Supporting Information

A Highly Efficient DBU-Catalyzed Green Synthesis of Spirooxindoles

Liqun Wang, a Daming Zhang, a Jian Li, a Guangyang Xu, a and Jiangtao Sun a

aSchool of Pharmaceutical Engineering & Life Science, Changzhou University, Changzhou
213164, P. R. China
General Information

All experiments were carried out under air unless otherwise indicated. All solvents were used directly without further purification. $^1$H NMR and $^{13}$C NMR spectra were reported on a Brucker 300 MHz, 400 MHz, 500 MHz spectrometer in CDCl$_3$ or DMSO-$d_6$ using trimethylsilane (TMS) as internal standard unless otherwise noted. HRMS were performed using electrospray ionization (ESI) with Bruker Daltonics, Inc. APEXIII 7.0 TESLA FTMS. Agilent 7890/5975C-GC/MSD. Melting points were determined on a SGW X-4B melting point apparatus. Reactions were monitored by thin layer chromatography (TLC), column chromatography purifications were carried out using silica gel GF254. Ethoxycarbonyl methyl triphenylphosphonium bromide$^1$, isothiocyanatocetate ester$^2$ and 1-(3,5-dimethyl-1H-pyrazol-1-yl)-2-isothiocyanatoethanone$^3,4$ was prepared according the literature procedure.

Preparation of the methyleneindolinones substrates$^5,6$

\[
\text{R}^1\text{H} \quad \text{Ph}_3\text{P}=\text{CO}_2\text{Et} \quad \text{toluene, reflux} \quad \text{EtO}_2\text{C} \quad \text{R}^1\text{H} \quad \text{N} \quad \text{Me}
\]

General procedure: To a solution of substituted 1-methylisatin (5 mmol, 1equiv) in toluene (30 mL) was added the Ethyl 2-(triphenylphosphoranylidene)acetate (5 mmol, 1 equiv); the mixture was heated to reflux. After the reaction was complete, the solvent was removed under reduced pressure and the residue was purified by flash chromatography to give the product.

(E)-ethyl 2-(1-methyl-2-oxoindolin-3-ylidene)acetate: $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ (ppm) 8.57-8.54(m, 1H), 8.40-8.34(td, $J = 7.5$ Hz, $J = 1.2$ Hz, 1H), 7.09-7.03(m, 1H), 6.91(s, 1H), 6.81-6.78(d, $J = 7.8$ Hz , 1H), 4.37-4.29(q, $J = 7.2$ Hz, 2H), 3.24(s, 3H), 1.38(t, $J = 7.2$ Hz, 3H).

(E)-ethyl 2-(5-chloro-1-methyl-2-oxoindolin-3-ylidene)acetate: $^1$H NMR (300 MHz, CDCl$_3$); $\delta$ (ppm) 8.60-8.59(d, $J = 2.1$ Hz, 1H), 7.37-7.33(dd, $J = 8.4$ Hz, $J = 2.1$ Hz, 1H), 6.94(s, 1H), 6.74-6.71(d, $J = 8.4$ Hz ,1H), 4.38-4.30(q, $J = 7.2$ Hz, 2H), 3.23(s, 3H), 1.38(t, $J = 7.2$ Hz, 3H).
(E)-ethyl 2-(6-chloro-1-methyl-2-oxoindolin-3-ylidene)acetate: $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ (ppm) 8.53-8.51(d, $J = 8.4$ Hz, 1H), 7.04-7.01(dd, $J = 8.4$ Hz, $J = 1.6$ Hz, 1H), 6.90(s, 1H), 6.80-6.79(d, $J = 2.0$ Hz ,1H), 4.34-4.29(q, $J = 7.2$ Hz, 2H), 3.22(s, 3H), 1.37(t, $J = 7.2$ Hz, 3H).

(E)-ethyl 2-(7-chloro-1-methyl-2-oxoindolin-3-ylidene)acetate: $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ (ppm) 8.61-8.58 (dd, $J = 7.5$ Hz, $J = 0.9$ Hz, 1H), 7.49-7.45(dd, $J = 8.1$ Hz, $J = 1.2$ Hz, 1H), 6.95 (s, 1H), 6.94-6.88 (t, $J = 8.1$ Hz ,1H), 4.36-4.28 (q, $J = 7.2$ Hz, 2H), 3.64 (s, 3H), 1.37 (t, $J = 7.2$ Hz, 3H).

(E)-ethyl 2-(4-bromo-1-methyl-2-oxoindolin-3-ylidene)acetate: $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ (ppm) 7.7 (s, 1H), 7.22-7.12 (m, 2H), 6.78-6.75 (dd, $J = 6.8$ Hz, $J = 1.6$ Hz, 1H), 4.38-4.45 (q, $J = 7.2$ Hz, 2H), 3.2 (s, 3H), 1.39 (t, $J = 7.2$ Hz, 3H).

(E)-ethyl 2-(5-bromo-1-methyl-2-oxoindolin-3-ylidene)acetate: $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ (ppm) 8.73-8.72 (d, $J = 1.6$ Hz, 1H), 7.51-7.48 (dd, $J = 8.4$ Hz, $J = 2.0$ Hz, 1H), 6.93 (s, 1H), 6.69-6.66 (d, $J = 8.4$ Hz ,1H), 4.37-4.31 (q, $J = 7.2$ Hz, 2H), 3.22 (s, 3H), 1.38 (t, $J = 7.2$ Hz, 3H).
(E)-ethyl 2-(6-bromo-1-methyl-2-oxoindolin-3-ylidene)acetate: $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ (ppm) 8.51-8.53(d, $J = 8.4$ Hz, 1H), 7.05-7.10(dd, $J = 8.4$ Hz, $J = 1.6$ Hz, 1H), 6.93(s, 1H), 6.8-6.75(d, $J = 2$ Hz, 1H), 4.35-4.28(q, $J = 7.2$ Hz, 2H), 3.22(s, 3H), 1.37(t, $J = 7.2$ Hz, 3H).

(E)-ethyl 2-(7-bromo-1-methyl-2-oxoindolin-3-ylidene)acetate: $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ (ppm) 8.60-8.58(dd, $J = 7.6$ Hz, $J = 0.8$ Hz, 1H), 7.47-7.45(dd, $J = 8.0$ Hz, $J = 0.8$ Hz, 1H), 6.94(s, 1H), 6.92-6.88(t, $J = 8.0$ Hz, 1H), 4.35-4.29(q, $J = 7.2$ Hz, 2H), 3.63(s, 3H), 1.37(t, $J = 7.2$ Hz, 3H).

(E)-ethyl 2-(5-fluoro-1-methyl-2-oxoindolin-3-ylidene)acetate: $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ (ppm) 8.39-8.36(dd, $J = 9.2$ Hz, $J = 2.0$ Hz, 1H), 7.11-7.06(td, $J = 8.4$ Hz, $J = 2.4$ Hz, 1H), 6.94(s, 1H), 6.73-6.69(dd, $J = 8.8$ Hz, $J = 4.0$ Hz, 1H), 4.36-4.31(q, $J = 7.2$ Hz, 2H), 3.22(s, 3H), 1.38(t, $J = 7.2$ Hz, 3H).

(E)-ethyl 2-(1-methyl-2-oxo-5-(trifluoromethoxy)indolin-3-ylidene)acetate: $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ (ppm) 8.54(d, $J = 1.6$ Hz, 1H), 7.27-7.23(m, 1H), 6.96(s, 1H), 6.81-6.75(d, $J = 11.2$ Hz, 1H), 4.39-4.31(q, $J = 9.6$ Hz, 2H), 3.24(s, 3H), 1.38(t, $J = 9.6$ Hz, 3H).

(E)-ethyl 2-(1,5-dimethyl-2-oxoindolin-3-ylidene)acetate: $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ (ppm) 8.38(s, 1H), 7.19-7.16(d, $J = 8.1$ Hz, 1H), 6.88(s, 1H), 6.69-6.66(d, $J = 8.1$ Hz, 1H), 4.37-4.29(q, $J = 7.2$ Hz, 2H), 3.20(s, 3H), 2.35(s, 3H), 1.38(t, $J = 7.2$ Hz, 3H).
**(E)-ethyl 2-(1,5,7-trimethyl-2-oxoindolin-3-ylidene)acetate:** $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ (ppm) 8.28(s, 1H), 6.91(s, 1H), 6.86(s, 1H), 4.35-4.29(q, $J = 7.2$ Hz, 2H), 3.48(s, 3H), 2.50(s, 3H), 2.29(s, 3H), 1.37(t, $J = 7.2$ Hz, 3H).

**General procedure for the synthesis of spirooxindoles**

![Chemical structure](image)

To a Schlenk tube was added methyleneindolinone (1 mmol), ethyl 2-isothiocyanatoacetate (38 mg, 1.1 mmol) and EtOH (3 mL) under air, then DBU (1 mol%) was added. The resulting solution was stirred at room temperature for 1.5 h. Then the reaction solution was directly evaporated to remove the ethanol to give the crude product as solid. Then the solid was washed with cold methanol to give the spirooxindole.

**Diethyl 1-methyl-2-oxo-2'-thioxospiro[indoline-3,3'-pyrrolidine]-4',5'-dicarboxylate (3a)**

Following the typical procedure above, the title compound was obtained as white solid, mp 231-233°C; $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ (ppm) 8.15 (s, 1H), 7.38-7.32 (td, $J = 7.8$ Hz, $J = 1.8$ Hz, 1H), 7.09-7.01 (m, 2H), 6.91-6.88 (d, $J = 7.8$ Hz, 1H), 5.27-5.24 (d, $J = 8.7$ Hz, 1H), 4.39-4.23 (m, 3H), 3.32 (s,3H), 1.33 (t, $J = 7.2$ Hz, 3H), 0.69 (t, $J = 7.2$ Hz, 3H); $^{13}$C NMR (75 MHz, CDCl$_3$):200.0, 173.5, 167.6, 167.4, 144.5, 130.0, 127.4, 123.3, 123.1, 108.8, 68.3, 62.9, 61.6, 61.4, 51.8, 27.1, 14.1, 13.4.

**Diethyl 5-chloro-1-methyl-2-oxo-2'-thioxospiro[indoline-3,3'-pyrrolidine]-4',5'-dicarboxylate (3b)**

Following the typical procedure above, the title compound was white solid, mp 242-244°C; $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ (ppm) 8.16 (s, 1H), 7.34-7.32 (dd, $J = 8.4$ Hz, $J = 2.0$ Hz, 1H), 7.07-7.06 (d, $J = 2.0$ Hz, 1H), 6.83-6.81 (d, $J = 8.3$ Hz, 1H), 5.24-5.22 (d, $J = 8.6$ Hz, 1H), 4.36-4.26 (m, 3H), 3.95-3.88 (m, 1H), 3.85-3.78 (m, 1H), 3.30 (s,3H), 1.33 (t, $J = 7.2$ Hz, 3H), 0.77 (t, $J = 7.2$ Hz, 3H); $^{13}$C NMR (125 MHz, CDCl$_3$):199.1, 173.0, 167.4, 167.2, 143.2, 129.9, 128.9, 128.3, 124.0, 109.6, 68.2, 63.0, 61.7, 61.6, 51.7, 27.2, 14.1, 13.5. HRMS (ESI) calcd for C$_{18}$H$_{20}$ClN$_2$O$_5$S (M+H)$^+$ 411.0776, found 411.0782.
Diethyl 6-chloro-1-methyl-2-oxo-2'-thioxospiro[indoline-3,3'-pyrrolidine]-4',5'-dicarboxylate (3c)

Following the typical procedure above, the title compound was obtained as white solid, mp 232-234\(^\circ\)C; \(^1\)H NMR (500 MHz, CDCl\(_3\)): \(\delta\) (ppm) 8.23 (s, 1H), 7.04-7.01 (d, \(J = 8.0\), 1H), 7.00-6.98 (d, \(J = 8.0\) Hz, 1H), 6.90 (s, 1H), 5.22-5.20 (d, \(J = 9.0\) Hz, 1H), 4.34-4.27 (m, 2H), 4.26-4.24 (d, \(J = 9.0\) Hz, 1H), 3.90-3.77 (m, 2H), 3.30 (s, 3H), 1.32 (t, \(J = 7.2\) Hz, 3H), 0.78 (t, \(J = 7.2\) Hz, 3H); \(^13\)C NMR (125 MHz, CDCl\(_3\)): 199.3, 173.5, 167.3, 145.8, 136.0, 125.7, 124.4, 122.9, 109.6, 67.9, 63.0, 61.7, 61.6, 51.6, 27.2, 14.1, 13.5. HRMS (ESI) calcd for C\(_{18}\)H\(_{20}\)ClN\(_2\)O\(_5\)S (M+H\(^+\)) 411.0776, found 411.0785.

Diethyl 7-chloro-1-methyl-2-oxo-2'-thioxospiro[indoline-3,3'-pyrrolidine]-4',5'-dicarboxylate (3d)

Following the typical procedure above, the title compound was obtained as white solid, mp 216-218\(^\circ\)C; \(^1\)H NMR (500 MHz, CDCl\(_3\)): \(\delta\) (ppm) 8.10 (s, 1H), 7.46-7.44 (dd, \(J = 8.2\), \(J = 0.8\) Hz, 1H), 7.00-6.97 (dd, \(J = 7.4\), \(J = 0.8\) Hz, 1H), 6.88 (t, \(J = 7.8\) Hz, 1H), 5.22-5.20 (d, \(J = 8.8\) Hz, 1H), 4.36-4.25 (m, 2H), 3.69 (s, 3H), 1.33 (t, \(J = 7.2\) Hz, 3H), 0.78 (t, \(J = 7.2\) Hz, 3H); \(^13\)C NMR (125 MHz, CDCl\(_3\)): 199.3, 174.0, 167.4, 167.2, 141.9, 135.7, 135.6, 130.2, 124.2, 122.4, 102.9, 67.9, 63.0, 61.6, 61.5, 52.6, 52.0, 30.8, 14.1, 13.5. HRMS (ESI) calcd for C\(_{18}\)H\(_{20}\)ClN\(_2\)O\(_5\)S (M+H\(^+\)) 411.0776, found 411.0785.

Diethyl 4-bromo-1-methyl-2-oxo-2'-thioxospiro[indoline-3,3'-pyrrolidine]-4',5'-dicarboxylate (3e)

Following the typical procedure above, the title compound was obtained as white solid, mp 216-218\(^\circ\)C; \(^1\)H NMR (500 MHz, CDCl\(_3\)): \(\delta\) (ppm) 7.29-7.23 (m, 2H), 6.86-6.84 (dd, \(J = 7.5\) Hz, \(J = 0.8\) Hz, 1H), 5.23-5.30 (d, \(J = 8.0\) Hz, 1H), 4.77-4.75 (d, \(J = 8.0\) Hz, 1H), 4.37-4.28 (m, 2H), 4.21-4.14 (m, 1H), 4.04-3.97 (m, 1H), 3.21 (s, 3H), 1.34 (t, \(J = 7.2\) Hz, 3H), 1.09 (t, \(J = 7.2\) Hz, 3H); \(^13\)C NMR (125 MHz, CDCl\(_3\)): 197.2, 172.4, 168.0, 167.9, 147.0, 131.2, 127.3, 127.0, 119.4, 107.6, 100.0, 69.9, 62.7, 61.8, 61.4, 48.7, 26.9, 14.2, 13.8. HRMS (ESI) calcd for C\(_{18}\)H\(_{20}\)BrN\(_2\)O\(_5\)S (M+H\(^+\)) 455.0271, found 455.0283.

Diethyl 5-bromo-1-methyl-2-oxo-2'-thioxospiro[indoline-3,3'-pyrrolidine]-4',5'-dicarboxylate (3f)

Following the typical procedure above, the title compound was obtained as white solid, mp 216-218\(^\circ\)C; \(^1\)H NMR (500 MHz, CDCl\(_3\)): \(\delta\) (ppm) 7.29-7.23 (m, 2H), 6.86-6.84 (dd, \(J = 7.5\) Hz, \(J = 0.8\) Hz, 1H), 5.23-5.30 (d, \(J = 8.0\) Hz, 1H), 4.37-4.28 (m, 2H), 4.21-4.14 (m, 1H), 4.04-3.97 (m, 1H), 3.21 (s, 3H), 1.34 (t, \(J = 7.2\) Hz, 3H), 1.09 (t, \(J = 7.2\) Hz, 3H); \(^13\)C NMR (125 MHz, CDCl\(_3\)): 199.3, 174.0, 167.4, 147.0, 131.2, 127.3, 127.0, 119.4, 107.6, 100.0, 69.9, 62.7, 61.8, 61.4, 48.7, 26.9, 14.2, 13.8. HRMS (ESI) calcd for C\(_{18}\)H\(_{20}\)BrN\(_2\)O\(_5\)S (M+H\(^+\)) 455.0271, found 455.0283.
dicarboxylate (3g)
Following the typical procedure above, the title compound was isolated as a white solid, mp 216-218°C; $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ (ppm) 8.42 (s, 1H), 7.46-7.44 (d, $J = 8.2$ Hz, 1H), 7.00-6.98 (d, $J = 7.4$ Hz, 1H), 6.90-6.87 (t, $J = 7.9$ Hz, 1H), 5.22-5.20 (d, $J = 8.8$ Hz, 1H), 4.34-4.25 (m, 3H), 3.90-3.87 (m, 1H), 3.80-3.74 (m, 1H), 3.69 (s, 3H), 1.31 (t, $J = 7.2$ Hz, 3H), 0.78 (t, $J = 7.2$ Hz, 3H); $^{13}$C NMR (125 MHz, CDCl$_3$): 199.3, 174.1, 167.4, 167.2, 141.9, 135.6, 130.3, 124.2, 122.4, 102.9, 67.9, 63.0, 61.6, 61.6, 52.0, 50.8, 30.8, 14.1, 13.5. HRMS (ESI) calcd for C$_{18}$H$_{20}$BrN$_2$O$_5$S (M+H)$^+$ 455.0271, found 455.0278.

Diethyl 7-bromo-1-methyl-2-oxo-2'-thioxospiro[indoline-3,3'-pyrrolidine]-4',5'-dicarboxylate (3h)
Following the typical procedure above, the title compound was obtained as a white solid, mp 210-212°C; $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ (ppm) 8.10 (s, 1H), 7.46-7.44 (dd, $J = 8.2$ Hz, $J = 0.8$ Hz, 1H), 7.00-6.97 (dd, $J = 7.4$, $J = 0.8$ Hz, 1H), 6.88 (t, $J = 7.8$ Hz, 1H), 5.22-5.20 (d, $J = 8.8$ Hz, 1H), 4.36-4.25 (m, 3H), 3.92-3.92 (m, 1H), 3.81-3.74 (m, 1H), 3.69 (s, 3H), 1.33 (t, $J = 7.2$ Hz, 3H), 0.78 (t, $J = 7.2$ Hz, 3H); $^{13}$C NMR (125 MHz, CDCl$_3$): 199.3, 174.0, 167.4, 167.2, 141.9, 135.7, 135.6, 130.2, 124.2, 122.4, 102.9, 67.9, 63.0, 61.6, 61.5, 52.6, 52.0, 30.8, 14.1, 13.5. HRMS (ESI) calcd for C$_{18}$H$_{20}$BrN$_2$O$_5$S (M+H)$^+$ 455.0271, found 455.0272.

Diethyl 5-fluoro-1-methyl-2-oxo-2'-thioxospiro[indoline-3,3'-pyrrolidine]-4',5'-dicarboxylate (3i)
Following the typical procedure above, the title compound was obtained as a white solid, mp 199-201°C; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ (ppm) 8.42 (s, 1H), 7.12-7.06 (td, $J = 8.4$ Hz, $J = 2.4$ Hz, 1H), 7.01-6.98 (dd, $J = 8.4$ Hz, $J = 2.8$ Hz, 1H), 6.85-6.81 (m, 1H), 5.24-5.22 (d, $J = 7.6$ Hz, 1H), 4.32-4.27 (q, $J = 7.2$ Hz, 2H), 4.07-4.00 (m, 3H), 3.26 (s, 3H), 1.31 (t, $J = 7.2$ Hz, 3H), 1.03 (t, $J = 7.2$ Hz, 3H); $^{13}$C NMR (125 MHz, CDCl$_3$): 198.9, 173.5, 168.1, 168.0, 160.3, 158.4, 140.7, 127.7, 127.6, 116.5, 116.3, 114.2, 114.0, 109.2, 109.1, 68.3, 62.4, 61.8, 61.6, 52.1, 27.1, 14.0, 13.8. HRMS (ESI) calcd for C$_{18}$H$_{20}$F$_2$N$_2$O$_5$S (M+H)$^+$ 395.1071, found 395.1082.

Diethyl 1-methyl-2-oxo-2'-thioxo-5-(trifluoromethoxy)spiro[indoline-3,3'-pyrrolidine]-4',5'-dicarboxylate (3j)
Following the typical procedure above, the title compound was obtained as a white solid, mp 235-237°C; $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ (ppm) 8.36 (s, 1H), 7.27-7.25 (d, $J = 4.8$ Hz, 2H), 6.91-6.88 (d, $J = 8.5$ Hz, 1H), 5.26-5.23 (d, $J = 7.6$ Hz, 1H), 4.33-4.26 (q, $J = 7.2$ Hz, 2H), 4.11-3.90 (m, 3H), 3.27 (s, 3H), 1.31 (t, $J = 7.2$ Hz, 3H), 1.02 (t, $J = 7.2$ Hz, 3H); $^{13}$C NMR (75 MHz, CDCl$_3$): 198.5, 173.5, 168.0, 145.0, 143.4, 127.5, 123.3, 120.0, 109.2, 68.1, 62.5, 61.8, 61.7, 52.1, 27.1, 14.0, 13.6. HRMS (ESI) calcd for C$_{19}$H$_{20}$F$_3$N$_2$O$_5$S (M+H)$^+$ 461.0989, found 461.0997.

Diethyl 1,5-dimethyl-2-oxo-2'-thioxospiro[indoline-3,3'-pyrrolidine]-4',5'-dicarboxylate (3k)
Following the typical procedure above, the title compound was obtained as a white solid, mp 209-211°C; $^1$H NMR (500 MHz, CDCl$_3$): δ (ppm) 8.35 (s, 1H), 7.17-7.16 (dd, $J = 8.0$ Hz, $J = 1.0$ Hz, 1H), 6.95 (s, 1H), 6.79-6.77 (d, $J = 8.0$ Hz, 1H), 5.27-5.25 (d, $J = 7.5$ Hz, 1H), 4.32 – 4.25 (m, 2H), 4.05 – 3.94 (m, 3H), 3.23 (s, 3H), 2.30 (s, 3H), 1.30 (t, $J = 7.2$ Hz, 3H), 1.02 (t, $J = 7.1$ Hz, 3H); $^{13}$C NMR (125 MHz, CDCl$_3$): δ 199.7, 173.6, 168.4, 168.1, 142.3, 132.8, 130.4, 126.5, 125.9, 108.4, 68.4, 62.3, 61.7, 61.4, 52.3, 27.0, 21.2, 14.1, 13.8. HRMS (ESI) calcd for C$_{19}$H$_{23}$N$_2$O$_5$S (M+H)$^+$ 391.1322, found 391.1338.

**Diethyl 1,5,7-trimethyl-2-oxo-2'-thioxospiro[indoline-3,3'-pyrrolidine]-4',5'-dicarboxylate (3l)**

Following the typical procedure above, the title compound was obtained as a white solid, mp 217-219°C; $^1$H NMR (400 MHz, CDCl$_3$): δ (ppm) 8.39 (s, 1H), 6.90 (s, 1H), 6.76 (s, 1H), 5.30-5.28 (d, $J = 7.2$ Hz, 1H), 4.30-4.25 (m, 2H), 4.04–3.92 (m, 3H), 3.50 (s, 3H), 2.54 (s, 3H), 2.24 (s, 3H), 1.29 (t, $J = 7.2$ Hz, 3H), 1.03 (t, $J = 7.2$ Hz, 3H); $^{13}$C NMR (125 MHz, CDCl$_3$): 200.0, 174.3, 168.5, 168.2, 140.0, 134.5, 132.6, 126.4, 124.4, 119.8, 68.0, 62.3, 61.7, 61.4, 52.8, 30.4, 20.9, 19.0, 14.1, 13.8. HRMS (ESI) calcd for C$_{20}$H$_{25}$N$_2$O$_5$S (M+H)$^+$ 405.1479, found 405.1486.

**Ethyl 5-chloro-5'-(3,5-dimethyl-1H-pyrazole-1-carbonyl)-1-methyl-2-oxo-2'-thioxospiro[indoline-3,3'-pyrrolidine]-4'-carboxylate (3m)**

Following the typical procedure above, the title compound was obtained as a white solid, mp 207-209°C; $^1$H NMR (500 MHz, CDCl$_3$): δ (ppm) 8.87 (s, 1H), 7.35-7.32 (dd, $J = 8.4$ Hz, $J = 2.0$ Hz, 1H), 7.14-7.13 (d, $J = 2.0$ Hz, 1H), 6.85-6.83 (d, $J = 8.4$ Hz, 1H), 6.08 (s, 1H), 5.82-5.79 (d, $J = 8.7$ Hz, 1H), 4.69-4.67 (d, $J = 8.7$ Hz, 1H), 3.94-3.87 (m, 1H), 3.83-3.76 (m, 1H), 3.32 (s, 3H), 2.58 (s, 3H), 2.31 (s, 3H), 0.76 (t, $J = 7.2$ Hz, 3H); $^{13}$C NMR (125 MHz, CDCl$_3$): 198.8, 173.2, 167.4, 167.1, 144.5, 130.0, 127.4, 123.7, 112.2, 109.6, 67.4, 63.6, 61.5, 50.1, 27.2, 14.0, 13.9, 13.5. HRMS (ESI) calcd for C$_{21}$H$_{22}$ClN$_4$O$_4$S (M+H)$^+$ 461.1045, found 461.1049.

**Ethyl 5'-(1S,2R,5S)-2-isopropyl-5-methyl cyclohexyl) 1-methyl-2-oxo-2'-thioxospiro[indoline-3,3'-pyrrolidine]-4',5'-dicarboxylate (3n)**

Following the typical procedure above, the title compound was obtained as a white solid, mp 257-259°C; $^1$H NMR (500 MHz, CDCl$_3$): δ (ppm) 8.06 (s, 1H), 7.36-7.32 (dd, $J = 8.4$ Hz, $J = 2.0$ Hz, 1H), 7.09-7.01 (m, 1H), 6.89-6.87 (d, $J = 7.6$ Hz, 1H), 6.08 (s, 1H), 5.29-5.22 (m, 1H), 4.84-4.77 (td, $J = 10.8$ Hz, $J = 4.4$ Hz, 1H), 4.24-4.20 (q, $J = 4.4$ Hz, 1H), 3.84-3.71 (m, 2H), 3.31 (s, 3H), 2.09-2.05 (m, 1H), 1.87-1.76 (m, 1H), 1.70 (s, 1H), 1.68 (s, 1H), 1.61 (s, 3H), 1.52-1.47 (m, 1H), 1.45-1.35 (m, 1H), 1.11-0.97 (s, 2H), 0.94-0.82 (m, 7H), 0.78-0.77 (d, $J = 6.8$ Hz, 3H), 0.71 (t, $J = 7.2$ Hz, 3H); $^{13}$C NMR (125 MHz, CDCl$_3$): 200.1, 173.4, 167.4, 167.1, 144.5, 130.0, 127.4, 123.5, 123.0, 108.7, 77.4, 68.4, 61.7, 52.0, 46.9, 40.7, 34.0, 31.4, 27.0, 26.4, 23.3, 21.9, 20.8, 16.3, 13.5, HRMS (ESI) calcd for C$_{26}$H$_{35}$N$_2$O$_5$S (M+H)$^+$ 487.2261, found 487.2275.
Large scale synthesis of spirooxindole (3f)

To a Schlenk tube was added methyleneindolinone 1f (31 g, 0.1 mmol), ethyl 2-isothiocyanatoacetate 2a (16 g, 1.1 mmol) and EtOH (300 mL) under air, then DBU (152 mg, 1 mol%) was added. The resulting mixture was stirred at room temperature for 2 h. Then the reaction solution was directly evaporated to remove the ethanol to give the crude product as solid. Then the solid was washed with cold methanol to give the spirooxindole (3f) in 34.6 g (76% yield).

The crystal structure of 3b has been deposited at the Cambridge Crystallographic Data Centre (CCDC 1016506). The data can be obtained free of charge via the Internet at www.ccdc.cam.ac.uk/conts/retrieving.html.

Reference: