Silver Catalyzed Cascade Synthesis of Alkaloid Ring Systems: Concise Total Synthesis of Fascaplysin, Homofascaplysin C and Analogues

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General:

$^1$H and $^{13}$C NMR spectroscopic data were recorded on a Varian Mercury VX 400 spectrometer at room temperature. NMR spectra were calibrated to the solvent signals of CDCl$_3$ ($\delta = 7.26$ and 77.00 ppm). Electrospray ionization (ESI)-MS were measured by using an Agilent 1100 series binary pump together with a reversed-phase HPLC column (Macherey-Nagel). TLC was performed on Merck silica gel 60 F$_{254}$ aluminum sheet. For flash chromatography Baker silica gel (40-70 $\mu$m) was used. Compounds 1, 2, 9 and 15 were synthesized as described in the literature references. Analytical data of compounds 14, 16 and 17 are in accordance with literature references.

All microwave irradiations were performed with a CEM Discover 1-300 W in sealed tubes (10 mL) equipped with a Teflon-coated stirring bar under an argon atmosphere.

General procedure for the synthesis:

Method A:

To the corresponding alkyne (0.40 mmol) dissolved in absolute ethanol (3 mL) were added the aniline derivative (0.42 mmol) and the 2,6-lutidine (47 $\mu$L, 0.40 mmol) at room temperature. To this mixture was added the AgOTf (22 mg, 80 $\mu$mol) and the solution was heated to 60° C for 24 h. The solvent was evaporated under reduced pressure and replaced by ethyl acetate. The solution was neutralized with an aqueous solution of sodium bicarbonate at room temperature and extracted with ethyl acetate. This crude mixture was adsorbed on basified silica gel and purified by flash chromatography using a gradient of ethyl acetate in petroleum ether.

Method B:

To the corresponding alkyne (0.40 mmol) dissolved in dry Ethanol (3 mL) were added the aniline derivative (0.42 mmol) and the 2,6-lutidine (4.7 $\mu$L, 40 $\mu$mol) at room temperature. To this mixture was added the AgOTf (11 mg, 40 $\mu$mol) and the solution was heated under microwave irradiation (150 W) to 150° C for 45 min. The solvent was evaporated under reduced pressure and replaced by ethyl acetate. The solution was neutralized with an aqueous solution of sodium bicarbonate at room temperature and extracted with ethyl acetate. Purification the desired compound afforded as reported for Method A.

*tert*-butyl 6-phenylindolo[2,1-a]isoquinoline-12-carboxylate (3a):
mp 82 – 84°C; $^1$H NMR (400 MHz, CDCl$_3$): $\delta = 9.28$ (d, 1H, $J = 7.6$ Hz.), 8.29 (d, 1H, $J = 8.0$ Hz.), 7.62-7.52 (m, 8H), 7.32 (t, 1H, $J = 7.4$ Hz.), 6.92 (t, 1H, $J = 7.8$ Hz.), 6.78 (s, 1H), 6.44 (d, 1H, $J = 8.8$ Hz.), 1.80 (s, 9H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta = 166.2$, 137.9, 137.5, 136.3, 131.6, 130.7, 129.4, 129.2, 129.0, 127.6, 126.9, 126.4, 124.3, 123.1, 121.1, 114.8, 114.3, 103.7, 81.0, 28.7; HRMS (ESI): Calculated for C$_{27}$H$_{24}$NO$_2$ [M+H$^+$]: 394.18071, Found: 394.1805.

**tert-butyl 6-(thiophen-3-yl)indolo[2,1-a]isoquinoline-12-carboxylate (3b):**

mp 85 – 87°C; $^1$H NMR (400 MHz, CDCl$_3$): $\delta = 9.28$ (d, 1H, $J = 7.5$ Hz.), 8.29 (d, 1H, $J = 8.4$ Hz.), 7.62 – 7.55 (m, 2H), 7.43 (d, 1H, $J = 8.8$ Hz.), 7.34 – 7.30 (m, 2H), 7.07 (d, 1H, $J = 8.8$ Hz.), 7.00 – 6.89 (m, 2H), 6.75 (s, 1H), 6.55 (s, 1H), 1.80 (s, 9H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta = 166.5$, 160.7, 138.3, 137.7, 131.1, 130.7, 129.5, 129.3, 129.2, 129.0, 127.9, 127.0, 126.6, 126.5, 124.5, 123.3, 121.3, 115.2, 114.6, 114.1, 104.0, 81.2, 29.0; HRMS (ESI): Calculated for C$_{25}$H$_{22}$NO$_2$S [M+H$^+$]: 400.1371, Found: 400.1369.

**tert-butyl 6-propylindolo[2,1-a]isoquinoline-12-carboxylate (3c):**

$^1$H NMR (400 MHz, CDCl$_3$): $\delta = 8.04$ (d, 1H, $J = 8.8$ Hz.), 7.90 (d, 1H, $J = 8.8$ Hz.), 7.54 – 7.36 (m, 4H), 7.00 – 6.80 (m, 2H), 6.69 (s, 1H), 2.62 (t, 2H, $J = 7.6$ Hz.), 1.93 – 1.88 (m, 2H), 1.75 (s, 9H), 0.96 (t, 3H, $J = 7.5$ Hz.); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta = 165.9$, 142.5, 141.2, 139.1, 137.4, 135.2, 134.1, 132.6, 129.8, 129.5, 129.0, 126.2, 124.9, 124.8, 124.6, 118.8, 116.9, 83.2, 35.2, 28.9, 21.3, 13.9; HRMS (ESI): Calculated for C$_{24}$H$_{26}$NO$_2$ [M+H$^+$]: 360.19636, Found: 360.1961.

**tert-butyl 6-(3-methoxyphenyl)indolo[2,1-a]isoquinoline-12-carboxylate (3d):**

mp 80 – 82°C; $^1$H NMR (400 MHz, CDCl$_3$): $\delta = 8.18 – 7.81$ (m, 3H), 7.89 (s, 1H), 7.73-7.50 (m, 4H), 7.16 – 6.97 (m, 4H), 6.60 (s, 1H), 3.85 (s, 3H), 1.81 (s, 9H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta = 166.9$, 159.9, 151.4, 138.0, 137.1, 133.2, 132.1, 131.0, 129.3, 128.7, 128.1, 127.5, 127.6, 126.7, 125.9, 125.1,
124.0, 121.8, 121.1, 115.4, 114.9, 110.2, 105.0, 81.2 (CCH$_3$), 55.8, 29.4; HRMS (ESI): Calculated for C$_{28}$H$_{26}$NO$_3$ [M+H$^+$]: 424.19128, Found: 424.1915.

**tert-butyl 6-(4-(trifluoromethyl)phenyl)indolo[2,1-a]isoquinoline-12-carboxylate (3e):**

![Chemical Structure](image)

mp 81 – 83°C; $^1$H NMR (400 MHz, CDCl$_3$): $\delta = 8.27$ (d, 2H, $J = 7.6$ Hz.), 7.74 (d, 2H, $J = 7.6$ Hz.), 7.69-7.51 (m, 5H), 7.29 (t, 1H, $J = 7.4$ Hz.), 6.94 (t, 1H, $J = 7.8$ Hz.), 6.80 (s, 1H), 6.43 (d, 1H, $J = 8.8$ Hz.), 1.79 (s, 9H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta = 166.1, 137.9, 137.3, 136.4, 135.1, 133.6$ (q, $J = 40$ Hz., CCF$_3$), 131.6, 130.7, 129.5, 129.2, 129.1, 127.2, 126.9, 126.3 (q, $J = 5$ Hz.), 124.3, 123.7 (q, $J = 330$ Hz., CF$_3$), 121.0, 115.0, 114.2, 103.7, 79.8, 28.6; HRMS (ESI): Calculated for C$_{28}$H$_{23}$F$_3$NO$_2$ [M+H$^+$]: 462.16809, Found: 462.1681.

**tert-butyl 6-(4-methoxyphenyl)indolo[2,1-a]isoquinoline-12-carboxylate (3f):**

![Chemical Structure](image)

mp 89 – 91°C; $^1$H NMR (400 MHz, CDCl$_3$): $\delta = 8.29$ (d, 2H, $J = 8.0$ Hz.), 7.16 (d, 2H, $J = 8.0$ Hz.), 7.62-7.42 (m, 4H), 7.13 – 6.94 (m, 4H), 6.56 (s, 1H), 3.82 (s, 3H), 1.80 (s, 9H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta = 166.5, 159.4, 138.2, 137.0, 132.9, 131.9, 130.8, 129.3, 129.0, 128.0, 127.3, 126.7, 125.8, 124.8, 123.6, 121.7, 121.4, 115.0, 114.6, 109.8, 104.1, 81.3, 56.1, 29.0; HRMS (ESI): Calculated for C$_{28}$H$_{26}$NO$_3$ [M+H$^+$]: 424.19128, Found: 394.1911.

**tert-butyl 2,3-dimethoxy-6-phenylindolo[2,1-a]isoquinoline-12-carboxylate (3g):**

![Chemical Structure](image)

mp 82 – 84°C; $^1$H NMR (400 MHz, CDCl$_3$): $\delta = 8.95$ (s, 1H), 7.83 (s, 1H), 7.58 – 7.49 (m, 3H), 7.38 – 7.23 (m, 2H), 7.12 – 7.00 (m, 3H), 6.89 – 6.84 (m, 1H), 6.73 (s, 1H), 4.10 (s, 3H), 4.00 (s, 3H), 1.78 (s, 9H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta = 168.3, 151.8, 150.9, 150.5, 150.1, 148.9, 138.3, 131.7, 131.2, 129.5, 129.2, 128.9, 128.8, 128.7, 126.3, 126.2, 123.2, 118.9, 117.8, 114.2, 108.8, 81.8, 56.2, 55.8, 29.0; HRMS (ESI): Calculated for C$_{29}$H$_{28}$NO$_4$ [M+H$^+$]: 454.20185, Found: 454.2020.

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**Supplementary Material (ESI) for Chemical Communications**

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**tert-butyl 2,3-dimethoxy-6-propylindolo[2,1-a]isoquinoline-12-carboxylate (3h):**

\[
\begin{align*}
\text{1H NMR (400 MHz, CDCl}_3\text{): } & \delta = 8.02 (d, 1H, J = 8.6 \text{ Hz}), 7.87 (d, 1H, J = 8.6 \text{ Hz}), 7.13 (s, 1H), 7.00 - 6.80 (m, 2H), 6.90 (s, 1H), 6.71 (s, 1H), 4.12 (t, 2H, J = 7.4 \text{ Hz}), 1.92 - 1.85 (m, 2H), 1.79 (s, 9H), 0.95 (t, 3H, J = 7.6 \text{ Hz}); \\
\text{13C NMR (100 MHz, CDCl}_3\text{): } & \delta = 165.6, 152.4, 150.8, 142.5, 141.2, 139.0, 137.7, 135.2, 134.0, 132.5, 130.0, 129.3, 124.9, 124.8, 124.5, 119.0, 116.3, 83.0, 58.2, 57.4, 35.4, 29.0, 21.1, 13.7; \\
\text{HRMS (ESI): Calculated for } C_{26}H_{30}NO_4 \text{ [M+H]^+: 420.21750, Found: 420.2173.}
\end{align*}
\]

**tert-butyl 2,3-dimethoxy-6-(4-(trifluoromethyl)phenyl)indolo[2,1-a]isoquinoline-12-carboxylate (3i):**

\[
\begin{align*}
\text{mp 93 – 95°C; 1H NMR (400 MHz, CDCl}_3\text{): } & \delta = 8.25 (d, 2H, J = 7.4 \text{ Hz}), 7.75 (d, 2H, J = 7.4 \text{ Hz}), 8.17 (d, 1H, J = 7.6 \text{ Hz}), 7.49 (d, 1H), 7.26 - 7.00 (m, 2H), 7.09 (s, 1H), 6.89 (s, 1H), 6.80 (s, 1H), 4.12 (s, 3H), 3.99 (s, 3H), 1.79 (s, 9H); \\
\text{13C NMR (100 MHz, CDCl}_3\text{): } & \delta = 167.8, 151.7, 151.2, 150.5, 150.0, 148.9, 143.3, 133.6 (q, J = 38 \text{ Hz, CCF}_3), 131.7, 131.4, 130.4, 129.5, 129.3, 129.1, 128.7, 126.1 (q, J = 5 \text{ Hz}), 124.7 (q, J = 340 \text{ Hz, CF}_3), 123.2, 119.4, 117.7, 114.2, 108.5, 81.7, 56.0, 55.1, 28.9; \\
\text{HRMS (ESI): Calculated for } C_{30}H_{27}F_3NO_4 \text{ [M+H]^+: 522.18923, Found: 522.1890.}
\end{align*}
\]

**tert-butyl 9,10-dimethoxy-6-phenylindolo[2,1-a]isoquinoline-12-carboxylate (3j):**

\[
\begin{align*}
\text{mp 88 – 90°C; 1H NMR (400 MHz, CDCl}_3\text{): } & \delta = 8.39 - 7.67 (m, 5H), 7.44 (s, 1H), 7.38 - 7.11 (m, 4H), 6.93 (s, 1H), 6.75 (s, 1H), 3.81 (s, 6H), 1.81 (s, 9H); \\
\text{13C NMR (100 MHz, CDCl}_3\text{): } & \delta = 168.0, 151.7, 150.9, 150.4, 150.0, 149.2, 148.9, 145.9, 138.4, 131.7, 131.3, 129.9, 129.3, 129.0, 128.9, 128.7, 126.3, 126.2, 124.7, 123.5, 118.9, 118.0, 114.0, 108.5, 81.7, 56.0, 55.9, 28.8; \\
\text{HRMS (ESI): Calculated for } C_{29}H_{28}NO_4 \text{ [M+H]^+: 454.20185, Found: 454.2020.}
\end{align*}
\]
tert-butyl 9,10-dimethoxy-6-propylindolo[2,1-a]isoquinoline-12-carboxylate (3k):

1H NMR (400 MHz, CDCl₃): δ = 8.02 (d, 1H, J = 8.6 Hz.), 7.90 – 7.63 (m, 2H), 7.57 (d, 1H, J = 8.6 Hz.), 7.12 (s, 1H), 6.81 (s, 1H), 6.69 (s, 1H), 3.89 (s, 3H), 3.76 (s, 3H), 2.57 (t, 2H, J = 7.2 Hz.), 1.89 – 1.81 (m, 2H), 1.74 (s, 9H), 0.98 (t, 3H, J = 7.4 Hz.); 13C NMR (100 MHz, CDCl₃): δ = 165.8, 152.3, 150.6, 142.5, 141.5, 138.8, 137.7, 135.0, 134.3, 132.6, 130.0, 129.1, 124.9, 124.5, 124.1, 118.7, 116.3, 82.4, 57.2, 56.5, 35.7, 29.1, 22.1, 13.9; HRMS (ESI): Calculated for C₂₆H₃₀NO₄ [M+H⁺]: 420.2175, Found: 420.2176.

tert-butyl 9,10-dimethoxy-6-(4-(trifluoromethyl)phenyl)indolo[2,1-a]isoquinoline-12-carboxylate (3l):

mp 94 – 96°C; 1H NMR (400 MHz, CDCl₃): δ = 8.29 (d, 2H, J = 7.6 Hz.), 7.73 (d, 2H, J = 7.6 Hz.), 7.81 (d, 1H, J = 7.4 Hz.), 7.38 – 7.21 (m, 2H), 7.30 (s, 1H), 7.49 (d, 1H, J = 7.4 Hz.), 7.09 (s, 1H), 6.80 (s, 1H), 3.89 (s, 3H), 3.79 (s, 3H), 1.70 (s, 9H); 13C NMR (100 MHz, CDCl₃): δ = 166.9, 152.0, 151.4, 150.1, 150.3, 147.1, 141.0, 137.8, 133.9 (q, J = 40 Hz., CCF₃), 131.6, 131.4, 130.6, 129.3, 129.4, 129.1, 129.0, 128.8, 128.6, 126.2 (q, J = 5 Hz.), 125.2 (q, J = 336 Hz., CCF₃), 123.2, 119.1, 117.2, 114.8, 108.0, 82.1, 57.2, 55.9, 29.6; HRMS (ESI): Calculated for C₃₀H₂₇F₃NO₄ [M+H⁺]: 522.18923, Found: 522.1894.

tert-butyl 9-methoxy-6-phenylindolo[2,1-a]isoquinoline-12-carboxylate (3m):

mp 88 – 90°C; 1H NMR (400 MHz, CDCl₃): δ = 8.31 – 7.78 (m, 5H), 7.69 (d, 1H, J = 7.8 Hz.), 7.40 – 7.05 (m, 4H), 6.97 (s, 1H), 6.70 (d, 1H, J = 7.8 Hz.), 6.67 (s, 1H), 3.88 (s, 3H), 1.84 (s, 9H); 13C NMR (100 MHz, CDCl₃): δ = 168.4, 150.9, 150.5, 150.2, 150.0, 147.3, 146.0, 137.5, 137.4, 131.1, 130.6, 129.8, 129.3, 129.1, 128.9, 127.9, 126.0, 125.1, 123.5, 118.6, 118.1, 116.4, 113.8, 108.6, 82.2, 56.6,
28.5; HRMS (ESI): Calculated for C_{28}H_{26}NO_{3} [M+H^+]: 424.19128, Found: 424.1914.

*tert*-butyl 2,3,9,10-tetramethoxy-6-phenylindolo[2,1-a]isoquinoline-12-carboxylate (3n):

mp 101 – 103°C; \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta = 8.26\) (d, 2H, \(J = 8.0\) Hz.), 7.68 – 7.31 (m, 3H), 7.21 (s, 1H), 7.08 (s, 1H), 6.81 (s, 1H), 6.69 (s, 1H), 6.64 (s, 1H), 4.01 (s, 3H), 3.90 (s, 3H), 3.87 (s, 3H), 3.76 (s, 3H), 1.69 (s, 9H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta = 165.4, 142.0, 141.1, 139.7, 138.1, 137.9, 135.8, 135.0, 134.4, 133.6, 133.0, 131.2, 130.5, 129.5, 129.1, 126.2, 125.4, 125.1, 124.8, 124.6, 120.4, 118.2, 115.1, 84.2, 58.0, 57.2, 56.8, 55.7, 28.2; HRMS (ESI): Calculated for C\(_{31}\)H\(_{32}\)NO\(_6\) [M+H\(^+\)]: 514.22299, Found: 514.22301.

*tert*-butyl 2,3,9,10-tetramethoxy-6-propylindolo[2,1-a]isoquinoline-12-carboxylate (3o):

mp 96 – 98°C; \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta = 7.41\) (s, 1H), 7.19 (s, 1H), 6.94 (s, 1H), 6.82 (s, 1H), 6.70 (s, 1H), 4.12 (s, 3H), 3.97 (s, 3H), 3.97 (s, 3H), 3.88 (s, 3H), 3.80 (s, 3H), 2.72 (t, 2H, \(J = 7.4\) Hz.), 1.98 – 1.77 (m, 2H), 1.82 (s, 9H), 0.91 (t, 3H, \(J = 7.6\) Hz.); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta = 166.3, 144.2, 141.9, 139.0, 136.8, 135.6, 134.0, 130.4, 129.5, 129.0, 127.6, 126.3, 125.6, 125.1, 124.0, 116.5, 114.7, 82.2, 58.0, 57.6, 57.1, 56.4, 36.0, 28.3, 20.8, 13.4; HRMS (ESI): Calculated for C\(_{28}\)H\(_{34}\)NO\(_6\) [M+H\(^+\)]: 480.23864, Found: 480.2388.

*tert*-butyl 2,3,9,10-tetramethoxy-6-(4-(trifluoromethyl)phenyl)indolo[2,1-a]isoquinoline-12-carboxylate (3p):

mp 107 – 109°C; \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta = 8.21\) (d, 2H, \(J = 7.8\) Hz.), 7.69 (d, 2H, \(J = 7.8\) Hz.), 7.29 (s, 1H), 7.11 (s, 1H), 6.80 (s, 1H), 6.63 (s, 1H), 6.59 (s, 1H), 4.08 (s, 3H), 3.91 (s, 3H), 3.82 (s, 3H), 3.79 (s, 3H), 1.75 (s, 9H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta = 166.3, 142.1, 141.8, 140.0, 139.1, 138.6, 137.7, 135.4, 134.0, 133.6 (q, \(J = 40\) Hz., CCF\(_3\)), 131.1, 130.6, 129.7, 129.0, 127.2, 126.1 (q, \(J = 5\) Hz.), 124.5 (q, \(J = 336\) Hz., CF\(_3\)), 124.1, 120.9, 118.3, 116.4, 114.6, 85.0, 58.8, 57.4, 56.9,
tert-butyl indolo[2,1-a]isoquinoline-12-carboxylate (3q):

\[
\begin{align*}
\text{H NMR (400 MHz, CDCl}_3\text{): } & \delta = 8.21 (d, 1H, J = 7.2 \text{ Hz.}), 7.67 - 7.56 (m, 4H), 7.51 - 7.37 (m, 4H), \\
& 6.98 (d, 1H, J = 7.2 \text{ Hz.}), 1.78 (s, 9H); \\
\text{C NMR (100 MHz, CDCl}_3\text{): } & \delta = 166.7, 143.4, 142.2, 139.8, \\
& 138.4, 135.9, 134.6, 132.9, 130.5, 129.2, 127.8, 126.3, 124.4, 124.0, 122.6, 120.7, 115.2, 82.7, 28.0; \\
\text{HRMS (ESI): Calculated for C}_{21}H_{20}NO_2 [M+H\text{]}^+: 318.14941, \text{ Found: 318.1495.}
\end{align*}
\]

Preparation of Benzoindolizine fused indoles 8a-c

Starting materials 7a-c were prepared according to literature procedures.\(^6\)

General procedure for the preparation of benzoindolizine fused indoles:

A mixture of 7 (0.34 mmol), 2a (104 mg, 0.34 mmol), 2,6-Lutidine (4 µL, 34 µmol) and AgOTf (9 mg, 34 µmol) in EtOH (2 ml) was stirred for 8 min under microwave irradiation (150°C, 150 W). It was filtered through a pad of silica (washed with EtOH) and 10 mL of 20 % HCOOH/H\text{2}O was added. The resulting mixture was stirred over night in room temperature. The solution was neutralized by the addition of aqueous NaOH (2 M) and extracted with EtOAc four times. The combined organic phase was dried over Na\text{2}SO\text{4}, filtered and the solvent removed under reduced pressure.

Benzoindolizine-fused indole (8a)

\[
\begin{align*}
8\text{a prepared as described above was purified on silica gel with 8 }\% \text{ EtOAc in petroleum ether as a yellow amorphous solid.} \\
\text{H NMR (400 MHz, CDCl}_3\text{): } & \delta 8.33 (d, 1H, J = 7.5 \text{ Hz.}), 8.01 (d, 1H, J = 8.0 \text{ Hz.}), 7.64 - 7.58 (m, 3H), \\
& 7.57 - 7.53 (m, 2H), 7.49 (dd, 2H, J = 4.9 and 1.1 \text{ Hz.}), 7.44 - 7.39 (m, 1H), 7.36 -7.32 (m, 1H), \\
& 6.87 - 6.82 (m, 1H), 6.85 (s, 1H), 6.46 (d, 1H, J = 8.6 \text{ Hz.}), 3.93 (s, 3H), 1.82 (s, 9H); \\
\text{C NMR (100 MHz, CDCl}_3\text{): } & \delta 165.29, 139.84, 139.47, 138.91, 138.55, 136.71, 131.39, 130.06, 129.66, 129.19, \\
& 129.13, 125.76, 123.93, 123.68, 122.98, 120.22, 120.13, 119.50, 114.86, 108.55, 106.57, 100.64, \\
& 98.16, 79.89, 29.69, 28.93; \text{HRMS (LC/MS) calcd for C}_{30}H_{28}N_2O_2 [M+H\text{]}^+: 447.1994, \text{ found 447.2066.}
\end{align*}
\]
Benzacondolizine fused indole (8b)

8b prepared as described above was purified on silica gel with 5 to 8 % EtOAc in petroleum ether as a red-brown amorphous solid.

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 8.41 (d, 1H, $J = 7.9$ Hz.), 7.93 (dd, 2H, $J = 23.3$ and 8.3 Hz.), 7.49 - 7.36 (m, 4H), 7.27 – 7.23 (m, 1H), 6.66 (s, 1H), 3.76 (s, 3H), 3.25 (t, 2H, $J = 8.0$ Hz.), 1.88 (dd, 2H, $J = 15.2$ and 7.5 Hz.), 1.82 (s, 9H), 1.13 (t, 3H, $J = 7.3$ Hz.); HRMS (LC/MS) calcd for C$_{27}$H$_{28}$N$_2$O$_2$ [M+H$^+$] 413.2151, found 413.2219.

Benzacondolizine fused indole (8c)

8c prepared as described above was purified on silica gel with 2 to 5 % EtOAc in petroleum ether as yellow oil.

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 8.64 (d, 1H, $J = 7.5$ Hz.), 8.14 (d, 1H, $J = 8.8$ Hz.), 7.90 (d, 1H, $J = 7.1$ Hz.), 7.73 (d, 1H, $J = 8.3$ Hz.), 7.53 – 7.48 (m, 2H), 7.42 – 7.32 (m, 2H), 7.05 (s, 1H), 3.47 – 3.40 (m, 2H), 1.97 (dd, 2H, $J = 15.0$ and 7.4 Hz.), 1.83 (s, 9H), 1.18 (t, 3H, $J = 7.3$, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 164.46, 156.29, 145.17, 138.93, 132.51, 130.11, 126.98, 124.13, 123.38, 123.29, 121.85, 121.58, 120.25, 119.16, 115.19, 112.17, 106.95, 103.54, 96.97, 80.39, 37.18, 28.85, 21.04, 13.67; LC/MS calcd for C$_{26}$H$_{25}$NO$_3$ [M+H$^+$] 400.2, found 399.9.

[2-(2-Aminophenyl)-1-(phenyl)ethyl]-propanedioic acid, diethyl ester (10a):

This product was synthesized according to the procedure described in the literature from diethyl (benzylidene)malonate and 2-nitrotoluene in 44% yield over 2 steps.
mp 78 – 80°C; \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta = 7.19\)–7.12 (m, 3H), 7.04–7.02 (m, 2H), 6.93–6.89 (m, 1H), 6.59 (d, 1H, \(J = 8.0\) Hz.), 6.39–6.31 (m, 2H), 4.27 (q, 2H, \(J = 8.0\) Hz.), 3.83 (q, 2H, \(J = 8.0\) Hz.), 3.81 (d, 1H, \(J = 12.0\) Hz.), 3.57 (ddd, 1H, \(J = 12.0\), \(J = 4.0\), \(J = 8.0\), C\(\text{HCH}_2\)), 3.04 and 2.64 (ABX spectrum, 2H, \(J_{AB} = 12.0\), \(J_{AX} = 4.0\), \(J_{BX} = 8.0\), CH\(\text{C}_2\)), 1.30 (t, 3H, \(J = 8.0\) Hz.), 0.87 (t, 3H, \(J = 8.0\) Hz.);

\(^{13}\)C NMR (MHz, CDCl\(_3\)): \(\delta = 169.6, 167.9, 145.2, 140.1, 131.4, 128.8, 128.3, 127.6, 127.2, 122.9, 117.7, 115.5, 62.2, 61.5, 57.4, 44.9, 37.6, 14.0, 13.6; HRMS (ESI): Calculated for C\(_{21}\)H\(_{26}\)NO\(_4\) [M+H\(^+\)]: 356.18620, Found: 356.1863.

[2-(2-Aminophenyl)-1-(4-ethylphenyl)ethyl]-propanedioic acid, diethyl ester (10b):

This product was synthesized according to the procedure described in the literature from diethyl 2-(4-ethylbenzylidene)malonate and 2-nitrotoluene in 49% yield over 2 steps.\(^6\)

\(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta = 7.03\)–6.91 (m, 5H), 6.60 (d, 1H, \(J = 7.6\) Hz.), 6.41–6.39 (m, 2H), 4.28 (q, 2H, \(J = 8.0\) Hz.), 3.85 (q, 2H, \(J = 8.0\) Hz.), 3.79 (d, 1H, \(J = 12.0\) Hz., \(J = 4.0\), \(J = 8.0\), CH\(\text{C}_2\)), 2.56 (q, 2H \(J = 7.6\) Hz.), 1.30 (t, 3H, \(J = 8.0\) Hz.), 1.17 (t, 3H, \(J = 7.6\) Hz.), 0.87 (t, 3H, \(J = 4.0\) Hz.);

\(^{13}\)C NMR (MHz, CDCl\(_3\)): \(\delta = 169.8, 168.2, 145.3, 143.2, 137.3, 131.6, 128.8, 128.7, 127.9, 127.6, 123.3, 117.8, 115.6, 62.2, 61.5, 57.9, 45.0, 37.9, 28.7, 15.8, 14.4, 13.9; HRMS (ESI): Calculated for C\(_{23}\)H\(_{30}\)NO\(_4\) [M+H\(^+\)]: 384.21750, Found: 384.2176.

diethyl (3-phenyl-1,2-dihydroisoquinolinyl)-4-phenyl-4,5-dihydro-1H-benzo[b]azepine-3,3(2H)-dicarboxylate (11a):

mp 107 – 109°C; \(^1\)H NMR (500 MHz, CDCl\(_3\)): \(\delta = 7.49\) (d, 2H, \(J = 7.0\) Hz.), 7.37 (d, 2H, \(J = 8.0\) Hz.), 7.20–7.10 (m, 8H), 7.02–6.97 (m, 3H), 6.70 (t, 1H, \(J = 7.5\) Hz.), 6.60 (t, 1H, \(J = 7.5\) Hz.), 6.27 (s, 1H), 6.26 (d, 1H, \(J = 8.0\) Hz.), 5.98 (s, 1H), 5.01 and 3.09 (broad ABX spectrum, 2H, \(J_{AX} = 12.5\), \(J_{BX} = 17.5\), CH\(\text{C}_2\)), 4.44 (dd, 1H, \(J = 12.4\) and 17.5 Hz.), 3.95 (qd, 1H, \(J = 12.0\) and 7.0 Hz.), 3.80 (qd, 1H, \(J = 7.0\) and 12.0 Hz.), 3.44 (m, 2H), 0.69 (t, 3H, \(J = 7.0\) Hz.), 0.65 (t, 3H, \(J = 7.0\) Hz.);

\(^{13}\)C NMR (125 MHz, CDCl\(_3\)): \(\delta = 169.4, 169.0, 145.5, 142.9, 142.0, 138.0, 133.7, 131.4, 131.1, 129.0,
128.5, 128.4, 128.0, 127.9, 127.8, 127.7, 127.5, 127.0, 126.3, 125.5, 125.4, 123.8, 122.7, 108.8, 68.2, 66.5, 61.3, 61.0, 44.2, 37.6, 13.5, 13.3; HRMS (ESI): Calculated for C$_{36}$H$_{34}$NO$_4$ [M+H$^+$]: 544.24880, Found: 544.2489.

diethyl (3-propyl-1,2-dihydroisoquinolinyl)-4-phenyl-4,5-dihydro-1H-benzo[b]azepine-3,3(2H)-dicarboxylate (11b):

mp 106 – 108°C; $^1$H NMR (500 MHz, CDCl$_3$): $\delta = 7.36$ (d, 1H, $J = 7.5$ Hz.), 7.26 – 6.95 (m, 11H), 6.78 (d, 1H, $J = 8.0$ Hz.), 6.15 (s, 1H), 5.78 (s, 1H), 4.63 and 3.07 (broad ABX spectrum, 2H, $J_{A,X} = 12.5, J_{B,X} = 17.5$, CHC$_2$H), 4.37 (dd, 1H, $J = 12.5$ and 17.5 Hz.), 4.08 (qd, 1H, $J = 7.0$ and 10.5 Hz.), 3.95 (qd, 1H, $J = 7.0$ and 10.5 Hz.), 3.55 (qd, 1H, $J = 7.0$ and 11.0 Hz.), 3.46 (qd, 1H, $J = 7.0$ and 11.0 Hz.), 2.46 – 2.35 (m, 2H), 1.79 – 1.62 (m, 2H), 0.97 (t, 3H, $J = 7.5$ Hz.), 0.80 (t, 3H, $J = 7.0$ Hz.), 0.73 (t, 3H, $J = 7.0$ Hz.); $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta = 169.6, 169.4, 144.3, 143.2, 142.9, 133.8, 132.9, 131.3, 129.2, 127.8, 127.6, 127.5, 127.1, 126.8, 125.8, 125.4, 124.6, 123.3, 122.9, 106.1, 67.6, 66.3, 61.0, 60.9, 44.4, 37.5, 35.2, 21.0, 14.6, 13.5, 13.3; HRMS (ESI): Calculated for C$_{33}$H$_{36}$NO$_4$ [M+H$^+$]: 510.26445, Found: 510.2643.

diethyl (3-phenyl-1,2-dihydrobenzo[b][1,6]naphthyridinyl)-4-phenyl-4,5-dihydro-1H-benzo[b]azepine-3,3(2H)-dicarboxylate (11c):

mp 122 – 124°C; $^1$H NMR (500 MHz, CDCl$_3$): $\delta = 8.05$ (d, 1H, $J = 9.6$ Hz.), 8.04 (s, 1H), 7.89 (dd, 2H, $J = 8.0$ and 1.6 Hz.), 7.80 (dd, 1H, $J = 8.0$ and 0.8 Hz.), 7.70 – 7.42 (m, 7H), 7.22 – 7.13 (m, 3H), 7.07 – 7.04 (m, 1H), 7.00 (s, 1H), 6.95 – 6.91 (m, 1H), 6.61 (d, 1H, $J = 8.0$ Hz.), 6.46 (s, 1H), 6.41 – 6.34 (m, 1H), 4.56 and 2.94 (ABX spectrum, 2H, $J_{A,X} = 12.4, J_{B,X} = 16.8, J_{A,B} = 13.6$, CHC$_2$H), 4.29 (q, 1H, $J = 7.2$ Hz.), 4.13 (qd, 1H, $J = 7.2$ and 9.2 Hz.), 3.92 (qd, 1H, $J = 7.2$ and 9.2 Hz.), 3.88 – 3.81 (m, 2H), 1.32 (t, 3H, $J = 7.2$ Hz.), 0.89 (t, 3H, $J = 7.2$ Hz.), $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta = 169.7, 168.0, 150.3, 145.3, 140.2, 134.2, 133.4, 131.5, 130.5, 130.2, 129.0, 128.9, 128.4, 128.2, 127.7, 127.4, 127.3, 125.9, 125.8, 123.2, 123.0, 117.8, 115.6, 110.1, 102.4, 99.3, 66.9, 64.6, 62.3, 61.5, 45.3, 38.0, 14.4, 13.9; HRMS (ESI): Calculated for C$_{39}$H$_{36}$N$_2$O$_4$ [M+H$^+$]: 595.25971, Found: 595.2599.
diethyl (3-phenyl-1,2-dihydroisoquinolinyl)-4-(4-ethylphenyl)-4,5-dihydro-1H-benzo[b]azepine-3,3(2H)-dicarboxylate (11d):

\[
\begin{align*}
\text{1H NMR (500 MHz, CDCl}_3\text{): } &\delta = 7.51 – 7.39 (m, 4H), 7.31 – 7.10 (m, 6H), 7.03 – 6.69 (m, 5H), 6.63 – 6.59 (m, 1H), 6.28 – 6.25 (m, 1H), 6.27 (s, 1H), 5.99 (s, 1H), 5.00 and 3.10 (broad ABX spectrum, 2H, \( J_{A,X} = 12.4, J_{B,X} = 17.2, CHC_2 \)), 4.43 (dd, 1H, \( J = 12.4 \) and 17.2 Hz.), 3.95 (qd, 1H, \( J = 7.2 \) and 10.4 Hz.), 3.81 (qd, 1H, \( J = 7.2 \) and 10.4 Hz.), 3.47 (m, 2H), 2.83 (q, 2H, \( J = 7.2 \) Hz.), 1.21 (t, 3H, \( J = 7.2 \) Hz.), 0.71 (t, 3H, \( J = 7.2 \) Hz.), 0.67 (t, 3H, \( J = 7.2 \) Hz.); \text{13C NMR (125 MHz, CDCl}_3\text{): } &\delta = 169.5, 169.1, 145.5, 143.0, 142.0, 140.2, 138.0, 134.1, 133.9, 133.8, 131.5, 131.1, 129.0, 128.9, 128.7, 128.4, 128.0, 127.9, 127.8, 127.6, 127.5, 126.3, 125.5, 123.8, 122.7, 108.8, 68.3, 66.5, 61.3, 61.1, 37.7, 37.0, 28.8, 16.0, 13.5, 13.3; HRMS (ESI): Calculated for C\(_{38}\)H\(_{38}\)NO\(_4\) [M+H\(^+\)]: 572.28001, Found: 572.2798.
\end{align*}
\]

diethyl (3-(3-methoxyphenyl)-1,2-dihydroisoquinolinyl)-4-(4-ethylphenyl)-4,5-dihydro-1H-benzo[b]azepine-3,3(2H)-dicarboxylate (11e):

\[
\begin{align*}
\text{mp 120 – 122°C; \text{1H NMR (500 MHz, CDCl}_3\text{): } &\delta = 7.37 – 7.30 (m, 3H), 7.25 – 7.17 (m, 3H), 7.13 – 7.05 (m, 5H), 6.82 – 6.70 (m 3H), 6.40 – 6.37 (m, 2H), 6.35 (s, 1H), 6.09 (s, 1H), 5.06 and 3.17 (broad ABX spectrum, 2H, \( J_{A,X} = 12.4, J_{B,X} = 17.2, CHC_2 \)), 4.51 (dd, 1H, \( J = 12.4 \) and 17.2 Hz.), 4.02 (qd, 1H, \( J = 7.2 \) and 10.4 Hz.), 3.90 (qd, 1H, \( J = 7.2 \) and 10.4 Hz.), 3.71 (s, 3H), 3.55 (m, 2H), 2.62 (q, 2H, \( J = 7.2 \) Hz.), 1.22 (t, 3H, \( J = 7.2 \) Hz.), 0.78 (t, 3H, \( J = 7.2 \) Hz.), 0.74 (t, 3H, \( J = 7.2 \) Hz.); \text{13C NMR (125 MHz, CDCl}_3\text{): } &\delta = 169.4, 169.0, 159.5, 145.5, 143.0, 141.8, 140.1, 139.4, 133.7, 131.3, 131.0, 129.3, 128.8, 128.6, 127.9, 127.8, 127.5, 126.3, 125.5, 125.2, 123.8, 122.7, 121.0, 114.1, 113.7, 108.7, 68.3, 66.4, 61.3, 61.0, 55.3, 43.5, 37.6, 28.7, 15.9, 13.5, 13.3; HRMS (ESI): Calculated for C\(_{39}\)H\(_{40}\)NO\(_5\) [M+H\(^+\)]: 602.29067, Found: 602.2910.
\end{align*}
\]
diethyl (1,2-dihydroisoquinolinyl)-4-(4-ethylphenyl)-4,5-dihydro-1H-benzo[b]azepine-3,3(2H)-
dicarboxylate (11f):

\[\text{1H NMR (500 MHz, CDCl}_3\text{): } \delta = 7.47 - 7.36 (m, 2H), 7.32 - 7.05 (m, 4H), 7.00 - 6.79 (m, 4H), 6.71 - 6.64 (m, 2H), 6.61 (d, 1H, } J = 7.2 \text{ Hz.), 6.19 (s, 1H), 6.00 (d, 1H, } J = 7.2 \text{ Hz.), 4.96 and 3.09 (broad ABX spectrum, 2H, } J_{A,X} = 12.4, J_{B,X} = 17.2, \text{ CHCH}_2\text{), 4.49 (dd, 1H, } J = 12.4 \text{ and 17.2 Hz.), 3.90 (qd, 1H, } J = 7.2 \text{ and 10.4 Hz.), 3.82 (qd, 1H, } J = 7.2 \text{ and 10.4 Hz.), 3.50 (m, 2H), 2.84 (q, 2H, } J = 7.2 \text{ Hz.), 1.19 (t, 3H, } J = 7.2 \text{ Hz.), 0.70 (t, 3H, } J = 7.2 \text{ Hz.), 0.68 (t, 3H, } J = 7.2 \text{ Hz.); 13C NMR (125 MHz, CDCl}_3\text{): } \delta = 170.1, 168.8, 144.9, 143.4, 139.8, 138.1, 135.1, 134.0, 132.5, 130.7, 129.0, 128.6, 128.3, 127.9, 127.5, 126.3, 125.1, 124.0, 122.6, 107.6, 69.1, 67.0, 63.3, 62.1, 42.3, 38.1, 28.5, 16.6, 13.2, 12.8; HRMS (ESI): Calculated for C32H34NO4 [M+H\(^+\)]: 496.24880, Found: 496.2490.

diethyl (6,7-dimethoxy-3-(4-(trifluoromethyl)phenyl)-1,2-dihydroisoquinolinyl)-4-(4-
ethylphenyl)-4,5-dihydro-1H-benzo[b]azepine-3,3(2H)-dicarboxylate (11g):

mp 143 – 145°C; \[\text{1H NMR (500 MHz, CDCl}_3\text{): } \delta = 7.97 (d, 2H, } J = 7.6 \text{ Hz.), 7.54 (d, 2H, } J = 7.6 \text{ Hz.), 7.39 – 7.22 (m, 2H), 7.17 (s, 1H), 7.14 – 6.99 (m, 4H), 6.96 (s, 1H), 6.80 – 6.67 (m, 2H), 6.25 (s, 1H), 6.12 (s, 1H), 5.10 and 3.15 (broad ABX spectrum, 2H, } J_{A,X} = 12.4, J_{B,X} = 17.0, \text{ CHCH}_2\text{), 4.49 (dd, 1H, } J = 12.4 \text{ and 17.2 Hz.), 4.04 (qd, 1H, } J = 7.2 \text{ and 10.4 Hz.), 3.88 (qd, 1H, } J = 7.2 \text{ and 10.4 Hz.), 3.71 (s, 3H), 3.69 (s, 3H), 3.51 (m, 2H), 2.61 (q, 2H, } J = 7.2 \text{ Hz.), 1.22 (t, 3H, } J = 7.2 \text{ Hz.), 0.76 (t, 3H, } J = 7.2 \text{ Hz.), 0.73 (t, 3H, } J = 7.2 \text{ Hz.); 13C NMR (125 MHz, CDCl}_3\text{): } \delta = 170.5, 168.6, 159.5, 144.5, 143.1, 141.8, 140.7, 139.5, 134.0 (q, } J = 38 \text{ Hz., CCF}_3\text{), 131.7, 131.1, 129.3, 128.8, 128.6, 127.8, 127.2, 126.0 (q, } J = 5 \text{ Hz.), 125.1 (q, } J = 330 \text{ Hz., CCF}_3\text{), 122.9, 122.2, 121.0, 119.6, 117.2, 115.3, 114.0, 108.8, 67.7, 66.8, 61.1, 60.9, 57.0, 56.7, 37.4, 30.5, 29.2, 16.1, 13.7, 13.6; HRMS (ESI): Calculated for C41H41F3NO6 [M+H\(^+\)]: 700.28862, Found: 700.2889.\]
**tert-butyl 2-formyl-3-iodo-1H-indole-1-carboxylate:**

![Chemical Structure](image1)

To a solution of 3-iodo-1H-indole-2-carbaldehyde (843 mg, 3.110 mmol) in acetonitrile (35 mL) at room temperature was added DMAP (38 mg, 0.311 mmol) and Boc₂O (815 mg, 3.730 mmol). After stirring for 4 h, the reaction was quenched with water and extracted with EtOAc to give the desired product in quantitative yield (1.154 g); mp 141 – 143.

**1H NMR (400 MHz, CDCl₃):** δ = 10.23 (s, 1H), 8.11 (d, 1H, J = 8.4 Hz.), 7.60 (d, 1H, J = 8.0 Hz.), 7.54 (ddd, 1H, J = 8.4, 7.2 and 1.2 Hz.), 7.38 (ddd, 1H, J = 8.0, 7.2 and 1.2 Hz.), 1.69 (s, 9H); **13C NMR (100 MHz, CDCl₃):** δ = 183.2, 150.5, 137.6, 136.4, 130.0, 129.4, 124.7, 121.0, 115.7, 86.0, 76.8, 28.0; HRMS (ESI): Calculated for C₁₄H₁₄INO₃ [M⁺]: 371.00186, Found: 371.0020.

**tert-butyl 2-formyl-3-((trimethylsilyl)ethynyl)-1H-indole-1-carboxylate:**

![Chemical Structure](image2)

A mixture of tert-butyl 2-formyl-3-iodo-1H-indole-1-carboxylate (575 mg, 1.550 mmol), Pd(PPh₃)₂Cl₂ (55 mg, 0.078 mmol), triphenylphosphine (12.5 mg, 0.048 mmol), trimethylsilylacetylene (260 mg, 245 μL, 2.650 mmol), cuprous iodide (30 mg, 0.158 mmol) and triethylamine (370 μL, 2.654 mmol) in DMF (40 mL) was stirred overnight at room temperature. The solvent was than evaporated under reduced pressure and the residue was purified by column chromatography (1% EtOAc in Petroleum Ether) yielding the desired product in 89 % (471 mg); mp 71 – 73° C.

**1H NMR (400 MHz, CDCl₃):** δ = 10.30 (s, 1H), 8.10 (d, 1H, J = 8.4 Hz.), 7.79 (d, 1H, J = 8.0 Hz.), 7.51 (ddd, 1H, J = 8.4, 7.2 and 1.2 Hz.), 7.36 (ddd, 1H, J = 8.0, 7.2 and 1.0 Hz.), 1.67 (s, 9H), 0.33 (s, 9H); **13C NMR (100 MHz, CDCl₃):** δ = 181.8, 149.5, 139.0, 137.0, 129.1, 128.9, 124.6, 122.3, 115.8, 94.7, 95.0, 86.5, 86.3, 28.2, 0.5; HRMS (ESI): Calculated for C₁₉H₂₄NO₃Si [M+H⁺]: 342.15256, Found: 342.1527.
**tert-butyl 3-ethynyl-2-formyl-1H-indole-1-carboxylate (12):**

To a solution of tert-butyl 2-formyl-3-((trimethylsilyl)ethynyl)-1H-indole-1-carboxylate (33 mg, 0.097 mmol) in THF (2 mL) and MeOH (37 µL, 0.966 mmol) cooled to -22°C was added n-Bu₄NF (1.0 M solution of THF, 37 µL, 0.039 mmol). After stirring at -22°C for 1 h, aq. NH₄Cl solution was added, extracted with CH₂Cl₂, dried over anhydrous Na₂SO₄ and concentrated under reduced pressure. The product was obtained in quantitative yield (26 mg).

**¹H NMR (400 MHz, CDCl₃):** δ = 10.35 (s, 1H), 8.10 (d, 1H, J = 8.8 Hz.), 7.79 (d, 1H, J = 8.0, arom. H), 7.51 (ddd, 1H, J = 8.4, 6.4 and 1.2 Hz.), 7.35 (ddd, 1H, J = 8.0, 7.2 and 0.8 Hz.), 4.16 (s, 1H), 1.68 (s, 9H);

**¹³C NMR (100 MHz, CDCl₃):** δ = 182.1, 149.4, 138.8, 136.9, 129.3, 129.1, 124.5, 122.0, 116.0, 86.5, 86.4, 75.1, 69.3, 28.3; HRMS (ESI): Calculated for C₁₆H₁₆NO₃ [M+H⁺]: 270.11303, Found: 270.1128.

**12H-Indolo[2',3':3,4]pyrido[1,2-a]indole-13-tert-butylcarboxylic acid ester (13):**

To a solution of tert-butyl 3-ethynyl-2-formyl-1H-indole-1-carboxylate (136 mg, 0.505 mmol) in EtOH (3 mL) were added di-tert-butyl 2-(2-aminophenyl)malonate (163 mg, 0.530 mmol) and the 2,6-lutidine (6.0 µL, 51 µmol) at room temperature. To this mixture was added the AgOTf (3.2 mg, 13 µmol) and the solution was heated under microwave irradiation (150 W) to 150°C for 45 min. The solvent was evaporated under reduced pressure and replaced by 10 mL of ethyl acetate. The solution was treated for some hours with 10 mL of an aqueous solution of hydrochloric acid (2N) at room temperature, than it was concentrated, neutralized with an aqueous solution of sodium bicarbonate and extracted with ethyl acetate. Purification the desired compound afforded as reported for Method A.

mp 122 – 124°C; **¹H NMR (400 MHz, CDCl₃):** δ = 12.2 (br s, 1H), 8.35 (d, 1H, J = 8.4 Hz.), 8.24 (d, 1H, J = 6.8 Hz.), 8.03 (d, 1H, J = 8.4 Hz.), 7.90 (d, 1H, J = 8.0 Hz.), 7.70 (d, 1H, J = 8.4 Hz.), 7.51 – 7.46 (m, 3H), 7.37 (ddd, 1H, J = 8.4, 7.2 and 1.2 Hz.), 7.30 (ddd, 1H, J = 8.0, 7.2 and 1.2 Hz.), 1.81 (s, 9H); **¹³C NMR (100 MHz, CDCl₃):** δ = 167.4, 138.2, 133.9, 132.0, 129.0, 128.2, 125.9, 124.9, 122.8, 122.4, 121.7, 120.4, 120.2, 117.0, 116.8, 112.6, 110.6, 106.3, 97.0, 80.9, 29.2; HRMS (ESI): Calculated for C₂₃H₂₁N₂O₂ [M+H⁺]: 357.16032, Found: 357.1601.
References:


