Electrocatalytic intramolecular dehydrogenative annulation for the synthesis of indoles

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General information

All glassware was oven dried at 110 °C for hours and cooled down under vacuum. 1a-1o, 1p-1q were prepared according to reported procedures. The instrument for electrolysis is dual display potentiostat (DJS-292B) (made in China). The anode electrode and cathode electrode all are platinum plate (15 mm×15 mm×0.3 mm). Thin layer chromatography (TLC) employed glass 0.25 mm silica gel plates. Flash chromatography columns were packed with 200-300 mesh silica gel in petroleum (bp. 60-90 °C). Gas chromatographic analyses were performed on SHIMADZU GC-2014 gas chromatography instrument with a FID detector and naphthalene was added as internal standard. GC-MS spectra were recorded on Varian GC MS 3900-2100T or SHIMADZU GC MS-2010. 1H and 13C NMR data were recorded with Bruker Advance III (400 MHz) spectrometers with tetramethylsilane as an internal standard. All chemical shifts (δ) are reported in ppm and coupling constants (J) in Hz. All chemical shifts are reported relative to tetramethylsilane and d-solvent peaks (77.00 ppm, CDCl3; 39.60 ppm, DMSO), respectively.

General procedure

In an oven-dried undivided three-necked bottle (25 mL) equipped with a stir bar, substrate (0.2 mmol), KI (249 mg, 1.5 mmol), DMF (10 mL) and H2O (0.2 mL) were combined and added. The bottle was equipped with platinum plate (15 mm×15 mm×0.3 mm) as both the anode and cathode and was then charged with nitrogen. The reaction mixture was stirred and electrolyzed at a constant current of 7 mA (J_{anode} = 12 mA/cm²) under room temperature for 3 h (3.9 F). When the reaction was finished, the resulting reaction solution was quenched with 100 mL brine and extracted with 4 × 60 mL ethylacetate. The extract was dried with Na2SO4. The solvent was removed with a rotary evaporator. The pure product was obtained by flash column chromatography on silica gel (petroleum: ethyl ether = 10:1).
Detail descriptions for products

**Ethyl 2-phenyl-1H-indole-3-carboxylate (2a):** A white solid (mp. 145-148 °C) was obtained in 96% isolated yield. $^1$H NMR (400 MHz, CDCl$_3$) δ 8.84 (s, 1H), 8.30 – 8.11 (m, 1H), 7.68 – 7.48 (m, 2H), 7.39 – 7.32 (m, 3H), 7.32 – 7.19 (m, 3H), 4.23 (q, $J = 7.1$ Hz, 2H), 1.27 (t, $J = 7.0$ Hz, 3H). $^{13}$C NMR (101 MHz, CDCl$_3$) δ 165.55, 144.63, 135.15, 131.90, 129.52, 129.02, 127.94, 127.48, 123.03, 121.93, 111.13, 104.34, 59.69, 14.22.

**Ethyl 5-methyl-2-phenyl-1H-indole-3-carboxylate (2b):** A white solid (mp. 144-145 °C) was obtained in 93% isolated yield. $^1$H NMR (400 MHz, CDCl$_3$) δ 8.43 (s, 1H), 8.03 (s, 1H), 7.67 – 7.59 (m, 2H), 7.48 – 7.39 (m, 3H), 7.26 (d, $J = 9.3$ Hz, 1H), 7.09 (dd, $J = 8.2$, 1.8 Hz, 1H), 4.29 (q, $J = 7.1$ Hz, 2H), 2.50 (s, 3H), 1.29 (t, $J = 7.1$ Hz, 3H). $^{13}$C NMR (101 MHz, CDCl$_3$) δ 165.43, 144.38, 133.42, 132.19, 131.50, 129.55, 129.03, 128.03, 127.87, 124.71, 121.73, 110.60, 104.21, 59.61, 21.73, 14.28.

**Ethyl 4,6-dimethyl-2-phenyl-1H-indole-3-carboxylate (2c):** A white solid (mp. 108-110 °C) was obtained in 94% isolated yield. $^1$H NMR (400 MHz, CDCl$_3$) δ 8.57 (s, 1H), 7.47 – 7.41 (m, 2H), 6.87 (s, 1H), 6.81 (s, 1H), 4.17 (q, $J = 7.2$ Hz, 2H), 2.61 (s, 3H), 2.35 (s, 3H), 1.11 (t, $J = 7.2$ Hz, 3H). $^{13}$C NMR (101 MHz, CDCl$_3$) δ 167.08, 140.42, 136.07, 132.98, 132.38, 130.79, 128.61, 128.41, 128.18, 125.20, 123.51, 108.72, 106.80, 60.40, 21.34, 21.04, 13.83. HRMS (ESI) calculated for C$_{19}$H$_{19}$NO$_2$ [M+H]$^+$: 294.1489; found: 294.1488.

**Ethyl 7-methyl-2-phenyl-1H-indole-3-carboxylate (2d):** A white solid (mp. 145-146 °C) was obtained in 79% isolated yield. $^1$H NMR (400 MHz, CDCl$_3$) δ 8.63 (s, 1H), 8.05 (d, $J = 8.0$ Hz, 1H), 7.66 – 7.57 (m, 2H), 7.42 – 7.34 (m, 3H), 7.21 – 7.15 (m, 1H), 7.08 – 7.01 (m, 1H), 4.25 (q, $J = 7.1$ Hz, 2H). $^{13}$C NMR (101 MHz, CDCl$_3$) δ 165.43, 144.38, 133.42, 132.19, 131.50, 129.55, 129.03, 128.03, 127.87, 124.71, 121.73, 110.60, 104.21, 59.61, 21.73, 14.28.
Hz, 2H), 2.47 (s, 3H), 1.28 (t, J = 7.1 Hz, 3H). $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 165.43, 144.25, 134.66, 132.12, 129.58, 128.98, 127.94, 127.11, 123.69, 122.15, 120.22, 119.71, 105.03, 59.61, 16.49, 14.23.

**Ethyl 5-fluoro-2-phenyl-1H-indole-3-carboxylate (2e):** A white solid (mp. 146-148 °C) was obtained in 86% isolated yield. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.89 (s, 1H), 7.84 (dd, $J$ = 10.1, 2.6 Hz, 1H), 7.80 – 7.51 (m, 2H), 7.40 – 7.31 (m, 3H), 7.20 (dd, $J$ = 8.8, 4.4 Hz, 1H), 6.96 (td, $J$ = 9.0, 2.6 Hz, 1H), 4.23 (q, $J$ = 7.1 Hz, 2H), 1.28 (t, $J$ = 7.1 Hz, 3H). $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 165.06, 159.16 (d, $J_{C-F}$ = 237.2 Hz), 145.96, 131.58 (d, $J_{C-F}$ = 8.4 Hz), 129.47, 129.34, 128.31 (d, $J_{C-F}$ = 11.2 Hz), 128.11, 111.79 (d, $J_{C-F}$ = 9.9 Hz), 111.54 (d, $J_{C-F}$ = 26.6 Hz), 107.44 (d, $J_{C-F}$ = 25.5 Hz), 104.82 (d, $J_{C-F}$ = 4.5 Hz), 59.84, 14.27. $^{19}$F NMR (377 MHz, CDCl$_3$) $\delta$ -121.22.

**Ethyl 5-chloro-2-phenyl-1H-indole-3-carboxylate (2f):** A white solid (mp. 149-151 °C) was obtained in 86% isolated yield. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.84 (s, 1H), 8.17 (d, $J$ = 2.0 Hz, 1H), 7.61 – 7.55 (m, 2H), 7.42 – 7.35 (m, 3H), 7.26 – 7.17 (m, 2H), 4.25 (q, $J$ = 7.1 Hz, 2H), 1.29 (t, J = 7.1 Hz, 3H). $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 165.02, 145.64, 133.47, 131.46, 129.48, 129.34, 128.31 (d, $J_{C-F}$ = 11.2 Hz), 128.11, 111.79 (d, $J_{C-F}$ = 9.9 Hz), 111.54 (d, $J_{C-F}$ = 26.6 Hz), 107.44 (d, $J_{C-F}$ = 25.5 Hz), 104.82 (d, $J_{C-F}$ = 4.5 Hz), 59.84, 14.28.

**Ethyl 5-bromo-2-phenyl-1H-indole-3-carboxylate (2g):** A white solid (mp. 148-150 °C) was obtained in 92% isolated yield. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.72 (s, 1H), 8.35 (d, $J$ = 1.9 Hz, 1H), 7.64 – 7.55 (m, 2H), 7.43 – 7.37 (m, 3H), 7.36 – 7.31 (m, 1H), 7.19 (d, $J$ = 8.6 Hz, 1H), 4.26 (q, $J$ = 7.1 Hz, 2H), 1.29 (t, J = 7.1 Hz, 3H). $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 165.02, 145.46, 133.75, 131.38, 129.47, 129.37, 129.18, 128.07, 126.04, 124.66, 115.46, 112.51, 104.13, 59.93, 14.28.

**Ethyl 5-iodo-2-phenyl-1H-indole-3-carboxylate (2h):** A white solid (mp. 140-142 °C) was obtained in 92% isolated yield. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 9.06 (s, 1H), 8.58 (d, $J$ = 1.8 Hz, 1H), 7.60 –
7.55 (m, 2H), 7.51 (dd, \( J = 8.5, 1.7 \) Hz, 1H), 7.41 – 7.35 (m, 3H), 7.08 (d, \( J = 8.5 \) Hz, 1H), 4.25 (q, \( J = 7.1 \) Hz, 2H), 1.30 (t, \( J = 7.1 \) Hz, 3H). \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \( \delta \) 165.15, 145.12, 134.23, 131.45, 131.27, 130.75, 129.78, 129.43, 129.28, 127.98, 113.07, 103.60, 86.03, 59.92, 14.18.

**Ethyl 5-methoxy-2-phenyl-1H-indole-3-carboxylate (2i):** \(^3\) white solid (mp. 145-147 °C) was obtained in 86% isolated yield. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 8.47 (s, 1H), 7.74 (d, \( J = 2.5 \) Hz, 1H), 7.63 (dd, \( J = 6.7, 3.0 \) Hz, 2H), 7.43 (q, \( J = 3.2, 2.5 \) Hz, 3H), 7.26 (s, 1H), 6.91 (dd, \( J = 8.8, 2.5 \) Hz, 1H), 4.28 (q, \( J = 7.1 \) Hz, 2H), 3.90 (s, 3H), 1.28 (t, \( J = 7.1 \) Hz, 3H). \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \( \delta \) 165.42, 155.72, 144.69, 132.15, 129.51, 128.52, 128.02, 113.46, 111.77, 104.42, 103.56, 59.59, 55.67, 14.22.

**3-Ethyl 5-methyl 2-phenyl-1H-indole-3,5-dicarboxylate (2j):** white solid (mp. 192-193 °C) was obtained in 82% isolated yield. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 9.33 (s, 1H), 8.89 (s, 1H), 7.93 (d, \( J = 8.6 \) Hz, 1H), 7.65 (dd, \( J = 6.6, 3.1 \) Hz, 2H), 7.50 – 7.34 (m, 4H), 4.31 (q, \( J = 7.1 \) Hz, 2H), 2.69 (s, 3H), 1.32 (t, \( J = 7.1 \) Hz, 3H). \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \( \delta \) 198.70, 164.93, 145.86, 137.84, 131.62, 131.37, 129.56, 129.49, 128.14, 127.21, 124.54, 123.11, 111.25, 105.67, 59.98, 26.62, 14.20. HRMS (ESI) calculated for C\(_{19}\)H\(_{17}\)NO\(_3\) [M+H]\(^+\): 308.1281; found: 308.1286.

**Ethyl 2-phenyl-5-(trifluoromethyl)-1H-indole-3-carboxylate (2k):** \(^3\) white solid (mp. 172-174 °C) was obtained in 56% isolated yield. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 9.04 (s, 1H), 8.51 (s, 1H), 7.63 – 7.55 (m, 2H), 7.50 – 7.43 (m, 1H), 7.42 – 7.33 (m, 4H), 4.27 (q, \( J = 7.1 \) Hz, 2H), 1.30 (t, \( J = 7.1 \) Hz, 3H). \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \( \delta \) 164.82, 145.99, 136.45, 131.25, 129.58, 129.51, 128.19, 127.06, 125.05 (q, \( J_{CF} = 272.7 \)Hz), 124.37 (q, \( J_{CF} = 31.9 \)Hz), 119.99 (q, \( J_{CF} = 4.3 \)Hz), 111.36, 105.37, 60.07, 14.19.
Ethyl 2-phenyl-3H-benzo[e]indole-1-carboxylate (2l): white solid (mp. 164-166 °C) was obtained in 95% isolated yield. $^1$H NMR (400 MHz, CDCl$_3$) δ 8.96 (d, $J = 8.4$ Hz, 1H), 8.77 (s, 1H), 7.95 – 7.85 (m, 1H), 7.64 (d, $J = 8.8$ Hz, 1H), 7.59 – 7.49 (m, 3H), 7.48 – 7.37 (m, 5H), 4.29 (q, $J = 7.2$ Hz, 2H), 1.13 (t, $J = 7.2$ Hz, 3H). $^{13}$C NMR (101 MHz, CDCl$_3$) δ 167.60, 139.88, 132.53, 132.47, 130.38, 128.74, 128.44, 128.24, 128.00, 125.94, 125.07, 124.87, 123.94, 120.91, 112.21, 108.56, 60.67, 13.76. HRMS (ESI) calculated for C$_{21}$H$_{17}$NO$_2$ [M+H]$^+$: 316.1332; found: 316.1333.

Ethyl 2-phenyl-1H-benzo[g]indole-3-carboxylate (2m): white solid (mp. 197-198 °C) was obtained in 80% isolated yield. $^1$H NMR (400 MHz, DMSO-d$_6$) δ 12.77 (s, 1H), 8.59 (dd, $J = 8.2$, 1.1 Hz, 1H), 8.21 (d, $J = 8.8$ Hz, 1H), 7.99 (dd, $J = 8.1$, 1.1 Hz, 1H), 7.78 – 7.71 (m, 2H), 7.68 (d, $J = 8.8$ Hz, 1H), 7.63 – 7.57 (m, 1H), 7.57 – 7.46 (m, 4H), 4.23 (q, $J = 7.1$ Hz, 2H), 1.24 (t, $J = 7.1$ Hz, 3H). $^{13}$C NMR (101 MHz, DMSO-d$_6$) δ 164.66, 142.75, 132.14, 130.51, 130.44, 130.20, 128.79, 128.51, 127.89, 126.01, 124.60, 123.63, 122.24, 121.71, 121.28, 120.87, 104.99, 59.28, 14.29.

Phenyl(2-phenyl-1H-indol-3-yl)methanone (2n): white solid was obtained in 62% isolated yield. $^1$H NMR (400 MHz, DMSO-d$_6$) δ 12.23 (s, 1H), 7.78 – 7.72 (m, 1H), 7.55 – 7.50 (m, 3H), 7.42 – 7.34 (m, 3H), 7.30 – 7.14 (m, 7H). $^{13}$C NMR (101 MHz, DMSO) δ 192.63, 144.60, 140.25, 136.28, 132.01, 131.82, 130.01, 129.53, 128.95, 128.63, 128.51, 128.25, 123.35, 121.90, 121.04, 112.56, 112.34.

Methyl 2-isopropyl-1H-indole-3-carboxylate (2o): pale yellow oil was obtained in 62% isolated yield. $^1$H NMR (400 MHz, CDCl$_3$) δ 8.80 (s, 1H), 8.19 – 8.08 (m, 1H), 7.39 – 7.30 (m, 1H), 7.25 – 7.16 (m, 2H), 4.15 (p, $J = 7.0$ Hz, 1H), 3.94 (s, 3H), 1.36 (d, $J = 7.0$ Hz, 6H). $^{13}$C NMR (101 MHz, CDCl$_3$) δ 166.44, 153.73, 134.41, 127.00, 122.29, 121.68, 121.43, 110.77, 102.64, 50.78, 26.28, 21.74.
Ethyl 2-(4-fluorophenyl)-1H-indole-3-carboxylate (2p): a white solid (mp. 167-168 °C) was obtained in 89% isolated yield. $^1$H NMR (400 MHz, CDCl$_3$) δ 8.82 (s, 1H), 8.23 – 8.15 (m, 1H), 7.61 – 7.53 (m, 2H), 7.35 – 7.30 (m, 1H), 7.29 – 7.21 (m, 2H), 7.04 (t, $J = 8.7$ Hz, 2H), 4.27 (q, $J = 7.1$ Hz, 2H), 1.31 (t, $J = 7.1$ Hz, 3H). $^{13}$C NMR (101 MHz, CDCl$_3$) δ 165.49, 163.11, 143.50, 135.11, 131.45, 127.94, 127.39, 123.23, 122.06, 115.17, 114.95, 111.08, 104.56, 59.78, 14.26. $^{19}$F NMR (377 MHz, CDCl$_3$) δ -111.59.

Ethyl 2-(4-methoxyphenyl)-1H-indole-3-carboxylate (2q): a white solid (mp. 164-165 °C) was obtained in 86% isolated yield. $^1$H NMR (400 MHz, CDCl$_3$) δ 8.75 (s, 1H), 8.26 – 8.10 (m, 1H), 7.53 (d, $J = 8.8$ Hz, 2H), 7.35 – 7.28 (m, 1H), 7.27 – 7.18 (m, 2H), 6.86 (d, $J = 8.7$ Hz, 2H), 4.28 (q, $J = 7.1$ Hz, 2H), 3.76 (s, 3H), 1.32 (t, $J = 7.1$ Hz, 3H). $^{13}$C NMR (101 MHz, CDCl$_3$) δ 165.68, 160.18, 144.76, 135.03, 130.86, 127.59, 124.06, 122.84, 121.91, 121.84, 113.44, 111.00, 103.85, 59.67, 55.24, 14.34.

Ethyl 2-(4-(trifluoromethyl)phenyl)-1H-indole-3-carboxylate (2r): white solid (mp. 151-152 °C) was obtained in 80% isolated yield. $^1$H NMR (400 MHz, CDCl$_3$) δ 8.96 (s, 1H), 7.69 (d, $J = 8.1$ Hz, 2H), 7.59 (d, $J = 8.1$ Hz, 2H), 7.38 – 7.31 (m, 1H), 7.31 – 7.22 (m, 2H), 4.26 (q, $J = 7.1$ Hz, 2H), 1.29 (t, $J = 7.1$ Hz, 3H). $^{13}$C NMR (101 MHz, CDCl$_3$) δ 165.39, 142.52, 135.47, 135.35, 130.81, 129.95, 127.25, 124.88 (q, $J_{C-F} = 3.7$ Hz), 123.87 (q, $J_{C-F} = 273.1$ Hz), 123.64, 122.33, 122.16, 111.25, 105.33, 59.97, 14.19. $^{19}$F NMR (377 MHz, CDCl$_3$) δ -62.68. HRMS (ESI) calculated for C$_{18}$H$_{14}$F$_3$NO$_2$ [M+H]$^+$: 334.1049; found: 334.1056.

Phenyl(2-(p-tolyl)imidazo[1,2-a]pyridin-3-yl)methanone (3a): white solid was obtained in 97% isolated yield. $^1$H NMR (400 MHz, CDCl$_3$) δ 9.52 (dt, $J = 6.9, 1.2$ Hz, 1H), 7.79 (dt, $J = 8.9, 1.2$ Hz,
1H), 7.56 – 7.46 (m, 3H), 7.29 – 7.24 (m, 1H), 7.24 – 7.19 (m, 2H), 7.13 – 7.04 (m, 3H), 6.88 (d, J = 7.9 Hz, 2H), 2.22 (s, 3H). 13C NMR (101 MHz, CDCl3) δ 187.41, 155.03, 147.37, 138.68, 138.16, 131.64, 130.97, 130.09, 129.58, 129.12, 128.45, 128.20, 127.75, 119.85, 117.34, 114.48, 21.23. HRMS (ESI) calculated for C21H16N2O [M+H]+: 313.1335; found: 313.1324.

Phenyl(2-(p-tolyl)imidazo[1,2-a]pyrazin-3-yl)methanone (3b): white solid was obtained in 94% isolated yield. 1H NMR (400 MHz, CDCl3) δ 9.29 (d, J = 1.5 Hz, 1H), 9.21 (dd, J = 4.6, 1.5 Hz, 1H), 8.16 (d, J = 4.7 Hz, 1H), 7.62 – 7.51 (m, 2H), 7.38 – 7.31 (m, 1H), 7.28 – 7.23 (m, 2H), 7.15 (t, J = 7.8 Hz, 2H), 6.93 (d, J = 7.9 Hz, 2H), 2.25 (s, 3H). 13C NMR (101 MHz, CDCl3) δ 187.57, 154.36, 143.62, 141.33, 138.86, 137.40, 132.47, 131.85, 129.99, 129.89, 129.53, 128.66, 127.95, 120.06, 21.19. HRMS (ESI) calculated for C20H15N3O [M+H]+: 313.1288; found: 314.1293.

References


Copies of product NMR Spectra

2a

$^1$H NMR

$^{13}$C NMR
$^1$H NMR

$^13$C NMR
$^1$H NMR

![NMR spectrum of 2d](image)

$^{13}$C NMR

![NMR spectrum of 2d](image)
$^{19}$F NMR
$^1$H NMR

$^{13}$C NMR
$^{1}H$ NMR

$^{13}C$ NMR
**1H NMR**

- Peak at 9.4 ppm
- Peak at 7.5 ppm
- Peak at 7.0 ppm
- Peak at 4.2 ppm

**13C NMR**

- Peak at 165.1 ppm
- Peak at 154.2 ppm
- Peak at 131.2 ppm
- Peak at 129.2 ppm
- Peak at 128.4 ppm
- Peak at 127.3 ppm
- Peak at 120.3 ppm
- Peak at 86.0 ppm
- Peak at 59.3 ppm
- Peak at 14.1 ppm
$^1$H NMR

$^{13}$C NMR
$^1$H NMR

$^{13}$C NMR
$^1$H NMR

$^{13}$C NMR
$^1$H NMR

$^{13}$C NMR
$^{19}$F NMR
$^{1}H$ NMR

$^{13}C$ NMR
$^{19}$F NMR
$^1$H NMR

$^{13}$C NMR