SUPPLEMENTARY CONTENT

SYNTHESIS OF NOVEL DISPIRO 1,4-BENZOTHAZINE HYBRID HETEROCYCLES THROUGH 1,3-DIPOLAR CYCLOADDITION

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EXPERIMENTAL

General. The melting points were measured in open capillary tubes and are uncorrected. The ^1H , ^{13}C and the 2D NMR spectra were recorded on a Bruker (Avance) 300 MHz NMR instrument using TMS as internal standard and CDCl_3 or DMSO-d_6 as solvent. Standard Bruker software was used throughout. Chemical shifts are given in parts per million (δ -scale) and the coupling constants are given in Hertz. Elemental analyses were performed on a Perkin Elmer 2400 Series II Elemental CHNS analyzer. Silica gel-G plates (Merck) were used for tlc analysis with a mixture of petroleum ether (60–80°C) and ethyl acetate as eluent. All the chemicals were purchased from Sigma-Aldrich and used without any further purification.

General procedure for the synthesis of dispiro 1,4-benzothiazine hybrid heterocycles: A mixture of (**3**, 1 mmol), acenaphthylene-1,2-dione or isatins (**4** or **13**, 1.2 mmol) and the respective α -amino acid (**5–8**, 1.5 mmol) in ethanol (10 mL) was heated to reflux on a water bath for 3 h. After completion of the reaction as evident from TLC, the mixture was poured into crushed ice and the resulting solid was filtered off and purified by column chromatography on silica gel employing ethyl acetate/petroleum ether (10:90 v/v) as eluent to obtain pure products **9–12** and **14–16**.

*Methyl 1'-methyl-[spiro[2',2'']-acenaphthene-1''-one]-3-oxo-3,4-dihydrospiro[benzo[b][1,4]thiazine-2,3'-pyrrolidine]-4'-carboxylate (**9a**):* Obtained as colourless solid; Yield 75%; m.p. 219–221°C; Anal. Calcd. for $\text{C}_{25}\text{H}_{20}\text{N}_2\text{O}_4\text{S}$: C, 67.55; H, 4.54; N, 6.30; S, 7.21. Found: C, 67.62; H, 4.46; N, 6.23; S, 7.28. ^1H NMR (300 MHz, CDCl_3) δ_{H} : 2.08 (s, 3H), 3.49 (t, $J=8.4\text{Hz}$, 1H), 3.73–3.82 (m, 3H), 4.19 (t, $J=9.3\text{Hz}$, 1H), 4.94 (t, $J=9.0\text{ Hz}$, 1H), 5.92 (d, $J=7.8\text{Hz}$, 1H), 6.34 (t, $J=7.5\text{ Hz}$, 1H), 6.44 (t, $J=7.8\text{ Hz}$, 1H), 6.66 (d, $J=7.5\text{ Hz}$, 1H), 7.41 (d, $J=4.5\text{Hz}$, 1H), 7.44–7.50 (m, 2H), 7.52–7.56 (m, 2H), 7.63 (d, $J=7.8\text{ Hz}$, 1H), 7.78 (d, $J=8.1\text{ Hz}$, 1H), 9.57 (s, 1H). ^{13}C NMR (75 MHz, CDCl_3) δ_{C} : 34.8, 39.3, 39.6, 39.8, 46.6, 51.6,

54.1, 58.1, 81.2, 114.9, 119.4, 121.2, 122.3, 125.1, 126.5, 126.6, 127.1, 127.7, 129.1, 130.3, 131.3, 135.6, 165.6, 170.1, 202.8.

Ethyl 1'-methyl-[spiro[2',2'']-acenaphthene-1''-one]-3-oxo-3,4-dihydrospiro[benzo[b][1,4]thiazine-2,3'-pyrrolidine]-4'-carboxylate (9b): Obtained as colourless solid; Yield 72%; m.p. 176–178°C; Anal. Calcd. for C₂₆H₂₂N₂O₄S: C, 68.10; H, 4.84; N, 6.11; S, 6.99. Found: C, 68.18; H, 4.77; N, 6.03; S, 7.07. ¹H NMR (300 MHz, CDCl₃) δ_H: 1.33 (t, *J*=7.2Hz, 3H), 2.08 (s, 3H), 3.51 (t, *J*=8.4Hz, 1H), 4.19 (t, *J*=9.3Hz, 1H), 4.29 (dd, *J*= 13.8, 6.6Hz, 2H), 4.88 (t, *J*=9.0Hz, 1H), 5.87 (d, *J*=7.5Hz, 1H), 6.39 (t, *J*=7.5Hz, 1H), 6.50 (t, *J*=6.6Hz, 1H), 6.71 (d, *J*=7.5Hz, 1H), 7.42–7.52 (m, 3H), 7.56–7.62 (m, 2H), 7.77 (d, *J*=7.6Hz, 1H), 8.44 (s, 1H). ¹³C NMR (75 MHz, CDCl₃) δ_C: 14.2, 35.2, 47.1, 54.6, 58.6, 61.2, 81.6, 115.1, 117.5, 119.9, 121.4, 123.1, 125.4, 127.0, 127.1, 127.5, 128.1, 129.5, 130.6, 131.7, 135.5, 136.0, 142.1, 166.7, 169.9, 203.1.

Methyl [spiro[3',2'']-acenaphthene-1''-one]-3-oxo-5'-phenyl-3,4-dihydrospiro[benzo[b][1,4]thiazine-2,3'-pyrrolidine]-4'-carboxylate (10a): Obtained as pale white solid; Yield 68%; m.p. 204–206°C; Anal. Calcd. for C₃₁H₂₄N₂O₄S: C, 71.13; H, 4.38; N, 5.53; S, 6.33. Found: C, 71.21; H, 4.32; N, 5.46; S, 6.41. ¹H NMR (300 MHz, DMSO-D₆/CDCl₃) δ_H: 1.20 (t, *J*=6.6Hz, 3H), 4.13 (d, *J*=6.9Hz, 2H), 4.79 (d, *J*=10.5Hz, 1H), 5.60 (d, *J*=6.3Hz, 1H), 5.83 (d, *J*=7.8Hz, 1H), 6.54 (d, *J*=7.8Hz, 1H), 6.58–6.63 (m, 1H), 6.93 (d, *J*=7.5Hz, 1H), 7.30–7.46 (m, 5H), 7.56–7.60 (m, 2H), 7.62–7.75 (m, 4H), 7.86 (d, *J*=7.8Hz, 1H), 9.83 (s, 1H). ¹³C NMR (75 MHz, CDCl₃) δ_C: 13.1, 56.3, 59.1, 59.9, 61.7, 76.6, 114.5, 115.7, 119.0, 120.5, 121.7, 124.2, 126.3, 126.5, 126.6, 126.8, 127.0, 127.3, 128.3, 129.7, 130.2, 135.9, 137.3, 139.1, 139.9, 163.9, 168.2, 202.4.

Ethyl [spiro[3',2'']-acenaphthene-1''-one]-3-oxo-5'-phenyl-3,4-dihydrospiro[benzo[b][1,4]thiazine-2,3'-pyrrolidine]-4'-carboxylate (10b): Obtained as pale white solid; Yield 86%; m.p. 201–203°C; Anal. Calcd. for C₃₁H₂₄N₂O₄S: C, 71.52; H, 4.65; N, 5.38; O, 12.29; S, 6.16

C, 71.44; H, 4.71; N, 5.45; S, 6.10. ^1H NMR (300 MHz, DMSO- D_6/CDCl_3) δ_{H} : 1.20 (t, $J=6.9\text{Hz}$, 3H), 4.17 (dd, $J=14.1$, 6.9Hz , 1H), 4.76 (d, $J=10.2\text{Hz}$, 1H), 5.64–5.69 (m, 2H), 6.57 (t, $J=7.8\text{Hz}$, 1H), 6.67 (t, $J=7.5\text{Hz}$, 1H), 7.02 (d, $J=7.8\text{Hz}$, 1H), 7.30–7.41 (m, 5H), 7.57 (d, $J=7.8\text{Hz}$, 1H), 7.65 (d, $J=6.9\text{Hz}$, 1H), 7.68–7.71 (m, 3H), 7.93 (dd, $J=6.3$, 2.4Hz , 1H). ^{13}C NMR (75 MHz, CDCl_3) δ_{C} : 14.1, 22.6, 29.6, 57.2, 60.2, 61.2, 62.8, 77.9, 115.3, 117.5, 120.3, 121.5, 123.5, 127.5, 127.6, 127.8, 128.0, 128.2, 128.4, 128.6, 129.4, 130.8, 131.1, 136.1, 136.1, 137.9, 140.3, 140.8, 165.8, 169.1, 203.6.

Methyl [spiro[3',2'']-acenaphthene-1''-one]-3-oxo-1',3,3',4,5',6',7',7a'-octahydrospiro[benzo[b][1,4]thiazine-2,2'-pyrrolizine]-1'-carboxylate (IIa): Obtained as pale white solid; Yield 75%; m.p. 199–201°C; Anal. Calcd. for $\text{C}_{27}\text{H}_{22}\text{N}_2\text{O}_3\text{S}$: C, 68.92; H, 4.71; N, 5.95; S, 6.81. Found: C, 68.99; H, 4.64; N, 6.03; S, 6.87. ^1H NMR (300 MHz, DMSO- D_6/CDCl_3) δ_{H} : 1.11 (t, $J=7.2\text{Hz}$, 3H), 2.17 (d, $J=5.7\text{Hz}$, 3H), 2.42–2.45 (m, 1H), 2.65 (t, $J=4.8\text{Hz}$, 1H), 3.72–3.78 (m, 1H), 3.94–4.03 (m, 1H), 4.45 (dd, $J=16.8\text{Hz}$, 7.8Hz , 1H), 4.83 (d, $J=9.6\text{Hz}$, 1H), 5.30 (s, 1H), 6.03 (d, $J=7.5\text{Hz}$, 1H), 6.80 (t, $J=7.5\text{Hz}$, 1H), 6.88 (t, $J=7.5\text{Hz}$, 1H), 7.19 (d, $J=6.0\text{Hz}$, 1H), 7.64 (d, $J=8.7\text{Hz}$, 2H), 7.79 (d, $J=6.9\text{Hz}$, 1H), 7.82 (d, $J=6.9\text{Hz}$, 1H), 7.95 (d, $J=8.4\text{Hz}$, 1H). ^{13}C NMR (75 MHz, CDCl_3) δ_{C} : 29.2, 30.7, 39.2, 39.4, 40.0, 40.2, 46.1, 51.4, 52.7, 64.3, 66.2, 81.8, 115.7, 117.8, 119.4, 122.9, 124.6, 124.6, 124.8, 125.8, 127.2, 129.6, 130.6, 132.1, 134.4, 162.1, 169.5, 205.3.

Ethyl [spiro[3',2'']-acenaphthene-1''-one]-3-oxo-1',3,3',4,5',6',7',7a'-octahydrospiro[benzo[b][1,4]thiazine-2,2'-pyrrolizine]-1'-carboxylate (IIb): Obtained as pale white solid; Yield 84%; m.p. 197–199°C; Anal. Calcd. for $\text{C}_{28}\text{H}_{24}\text{N}_2\text{O}_4\text{S}$: C, 69.40; H, 4.99; N, 5.78; S, 6.62. Found: C, 69.33; H, 5.86; N, 5.72; S, 6.69. ^1H NMR (300 MHz, DMSO- D_6/CDCl_3) δ_{H} : 1.11 (t, $J=7.2\text{Hz}$, 3H), 2.17 (d, $J=5.7\text{Hz}$, 3H), 2.42–2.45 (m, 1H), 2.65 (t, $J=4.8\text{Hz}$, 1H), 3.72–3.78 (m, 1H), 3.94–4.03 (m, 1H), 4.45 (dd, $J=16.8$, 7.8Hz , 1H), 4.83 (d, $J=9.6\text{Hz}$, 1H), 5.30 (s, 1H), 6.03 (d, $J=7.5\text{Hz}$, 1H), 6.80 (t, $J=7.5\text{Hz}$, 1H), 6.88 (t, $J=7.5\text{Hz}$, 1H), 7.19 (d, $J=6.0\text{Hz}$,

1H), 7.64 (d, $J=8.7$ Hz, 2H), 7.79 (d, $J=6.9$ Hz, 1H), 7.82 (d, $J=6.9$ Hz, 1H), 7.95 (d, $J=8.4$ Hz, 1H). ^{13}C NMR (75 MHz, CDCl_3) δ_{C} : 13.5, 29.4, 30.6, 46.1, 52.7, 60.5, 64.2, 66.3, 81.7, 115.7, 117.6, 119.4, 123.0, 124.6, 124.8, 125.7, 125.8, 127.2, 129.6, 130.6, 132.1, 134.2, 134.4, 140.9, 162.4, 169.0, 205.5

Methyl [spiro[3',2'']-acenaphthene-1''-one]-3-oxo-3,3',4,5',7',7a'-hexahydro-1'H-spiro[benzo[b][1,4]thiazine-2,6'-pyrrolo[1,2-c]thiazole]-7'-carboxylate (12a): Obtained as pale white solid; Yield 74%; m.p. 220–222°C; Anal. Calcd. for $\text{C}_{26}\text{H}_{20}\text{N}_2\text{O}_3\text{S}$: C, 63.92; H, 4.13; N, 5.73; S, 13.13. Found: C, 63.84; H, 4.18; N, 5.78; S, 13.06. ^1H NMR (300 MHz, $\text{DMSO-}d_6/\text{CDCl}_3$) δ_{H} : 3.12 (d, $J=7.5$ Hz, 1H), 3.32–3.38 (m, 1H), 3.42 (d, $J=8.7$ Hz, 1H), 3.76–3.83 (m, 4H), 4.62 (d, $J=10.2$ Hz, 1H), 4.89 (d, $J=4.2$ Hz, 1H), 5.89 (d, $J=7.8$ Hz, 1H), 6.70 (t, $J=7.5$ Hz, 1H), 6.81 (t, $J=7.2$ Hz, 1H), 7.11 (d, $J=7.5$ Hz, 1H), 7.27 (d, $J=6.6$ Hz, 1H), 7.43–7.48 (m, 1H), 7.57–7.62 (m, 1H), 7.82 (d, $J=8.4$ Hz, 1H), 7.95 (t, $J=8.7$ Hz, 2H), 9.51 (s, 1H). ^{13}C NMR (75 MHz, CDCl_3) δ_{C} : 34.6, 50.0, 51.2, 62.7, 66.6, 79.1, 114.9, 116.0, 119.1, 122.0, 123.2, 124.8, 126.1, 126.5, 126.7, 127.2, 128.5, 129.7, 130.2, 132.2, 135.5, 139.3, 161.3, 168.1, 199.6.

Ethyl [spiro[3',2'']-acenaphthene-1''-one]-3-oxo-3,3',4,5',7',7a'-hexahydro-1'H-spiro[benzo[b][1,4]thiazine-2,6'-pyrrolo[1,2-c]thiazole]-7'-carboxylate (12b): Obtained as pale white solid; Yield 71%; m.p. 222–224°C; Anal. Calcd. for $\text{C}_{27}\text{H}_{22}\text{N}_2\text{O}_4\text{S}_2$: C, 64.52; H, 4.41; N, 5.57; S, 12.76. Found: C, 64.59; H, 4.34; N, 5.63; S, 12.68. ^1H NMR (300 MHz, $\text{DMSO-}d_6/\text{CDCl}_3$) δ_{H} : 1.28 (t, $J=7.2$ Hz, 3H), 3.30–3.36 (m, 1H), 3.42 (d, $J=8.7$ Hz, 1H), 3.77 (d, $J=8.7$ Hz, 1H), 4.23 (dd, $J=14.1, 7.2$ Hz, 2H), 4.59 (d, $J=10.2$ Hz, 1H), 4.83–4.9 (m, 1H), 5.84 (d, $J=7.8$ Hz, 1H), 6.68 (t, $J=7.8$ Hz, 1H), 6.79 (t, $J=7.5$ Hz, 1H), 7.08 (d, $J=7.5$ Hz, 1H), 7.26 (d, $J=6.9$ Hz, 1H), 7.46 (t, $J=7.5$ Hz, 1H), 7.59–7.64 (m, 1H), 7.83 (d, $J=8.4$ Hz, 1H), 7.91 (d, $J=7.2$ Hz, 1H), 7.98 (d, $J=8.1$ Hz, 1H), 9.74 (s, 1H). ^{13}C NMR (75 MHz, CDCl_3) δ_{C} : 13.3, 35.0, 38.1, 50.5,

51.6, 60.5, 63.0, 66.9, 79.6, 115.2, 116.5, 119.4, 122.3, 123.5, 125.0, 126.4, 126.8, 126.9, 127.6, 128.8, 130.0, 130.4, 132.4, 135.6, 139.6, 161.7, 167.8, 200.1.

Methyl 1'-methyl-[spiro[2',3'']-oxindole]-3-oxo-3,4-dihydrospiro[benzo[b][1,4]thiazine-2,3'-pyrrolidine]-4'-carboxylate (14a): Obtained as colourless solid; Yield 71%; m.p. 266-268°C; Anal. Calcd. for C₂₁H₁₉N₃O₄S: C, 61.60; H, 4.68; N, 10.26; S, 7.83. Found: C, 61.67; H, 4.61; N, 10.29; S, 7.75. ¹H NMR (300 MHz, DMSO-D₆/CDCl₃) δ_H: 3.11 (s, 3H), 3.31 (t, J=11.2Hz, 1H), 3.74 (s, 3H), 4.07 (t, J=9.3Hz, 1H), 4.82–4.89 (m, 1H), 6.33 (d, J=7.5Hz, 1H), 6.29 (d, J=6.9Hz, 1H), 6.71–6.78 (m, 2H), 6.80–6.91 (m, 2H), 7.05 (d, J=6.9Hz, 1H), 7.13–7.15 (m, 1H), 9.56 (s, 1H), 10.30 (s, 1H). C¹³ NMR (75 MHz, CDCl₃) δ_C: 33.8, 44.8, 50.4, 52.1, 55.4, 76.6, 107.4, 114.1, 115.2, 119.8, 121.4, 124.4, 125.8, 128.1, 135.1, 141.8, 164.5, 169.0, 173.5.

Ethyl 1'-methyl-[spiro[2',3'']-oxindole]-3-oxo-3,4-dihydrospiro[benzo[b][1,4]thiazine-2,3'-pyrrolidine]-4'-carboxylate (14b): Obtained as pale white solid; Yield 70%; m.p. 279–281°C; Anal. Calcd. for C₂₂H₂₁N₃O₄S: C, 62.40; H, 5.00; N, 9.92, S, 7.57. Found: C, 62.32; H, 4.93; N, 9.98; S, 7.49. ¹H NMR (300 MHz, DMSO-D₆/CDCl₃) δ_H: 1.29 (t, J=7.2Hz, 3H), 2.05 (s, 3H), 3.32 (t, J=8.7Hz, 1H), 4.06 (t, J=9.0Hz, 1H), 4.21 (dd, J=14.4, 7.2Hz, 2H), 4.81 (t, J=8.7Hz, 1H), 6.22 (d, J=7.5Hz, 1H), 6.28 (d, J=7.8Hz, 1H), 6.75 (t, J=6.3Hz, 2H), 6.79–6.88 (m, 2H), 7.06 (d, J=7.2Hz, 1H), 7.14 (d, J=6.9Hz, 1H), 9.52 (s, 1H), 10.26 (s, 1H). ¹³C NMR (75 MHz, CDCl₃) δ_C: 12.8, 33.7, 44.6, 52.0, 55.2, 59.2, 76.6, 107.2, 113.9, 115.2, 119.6, 121.1, 123.2, 124.3, 125.6, 128.0, 135.0, 141.7, 164.4, 168.3, 173.3.

Methyl 1'-methyl-[spiro[2',3'']-5-chlorooxindole]-3-oxo-3,4-dihydrospiro[benzo[b][1,4]thiazine-2,3'-pyrrolidine]-4'-carboxylate (14c): Obtained as colourless solid; Yield 81%; m.p. 272-274°C; Anal. Calcd. for C₂₁H₁₈ClN₃O₄S: C, 56.82; H, 4.09; N, 9.47; S, 7.22. Found: C, 56.76; H, 4.03; N, 9.40; S, 7.18. ¹H NMR (300 MHz, DMSO-D₆/CDCl₃) δ_H: 2.23 (s, 3H), 3.50 (t, J=8.7 Hz, 1H), 3.70 (s, 1H), 3.91–3.95 (m, 3H), 4.20 (t, J=9.3Hz, 1H), 4.95–5.01 (m,

1H), 6.34–6.38 (m, 1H), 6.55–6.57 (m, 1H), 6.95–6.98 (m, 1H), 7.11 (d, $J=8.1\text{Hz}$, 2H), 7.22 (d, $J=2.1\text{Hz}$, 1H), 7.30–7.32 (m, 1H), 9.93 (s, 1H), 10.81 (s, 1H). ^{13}C NMR (75 MHz, CDCl_3) δ_{C} : 34.4, 45.2, 50.9, 52.7, 56.0, 76.6, 109.0, 114.7, 115.7, 121.9, 123.9, 125.4, 126.4, 126.6, 126.8, 128.4, 135.6, 140.9, 165.0, 169.4, 173.8.

Ethyl 1'-methyl-[spiro[2',3'']-5-chlorooxindole]-3-oxo-3,4-dihydrospiro[benzo[b][1,4]thiazine-2,3'-pyrrolidine]-4'-carboxylate (14d): Obtained as colourless solid; Yield 82%; m.p. 289–291°C; Anal. Calcd. for $\text{C}_{22}\text{H}_{20}\text{ClN}_3\text{O}_4\text{S}$: C, 57.70; H, 4.40; Cl, 7.74; N, 9.18; S, 7.00. Found: C, 57.77; H, 4.32; Cl, 7.81; N, 9.23; S, 7.06. ^1H NMR (300 MHz, $\text{DMSO-}d_6/\text{CDCl}_3$) δ_{H} : 2.08 (s, 3H), 3.34–3.40 (m, 1H), 4.04 (t, $J=9.0\text{Hz}$, 1H), 4.22 (dd, $J=13.1$, 7.2Hz, 2H), 4.78 (t, $J=9.0\text{Hz}$, 1H), 6.19 (d, $J=7.1\text{Hz}$, 1H), 6.38–6.41 (m, 1H), 6.76–6.79 (m, 2H), 6.84–6.87 (m, 1H), 7.13–7.16 (m, 1H), 9.47 (s, 1H), 10.40 (s, 1H). ^{13}C NMR (75 MHz, CDCl_3) δ_{C} : 13.7, 29.0, 34.7, 45.6, 53.2, 56.3, 60.4, 78.4, 109.2, 115.0, 116.3, 122.2, 124.3, 125.9, 126.7, 126.9, 127.2, 128.8, 136.0, 141.2, 165.5, 169.3, 171.3.

Methyl [spiro[2',3'']-oxindole]-3-oxo-5'-phenyl-3,4-dihydrospiro[benzo[b][1,4]thiazine-2,3'-pyrrolidine]-4'-carboxylate (15a): Obtained as pale white solid; Yield 99%; m.p. 228–230°C; Anal. Calcd. for $\text{C}_{26}\text{H}_{21}\text{N}_3\text{O}_4\text{S}$: C, 66.23; H, 4.49; N, 8.91; S, 6.80. Found: C, 66.31; H, 4.41; N, 8.97; S, 6.73. ^1H NMR (300 MHz, $\text{DMSO-}d_6/\text{CDCl}_3$) δ_{H} : 2.81 (d, $J=6.9\text{Hz}$, 1H), 3.67 (s, 3H), 4.75 (d, $J=9.9\text{Hz}$, 1H), 5.58–5.64 (m, 1H), 6.31 (d, $J=7.5\text{Hz}$, 1H), 6.34–6.37 (m, 1H), 6.84–6.88 (m, 3H), 7.17–7.24 (m, 3H), 7.28–7.34 (m, 3H), 7.61 (d, $J=7.5\text{Hz}$, 2H), 9.64 (s, 1H), 10.35 (s, 1H). ^{13}C NMR: 50.1, 55.3, 56.0, 59.7, 73.0, 107.0, 113.9, 114.9, 115.7, 119.3, 121.1, 121.8, 123.0, 125.4, 125.6, 125.8, 126.1, 126.4, 126.7, 127.7, 134.9, 139.5, 140.8, 164.2, 168.2, 175.9.

Ethyl [spiro[2',3'']-oxindole]-3-oxo-5'-phenyl-3,4-dihydrospiro[benzo[b][1,4]thiazine-2,3'-pyrrolidine]-4'-carboxylate (15b): Obtained as colourless solid; Yield 73%; m.p. 218–220°C; Anal. Calcd. for $\text{C}_{27}\text{H}_{23}\text{N}_3\text{O}_4\text{S}$: C, 66.79; H, 4.77; N, 8.65; S, 6.60. Found: C, 66.71; H,

4.82; N, 8.57; S, 6.67. ^1H NMR (300 MHz, DMSO- D_6/CDCl_3) δ_{H} : 1.21 (t, $J=7.2\text{Hz}$, 3H), 2.73 (d, $J=7.5\text{Hz}$, 1H), 4.10–4.18 (m, 2H), 4.71 (d, $J=9.9\text{Hz}$, 1H), 6.00 (m, 1H), 6.31 (d, $J=7.5\text{Hz}$, 1H), 6.35–6.38 (m, 1H), 6.82–6.88 (m, 3H), 6.95 (t, $J=7.8\text{Hz}$, 1H), 7.18–7.24 (m, 1H), 7.29–7.37 (m, 3H), 7.62 (d, $J=7.2\text{Hz}$, 2H), 7.67 (s, 1H), 9.58 (s, 1H), 10.27 (s, 1H). ^{13}C NMR (75 MHz, CDCl_3) δ_{C} : 13.1, 56.0, 57.5, 60.0, 61.1, 73.7, 108.0, 114.7, 120.3, 121.9, 123.7, 126.3, 126.5, 126.7, 126.8, 127.0, 127.4, 128.5, 135.5, 139.8, 141.0, 164.8, 168.4, 176.6.

Methyl [spiro[2',3'']-oxindole]-3-oxo-5'-phenyl-3,4-dihydrospiro[benzo[b][1,4]thiazine-2,3'-pyrrolidine]-4'-carboxylate (15c): Obtained as pale white solid; Yield 99%; m.p. 212–214°C; Anal. Calcd. for $\text{C}_{26}\text{H}_{20}\text{ClN}_3\text{O}_4\text{S}$: C, 61.72; H, 3.98; Cl, 7.01; N, 8.30; S, 6.34. Found: C, 61.80; H, 3.91; Cl, 7.08; N, 8.37; S, 6.34. ^1H NMR (300 MHz, DMSO- D_6/CDCl_3) δ_{H} : 2.81 (d, $J=6.9\text{Hz}$, 1H), 3.66 (s, 3H), 3.80 (s, 1H), 4.75 (d, $J=9.9\text{Hz}$, 1H), 5.58–5.63 (m, 1H), 6.29 (d, $J=7.5\text{Hz}$, 1H), 6.35–6.37 (m, 1H), 6.83–6.88 (m, 3H), 6.93 (d, $J=7.3\text{Hz}$, 1H), 7.17–7.23 (m, 3H), 7.28–7.34 (m, 3H), 7.61 (d, $J=7.5\text{Hz}$, 2H), 9.63 (s, 1H), 10.35 (s, 1H). ^{13}C NMR (75 MHz, CDCl_3) δ_{C} : 50.1, 55.3, 56.0, 59.7, 73.0, 107.0, 113.9, 114.9, 115.7, 119.3, 121.1, 121.8, 123.0, 125.4, 125.6, 125.8, 126.1, 126.4, 126.7, 127.7, 134.9, 139.5, 139.5, 140.8, 164.2, 168.2, 175.8.

Ethyl [spiro[2',3'']-5-chlorooxindole]-3-oxo-5'-phenyl-3,4-dihydrospiro[benzo[b][1,4]thiazine-2,3'-pyrrolidine]-4'-carboxylate (15d): Obtained as pale white solid; Yield 98%; m.p. 240–242°C; Anal. Calcd. for $\text{C}_{27}\text{H}_{22}\text{ClN}_3\text{O}_4\text{S}$: C, 62.36; H, 4.26; N, 8.08; S, 6.17. Found: C, 62.44; H, 4.19; N, 8.02; S, 6.24. ^1H NMR (300 MHz, DMSO- D_6/CDCl_3) δ_{H} : 1.20 (t, $J=7.2\text{Hz}$, 3H), 4.08–4.14 (m, 2H), 4.60 (d, $J=9.3\text{Hz}$, 1H), 5.55 (dd, $J=9.6, 6.3\text{Hz}$, 1H), 6.21 (d, $J=5.1\text{Hz}$, 1H), 6.39–6.41 (m, 1H), 6.84–6.92 (m, 3H), 7.15–7.20 (m, 2H), 7.27–7.37 (m, 3H), 7.58 (d, $J=7.5\text{Hz}$, 2H), 9.87 (s, 1H), 10.7 (s, 1H). ^{13}C NMR (75 MHz, CDCl_3) δ_{C} :

12.6, 27.8, 55.1, 56.0, 59.1, 59.8, 72.9, 108.2, 114.1, 115.1, 121.2, 123.4, 124.1, 125.9, 126.0, 126.2, 126.7, 127.4, 128.6, 135.1, 139.5, 139.7, 164.1, 167.6, 175.9.

Methyl [spiro[5',3'']-oxindole]-3-oxo-3,3',4,5',7',7a'-hexahydro-1'H-spiro[benzo[b][1,4]thiazine-2,6'-pyrrolo[1,2-c]thiazole]-7'-carboxylate (16a): Obtained as pale white solid; Yield 73%; m.p. 252–254°C; Anal. Calcd. for C₂₂H₁₉N₃O₄S₂: C, 58.26; H, 4.22; N, 9.27; S, 14.14. Found: C, 58.19; H, 4.27; N, 9.31; S, 14.07. ¹H NMR (300 MHz, DMSO-D₆/CDCl₃) δ_H: 2.59 (t, *J*=1.8Hz, 1H), 2.96 (dd, *J*=10.5, 5.4Hz, 1H), 3.34 (d, *J*= 7.8Hz, 1H), 3.64 (d, *J*=7.8Hz, 1H), 3.74 (s, 3H), 4.54 (d, *J*=10.2Hz, 1H). 4.77–4.85 (m, 1H), 6.50 (dd, *J*=11.1, 7.2Hz, 2H), 6.86–6.92 (m, 3H), 7.05 (d, *J*=7.8Hz, 1H), 7.18 (d, *J*=7.5Hz, 1H), 7.41 (d, *J*=7.5Hz, 1H), 9.77 (s, 1H), 10.37 (s, 1H). ¹³C NMR (75 MHz, CDCl₃) δ_C: 32.5, 47.5, 49.7, 50.6, 61.0, 65.3, 73.4, 107.7, 114.4, 115.2, 119.4, 121.3, 122.6, 125.3, 125.7, 126.2, 128.3, 135.0, 141.1, 161.6, 167.7, 173.1.

Ethyl [spiro[5',3'']-oxindole]-3-oxo-3,3',4,5',7',7a'-hexahydro-1'H-spiro[benzo[b][1,4]thiazine-2,6'-pyrrolo[1,2-c]thiazole]-7'-carboxylate (16b): Obtained as pale white solid; Yield 88%; m.p. 271–273°C; Anal. Calcd. for C₂₃H₂₁N₃O₄S₂: C, 59.08; H, 4.53; N, 8.99; S, 13.72. Found: C, 59.16; H, 4.46; N, 9.05; S, 13.65. ¹H NMR (300 MHz, DMSO-D₆/CDCl₃) δ_H: 1.21–1.30(m, 3H), 3.00 (dd, *J*=10.8, 6.3Hz, 2H), 3.24 (dd, *J*=10.8, 6.3Hz, 1H), 3.41(d, *J*=8.1Hz, 1H), 3.72 (d, *J*=8.1Hz, 1H), 4.19–4.28 (m, 2H), 4.52 (d, *J*=10.2Hz, 1H), 4.80–4.8 (m, 1H), 6.54 (d, *J*=7.8Hz, 2H), 6.82–6.96 (m, 3H), 7.06–7.11 (m, 1H), 7.35 (d, *J*=7.5Hz, 1H), 9.40 (s, 1H), 10.0 (s, 1H). ¹³C NMR (75 MHz, CDCl₃) δ_C: 13.6, 34.7, 50.1, 51.4, 60.8, 62.2, 66.6, 75.1, 108.9, 115.5, 116.8, 120.4, 122.4, 123.2, 126.6, 127.2, 127.4, 129.4, 135.8, 141.7, 161.9, 168.2, 173.9.

Methyl [spiro[5',3'']-5-chlorooxindole]-3-oxo-3,3',4,5',7',7a'-hexahydro-1'H-spiro[benzo[b][1,4]thiazine-2,6'-pyrrolo[1,2-c]thiazole]-7'-carboxylate (16c): Obtained as pale white solid; Yield 76%; m.p. 266–268°C; Anal. Calcd. for C₂₂H₁₈ClN₃O₄S₂: C, 54.15; H, 3.72; N,

8.61; S, 13.14. Found: C, 54.07 H, 3.80 N, 8.68; S, 13.05. ^1H NMR (300 MHz, DMSO- D_6/CDCl_3) δ_{H} : 3.20 (dd, $J=10.5$, 6.0Hz, 1H), 3.37 (d, $J=8.1$ Hz, 1H), 3.66 (t, $J=7.8$ Hz, 2H), 3.76 (s, 3H), 4.51 (d, $J=9.9$ Hz, 1H), 4.77–4.82 (m, 1H), 6.46 (d, $J=8.4$ Hz, 1H), 6.56 (d, $J=7.8$ Hz, 1H), 6.84–6.89 (m, 1H), 6.92–6.97 (m, 1H), 7.06 (dd, $J=8.1$, 1.8Hz, 1H), 7.20 (d, $J=7.2$ Hz, 1H), 7.45 (d, $J=1.8$ Hz, 1H), 9.74 (s, 1H), 10.42 (s, 1H). ^{13}C NMR (75 MHz, CDCl_3) δ_{C} : 33.5, 48.6, 50.5, 51.3, 56.2, 61.9, 66.0, 74.1, 109.4, 115.1, 115.8, 122.0, 125.0, 126.4, 127.0, 128.8, 135.5, 140.3, 161.7, 168.2, 173.6.

Ethyl [spiro[5',3'']-5-chlorooxindole]-3-oxo-3,3',4,5',7',7a'-hexahydro-1'H-spiro[benzo[b][1,4]thiazine-2,6'-pyrrolo[1,2-c]thiazole]-7'-carboxylate (16d): Obtained as pale white solid; Yield 94%; m.p. 266–268°C; Anal. Calcd. for $\text{C}_{23}\text{H}_{20}\text{ClN}_3\text{O}_4\text{S}_2$: C, 55.03; H, 4.02; N, 8.37; S, 12.77. Found: C, 55.09; H, 3.95; N, 8.29; S, 12.83. ^1H NMR (300 MHz, DMSO- D_6/CDCl_3) δ_{H} : 1.23–1.33 (m, 3H), 2.95 (dd, $J=7.2$, 6.0Hz, 1H), 3.15–3.20 (m, 2H), 3.36 (d, $J=10.5$ Hz, 1H), 3.63 (d, $J=7.8$ Hz, 1H), 4.17–4.26 (m, 2H), 4.58 (d, $J=9.9$ Hz, 1H), 4.74–4.79 (m, 1H), 6.43 (d, $J=7.1$ Hz, 1H), 6.54 (d, $J=7.8$ Hz, 1H), 6.84–6.96 (m, 2H), 7.03–7.06 (m, 1H), 7.19 (d, $J=7.5$ Hz, 1H), 9.86 (s, 1H), 10.52 (s, 1H). ^{13}C NMR (75 MHz, CDCl_3) δ_{C} : 13.2, 28.5, 33.6, 48.7, 50.5, 60.4, 61.9, 66.0, 74.2, 109.4, 115.1, 115.9, 122.0, 124.9, 125.0, 126.4, 127.0, 128.8, 135.6, 140.3, 161.8, 167.6, 173.7.

Figure 1. ^1H NMR spectrum of 9a

Figure 2. ^{13}C NMR spectrum of 9a

Figure 3. ^1H NMR spectrum of **9b**

Figure 4. ^{13}C NMR spectrum of **9b**

Figure 5. ^1H NMR spectrum of 10a

Figure 6. ^{13}C NMR spectrum of 10a

Figure 7. ^1H NMR spectrum of **10b**

Figure 8. ^{13}C NMR spectrum of **10b**

Figure 13. ^1H NMR spectrum of 12a

Figure 14. ^{13}C NMR spectrum of 12a

Figure 15. ^1H NMR spectrum of 12b

Figure 16. ^{13}C NMR spectrum of 12b

Figure 19. C,H-COSY spectrum of 12b

Figure 20. HMBC spectrum of 12b

Figure 21. ^1H NMR spectrum of 14a

Figure 22. ^{13}C NMR spectrum of 14a

Figure 25. ^1H NMR spectrum of **14c**

Figure 26. ^{13}C NMR spectrum of **14c**

Figure 27. ^1H NMR spectrum of 14d

Figure 28. ^{13}C NMR spectrum of 14d

Figure 33. ^1H NMR spectrum of **15c**

Figure 34. ^{13}C NMR spectrum of **15c**

Figure 35. ^1H NMR spectrum of **15d**

Figure 36. ^{13}C NMR spectrum of **15d**

Figure 37. ¹H NMR spectrum of 16a

Figure 38. ^{13}C NMR spectrum of **16a**

Figure 39. ^1H NMR spectrum of **16b**

Figure 40. ^{13}C NMR spectrum of **16b**

Figure 41. ^1H NMR spectrum of 16c

Figure 42. ^{13}C NMR spectrum of 16c

Figure 43. ^1H NMR spectrum of 16d

Figure 44. ^{13}C NMR spectrum of 16d