

Assembly of spirocyclic pyrazolone-pyrrolo[4,3,2-*de*]quinoline skeleton via cascade [1,5] hydride transfer/cyclization by C(sp³)-H functionalization

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Supplementary Material

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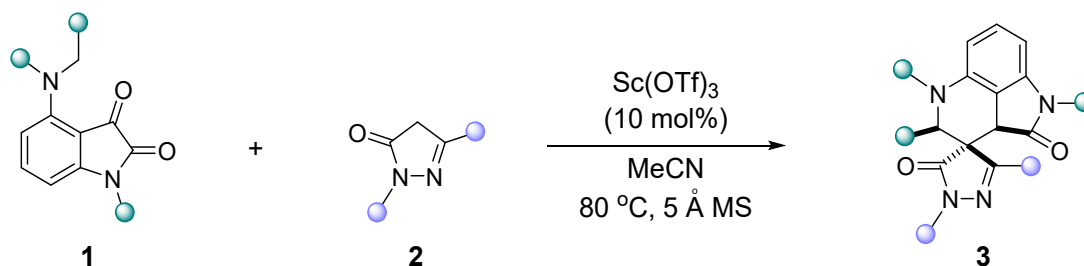
1. General Information

Nuclear magnetic resonance (NMR) spectra were recorded in CDCl_3 and $\text{DMSO-}d_6$ on Bruker 600, 700 MHz, or JEOL 600 NMR instrument (at 600 or 700 MHz for ^1H , and at 150, or 175 MHz for ^{13}C). Proton chemical shifts were reported in parts per million (δ scale). The ^1H NMR chemical shifts were reported in ppm with the residual non-deuterated solvents: CDCl_3 at 7.26 ppm as standard. The ^{13}C NMR chemical shifts were given using CDCl_3 as the internal standard (CDCl_3 : $\delta = 77.2$ ppm and $\text{DMSO-}d_6$: $\delta = 39.5$ ppm). High-resolution mass spectra (HRMS) were obtained using Agilent P/N G1969-90010. High-resolution mass spectra were reported for the molecular ion $[\text{M}+\text{Na}]^+$ or $[\text{M}+\text{H}]^+$. X-ray diffraction experiment was carried out on an Agilent Gemini and the data obtained was deposited at the Cambridge Crystallographic Data Centre. Column chromatography was performed on silica gel (200-300 mesh) using an eluent of ethyl acetate (EA) and petroleum ether (PE). All reagents and solvents were obtained from commercial sources and used without further purification. Oil baths were used as the heat source. 1-benzyl-4-(pyrrolidin-1-yl)indoline-2,3-dione¹ were prepared according to the literature procedures.

References

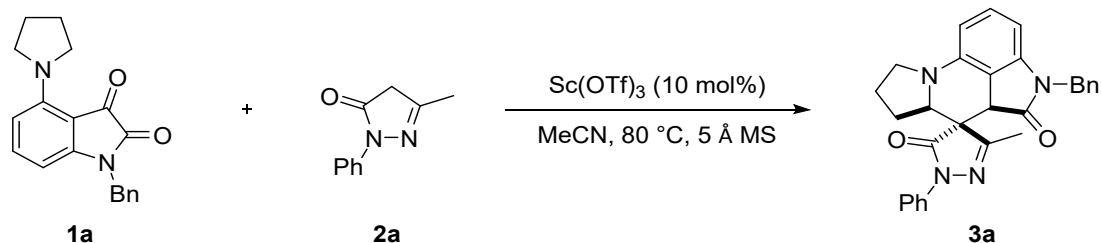
(1) S. Wang, X.-D. An, S.-S. Li, X. Liu, Q. Liu and J. Xiao, Hydride transfer initiated ring expansion of pyrrolidines toward highly functionalized tetrahydro-1-benzazepines, *Chem. Commun.*, 2018, **54**, 13833-13836.

2. Synthesis of Compound 3



A mixture of C-4 pyrrolidine substituted isatins **1** (0.1 mmol), pyrazolone substrates **2** (0.15 mmol), $\text{Sc}(\text{OTf})_3$ (10 mol%), 5 Å MS (50 mg) and MeCN (1.0 mL) was stirred at 80 °C and monitored by TLC. After reactions completed, the residue was purified by silica gel flash column chromatography (petroleum ether/ethyl acetate) to afford the compound **3** as brown solids.

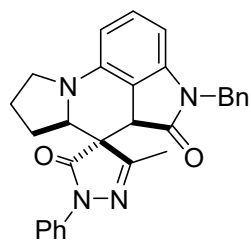
3. Gram-scale Synthesis of Compound 3a



To a Schlenk tube were added 1-benzyl-4-(pyrrolidin-1-yl)indoline-2,3-dione **1a** (4 mmol, 1.23 g), pyrazolone substrate **2a** (6 mmol, 1.05 g), Sc(OTf)₃ (10 mol%), 5 Å MS (500 mg) and MeCN (10 mL) was stirred at 80 °C for overnight. The reaction was monitored by TLC. After completion of the reaction, the reaction mixture was concentrated and directly purified by flash column chromatography on silica gel (PE/EA = 20:1 to 15:1 v/v) to afford the pure products **3a** as a brown solid in 88% yield (1.63 g).

4. Analytical Data of Compounds 3

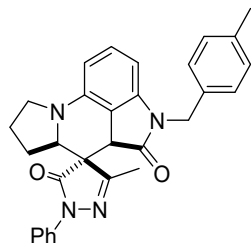
4-benzyl-3'-methyl-1'-phenyl-4,5a,6a,7,8,9-hexahydro-5H-spiro[dipyrrolo[1,2-a:4',3',2'-de]quinoline-6,4'-pyrazole]-5,5'(1'H)-dione (**3a**)



3a

The crude product was purified by flash chromatography on silica gel (EtOAc/petroleum ether = 1/15) to give the product as a brown solid in 92% yield (42.5 mg), >16:1 dr, m.p. 142.6-144.5 °C. ¹H NMR (600 MHz, CDCl₃) δ 7.97 – 7.93 (m, 2H), 7.44 – 7.38 (m, 2H), 7.31 – 7.27 (m, 4H), 7.25 – 7.23 (m, 1H), 7.20 (tt, *J* = 7.2, 1.2 Hz, 1H), 7.12 (t, *J* = 7.8 Hz, 1H), 6.25 (d, *J* = 8.4 Hz, 1H), 6.19 (d, *J* = 7.8 Hz, 1H), 4.89 (d, *J* = 15.6 Hz, 1H), 4.67 (d, *J* = 15.6 Hz, 1H), 4.12 (s, 1H), 4.04 (dd, *J* = 10.8, 6.0 Hz, 1H), 3.66 – 3.62 (m, 1H), 3.05 (q, *J* = 8.4 Hz, 1H), 2.13 – 2.03 (m, 3H), 1.25 – 1.17 (m, 1H), 1.10 (s, 3H). ¹³C NMR (151 MHz, CDCl₃) δ 174.5, 173.5, 156.8, 143.8, 142.1, 138.0, 136.3, 130.8, 128.9, 128.7, 127.70, 127.65, 125.4, 119.3, 105.3, 104.6, 98.5, 64.8, 50.4, 47.4, 47.2, 44.1, 26.5, 24.5, 16.1. HRMS (ESI-TOF) *m/z*: [M+Na]⁺ Calcd for C₂₉H₂₆N₄NaO₂⁺ 485.1948, found 485.1953.

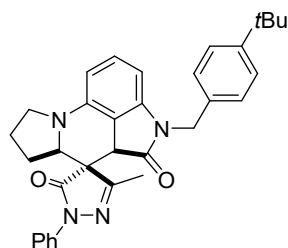
3'-methyl-4-(4-methylbenzyl)-1'-phenyl-4,5a,6a,7,8,9-hexahydro-5H-spiro[dipyrrolo[1,2-a:4',3',2'-de]quinoline-6,4'-pyrazole]-5,5'(1'H)-dione (3b)



3b

The crude product was purified by flash chromatography on silica gel (EtOAc/petroleum ether = 1/15) to give the product as a brown solid in 82% yield (39.0 mg), >16:1 dr, m.p. 149.6-151.4 °C. ¹H NMR (600 MHz, CDCl₃) δ 7.99 – 7.94 (m, 2H), 7.45 – 7.40 (m, 2H), 7.21 (tt, *J* = 7.2, 1.2 Hz, 1H), 7.19 (d, *J* = 7.8 Hz, 2H), 7.13 (td, *J* = 7.8, 1.2 Hz, 1H), 7.10 (d, *J* = 7.8 Hz, 2H), 6.25 (d, *J* = 8.4 Hz, 1H), 6.20 (d, *J* = 7.8 Hz, 1H), 4.85 (d, *J* = 15.0 Hz, 1H), 4.64 (d, *J* = 15.6 Hz, 1H), 4.12 (s, 1H), 4.04 (dd, *J* = 10.8, 6.0 Hz, 1H), 3.67 – 3.63 (m, 1H), 3.06 (q, *J* = 9.0 Hz, 1H), 2.30 (s, 3H), 2.14 – 2.06 (m, 3H), 1.25 – 1.20 (m, 1H), 1.11 (s, 3H). ¹³C NMR (151 MHz, CDCl₃) δ 174.4, 173.5, 156.8, 143.8, 142.0, 137.9, 137.4, 133.2, 130.7, 129.4, 128.8, 127.6, 125.3, 119.3, 105.3, 104.5, 98.6, 64.8, 50.4, 47.4, 47.1, 43.8, 26.5, 24.5, 21.1, 16.1. HRMS (ESI-TOF) *m/z*: [M+Na]⁺ Calcd for C₃₀H₂₈N₄NaO₂⁺ 499.2104, found 499.2108.

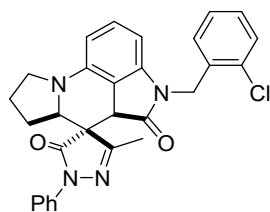
4-(4-(tert-butyl)benzyl)-3'-methyl-1'-phenyl-4,5a,6a,7,8,9-hexahydro-5H-spiro[dipyrrolo[1,2-a:4',3',2'-de]quinoline-6,4'-pyrazole]-5,5'(1'H)-dione (3c)



3c

The crude product was purified by flash chromatography on silica gel (EtOAc/petroleum ether = 1/15) to give the product as a brown solid in 90% yield (46.7 mg), >16:1 dr, m.p. 156.2-157.9 °C. ¹H NMR (600 MHz, CDCl₃) δ 7.97 (dt, *J* = 7.8, 1.2 Hz, 2H), 7.44 – 7.40 (m, 2H), 7.31 (d, *J* = 7.8 Hz, 2H), 7.25 – 7.19 (m, 3H), 7.18 – 7.12 (m, 1H), 6.27 (d, *J* = 7.8 Hz, 1H), 6.24 (d, *J* = 7.8 Hz, 1H), 4.92 (d, *J* = 15.0 Hz, 1H), 4.59 (d, *J* = 15.0 Hz, 1H), 4.12 (s, 1H), 4.05 (dd, *J* = 10.8, 5.4 Hz, 1H), 3.68 – 3.64 (m, 1H), 3.07 (q, *J* = 8.4 Hz, 1H), 2.14 – 2.06 (m, 3H), 1.28 (s, 9H), 1.25 – 1.20 (m, 1H), 1.13 (s, 3H). ¹³C NMR (151 MHz, CDCl₃) δ 174.4, 173.5, 156.8, 150.7, 143.9, 142.1, 138.0, 133.2, 130.7, 128.9, 127.4, 125.6, 125.3, 119.3, 105.4, 104.5, 98.6, 64.8, 50.4, 47.5, 47.2, 43.7, 34.5, 31.3, 26.5, 24.5, 16.1. HRMS (ESI-TOF) *m/z*: [M+Na]⁺ Calcd for C₃₃H₃₄N₄NaO₂⁺ 541.2574, found 541.2572.

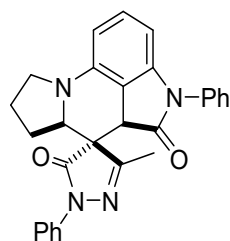
4-(2-chlorobenzyl)-3'-methyl-1'-phenyl-4,5a,6a,7,8,9-hexahydro-5H-spiro[dipyrrolo[1,2-a:4',3',2'-de]quinoline-6,4'-pyrazole]-5,5'(1'H)-dione (3d)



3d

The crude product was purified by flash chromatography on silica gel (EtOAc/petroleum ether = 1/15) to give the product as a brown solid in 94% yield (46.7 mg), >16:1 dr, m.p. 155.9-157.4 °C. ¹H NMR (600 MHz, CDCl₃) δ 7.98 – 7.93 (m, 2H), 7.44 – 7.40 (m, 2H), 7.39 – 7.37 (m, 1H), 7.23 – 7.17 (m, 4H), 7.16 – 7.13 (m, 1H), 6.28 (d, *J* = 7.8 Hz, 1H), 6.19 (d, *J* = 7.8 Hz, 1H), 5.11 (d, *J* = 16.2 Hz, 1H), 4.75 (d, *J* = 16.8 Hz, 1H), 4.18 (s, 1H), 4.06 (dd, *J* = 10.8, 6.0 Hz, 1H), 3.69 – 3.65 (m, 1H), 3.08 (q, *J* = 8.4 Hz, 1H), 2.14 – 2.08 (m, 3H), 1.27 – 1.24 (m, 1H), 1.18 (s, 3H). ¹³C NMR (151 MHz, CDCl₃) δ 174.7, 173.5, 156.7, 143.6, 142.1, 137.9, 133.5, 133.1, 130.9, 129.7, 129.0, 128.9, 128.7, 127.2, 125.4, 119.3, 105.2, 104.8, 98.5, 64.8, 50.4, 47.5, 47.1, 41.3, 26.5, 24.5, 16.2. HRMS (ESI-TOF) *m/z*: [M+Na]⁺ Calcd for C₂₉H₂₅ClN₄NaO₂⁺ 519.1558, found 519.1562.

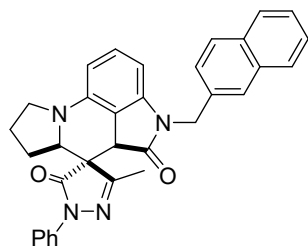
3'-methyl-1',4-diphenyl-4,5a,6a,7,8,9-hexahydro-5H-spiro[dipyrrolo[1,2-a:4',3',2'-de]quinoline-6,4'-pyrazole]-5,5'(1'H)-dione (3e)



3e

The crude product was purified by flash chromatography on silica gel (EtOAc/petroleum ether = 1/15) to give the product as a brown solid in 53% yield (23.8 mg), >16:1 dr, m.p. 151.7-153.4 °C. ¹H NMR (600 MHz, CDCl₃) δ 7.93 (d, *J* = 7.8 Hz, 2H), 7.46 (t, *J* = 7.8 Hz, 2H), 7.42 – 7.39 (m, 4H), 7.34 (t, *J* = 7.2 Hz, 1H), 7.19 (q, *J* = 7.2 Hz, 2H), 6.34 (d, *J* = 8.4 Hz, 1H), 6.29 (d, *J* = 7.8 Hz, 1H), 4.24 (s, 1H), 4.10 (dd, *J* = 10.8, 6.0 Hz, 1H), 3.73 – 3.69 (m, 1H), 3.12 (q, *J* = 8.4 Hz, 1H), 2.17 – 2.09 (m, 3H), 1.31 – 1.26 (m, 4H). ¹³C NMR (151 MHz, CDCl₃) δ 172.4, 172.3, 155.6, 143.4, 141.3, 136.9, 133.6, 129.7, 128.3, 127.8, 126.6, 124.6, 124.4, 118.3, 104.3, 103.8, 97.9, 63.7, 49.3, 46.6, 46.2, 25.5, 23.5, 15.0. HRMS (ESI-TOF) *m/z*: [M+Na]⁺ Calcd for C₂₈H₂₄N₄NaO₂⁺ 471.1791, found 471.1799.

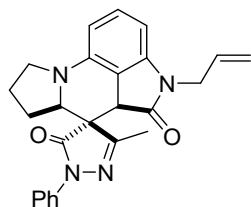
3'-methyl-4-(naphthalen-2-ylmethyl)-1'-phenyl-4,5a,6a,7,8,9-hexahydro-5H-spiro[dipyrrolo[1,2-a:4',3',2'-de]quinoline-6,4'-pyrazole]-5,5'(1'H)-dione (3f)



3f

The crude product was purified by flash chromatography on silica gel (EtOAc/petroleum ether = 1/15) to give the product as a brown solid in 91% yield (46.6 mg), 12:1 dr, m.p. 160.5-162.3 °C. ¹H NMR (600 MHz, Chloroform-*d*) δ 7.98 (d, *J* = 7.8 Hz, 2H), 7.78 – 7.73 (m, 3H), 7.73 (s, 1H), 7.46 – 7.41 (m, 4H), 7.37 (dd, *J* = 8.4, 1.8 Hz, 1H), 7.20 (t, *J* = 7.2 Hz, 1H), 7.08 (t, *J* = 7.8 Hz, 1H), 6.21 (t, *J* = 7.8 Hz, 2H), 5.00 (d, *J* = 15.6 Hz, 1H), 4.87 (d, *J* = 15.6 Hz, 1H), 4.15 (s, 1H), 4.03 (dd, *J* = 10.8, 6.0 Hz, 1H), 3.62 – 3.29 (m, 1H), 3.02 (d, *J* = 7.8 Hz, 1H), 2.09 – 2.04 (m, 3H), 1.25 – 1.16 (m, 1H), 1.11 (s, 3H). ¹³C NMR (151 MHz, Chloroform-*d*) δ 174.6, 173.6, 156.8, 143.7, 142.1, 138.0, 133.8, 133.3, 132.9, 130.8, 128.9, 128.7, 127.8, 127.7, 126.6, 126.4, 126.1, 125.5, 125.4, 119.3, 105.3, 104.6, 98.7, 64.8, 50.5, 47.5, 47.1, 44.3, 26.5, 24.5, 16.2. HRMS (ESI-TOF) *m/z*: [M+Na]⁺ Calcd for C₃₃H₂₈N₄NaO₂⁺ 535.2104, found 535.2106.

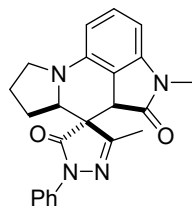
4-allyl-3'-methyl-1'-phenyl-4,5a,6a,7,8,9-hexahydro-5H-spiro[dipyrrolo[1,2-a:4',3',2'-de]quinoline-6,4'-pyrazole]-5,5'(1'H)-dione (3g)



3g

The crude product was purified by flash chromatography on silica gel (EtOAc/petroleum ether = 1/15) to give the product as a brown solid in 90% yield (37.1 mg), >16:1 dr, m.p. 163.2-165.0 °C. ¹H NMR (600 MHz, CDCl₃) δ 7.96 – 7.91 (m, 2H), 7.44 – 7.38 (m, 2H), 7.23 – 7.17 (m, 2H), 6.28 (t, *J* = 7.8 Hz, 2H), 5.79 (ddt, *J* = 17.4, 10.2, 5.4 Hz, 1H), 5.25 (dq, *J* = 17.4, 1.2 Hz, 1H), 5.20 (dq, *J* = 10.2, 1.2 Hz, 1H), 4.35 (ddt, *J* = 16.2, 6.0, 1.8 Hz, 1H), 4.12 – 4.06 (m, 2H), 4.04 (dd, *J* = 10.8, 6.0 Hz, 1H), 3.69 – 3.64 (m, 1H), 3.08 (q, *J* = 9.0 Hz, 1H), 2.22 – 2.02 (m, 3H), 1.27 – 1.19 (m, 1H), 1.18 – 1.11 (s, 3H). ¹³C NMR (151 MHz, CDCl₃) δ 174.1, 173.5, 156.7, 143.9, 142.1, 138.0, 131.7, 130.8, 128.9, 125.3, 119.3, 117.9, 105.3, 104.5, 98.4, 64.8, 50.4, 47.4, 47.2, 42.6, 26.5, 24.5, 16.0. HRMS (ESI-TOF) *m/z*: [M+Na]⁺ Calcd for C₂₅H₂₄N₄NaO₂⁺ 435.1791, found 435.1798.

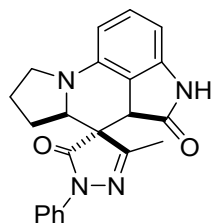
3',4-dimethyl-1'-phenyl-4,5a,6a,7,8,9-hexahydro-5H-spiro[dipyrrolo[1,2-a:4',3',2'-de]quinoline-6,4'-pyrazole]-5,5'(1'H)-dione (3h)



3h

The crude product was purified by flash chromatography on silica gel (EtOAc/petroleum ether = 1/15) to give the product as a brown solid in 50% yield (19.3 mg), >16:1 dr, m.p. 157.8-159.1 °C. ¹H NMR (600 MHz, CDCl₃) δ 7.94 (dd, *J* = 8.4, 1.2 Hz, 2H), 7.42 – 7.39 (m, 2H), 7.25 – 7.22 (m, 1H), 7.20 (t, *J* = 7.8 Hz, 1H), 6.30 (d, *J* = 8.4 Hz, 1H), 6.28 (d, *J* = 7.2 Hz, 1H), 4.05 – 4.02 (m, 2H), 3.69 – 3.66 (m, 1H), 3.13 (s, 3H), 3.08 (q, *J* = 9.0 Hz, 1H), 2.14 – 2.06 (m, 3H), 1.26 – 1.20 (m, 1H), 1.12 (s, 3H). ¹³C NMR (151 MHz, CDCl₃) δ 173.5, 172.5, 155.7, 143.7, 141.0, 136.9, 129.9, 127.8, 124.3, 118.2, 104.3, 103.6, 96.4, 63.8, 49.4, 46.3, 46.1, 25.47, 25.45, 23.5, 15.0. HRMS (ESI-TOF) *m/z*: [M+Na]⁺ Calcd for C₂₃H₂₂N₄NaO₂⁺ 409.1635, found 409.1636.

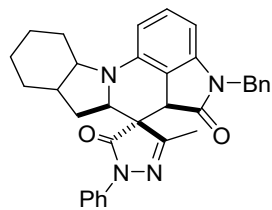
3'-methyl-1'-phenyl-4,5a,6a,7,8,9-hexahydro-5H-spiro[dipyrrolo[1,2-a:4',3',2'-de]quinoline-6,4'-pyrazole]-5,5'(1'H)-dione (3i)



3i

The crude product was purified by flash chromatography on silica gel (EtOAc/petroleum ether = 1/15) to give the product as a brown solid in 78% yield (29.0 mg), 14:1 dr, m.p. 148.2-150.2 °C. ¹H NMR (600 MHz, DMSO-*d*₆) δ 10.35 (s, 1H), 7.85 – 7.83 (m, 2H), 7.47 – 7.43 (m, 2H), 7.23 (tt, *J* = 7.2, 1.2 Hz, 1H), 7.15 – 7.12 (m, 1H), 6.27 (d, *J* = 7.8 Hz, 1H), 6.23 (d, *J* = 7.8 Hz, 1H), 4.00 (s, 1H), 3.88 (dd, *J* = 10.2, 6.0 Hz, 1H), 3.62 – 3.58 (m, 1H), 3.00 (q, *J* = 9.6 Hz, 1H), 2.05 – 2.01 (m, 2H), 1.94 – 1.89 (m, 1H), 1.14 – 1.09 (m, 1H), 1.08 (s, 3H). ¹³C NMR (151 MHz, DMSO-*D*₆) δ 176.7, 173.9, 158.0, 143.3, 142.7, 138.2, 131.1, 129.6, 125.6, 118.8, 106.9, 104.3, 99.3, 65.0, 50.5, 47.8, 47.5, 26.5, 24.6, 16.1. HRMS (ESI-TOF) *m/z*: [M+Na]⁺ Calcd for C₂₂H₂₀N₄NaO₂⁺ 395.1478, found 395.1478.

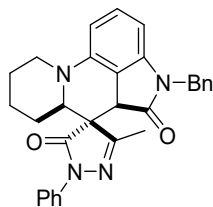
4-benzyl-3'-methyl-1'-phenyl-4,5a,6a,7,7a,8,9,10,11,11a-decahydro-5H-spiro[indolo[1,2-a]pyrrolo[4,3,2-de]quinoline-6,4'-pyrazole]-5,5'(1H)-dione (3j)



3j

The crude product was purified by flash chromatography on silica gel (EtOAc/petroleum ether = 1/15) to give the product as a brown solid in 97% yield (50.1 mg), >16:1 dr, m.p. 158.2-159.7 °C. ¹H NMR (600 MHz, CDCl₃) δ 7.94 – 7.91 (m, 2H), 7.41 – 7.38 (m, 2H), 7.29 – 7.25 (m, 3H), 7.25 – 7.20 (m, 2H), 7.19 (tt, *J* = 7.2, 1.2 Hz, 1H), 7.11 – 7.07 (m, 1H), 6.21 (d, *J* = 8.4 Hz, 1H), 6.15 (d, *J* = 7.8 Hz, 1H), 4.85 (d, *J* = 15.0 Hz, 1H), 4.66 (d, *J* = 15.0 Hz, 1H), 4.19 (d, *J* = 10.2 Hz, 1H), 4.11 (s, 1H), 3.27 (d, *J* = 9.0 Hz, 1H), 3.11 (dd, *J* = 10.2, 6.0 Hz, 1H), 2.23 – 2.12 (m, 1H), 1.83 – 1.79 (m, 1H), 1.75 – 1.69 (m, 2H), 1.55 – 1.42 (m, 5H), 1.25 – 1.19 (m, 1H), 1.08 (s, 3H). ¹³C NMR (151 MHz, CDCl₃) δ 174.6, 173.8, 157.4, 143.7, 142.9, 138.0, 136.4, 130.8, 129.0, 128.8, 127.80, 127.75, 125.5, 119.6, 105.3, 104.6, 98.5, 64.2, 53.5, 50.0, 48.0, 44.1, 39.8, 38.2, 28.3, 25.6, 25.0, 20.9, 16.3. HRMS (ESI-TOF) *m/z*: [M+Na]⁺ Calcd for C₃₃H₃₂N₄NaO₂⁺ 539.2417, found 539.2420.

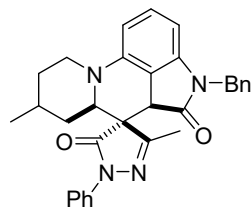
4'-benzyl-3-methyl-1-phenyl-4',5a',6a',7',9',10'-hexahydro-5'H,8'H-spiro[pyrazole-4,6'-pyrido[1,2-a]pyrrolo[4,3,2-de]quinoline]-5,5'(1H)-dione (3k)



3k

The crude product was purified by flash chromatography on silica gel (EtOAc/petroleum ether = 1/15) to give the product as a brown solid in 82% yield (39.1 mg), >16:1 dr, m.p. 150.0-152.2 °C. ¹H NMR (600 MHz, CDCl₃) δ 8.00 – 7.94 (m, 2H), 7.46 – 7.39 (m, 2H), 7.32 – 7.24 (m, 5H), 7.21 (tt, *J* = 7.2, 1.2 Hz, 1H), 7.09 (td, *J* = 7.8, 1.2 Hz, 1H), 6.55 (d, *J* = 8.4 Hz, 1H), 6.19 (d, *J* = 7.8 Hz, 1H), 4.88 (d, *J* = 15.6 Hz, 1H), 4.68 (d, *J* = 15.6 Hz, 1H), 4.14 (s, 1H), 4.07 – 4.02 (m, 1H), 3.46 (dd, *J* = 11.4, 2.4 Hz, 1H), 2.95 (td, *J* = 12.6, 3.0 Hz, 1H), 1.84 – 1.79 (m, 2H), 1.72 (dt, *J* = 12.6, 2.4 Hz, 1H), 1.52 (tt, *J* = 13.2, 4.2 Hz, 1H), 1.48 (s, 3H), 1.43 (tt, *J* = 13.2, 3.6 Hz, 1H), 1.08 (qd, *J* = 12.0, 4.2 Hz, 1H). ¹³C NMR (151 MHz, CDCl₃) δ 174.1, 172.5, 157.9, 143.4, 143.1, 137.8, 136.1, 130.0, 128.9, 128.7, 127.7, 127.6, 125.4, 119.4, 107.6, 106.8, 99.6, 61.3, 55.7, 47.8, 45.9, 44.0, 26.4, 25.5, 23.8, 16.1. HRMS (ESI-TOF) *m/z*: [M+Na]⁺ Calcd for C₃₀H₂₈N₄NaO₂⁺ 499.2104, found 499.2110.

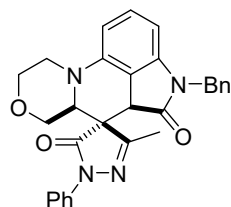
4'-benzyl-3,8'-dimethyl-1-phenyl-4',5a',6a',7',9',10'-hexahydro-5'H,8'H-spiro[pyrazole-4,6'-pyrido[1,2-a]pyrrolo[4,3,2-de]quinoline]-5,5'(1H)-dione (3l)



3l

The crude product was purified by flash chromatography on silica gel (EtOAc/petroleum ether = 1/15) to give the product as a brown solid in 90% yield (44.2 mg), 10:1 dr, m.p. 153.2-155.3 °C. ¹H NMR (600 MHz, CDCl₃) δ 8.02 – 7.97 (m, 2H), 7.47 – 7.40 (m, 2H), 7.32 – 7.25 (m, 5H), 7.22 (tt, *J* = 7.2, 1.2 Hz, 1H), 7.10 – 7.07 (m, 1H), 6.56 (d, *J* = 9.0 Hz, 1H), 6.19 (d, *J* = 7.8 Hz, 1H), 4.87 (d, *J* = 15.6 Hz, 1H), 4.69 (d, *J* = 15.6 Hz, 1H), 4.14 (s, 1H), 4.05 (ddd, *J* = 12.6, 4.2, 2.4 Hz, 1H), 3.49 (dd, *J* = 11.4, 2.4 Hz, 1H), 2.97 (td, *J* = 12.6, 3.0 Hz, 1H), 1.82 – 1.77 (m, 1H), 1.68 – 1.64 (m, 1H), 1.63 – 1.59 (m, 1H), 1.48 (s, 3H), 1.22 – 1.15 (m, 1H), 0.91 (d, *J* = 6.0 Hz, 3H), 0.74 (q, *J* = 12.0 Hz, 1H). ¹³C NMR (151 MHz, CDCl₃) δ 174.0, 172.5, 157.9, 143.4, 142.9, 137.9, 136.1, 130.0, 128.9, 128.9, 128.7, 127.7, 127.6, 125.4, 119.4, 119.4, 107.6, 106.8, 99.6, 60.8, 55.6, 47.2, 46.1, 44.0, 34.6, 33.9, 30.7, 21.8, 16.1. HRMS (ESI-TOF) *m/z*: [M+Na]⁺ Calcd for C₃₁H₃₀N₄NaO₂⁺ 513.2261, found 513.2263.

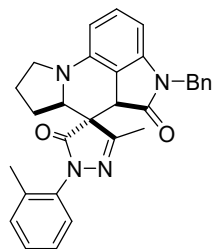
4'-benzyl-3-methyl-1-phenyl-4',5a',6a',7',9',10'-hexahydro-5'H-spiro[pyrazole-4,6'-[1,4]oxazino[4,3-a]pyrrolo[4,3,2-de]quinoline]-5,5'(1H)-dione (3m)



3m

The crude product was purified by flash chromatography on silica gel (EtOAc/petroleum ether = 1/15) to give the product as a brown solid in 55% yield (26.3 mg), >16:1 dr, m.p. 146.6-148.4 °C. ¹H NMR (600 MHz, DMSO-*d*₆) δ 7.85 (d, *J* = 8.4 Hz, 2H), 7.49 (t, *J* = 8.4 Hz, 2H), 7.33 (t, *J* = 7.2 Hz, 2H), 7.30 – 7.23 (m, 4H), 7.14 (t, *J* = 8.4 Hz, 1H), 6.71 (d, *J* = 7.8 Hz, 1H), 6.38 (d, *J* = 7.8 Hz, 1H), 4.85 (d, *J* = 16.2 Hz, 1H), 4.73 (d, *J* = 16.2 Hz, 1H), 4.36 (s, 1H), 3.97 (d, *J* = 12.0 Hz, 1H), 3.93 (dd, *J* = 11.4, 3.6 Hz, 1H), 3.69 (dd, *J* = 10.8, 3.0 Hz, 1H), 3.64 (dd, *J* = 10.8, 3.0 Hz, 1H), 3.52 (td, *J* = 11.4, 2.4 Hz, 1H), 3.15 (td, *J* = 12.6, 3.6 Hz, 1H), 3.06 (t, *J* = 10.8 Hz, 1H), 1.44 (s, 3H). ¹³C NMR (150 MHz, DMSO-*d*₆) δ 174.1, 171.9, 158.0, 143.4, 142.2, 137.8, 137.0, 130.4, 129.5, 129.0, 128.0, 127.7, 126.0, 119.3, 107.2, 106.8, 100.5, 66.7, 65.9, 59.2, 52.5, 46.0, 45.9, 43.5, 16.1. HRMS (ESI-TOF) *m/z*: [M+Na]⁺ Calcd for C₂₉H₂₆N₄NaO₃⁺ 501.1897, found 501.1904.

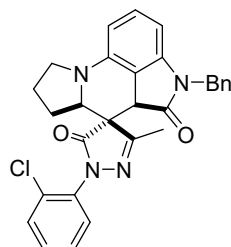
4-benzyl-3'-methyl-1'-(*o*-tolyl)-4,5a,6a,7,8,9-hexahydro-5*H*-spiro[dipyrrolo[1,2-*a*:4',3',2'-*de*]quinoline-6,4'-pyrazole]-5,5'(1'*H*)-dione (3n)



3n

The crude product was purified by flash chromatography on silica gel (EtOAc/petroleum ether = 1/15) to give the product as a brown solid in 52% yield (24.8 mg), >16:1 dr, m.p. 148.3-150.6 °C. ¹H NMR (600 MHz, CDCl₃) δ 7.44 – 7.41 (m, 1H), 7.34 – 7.29 (m, 6H), 7.29 – 7.28 (m, 1H), 7.26 – 7.23 (m, 1H), 7.13 (td, *J* = 7.8, 1.2 Hz, 1H), 6.26 (d, *J* = 8.4 Hz, 1H), 6.19 (d, *J* = 7.8 Hz, 1H), 4.91 (d, *J* = 15.6 Hz, 1H), 4.76 (d, *J* = 15.0 Hz, 1H), 4.14 (s, 1H), 4.07 (dd, *J* = 10.8, 6.0 Hz, 1H), 3.68 (tt, *J* = 7.8, 2.4 Hz, 1H), 3.10 – 3.04 (m, 1H), 2.42 (s, 3H), 2.23 – 2.11 (m, 3H), 1.40 – 1.28 (m, 1H), 1.08 (s, 3H). ¹³C NMR (151 MHz, CDCl₃) δ 174.7, 174.2, 156.8, 143.9, 142.2, 136.4, 135.9, 135.8, 131.1, 130.8, 128.8, 127.8, 127.7, 127.2, 126.7, 105.4, 104.6, 98.6, 64.6, 49.2, 47.5, 47.2, 44.2, 26.7, 24.6, 18.4, 16.2. HRMS (ESI-TOF) *m/z*: [M+Na]⁺ Calcd for C₃₀H₂₈N₄NaO₂⁺ 499.2104, found 499.2107.

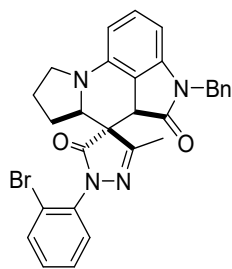
4-benzyl-1'-(2-chlorophenyl)-3'-methyl-4,5a,6a,7,8,9-hexahydro-5*H*-spiro[dipyrrolo[1,2-*a*:4',3',2'-*de*]quinoline-6,4'-pyrazole]-5,5'(1'*H*)-dione (3o)



3o

The crude product was purified by flash chromatography on silica gel (EtOAc/petroleum ether = 1/15) to give the product as a brown solid in 42% yield (20.9 mg), >16:1 dr, m.p. 154.8-156.5 °C. ¹H NMR (600 MHz, CDCl₃) δ 7.58 (dd, *J* = 7.2, 1.8 Hz, 1H), 7.44 (dd, *J* = 7.8, 1.8 Hz, 1H), 7.31 (td, *J* = 7.8, 1.8 Hz, 1H), 7.28 (td, *J* = 7.8, 1.8 Hz, 1H), 7.24 – 7.14 (m, 5H), 7.05 (td, *J* = 7.8, 1.2 Hz, 1H), 6.19 (d, *J* = 8.4 Hz, 1H), 6.11 (d, *J* = 7.8 Hz, 1H), 4.83 (d, *J* = 15.0 Hz, 1H), 4.67 (d, *J* = 15.0 Hz, 1H), 4.06 (s, 1H), 3.99 (dd, *J* = 10.2, 6.0 Hz, 1H), 3.61 – 3.57 (m, 1H), 3.04 – 2.95 (m, 1H), 2.21 – 2.16 (m, 1H), 2.13 – 2.01 (m, 2H), 1.35 – 1.27 (m, 1H), 1.01 (s, 3H). ¹³C NMR (151 MHz, CDCl₃) δ 173.7, 173.3, 156.0, 142.7, 141.2, 135.2, 133.5, 131.0, 129.7, 129.2, 129.0, 128.7, 127.7, 126.8, 126.7, 126.6, 104.2, 103.6, 97.5, 63.4, 48.1, 46.6, 46.1, 43.1, 25.8, 23.6, 15.1. HRMS (ESI-TOF) *m/z*: [M+Na]⁺ Calcd for C₂₉H₂₅ClN₄NaO₂⁺ 519.1558, found 519.1561.

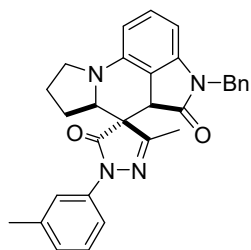
4-benzyl-1'-(2-bromophenyl)-3'-methyl-4,5a,6a,7,8,9-hexahydro-5H-spiro[dipyrrolo[1,2-a:4',3',2'-de]quinoline-6,4'-pyrazole]-5,5'(1'H)-dione (3p)



3p

The crude product was purified by flash chromatography on silica gel (EtOAc/petroleum ether = 1/15) to give the product as a brown solid in 69% yield (37.4 mg), >16:1 dr, m.p. 149.2-151.1 °C. ¹H NMR (600 MHz, CDCl₃) δ 7.65 (dd, *J* = 8.4, 1.8 Hz, 1H), 7.62 (dd, *J* = 7.8, 1.8 Hz, 1H), 7.39 (td, *J* = 7.8, 1.8 Hz, 1H), 7.27 – 7.17 (m, 6H), 7.11 – 7.05 (m, 1H), 6.22 (d, *J* = 8.4 Hz, 1H), 6.15 (d, *J* = 7.8 Hz, 1H), 4.85 (d, *J* = 15.6 Hz, 1H), 4.71 (d, *J* = 15.6 Hz, 1H), 4.08 (s, 1H), 4.03 (dd, *J* = 10.8, 6.0 Hz, 1H), 3.66 – 3.56 (m, 1H), 3.06 – 2.97 (m, 1H), 2.31 – 2.22 (m, 1H), 2.15 – 2.05 (m, 2H), 1.40 – 1.33 (m, 1H), 1.04 (s, 3H). ¹³C NMR (151 MHz, CDCl₃) δ 174.7, 174.3, 156.9, 143.8, 142.2, 136.3, 136.2, 133.4, 130.8, 130.4, 130.1, 128.8, 128.6, 127.8, 127.6, 121.9, 105.2, 104.6, 98.6, 64.4, 49.1, 47.8, 47.2, 44.1, 27.1, 24.7, 16.1. HRMS (ESI-TOF) *m/z*: [M+Na]⁺ Calcd for C₂₉H₂₅BrN₄NaO₂⁺ 563.1053, found 563.1058.

4-benzyl-3'-methyl-1'-(*m*-tolyl)-4,5a,6a,7,8,9-hexahydro-5H-spiro[dipyrrolo[1,2-a:4',3',2'-de]quinoline-6,4'-pyrazole]-5,5'(1'H)-dione(3q)

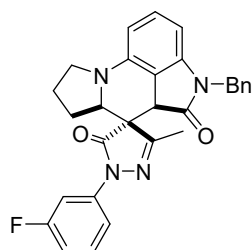


3q

The crude product was purified by flash chromatography on silica gel (EtOAc/petroleum ether = 1/15) to give the product as a brown solid in 67% yield (32.0 mg), 9:1 dr, m.p. 155.2-157.0 °C. ¹H NMR (600 MHz, CDCl₃) δ 7.76 (t, *J* = 1.8 Hz, 1H), 7.75 – 7.69 (m, 1H), 7.30 – 7.25 (m, 3H), 7.26 – 7.12 (m, 3H), 7.10 (td, *J* = 7.8, 1.2 Hz, 1H), 7.00 (dt, *J* = 7.2, 1.8 Hz, 1H), 6.22 (d, *J* = 8.4 Hz, 1H), 6.16 (d, *J* = 7.8 Hz, 1H), 4.86 (d, *J* = 15.6 Hz, 1H), 4.65 (d, *J* = 15.0 Hz, 1H), 4.09 (s, 1H), 4.01 (dd, *J* = 10.8, 6.0 Hz, 1H), 3.64 – 3.60 (m, 1H), 3.02 (q, *J* = 8.4 Hz, 1H), 2.37 (s, 3H), 2.10 – 2.00 (m, 3H), 1.22 – 1.14 (m, 1H), 1.08 (s, 3H). ¹³C NMR (151 MHz, CDCl₃) δ 174.5, 173.5, 156.7, 143.8, 142.1, 138.8, 137.9, 136.3, 130.7, 128.7, 127.73, 127.69, 126.2, 119.9, 116.5, 105.3, 104.6, 98.5, 64.8, 50.4, 47.4, 47.2, 44.1, 26.5, 24.5, 21.6, 16.1. HRMS (ESI-TOF) *m/z*: [M+Na]⁺ Calcd for C₃₀H₂₈N₄NaO₂⁺ 499.2104, found 499.2111.

4-benzyl-1'-(3-fluorophenyl)-3'-methyl-4,5a,6a,7,8,9-hexahydro-5H-

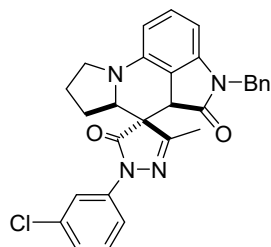
spiro[dipyrrolo[1,2-a:4',3',2'-de]quinoline-6,4'-pyrazole]-5,5'(1'H)-dione (3r)



3r

The crude product was purified by flash chromatography on silica gel (EtOAc/petroleum ether = 1/15) to give the product as a brown solid in 90% yield (43.2 mg), 15:1 dr, m.p. 158.6-160.4 °C. ¹H NMR (600 MHz, CDCl₃) δ 7.79 (ddd, *J* = 7.8, 1.8, 0.6 Hz, 1H), 7.74 (dt, *J* = 10.8, 2.4 Hz, 1H), 7.33 (dt, *J* = 8.4, 6.6 Hz, 1H), 7.29 – 7.25 (m, 4H), 7.24 – 7.21 (m, 1H), 7.10 (td, *J* = 7.8, 1.2 Hz, 1H), 6.87 (tdd, *J* = 8.4, 2.4, 1.2 Hz, 1H), 6.23 (d, *J* = 8.4 Hz, 1H), 6.17 (d, *J* = 7.8 Hz, 1H), 4.86 (d, *J* = 15.6 Hz, 1H), 4.64 (d, *J* = 15.0 Hz, 1H), 4.09 (s, 1H), 4.01 (dd, *J* = 10.8, 6.0 Hz, 1H), 3.64 – 3.61 (m, 1H), 3.03 (q, *J* = 9.0 Hz, 1H), 2.15 – 1.99 (m, 3H), 1.20 – 1.13 (m, 1H), 1.08 (s, 3H). ¹³C NMR (151 MHz, CDCl₃) δ 174.5, 173.7, 163.5 (d, *J*_{CF} = 243.0 Hz), 157.2, 143.8, 142.1, 139.4 (d, *J*_{CF} = 10.5 Hz), 136.3, 130.9, 130.2 (d, *J*_{CF} = 9.0 Hz), 128.8, 127.9, 127.8, 114.4, 114.3, 112.0 (d, *J*_{CF} = 21.0 Hz), 106.5 (d, *J*_{CF} = 27.0 Hz), 105.3, 104.7, 98.7, 64.9, 50.7, 47.6, 47.2, 44.2, 26.6, 24.5, 16.1. HRMS (ESI-TOF) *m/z*: [M+Na]⁺ Calcd for C₂₉H₂₅FN₄NaO₂⁺ 503.1854, found 503.1858.

4-benzyl-1'-(3-chlorophenyl)-3'-methyl-4,5a,6a,7,8,9-hexahydro-5H-spiro[dipyrrolo[1,2-a:4',3',2'-de]quinoline-6,4'-pyrazole]-5,5'(1'H)-dione (3s)

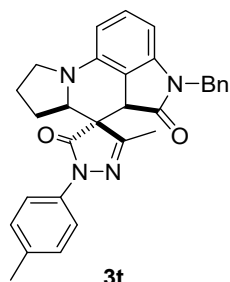


3s

The crude product was purified by flash chromatography on silica gel (EtOAc/petroleum ether = 1/15) to give the product as a brown solid in 41% yield (20.4 mg), 8:1 dr, m.p. 160.2-161.8 °C. ¹H NMR (600 MHz, Chloroform-*d*) δ 8.02 (t, *J* = 2.4 Hz, 1H), 7.94 (d, *J* = 7.8 Hz, 1H), 7.33 (t, *J* = 7.8 Hz, 1H), 7.30 – 7.28 (m, 4H), 7.26 – 7.24 (m, 1H), 7.16 (d, *J* = 7.8 Hz, 1H), 7.13 (t, *J* = 7.8 Hz, 1H), 6.25 (d, *J* = 8.2 Hz, 1H), 6.20 (d, *J* = 7.7 Hz, 1H), 4.88 (d, *J* = 15.6 Hz, 1H), 4.67 (d, *J* = 15.6 Hz, 1H), 4.11 (s, 1H), 4.03 (dd, *J* = 10.8, 6.0 Hz, 1H), 3.67 – 3.63 (m, 1H), 3.09 – 3.01 (m, 1H), 2.03 – 2.05 (m, 3H), 1.25 – 1.15 (m, 1H), 1.10 (s, 3H). ¹³C NMR (150 MHz, Chloroform-*d*) δ 172.0, 171.2, 154.8, 141.3, 139.6, 136.5, 133.8, 132.2, 128.4, 127.5, 126.3, 125.4, 125.3, 122.8, 116.6, 114.4, 102.7, 102.2, 96.2, 62.4, 48.2, 45.1, 44.7, 41.7, 24.1, 22.0, 13.7. HRMS (ESI-TOF) *m/z*: [M+Na]⁺ Calcd for C₂₉H₂₅ClN₄NaO₂⁺ 519.1558, found 519.1563.

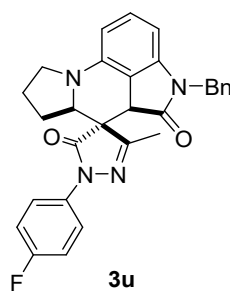
4-benzyl-3'-methyl-1'-(p-tolyl)-4,5a,6a,7,8,9-hexahydro-5H-spiro[dipyrrolo[1,2-

a:4',3',2'-de]quinoline-6,4'-pyrazole]-5,5'(1'H)-dione (3t)



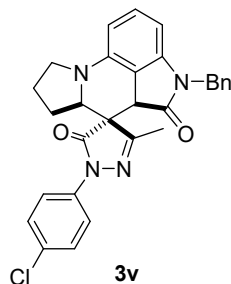
The crude product was purified by flash chromatography on silica gel (EtOAc/petroleum ether = 1/15) to give the product as a brown solid in 78% yield (37.2 mg), 10:1 dr, m.p. 156.7-158.6 °C. ¹H NMR (600 MHz, CDCl₃) δ 7.93 – 7.76 (m, 2H), 7.33 – 7.27 (m, 4H), 7.26 – 7.18 (m, 3H), 7.13 (td, *J* = 7.8, 1.2 Hz, 1H), 6.25 (d, *J* = 8.4 Hz, 1H), 6.19 (d, *J* = 7.8 Hz, 1H), 4.90 (d, *J* = 15.6 Hz, 1H), 4.68 (d, *J* = 15.6 Hz, 1H), 4.12 (s, 1H), 4.04 (dd, *J* = 10.8, 5.4 Hz, 1H), 3.68 – 3.56 (m, 1H), 3.05 (q, *J* = 8.4 Hz, 1H), 2.36 (s, 3H), 2.17 – 1.96 (m, 3H), 1.28 – 1.18 (m, 1H), 1.11 (s, 3H). ¹³C NMR (151 MHz, CDCl₃) δ 174.5, 143.8, 156.6, 142.1, 136.3, 135.1, 130.7, 129.4, 128.7, 127.73, 127.69, 119.5, 105.4, 104.5, 98.5, 64.8, 50.3, 47.4, 47.2, 44.1, 26.5, 24.5, 21.0, 16.1. HRMS (ESI-TOF) *m/z*: [M+Na]⁺ Calcd for C₃₀H₂₈N₄NaO₂⁺ 499.2104, found 499.2107.

4-benzyl-1'-(4-fluorophenyl)-3'-methyl-4,5a,6a,7,8,9-hexahydro-5H-spiro[dipyrrolo[1,2-a:4',3',2'-de]quinoline-6,4'-pyrazole]-5,5'(1'H)-dione (3u)



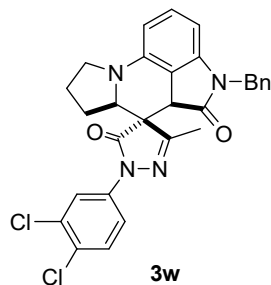
The crude product was purified by flash chromatography on silica gel (EtOAc/petroleum ether = 1/15) to give the product as a brown solid in 80% yield (38.4 mg), >16:1 dr, m.p. 172.2-173.9 °C. ¹H NMR (600 MHz, CDCl₃) δ 7.95 – 7.85 (m, 2H), 7.29 – 7.25 (m, 4H), 7.24 – 7.20 (m, 1H), 7.12 – 7.04 (m, 3H), 6.23 (d, *J* = 7.8 Hz, 1H), 6.17 (d, *J* = 7.8 Hz, 1H), 4.86 (d, *J* = 15.6 Hz, 1H), 4.65 (d, *J* = 15.6 Hz, 1H), 4.08 (s, 1H), 4.01 (dd, *J* = 10.2, 5.4 Hz, 1H), 3.65 – 3.61 (m, 1H), 3.03 (q, *J* = 9.0 Hz, 1H), 2.14 – 2.02 (m, 3H), 1.31 – 1.15 (m, 1H), 1.07 (s, 3H). ¹³C NMR (151 MHz, CDCl₃) δ 174.6, 173.5, 161.2 (d, *J*_{CF} = 243.0 Hz), 157.1, 143.8, 142.1, 136.3, 134.2, 130.9, 128.8, 127.8, 127.7, 121.2 (d, *J*_{CF} = 9.0 Hz), 115.7 (d, *J*_{CF} = 22.5 Hz), 105.3, 104.7, 98.7, 64.8, 50.4, 47.6, 47.2, 44.2, 26.6, 24.5, 16.1. HRMS (ESI-TOF) *m/z*: [M+Na]⁺ Calcd for C₂₉H₂₅FN₄NaO₂⁺ 503.1854, found 503.1859.

4-benzyl-1'-(4-chlorophenyl)-3'-methyl-4,5a,6a,7,8,9-hexahydro-5H-spiro[dipyrrolo[1,2-a:4',3',2'-de]quinoline-6,4'-pyrazole]-5,5'(1'H)-dione (3v)



The crude product was purified by flash chromatography on silica gel (EtOAc/petroleum ether = 1/15) to give the product as a brown solid in 76% yield (37.8 mg), 8:1 dr, m.p. 167.6-169.3 °C. ¹H NMR (600 MHz, CDCl₃) δ 7.90 – 7.83 (m, 2H), 7.33 – 7.26 (m, 2H), 7.25 – 7.18 (m, 3H), 7.20 – 7.05 (m, 2H), 7.07 – 7.03 (m, 1H), 6.18 (d, *J* = 7.8 Hz, 1H), 6.12 (d, *J* = 7.8 Hz, 1H), 4.81 (d, *J* = 15.6 Hz, 1H), 4.59 (d, *J* = 15.0 Hz, 1H), 4.03 (s, 1H), 3.95 (dd, *J* = 10.2, 5.4 Hz, 1H), 3.59 – 3.55 (m, 1H), 2.97 (q, *J* = 9.0 Hz, 1H), 2.09 – 1.94 (m, 3H), 1.19 – 1.07 (m, 1H), 1.02 (s, 3H). ¹³C NMR (151 MHz, CDCl₃) δ 173.4, 172.5, 156.1, 142.7, 141.0, 135.5, 135.2, 129.8, 129.3, 127.9, 127.7, 126.7, 126.6, 119.2, 104.1, 103.6, 97.6, 63.7, 49.4, 46.5, 46.1, 43.1, 25.5, 23.4, 15.0. HRMS (ESI-TOF) *m/z*: [M+Na]⁺ Calcd for C₂₉H₂₅ClN₄NaO₂⁺ 519.1558, found 519.1561.

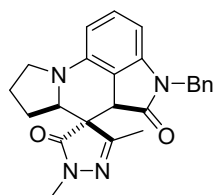
4-benzyl-1'-(3,4-dichlorophenyl)-3'-methyl-4,5a,6a,7,8,9-hexahydro-5H-spiro[dipyrrolo[1,2-a:4',3',2'-de]quinoline-6,4'-pyrazole]-5,5'(1'H)-dione (3w)



The crude product was purified by flash chromatography on silica gel (EtOAc/petroleum ether = 1/15) to give the product as a brown solid in 98% yield (52.1 mg), 8:1 dr, m.p. 171.2-173.4 °C. ¹H NMR (600 MHz, CDCl₃) δ 8.08 (d, *J* = 2.4 Hz, 1H), 7.84 (dd, *J* = 9.0, 2.4 Hz, 1H), 7.38 (d, *J* = 9.0 Hz, 1H), 7.24 – 7.19 (m, 4H), 7.17 – 7.08 (m, 1H), 7.06 (td, *J* = 8.4, 1.2 Hz, 1H), 6.18 (d, *J* = 8.4 Hz, 1H), 6.12 (d, *J* = 7.8 Hz, 1H), 4.80 (d, *J* = 15.0 Hz, 1H), 4.59 (d, *J* = 15.0 Hz, 1H), 4.02 (s, 1H), 3.95 (dd, *J* = 10.8, 6.0 Hz, 1H), 3.59 – 3.56 (m, 1H), 2.98 (q, *J* = 8.4 Hz, 1H), 2.12 – 1.89 (m, 3H), 1.16 – 1.07 (m, 1H), 1.02 (s, 3H). ¹³C NMR (151 MHz, CDCl₃) δ 174.4, 173.6, 157.6, 143.7, 142.0, 137.2, 136.2, 132.8, 130.9, 130.5, 128.8, 128.4, 127.8, 127.7, 120.4, 117.9, 105.1, 104.7, 98.7, 64.8, 50.6, 47.6, 47.1, 44.1, 26.5, 24.5, 16.1. HRMS (ESI-TOF) *m/z*: [M+Na]⁺ Calcd for C₂₉H₂₄Cl₂N₄NaO₂⁺ 553.1196, found 553.1201.

4-benzyl-1',3'-dimethyl-4,5a,6a,7,8,9-hexahydro-5H-spiro[dipyrrolo[1,2-

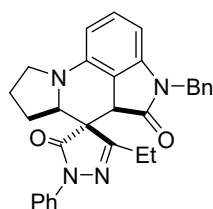
a:4',3',2'-de]quinoline-6,4'-pyrazole]-5,5'(1'H)-dione (3x)



3x

The crude product was purified by flash chromatography on silica gel (EtOAc/petroleum ether = 1/16) to give the product as a brown solid in 35% yield (14.0 mg), >16:1 dr, m.p. 142.3-143.5 °C. ¹H NMR (600 MHz, DMSO-*d*₆) δ 7.35 – 7.23 (m, 5H), 7.11 (t, *J* = 7.8 Hz, 1H), 6.28 (dd, *J* = 10.2, 8.4 Hz, 2H), 4.83 (d, *J* = 15.6 Hz, 1H), 4.72 (d, *J* = 15.6 Hz, 1H), 4.05 (s, 1H), 3.81 (dd, *J* = 10.2, 6.0 Hz, 1H), 3.61 – 3.58 (m, 1H), 3.26 (s, 3H), 2.97 (td, *J* = 9.6, 6.6 Hz, 1H), 2.05 – 1.99 (m, 2H), 1.88 – 1.84 (m, 1H), 1.06 – 0.99 (m, 1H), 0.89 (s, 3H). ¹³C NMR (150 MHz, DMSO-*d*₆) δ 174.8, 174.7, 155.9, 143.7, 142.5, 137.2, 130.8, 129.0, 127.9, 127.8, 105.7, 105.0, 98.7, 64.4, 48.7, 47.4, 46.8, 43.5, 31.6, 26.4, 24.5, 15.8. HRMS (ESI-TOF) *m/z*: [M+Na]⁺ Calcd for C₂₄H₂₄N₄NaO₂⁺ 423.1791, found 423.1793.

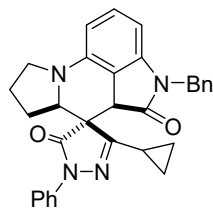
4-benzyl-3'-ethyl-1'-phenyl-4,5a,6a,7,8,9-hexahydro-5H-spiro[dipyrrolo[1,2-a:4',3',2'-de]quinoline-6,4'-pyrazole]-5,5'(1'H)-dione (3y)



3y

The crude product was purified by flash chromatography on silica gel (EtOAc/petroleum ether = 1/15) to give the product as a brown solid in 45% yield (21.4 mg), 8:1 dr, m.p. 157.4-159.1 °C. ¹H NMR (600 MHz, DMSO-*d*₆) δ 7.92 – 7.86 (m, 2H), 7.51 – 7.44 (m, 2H), 7.33 – 7.27 (m, 2H), 7.28 – 7.23 (m, 4H), 7.17 – 7.10 (m, 1H), 6.32 (d, *J* = 3.0 Hz, 1H), 6.30 (d, *J* = 3.0 Hz, 1H), 4.78 (s, 2H), 4.20 (s, 1H), 3.92 (dd, *J* = 10.8, 6.0 Hz, 1H), 3.75 – 3.55 (m, 1H), 3.00 (q, *J* = 8.4 Hz, 1H), 2.11 – 1.88 (m, 4H), 1.37 – 1.29 (m, 1H), 1.15 – 1.04 (m, 1H), 0.83 (t, *J* = 7.2 Hz, 3H). ¹³C NMR (151 MHz, DMSO-*d*₆) δ 174.3, 173.4, 160.9, 143.2, 141.7, 137.8, 136.7, 130.5, 129.1, 128.5, 127.5, 127.3, 125.2, 118.4, 105.2, 104.6, 98.4, 64.4, 50.1, 46.9, 46.8, 43.1, 25.9, 24.0, 22.4, 8.2. HRMS (ESI-TOF) *m/z*: [M+Na]⁺ Calcd for C₃₀H₂₈N₄NaO₂⁺ 499.2104, found 499.2105.

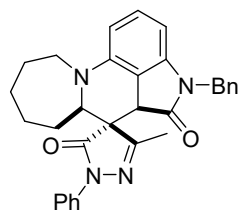
4-benzyl-3'-cyclopropyl-1'-phenyl-4,5a,6a,7,8,9-hexahydro-5H-spiro[dipyrrolo[1,2-a:4',3',2'-de]quinoline-6,4'-pyrazole]-5,5'(1'H)-dione (3z)



3z

The crude product was purified by flash chromatography on silica gel (EtOAc/petroleum ether = 1/13) to give the product as a brown solid in 94% yield (46.0 mg), 10:1 dr, m.p. 207.1-208.5 °C. ¹H NMR (600 MHz, Chloroform-*d*) δ 7.94 (d, *J* = 8.4 Hz, 2H), 7.39 (t, *J* = 7.8 Hz, 2H), 7.35 – 7.28 (m, 4H), 7.27 – 7.23 (m, 1H), 7.17 (d, *J* = 7.2 Hz, 1H), 7.11 (t, *J* = 7.8 Hz, 1H), 6.23 (d, *J* = 8.4 Hz, 1H), 6.18 (d, *J* = 8.4 Hz, 1H), 4.99 (d, *J* = 9.6 Hz, 1H), 4.53 (d, *J* = 9.6 Hz, 1H), 4.14 (s, 1H), 4.06 (dd, *J* = 10.8, 6.0 Hz, 1H), 3.67 – 3.64 (m, 1H), 3.07 (q, *J* = 8.4 Hz, 1H), 2.13 – 2.06 (m, 3H), 1.39 – 1.32 (m, 1H), 1.05 – 1.00 (m, 1H), 0.52 – 0.43 (m, 1H), 0.14 – 0.06 (m, 2H). ¹³C NMR (150 MHz, CDCl₃) δ 175.0, 173.6, 161.3, 144.1, 142.2, 138.2, 136.2, 130.7, 128.8, 128.7, 127.8, 127.7, 125.2, 119.1, 105.9, 104.4, 98.4, 65.0, 51.0, 47.7, 47.3, 44.1, 26.7, 24.6, 9.33, 9.31, 6.8. HRMS (ESI-TOF) *m/z*: [M+Na]⁺ Calcd for C₃₁H₂₈N₄NaO₂⁺ 511.2104, found 511.2106.

4-benzyl-3'-methyl-1'-phenyl-4,5a,6a,7,8,9,10,11-octahydro-5H-spiro[azepino[1,2-a]pyrrolo[4,3,2-de]quinoline-6,4'-pyrazole]-5,5'(1'H)-dione (3aa)

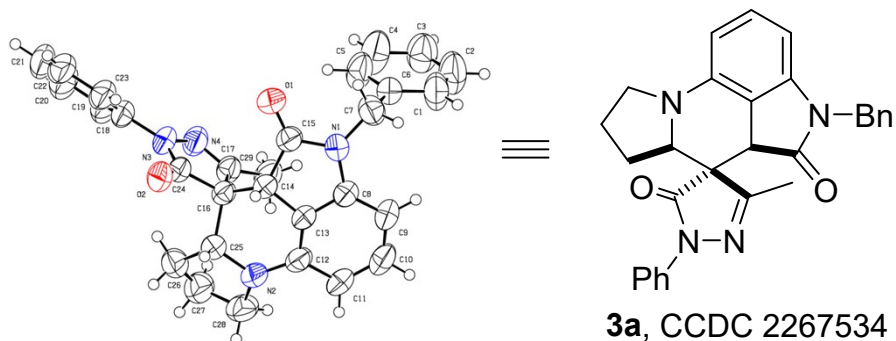


3aa

The crude product was purified by flash chromatography on silica gel (EtOAc/petroleum ether = 1/15) to give the product as a brown solid in 43% yield (21.2 mg), 2:1 dr, m.p. 178.4-181.2 °C. ¹H NMR (600 MHz, Chloroform-*d*) δ 8.00 – 7.97 (m, 2H), 7.45 – 7.42 (m, 2H), 7.30 – 7.28 (m, 4H), 7.26 – 7.19 (m, 2H), 7.10 – 7.08 (m, 1H), 6.42 (d, *J* = 8.4 Hz, 1H), 6.15 (d, *J* = 7.2 Hz, 1H), 4.87 (d, *J* = 15.6 Hz, 1H), 4.69 (d, *J* = 15.6 Hz, 1H), 4.13 (s, 1H), 3.99 (t, *J* = 4.2 Hz, 1H), 3.59 – 3.54 (m, 2H), 1.81 – 1.73 (m, 4H), 1.60 – 1.55 (m, 4H), 1.37 (s, 3H). ¹³C NMR (151 MHz, CDCl₃) δ 174.2, 173.3, 157.8, 143.7, 143.5, 137.9, 136.3, 130.4, 128.9, 128.7, 127.7, 125.4, 119.4, 105.8, 103.3, 98.4, 63.8, 55.1, 48.5, 46.9, 44.1, 29.3, 28.9, 26.1, 25.9, 16.6. HRMS (ESI-TOF) *m/z*: [M+Na]⁺ Calcd for C₃₁H₃₀N₄NaO₂⁺ 513.2261, found 513.2266.

5. X-ray Crystal Structures of 3a

To a 10 mL tube containing **3a** (50.0 mg) was added a mixture of solvent (PE:EA = 5:1) (6.0 mL). A clear solution was obtained through ultrasound treatment and was kept at room temperature and the crystals were obtained after the solvent evaporated, which were characterized by X-ray single crystal diffraction. X-ray diffraction experiment was carried out on an Agilent Gemini and the data obtained were deposited at the Cambridge Crystallographic Data Centre.



Identification code	3a
Chemical formula	C ₂₉ H ₂₆ N ₄ O ₂
Formula weight	462.54 g/mol
Temperature	293(2) K
Crystal system	orthorhombic
Space group	Pbca
Unit cell dimensions	a = 11.0161(16) Å α = 90° b = 8.8582(11) Å β = 90° c = 48.322(7) Å γ = 90°
Volume	4715.4(12) Å ³
Z	8
Density (calculated)	1.303 g/cm ³
Absorption coefficient	0.666 mm ⁻¹
F (000)	1952.0
Theta range for data collection	7.318 to 134.484°
Index ranges	-13 ≤ h ≤ 12, -6 ≤ k ≤ 10, -57 ≤ l ≤ 54
Reflections collected	9420
Independent reflections	4193 [R(int) = 0.0462, R(sigma) = 0.0797]
Data / restraints / parameters	4193 / 0 / 318
Goodness-of-fit on F²	0.991
Final R indices	I > 2σ(I) R1 = 0.1004, wR2 = 0.2621 all data R1 = 0.1623, wR2 = 0.3352
Largest diff. peak and hole	0.26 and -0.45 eÅ ⁻³

6. NMR Spectra

