</tr>
</tbody>
</table>

**MS ES+**
1.7e+005

<table>
<thead>
<tr>
<th>Peak ID</th>
<th>Compound</th>
<th>Time (s)</th>
<th>Mass Found</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
<td>(Time: 1.75)</td>
<td>1.75</td>
<td>227.1</td>
</tr>
<tr>
<td></td>
<td>249.1</td>
<td>395.3</td>
<td>479.6</td>
</tr>
<tr>
<td></td>
<td>509.1</td>
<td>629.1</td>
<td>668.5</td>
</tr>
<tr>
<td></td>
<td>692.1</td>
<td>777.3</td>
<td>828.8</td>
</tr>
<tr>
<td></td>
<td>922.2</td>
<td>992.8</td>
<td>1000.0</td>
</tr>
</tbody>
</table>

**MS ES-**
9.1e+004
### 6.2. HT-LC-MS Methods for the Control of Identity and Purity of Compounds 4a-u and 5

<table>
<thead>
<tr>
<th>Problem Definition</th>
<th>Identity and Purity</th>
</tr>
</thead>
<tbody>
<tr>
<td>SOP</td>
<td>2200</td>
</tr>
<tr>
<td>Methods</td>
<td>HT-LC-MS</td>
</tr>
<tr>
<td>System</td>
<td>Waters Acquity UPLC© with PDA and ELSD</td>
</tr>
<tr>
<td></td>
<td>Waters SQD (ESI+/- and APCI+/-)</td>
</tr>
<tr>
<td>Software</td>
<td>MassLynx with OpenLynx</td>
</tr>
<tr>
<td>Column</td>
<td>Waters XBridge™ C8 3.5 μm</td>
</tr>
<tr>
<td></td>
<td>4.6 x 50 mm Column</td>
</tr>
<tr>
<td></td>
<td>Part No. 186003053</td>
</tr>
<tr>
<td>Eluent</td>
<td>A: 99.9 % acetonitrile + 0.1 % TFA</td>
</tr>
<tr>
<td></td>
<td>B: 99.9 % water + 0.1 % TFA</td>
</tr>
<tr>
<td>Gradient</td>
<td>time (min)</td>
</tr>
<tr>
<td></td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>8.00</td>
</tr>
<tr>
<td></td>
<td>8.10</td>
</tr>
<tr>
<td></td>
<td>8.50</td>
</tr>
<tr>
<td></td>
<td>11.00</td>
</tr>
<tr>
<td>Column temperature</td>
<td>Room temperature</td>
</tr>
<tr>
<td>Injection volume</td>
<td>3 μl</td>
</tr>
<tr>
<td>Sample Preparation</td>
<td>Approx. 0.1 mg were dissolved in acetonitrile + water 50/50 in an ultrasonic bath, so that the concentration was 0.5 mM.</td>
</tr>
<tr>
<td></td>
<td>If necessary, the sample was additionally diluted: 100 μl in 500 μl acetonitrile + water 5/95.</td>
</tr>
</tbody>
</table>
**Problem Definition**  
Identity and Purity

**SOP**  
2222

**Methods**  
HT-LC-MS

**System**  
4 x Waters 1525 Binary HPLC Pump  
2 x Waters In-Line Degasser AF  
1 x Waters 2777 Sample Manager  
1 x Waters 2488 Mux-UV Detector  
4 x Waters 2420 ELS Detector  
1 x Waters ZQ-MUX

**Software**  
MassLynx with OpenLynx

**Column**  
Chromolith® Flash RP-18e (25-2mm)

**Eluent**  
A: 99.9 % acetonitrile + 0.1 % formic acid  
B: 99.9 % water + 0.1 % formic acid

**Gradient**  
<table>
<thead>
<tr>
<th>time (min)</th>
<th>A %</th>
<th>B %</th>
<th>flow (mL/min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>5</td>
<td>95</td>
<td>0.8</td>
</tr>
<tr>
<td>1.7</td>
<td>100</td>
<td>0</td>
<td>0.8</td>
</tr>
<tr>
<td>3.0</td>
<td>100</td>
<td>0</td>
<td>0.8</td>
</tr>
<tr>
<td>3.01</td>
<td>0</td>
<td>100</td>
<td>0.8</td>
</tr>
<tr>
<td>6.25</td>
<td>5</td>
<td>95</td>
<td>0.8</td>
</tr>
</tbody>
</table>

**Column temperature**  
Room temperature

**Throughput**  
416 samples: approx. 11 hours
7. References