

Zinc Chloride Catalyzed Stereoselective Construction of Spiropyrazolone Tetrahydroquinolines via Tandem [1,5]-Hydride Shift/Cyclization Sequence

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Supporting Information

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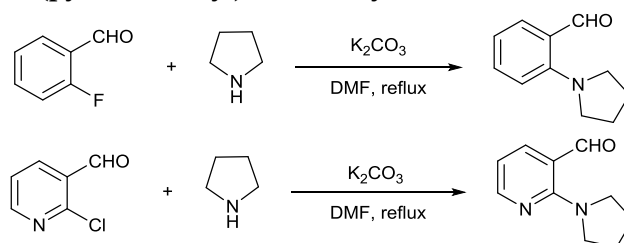
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1. General information

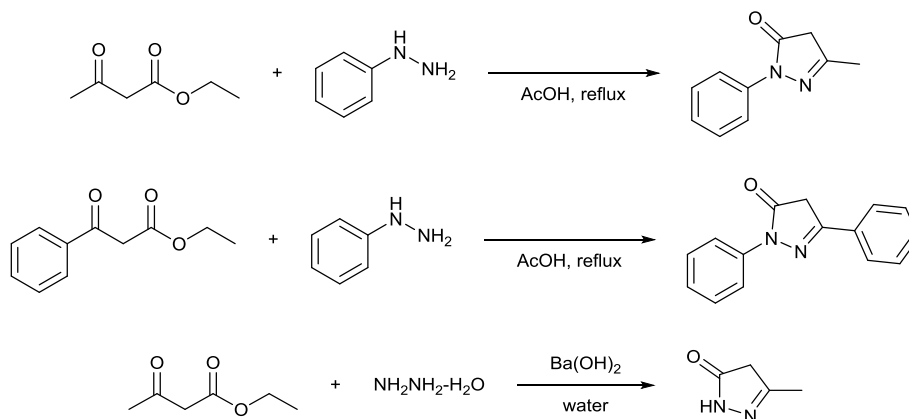
Unless otherwise noted, all reagents and chemicals (AR grade) were purchased from commercial suppliers and used without further purification. All the solvents were treated according to general methods. Anhydrous furanidine (THF) was freshly distilled from sodium. Petroleum ether (PE) refers to the fraction boiling in the 60-90°C range. The progress of the reactions was monitored by TLC (silica gel, Polygram SILG/UV 254 plates). Column chromatography was performed on silica gel (100~200 mesh). All ^1H NMR spectra were recorded on a Bruker Avance II 400 MHz and Bruker Avance III 471 MHz respectively, ^{13}C NMR spectra were recorded on a Bruker Avance II 101 MHz or Bruker Avance III 126 MHz. CDCl_3 were used for NMR spectroscopy, using tetramethylsilane as the internal reference. Data for ^1H NMR are recorded as follows: chemical shift (δ , ppm), multiplicity (s = singlet, d = doublet, t = triplet, m = multiplet or unresolved, br = broad singlet, dd = doublet doublet, coupling constants in Hz, integration). Data for ^{13}C NMR are reported in terms of chemical shift (δ , ppm). HRMS (ESI) was determined by a HRMS/MS instrument (LTQ Orbitrap XL TM).

2. Typical procedure for substrates preparation

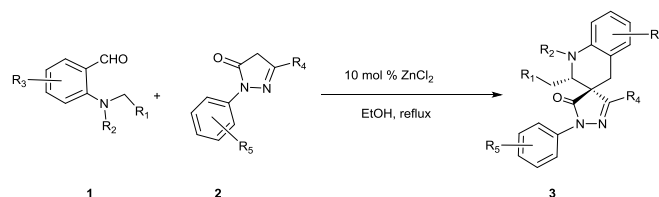
a). The synthesis of 2-(pyrrolidin-1-yl)benzaldehyde¹⁻³.



b). The synthesis of pyrazolones.^{4,5}

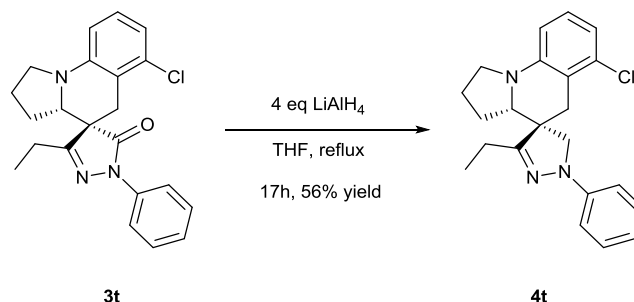


3. General procedure for the intramolecular redox reaction catalyzed by zinc chloride



A mixture of **1** (0.40 mmol), **2** (0.42 mmol) and ZnCl_2 (0.04 mmol) was added solvent (4 mL), then the reaction mixture was stirred at refluxing temperature until the complete consumption of **1** as judged by TLC analysis. When the reactions completed, the reaction

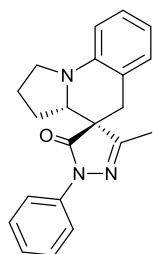
mixture was adsorbed onto silica gel and purified by column chromatography to desired product **3**.



In the argon atmosphere, LiAlH_4 (1.6 mmol, 4eq) was added into **anhydrous** THF (1.0 mL), then the mixture was stirred for 20 min in 0 °C. A solution of **3t** (0.4 mmol, 1 eq) in **anhydrous** THF (1.0 mL) was added into the solution of LiAlH_4 in drops. Then the reaction mixture was stirred at refluxing temperature. After completion of the reaction (17 h) the reaction mixture was quenched with water, extracted with EtOAc. The combined organic layers were washed with water, brine, dried (Na_2SO_4) and concentrated to **4t** in 56% yield. The product **4t** should be preserved under low temperature and oxygen free conditions.

4. Characterization data of products

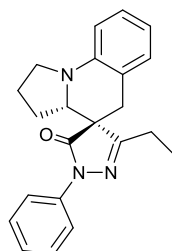
3-methyl-1-phenyl-1',2',3',3a'-tetrahydro-5'H-spiro[pyrazole-4,4'-pyrrolo[1,2-a]quinolin]-5(1H)-one (**3a**)



3a

White solid, mp 117.4 - 120.3 °C; yield 91%, *dr* 92:8. ^1H NMR (400 MHz, CDCl_3) δ 7.95 (d, J = 7.7 Hz, 2H), 7.45 – 7.37 (m, 2H), 7.19 (dd, J = 14.6, 7.3 Hz, 2H), 7.10 (d, J = 7.4 Hz, 1H), 6.67 (t, J = 7.3 Hz, 1H), 6.53 (d, J = 8.1 Hz, 1H), 3.77 (dd, J = 10.3, 5.2 Hz, 1H), 3.53 (dd, J = 13.2, 4.4 Hz, 1H), 3.39 (d, J = 16.4 Hz, 1H), 3.27 (dd, J = 16.2, 8.9 Hz, 1H), 2.82 (d, J = 16.4 Hz, 1H), 2.13 – 1.97 (m, 3H), 1.68 (s, 3H), 1.34 – 1.22 (m, 1H); ^{13}C NMR (126 MHz, CDCl_3) δ 174.2, 162.1, 143.1, 138.1, 129.0, 128.9, 128.1, 125.1, 118.7, 117.4, 116.2, 110.6, 61.6, 52.8, 46.9, 34.4, 27.5, 23.2, 16.6. HRMS (ESI) Calculated for $\text{C}_{21}\text{H}_{22}\text{N}_3\text{O}$ ($[\text{M}+\text{H}]^+$) 332.1757, Found 332.1754.

3-ethyl-1-phenyl-1',2',3',3a'-tetrahydro-5'H-spiro[pyrazole-4,4'-pyrrolo[1,2-a]quinolin]-5(1H)-one (**3b**)

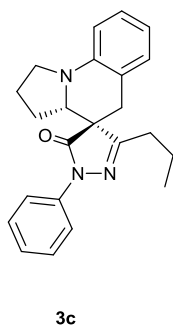


3b

Pink solid, mp 132.1 - 134.2 °C, yield 77%, *dr* >95:5. ^1H NMR (400 MHz, CDCl_3) δ 8.00 (dd, J = 8.7, 1.1 Hz, 2H), 7.47 – 7.37 (m, 2H), 7.23 – 7.14 (m, 2H), 7.09 (d, J = 7.5 Hz, 1H), 6.67 (t, J = 7.0 Hz, 1H), 6.52 (d, J = 8.0 Hz, 1H), 3.74 (dd, J = 10.4, 5.1 Hz, 1H), 3.51 (td, J = 9.1, 3.0 Hz, 1H), 3.37 (d, J = 16.4 Hz, 1H), 3.28 (dd, J = 16.2, 8.8 Hz, 1H), 2.80 (d, J = 16.5 Hz, 1H), 2.13 – 1.90 (m, 4H), 1.87 – 1.79 (m, 1H), 1.32 – 1.16 (m, 1H), 1.09 (t, J = 7.2 Hz, 3H); ^{13}C NMR (126 MHz, CDCl_3) δ 174.3, 165.7, 143.1, 138.4, 129.0, 128.9, 128.1, 125.0, 118.7, 117.7, 116.2, 110.6, 61.6, 52.9, 46.8, 34.3, 27.5, 23.4, 23.1, 8.9.

HRMS (ESI) Calculated for $C_{22}H_{24}N_3O$ ($[M+H]^+$) 346.1914, Found 346.1909.

1-phenyl-3-propyl-1',2',3',3a'-tetrahydro-5'H-spiro[pyrazole-4,4'-pyrrolo[1,2-a]quinolin]-5(1H)-one (3c)

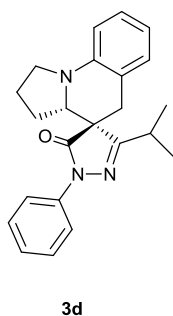


3c

Yellow solid, mp 102.1- 104.0 °C; yield 83%, *dr* 92:8. 1H NMR (400 MHz, $CDCl_3$) δ 7.98 (d, J = 7.8 Hz, 2H), 7.42 (t, J = 8.0 Hz, 2H), 7.19 (dd, J = 13.3, 7.1 Hz, 2H), 7.08 (d, J = 7.4 Hz, 1H), 6.67 (t, J = 7.3 Hz, 1H), 6.52 (d, J = 8.0 Hz, 1H), 3.73 (dd, J = 10.3, 5.1 Hz, 1H), 3.51 (td, J = 9.2, 3.0 Hz, 1H), 3.37 (d, J = 16.4 Hz, 1H), 3.27 (dd, J = 16.3, 8.8 Hz, 1H), 2.79 (d, J = 16.5 Hz, 1H), 1.98 (dddd, J = 17.9, 11.1, 8.1, 2.3 Hz, 4H), 1.82 – 1.73 (m, 1H), 1.61 – 1.54 (m, 2H), 1.30 – 1.24 (m, 1H), 0.81 (t, J = 7.3 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.2, 164.7, 143.1, 138.3, 129.0, 128.9, 128.0, 124.9, 118.7, 117.7, 116.2, 110.6, 61.8, 52.9, 46.8, 34.3, 31.8, 27.4, 23.1, 18.1, 13.9. HRMS (ESI)

Calculated for $C_{23}H_{26}N_3O$ ($[M+H]^+$) 360.2070, Found 360.2070.

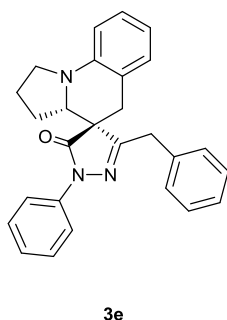
3-isopropyl-1-phenyl-1',2',3',3a'-tetrahydro-5'H-spiro[pyrazole-4,4'-pyrrolo[1,2-a]quinolin]-5(1H)-one (3d)



3d

Pink solid, mp 146.3 - 152.4 °C; yield 85%, *dr* 89:11. 1H NMR (400 MHz, $CDCl_3$) δ 7.98 (d, J = 8.2 Hz, 2H), 7.41 (t, J = 7.9 Hz, 2H), 7.21 – 7.15 (m, 2H), 7.10 (d, J = 7.4 Hz, 1H), 6.68 (d, J = 7.5 Hz, 1H), 6.53 (d, J = 8.1 Hz, 1H), 3.69 (dd, J = 10.1, 5.2 Hz, 1H), 3.50 – 3.37 (m, 2H), 3.28 (dd, J = 16.5, 8.2 Hz, 1H), 2.86 (d, J = 16.6 Hz, 1H), 2.24 – 2.16 (m, 1H), 2.09 – 1.93 (m, 3H), 1.34 – 1.25 (m, 1H), 1.14 (d, J = 6.8 Hz, 3H), 0.87 (d, J = 6.8 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.0, 169.7, 143.2, 138.3, 129.0, 128.9, 128.0, 125.0, 118.7, 118.2, 116.4, 110.7, 62.3, 53.3, 46.7, 34.3, 29.1, 27.5, 23.0, 22.2, 20.3. HRMS (ESI) Calculated for $C_{23}H_{26}N_3O$ ($[M+H]^+$) 360.2070, Found 360.2069.

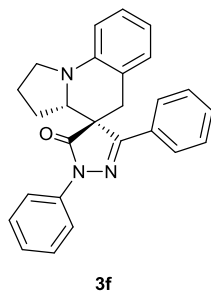
3-benzyl-1-phenyl-1',2',3',3a'-tetrahydro-5'H-spiro[pyrazole-4,4'-pyrrolo[1,2-a]quinolin]-5(1H)-one (3e)



3e

Orange liquid, yield 95%, *dr* 92:8. 1H NMR (400 MHz, $CDCl_3$) δ 8.00 (d, J = 8.5 Hz, 2H), 7.44 (t, J = 8.0 Hz, 2H), 7.25 – 7.12 (m, 5H), 6.90 – 6.81 (m, 3H), 6.63 (t, J = 7.4 Hz, 1H), 6.54 (d, J = 8.1 Hz, 1H), 3.70 (dd, J = 10.1, 5.4 Hz, 1H), 3.44 (d, J = 15.3 Hz, 1H), 3.40 – 3.30 (m, 3H), 3.08 (dd, J = 16.8, 7.9 Hz, 1H), 2.66 (d, J = 16.6 Hz, 1H), 2.03 – 1.79 (m, 3H), 1.28 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.0, 163.1, 143.1, 138.2, 134.7, 129.2, 128.9, 128.9, 128.1, 127.9, 126.5, 125.1, 118.7, 117.8, 116.5, 110.8, 62.0, 53.6, 46.3, 36.2, 34.1, 27.2, 22.7. HRMS (ESI) Calculated for $C_{27}H_{26}N_3O$ ($[M+H]^+$) 408.2070, Found 408.2073.

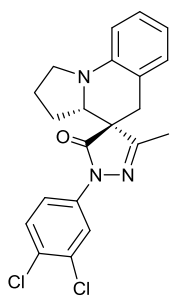
1,3-diphenyl-1',2',3',3a'-tetrahydro-5'H-spiro[pyrazole-4,4'-pyrrolo[1,2-a]quinolin]-5(1H)-one (3f)



3f

Yellow solid, mp 131.3 – 133.5 °C; yield 94%, *dr* 78:22. ¹H NMR (400 MHz, CDCl₃) δ 8.07 (d, *J* = 8.1 Hz, 2H), 7.52 – 7.42 (m, 2H), 7.25 (dd, *J* = 6.3, 4.0 Hz, 4H), 7.12 (dt, *J* = 15.3, 7.6 Hz, 4H), 6.69 (t, *J* = 7.5 Hz, 1H), 6.31 (d, *J* = 8.1 Hz, 1H), 3.75 (dd, *J* = 8.9, 6.7 Hz, 1H), 3.61 (d, *J* = 17.1 Hz, 1H), 3.28 (td, *J* = 8.6, 4.1 Hz, 1H), 3.20 (d, *J* = 17.1 Hz, 1H), 2.71 (q, *J* = 8.1 Hz, 1H), 2.04 (dt, *J* = 10.4, 6.5 Hz, 1H), 1.94 – 1.78 (m, 2H), 1.49 (dd, *J* = 19.9, 9.9 Hz, 1H); ¹³C NMR (126 MHz, CDCl₃) δ 174.1, 162.4, 143.5, 138.1, 132.1, 129.7, 129.0, 128.6, 127.8, 127.8, 127.7, 125.4, 119.0, 116.5, 111.2, 62.5, 54.9, 46.4, 34.1, 27.1, 23.0. HRMS (ESI) Calculated for C₂₆H₂₄N₃O ([M+H]⁺) 394.1914, Found 394.1914.

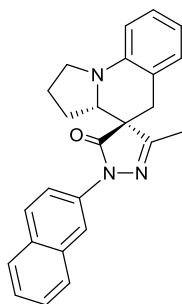
1-(3,4-dichlorophenyl)-3-methyl-1',2',3',3a'-tetrahydro-5'H-spiro[pyrazole-4,4'-pyrrolo[1,2-a]quinolin]-5(1H)-one (3g)



3g

Yellow solid, mp 125.8 - 128.5 °C; yield 84 %, *dr* 94:6. ¹H NMR (400 MHz, CDCl₃) δ 8.15 (d, *J* = 2.5 Hz, 1H), 7.90 (dd, *J* = 8.9, 2.5 Hz, 1H), 7.46 (d, *J* = 8.9 Hz, 1H), 7.19 (t, *J* = 7.8 Hz, 1H), 7.09 (d, *J* = 7.3 Hz, 1H), 6.68 (t, *J* = 7.1 Hz, 1H), 6.53 (d, *J* = 7.9 Hz, 1H), 3.75 (dd, *J* = 10.4, 5.4 Hz, 1H), 3.54 (t, *J* = 7.5 Hz, 1H), 3.32 (dd, *J* = 40.7, 11.9 Hz, 2H), 2.82 (d, *J* = 16.5 Hz, 1H), 2.13 – 1.95 (m, 3H), 1.67 (s, 3H), 1.25 (t, *J* = 9.1 Hz, 1H); ¹³C NMR (126 MHz, CDCl₃) δ 174.2, 162.8, 143.0, 137.4, 132.8, 130.5, 129.0, 128.2, 128.1, 120.0, 117.5, 117.0, 116.4, 110.7, 61.6, 53.0, 46.9, 34.4, 27.5, 23.1, 16.6. HRMS (ESI) Calculated for C₂₁H₂₀Cl₂N₃O ([M+H]⁺) 400.0978, Found 400.0984.

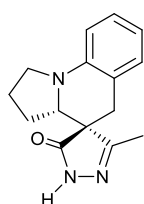
3-methyl-1-(naphthalen-2-yl)-1',2',3',3a'-tetrahydro-5'H-spiro[pyrazole-4,4'-pyrrolo[1,2-a]quinolin]-5(1H)-one (3h)



3h

Yellow liquid, yield 76%, *dr* 93:7. ¹H NMR (400 MHz, CDCl₃) δ 8.45 (d, *J* = 1.8 Hz, 1H), 8.18 (dd, *J* = 8.9, 2.2 Hz, 1H), 7.94 – 7.80 (m, 3H), 7.47 (dtd, *J* = 14.7, 6.9, 1.3 Hz, 2H), 7.21 (t, *J* = 7.7 Hz, 1H), 7.12 (d, *J* = 7.4 Hz, 1H), 6.69 (t, *J* = 7.4 Hz, 1H), 6.55 (d, *J* = 8.0 Hz, 1H), 3.82 (dd, *J* = 10.2, 5.2 Hz, 1H), 3.60 – 3.49 (m, 1H), 3.44 (d, *J* = 16.4 Hz, 1H), 3.29 (dd, *J* = 16.2, 8.8 Hz, 1H), 2.87 (d, *J* = 16.4 Hz, 1H), 2.17 – 1.93 (m, 3H), 1.73 (s, 3H), 1.38 – 1.29 (m, 1H); ¹³C NMR (126 MHz, CDCl₃) δ 174.4, 162.3, 143.1, 135.7, 133.6, 131.0, 129.0, 128.8, 128.2, 128.0, 127.6, 126.5, 125.4, 118.3, 117.4, 116.3, 115.8, 110.6, 61.7, 52.9, 46.9, 34.4, 27.5, 23.2, 16.6. HRMS (ESI) Calculated for C₂₅H₂₄N₃O ([M+H]⁺) 382.1914, Found 382.1919.

methyl-1',2',3',3a'-tetrahydro-5'H-spiro[pyrazole-4,4'-pyrrolo[1,2-a]quinolin]-5(1H)-one (3i)

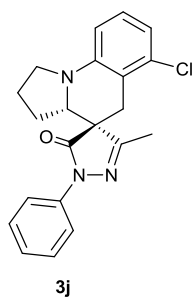


3i

Yellow solid, mp 190.9 - 194.6 °C; yield 73%, *dr* 95:5. ¹H NMR (400 MHz, CDCl₃) δ 9.50 (d, *J* = 14.6 Hz, 1H), 7.16 (t, *J* = 7.7 Hz, 1H), 7.06 (d, *J* = 7.4 Hz, 1H), 6.64 (t, *J* = 7.4 Hz, 1H), 6.50 (d, *J* = 8.1 Hz, 1H), 3.68 (dd, *J* = 10.3, 5.1 Hz, 1H), 3.50 (t, *J* = 8.8 Hz, 1H), 3.35 – 3.16 (m, 2H), 2.71 (d, *J* = 16.4 Hz, 1H), 2.16

– 1.92 (m, 3H), 1.56 (s, 3H), 1.33 – 1.14 (m, 1H); ^{13}C NMR (126 MHz, CDCl_3) δ 178.7, 162.5, 143.2, 128.9, 128.1, 117.3, 116.1, 110.5, 61.1, 50.4, 46.9, 34.0, 27.5, 23.2, 16.6. HRMS (ESI) Calculated for $\text{C}_{15}\text{H}_{18}\text{N}_3\text{O}$ ($[\text{M}+\text{H}]^+$) 256.1444, Found 256.1448.

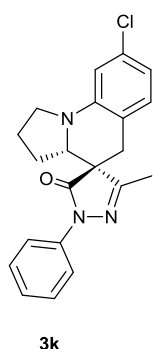
6'-chloro-3-methyl-1-phenyl-1',2',3',3a'-tetrahydro-5'H-spiro[pyrazole-4,4'-pyrrolo[1,2-a]quinolin]-5(1H)-one (3j)



White solid, mp 128.2 - 132.0 °C; yield 95%, *dr* 91:9. ^1H NMR (400 MHz, CDCl_3) δ 7.96 (dd, J = 8.6, 1.0 Hz, 2H), 7.47 – 7.38 (m, 2H), 7.21 (t, J = 7.4 Hz, 1H), 7.10 (t, J = 8.1 Hz, 1H), 6.75 (d, J = 7.4 Hz, 1H), 6.44 (d, J = 8.1 Hz, 1H), 3.71 (dd, J = 10.2, 5.2 Hz, 1H), 3.51 (td, J = 8.6, 2.1 Hz, 1H), 3.30 (dd, J = 16.2, 8.7 Hz, 1H), 3.16 (s, 2H), 2.13 – 1.96 (m, 3H), 1.71 (s, 3H), 1.35 – 1.25 (m, 1H); ^{13}C NMR (101 MHz, CDCl_3) δ 173.8, 161.6, 144.2, 138.0, 130.2, 129.0, 125.2, 121.8, 118.9, 118.7, 116.4, 113.2, 61.4, 52.4, 47.0, 33.9, 27.5, 23.2, 16.7. HRMS (ESI) Calculated for $\text{C}_{21}\text{H}_{20}\text{ClN}_3\text{NaO}$ ($[\text{M}+\text{Na}]^+$)

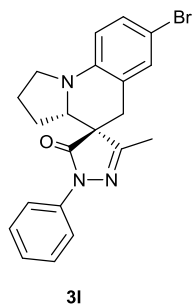
388.1187, Found 388.1187.

8'-chloro-3-methyl-1-phenyl-1',2',3',3a'-tetrahydro-5'H-spiro[pyrazole-4,4'-pyrrolo[1,2-a]quinolin]-5(1H)-one (3k)



White solid, mp 172.8 - 175.0 °C; yield 90%, *dr* 91:9. ^1H NMR (400 MHz, CDCl_3) δ 7.96 (dd, J = 8.6, 1.0 Hz, 2H), 7.48 – 7.39 (m, 2H), 7.23 (t, J = 7.4 Hz, 1H), 7.02 (d, J = 7.9 Hz, 1H), 6.66 (dd, J = 8.0, 2.0 Hz, 1H), 6.52 (d, J = 1.9 Hz, 1H), 3.77 (dd, J = 10.5, 5.2 Hz, 1H), 3.59 – 3.48 (m, 1H), 3.38 – 3.22 (m, 2H), 2.81 (d, J = 16.4 Hz, 1H), 2.18 – 1.99 (m, 3H), 1.70 (s, 3H), 1.34 – 1.26 (m, 1H); ^{13}C NMR (101 MHz, CDCl_3) δ 173.8, 161.6, 144.0, 138.0, 133.7, 129.8, 128.9, 125.2, 118.7, 116.0, 115.9, 110.3, 61.4, 52.4, 47.0, 33.9, 27.5, 23.2, 16.6. HRMS (ESI) Calculated for $\text{C}_{21}\text{H}_{21}\text{ClN}_3\text{O}$ ($[\text{M}+\text{H}]^+$) 366.1368, Found 366.1369.

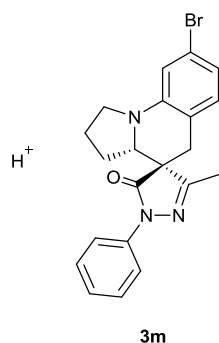
7'-bromo-3-methyl-1-phenyl-1',2',3',3a'-tetrahydro-5'H-spiro[pyrazole-4,4'-pyrrolo[1,2-a]quinolin]-5(1H)-one (3l)



Pink solid, mp 160.3 - 162.1 °C; yield 80%, *dr* >95:5. ^1H NMR (400 MHz, CDCl_3) δ 7.98 – 7.90 (m, 2H), 7.43 (t, J = 8.0 Hz, 2H), 7.26 (m, 1H), 7.24 – 7.18 (m, 2H), 6.40 (d, J = 8.6 Hz, 1H), 3.74 (dd, J = 10.4, 5.2 Hz, 1H), 3.51 (dd, J = 13.2, 4.4 Hz, 1H), 3.35 (d, J = 16.5 Hz, 1H), 3.24 (dd, J = 16.2, 9.0 Hz, 1H), 2.78 (d, J = 16.6 Hz, 1H), 2.17 – 1.96 (m, 3H), 1.69 (s, 3H), 1.36 – 1.25 (m, 1H). ^{13}C NMR (101 MHz, CDCl_3) δ 173.7, 161.5, 142.1, 138.0, 131.3, 130.8, 128.9, 125.2, 119.5, 118.7, 112.1, 107.8, 61.6, 52.4, 47.0, 34.0, 27.4, 23.2, 16.6. HRMS (ESI) Calculated for $\text{C}_{21}\text{H}_{21}\text{BrN}_3\text{O}$ ($[\text{M}+\text{H}]^+$)

410.0863 Found 410.0867 .

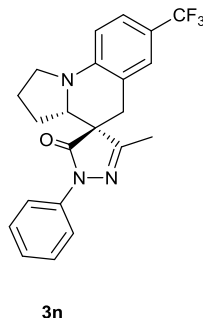
8'-bromo-3-methyl-1-phenyl-1',2',3',3a'-tetrahydro-5'H-spiro[pyrazole-4,4'-pyrrolo[1,2-a]quinolin]-5(1H)-one (3m)



410.0867.

White solid, mp 184.9 – 187.5 °C; yield 85%, *dr* 88:12. ¹H NMR (400 MHz, CDCl₃) δ 7.94 (dd, *J* = 8.7, 1.0 Hz, 2H), 7.45 – 7.37 (m, 2H), 7.20 (t, *J* = 7.4 Hz, 1H), 6.94 (d, *J* = 7.9 Hz, 1H), 6.78 (dd, *J* = 7.9, 1.8 Hz, 1H), 6.65 (d, *J* = 1.8 Hz, 1H), 3.75 (dd, *J* = 10.5, 5.3 Hz, 1H), 3.51 (dd, *J* = 13.3, 4.6 Hz, 1H), 3.26 (dd, *J* = 19.5, 11.3 Hz, 2H), 2.78 (d, *J* = 16.5 Hz, 1H), 2.16 – 1.94 (m, 3H), 1.68 (s, 3H), 1.28 (dd, *J* = 10.4, 7.9 Hz, 1H); ¹³C NMR (101 MHz, CDCl₃) δ 173.8, 161.6, 144.2, 138.0, 130.2, 129.0, 125.2, 121.8, 118.9, 118.7, 116.3, 113.2, 61.4, 52.4, 47.0, 33.9, 27.5, 23.2, 16.7. HRMS (ESI) Calculated for C₂₁H₂₁BrN₃O ([M+H]⁺) 410.0863 Found

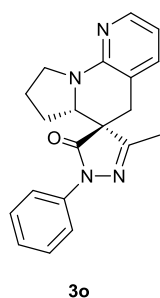
3-methyl-1-phenyl-7'-(trifluoromethyl)-1',2',3',3a'-tetrahydro-5'H-spiro[pyrazole-4,4'-pyrrolo[1,2-a]quinolin]-5(1H)-one (3n)



Calculated for C₂₂H₂₁F₃N₃O ([M+H]⁺) 400.1631, Found 400.1629.

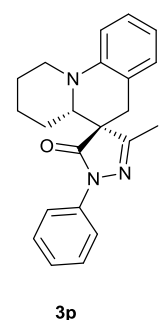
Pink solid, mp 158.5 – 162.4 °C; yield 87%, *dr* 90:10. ¹H NMR (400 MHz, CDCl₃) δ 7.94 (d, *J* = 8.1 Hz, 2H), 7.42 (t, *J* = 7.9 Hz, 3H), 7.33 (s, 1H), 7.21 (t, *J* = 7.4 Hz, 1H), 6.54 (d, *J* = 8.5 Hz, 1H), 3.80 (dd, *J* = 10.4, 4.8 Hz, 1H), 3.60 (t, *J* = 8.5 Hz, 1H), 3.38 (d, *J* = 16.5 Hz, 1H), 3.29 (dd, *J* = 16.5, 8.3 Hz, 1H), 2.85 (d, *J* = 16.5 Hz, 1H), 2.19 – 1.97 (m, 3H), 1.66 (s, 3H), 1.29 (dd, *J* = 19.2, 11.2 Hz, 1H); ¹³C NMR (126 MHz, CDCl₃) δ 173.6, 161.2, 145.3, 138.0, 129.0, 125.9 (³*J*_{C-F} = 3.78 Hz), 125.53 (³*J*_{C-F} = 3.78 Hz), 125.25, 125.0 (¹*J*_{C-F} = 270.90 Hz), 118.7, 117.8 (²*J*_{C-F} = 32.76 Hz), 117.3, 109.9, 61.6, 52.1, 47.0, 34.1, 27.5, 23.2, 16.6. HRMS (ESI)

3-methyl-1-phenyl-6a',7',8',9'-tetrahydro-5'H-spiro[pyrazole-4,6'-pyrrolo[1,2-a][1,8]naphthyridin]-5(1H)-one (3o)



Yellow liquid, yield 84%, *dr* 87:13. ¹H NMR (400 MHz, CDCl₃) δ 8.07 (d, *J* = 4.8 Hz, 1H), 7.94 – 7.86 (m, 2H), 7.38 (t, *J* = 7.9 Hz, 2H), 7.26 (d, *J* = 7.1 Hz, 1H), 7.16 (t, *J* = 7.2 Hz, 1H), 6.55 – 6.48 (m, 1H), 3.89 – 3.76 (m, 2H), 3.51 – 3.39 (m, 1H), 3.31 (d, *J* = 16.4 Hz, 1H), 2.76 (d, *J* = 16.4 Hz, 1H), 2.00 (qd, *J* = 18.5, 10.3 Hz, 3H), 1.65 (s, 3H), 1.36 – 1.20 (m, 1H); ¹³C NMR (126 MHz, CDCl₃) δ 173.6, 161.2, 153.5, 147.1, 137.9, 135.8, 128.9, 125.2, 118.7, 113.0, 112.0, 61.5, 52.1, 46.2, 34.0, 27.8, 23.1, 16.5. HRMS (ESI) Calculated for C₂₀H₂₁N₄O ([M+H]⁺) 333.1710, Found 333.1710.

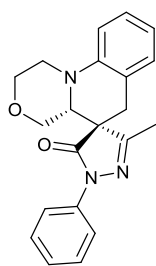
3-methyl-1-phenyl-2',3',4',4a'-tetrahydro-1'H,6'H-spiro[pyrazole-4,5'-pyrido[1,2-a]quinolin]-5(1H)-one (3p)



Yellow solid, mp 89.0 - 93.2 °C; yield 94%, *dr* 94:6. ¹H NMR (400 MHz, CDCl₃) δ 8.00 – 7.92 (m, 2H), 7.45 – 7.38 (m, 2H), 7.23 – 7.14 (m, 2H), 7.01 (d, *J* = 7.1 Hz, 1H), 6.95 (d, *J* = 8.4 Hz, 1H), 6.74 (t, *J* = 7.3 Hz, 1H), 4.07 (d, *J* = 12.1 Hz, 1H), 3.43 (d, *J* = 16.4 Hz, 1H), 3.24 (dd, *J* = 11.6, 2.7 Hz, 1H), 2.79 –

2.65 (m, 2H), 1.96 (s, 3H), 1.89 – 1.72 (m, 2H), 1.67 (dd, $J = 12.6, 2.6$ Hz, 1H), 1.60 – 1.51 (m, 1H), 1.44 – 1.32 (m, 1H), 1.07 (ddd, $J = 24.5, 12.7, 3.8$ Hz, 1H); ^{13}C NMR (126 MHz, CDCl_3) δ 174.0, 163.3, 146.0, 138.0, 129.4, 128.9, 127.9, 125.1, 119.6, 118.7, 118.5, 113.6, 59.2, 56.4, 48.5, 34.3, 27.5, 25.8, 23.4, 16.5. HRMS (ESI) Calculated for $\text{C}_{22}\text{H}_{24}\text{N}_3\text{O}$ ($[\text{M}+\text{H}]^+$) 346.1914, Found 346.1910.

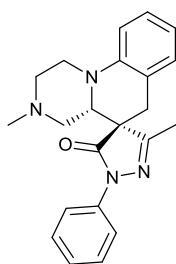
3-methyl-1-phenyl-1',2',4',4a'-tetrahydro-6'H-spiro[pyrazole-4,5'-[1,4]oxazino[4,3-a]quinolin]-5(1H)-one (3q)



3q

White solid, mp 138.1 -141.2 °C; yield 85%, *dr* 92:8. ^1H NMR (500 MHz, CDCl_3) δ 7.97 – 7.90 (m, 2H), 7.42 (t, $J = 8.0$ Hz, 2H), 7.23 – 7.18 (m, 2H), 7.05 (d, $J = 7.4$ Hz, 1H), 6.89 (d, $J = 8.4$ Hz, 1H), 6.82 (t, $J = 7.3$ Hz, 1H), 4.05 (dd, $J = 11.5, 3.6$ Hz, 1H), 3.81 (dd, $J = 11.1, 2.6$ Hz, 1H), 3.76 (d, $J = 12.1$ Hz, 1H), 3.64 (td, $J = 11.8, 2.8$ Hz, 1H), 3.52 – 3.43 (m, 2H), 3.07 (t, $J = 11.0$ Hz, 1H), 3.00 (td, $J = 12.1, 3.7$ Hz, 1H), 2.73 (d, $J = 16.7$ Hz, 1H), 2.05 (s, 3H); ^{13}C NMR (126 MHz, CDCl_3) δ 172.8, 162.4, 145.8, 137.8, 130.6, 129.0, 128.0, 125.3, 119.4, 119.3, 118.8, 112.6, 67.1, 67.02, 57.1, 53.2, 46.5, 34.1, 16.5. HRMS (ESI) Calculated for $\text{C}_{21}\text{H}_{22}\text{N}_3\text{O}_2$ ($[\text{M}+\text{H}]^+$) 348.1707, Found 348.1701.

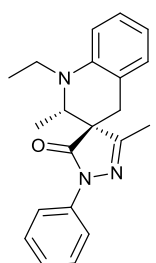
3,3'-dimethyl-1'-phenyl-2,3,4,4a-tetrahydro-1H,6H-spiro[pyrazino[1,2-a]quinoline-5,4'-pyrazol]-5'(1'H)-one (3r)



3r

Yellow liquid, yield 75%, *dr* >95:5. ^1H NMR (400 MHz, CDCl_3) δ 7.97 (d, $J = 8.2$ Hz, 2H), 7.43 (t, $J = 7.8$ Hz, 2H), 7.21 (dd, $J = 14.5, 7.3$ Hz, 2H), 7.04 (d, $J = 7.4$ Hz, 1H), 6.92 (d, $J = 8.4$ Hz, 1H), 6.81 (t, $J = 7.3$ Hz, 1H), 3.93 (d, $J = 11.8$ Hz, 1H), 3.62 (d, $J = 9.8$ Hz, 1H), 3.48 (d, $J = 16.6$ Hz, 1H), 3.12 (d, $J = 10.0$ Hz, 2H), 2.86 (d, $J = 10.7$ Hz, 1H), 2.72 (d, $J = 16.6$ Hz, 1H), 2.37 (s, 4H), 2.00 (s, 3H), 1.25 (s, 1H); ^{13}C NMR (126 MHz, CDCl_3) δ 172.8, 162.5, 144.6, 137.9, 129.5, 129.0, 128.0, 125.3, 119.5, 119.4, 118.6, 113.2, 56.5, 55.3, 54.5, 54.2, 45.9, 45.3, 34.3, 16.5. HRMS (ESI) Calculated for $\text{C}_{22}\text{H}_{25}\text{N}_4\text{O}$ ($[\text{M}+\text{H}]^+$) 361.2023, Found 361.2035.

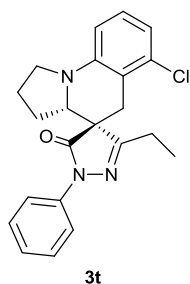
1'-ethyl-2',3-dimethyl-1-phenyl-1',4'-dihydro-2'H-spiro[pyrazole-4,3'-quinolin]-5(1H)-one (3s)



3s

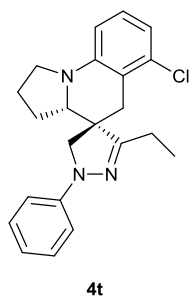
Yellow liquid, yield 88%, *dr* 56:44. ^1H NMR (400 MHz, CDCl_3) δ (major + minor) 7.98 (td, $J = 9.1, 4.4$ Hz, 2H), 7.44 (ddd, $J = 8.5, 6.4, 3.7$ Hz, 2H), 7.21 (dt, $J = 15.6, 7.8$ Hz, 2H), 7.06 (dd, $J = 34.8, 7.3$ Hz, 1H), 6.75 (ddd, $J = 23.9, 11.6, 6.3$ Hz, 2H), 3.75 – 3.33 (m, 4H), 2.70 (dd, $J = 16.7, 5.3$ Hz, 1H), 1.92 (d, $J = 16.2$ Hz, 3H), minor 1.38 (d, $J = 6.5$ Hz, 1.3H), minor 1.31 (t, $J = 7.1$ Hz, 1.3H), major 1.21 (t, $J = 7.1$ Hz, 1.7H), major 1.17 (d, $J = 6.5$ Hz, 1.7H); ^{13}C NMR (126 MHz, CDCl_3) δ 173.2, 172.5, 163.4, 161.8, 143.9, 141.4, 137.1, 137.0, 128.5, 128.1, 127.9, 127.8, 127.0, 126.9, 124.0, 123.9, 117.7, 117.7, 117.7, 116.2, 115.9, 115.5, 111.5, 110.1, 55.5, 55.0, 53.3, 52.4, 43.9, 40.1, 33.3, 27.6, 15.4, 15.4, 14.7, 12.4, 12.4, 11.4. HRMS (ESI) Calculated for $\text{C}_{21}\text{H}_{24}\text{N}_3\text{O}$ ($[\text{M}+\text{H}]^+$) 334.1914, Found 334.1914.

6'-chloro-3-ethyl-1-phenyl-1',2',3',3a'-tetrahydro-5'H-spiro[pyrazole-4,4'-pyrrolo[1,2-a]quinolin]-5(1H)-one (3t)



White solid, mp 117 – 120 °C; yield 95%, *dr* 89:11. ¹H NMR (400 MHz, CDCl₃) δ 8.00 (d, *J* = 7.8 Hz, 2H), 7.43 (t, *J* = 8.0 Hz, 2H), 7.20 (t, *J* = 7.4 Hz, 1H), 7.10 (t, *J* = 8.1 Hz, 1H), 6.74 (d, *J* = 7.9 Hz, 1H), 6.43 (d, *J* = 8.2 Hz, 1H), 3.68 (dd, *J* = 10.2, 5.2 Hz, 1H), 3.48 (dt, *J* = 9.1, 4.6 Hz, 1H), 3.29 (dd, *J* = 16.4, 8.6 Hz, 1H), 3.13 (s, 2H), 2.12 – 1.94 (m, 4H), 1.89 – 1.78 (m, 1H), 1.34 – 1.20 (m, 1H), 1.10 (t, *J* = 7.2 Hz, 3H); ¹³C NMR (126 MHz, CDCl₃) δ 173.9, 165.4, 144.4, 138.3, 134.5, 128.9, 128.4, 125.1, 118.7, 117.0, 115.9, 109.1, 61.1, 53.0, 47.2, 31.8, 27.4, 23.3, 23.2, 9.0. HRMS (ESI) Calculated for C₂₂H₂₃ClN₃O ([M+H]⁺) 380.1524, Found 380.1530.

6'-chloro-3-ethyl-1-phenyl-1',1',2',3',3a',5-hexahydro-5'H-spiro[pyrazole-4,4'-pyrrolo[1,2-a]quinoline] (4t)



Yellow liquid, yield 56%. ¹H NMR (400 MHz, CDCl₃) δ 7.31 (d, *J* = 8.5 Hz, 2H), 7.07 (dt, *J* = 8.0, 4.0 Hz, 3H), 6.85 (t, *J* = 7.3 Hz, 1H), 6.72 (d, *J* = 7.8 Hz, 1H), 6.37 (d, *J* = 8.1 Hz, 1H), 3.77 (d, *J* = 9.8 Hz, 1H), 3.51 – 3.21 (m, 5H), 2.87 (d, *J* = 17.5 Hz, 1H), 2.11 (dq, *J* = 8.2, 5.6 Hz, 2H), 2.02 – 1.89 (m, 2H), 1.83 (dq, *J* = 17.9, 7.2 Hz, 1H), 1.49 (ddd, *J* = 20.2, 11.5, 8.0 Hz, 1H), 1.08 (t, *J* = 7.3 Hz, 3H); ¹³C NMR (126 MHz, CDCl₃) δ 156.6, 146.7, 145.3, 134.1, 129.1, 128.0, 118.9, 117.7, 116.6, 112.8, 108.7, 63.3, 60.7, 50.7, 46.9, 35.2, 28.1, 23.2, 22.1, 10.7. HRMS (ESI) Calculated for C₂₂H₂₅ClN₃O ([M+H]⁺) 366.1732, Found 366.1727.

5. Reference

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6. NMR spectra for compounds

