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

Tuan Zhao, Huanrui Zhang, Longchen Cui, Jingping Qu and Baomin Wang*

State Key Laboratory of Fine Chemicals, School of Pharmaceutical Science and Technology, Dalian University of Technology, 2 Linggong Road, Dalian 116024, P. R. China

Supporting Information

Contents:
1. General information ......................................................... S2
2. General procedure for substrates preparation .................................. S2
3. General procedure for the intramolecular redox reaction catalyzed by zinc chloride .... S2
4. Characterization data of products .................................................. S3
5. Reference .................................................................................. S10
6. NMR spectra for compounds ........................................................... S11
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. ¹³C NMR spectra were recorded on a Bruker Avance II 101 MHz or Bruker Avance III 126 MHz. CDCl₃ 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 ¹³C 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)benzaldehyde

\[
\begin{align*}
\text{CHO} & \quad \text{CHO} \\
\text{F} & \quad \text{H} \\
\text{CHO} & \quad \text{CHO} \\
\text{Cl} & \quad \text{N} \\
\end{align*}
\]

K₂CO₃, DMF, reflux

b). The synthesis of pyrazolones

\[
\begin{align*}
\text{N} & \quad \text{NH₂} \\
\text{H} & \quad \text{O} \\
\text{O} & \quad \text{H} \\
\text{N} & \quad \text{NH₂} \\
\text{O} & \quad \text{H} \\
\end{align*}
\]

AcOH, reflux

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

A mixture of 1 (0.40 mmol), 2 (0.42 mmol) and ZnCl₂ (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, LiAlH₄ (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 LiAlH₄ 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 (Na₂SO₄) 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)

White solid, mp 117.4 - 120.3 °C; yield 91%, dr 92:8. ¹H NMR (400 MHz, CDCl₃) 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); ¹³C NMR (126 MHz, CDCl₃) 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 C₂₁H₂₂N₃O ([M+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)

Pink solid, mp 132.1 - 134.2 °C, yield 77%, dr >95:5. ¹H NMR (400 MHz, CDCl₃) 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); ¹³C NMR (126 MHz, CDCl₃) 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_{22}N_{2}O ([M+H]^+) 346.1914, Found 346.1909.

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

Yellow solid, mp 102.1 - 104.0 °C; yield 83%, dr 92:8. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 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 (dd, \(J = 9.2, 3.0\) 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 (ddd, \(J = 17.9, 11.1, 8.1\) Hz, 1H), 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); \(^1\)C NMR (126 MHz, CDCl\(_3\)) \(\delta\) 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_{24}N_{2}O ([M+H]^+) 360.2070, Found 360.2070.

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

Pink solid, mp 146.3 - 152.4 °C; yield 85%, dr 89:11. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 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); \(^1\)C NMR (126 MHz, CDCl\(_3\)) \(\delta\) 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_{2}O ([M+H]^+) 360.2070, Found 360.2069.

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

Orange liquid, yield 95%, dr 92:8. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 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); \(^1\)C NMR (126 MHz, CDCl\(_3\)) \(\delta\) 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_{28}N_{2}O ([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)

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 C25H23N3O ([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)

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 C22H17Cl2N3O ([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)

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 (dd, 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 C25H23N3O ([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)

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); 13C NMR (126 MHz, CDCl3) 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 C15H18N3O ([M+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, CDCl3) 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); 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, 116.4, 113.2, 61.4, 52.4, 47.0, 33.9, 27.5, 23.2, 16.7. HRMS (ESI) Calculated for C21H19ClN3NaO ([M+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, CDCl3) 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); 13C NMR (101 MHz, CDCl3) 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 C21H21ClN3O ([M+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, CDCl3) 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). 13C NMR (101 MHz, CDCl3) 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 C21H23BrN3O ([M+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)

White solid, mp 184.9 – 187.5 °C; yield 85%, dr 88:12. $^1$H NMR (400 MHz, CDCl$_3$) 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); $^{13}$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, 116.3, 113.2, 61.4, 52.4, 47.0, 33.9, 27.5, 23.2, 16.7. HRMS (ESI) Calculated for C$_{27}$H$_{25}$BrN$_3$O ([M+H]$^+$) 410.0863 Found 410.0867.

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)

Pink solid, mp 158.5 – 162.4 °C; yield 87%, dr 90:10. $^1$H NMR (400 MHz, CDCl$_3$) 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); $^{13}$C NMR (126 MHz, CDCl$_3$) δ 173.6, 161.2, 145.3, 138.0, 129.0, 125.9 ($^2$J$_{CF}$ = 3.78 Hz), 125.53 ($^2$J$_{CF}$ = 3.78 Hz), 125.25, 125.0 ($^2$J$_{CF}$ = 270.90 Hz), 117.8, 117.8 ($^2$J$_{CF}$ = 32.76 Hz), 117.3, 109.9, 61.6, 52.1, 47.0, 34.1, 27.5, 23.2, 16.6. HRMS (ESI) Calculated for C$_{29}$H$_{29}$F$_3$N$_3$O ([M+H]$^+$) 400.1631, Found 400.1629.

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

Yellow liquid, yield 84%, dr 87:13. $^1$H NMR (400 MHz, CDCl$_3$) 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); $^{13}$C NMR (126 MHz, CDCl$_3$) 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 C$_{30}$H$_{29}$N$_2$O ([M+H]$^+$) 333.1710, Found 333.1710.

3-methyl-1-phenyl-2',3',4'-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. $^1$H NMR (400 MHz, CDCl$_3$) 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 (dd, J = 24.5, 12.7, 3.8 Hz, 1H); 13C NMR (126 MHz, CDCl3) 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 C22H23N3O ([M+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)

White solid, mp 138.1 -141.2 °C; yield 85%, dr 92:8. 1H NMR (500 MHz, CDCl3) 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 (dd, 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); 13C NMR (126 MHz, CDCl3) 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 C21H22N3O2 ([M+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)

Yellow liquid, yield 75%, dr >95:5. 1H NMR (400 MHz, CDCl3) 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); 13C NMR (126 MHz, CDCl3) δ 172.8, 162.5, 144.6, 137.9, 129.7, 129.0, 128.0, 125.3, 119.4, 119.3, 118.6, 113.2, 56.5, 55.3, 54.5, 54.2, 45.9, 45.3, 34.3, 16.5. HRMS (ESI) Calculated for C21H22N3O ([M+H]+) 361.2035, Found 361.2035.

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

Yellow liquid, yield 88%, dr 56:44. 1H NMR (400 MHz, CDCl3) 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 (ddd, 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, 1H), minor 1.31 (t, J = 7.1 Hz, 1H), major 1.21 (t, J = 7.1 Hz, 1H), major 1.17 (d, J = 6.5 Hz, 1H); 13C NMR (126 MHz, CDCl3) 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 C21H22N3O ([M+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%. \( ^1 \)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 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); \( ^{13} \)C NMR (126 MHz, CDCl\(_3\)) \( \delta \) 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 C\(_{22}\)H\(_{24}\)ClN\(_3\)O ([M+H]\(^+\)) 380.1524, Found 380.1530.

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

Yellow liquid, yield 56%. \( ^1 \)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 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); \( ^{13} \)C NMR (126 MHz, CDCl\(_3\)) \( \delta \) 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 C\(_{22}\)H\(_{25}\)ClN\(_3\)O ([M+H]\(^+\)) 366.1732, Found 366.1727.
5. Reference


6. NMR spectra for compounds