

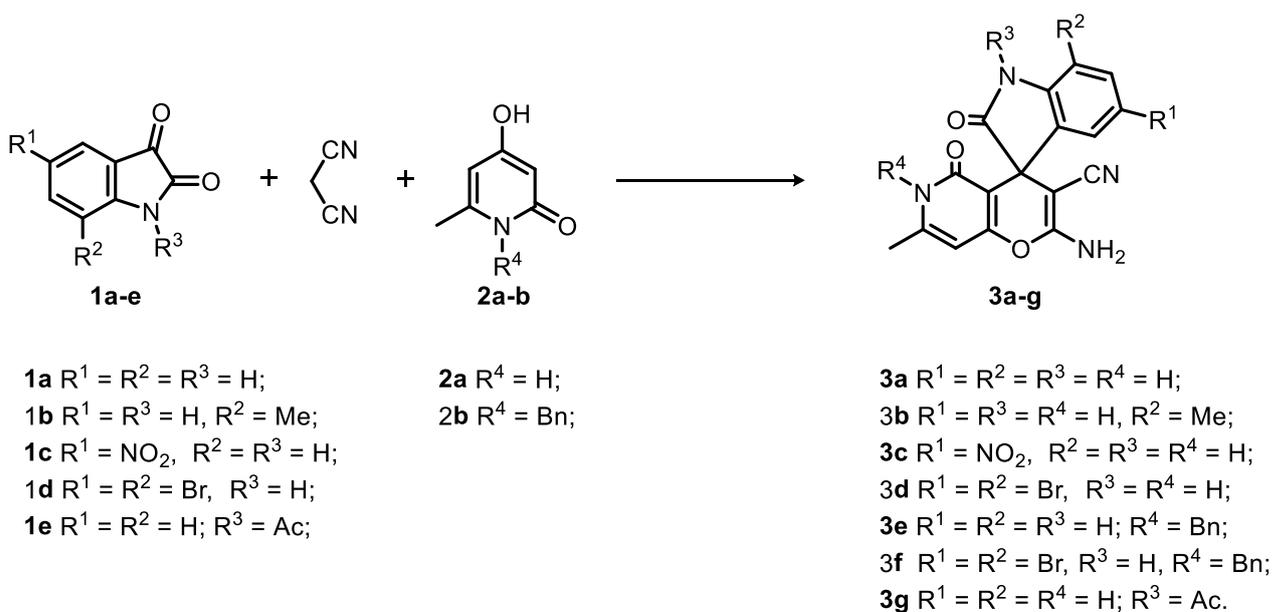
**Multicomponent assembling of isatins, malononitrile and 4-hydroxy-6-methylpyridin-2(1*H*)-ones: one-pot efficient approach to privileged spiro[indoline-3,4'-pyrano[3,2-*c*]pyridine]-2,5'(6'*H*)-dione scaffold**

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All melting points were measured with a Gallenkamp melting point apparatus and are uncorrected. <sup>1</sup>H and <sup>13</sup>C-NMR spectra were recorded with a Bruker AM-300 at ambient temperature in DMSO-*d*<sub>6</sub> solutions. Chemical shift values are given in δ scale relative to Me<sub>4</sub>Si. IR spectra were registered with a Bruker ALPHA-T FT-IR spectrometer in KBr pellets. Mass-spectra (EI = 70 eV) were obtained directly with a Finnigan MAT INCOS 50 spectrometer. All reagents were obtained from commercial sources and used without further purification.

**General procedure**

Isatin **1** (3 mmol), malononitrile (3 mmol), 4-hydroxy-6-methylpyridin-2(1*H*)-one **2** (3 mmol) were refluxed in ethanol (5 ml) in the presence of 10 mol% AcONa for 1 h (Scheme 1). After the reaction was finished the solid was filtered, washed with ice ethanol and dried to isolate pure substituted 2'-amino-7'-methyl-2,5'-dioxo-5',6'-dihydrospiro[indoline-3,4'-pyrano[3,2-*c*]pyridine]-3'-carbonitrile **3**.



**Scheme 1**

**2'-Amino-7'-methyl-2,5'-dioxo-5',6'-dihydrospiro[indoline-3,4'-pyrano[3,2-*c*]pyridine]-3'-carbonitrile(3a)**, obtained from **1a**, malononitrile and **2a**.

White solid; yield 0.94 g, (98%); mp >320 °C; <sup>1</sup>H NMR (300 MHz, DMSO-*d*<sub>6</sub>): δ 2.19 (s, 3H, CH<sub>3</sub>), 5.95 (s, 1H, CH), 6.80 (d, *J* = 7.6 Hz, 1H, Ar), 6.90-6.97 (m, 2H, Ar), 7.15-7.17 (m, 1H, Ar), 7.20 (s, 2H, NH<sub>2</sub>), 10.43 (s, 1H, NH), 11.51 (s, 1H, NH); <sup>13</sup>C NMR (DMSO-*d*<sub>6</sub>): 18.4, 47.3, 57.2, 95.7, 103.7, 109.1, 117.8, 121.6, 123.3, 128.0, 134.5, 142.4, 146.5, 157.4, 159.2, 160.7, 178.1 ppm; IR (KBr): ν = 3315, 3187, 2200, 1730, 1668, 1624, 1375, 1246, 739, 590 cm<sup>-1</sup>; Found (%): C, 63.72; H, 3.80; N, 17.47. Calcd. for C<sub>17</sub>H<sub>12</sub>N<sub>4</sub>O<sub>3</sub> (320.09) (%): C, 63.75; H, 3.78; N, 17.49; MS (m/z, relative intensity %): 320 [M<sup>+</sup>] (78), 294 (34), 292 (43), 291 (100), 276 (11), 267 (17), 266 (100), 120 (12), 82 (11), 44 (24).

**2'-Amino-7,7'-dimethyl-2,5'-dioxo-5',6'-dihydrospiro[indoline-3,4'-pyrano[3,2-*c*]pyridine]-3'-carbonitrile(3b)**, obtained from **1b**, malononitrile and **2a**.

White solid; yield 0.95 g, (95%); mp > 320 °C; <sup>1</sup>H NMR (300 MHz, DMSO-*d*<sub>6</sub>): δ 2.17 (s, 3H, CH<sub>3</sub>), 2.23 (s, 3H, CH<sub>3</sub>), 5.92 (s, 1H, CH), 6.73-6.82 (m, 2H, Ar), 6.97 (d, *J* = 7.3 Hz, 1H, Ar), 7.14 (s, 2H, NH<sub>2</sub>), 11.45 (s, 1H, NH), 11.45 (s, 1H, NH); <sup>13</sup>C NMR (DMSO-*d*<sub>6</sub>): 16.4, 18.3, 47.5, 56.1, 95.7, 103.8, 117.7, 118.0, 120.6, 121.5, 129.5, 134.2, 141.0, 146.4, 157.4, 159.2, 160.6, 178.5 ppm; IR (KBr): ν = 346, 3426, 3117, 2201, 1712, 1664, 1626, 1468, 1375, 1246 cm<sup>-1</sup>; Found (%): C, 64.67; H, 4.27; N, 16.77. Calcd. for C<sub>18</sub>H<sub>14</sub>N<sub>4</sub>O<sub>3</sub> (334.11) (%): C, 64.62; H, 4.22; N, 16.76; MS (m/z, relative intensity %): 335 (4), 334 [M<sup>+</sup>] (13), 306 (2), 305 (11), 291 (7), 280 (10), 255 (3), 199 (7), 184 (100), 45 (13).

**2'-Amino-7'-methyl-7-nitro-2,5'-dioxo-5',6'-dihydrospiro[indoline-3,4'-pyrano[3,2-*c*]pyridine]-3'-carbonitrile(3c)**, obtained from **1c**, malononitrile and **2a**.

Brown solid; yield 0.99 g, (90%); mp > 320 °C; <sup>1</sup>H NMR (300 MHz, DMSO-*d*<sub>6</sub>): δ 2.20 (s, 3H, CH<sub>3</sub>), 6.00 (s, 1H, CH), 7.03 (d, *J* = 8.6 Hz, 1H, Ar), 7.41 (s, 2H, NH<sub>2</sub>), 7.92 (s, 1H, Ar), 8.17 (d, *J* = 8.6 Hz, 1H, Ar), 11.20 (s, 1H, NH), 11.61 (s, 1H, NH); <sup>13</sup>C NMR (DMSO-*d*<sub>6</sub>): 18.4, 47.4, 55.5, 96.0, 102.5, 109.3, 117.5, 118.9, 125.7, 135.5, 142.4, 147.2, 149.0, 157.8, 159.6, 160.7, 178.7 ppm; IR (KBr): ν = 3360, 3190, 2202, 1738, 1668, 1627, 1381, 1341, 1246, 594 cm<sup>-1</sup>; Found (%): C, 55.82; H, 3.09; N, 19.16. Calcd. for C<sub>17</sub>H<sub>11</sub>N<sub>5</sub>O<sub>5</sub> (365.08) (%): C, 55.89; H, 3.04; N, 19.17; MS (m/z, relative intensity %): 365 [M<sup>+</sup>] (17), 348 (88), 320 (100), 296 (28), 240 (8), 215 (11), 146 (11), 125 (10), 73 (7), 66 (32).

**2'-Amino-5,7-dibromo-7'-methyl-2,5'-dioxo-5',6'-dihydrospiro[indoline-3,4'-pyrano[3,2-*c*]pyridine]-3'-carbonitrile(3d)**, obtained from **1d**, malononitrile and **2a**.

Beige solid; yield 1.36 g, (95%); mp > 320 °C; <sup>1</sup>H NMR (300 MHz, DMSO-*d*<sub>6</sub>): δ 2.20 (s, 3H, CH<sub>3</sub>), 5.97 (s, 1H, CH), 7.26 (s, 1H, Ar), 7.36 (s, 2H, NH<sub>2</sub>), 7.61 (s, 1H, Ar), 10.92 (s, 1H, NH), 11.58 (s, 1H, NH); <sup>13</sup>C NMR (DMSO-*d*<sub>6</sub>): 18.4, 48.6, 55.9, 95.9, 102.3, 102.6, 113.7, 117.4, 125.5, 132.8, 137.9, 141.5, 147.0, 157.6, 159.4, 160.6, 177.7 ppm; IR (KBr): ν = 3455, 3347, 3082, 2202, 1730, 1670, 1463, 1378, 1246, 565 cm<sup>-1</sup>; Found (%): C, 42.68; H, 2.15; Br, 33.43; N, 11.69. Calcd. for C<sub>17</sub>H<sub>10</sub>Br<sub>2</sub>N<sub>4</sub>O<sub>3</sub> (478.09) (%): C, 42.71; H, 2.11; Br, 33.43; N, 11.72; MS (m/z, relative intensity %): 480 [M<sup>+</sup>] (28), 478 [M<sup>+</sup>] (61), 476 [M<sup>+</sup>] (29), 426 (48), 424 (100), 422 (52), 352 (9), 307 (12), 289 (11), 28 (11).

**2'-Amino-1-benzyl-7'-methyl-2,5'-dioxo-5',6'-dihydrospiro[indoline-3,4'-pyrano[3,2-c]-pyridine]-3'-carbonitrile(3e)**, obtained from **1a**, malononitrile and **2b**.

White solid; yield 0.98 g, (80%); mp > 320 °C; <sup>1</sup>H NMR (300 MHz, DMSO-d<sub>6</sub>): δ 2.22 (s, 3H, CH<sub>3</sub>), 5.03 (d, *J* = 16.1 Hz, 1H, CH), 5.14 (d, *J* = 16.1 Hz, 1H, CH), 6.10 (s, 1H, CH), 6.75 (d, *J* = 7.6 Hz, 1H, Ar), 6.83-6.95 (m, 4H, Ar), 7.10 (s, 2H, NH<sub>2</sub>), 7.13-7.26 (m, 4H, Ar), 10.31 (s, 1H, NH); <sup>13</sup>C NMR (DMSO-d<sub>6</sub>): 19.6, 46.1, 47.8, 57.2, 97.7, 103.8, 109.1, 117.6, 121.6, 123.1, 126.0 2C, 127.1, 128.1, 128.6 2C, 134.6, 136.6, 142.5, 148.1, 156.0, 159.2, 160.3, 172.0 ppm; IR (KBr): ν = 3467, 3298, 3166, 2200, 1715, 1666, 1580, 1369, 1130, 735 cm<sup>-1</sup>; Found (%): C, 70.18; H, 3.47; N, 13.60. Calcd. for C<sub>24</sub>H<sub>18</sub>N<sub>4</sub>O<sub>3</sub> (410.14) (%): C, 70.23; H, 4.42; N, 13.65; MS (m/z, relative intensity %): 411 (23), 410 [M<sup>+</sup>] (100), 381 (18), 356 (11), 320 (20), 319 (97), 276 (9), 215 (2), 91 (20), 18 (15).

**2'-Amino-1-benzyl-5,7-dibromo-7'-methyl-2,5'-dioxo-5',6'-dihydrospiro[indoline-3,4'-pyrano[3,2-c]pyridine]-3'-carbonitrile(3f)**, obtained from **1d**, malononitrile and **2b**.

Brown solid; yield 1.44 g, (85%); mp > 320 °C; <sup>1</sup>H NMR (300 MHz, DMSO-d<sub>6</sub>): δ 2.29 (s, 3H, CH<sub>3</sub>), 5.06 (d, *J* = 16.1 Hz, 1H, CH), 5.23 (d, *J* = 16.1 Hz, 1H, CH), 6.21 (s, 1H, CH), 6.98 (d, *J* = 7.0 Hz, 2H, CH), 7.24-7.43 (m, 6H, Ar+NH<sub>2</sub>), 7.60 (s, 1H, Ar), 10.95 (s, 1H, NH); <sup>13</sup>C NMR (DMSO-d<sub>6</sub>): 19.6, 46.2, 49.2, 55.8, 97.9, 102.3, 102.9, 113.7, 117.4, 125.4, 126.0 2C, 127.1, 128.5 2C, 132.8, 136.4, 137.8, 141.6, 148.7, 156.2, 159.4, 160.3, 177.7 ppm; IR (KBr): ν = 3457, 3208, 2199, 1741, 1664, 1590, 1462, 1371, 1134, 727 cm<sup>-1</sup>; Found (%): C, 50.70; H, 2.89; Br, 28.12; N, 9.82. Calcd. for C<sub>24</sub>H<sub>16</sub>Br<sub>2</sub>N<sub>4</sub>O<sub>3</sub> (568.22) (%): C, 50.73; H, 2.84; Br, 28.11; N, 9.82; MS (m/z, relative intensity %): 570 [M<sup>+</sup>] (27), 568 [M<sup>+</sup>] (65), 566 [M<sup>+</sup>] (26), 479 (41), 477 (100), 475 (44), 436 (11), 364 (7), 91 (36), 28 (6).

**1-Acetyl-2'-amino-7'-methyl-2,5'-dioxo-5',6'-dihydrospiro[indoline-3,4'-pyrano[3,2-c]-pyridine]-3'-carbonitrile(3g)**, obtained from **1e**, malononitrile and **2a**.

White solid; yield 0.91 g, (84%); mp > 320 °C; <sup>1</sup>H NMR (300 MHz, DMSO-d<sub>6</sub>): δ 2.16 (s, 3H, CH<sub>3</sub>), 2.47 (s, 3H, CH<sub>3</sub>), 5.98 (s, 1H, CH), 7.07-7.17 (m, 2H, Ar), 7.29 (t, *J* = 7.7 Hz, 1H, Ar), 7.41 (s, 2H, NH<sub>2</sub>), 8.02 (d, *J* = 8.1 Hz, 1H, Ar), 11.58 (s, 1H, NH); <sup>13</sup>C NMR (DMSO-d<sub>6</sub>): 18.4, 25.9, 47.2, 56.8, 95.9, 103.6, 115.1, 117.4, 123.6, 125.4, 128.5, 132.8, 139.7, 147.4, 157.4, 159.2, 160.7, 170.3, 178.0 ppm; IR (KBr): ν = 3397, 3185, 2201, 1762, 1675, 1606, 1396, 1274, 1157, 747 cm<sup>-1</sup>; Found (%): C, 62.92; H, 3.94; N, 15.41. Calcd. for C<sub>19</sub>H<sub>14</sub>N<sub>4</sub>O<sub>4</sub> (362.10) (%): C, 62.98; H, 3.89; N, 15.46; MS (m/z, relative intensity %): 362 [M<sup>+</sup>] (28), 319 (100), 276 (17), 230 (1), 205 (1), 182 (1), 144 (1), 91 (1), 55 (1), 18 (5).