A Ruthenium-Catalyzed Alkenylation-Annulation Approach for the Synthesis of Indazole Derivatives via C-H Bond Activation

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1. General information:

Solvents, Ruthenium catalyst, alkenes, phenylhydrazine, maleic anhydride and phthalic anhydride derivatives were purchased from Merck and Sigma. Other reagents were purchased from commercial distributors and used without further purification. N-arylated hydratedione and N-arylated phthalazine derivatives were synthesized according to the literature. Analytical thin layer chromatography (TLC) was performed on pre-coated silica gel 60 F254 plates. The products were purified by preparative column chromatography on silica gel (0.063-0.200 mm; Merck). $^1$H and $^{13}$C-NMR Spectra: were recorded on Bruker, 500 and 400 Advance instrument in CDCl$_3$ and DMSO; $\delta$ in ppm, $J$ in Hz. Mass spectrometry was obtained on Agilent 5975C VL MSD (Ion source: EI+, 70eV, 230°C).

2. General procedure for synthesis of indazolo[1,2-b]phthalazines and pyridazino[1,2-a]indazoles:

A 15 mL microwave vial was charged with N-aryl pyridazinedione or N-aryl phthalazine or maleic anhydride derivatives (1 equiv, 0.5 mmol), alkene (3 equiv, 1.5 mmol), copper acetate monohydrate (1 equiv, 0.5 mmol), Ru catalyst (5 mol %), potassium hexafluorophosphate (10 mol %) and H$_2$O or DCE (2 mL). The vial was then sealed and immersed in an oil bath at 120 °C, for 24 h. After this time the reaction mixture was cooled to room temperature and then diluted with water and extracted by chloroform. The residue was purified by using column chromatography (n-hexane/EtOAc, 1/1) to yield the desired products.

3. General Synthetic procedure for the preparation of N- aryl phthalazine/pyridazine dione:

![Chemical Structure](image)

The appropriate phenylhydrazine (1.1 equiv) was added to a stirred mixture of phthalic or malonic anhydride (1.0 equiv) in 10% HCl and the mixture was heated at 120 °C for 9 h. After this time, the reaction mixture was cooled and the resulting solid was collected by filtration and washed with water and then recrystallized by using ethanol.

4. Characterization of starting materials:

2-phenyl-2,3-dihydropthalazine-1,4-dione:

![Chemical Structure](image)

$^1$H NMR (500 MHz, DMSO) $\delta$ 11.85 (s, 1H), 8.30 (d, $J$ = 7.6 Hz, 1H), 8.01 (d, $J$ = 7.6 Hz, 1H), 7.96- 7.88 (m, 2H), 7.66 (d, $J$ = 8.1 Hz, 2H), 7.49 (t, $J$ = 7.6 Hz, 2H), 7.36 (t, $J$ = 7.2 Hz, 1H). $^{13}$C NMR (126 MHz, DMSO) $\delta$ 157.8, 150.9, 142.3, 133.9, 132.8, 129.7, 128.8, 127.5, 127.3, 126.4, 125.1, 124.6.

6-methyl-2-(p-tolyl)-2,3-dihydropthalazine-1,4-dione:

![Chemical Structure](image)

$^1$H NMR (500 MHz, DMSO) $\delta$ 11.72 (s, 1H), 8.17 (d, $J$ = 8.2 Hz, 1H), 8.09 (s, 1H), 7.89 (d, $J$ = 7.9 Hz, 1H), 7.51 (d, $J$ = 8.2 Hz, 2H), 7.27 (d, $J$ = 7.9 Hz, 2H), 2.53 (s, 3H), 2.36 (s, 3H). $^{13}$C NMR (126 MHz, DMSO) $\delta$ 157.7, 150.9, 144.4, 143.3, 136.7, 135.0, 134.0, 129.7, 129.3, 127.5, 126.1, 124.6, 21.8, 21.1.
6-fluoro-2-phenyl-2,3-dihydrophthalazine-1,4-dione:

$^1$H NMR (500 MHz, DMSO) $\delta$ 11.99 (s, 1H), 8.35 (dd, $J = 8.7, 5.2$ Hz, 1H), 8.09 (dd, $J = 8.7, 5.2$ Hz, 1H), 7.96 (dd, $J = 8.9, 2.2$ Hz, 1H), 7.63 (t, $J = 6.1$ Hz, 2H), 7.54 – 7.42 (m, 2H), 7.38 (t, $J = 7.3$ Hz, 1H). $^{13}$C NMR (126 MHz, DMSO) $\delta$ 165.3 (d, $^1J_{CF} = 252.6$ Hz), 157.1, 157.0, 142.0, 132.2 (d, $^3J_{CF} = 9.2$ Hz), 128.9, 127.7, 127.6, 126.6, 126.3, 122.3 (d, $^2J_{CF} = 23.8$ Hz), 112.8 (d, $^2J_{CF} = 24.8$ Hz). Anal. Calcd for C$_{14}$H$_9$FN$_2$O$_2$: C, 65.62; H, 3.54; N, 10.93; found: C, 65.81; H, 3.57; N, 10.88.

6-methyl-2-phenyl-2,3-dihydrophthalazine-1,4-dione:

$^1$H NMR (500 MHz, DMSO) $\delta$ 11.75 (s, 1H), 8.18 (d, $J = 7.9$ Hz, 1H), 8.10 (s, 1H), 7.90 (d, $J = 7.9$ Hz, 1H), 7.64 (d, $J = 7.6$ Hz, 2H), 7.48 (t, $J = 7.4$ Hz, 2H), 7.40 – 7.32 (m, 1H), 2.53 (s, 3H). $^{13}$C NMR (126 MHz, DMSO) $\delta$ 144.5, 143.3, 142.3, 135.0, 134.1, 129.7, 128.8, 127.4, 127.0, 126.3, 124.6, 124.2, 21.8.

2-(4-bromophenyl)-2,3-dihydrophthalazine-1,4-dione:

$^1$H NMR (500 MHz, DMSO) $\delta$ 11.94 (s, 1H), 8.28 (d, $J = 7.7$ Hz, 1H), 8.00 (d, $J = 7.9$ Hz, 1H), 7.96 - 7.88 (m, 2H), 7.80 - 7.40 (m, 4H). $^{13}$C NMR (126 MHz, DMSO) $\delta$ 157.80, 151.1, 141.4, 134.1, 133.0, 131.7, 129.6, 128.2, 127.3, 126.4, 124.7, 120.0.

1-(4-fluorophenyl)-1,2-dihydropyridazine-3,6-dione:

$^1$H NMR (500 MHz, DMSO) $\delta$ 11.37 (s, 1H), 7.61 (dd, $J = 8.3, 5.2$ Hz, 2H), 7.30 (t, $J = 8.7$ Hz, 2H), 7.17 (d, $J = 9.9$ Hz, 1H), 7.02 (d, $J = 9.9$ Hz, 1H). $^{13}$C NMR (126 MHz, DMSO) $\delta$ 161.1 (d, $^1J_{CF} = 244.5$ Hz), 158.2, 153.3, 138.2 (d, $^1J_{CF} = 3.3$ Hz), 134.4 (d, $^3J_{CF} = 9.3$ Hz), 128.1, 128.0, 115.7 (d, $^2J_{CF} = 26.4$ Hz).

1-(p-tolyl)-1,2-dihydropyridazine-3,6-dione:

$^1$H NMR (500 MHz, DMSO) $\delta$ 11.28 (s, 1H), 7.44 (d, $J = 8.0$ Hz, 2H), 7.26 (d, $J = 8.0$ Hz, 2H), 7.15 (d, $J = 9.7$ Hz, 1H), 7.00 (d, $J = 9.7$ Hz, 1H), 2.34 (s, 3H). $^{13}$C NMR (126 MHz, DMSO) $\delta$ 158.2, 153.1, 139.5, 137.2, 134.4, 129.3, 127.9, 125.7, 21.1. Anal. Calcd for C$_{14}$H$_{10}$N$_2$O$_2$: C, 65.34; H, 4.98; N, 13.85; found: C, 65.59; H, 4.96; N, 13.92.
5. Characterization of the products

**Methyl 2-(6,9-dioxo-6,9-dihydro-11H-pyrazino[1,2-a]indazol-11-yl)acetate (3a):**

![Structure of 3a](image)

3a (95% yield) as a yellow solid; M.p.: 157-159 °C; $^1$H NMR (500 MHz, CDCl₃) δ 8.29 (d, $J = 7.9$ Hz, 1H), 7.44-7.40 (m, 2H), 7.28 (s, $J = 7.4$ Hz, 1H), 7.00 (d, $J = 10.2$ Hz, 1H), 6.91 (d, $J = 10.2$ Hz, 1H), 5.98 (dd, $J = 7.1$, 3.4 Hz, 1H), 3.63 (s, 3H), 3.40 (dd, $J = 16.5$, 3.5 Hz, 1H), 3.08 (dd, $J = 16.5$, 7.3 Hz, 1H); $^1$C NMR (100 MHz, CDCl₃) δ 169.8, 154.3, 153.7, 136.2, 136.0, 134.1, 129.9, 126.8, 126.5, 122.9, 115.5, 59.4, 52.1, 36.3; MS (EI): m/z (%): 272 (59) [M]$^+$, 199 (100), 171 (100), 131 (70), 102 (15), 82 (40), 54 (39). Anal. Calcd for C$_{18}$H$_2$N$_2$O$_4$: C, 61.76; H, 4.44; N, 10.29; found: C, 61.48; H, 4.46; N, 10.33.

**Methyl 2-(2-bromo-6,11-dioxo-6,11-dihydro-13H-indazolo[1,2-b]phthalazin-13-yl)acetate (3b):**

![Structure of 3b](image)

3b (99% yield) as an off white solid; M.p.: 205-207 °C; $^1$H NMR (500 MHz, CDCl₃) δ 8.43 (dd, $J = 6.0$, 3.1 Hz, 1H), 8.38 (dd, $J = 6.0$, 3.1 Hz, 1H), 8.31 (d, $J = 8.5$ Hz, 1H), 7.90 - 7.81 (m, 2H), 7.71 - 7.45 (m, 2H), 6.14 (dd, $J = 7.5$, 3.2 Hz, 1H), 3.69 (s, 3H), 3.48 (dd, $J = 16.8$, 3.3 Hz, 1H), 3.15 (dd, $J = 16.8$, 7.6 Hz, 1H); $^1$C NMR (125 MHz, CDCl₃) δ 162.2, 155.3, 152.7, 136.0, 133.7, 133.6, 132.9, 128.9, 127.7, 127.4, 126.3, 125.9, 124.9, 119.1, 117.0, 58.5, 52.0, 37.0; MS (EI): m/z (%) = 402 (1), m/z (%) = 340 (21), m/z (%) = 290 (48) [M]$^+$, 230 (50), 217 (100), 208 (33), 189 (90), 149 (85), 137 (22), 101 (21), 82 (66), 69 (9), 54 (48), 43 (20). Anal. Calcd for C$_{14}$H$_{13}$BrN$_2$O$_4$: C, 53.89; H, 3.27; N, 6.98; found: C, 53.89; H, 3.29; N, 6.94.

**Methyl 2-(2-fluoro-6,9-dioxo-6,9-dihydro-11H-pyrazino[1,2-a]indazol-11-yl)acetate (3c):**

![Structure of 3c](image)

3c (71% yield) as an off white solid; M.p.: 205-208 °C; $^1$H NMR (500 MHz, CDCl₃) δ 8.32 (dd, $J = 8.9$, 4.6 Hz, 1H), 7.22 - 7.12 (m, 2H), 7.04 (d, $J = 10.2$ Hz, 1H), 6.94 (d, $J = 10.2$ Hz, 1H), 6.00 (dd, $J = 7.9$, 2.9 Hz, 1H), 3.69 (s, 3H), 3.48 (dd, $J = 16.8$, 3.4 Hz, 1H), 3.08 (dd, $J = 16.8$, 7.8 Hz, 1H); $^1$C NMR (100 MHz, CDCl₃) δ 169.7, 161.0 (d, $J_{CF} = 247.4$ Hz), 154.4, 153.5, 136.0, 134.0, 132.5, 128.6 (d, $J_{CF} = 9.4$ Hz), 117.0, 116.8 (d, $J_{CF} = 24.1$ Hz), 111.0 (d, $J_{CF} = 26.3$ Hz), 59.2, 52.2, 36.0; MS (EI): m/z (%) = 290 (48) [M]$^+$, 230 (50), 217 (100), 208 (33), 189 (90), 149 (85), 137 (22), 101 (21), 82 (66), 69 (9), 54 (48), 43 (20). Anal. Calcd for C$_{14}$H$_{11}$FN$_2$O$_4$: C, 57.93; H, 3.82; N, 9.65; found: C, 57.55; H, 3.85; N, 9.69.

**Ethyl 2-(2-bromo-6,11-dioxo-6,11-dihydro-13H-indazolo[1,2-b]phthalazin-13-yl)acetate (3d):**

![Structure of 3d](image)

3d (96% yield) as a white solid; M.p.: 173-176 °C; $^1$H NMR (500 MHz, CDCl₃) δ 8.42 (dd, $J = 6.0$, 3.2 Hz, 1H), 8.36 (dd, $J = 5.8$, 3.4 Hz, 1H), 8.30 (d, $J = 8.6$ Hz, 1H), 7.89 - 7.86 (m, 2H), 7.61 (s, 1H), 7.60 - 7.57 (m, 1H), 6.13 (dd, $J = 7.5$, 3.3 Hz, 1H), 4.11 (q, $J = 7.2$ Hz, 2H), 3.44 (dd, $J = 16.7$, 3.4 Hz, 1H), 3.19 (dd, $J = 16.7$, 7.5 Hz, 1H), 1.16 (t, $J = 7.1$ Hz, 3H); $^1$C NMR (125 MHz, CDCl₃) δ 169.2, 155.1, 154.7, 135.8, 133.7, 133.6, 132.8, 129.6, 128.9, 128.6, 127.7, 127.4, 126.3, 119.0, 117.0, 61.1, 58.6, 37.2, 14.0; MS (EI): m/z (%) = 416 (29) [M+1]$^+$, 415 (28) [M]$^+$, 342 (14), 341 (13), 329 (100), 328 (90), 283 (7), 248 (8), 220 (10), 192 (7), 164 (7), 104 (10), 76 (13). Anal. Calcd for C$_{18}$H$_{13}$BrN$_2$O$_4$: C, 54.96; H, 3.64; N, 6.75; found: C, 54.85; H, 3.67; N, 6.70.
Methyl 2-(2-methyl-6,11-dioxo-6,11-dihydro-13H-indazolo[1,2-b]phthalazin-13-y]acetate (3e):

3e (89% yield) as a white solid; M.p.: 182-184 °C; ¹H NMR (500 MHz, CDCl₃) δ 8.43 (dd, J = 6.3, 2.9 Hz, 1H), 8.36 (dd, J = 6.4, 2.8 Hz, 1H), 8.29 (dd, J = 8.2 Hz, 1H), 7.93 – 7.61 (m, 2H), 7.29 – 7.20 (m, 2H), 6.13 (dd, J = 7.3, 3.6 Hz, 1H), 3.67 (s, 3H), 3.47 (dd, J = 16.5, 3.6 Hz, 1H), 3.13 (dd, J = 16.5, 7.4 Hz, 1H), 2.40 (s, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 170.0, 155.1, 154.3, 136.3, 134.5, 133.4, 133.3, 130.3, 128.6, 127.6, 127.2, 127.0, 123.3, 115.5, 59.0, 51.9, 37.4, 21.3; MS (EI): m/z (%) = 336 (18) [M⁺], 276 (7), 263 (100), 178 (8), 104 (10), 76 (10), 50 (7). Anal. Calcd for C₁₂₇H₁₆₆N₂O₁₂; C, 67.85; H, 4.79; N, 8.33; found: C, 67.57; H, 4.82; N, 8.29.

Ethyl 2-(2-methyl-6,11-dioxo-6,11-dihydro-13H-indazolo[1,2-b]phthalazin-13-yl)acetate (3f):

3f (98% yield) as an off white solid; M.p.: 168-169 °C; ¹H NMR (500 MHz, CDCl₃) δ 8.42 (dd, J = 5.9, 3.0 Hz, 1H), 7.19 (dd, J = 8.7 Hz, 1H), 7.92 – 7.65 (m, 2H), 7.50 – 7.07 (m, 2H), 6.10 (dd, J = 7.0, 3.4 Hz, 1H), 4.07 (q, J = 7.1 Hz, 2H), 3.39 (dd, J = 16.3, 3.5 Hz, 1H), 3.20 (dd, J = 16.3, 7.1 Hz, 1H), 2.39 (s, 3H), 1.11 (t, J = 7.1 Hz, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 169.5, 155.1, 154.3, 136.3, 134.5, 133.4, 133.30, 131.4, 130.3, 127.5, 127.2, 126.9, 123.4, 115.5, 60.9, 49.9, 37.4, 21.3, 14.0; MS (EI): m/z (%) = 350 (18) [M⁺], 276 (8), 263 (100), 178 (6), 104 (7), 76 (7), 50 (3). Anal. Calcd for C₁₂₇H₁₆₆N₂O₁₂; C, 68.56; H, 5.18; N, 8.00; found: C, 68.24; H, 5.20; N, 8.04.

Ethyl 2-(2-fluoro-6,9-dioxo-6,9-dihydro-11H-pyridazino[1,2-ajindazol-11-yl)acetate (3g):

3g (74% yield) as a yellow solid; M.p.: 147-149 °C; ¹H NMR (500 MHz, CDCl₃) δ 8.28 (dd, J = 8.9, 4.5 Hz, 1H), 7.20 – 7.11 (m, 2H), 7.01 (d, J = 10.2 Hz, 1H), 6.92 (d, J = 10.2 Hz, 1H), 5.96 (dd, J = 7.4, 3.0 Hz, 1H), 4.09 (q, J = 7.1 Hz, 2H), 3.39 (dd, J = 16.7, 3.3 Hz, 1H), 3.12 (dd, J = 16.7, 7.5 Hz, 1H), 1.16 (t, J = 7.1 Hz, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 169.0, 160.8 (d, J C=CH = 248.2 Hz), 154.3, 153.4, 153.9, 133.0, 128.6 (d, J C=CH = 12.2 Hz), 116.7 (d, J C=CH = 23.2 Hz), 110.9 (d, J C=CH = 28.0 Hz), 61.1, 59.2, 36.1, 14.0; MS (EI): m/z (%) = 305 (30) [M⁺+1], 304(81) [M⁺], 275 (11), 258 (11), 230 (66), 217 (100), 189 (89), 188(69), 149 (67), 137 (11), 101 (11), 82 (37), 54 (37). Anal. Calcd for C₁₅₁H₁₄₃F₂N₂O₁₂; C, 59.21; H, 4.31; N, 9.21; found: C, 59.50; H, 4.33; N, 9.18.

Methyl 2-(2,9-dimethyl-6,11-dioxo-6,11-dihydro-13H-indazolo[1,2-b]phthalazin-13-yl)acetate (3h):

3h (86% yield) as a white solid; M.p.: 155-158 °C; ¹H NMR (500 MHz, CDCl₃) δ 8.34 – 8.20 (m, 3H), 8.15 (s, 1H), 7.65 (t, J = 8.0 Hz, 1H), 7.23 (s, 1H), 6.11 (dt, J = 7.4, 3.7 Hz, 1H), 3.67 (s, 3H), 3.46 (dt, J = 16.4, 3.7 Hz, 1H), 3.12 (dd, J = 16.5, 7.4 Hz, 1H), 2.56 (d, J = 4.7 Hz, 3H), 2.40 (s, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 170.0, 155.3, 154.5, 144.5, 136.3, 134.5, 134.4, 130.3, 127.6, 127.5, 127.3, 123.5, 115.5, 59.9, 51.9, 37.4, 21.8, 21.3; MS (EI): m/z (%) = 350 (21) [M⁺], 277 (100), 178 (7), 145 (7), 118 (9), 89 (10). Anal. Calcd for C₁₂₇H₁₆₆N₂O₁₂; C, 68.56; H, 5.18; N, 8.00; found: C, 68.92; H, 5.21; N, 8.05.

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Ethyl 2-(2,9-dimethyl-6,11-dioxo,6,11-dihydro-13H-indazolo[1,2-b]phthalazin-13-yl)acetate (3i):

3i (89% yield) as a white solid; M.p.: 148-150 °C; 1H NMR (500 MHz, CDCl₃) δ 8.32 – 8.21 (m, 3H), 8.15 (s, 1H), 7.65 (dd, J = 8.0, 1.6 Hz, 1H), 7.24 (s, 1H), 7.10 (dt, J = 7.3, 3.7 Hz, 1H), 4.07 (q, J = 7.1 Hz, 2H), 3.40 (dt, J = 16.5, 3.4 Hz, 1H), 3.19 (dd, J = 16.3, 7.2 Hz, 1H), 2.56 (dd, J = 4.1 Hz, 3H), 2.39 (s, 3H), 1.16 (t, J = 7.1 Hz, 3H); 13C NMR (125 MHz, CDCl₃) δ 169.5, 155.3, 154.5, 144.5, 130.3, 127.6, 127.5, 127.3, 127.2, 123.3, 115.5, 115.4, 60.8, 58.9, 37.4, 21.8, 21.3, 14.0; MS (EI): m/z (%) = 364 (18) [M]+, 290 (7), 277 (100), 178 (6), 145 (3), 118 (7), 89 (7). Anal. Caled for C₂₁H₂₀N₂O₄: C, 69.22; H, 5.53; N, 7.69; found: C, 69.54; H, 5.56; N, 7.74.

Methyl 2-(9-fluoro-6,11-dioxo,6,11-dihydro-13H-indazolo[1,2-b]phthalazin-13-yl)acetate (3j):

3j (63% yield) as a yellow solid; M.p.: 154-155 °C; 1H NMR (500 MHz, CDCl₃) δ 8.41 – 8.35 (m, 2H), 8.06 (dd, J = 8.6, 2.6 Hz, 1H), 7.54 – 7.48 (m, 1H), 7.48 – 7.43 (m, 2H), 7.30 (t, J = 7.6 Hz, 1H), 6.15 (dd, J = 7.3, 3.6 Hz, 1H), 3.65 (s, 3H), 3.45 (dd, J = 16.5, 3.6 Hz, 1H), 3.16 (dd, J = 16.5, 7.3 Hz, 1H); 13C NMR (100 MHz, CDCl₃) δ 170.0, 165.9 (d, J₁C= = 256.4 Hz), 154.5, 153.6, 136.4, 132.6, 130.6 (d, J₁C= = 9.0 Hz), 129.9, 126.9, 126.6, 125.7, 123.0, 121.6 (d, J₁C= = 23.0 Hz), 115.9, 113.9 (d, J₁C= = 24.0 Hz), 59.1, 52.1, 37.2; MS (EI): m/z (%) = 340 (28) [M]+, 280 (25), 267 (100), 256 (51), 238 (7), 211 (9), 183 (49), 122 (45), 94 (40), 77 (21), 51 (9). Anal. Caled for C₁₁H₁₁FNO₂: C, 63.53; H, 3.85; N, 8.23; found: C, 63.18; H, 3.82; N, 8.18.

Methyl 2-(6,11-dioxo,6,11-dihydro-13H-indazolo[1,2-b]phthalazin-13-yl)acetate (3k):

3k (81% yield) as a yellow solid; M.p.: 146-147 °C; 1H NMR (500 MHz, CDCl₃) δ 8.46 – 8.43 (m, 2H), 8.39 – 8.37 (m, 1H), 7.87 (dd, J = 6.2, 2.7 Hz, 2H), 7.48 – 7.44 (m, 2H), 7.30 (t, J = 7.2 Hz, 1H), 6.19 (dd, J = 6.8, 3.2 Hz, 1H), 3.66 (s, 3H), 3.49 (dd, J = 16.4, 3.6 Hz, 1H), 3.15 (dd, J = 16.4, 7.4 Hz, 1H); 13C NMR (100 MHz, CDCl₃) δ 170.0, 155.2, 154.7, 136.7, 133.6, 133.5, 129.9, 128.6, 127.7, 127.3, 126.8, 126.3, 123.0, 115.8, 59.0, 52.0, 37.4; MS (EI): m/z (%) = 322 (33) [M]+, 279 (7), 249 (100), 221 (7), 190 (21), 165 (55), 131 (41), 104 (48), 76 (49), 43 (25). Anal. Caled for C₁₁H₁₁N₂O₂: C, 67.08; H, 4.38; N, 8.69; found: C, 67.29; H, 4.40; N, 8.72.

Ethyl 2-(9-fluoro-6,11-dioxo,6,11-dihydro-13H-indazolo[1,2-b]phthalazin-13-yl)acetate (3l):

3l (66% yield) as a white solid; M.p.: 146-148 °C; 1H NMR (500 MHz, CDCl₃) δ 8.45 – 8.35 (m, 2H), 8.05 (dd, J = 8.5, 2.4 Hz, 1H), 7.53 (td, J = 8.3, 2.5 Hz, 1H), 7.48 – 7.42 (m, 2H), 7.30 (t, J = 7.5 Hz, 1H), 6.13 (dd, J = 6.9, 3.4 Hz, 1H), 4.06 (q, J = 7.1 Hz, 2H), 3.39 (dd, J = 16.4, 3.5 Hz, 1H), 3.22 (dd, J = 16.4, 7.1 Hz, 1H), 1.11 (t, J = 7.1 Hz, 3H); 13C NMR (125 MHz, CDCl₃) δ 169.3, 166.9 (d, J₁C= = 255.9 Hz), 154.4, 153.5, 136.5, 130.5 (d, J₁C= = 12.5 Hz), 129.8, 126.9, 126.5, 125.1, 122.9, 121.5 (d, J₁C= = 25.4 Hz), 115.8, 113.9 (d, J₁C= = 24.3 Hz), 60.9, 59.1, 37.3, 14.0; MS (EI): m/z (%) = 354 (18) [M]+, 280 (17), 268 (20), 267 (100), 183 (11), 122 (13), 102 (3), 94 (14). Anal. Caled for C₁₉H₁₅FNO₂: C, 64.40; H, 4.27; N, 7.91; found: C, 64.69; H, 4.29; N, 7.94.
Ethyl 2-(6,9-dioxo-6,9-dihydro-11H-pyridazino[1,2-a]indazol-11-yl)acetate (3m):

3m (98% yield) as a yellow solid; M.p.: 132-133 °C; 1H NMR (500 MHz, CDCl3) δ 8.35 (d, J = 8.1 Hz, 1H), 7.51 - 7.46 (m, 2H), 7.33 (t, J = 7.5 Hz, 1H), 7.06 (d, J = 10.2 Hz, 1H), 6.97 (d, J = 10.2 Hz, 1H), 6.05 (dd, J = 7.0, 3.5 Hz, 1H), 4.10 (q, J = 7.2 Hz, 2H), 3.39 (dd, J = 16.4, 3.6 Hz, 1H), 3.21 (dd, J = 16.4, 7.1 Hz, 1H), 1.17 (t, J = 7.2 Hz, 3H); 13C NMR (100 MHz, CDCl3) δ 168.7, 154.9, 153.7, 140.7, 130.8, 128.3, 125.6, 124.8, 124.3, 119.0, 116.6, 59.3, 51.1, 37.1, 14.2; MS (EI): m/z (%) = 286 (43) [M]+, 212 (42), 204 (9), 199 (100), 171 (66), 131 (37), 119 (11), 102 (11), 82 (18), 54 (23). Anal. Calcd for C13H14N2O3: C, 62.93; H, 4.93; N, 9.79; found: C, 62.64; H, 4.95; N, 9.85.

Methyl 2-(9-methyl-6,11-dioxo-6,11-dihydro-13H-indazolo[1,2-b]phthalazin-13-yl)acetate (3n):

3n (94% yield) as an orange solid; M.p.: 61-63 °C; 1H NMR (500 MHz, CDCl3) δ 8.47 - 8.41 (m, 1H), 8.33 (d, J = 8.2 Hz, 1H), 8.29 - 8.23 (m, 1H), 8.18 (s, 1H), 7.67 (t, J = 6.8 Hz, 1H), 7.53 - 7.41 (m, 2H), 6.16 (dd, J = 6.5, 3.2 Hz, 1H), 3.84 (s, 3H), 3.43 (dd, J = 16.2, 3.1 Hz, 1H), 3.22 (dd, J = 16.2, 7.1 Hz, 1H), 2.58 (d, J = 4.3 Hz, 3H); 13C NMR (100 MHz, CDCl3) δ 170.1, 154.4, 153.7, 136.4, 136.1, 134.6, 134.5, 130.1, 127.8, 123.8, 129.8, 127.7, 127.6, 127.3, 126.9, 126.3, 126.2, 123.0, 115.8, 58.9, 52.0, 37.4, 21.9; MS (EI): m/z (%) = 336 (14) [M]+, 263 (100), 237(15), 190 (60), 163 (14), 131 (100), 104 (14), 84 (29), 57 (20). Anal. Calcd for C19H16N2O2: C, 67.85; H, 4.79; N, 8.33; found: C, 67.71; H, 4.76; N, 8.37.

Methyl 2-(2-methyl-6,9-dioxo-6,9-dihydro-11H-pyridazino[1,2-a]indazol-11-yl)acetate (3o):

3o (98% yield) as a yellow solid; M.p.: 150-152 °C; 1H NMR (500 MHz, CDCl3) δ 8.22 (d, J = 8.2 Hz, 1H), 7.27-7.25 (m, 2H), 7.05 (d, J = 10.2 Hz, 1H), 6.95 (d, J = 10.2 Hz, 1H), 5.99 (dd, J = 7.3, 3.6 Hz, 1H), 3.69 (s, 3H), 3.43 (dd, J = 16.6, 3.6 Hz, 1H), 3.13 (dd, J = 16.6, 7.3 Hz, 1H), 2.43 (s, 3H); 13C NMR (125 MHz, DMSO) δ 170.1, 154.4, 153.7, 136.4, 136.1, 134.6, 134.5, 130.1, 127.8, 123.8, 114.5, 59.5, 52.0, 35.7, 21.3; MS (EI): m/z (%) = 286 (48) [M]+, 226 (21), 213 (100), 204 (14), 185 (35), 145 (29), 131 (7), 145 (29), 115 (14), 82 (14), 54 (20). Anal. Calcd for C13H14N2O3: C, 62.93; H, 4.93; N, 9.79; found: C, 62.70; H, 4.95; N, 9.75.

Ethyl 2-(2-methyl-6,9-dioxo-6,9-dihydro-11H-pyridazino[1,2-a]indazol-11-yl)acetate (3p):

3p (97% yield) as a yellow solid; M.p.: 156-158 °C; 1H NMR (500 MHz, CDCl3) δ 8.16 (d, J = 8.6 Hz, 1H), 7.25 (d, J = 8.9 Hz, 1H), 7.22 (s, 1H), 7.01 (d, J = 10.2 Hz, 1H), 6.91 (d, J = 10.2 Hz, 1H), 5.92 (dd, J = 7.0, 3.5 Hz, 1H), 4.06 (q, J = 7.1 Hz, 2H), 3.32 (dd, J = 16.4, 3.6 Hz, 1H), 3.16 (dd, J = 16.4, 7.0 Hz, 1H), 2.38 (s, 3H), 1.13 (t, J = 7.2 Hz, 3H); 13C NMR (125 MHz, CDCl3) δ 169.2, 154.3, 153.4, 136.9, 135.9, 134.1, 133.8, 130.3, 126.6, 123.3, 115.2, 60.9, 59.4, 36.4, 21.3, 14.0; MS (EI): m/z (%) = 300 (42) [M]+, 226 (36), 219 (14), 213 (100), 185 (42), 145 (36), 131 (7), 115 (14), 82 (14), 54 (16). Anal. Calcd for C16H16N2O2: C, 63.99; H, 5.37; N, 9.33; found: C, 63.78; H, 5.34; N, 9.37.
Butyl 2-(6,9-dioxo-6,9-dihydro-1H-pyridazino[1,2-a]indazol-11-yl)acetate (3q):

3q (82% yield) as a black oil; $^1$H NMR (500 MHz, CDCl$_3$) δ 8.33 (d, $J$ = 8.2 Hz, 1H), 7.46 – 7.43 (m, 2H), 7.31 (t, $J$ = 8.0 Hz, 1H), 7.04 (d, $J$ = 10.2 Hz, 1H), 6.95 (d, $J$ = 10.2 Hz, 1H), 6.00 (dd, $J = J_1$ = 6.9, 3.4 Hz, 1H), 4.02 (t, $J = J_2$ = 6.7 Hz, 2H), 3.38 (dd, $J = J_3$ = 16.4, 3.5 Hz, 1H), 3.19 (dd, $J = J_4$ = 16.4, 7.1 Hz, 1H), 1.51 - 1.46 (m, 2H), 1.30 – 1.22 (m, 2H), 0.87 (t, $J = 7.4$ Hz, 3H); $^{13}$C NMR (125 MHz, CDCl$_3$) δ 169.3, 154.3, 153.8, 136.3, 136.0, 134.1, 130.0, 126.8, 126.5, 123.0, 115.5, 65.0, 59.5, 36.3, 30.4, 19.0, 13.6; MS (EI): $m/z$ (%) = 348 (18) [M]$^+$, 231 (13), 212 (41), 199 (100), 171 (41), 149 (12), 131 (41), 82 (15), 57 (13). Anal. Calcd for C$_{19}$H$_{18}$N$_{2}$O$_{4}$: C, 64.96; H, 5.77; N, 8.91; found: C, 64.73; H, 5.79; N, 8.94.

Ethyl 2-(1-oxo-2,3-dihydro-1H,9H-pyrazolo[1,2-a]indazol-9-yl)acetate (3r):

3r (31% yield) as a yellow oil; $^1$H NMR (500 MHz, DMSO) δ 7.62 (d, $J$ = 7.9 Hz, 1H), 7.07 (t, $J = J_1$ = 7.6 Hz, 1H), 6.99 (t, $J = J_2$ = 7.7 Hz, 1H), 6.79 (d, $J$ = 7.9 Hz, 1H), 5.71 (t, $J = 6.8$ Hz, 1H), 4.17 (q, $J = J_3$ = 7.2 Hz, 2H), 2.99 – 2.80 (m, 3H), 2.68 (dd, $J = J_4$ = 15.9, 7.8 Hz, 1H), 2.64 – 2.53 (m, 2H), 1.20 (t, $J = 7.1$ Hz, 3H); $^{13}$C NMR (126 MHz, CDCl$_3$) δ 172.6, 170.1, 149.1, 1230.0, 129.0, 126.6, 123.7, 122.9, 66.5, 61.2, 55.9, 39.4, 32.7, 14.1; MS (EI): $m/z$ (%) = 260 (15) [M]$^+$, 232 (13), 217 (50), 204 (20), 173 (15), 159 (13), 131 (80), 104 (13), 93 (28), 84 (100), 59 (30), 43 (27). Anal. Calcd for C$_{19}$H$_{18}$N$_{2}$O$_{3}$: C, 64.60; H, 6.20; N, 10.76; found: C, 64.84; H, 6.23; N, 10.81.

9-(2-oxopropyl)-2,3-dihydro-1H,9H-pyrazolo[1,2-a]indazol-1-one (3s):

3s (42% yield) as a yellow oil; $^1$H NMR (500 MHz, DMSO ) δ 7.51 (d, $J$ = 8.0 Hz, 1H), 7.34 (t, $J = J_1$ = 7.6 Hz, 1H), 7.11 (t, $J = J_2$ = 7.2 Hz, 1H), 6.95 (d, $J$ = 8.0 Hz, 1H), 5.73 (t, $J = 6.0$ Hz 1H), 3.74 (dd, $J = J_3$ = 15.3, 2.8 Hz, 1H), 3.55 (dd, $J = J_4$ = 14.9, 5.3 Hz, 1H), 2.73 (t, $J = 6.8$ Hz, 2H), 2.51 (t, $J = J_5$ = 7.3 Hz, 2H), 2.14 (s, 3H); $^{13}$C NMR (126 MHz, CDCl$_3$) δ 194.8, 173.0, 149.6, 129.4, 128.8, 126.67, 124.1, 123.0, 66.6, 55.9, 40.8, 38.4, 29.5; MS (EI): $m/z$ (%) = 250 (21) [M]$^+$, 203 (40), 161 (50), 145 (15), 131 (70), 119 (11), 108 (16), 91 (10), 77 (90), 43 (100). Anal. Calcd for C$_{19}$H$_{18}$N$_{2}$O$_{2}$: C, 67.81; H, 6.13; N, 12.17; found: C, 67.57; H, 6.15; N, 12.21.

13-(2-oxopropyl)-13H-indazolo[1,2-b]phthalazine-6,11-dione (3t):

3t (33% yield) as a yellow oil; $^1$H NMR (500 MHz, DMSO ) δ 8.36-8.32 (m, 2H), 8.26 – 8.24 (m, 2H), 7.88 (d, $J = 6.6$ Hz, 1H), 7.68 (d, $J = 6.4$ Hz, 1H), 7.18 - 7.16 (m, 2H), 6.28 (dd, $J = J_1$ = 5.0, 2.5 Hz, 1H), 3.37 (dd, $J = J_2$ = 15.0, 2.6 Hz, 1H), 3.24 (dd, $J = J_3$ = 14.8, 5.0 Hz, 1H), 2.25 (s, 3H); $^{13}$C NMR (126 MHz, DMSO) δ 189.5, 188.9, 152.6, 141.4, 134.8, 132.0, 130.1, 125.3, 123.7, 123.6, 122.9, 118.9, 58.7, 36.8, 21.4; MS (EI): $m/z$ (%) = 306 (14) [M]$^+$, 291 (22), 264 (22), 191 (30), 165 (26), 135 (26), 107 (48), 71 (40), 43 (100). Anal. Calcd for C$_{19}$H$_{18}$N$_{2}$O$_{3}$: C, 70.58; H, 4.61; N, 9.15; found: C, 70.73; H, 4.59; N, 9.20.

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6. Spectral Data

2-phenyl-2,3-dihydrophthalazine-1,4-dione
6-methyl-2-(p-tolyl)-2,3-dihydropthalazine-1,4-dione
6-fluoro-2-phenyl-2,3-dihydropthalazine-1,4-dione
6-methyl-2-phenyl-2,3-dihydrophthalazine-1,4-dione
2-(4-bromophenyl)-2,3-dihydrophthalazine-1,4-dione
1-(4-fluorophenyl)-1,2-dihydropyridazine-3,6-dione
1-(p-tolyl)-1,2-dihydropyridazine-3,6-dione
Methyl 2-(6,9-dioxo-6,9-dihydro-11H-pyridazino[1,2-a]indazol-11-yl)acetate (3a)
Methyl 2-(2-bromo-6,11-dioxo-6,11-dihydro-13H-indazolo[1,2-b]phthalazin-13-yl)acetate (3b)
Methyl 2-(2-fluoro-6,9-dioxo-6,9-dihydro-11H-pyridazino[1,2-a]indazol-11-yl)acetate (3c)
Ethyl 2-(2-bromo-6,11-dioxo-6,11-dihydro-13H-indazolo[1,2-b]phthalazin-13-yl)acetate (3d)
Methyl 2-(2-methyl-6,11-dioxo-6,11-dihydro-13H-indazolo[1,2-b]phthalazin-13-yl)acetate (3e)
Ethyl 2-(2-methyl-6,11-dioxo-6,11-dihydro-13H-indazolo[1,2-b]phthalazin-13-yl)acetate (3f)
Ethyl 2-(2-fluoro-6,9-dioxo-6,9-dihydro-11H-pyridazino[1,2-a]indazol-11-yl)acetate (3g)
Methyl 2-(2,9-dimethyl-6,11-dioxo-6,11-dihydro-13H-indazolo[1,2-b]phthalazin-13-yl)acetate (3h)
Ethyl 2-(2,9-dimethyl-6,11-dioxo-6,11-dihydro-13H-indazolo[1,2-b]phthalazin-13-yl)acetate (3i)
Methyl 2-(9-fluoro-6,11-dioxo-6,11-dihydro-13H-indazolo[1,2-b]phthalazin-13-yl)acetate (3j)
Methyl 2-(6,11-dioxo-6,11-dihydro-13H-indazolo[1,2-b]phthalazin-13-yl)acetate (3k)

Solvent Impurity
Ethyl 2-(9-fluoro-6,11-dioxo-6,11-dihydro-13H-indazolo[1,2-b]phthalazin-13-yl)acetate (3l)
Ethyl 2-(6,9-dioxo-6,9-dihydro-11H-pyridazino[1,2-a]indazol-11-yl)acetate (3m)
Methyl 2-(9-methyl-6,11-dioxo-6,11-dihydro-13H-indazo[1,2-b]phthalazin-13-yl)acetate (3n)
Methyl 2-(2-methyl-6,9-dioxo-6,9-dihydro-11H-pyridazino[1,2-a]indazol-11-yl)acetate (3o)
Ethyl 2-(2-methyl-6,9-dioxo-6,9-dihydro-11H-pyridazino[1,2-a]indazol-11-yl)acetate (3p)
Butyl 2-(6,9-dioxo-6,9-dihydro-11H-pyridazino[1,2-a]indazol-11-yl)acetate (3q)
Ethyl 2-(1-oxo-2,3-dihydro-1H,9H-pyrazolo[1,2-a]indazol-9-yl)acetate (3r):
9-(2-oxopropyl)-2,3-dihydro-1H,9H-pyrazolo[1,2-a]indazol-1-one (3s):
13-(2-oxopropyl)-13H-indazolo[1,2-b]phthalazine-6,11-dione (3t):
7. Reference