Supporting information for

**General Approach to Spiro Indole-3,1'-naphthalen Tetracyclic System: Stereoselective Pseudo Four-component Reaction of Isatins and Cyclic Carbonyl Compounds with two Molecules of Malononitrile**

Michail N. Elinson a,*, Anatoly N. Vereshchagin a, Ruslan F. Nasybullin a, Sergey I. Bobrovsky a, Alexey I. Ilovaisky a, Valentina M. Merkulova a, Ivan S. Bushmarinov b, Mikhail P. Egorov a

*N. D. Zelinsky Institute of Organic Chemistry, Leninsky prospect 47, 119991 Moscow, Russia
E-mail: elinson@ioc.ac.ru

1. **General Information**

   All melting points were measured with a Gallenkamp melting point apparatus and are uncorrected. 1H and 13C NMR spectra were recorded with a Bruker Avance II-300 spectrometer at ambient temperature in DMSO-d_6 solutions. Chemical shifts values are given in δ scale relative to Me_4Si. 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 Finningan MAT INCOS 50 spectrometer. All starting materials were obtained from commercial sources and used without purification.

2. **General Multicomponent Procedure**

   A mixture of isatin 1 (1 mmol), cyclic ketone 2 (1 mmol), malononitrile (0.132g, 2 mmol), Et_3N (0.02 g, 0.2 mmol) and ethanol (3 mL) was magnetically stirred at 20 °C for 1.5-2 h until deep red color of isatilydene malononitrile 4 was disappeared. Then the reaction mixture was filtered to isolate the solid products 3a-p, which were then rinsed with ice-cold ethanol (2×2 mL) and dried under reduced pressure.

   ![Chemical Structure](image)

   (3R*,8a'R*)-3'-Amino-2-oxo-1,2,6',8',8a'-hexahydro-2'H-spiro[indole-3,1'-naphthalene]-2',2',4'-tricarbonitrile (3a) (known compound, see: T. H. Babu, A. A. Joseph, D. Muralidharan and P. T. Perumal, *Tetrahedron Lett.*, 2010, 51, 994): white solid; yield 0.29 g (85%); mp 271–273 °C (lit. mp 238–240 °C); 1H NMR (300 MHz, DMSO-d_6): 0.46 (q, J = 11.7 Hz, 1H), 1.36–1.71 (m, 3H),...
1.81–1.99 (m, 1H), 2.07–2.27 (m, 1H), 2.83–2.97 (m, 1H), 5.86–5.97 (m, 1H), 6.87 (d, J = 7.7 Hz, 1H, Ar), 7.00 (t, J = 7.7 Hz, 1H, Ar), 7.37 (t, J = 7.7 Hz, 1H, Ar), 7.53 (s, 2H, NH₂), 11.36 (s, 1H, NH) ppm; ¹³C NMR (75 MHz, DMSO-d₆): 20.2, 23.4, 24.5, 37.0, 42.2, 54.6, 81.6, 110.2, 110.6, 110.7, 115.5, 122.5, 122.9, 123.7, 125.0, 125.4, 130.8, 142.3, 142.9, 173.3 ppm; IR (KBr): ν = 3416, 3328, 3223, 2944, 2221, 1749, 1728, 1656, 1596, 1471 cm⁻¹; MS (EI): m/z (%) = 341 ([M]+, 100), 324 (25), 313 (21), 297 (15), 285 (13), 230 (11), 209 (10), 170 (10), 133 (28), 77 (13); Anal. calcd (%) for C₂₀H₁₅N₅O: C 70.37, H 4.43, N 20.52. Found (%): C 70.23, H 4.57, N 20.40.

(3R*,8a'R*)-3'-Amino-1-ethyl-2-oxo-1,2,6',7',8',8a'-hexahydro-2'H-spiro[indole-3,1'-naphthalene]-2',2',4'-tricarbonitrile (3b): white solid. Yield 0.32 g (86%); mp 268–269 ºC; ¹H NMR (300 MHz, DMSO-d₆) δ 0.40 (q, J = 12.1 Hz, 1H), 1.18 (t, J = 7.0 Hz, 3H, CH₃), 1.37–1.55 (m, 2H), 1.55–1.68 (m, 1H), 1.81–1.99 (m, 1H), 2.08–2.22 (m, 1H), 2.90–3.02 (m, 1H), 3.79–3.93 (m, 2H, CH₂), 5.89–5.98 (m, 1H), 6.94 (d, J = 7.7 Hz, 1H, Ar), 7.15 (t, J = 7.7 Hz, 1H, Ar), 7.29 (d, J = 7.7 Hz, 1H, Ar), 7.48 (t, J = 7.7 Hz, 1H, Ar), 7.55 (s, 2H, NH₂) ppm; ¹³C NMR (75 MHz, DMSO-d₆) δ 12.2, 20.2, 23.3, 24.5, 34.8, 37.0, 42.2, 54.0, 81.6, 109.8, 110.0, 110.6, 115.5, 122.0, 123.5, 123.8, 124.9, 125.3, 131.0, 142.2, 143.2, 171.2 ppm; IR (KBr): ν = 3635, 3347, 3187, 2936, 2215, 1716, 1664, 1597, 1371 cm⁻¹; MS (EI): m/z (%) = 369 ([M]+, 17), 326 (5), 287 (4), 161 (32), 130 (25), 77 (27), 29 (100). Anal. calcd (%) for C₂₂H₁₉N₅O: C 71.53, H 5.18, N 18.96. Found (%): C 71.27, H 5.25, N 18.78.

(3R*,8a'R*)-3'-Amino-1-benzyl-2-oxo-1,2,6',7',8',8a'-hexahydro-2'H-spiro[indole-3,1'-naphthalene]-2',2',4'-tricarbonitrile (3c): white solid. Yield 0.39 g (90%); mp 243–245 ºC; ¹H NMR (300 MHz, DMSO-d₆) δ 0.38 (q, J = 12.1 Hz, 1H), 1.37–1.67 (m, 3H), 1.78–1.98 (m, 1H), 2.06–2.24 (m, 1H), 2.94–3.07 (m, 1H), 4.99–5.13 (m, 2H, CH₂), 5.89–5.99 (m, 1H), 6.95 (d, J = 7.3 Hz, 1H, Ar), 7.10–7.20 (m, 2H, Ar), 7.24–7.47 (m, 6H, Ar), 7.58 (s, 2H, NH₂) ppm; ¹³C NMR (75 MHz, DMSO-d₆) δ 20.2, 23.4, 24.5, 37.3, 42.2, 43.5, 54.2, 81.7, 110.2, 110.4, 115.5, 121.8, 123.8, 124.0, 124.9, 125.2, 127.4 (2C), 127.8, 128.7 (2C), 131.0, 135.5, 142.2, 143.4, 171.9 ppm; IR (KBr): ν = 3353, 3216, 2944, 2217, 1716, 1664, 1600, 1378 cm⁻¹; MS (EI): m/z (%) = 431 ([M]+, 13), 340 (5), 285 (4), 91 (100), 65 (18). Anal. calcd (%) for C₂₇H₂₁N₅O: C 75.16, H 4.91, N 16.23. Found (%): C 74.97, H 5.02, N 16.11.

(3R*,8a'R*)-1-Acetyl-3'-amino-2-oxo-1,2,6',7',8',8a'-hexahydro-2'H-spiro[indole-3,1'-naphthalene]-2',2',4'-tricarbonitrile (3d): white solid. Yield
0.25 g (65%); mp 251–253 °C; $^1$H NMR (300 MHz, DMSO-d$_6$) δ 0.45 (q, $J = 12.1$ Hz, 1H), 1.39–1.74 (m, 3H), 1.82–2.01 (m, 1H), 2.08–2.25 (m, 1H), 2.71 (s, 3H, CH$_3$), 2.99–3.12 (m, 1H), 5.95–6.05 (m, 1H), 7.03 (d, $J = 7.3$ Hz, 1H, Ar), 7.35 (t, $J = 7.3$ Hz, 1H, Ar), 7.56 (d, $J = 7.7$ Hz, 1H, Ar), 7.64 (s, 2H, NH$_2$), 8.24 (d, $J = 8.0$ Hz, 1H, Ar) ppm; $^{13}$C NMR (75 MHz, DMSO-d$_6$) δ 20.1, 23.4, 24.5, 26.6, 38.1, 42.5, 55.3, 81.8, 109.8, 110.4, 115.3, 116.2, 121.3, 124.5, 124.7, 124.8, 126.3, 131.3, 140.6, 141.6, 170.1, 173.4 ppm; IR (KBr): $\nu = 3391, 3329, 3223, 2943, 2220, 1756, 1736, 1658, 1593, 1265$ cm$^{-1}$; MS (EI): $m/z$ (%) = 383 ([M]$^+$, 8), 341 (10), 285 (4), 133 (9), 43 (100). Anal. calcd (%) for C$_{22}$H$_{27}$N$_5$O$_2$: C 68.92, H 4.47, N 18.27. Found (%): C 68.79, H 4.58, N 18.01.

(3R*,8a'R*) Ethyl (3’-amino-2’,2’,4’-tricyano-2-oxo-6’,7’,8’,8a’-tetrahydro-2’H-spiro[indole-3,1’-naphthalene]-1(2H)-yl)acetate (3e): white solid. Yield 0.26 g (62%); mp 229–230 °C; $^1$H NMR (300 MHz, DMSO-d$_6$) δ 0.44 (q, $J = 12.1$ Hz, 1H), 1.39 (t, $J = 7.0$ Hz, 3H, CH$_3$), 1.19 (t, $J = 7.0$ Hz, 3H, CH$_3$), 1.38–1.55 (m, 1H), 1.55–1.70 (m, 2H), 1.82–2.01 (m, 1H), 2.07–2.25 (m, 1H), 2.89–3.03 (m, 1H), 4.16 (q, $J = 7.0$ Hz, 2H, CH$_2$), 4.67–4.83 (m, 2H, CH$_2$), 5.90–6.00 (m, 1H), 6.95 (d, $J = 7.7$ Hz, 1H, Ar), 7.17 (t, $J = 7.7$ Hz, 1H, Ar), 7.24 (d, $J = 7.7$ Hz, 1H, Ar), 7.46 (t, $J = 7.7$ Hz, 1H, Ar), 7.56 (s, 2H, NH$_2$) ppm; $^{13}$C NMR (75 MHz, DMSO-d$_6$) δ 14.0, 20.2, 23.4, 24.6, 37.3, 42.1, 54.0, 61.4, 81.8, 109.8, 109.9, 110.5, 115.5, 121.7, 123.9, 124.0, 124.8, 125.3, 130.9, 142.1, 143.2, 167.0, 171.9 ppm; IR (KBr): $\nu = 3324, 3219, 2940, 2216, 1758, 1727, 1645, 1373, 1207$ cm$^{-1}$; MS (EI): $m/z$ (%) = 427 ([M]$^+$, 68), 353 (92), 336 (38), 243 (18), 208 (22), 117 (71), 29 (100). Anal. calcd (%) for C$_{24}$H$_{21}$N$_5$O$_3$: C 67.44, H 4.95, N 16.38. Found (%): C 67.21, H 5.07, N 16.19.

(3R*,8a'R*)-3’-Amino-5-methyl-2-oxo-1,2,6’,7’,8’,8a’-hexahydro-2’H-spiro[indole-3,1’-naphthalene]-2’,2’,4’-tricarbonitrile (3f): white solid. Yield 0.24 g (68%); mp 259–262 °C; $^1$H NMR (300 MHz, DMSO-d$_6$) δ 0.48 (q, $J = 12.1$ Hz, 1H), 1.37–1.71 (m, 3H), 1.83–2.03 (m, 1H), 2.08–2.21 (m, 1H), 2.31 (s, 3H, CH$_3$), 2.83–2.95 (m, 1H), 5.88–5.98 (m, 1H), 6.65 (s, 1H, NH), 6.90 (d, $J = 8.0$ Hz, 1H, Ar), 7.19 (d, $J = 8.0$ Hz, 1H, Ar), 7.51 (s, 2H, NH$_2$), 11.26 (s, 1H, NH) ppm; $^{13}$C NMR (75 MHz, DMSO-d$_6$) δ 20.2, 21.0, 23.4, 24.5, 37.0, 42.2, 54.6, 81.6, 110.3, 110.5, 110.7, 115.5, 122.6, 123.6, 125.3, 125.5, 131.2, 131.6, 140.5, 142.3, 173.2 ppm; IR (KBr): $\nu = 3337, 3224, 2928, 2214, 1723, 1644, 1598, 1490$ cm$^{-1}$; MS (EI): $m/z$ (%) = 355 ([M]$^+$, 100), 209 (15), 146 (52), 115 (23), 77 (51), 39 (78). Anal. calcd (%) for C$_{21}$H$_{17}$N$_5$O: C 70.97, H 4.82, N 19.71. Found (%): C 70.74, H 4.93, N 19.59.

S3
(3R*,8a’R*)-3’-Amino-5-chloro-2-oxo-1,2,6’,7’,8’,8a’-hexahydro-2’H-spiro[indole-3,1’-naphthalene]-2’,2’,4’-tricarbonitrile (3g): white solid. Yield 0.23 g (61%); mp 232–234 °C; 1H NMR (300 MHz, DMSO-d6) δ 0.49 (q, J = 12.1 Hz, 1H), 1.37–1.77 (m, 3H), 1.88–2.07 (m, 1H), 2.07–2.32 (m, 1H), 2.86–3.01 (m, 1H), 5.92–6.03 (m, 1H), 6.78 (s, 1H, Ar), 7.06 (d, J = 8.4 Hz, 1H, Ar), 7.49 (d, J = 8.4 Hz, 1H, Ar), 7.64 (s, 2H, NH2), 11.58 (s, 1H, NH) ppm; 13C NMR (75 MHz, DMSO-d6) δ 20.2, 23.4, 24.5, 37.0, 42.0, 54.8, 81.5, 110.1, 110.3, 112.4, 115.3, 124.3, 124.4, 124.7, 124.9, 126.7, 131.0, 142.0 (2C), 172.9 ppm; IR (KBr): ν = 3335, 3221, 2941, 2216, 1726, 1642, 1599, 1476 cm−1; MS (EI): m/z (%) = 377 ([M]+, 17), 375 (58) [M]+, 169 (23), 167 (100), 102 (23), 77 (38), 41 (70). Anal. calcd (%) for C20H14ClN5O: C 63.92, H 3.75, Cl 9.43, N 18.64. Found (%): C 63.78, H 3.91, Cl 9.31, N 18.47.

(3R*,8a’R*)-3’-Amino-5-bromo-2-oxo-1,2,6’,7’,8’,8a’-hexahydro-2’H-spiro[indole-3,1’-naphthalene]-2’,2’,4’-tricarbonitrile (3h): white solid. Yield 0.26 g (63%); mp 242–245 °C; 1H NMR (300 MHz, DMSO-d6) δ 0.49 (q, J = 12.1 Hz, 1H), 1.38–1.76 (m, 3H), 1.88–2.06 (m, 1H), 2.09–2.31 (m, 1H), 2.87–3.00 (m, 1H), 5.92–6.03 (m, 1H), 6.90 (s, 1H, Ar), 7.01 (d, J = 8.4 Hz, 1H, Ar), 7.56–7.70 (m, 3H, Ar, NH2), 11.58 (s, 1H, NH) ppm; 13C NMR (75 MHz, DMSO-d6) δ 20.2, 23.4, 24.5, 37.0, 42.0, 54.7, 81.4, 110.1, 110.3, 112.8, 114.3, 115.3, 124.3, 124.7, 124.9, 133.9, 142.0, 142.4, 172.8 ppm; IR (KBr): ν = 3335, 3220, 2941, 2215, 1725, 1643, 1599, 1472 cm−1; MS (EI): m/z (%) = 421 ([M]+, 18), 419 ([M]+, 17), 213 (21), 211 (19), 115 (28), 77 (61), 41 (90), 39 (100); Anal. calcd (%) for C20H14BrN5O: C 57.16, H 3.36, Br 19.01, N 16.66. Found (%): C 56.97, H 3.48, Br 18.82, N 16.43.

(3R*,8a’R*)-3’-Amino-7-methyl-2-oxo-1,2,6’,7’,8’,8a’-hexahydro-2’H-spiro[indole-3,1’-naphthalene]-2’,2’,4’-tricarbonitrile (3i): white solid. Yield 0.21 g (60%); mp 263-268 °C; 1H NMR (300 MHz, DMSO-d6) δ 0.51 (q, J = 10.8 Hz, 1H), 1.47-1.64 (m, 3H), 1.87-1.92 (m, 1H), 2.13-2.20 (m, 1H), 2.90-2.93 (m, 1H), 2.26 (s, 3H, CH3), 5.90-5.92 (m, 1H), 6.72 (d, J = 7.6 Hz, 1H, Ar), 6.99 (s, J = 7.7 Hz, 1H, Ar), 7.22 (d, J = 7.7 Hz, 1H, Ar), 7.54 (s, 2H, NH2), 11.41 (s, 1H, NH) ppm; 13C NMR (75 MHz, DMSO-d6): 16.5, 20.2, 23.5, 24.5, 37.1, 42.2, 54.7, 81.6, 110.2, 110.8, 115.5, 120.1, 122.2 (2C), 122.8, 123.6, 125.5, 132.1, 141.4, 142.3, 173.8 ppm; IR (KBr): ν = 3445, 3317, 3218, 2224, 1742, 1719, 1647, 1599, 1462, 1395 cm−1; MS (EI): m/z (%) = 355 ([M]+, 46), 297 (66), 254 (25), 184 (19), 151 (95), 128 (28), 115 (20), 91 (28), 65 (31), 15 (100); Anal. calcd (%) for C21H17N5O: C 70.97, H 4.82, N 19.71. Found (%): C 70.85, H 4.93, N 19.60.
(3R*,8a'R*)-3'-Amino-5,7-dibromo-2-oxo-1,2,6',7',8',8a'-hexahydro-2'H-spiro[indole-3,1'-naphthalene]-2',2',4'-tricarbonitrile (3j): white solid. Yield 0.40 g (81%); mp 304–309 ºC; 1H NMR (300 MHz, DMSO-<sub>d6</sub>) \( \delta \) 0.54 (q, \( J = 11.4 \) Hz, 1H), 1.49-1.66 (m, 3H), 1.99-2.01 (m, 1H), 2.15-2.21 (m, 1H), 2.94-2.98 (m, 1H), 5.97-6.00 (m, 1H), 6.89 (s, 1H, Ar), 7.70 (s, 2H, NH₂), 7.96 (s, 1H, Ar), 11.99 (s, 1H, NH); 13C NMR (75 MHz, DMSO-<sub>d6</sub>): 21.1, 24.5, 25.5, 38.1, 43.0, 56.6, 82.5, 105.3, 110.9, 111.0, 115.8, 116.2, 125.6, 125.7, 126.7, 127.6, 137.0, 142.7, 143.2, 173.8 ppm; IR (KBr): \( \nu \) = 3443, 3347, 2221, 1747, 1633, 1622, 1457, 1392, 1296, 1163 cm⁻¹; MS (EI): \( m/z \) (%) = 501 ([M]+, 9), 499 ([M]+, 13), 391 (3), 291 (10), 209 (20), 184 (18), 128 (22), 114 (18), 77 (23), 27 (100); Anal. calcd (%) for C<sub>20</sub>H<sub>13</sub>Br<sub>2</sub>N<sub>5</sub>O: C 48.12, H 2.63, N 14.03, Br 32.02. Found (%): C 48.03, H 2.71, N 13.95, Br 31.95.

(3R*,7'R*,8a'R*)-3'-Amino-7'-methyl-2-oxo-1,2,6',7',8',8a'-hexahydro-2'H-spiro[indole-3,1'-naphthalene]-2',2',4'-tricarbonitrile (3k): white solid. Yield 0.24 g (68%); mp 219–222 ºC; 1H NMR (300 MHz, DMSO-<sub>d6</sub>) \( \delta \) 0.24 (q, \( J = 11.4 \) Hz, 1H), 0.79 (d, \( J = 6.3 \) Hz, 3H, CH₃), 1.40–1.60 (m, 2H), 1.63–1.80 (m, 1H), 2.16–2.30 (m, 1H), 2.92–3.04 (m, 1H), 5.85–5.94 (m, 1H), 6.86 (d, \( J = 7.3 \) Hz, 1H, Ar), 7.01 (d, \( J = 7.7 \) Hz, 1H, Ar), 7.06 (t, \( J = 7.7 \) Hz, 1H, Ar), 7.38 (t, \( J = 7.7 \) Hz, 1H, Ar), 7.54 (s, 2H, NH₂), 11.35 (s, 1H, NH) ppm; 13C NMR (75 MHz, DMSO-<sub>d6</sub>) \( \delta \) 21.5, 27.2, 31.7, 33.4, 37.6, 42.3, 54.5, 81.5, 110.2, 110.6, 110.7, 115.6, 122.4, 123.0, 123.5, 125.0, 125.3, 130.9, 142.4, 142.9, 173.2 ppm; IR (KBr): \( \nu \) = 3363, 3284, 2959, 2222, 1739, 1710, 1594, 1473 cm⁻¹; MS (EI): \( m/z \) (%) = 355 ([M]+, 100), 313 (21), 285 (17), 133 (41), 115 (20), 77 (25), 46 (64), 31 (88). Anal. calcd (%) for C<sub>21</sub>H<sub>17</sub>N<sub>5</sub>O: C 70.97, H 4.82, N 19.71. Found (%): C 70.78, H 4.98, N 19.57.

(3R*,7'R*,8a'R*)-3'-Amino-2-oxo-7'-phenyl-1,2,6',7',8',8a'-hexahydro-2'H-spiro[indole-3,1'-naphthalene]-2',2',4'-tricarbonitrile (3l): white solid. Yield 0.30 g (72%); mp 284–286 ºC; 1H NMR (300 MHz, DMSO-<sub>d6</sub>) \( \delta \) 0.74 (q, \( J = 12.4 \) Hz, 1H), 1.53–1.67 (m, 1H), 2.00–2.17 (m, 1H), 2.33–2.49 (m, 1H), 2.89–3.06 (m, 1H), 3.13–3.28 (m, 1H), 5.95–6.08 (m, 1H), 6.86 (d, \( J = 7.7 \) Hz, 1H, Ar), 6.97–7.30 (m, 7H, Ar), 7.40 (t, \( J = 7.3 \) Hz, 1H, Ar), 7.63 (s, 2H, NH₂), 11.32 (s, 1H, NH) ppm; 13C NMR (75 MHz, DMSO-<sub>d6</sub>) \( \delta \) 31.2, 32.6, 37.8, 37.9, 42.2, 54.5, 81.2, 110.1, 110.6, 110.8, 115.5, 122.3, 123.1, 123.3, 125.0, 125.3, 126.4, 126.5 (2C), 128.5 (2C), 131.0, 142.6, 142.8, 142.9, 173.1 ppm; IR (KBr): \( \nu \) = 3421, 3331, 3223, 2918, 2212, 1724, 1649, 1597, 1471 cm⁻¹; MS (EI): \( m/z \) (%) = 417 ([M]+, 85), 313 (28), 285...
(19), 115 (23), 104 (73), 91 (100), 77 (55), 44 (40). Anal. calcd (%): C 26H19N5O: C 74.80, H 4.59, N 16.78. Found (%): C 74.61, H 4.72, N 16.59.

\( (3 \text{R}^*,8 \text{a}^* \text{R}^*) \)-2'-Acetyl-6'-amino-2-oxo-1,1',2,2',3',8a'-hexahydro-7'H-spiro[indole-3,8'-isoquinoline]-5',7',7'-tricarbonitrile (3m): white solid. Yield 0.25 g (66%); mp 226–227 ºC; \(^1\)H NMR (300 MHz, DMSO-\(d_6\)) \( \delta \) 1.59 (t, \( J = 11.0 \) Hz, 1H), 1.96 (s, 3H, CH\(^3\)), 2.88–3.00 (m, 1H), 3.77–3.91 (m, 1H), 4.20–4.40 (m, 2H), 5.82–5.92 (m, 1H), 6.93 (d, \( J = 7.3 \) Hz, 1H, Ar), 7.01–7.16 (m, 2H, Ar), 7.41 (t, \( J = 7.7 \) Hz, 1H, Ar), 7.79 (s, 2H, NH\(^2\)), 11.51 (s, 1H, NH) ppm; \(^{13}\)C NMR (75 MHz, DMSO-\(d_6\)) \( \delta \) 21.5, 35.7, 37.7, 42.2, 44.9, 52.8, 80.0, 109.8, 110.3, 111.1, 115.2, 118.9, 121.4, 123.3, 124.6, 125.0, 131.3, 142.7, 143.3, 169.0, 172.5 ppm; IR (KBr): \( \nu = \) 3624, 3498, 3328, 3149, 2210, 1729, 1648, 1600, 1472 cm –1; MS (EI): \( m/z \) (%) = 384 ([M]+, 5), 341 (6), 298 (8), 210 (10), 147 (12), 133 (13), 77 (5), 43 (100). Anal. calcd (%) for C\(_{21}\)H\(_{16}\)N\(_6\)O\(_2\): C 65.62, H 4.20, N 21.86. Found (%): C 65.38, H 4.34, N 21.67.

\( (3 \text{R}^*,8 \text{a}^* \text{R}^*) \)-Ethyl 6'-amino-5',7',7'-tricyano-2-oxo-1,1',2,3',7',8a'-hexahydro-2'H-spiro[indole-3,8'-isoquinoline]-2'-carboxylate (3n): white solid. Yield 0.25 g (60%); mp 240 ºC (dec); \(^1\)H NMR (300 MHz, DMSO-\(d_6\)) \( \delta \) 1.15 (t, \( J = 7.3 \) Hz, 3H, CH\(^3\)), 2.95–3.08 (m, 1H), 3.52–3.72 (m, 1H), 3.76–3.96 (m, 2H), 4.02 (q, \( J = 7.3 \) Hz, 2H, CH\(^2\)), 4.22–4.38 (m, 1H), 5.82–5.93 (m, 1H), 6.92 (d, \( J = 7.3 \) Hz, 1H, Ar), 7.05 (d, \( J = 7.7 \) Hz, 1H, Ar), 7.10 (t, \( J = 7.7 \) Hz, 1H, Ar), 7.41 (t, \( J = 7.3 \) Hz, 1H, Ar), 7.78 (s, 2H, NH\(^2\)), 11.53 (s, 1H, NH) ppm; \(^{13}\)C NMR (75 MHz, DMSO-\(d_6\)) \( \delta \) 14.5, 35.7, 40.3, 42.2, 43.2, 52.6, 61.2, 80.1, 109.7, 110.2, 111.1, 115.1, 119.0, 121.4, 123.3, 124.2, 125.0, 131.3, 142.6, 143.2, 154.5, 172.5 ppm; IR (KBr): \( \nu = \) 3430, 3224, 2213, 1728, 1688, 1646, 1600, 1470 cm –1; MS (EI): \( m/z \) (%) = 414 ([M]+, 4), 341 (3), 313 (5), 259 (8), 210 (12), 133 (16), 77 (8), 29 (100). Anal. calcd (%) for C\(_{22}\)H\(_{18}\)N\(_6\)O\(_3\): C 63.76, H 4.38, N 20.28. Found (%): C 63.52, H 4.51, N 20.03.

\( (3 \text{R}^*,8 \text{a}^* \text{R}^*) \)-6'-Amino-5',7',7'-tricyano-2-oxo-1,1',2,3',7',8a'-hexahydro-2'H-spiro[indole-3,8'-isoquinoline]-2'-tricarbonitrile (3o): white solid. Yield 0.25 g (73%); mp 258–260 ºC; \(^1\)H NMR (300 MHz, DMSO-\(d_6\)) \( \delta \) 2.44–2.51 (m, 1H, CH), 3.07–3.15 (m, 1H, CH), 3.67–3.72 (m, 1H, CH), 4.00 (d, \( J = 17.7 \) Hz, 1H, CH), 4.21 (d, \( J = 17.7 \) Hz, 1H, CH), 5.91 (s, 1H, CH), 6.93 (d, \( J = 7.7 \) Hz, 1H, Ar), 7.03 (d, \( J = 7.7 \) Hz, 1H, Ar), 7.10 (t, \( J = 7.7 \) Hz, 1H, Ar), 7.41 (t, \( J = 7.7 \) Hz, 1H, Ar), 7.79 (s, 2H, NH\(^2\)), 11.46 (s, 1H, NH) ppm; \(^{13}\)C NMR (75 MHz, DMSO-\(d_6\)) \( \delta \) 35.4, 42.3, 51.9, 63.4, 65.3,
79.8, 109.7, 110.3, 111.0, 115.0, 120.4, 121.5, 123.2, 123.6, 124.9, 131.2, 142.5, 143.1, 172.3 ppm; MS (EI): \( m/z \) (%) = 343 ([M]⁺, 100), 298 (38), 287 (35), 269 (24), 230 (19), 158 (43), 140 (85), 112 (65), 69 (36), 28 (58); IR (KBr): \( \nu = \) 3339, 3196, 2825, 2224, 1736, 1666, 1598, 1472, 1390, 1127 cm⁻¹; Anal. calcd (%) for C₁₉H₁₃N₅O₂: C 66.47, H 3.82, N 20.40. Found (%): C 66.31, H 3.99, N 20.19.

(3\( R^*\),8\( a'R^*\))-6'-Amino-2-oxo-3',8a'-dihydrospiro[indoline-3,8'-isothiochromene]-5',7',7'(1'H)-tricarbonitrile (3p) white solid. Yield 0.28 g (77%); mp 181–183 °C; \(^1\)H NMR (300 MHz, DMSO-\( d_6 \)) \( \delta \) 1.71-1.79 (m, 1H, CH), 2.44-2.48 (m, 1H, CH), 3.11-3.19 (m, 2H), 3.38-3.44 (m, 1H, CH), 6.14 (s, 1H, CH), 6.90 (d, \( J = 7.6 \) Hz, 1H, Ar), 7.02-7.11 (m, 2H, Ar), 7.41 (t, \( J = 7.7 \) Hz, 1H, Ar), 7.71 (s, 2H, NH₂), 11.50 (s, 1H, NH) ppm; \(^{13}\)C NMR (75 MHz, DMSO-\( d_6 \)) \( \delta \) 25.4, 25.5, 38.3, 42.9, 55.1, 82.2, 110.3, 111.0, 111.6, 115.9, 121.5, 122.0, 123.8, 125.6, 126.9, 131.8, 143.3, 143.4, 173.3; MS (EI): \( m/z \) (%) = 359 ([M]⁺, 100), 326 (17), 258 (19), 298 (22), 230 (15), 195 (15), 164 (27), 133 (67), 77 (24), 45 (44); IR (KBr): \( \nu = \) 3337, 3213, 2213, 1722, 1640, 1619, 1599, 1472, 1330, 1238 cm⁻¹; Anal. calcd (%) for C₁₉H₁₃N₅O₂S: C 63.49, H 3.65, N 19.49, S 8.92. Found (%): C 63.30, H 3.81, N 19.32, S 8.79.
$^1$H-NMR for 3a:

$^{13}$C-NMR for 3a:
IR for 3a:
$^1$H-NMR for 3i:

$^{13}$C-NMR for 3i:
IR for 3i:
$^1$H-NMR for 3j:

$^{13}$C-NMR for 3j:
IR for 3j:
$^1$H-NMR for 3o:

[1H-NMR image]

$^{13}$C-NMR for 3o:

[13C-NMR image]
IR for 3ο:
$^1$H-NMR for 3p:

$^{13}$C-NMR for 3p:
IR for $3p$: 
3. **Single-crystal X-ray diffraction**

Single crystals of C$_{23}$H$_{24}$N$_5$O$_2.5$ (3a) were crystallized from EtOH. A suitable crystal was selected and mounted on a needle on a Bruker SMART 1000 diffractometer. The crystal was kept at 150 K during data collection. Using Olex2,$^1$ the structure was solved with the SHELXS$^2$ structure solution program using Direct Methods and refined with the SHELXL$^2$ refinement package using Least Squares minimization.

The crystal of 3a contained two independent disordered EtOH moieties, one of them positioned around an inversion centre, resulting in a composition of C$_{20}$H$_{15}$N$_5$O · 1.5EtOH. The disordered solvent molecules were refined using SAME and SIMU restraints as implemented in SHELXL 2014/7.

**Crystal Data** for C$_{23}$H$_{24}$N$_5$O$_2.5$ ($M=410.47$ g/mol): triclinic, space group P-1 (no. 2), a = 7.4809(18) Å, b = 11.265(3) Å, c = 13.576(3) Å, $\alpha = 77.760(6)^\circ$, $\beta = 83.288(7)^\circ$, $\gamma = 70.811(6)^\circ$, $V = 1054.6(4)$ Å$^3$, Z = 2, $T = 150$ K, $\mu$(MoK$\alpha$) = 0.087 mm$^{-1}$, $D_{calc} = 1.293$ g/cm$^3$, 9729 reflections measured ($3.074^\circ \leq 2\Theta \leq 52.742^\circ$), 4309 unique ($R_{int} = 0.0359$, $R_{sigma} = 0.0575$) which were used in all calculations. The final $R_1$ was 0.0631 (I > 2$\sigma$(I)) and $wR_2$ was 0.2092 (all data). The structure has been deposited with the CSD, deposition number CCDC 1050772.