Supplementary Information

Diversity-oriented synthesis of pyrazolo[4,3-b]indoles by gold-catalysed three-component annulation: application to the development of a new class of CK2 inhibitors

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Experimental section

Synthesis of aryl azides 6a–c and 12

Compounds S1a, S1b, S1c, and S2 were prepared according to the literature.

Representative procedure: synthesis of ethyl 3-azido-4-ethynylbenzoate (6b). To a solution of S1b (1286 mg, 6.8 mmol) in MeCN (24 mL), DMF (4 mL) and 10% aqueous H2SO4 (8 mL) was added dropwise a solution of NaNO2 (563 mg, 8.2 mmol) in H2O (2 mL) at 0 °C. The reaction mixture was stirred at the same temperature for 30 min. Then, a solution of NaN3 (530 mg, 8.2 mmol) in H2O (2 mL) was added dropwise to the mixture at 0 °C. The mixture was allowed to warm to room temperature and stirred for further 30 min. The resulting mixture was diluted with H2O and extracted with EtOAc twice. The combined extracts were washed with brine, dried over Na2SO4, and concentrated in vacuo. The residue was chromatographed on silica gel (hexane/EtOAc = 8/1) followed by recrystallization from EtOAc–hexane to afford the title compound 6b (1.20 g, 82%) as light yellow crystals: mp 75 °C; IR (neat): νmax/cm⁻¹ 3236 (C≡CH), 2111 (N3), 1699 (C=O); ¹H-NMR (500 MHz, CDCl3) δ: 1.41 (t, J = 7.2 Hz, 3H), 3.53 (s, 1H), 4.40 (q, J = 7.2 Hz, 2H), 7.53 (d, J = 8.0 Hz, 1H), 7.76 (d, J = 8.0 Hz, 1H), 7.80 (s, 1H); ¹³C-NMR (125 MHz, CDCl3) δ: 14.2, 61.6, 78.7, 85.4, 118.1, 119.4, 125.4, 132.0, 134.2, 142.1, 165.1; HRMS (FAB⁺) calcd for C11H10N3O2 [M+H]⁺: 216.0773, found: 216.0765.
1-Azido-2-ethynylbenzene (6a). By use of the procedure for the synthesis of 6b, S1a (1.02 g, 8.7 mmol) was converted to the title compound 6a (1.02 mg, 82%) as a yellow oil: IR (neat): $\nu_{\text{max}}$/cm$^{-1}$ 3295 (C≡CH), 2106 (N$_3$); $^1$H-NMR (500 MHz, CDCl$_3$) $\delta$: 3.38 (s, 1H), 7.08–7.15 (m, 2H), 7.36–7.39 (m, 1H), 7.47–7.49 (m, 1H); $^{13}$C-NMR (125 MHz, CDCl$_3$) $\delta$: 79.3, 82.9, 114.1, 118.5, 124.6, 130.1, 134.3, 141.7; HRMS (FAB$^+$) calcd for C$_8$H$_6$N$_3$ [M+H]$^+$: 144.0562, found: 144.0553.

2-Azido-1-ethynyl-4-methoxybenzene (6c). By use of the procedure for the synthesis of 6b, S1c (900 mg, 6.1 mmol) was converted to the title compound 6c (656 mg, 62%) as yellow crystals: mp 52 °C; IR (neat): $\nu_{\text{max}}$/cm$^{-1}$ 3281 (C≡CH), 2114 (N$_3$); $^1$H-NMR (500 MHz, CDCl$_3$) $\delta$: 3.30 (s, 1H), 3.82 (s, 3H), 6.61–6.64 (m, 2H), 7.38 (d, $J= 8.0$ Hz, 1H); $^{13}$C-NMR (125 MHz, CDCl$_3$) $\delta$: 55.5, 79.3, 81.3, 104.3, 106.5, 110.7, 135.2, 142.9, 161.0; HRMS (FAB$^+$) calcd for C$_9$H$_8$N$_3$O [M+H]$^+$: 174.0667, found: 174.0659.

Ethyl 3-azido-4-iodobenzoate (12). By use of the procedure for the synthesis of 6b, S2 (3.30 g, 11.3 mmol) was converted to the title compound 12 (2.48 g, 69%) as colourless crystals: mp 43 °C; IR (neat): $\nu_{\text{max}}$/cm$^{-1}$ 2110 (N$_3$), 1706 (C=O); $^1$H-NMR (500 MHz, CDCl$_3$) $\delta$: 1.41 (t, $J= 7.2$ Hz, 3H), 4.40 (q, $J= 7.2$ Hz, 2H), 7.48–7.51 (m, 1H), 7.76–7.77 (m, 1H), 7.87 (d, $J= 8.0$ Hz, 1H); $^{13}$C-NMR (125 MHz, CDCl$_3$) $\delta$: 14.3, 61.6, 93.8, 118.8, 126.8, 132.1, 140.2, 142.3, 165.3; HRMS (FAB$^+$) calcd for C$_9$H$_8$I$_3$N$_3$O$_2$ [M+H]$^+$: 317.9740, found: 317.9746.

S3
Methyl 5-[2-azido-4-(ethoxycarbonyl)phenyl]-3-isopropyl-2-(4-methoxybenzyl)-2,3-dihydro-1H-pyrazole-1-carboxylate (9b). By use of the procedure for the synthesis of 9a, 6b (108 mg, 0.5 mmol), hydrazine 8a (158 mg, 0.75 mmol) and isobutyraldehyde (68 μL, 0.75 mmol) were converted to the title compound 9b (230 mg, 96%) as a yellow oil: IR (neat): νmax/cm⁻¹ 2116 (N₃), 1710 (C=O); ¹H-NMR (500 MHz, CDCl₃) δ: 0.75–0.77 (m, 6H), 1.40 (t, J = 6.9 Hz, 3H), 1.52–1.58 (m, 1H), 3.38 (dd, J = 6.0, 2.9 Hz, 1H), 3.59 (s, 3H), 3.77 (d, J = 12.0 Hz, 1H), 3.81 (s, 3H), 4.08 (d, J = 12.0 Hz, 1H), 5.54 (d, J = 2.9 Hz, 1H), 6.87 (d, J = 8.6 Hz, 2H), 7.37–7.39 (m, 3H), 7.77–7.79 (m, 1H), 7.85 (s, 1H); ¹³C-NMR (125 MHz, CDCl₃) δ: 14.3, 18.1, 18.2, 32.8, 52.7, 55.2, 61.3, 61.7, 73.9, 113.3 (2C), 114.5, 119.4, 125.4, 128.5, 128.8, 130.1, 131.3, 131.5 (2C), 136.6, 138.1, 155.2, 159.1, 165.5; HRMS (FAB⁺) calcd for C₂₅H₃₀N₅O₅ [M+H]⁺: 480.2247, found: 480.2250.

Methyl 5-(2-azido-4-methoxyphenyl)-3-isopropyl-2-(4-methoxybenzyl)-2,3-dihydro-1H-pyrazole-1-carboxylate (9c). By use of the procedure for the synthesis of 9a, 6c (43 mg, 0.25 mmol), hydrazine 8a (79 mg, 0.38 mmol) and isobutyraldehyde (34 μL, 0.38 mmol) were converted to the title compound 9c (100 mg, 91%) as a yellow oil: IR (neat): νmax/cm⁻¹ 2109 (N₃), 1712 (C=O); ¹H-NMR (500 MHz, CDCl₃) δ: 0.74–0.76 (m, 6H), 1.40–1.55 (m, 1H), 3.32 (dd, J = 5.7, 2.9 Hz, 1H), 3.60 (s, 3H), 3.76 (d, J = 12.0 Hz, 1H), 3.81 (s, 3H), 3.83 (s, 3H), 4.06 (d, J = 12.0 Hz, 1H), 5.35 (d, J = 2.9 Hz, 1H), 6.65–6.70 (m, 2H), 6.86 (d, J = 8.6 Hz, 2H), 7.23 (d, J = 8.6 Hz, 1H), 7.37 (d, J = 8.6 Hz, 2H); ¹³C-NMR (125 MHz, CDCl₃) δ: 18.0, 18.2, 32.8, 52.5, 55.2, 55.4, 61.6, 73.5, 104.3,
109.9, 111.8, 113.3 (2C), 117.5, 129.1, 131.2, 131.5 (2C), 137.0, 138.8, 155.0, 159.0, 160.4; HRMS (FAB+) calcd for C$_{23}$H$_{28}$N$_{5}$O$_{4}$ [M+H]$^+$: 438.2142, found: 438.2134.

tert-Butyl 5-[2-azido-4-(ethoxycarbonyl)phenyl]-2-benzyl-3-isopropyl-2,3-dihydro-1H-pyrazole-1-carboxylate (9d). By use of the procedure for the synthesis of 9a, 6b (54 mg, 0.25 mmol), hydrazine 8b (83 mg, 0.38 mmol) and isobutyraldehyde (34 µL, 0.38 mmol) were converted to the title compound 9d (98 mg, 80%) as a yellow oil: IR (neat): $\nu_{\text{max}}$/cm$^{-1}$ 2114 (N$_3$), 1712 (C=O); $^1$H-NMR (500 MHz, CDCl$_3$) $\delta$: 0.75–0.78 (m, 6H), 1.24 (s, 9H), 1.41 (t, $J = 6.9$ Hz, 3H), 1.50–1.56 (m, 1H), 3.31 (dd, $J = 5.7$, 2.9 Hz, 1H), 3.79 (d, $J = 12.0$ Hz, 1H), 4.16 (d, $J = 12.0$ Hz, 1H), 4.40 (q, $J = 6.9$ Hz, 2H), 5.52 (d, $J = 2.9$ Hz, 1H), 7.26–7.29 (m, 1H), 7.31–7.34 (m, 2H), 7.40 (d, $J = 8.0$ Hz, 1H), 7.47–7.49 (m, 2H), 7.78 (d, $J = 8.0$ Hz, 1H), 7.84 (s, 1H); $^{13}$C-NMR (125 MHz, CDCl$_3$) $\delta$: 14.3, 18.08, 18.10, 27.9 (3C), 32.7, 61.3, 62.3, 73.8, 80.6, 114.1, 119.5, 125.3, 127.3, 127.9 (2C), 129.6, 130.0, 130.4 (2C), 131.0, 136.85, 136.94, 137.9, 153.3, 165.5; HRMS (FAB+) calcd for C$_{27}$H$_{34}$N$_{5}$O$_{4}$ [M+H]$^+$: 492.2611, found: 492.2609.

Methyl 5-[2-azido-4-(ethoxycarbonyl)phenyl]-2-(4-methoxybenzyl)-3-propyl-2,3-dihydro-1H-pyrazole-1-carboxylate (9e). By use of the procedure for the synthesis of 9a, 6b (54 mg, 0.25 mmol), hydrazine 8a (79 mg, 0.38 mmol) and n-butyraldehyde (34 µL, 0.38 mmol) were converted to the title compound 9e (94 mg, 78%) as a yellow oil. In this case, AgNTf$_2$ (2.9 mg, 0.0075 mmol) was used instead of AgOTf: IR (neat): $\nu_{\text{max}}$/cm$^{-1}$ 2112 (N$_3$), 1713 (C=O); $^1$H-NMR (500 MHz, CDCl$_3$) $\delta$: 0.77 (t, $J = 7.2$ Hz, 3H), 1.10–1.34 (m, 4H), 1.40 (t, $J = 7.2$ Hz, 3H), 3.57–3.60 (m, 4H), 3.78–3.81 (m, 4H), 4.09 (d, $J = 12.0$ Hz, 1H), 4.38–4.42 (m, 2H), 5.59 (d, $J = 2.9$ Hz, 1H), 6.87 (d, $J$
= 8.6 Hz, 2H), 7.37–7.39 (m, 3H), 7.77–7.79 (m, 1H), 7.85 (s, 1H); $^{13}$C-NMR (125 MHz, CDCl$_3$) δ: 13.8, 14.3, 18.5, 37.0, 52.7, 55.2, 60.9, 61.3, 67.8, 113.4 (2C), 116.5, 119.4, 125.4, 128.7, 128.8, 130.1, 131.2 (2C), 131.3, 136.0, 138.0, 155.2, 159.0, 165.4; HRMS (FAB$^+$) calcd for C$_{25}$H$_{30}$N$_5$O$_5$ [M+H]$^+$: 480.2247, found: 480.2241.

Methyl 5-[2-azido-4-(ethoxycarbonyl)phenyl]-3-benzyl-2-(4-methoxybenzyl)-2,3-dihydro-1H-pyrazole-1-carboxylate (9f). By use of the procedure for the synthesis of 9a, 6b (54 mg, 0.25 mmol), hydrazine 8a (79 mg, 0.38 mmol) and 2-phenylacetaldehyde (49 µL, 0.38 mmol) were converted to the title compound 9f (67 mg, 51%) as a yellow oil. In this case, AgNTf$_2$ (2.9 mg, 0.0075 mmol) was used instead of AgOTf: IR (neat): $\nu_{\text{max}}$/cm$^{-1}$ 2114 (N$_3$), 1714 (C=O); $^1$H-NMR (500 MHz, CDCl$_3$) δ: 1.39 (t, $J = 7.2$ Hz, 3H), 2.61–2.70 (m, 2H), 3.58 (s, 3H), 3.77 (d, $J = 12.0$ Hz, 1H), 3.79–3.82 (m, 4H), 4.09 (d, $J = 12.0$ Hz, 1H), 4.37–4.42 (m, 2H), 5.49 (d, $J = 2.9$ Hz, 1H), 6.81 (d, $J = 8.6$ Hz, 2H), 7.13–7.14 (m, 2H), 7.17–7.19 (m, 1H), 7.21–7.25 (m, 2H), 7.28–7.31 (m, 3H), 7.75–7.77 (m, 1H), 7.83 (s, 1H); $^{13}$C-NMR (125 MHz, CDCl$_3$) δ: 14.3, 41.5, 52.7, 55.2, 60.8, 61.3, 69.1, 113.5 (2C), 115.2, 119.4, 125.4, 126.2, 127.9 (2C), 128.50, 128.52, 129.7 (2C), 130.2, 130.9 (2C), 131.4, 136.9, 137.5, 138.1, 154.9, 158.9, 165.4; HRMS (FAB$^+$) calcd for C$_{29}$H$_{30}$N$_5$O$_5$ [M+H]$^+$: 528.2247, found: 528.2250.

Methyl 5-[2-azido-4-(ethoxycarbonyl)phenyl]-2-(4-methoxybenzyl)-3-phenyl-2,3-dihydro-1H-pyrazole-1-carboxylate (9g). By use of the procedure for the synthesis of 9a, 6b (108 mg, 0.5 mmol), hydrazine 8a (158 mg, 0.75 mmol) and benzaldehyde (76 µL, 0.75 mmol) were converted to
the title compound 9g (134 mg, 52%) as a yellow oil. In this case, the reaction was carried out at room temperature using AgNTf$_2$ (5.8 mg, 0.015 mmol) instead of AgOTf: IR (neat): $\nu_{\text{max}}$/cm$^{-1}$ 2114 (N$_3$), 1714 (C=O); $^1$H-NMR (500 MHz, CDCl$_3$) $\delta$: 1.40 (t, $J = 7.2$ Hz, 3H), 3.59 (s, 3H), 3.81 (s, 3H), 4.02 (d, $J = 12.0$ Hz, 1H), 4.30 (d, $J = 12.0$ Hz, 1H), 4.37–4.44 (m, 2H), 4.70 (d, $J = 3.4$ Hz, 1H), 5.73 (d, $J = 3.4$ Hz, 1H), 6.87 (d, $J = 8.0$ Hz, 2H), 7.14–7.15 (m, 2H), 7.20–7.28 (m, 3H), 7.41–7.43 (m, 3H), 7.78–7.80 (m, 1H), 7.87 (s, 1H); $^{13}$C-NMR (125 MHz, CDCl$_3$) $\delta$: 14.3, 52.9, 55.2, 61.4, 61.5, 70.4, 113.6 (2C), 114.8, 119.4, 125.4, 126.7 (2C), 127.4, 128.2, 128.4, 128.6 (2C), 130.3, 131.2 (2C), 131.6, 136.8, 138.3, 140.4, 154.9, 159.2, 165.4; HRMS (FAB$^+$) calcd for C$_{28}$H$_{28}$N$_5$O$_5$ [M+H]$^+$: 514.2091, found: 514.2089.

Methyl 5-[2-azido-4-(ethoxycarbonyl)phenyl]-2-(4-methoxybenzyl)-3-(4-nitrophenyl)-2,3-dihydro-1H-pyrazole-1-carboxylate (9h). By use of the procedure for the synthesis of 9a, 6b (54 mg, 0.25 mmol), hydrazine 8a (79 mg, 0.38 mmol) and 4-nitrobenzaldehyde (57 mg, 0.38 mmol) were converted to the title compound 9h (82 mg, 59%) as a yellow oil. In this case, AgNTf$_2$ (2.9 mg, 0.0075 mmol) was used instead of AgOTf: IR (neat): $\nu_{\text{max}}$/cm$^{-1}$ 2115 (N$_3$), 1714 (C=O), 1514, 1346 (NO$_2$); $^1$H-NMR (500 MHz, CDCl$_3$) $\delta$: 1.41 (t, $J = 6.9$ Hz, 3H), 3.63 (s, 3H), 3.81 (s, 3H), 4.02 (d, $J = 12.0$ Hz, 1H), 4.36 (d, $J = 12.0$ Hz, 1H), 4.39–4.44 (m, 2H), 4.78 (d, $J = 2.9$ Hz, 1H), 5.73 (d, $J = 2.9$ Hz, 1H), 6.88 (d, $J = 8.0$ Hz, 2H), 7.34 (d, $J = 9.2$ Hz, 2H), 7.39–7.42 (m, 3H), 7.79–7.81 (m, 1H), 7.88 (s, 1H), 8.13 (d, $J = 8.0$ Hz, 2H); $^{13}$C-NMR (125 MHz, CDCl$_3$) $\delta$: 14.3, 53.1, 55.2, 61.3, 61.5, 69.2, 112.8, 113.8 (2C), 119.4, 123.9 (2C), 125.4, 127.4 (2C), 127.5, 127.8, 130.2, 131.1 (2C), 132.0, 137.8, 138.4, 147.3, 147.8, 154.5, 159.4, 165.3; HRMS (FAB$^+$) calcd for C$_{28}$H$_{28}$N$_5$O$_7$ [M+H]$^+$: 559.1941, found: 559.1939.
Methyl 5-[2-azido-4-(ethoxycarbonyl)phenyl]-2-(4-methoxybenzyl)-3-(4-methoxyphenyl)-2,3-dihydro-1H-pyrazole-1-carboxylate (9i). By use of the procedure for the synthesis of 9a, 6b (54 mg, 0.25 mmol), hydrazine 8a (79 mg, 0.38 mmol) and p-anisaldehyde (46 µL, 0.38 mmol) were converted to the title compound 9i (42 mg, 31%) as a yellow oil. In this case, AgNTf₂ (2.9 mg, 0.0075 mmol) was used instead of AgOTf: IR (neat): νmax/cm⁻¹ 2116 (N₃), 1716 (C=O); ¹H-NMR (500 MHz, CDCl₃) δ: 1.41 (t, J = 7.2 Hz, 3H), 3.58 (s, 3H), 3.76 (s, 3H), 3.82 (s, 3H), 3.99 (d, J = 12.0 Hz, 1H), 4.28 (d, J = 12.0 Hz, 1H), 4.38–4.45 (m, 2H), 4.65 (d, J = 2.9 Hz, 1H), 5.71 (d, J = 2.9 Hz, 1H), 6.80 (d, J = 9.2 Hz, 2H), 6.88 (d, J = 8.6 Hz, 2H), 7.03 (d, J = 9.2 Hz, 2H), 7.40–7.45 (m, 3H), 7.79–7.81 (m, 1H), 7.88 (s, 1H); ¹³C-NMR (125 MHz, CDCl₃) δ: 14.3, 52.9, 55.2, 55.2, 61.4, 61.5, 70.0, 113.6 (2C), 114.0 (2C), 115.1, 119.4, 125.4, 128.0 (2C), 128.3, 128.5, 130.2, 131.2 (2C), 131.6, 132.5, 136.6, 138.3, 155.0, 159.0, 159.1, 165.4; HRMS (FAB⁺) calcd for C₂₉H₃₀N₅O₆ [M+H]⁺: 544.2196, found: 544.2194.

Methyl 3-[2-azido-4-(ethoxycarbonyl)phenyl]-1-(4-methoxybenzyl)-1,2-diazaspiro[4.5]dec-3-ene-2-carboxylate (9j). By use of the procedure for the synthesis of 9a, 6b (54 mg, 0.25 mmol), hydrazine 8a (79 mg, 0.38 mmol) and cyclohexanone (39 µL, 0.38 mmol) were converted to the title compound 9j (104 mg, 82%) as a yellow oil. In this case, AgNTf₂ (2.9 mg, 0.0075 mmol) was used instead of AgOTf: IR (neat): νmax/cm⁻¹ 2115 (N₃), 1715; (C=O); ¹H-NMR (500 MHz, CDCl₃) δ: 1.39 (t, J = 7.2 Hz, 3H), 1.48–1.77 (m, 10H), 3.37 (s, 3H), 3.81–3.82 (m, 5H), 4.39 (q, J = 7.2 Hz, 2H), 6.07 (s, 1H), 6.86 (d, J = 8.6 Hz, 2H), 7.32–7.33 (m, 1H), 7.39 (d, J = 8.6 Hz, 2H), 7.75–7.77 (m,
1H), 7.84 (s, 1H); $^{13}$C-NMR (125 MHz, CDCl$_3$) δ: 14.3, 23.4 (2C), 25.6, 33.9 (2C), 52.5, 54.0, 55.2, 61.3, 72.2, 113.0 (2C), 119.6, 123.6, 125.3, 128.6, 130.2, 130.3, 131.0, 131.1 (2C), 136.1, 137.6, 156.6, 158.7, 165.4; HRMS (FAB$^+$) calcd for C$_{27}$H$_{32}$N$_5$O$_5$ [M+H]$^+$: 506.2403, found: 506.2409.

![Image of molecule](image.png)

6-Ethyl 1-methyl 3-isopropyl-2-(4-methoxybenzyl)-1,2,3,4-tetrahydropyrazolo[4,3-b]indole-1,6-dicarboxylate (10b). By use of the procedure for the synthesis of 10a, 9b (210 mg, 0.44 mmol) was converted to the title compound 10b (170 mg, 85%) as a colourless oil: IR (neat): $\nu$$_{\text{max}}$/cm$^{-1}$ 1707 (C=O); $^1$H-NMR (500 MHz, CDCl$_3$) δ: 0.71–0.77 (m, 6H), 1.41 (t, $J$ = 7.2 Hz, 3H), 1.71–1.77 (m, 1H), 3.79–3.86 (m, 5H), 3.89 (s, 3H), 4.22 (d, $J$ = 12.0 Hz, 1H), 4.40 (q, $J$ = 7.2 Hz, 2H), 6.84 (d, $J$ = 8.6 Hz, 2H), 7.34 (d, $J$ = 8.6 Hz, 2H), 7.82–7.84 (m, 2H), 8.09–8.10 (m, 1H), 8.17 (s, 1H); $^{13}$C-NMR (125 MHz, CDCl$_3$) δ: 14.4, 17.8, 18.4, 33.2, 53.0, 55.2, 60.8, 62.5, 69.8, 113.5 (2C), 114.2, 119.1, 120.0, 121.3, 123.6, 128.4, 131.4 (2C), 133.7, 139.4, 140.6, 151.8, 159.2, 167.6; HRMS (FAB$^+$) calcd for C$_{25}$H$_{30}$N$_3$O$_5$ [M+H]$^+$: 452.2185, found: 452.2179.

![Image of molecule](image.png)

Methyl 3-isopropyl-6-methoxy-2-(4-methoxybenzyl)-1,2,3,4-tetrahydropyrazolo[4,3-b]indole-1-carboxylate (10c). By use of the procedure for the synthesis of 10a, 9c (100 mg, 0.23 mmol) was converted to the title compound 10c (67 mg, 72%) as a yellow oil: IR (neat): $\nu$$_{\text{max}}$/cm$^{-1}$ 1698 (C=O); $^1$H-NMR (500 MHz, CDCl$_3$) δ: 0.68–0.73 (m, 6H), 1.65–1.71 (m, 1H), 3.78–3.86 (m, 11H), 4.21 (d, $J$ = 12.0 Hz, 1H), 6.80–6.84 (m, 4H), 7.34 (d, $J$ = 8.6 Hz, 2H), 7.70–7.78 (m, 2H); $^{13}$C-NMR (125 MHz, CDCl$_3$) δ: 17.7, 18.3, 33.2, 52.9, 55.1, 55.8, 62.4, 70.0, 95.7, 110.0, 111.9, 113.3 (2C), 120.2,
123.6, 128.0, 128.8, 131.3 (2C), 140.9, 154.3, 156.2, 159.1; HRMS (FAB\(^+\)) calcd for C\(_{23}\)H\(_{28}\)N\(_3\)O\(_4\) \([M+H]^+\): 410.2080, found: 410.2078.

![](image)

**1-tert-Butyl 6-ethyl 2-benzyl-3-isopropyl-1,2,3,4-tetrahydropyrazolo[4,3-b]indole-1,6-dicarboxylate (10d).** By use of the procedure for the synthesis of 10a, 9d (90 mg, 0.18 mmol) was converted to the title compound 10d (70 mg, 84\%) as a colourless oil: IR (neat): \(\nu_{\text{max}}/\text{cm}^{-1}\) 1686 (C=O); \(^1\)H-NMR (500 MHz, CDCl\(_3\)) \(^1\)H-NMR (CDCl\(_3\)) \(\delta\): 0.71–0.77 (m, 6H), 1.40 (t, \(J = 7.2\) Hz, 3H), 1.56 (s, 9H), 1.68–1.75 (m, 1H), 3.76 (d, \(J = 5.2\) Hz, 1H), 3.82 (d, \(J = 12.0\) Hz, 1H), 4.25 (d, \(J = 12.0\) Hz, 1H), 4.39 (q, \(J = 7.2\) Hz, 2H), 7.24–7.31 (m, 3H), 7.41–7.42 (m, 2H), 7.80 (d, \(J = 8.6\) Hz, 1H), 7.88 (d, \(J = 8.6\) Hz, 1H), 8.14 (s, 1H), 8.63 (s, 1H); \(^{13}\)C-NMR (125 MHz, CDCl\(_3\)) \(\delta\): 14.4, 17.7, 18.2, 28.5 (3C), 33.1, 60.7, 63.4, 70.1, 81.2, 114.3, 119.3, 120.5, 120.9, 123.1, 124.6, 127.5, 128.1 (2C), 130.2 (2C), 134.2, 136.8, 139.4, 153.9, 167.9; HRMS (FAB\(^+\)) calcd for C\(_{27}\)H\(_{34}\)N\(_3\)O\(_4\) \([M+H]^+\): 464.2549, found: 464.2551.

6-Ethyl 1-methyl 2-(4-methoxybenzyl)-3-propyl-1,2,3,4-tetrahydropyrazolo[4,3-b]indole-1,6-dicarboxylate (10e). By use of the procedure for the synthesis of 10a, 9e (80 mg, 0.17 mmol) was converted to the title compound 10e (65 mg, 86\%) as a colourless oil: IR (neat): \(\nu_{\text{max}}/\text{cm}^{-1}\) 1701 (C=O); \(^1\)H-NMR (500 MHz, CDCl\(_3\)) \(\delta\): 0.71 (t, \(J = 7.2\) Hz, 3H), 1.14–1.22 (m, 2H), 1.41 (t, \(J = 7.2\) Hz, 3H), 1.46–1.58 (m, 2H), 3.79 (s, 3H), 3.85 (d, \(J = 12.0\) Hz, 1H), 3.89 (s, 3H), 4.05 (t, \(J = 6.3\) Hz, 1H), 4.24 (d, \(J = 12.0\) Hz, 1H), 4.39 (q, \(J = 7.2\) Hz, 2H), 6.84 (d, \(J = 8.6\) Hz, 2H), 7.33 (d, \(J = 8.6\) Hz, 2H), 7.81–7.87 (m, 2H), 8.11 (s, 1H), 8.51 (s, 1H); \(^{13}\)C-NMR (125 MHz, CDCl\(_3\)) \(\delta\): 13.7, 14.4, 18.4, 37.6, 53.1, 55.2, 60.8, 61.9, 64.0, 113.6 (2C), 114.3, 119.0, 120.1, 121.2, 123.1, 123.4, 128.4, 131.1
6-Ethyl 1-methyl 3-benzyl-2-(4-methoxybenzyl)-1,2,3,4-tetrahydropyrazolo[4,3-b]indole-1,6-dicarboxylate (10f). By use of the procedure for the synthesis of 10a, 9f (48 mg, 0.09 mmol) was converted to the title compound 10f (33 mg, 73%) as a light yellow oil: IR (neat): $\nu_{\text{max}}/\text{cm}^{-1}$ 1705 (C=O); $^1$H-NMR (500 MHz, CDCl$_3$) $\delta$: 1.40 (t, $J = 7.2$ Hz, 3H), 2.75–2.80 (m, 1H), 2.86–2.89 (m, 1H), 3.81 (s, 3H), 3.86 (d, $J = 12.0$ Hz, 1H), 3.90 (s, 3H), 4.28–4.34 (m, 2H), 4.37 (q, $J = 7.2$ Hz, 2H), 6.85 (d, $J = 8.6$ Hz, 2H), 6.90–6.92 (m, 2H), 7.21–7.22 (m, 3H), 7.35 (d, $J = 8.6$ Hz, 2H), 7.50 (s, 1H), 7.80–7.85 (m, 2H), 7.95 (s, 1H); $^{13}$C-NMR (125 MHz, CDCl$_3$) $\delta$: 14.4, 42.4, 53.1, 55.2, 60.7, 61.9, 65.7, 113.7 (2C), 114.2, 119.1, 119.8, 121.2, 123.4, 123.7, 126.8, 128.1, 128.4 (2C), 129.4 (2C), 131.0 (2C), 134.2, 136.9, 139.1, 154.4, 159.2, 167.5; HRMS (FAB$^+$) calcd for C$_{29}$H$_{30}$N$_3$O$_5$ [M+H]$^+$: 500.2186, found: 500.2185.

6-Ethyl 1-methyl 2-(4-methoxybenzyl)-3-phenyl-1,2,3,4-tetrahydropyrazolo[4,3-b]indole-1,6-dicarboxylate (10g) and 6-ethyl 1-methyl 3-phenyl-1,4-dihydropyrazolo[4,3-b]indole-1,6-dicarboxylate (11b). By use of the procedure for the synthesis of 10a, 9g (50 mg, 0.097 mmol) was converted to the compound 10g (32 mg, 68%) as a yellow oil, together with the compound 11b (12 mg, 27%) as colourless crystals.

10g: IR (neat): $\nu_{\text{max}}/\text{cm}^{-1}$ 1697 (C=O); $^1$H-NMR (500 MHz, CDCl$_3$) $\delta$: 1.23 (t, $J = 7.2$ Hz, 3H), 3.62 (s, 3H), 3.70 (s, 3H), 3.90 (d, $J = 12.0$ Hz, 1H), 4.16–4.22 (m, 2H), 4.26 (d, $J = 12.0$ Hz, 1H), 4.99 (s,
1H), 6.67 (d, J = 8.6 Hz, 2H), 6.79–6.81 (m, 2H), 6.99–7.01 (m, 3H), 7.19 (d, J = 8.6 Hz, 2H), 7.69 (d, J = 8.0 Hz, 1H), 7.77 (d, J = 8.0 Hz, 1H), 7.94 (s, 1H), 8.90 (s, 1H); $^{13}$C-NMR (125 MHz, CDCl₃) δ: 14.3, 53.2, 55.1, 60.8, 65.8, 66.7, 113.7 (2C), 114.6, 119.2, 119.8, 121.1, 123.4, 123.6, 126.7 (2C), 127.9, 128.1, 128.7 (2C), 131.2 (2C), 134.1, 139.2, 139.7, 154.4, 159.2, 167.8; HRMS (FAB⁺) calcd for C$_{28}$H$_{28}$N$_3$O$_5$ [M+H]$^+$: 486.2029, found: 486.2026.

**11b**: mp 229 °C; IR (neat): $\nu_{\max}$/cm$^{-1}$ 1737 (C=O), 1695 (C=O); $^1$H-NMR (500 MHz, CDCl₃) δ: 1.43 (t, J = 7.2 Hz, 3H), 4.21 (s, 3H), 4.43 (q, J = 7.2 Hz, 2H), 7.42–7.45 (m, 1H), 7.49–7.52 (m, 2H), 7.94–7.98 (m, 3H), 8.25 (s, 1H), 8.31–8.35 (m, 2H); $^{13}$C-NMR (125 MHz, CDCl₃) δ: 14.4, 54.8, 61.1, 114.7, 117.6, 121.5, 121.6, 127.0 (2C), 127.8, 129.1 (2C), 129.5, 131.2, 131.7, 133.5, 139.9, 143.3, 150.7, 167.0; HRMS (FAB⁺) calcd for C$_{20}$H$_{18}$N$_3$O$_4$ [M+H]$^+$: 364.1297, found: 364.1301.

**6-Ethyl 1-methyl 2-(4-methoxybenzyl)-3-(4-nitrophenyl)-1,2,3,4-tetrahydropyrazolo[4,3-b]indole-1,6-dicarboxylate (10h).** By use of the procedure for the synthesis of 10a, 9h (38 mg, 0.068 mmol) was converted to the title compound 10h (26 mg, 72%) as yellow needles: mp 167 °C; IR (neat): $\nu_{\max}$/cm$^{-1}$ 1689 (C=O), 1514, 1347 (NO$_2$); $^1$H-NMR (500 MHz, CDCl₃) δ: 1.40 (t, J = 7.1 Hz, 3H), 3.79 (s, 3H), 3.91 (s, 3H), 4.06 (d, J = 12.6 Hz, 1H), 4.37 (q, J = 7.1 Hz, 2H), 4.49 (d, J = 12.6 Hz, 1H), 5.23 (s, 1H), 6.84 (d, J = 8.6 Hz, 2H), 7.13 (d, J = 9.2 Hz, 2H), 7.35 (d, J = 8.6 Hz, 2H), 7.84 (d, J = 8.6 Hz, 1H), 7.90 (d, J = 8.6 Hz, 1H), 7.98 (d, J = 9.2 Hz, 2H), 8.08 (s, 1H), 8.70 (s, 1H); $^{13}$C-NMR (125 MHz, CDCl₃) δ: 14.4, 53.4, 55.3, 61.0, 62.4, 65.8, 113.9 (2C), 114.6, 119.6, 119.8, 121.5, 123.9 (2C), 124.2, 124.4, 127.5 (2C), 127.6, 131.1 (2C), 131.8, 139.9, 146.3, 147.4, 154.3, 159.5, 167.6; HRMS (FAB⁺) calcd for C$_{28}$H$_{27}$N$_4$O$_7$ [M+H]$^+$: 531.1880, found: 531.1873.
6-Ethyl 1-methyl 3-(4-methoxyphenyl)-1,4-dihydropyrazolo[4,3-b]indole-1,6-dicarboxylate (11c). By use of the procedure for the synthesis of 10a, 9i (38 mg, 0.07 mmol) was converted to the title compound 11c (13 mg, 48%) as a white solid: mp 221 °C; IR (neat): νmax/cm⁻¹ 1696 (C=O); ¹H-NMR (500 MHz, DMSO-d₆) δ: 1.36 (t, J = 7.0 Hz, 3H), 3.85 (s, 3H), 4.12 (s, 3H), 4.34 (q, J = 7.0 Hz, 2H), 7.13 (d, J = 8.0 Hz, 2H), 7.75 (d, J = 8.0 Hz, 1H), 8.01 (d, J = 8.0 Hz, 2H), 8.14–8.18 (m, 2H), 12.04 (s, 1H); ¹³C-NMR (125 MHz, DMSO-d₆) δ: 14.2, 54.6, 55.2, 60.6, 114.4, 114.5 (2C), 115.6, 119.6, 120.5, 122.9, 125.8, 127.9 (2C), 131.1, 131.3, 138.6, 142.9, 149.9, 160.2, 166.0; HRMS (FAB⁺) calcd for C₂₁H₂₀N₃O₅ [M+H]⁺: 394.1403, found: 394.1400.

6'-Ethyl 1'-methyl 2'-(4-methoxybenzyl)-1',2',3',4'-tetrahydropyrazolo[4,3-b]indole-1',6' dicarboxylate (10i). Under argon atmosphere, a solution of 9j (50 mg, 0.1 mmol) in o-dichlorobenzene (1 mL) was stirred at 150 °C for 2 h. After being cooled to room temperature, the resulting mixture was chromatographed on silica gel (hexane/EtOAc = 3/1) to afford the title compound 10i (29 mg, 62%) as a yellow oil: IR (neat): νmax/cm⁻¹ 1704 (C=O); ¹H-NMR (500 MHz, CDCl₃) δ: 1.41 (t, J = 7.2 Hz, 3H), 1.46–1.62 (m, 4H), 1.85–1.89 (m, 4H), 1.95–2.01 (m, 2H), 3.52 (br s, 3H), 3.79 (s, 3H), 3.88 (s, 2H), 4.41 (q, J = 7.2 Hz, 2H), 6.84 (d, J = 8.0 Hz, 2H), 7.29 (d, J = 8.0 Hz, 2H), 7.81–7.85 (m, 2H), 8.20 (s, 1H), 8.82 (s, 1H); ¹³C-NMR (125 MHz, CDCl₃) δ: 14.4, 23.7 (2C), 25.2, 34.1 (2C), 52.8, 55.1, 55.2, 60.7, 70.4, 113.2 (2C), 114.6, 118.8, 120.9, 121.4, 123.1, 123.2, 129.7, 131.3 (2C), 138.7, 141.8, 155.4, 158.8, 167.8; HRMS (FAB⁺) calcd for C₂₇H₃₂N₅O₅ [M+H]⁺: 478.2342, found: 478.2350.
6-Ethyl 1-methyl 4-benzyl-2-(4-methoxybenzyl)-1,2,3,4-tetrahydropyrazolo[4,3-b]indole-1,6-dicarboxylate (15a). By use of the procedure for the synthesis of 15c, 10j (50 mg, 0.12 mmol) was converted to the title compound 15a (43 mg, 71%) as a yellow oil: IR (neat): $\nu_{\text{max}}$/cm$^{-1}$ 1700 (C=O); $^1$H-NMR (500 MHz, CDCl$_3$) $\delta$: 1.41 (t, $J = 7.2$ Hz, 3H), 3.78 (s, 3H), 3.87 (s, 3H), 3.93 (br s, 2H), 3.97 (br s, 2H), 4.39 (q, $J = 7.2$ Hz, 2H), 5.23 (s, 2H), 6.80 (d, $J = 8.6$ Hz, 2H), 7.03–7.05 (m, 2H), 7.18 (d, $J = 8.6$ Hz, 2H), 7.30–7.32 (m, 3H), 7.83–7.88 (m, 2H), 8.09 (s, 1H); $^{13}$C-NMR (125 MHz, CDCl$_3$) $\delta$: 14.4, 48.7, 51.7, 53.1, 55.2, 60.8, 62.3, 112.3, 113.6 (2C), 119.1, 119.6, 121.1, 122.6, 123.4, 127.1 (2C), 127.8, 128.2, 129.0 (2C), 131.0 (2C), 133.9, 136.1, 139.7, 154.4, 159.2, 167.5; HRMS (FAB$^+$) calcd for C$_{29}$H$_{30}$N$_3$O$_5$ [M+H]$^+$: 500.2186, found: 500.2181.

6-Ethyl 1-methyl 2-(4-methoxybenzyl)-4-(4-nitrophenyl)-1,2,3,4-tetrahydropyrazolo[4,3-b]indole-1,6-dicarboxylate (15b). By use of the procedure for the synthesis of 15c, 10j (50 mg, 0.12 mmol) was converted to the title compound 15b (45 mg, 70%) as a yellow oil. In this case, 1-fluoro-4-nitrobenzene (16 $\mu$L, 0.15 mmol) was used: IR (neat): $\nu_{\text{max}}$/cm$^{-1}$ 1705 (C=O), 1513, 1343 (NO$_2$); $^1$H-NMR (500 MHz, CDCl$_3$) $\delta$: 1.41 (t, $J = 7.1$ Hz, 3H), 3.77 (s, 3H), 3.91 (s, 3H), 4.13 (s, 2H), 4.34 (br s, 2H), 4.40 (q, $J = 7.1$ Hz, 2H), 6.83 (d, $J = 8.6$ Hz, 2H), 7.32 (d, $J = 8.6$ Hz, 2H), 7.50 (d, $J = 8.6$ Hz, 2H), 7.93–7.98 (m, 2H), 8.22 (s, 1H), 8.40 (d, $J = 8.6$ Hz, 2H); $^{13}$C-NMR (125 MHz, CDCl$_3$) $\delta$: 14.4, 52.7, 53.3, 55.3, 61.1, 62.8, 113.2, 113.7 (2C), 120.1, 121.4 (2C), 123.0, 123.6, 125.4 (2C),
125.9, 126.4, 127.6, 130.8 (2C), 132.1, 139.0, 142.7, 145.6, 154.5, 159.4, 166.9; HRMS (FAB⁺) calcd for C<sub>28</sub>H<sub>27</sub>N<sub>4</sub>O<sub>7</sub> [M+H]<sup>+</sup>: 531.1880, found: 531.1884.

![Chemical structure](image)

**6-Ethyl 1-methyl 4-benzyl-2-(4-methoxybenzyl)-3-phenyl-1,2,3,4-tetrahydropyrazolo[4,3-b]indole-1,6-dicarboxylate (15d).** By use of the procedure for the synthesis of 15c, 10g (60 mg, 0.12 mmol) was converted to the title compound 15d (58 mg, 82%) as a yellow oil: IR (neat): ν<sub>max</sub>/cm<sup>-1</sup> 1703 (C=O); <sup>1</sup>H-NMR (500 MHz, CDCl<sub>3</sub>) δ: 1.40 (t, J = 7.2 Hz, 3H), 3.79 (s, 3H), 3.88 (s, 3H), 3.90 (d, J = 12.0 Hz, 1H), 4.31 (d, J = 12.0 Hz, 1H), 4.36–4.41 (m, 2H), 4.72 (d, J = 15.5 Hz, 1H), 4.75 (s, 1H), 5.30 (d, J = 15.5 Hz, 1H), 6.69–6.70 (m, 2H), 6.78 (d, J = 8.6 Hz, 2H), 6.84–6.85 (m, 2H), 7.13–7.18 (m, 5H), 7.22–7.27 (m, 3H), 7.87 (d, J = 8.0 Hz, 1H), 7.99 (d, J = 8.0 Hz, 1H), 8.06 (s, 1H); <sup>13</sup>C-NMR (125 MHz, CDCl<sub>3</sub>) δ: 14.5, 48.2, 53.3, 55.1, 60.8, 62.2, 66.3, 112.6, 113.8 (2C), 119.4, 121.0, 123.1, 123.8, 126.8, 127.1 (2C), 127.3, 127.8 (2C), 128.1, 128.6 (2C), 129.0 (2C), 131.2 (2C), 131.5, 135.7, 136.3, 138.9, 140.0, 154.2, 159.2, 167.4; HRMS (FAB⁺) calcd for C<sub>35</sub>H<sub>34</sub>N<sub>3</sub>O<sub>5</sub> [M+H]<sup>+</sup>: 576.2498, found: 576.2504.

![Chemical structure](image)

**6-Ethyl 1-methyl 1,4-dihydropyrazolo[4,3-b]indole-1,6-dicarboxylate (11d).** By use of the procedure for the synthesis of 11a, 10j (60 mg, 0.15 mmol) was converted to the title compound 11d (48 mg, 95%) as a white solid: mp 215 °C; IR (neat): ν<sub>max</sub>/cm<sup>-1</sup> 1749 (C=O), 1708 (C=O); <sup>1</sup>H-NMR (500 MHz, DMSO-<em>d</em><sub>6</sub>) δ: 1.35 (t, J = 7.2 Hz, 3H), 4.11 (s, 3H), 4.34 (q, J = 7.2 Hz, 2H), 7.74 (d, J = 8.6 Hz, 1H), 8.13–8.17 (m, 3H), 11.52 (s, 1H); <sup>13</sup>C-NMR (125 MHz, DMSO-<em>d</em><sub>6</sub>) δ: 14.2, 54.7, 60.7,

S15
114.7, 115.5, 119.5, 120.4, 125.7, 128.9, 129.9, 134.2, 142.5, 149.9, 166.1; HRMS (FAB⁺) calcd for C_{14}H_{14}N_{3}O_{4} [M+H]⁺: 288.0984, found: 288.0987.

6-Ethyl 1-methyl 3-isopropyl-1,4-dihydropyrazolo[4,3-b]indole-1,6-dicarboxylate (11e). By use of the procedure for the synthesis of 11a, 10b (49 mg, 0.11 mmol) was converted to the title compound 11e (25 mg, 70%) as a white solid: mp 201 °C; IR (neat): ν_{max}/cm⁻¹ 1737 (C=O), 1685 (C=O); ¹H-NMR (500 MHz, CDCl₃) δ: 1.44 (t, J = 7.2 Hz, 3H), 1.48 (d, J = 6.9 Hz, 6H), 3.29–3.38 (m, 1H), 4.17 (s, 3H), 4.45 (q, J = 7.2 Hz, 2H), 7.91–7.93 (m, 1H), 8.30–8.33 (m, 2H), 8.99 (s, 1H); ¹³C-NMR (125 MHz, CDCl₃) δ: 14.3, 21.5 (2C), 27.9, 54.6, 61.2, 114.7, 117.1, 120.8, 121.2, 126.8, 131.8, 132.3, 142.8, 147.6, 150.6, 167.5; HRMS (FAB⁺) calcd for C_{17}H_{20}N_{3}O_{4} [M+H]⁺: 330.1454, found: 330.1451.

6-Ethyl 1-methyl 4-benzyl-1,4-dihydropyrazolo[4,3-b]indole-1,6-dicarboxylate (11f). By use of the procedure for the synthesis of 11a, 15a (40 mg, 0.08 mmol) was converted to the title compound 11f (28 mg, 93%) as a white solid: mp 142 °C; IR (neat): ν_{max}/cm⁻¹ 1735 (C=O), 1703 (C=O); ¹H-NMR (500 MHz, CDCl₃) δ: 1.43 (t, J = 7.2 Hz, 3H), 4.18 (s, 3H), 4.43 (q, J = 7.2 Hz, 2H), 5.41 (s, 2H), 7.20–7.22 (m, 2H), 7.31–7.34 (m, 4H), 7.92–7.94 (m, 1H), 8.20 (s, 1H), 8.32–8.33 (m, 1H); ¹³C-NMR (125 MHz, CDCl₃) δ: 14.4, 49.0, 54.8, 61.1, 112.4, 113.8, 116.4, 120.6, 121.4, 127.1, 127.4, 127.5 (2C), 128.3, 129.0 (2C), 135.5, 135.6, 143.1, 150.3, 166.9; HRMS (FAB⁺) calcd for C_{21}H_{20}N_{3}O_{4} [M+H]⁺: 378.1454, found: 378.1449.
6-Ethyl 1-methyl 4-(4-nitrophenyl)-1,4-dihydropyrazolo[4,3-b]indole-1,6-dicarboxylate (11g).

By use of the procedure for the synthesis of 11a, 15b (120 mg, 0.23 mmol) was converted to the title compound 11g (80 mg, 87%) as a yellow solid: mp 228 °C; IR (neat): ν_max/cm⁻¹ 1754 (C=O), 1731 (C=O), 1523, 1348 (NO₂); ¹H-NMR (500 MHz, CDCl₃) δ: 1.43 (t, J = 6.9 Hz, 3H), 4.23 (s, 3H), 4.44 (q, J = 6.9 Hz, 2H), 7.79 (d, J = 8.0 Hz, 2H), 7.90 (s, 1H), 8.03 (d, J = 8.6 Hz, 1H), 8.41 (s, 1H), 8.43 (d, J = 8.6 Hz, 1H), 8.48 (d, J = 8.0 Hz, 2H); ¹³C-NMR (125 MHz, CDCl₃) δ: 14.4, 55.1, 61.4, 113.4, 118.5, 122.3, 123.0, 123.4 (2C), 126.0 (2C), 127.2, 128.8, 133.0, 134.6, 142.1, 143.4, 145.8, 150.2, 166.4; HRMS (FAB⁺) calcd for C₂₀H₁₇N₄O₆ [M+H]⁺: 409.1148, found: 409.1148.

6-Ethyl 1-methyl 4-benzyl-3-isopropyl-1,4-dihydropyrazolo[4,3-b]indole-1,6-dicarboxylate (11h). By use of the procedure for the synthesis of 11a, 15c (60 mg, 0.11 mmol) was converted to the title compound 11h (39 mg, 84%) as a yellow oil: IR (neat): ν_max/cm⁻¹ 1740 (C=O), 1709 (C=O); ¹H-NMR (500 MHz, CDCl₃) δ: 1.31 (d, J = 6.9 Hz, 6H), 1.40 (t, J = 7.2 Hz, 3H), 3.10–3.18 (m, 1H), 4.18 (s, 3H), 4.39 (q, J = 7.2 Hz, 2H), 5.58 (s, 2H), 6.97–6.99 (m, 2H), 7.24–7.29 (m, 3H), 7.90–7.92 (m, 1H), 8.09 (s, 1H), 8.36 (br s, 1H); ¹³C-NMR (125 MHz, CDCl₃) δ: 14.3, 21.8 (2C), 27.6, 48.2, 54.7, 61.0, 112.5, 116.6, 120.7, 121.5, 125.7 (2C), 127.0, 127.8, 128.9 (2C), 131.4, 133.4, 136.9, 143.3, 147.3, 150.5, 167.0; HRMS (FAB⁺) calcd for C₂₄H₂₆N₅O₄ [M+H]⁺: 420.1923, found: 420.1921.
6-Ethyl 1-methyl 4-benzyl-3-phenyl-1,4-dihydropyrazolo[4,3-b]indole-1,6-dicarboxylate (11i).

By use of the procedure for the synthesis of 11a, 15d (50 mg, 0.09 mmol) was converted to the title compound 11i (27 mg, 69%) as a white solid: mp 185 °C; IR (neat): \( \nu_{\text{max}}/\text{cm}^{-1} \) 1742 (C=O), 1710 (C=O); \(^1\)H-NMR (500 MHz, CDCl\(_3\)) \( \delta \): 1.41 (t, \( J = 7.2 \) Hz, 3H), 4.21 (s, 3H), 4.40 (q, \( J = 7.2 \) Hz, 2H), 5.46 (s, 2H), 6.84–6.90 (m, 2H), 7.18–7.23 (m, 3H), 7.57–7.58 (m, 2H), 7.95 (d, \( J = 8.0 \) Hz, 1H), 8.11 (s, 1H), 8.41–8.42 (m, 1H); \(^{13}\)C-NMR (125 MHz, CDCl\(_3\)) \( \delta \): 14.5, 48.1, 54.8, 61.1, 113.0, 116.6, 120.8, 121.7, 126.2 (2C), 127.4, 127.9, 128.5, 128.6 (2C), 128.8 (2C), 129.0 (2C), 129.4, 130.9, 133.2, 136.6, 141.1, 143.8, 150.6, 166.9; HRMS (FAB\(^+\)) calcd for C\(_{27}\)H\(_{32}\)N\(_3\)O\(_4\) [M+H]\(^+\): 454.1767, found: 454.1761.

3-Isopropyl-1,4-dihydropyrazolo[4,3-b]indole-6-carboxylic acid (5b). By use of the procedure for the synthesis of 5a, 11e (43 mg, 0.13 mmol) was converted to the title compound 5b (26 mg, 82%) as a white solid: mp >300 °C; IR (neat): \( \nu_{\text{max}}/\text{cm}^{-1} \) 1663 (C=O); \(^1\)H-NMR (500 MHz, DMSO-d\(_6\)) \( \delta \): 1.37 (d, \( J = 6.9 \) Hz, 6H), 3.14–3.20 (m, 1H), 7.63 (d, \( J = 8.4 \) Hz, 1H), 7.74 (d, \( J = 8.4 \) Hz, 1H), 7.98 (s, 1H), 10.67 (s, 1H), 12.55–12.64 (m, 2H); \(^{13}\)C-NMR (125 MHz, DMSO-d\(_6\)) \( \delta \): 22.3 (2C), 26.4, 113.6, 114.6, 117.1, 119.7, 128.6, 135.7, 144.6, 147.4, 168.4, 171.2; HRMS (FAB\(^+\)) calcd for C\(_{13}\)H\(_{14}\)N\(_3\)O\(_2\) [M+H]\(^+\): 244.1086, found: 244.1094; \( t_R \) (method A): 22.64 min.
3-Phenyl-1,4-dihydropyrazolo[4,3-b]indole-6-carboxylic acid (5c). By use of the procedure for the synthesis of 5a, 11b (12 mg, 0.03 mmol) was converted to the title compound 5c (8 mg, 87%) as a light yellow solid. In this case, compound 5c precipitated after the neutralization, which was collected by filtration: mp >300 °C; IR (neat): νmax/cm⁻¹ 1688 (C=O); ¹H-NMR (500 MHz, DMSO-d₆) δ: 7.31–7.34 (m, 1H), 7.49–7.52 (m, 2H), 7.71 (d, J = 7.6 Hz, 1H), 7.84 (d, J = 7.6 Hz, 1H), 7.95–7.99 (m, 2H), 8.06 (s, 1H), 11.27 (s, 1H), 12.81–13.22 (m, 2H); ¹³C-NMR (125 MHz, DMSO-d₆) δ: 113.9, 118.5, 119.5, 124.7, 124.9 (2C), 126.3, 126.7, 127.0, 128.8, 129.0 (2C), 129.5, 131.9, 144.3, 167.9; HRMS (FAB⁺) calcd for C₁₆H₁₂N₃O₂ [M+H]^⁺: 278.0929, found: 278.0935; tᵣ (method B): 13.07 min.

4-Benzyl-1,4-dihydropyrazolo[4,3-b]indole-6-carboxylic acid (5d). By use of the procedure for the synthesis of 5a, 11f (40 mg, 0.11 mmol) was converted to the title compound 5d (25 mg, 81%) as a white solid: mp >300 °C; IR (neat): νmax/cm⁻¹ 1683 (C=O); ¹H-NMR (500 MHz, DMSO-d₆) δ: 5.47 (s, 2H), 7.22–7.31 (m, 5H), 7.54 (s, 1H), 7.71 (d, J = 8.4 Hz, 1H), 7.86 (d, J = 8.4 Hz, 1H), 8.11 (s, 1H), 12.79–13.09 (m, 2H); ¹³C-NMR (125 MHz, DMSO-d₆) δ: 48.1, 111.8, 114.2, 117.4, 118.9, 119.4, 126.3, 127.2 (2C), 127.4, 128.6 (2C), 134.3, 135.9, 137.5, 143.8, 167.9; HRMS (FAB⁺) calcd for C₁₇H₁₄N₃O₂ [M+H]^⁺: 292.1086, found: 292.1085; tᵣ (method B): 13.08 min.
4-(4-Nitrophenyl)-1,4-dihydropyrazolo[4,3-b]indole-6-carboxylic acid (5e). By use of the procedure for the synthesis of 5a, 11g (37 mg, 0.09 mmol) was converted to the title compound 5e (23 mg, 79%) as a yellow solid. In this case, compound 5e precipitated after the neutralization, which was collected by filtration: mp >300 °C; IR (neat): \( \nu_{\text{max}}/\text{cm}^{-1} \) 1683 (C=O), 1503, 1308 (NO\(_2\)); \(^1\)H-NMR (500 MHz, DMSO-\(d_6\)) \( \delta \): 7.92 (d, \( J = 7.6 \) Hz, 1H), 7.98–8.03 (m, 3H), 8.09 (s, 1H), 8.42 (s, 1H), 8.46 (d, \( J = 8.4 \) Hz, 2H), 12.76–13.83 (m, 2H); \(^{13}\)C-NMR (125 MHz, DMSO-\(d_6\)) \( \delta \): 113.1, 119.7, 120.8, 121.4 (2C), 122.6, 125.6, 125.9 (2C), 127.8, 131.6, 138.8, 142.0, 143.3, 144.5, 167.4; HRMS (FAB\(^+\)) calcd for C\(_{16}\)H\(_{11}\)N\(_4\)O\(_4\) [M+H]\(^+\): 323.0780, found: 323.0774; \( t_R \) (method B): 17.46 min.

4-Benzyl-3-isopropyl-1,4-dihydropyrazolo[4,3-b]indole-6-carboxylic acid (5f). By use of the procedure for the synthesis of 5a, 11h (35 mg, 0.08 mmol) was converted to the title compound 5f (20 mg, 72%) as a white solid: mp >300 °C; IR (neat): \( \nu_{\text{max}}/\text{cm}^{-1} \) 1682 (C=O); \(^1\)H-NMR (500 MHz, DMSO-\(d_6\)) \( \delta \): 1.15 (d, \( J = 6.9 \) Hz, 6H), 3.13–3.19 (m, 1H), 5.58 (s, 2H), 6.98–6.99 (m, 2H), 7.19–7.22 (m, 1H), 7.25–7.28 (m, 2H), 7.69 (d, \( J = 8.4 \) Hz, 1H), 7.83 (d, \( J = 8.4 \) Hz, 1H), 8.02 (s, 1H), 12.69–12.85 (m, 2H); \(^{13}\)C-NMR (125 MHz, DMSO-\(d_6\)) \( \delta \): 22.9 (2C), 25.7, 47.4, 111.7, 117.0, 118.8, 119.4, 125.9 (2C), 126.2, 127.2, 128.6 (2C), 130.5, 134.3, 136.5, 138.4, 144.1, 167.9; HRMS (FAB\(^+\)) calcd for C\(_{20}\)H\(_{20}\)N\(_3\)O\(_2\) [M+H]\(^+\): 334.1555, found: 334.1559; \( t_R \) (method B): 18.82 min.
4-Benzyl-3-phenyl-1,4-dihydropyrazolo[4,3-b]indole-6-carboxylic acid (5g). By use of the procedure for the synthesis of 5a. 11i (25 mg, 0.06 mmol) was converted to the title compound 5g (18 mg, 89%) as a white solid: mp >300 °C; IR (neat): v_{max}/cm^{-1} 1687 (C=O); ^1H-NMR (500 MHz, DMSO-\textit{d}_6) \delta: 5.57 (s, 2H), 6.88–6.90 (m, 2H), 7.16–7.20 (m, 3H), 7.35–7.45 (m, 3H), 7.60–7.62 (m, 2H), 7.77 (d, J = 7.6 Hz, 1H), 7.93 (d, J = 7.6 Hz, 1H), 8.09 (s, 1H), 12.79–13.42 (m, 2H); ^13C-NMR (125 MHz, DMSO-\textit{d}_6) \delta: 47.6, 112.2, 117.2, 119.1, 120.0, 125.9 (2C), 126.2 (2C), 126.8, 127.0, 127.5, 127.9 (2C), 128.4, 128.6, 128.8 (2C), 130.8, 131.5, 137.7, 144.5, 167.8; HRMS (FAB\textsuperscript{+}) calcd for C_{23}H_{18}N_{3}O_{2} [\textit{M}+\textit{H}]^+: 368.1399, found: 368.1409; \textit{t}_R (method B): 15.32 min.

References
