Supporting Information for

A catalyst-free 1,3-dipolar cycloaddition of C,N-cyclic azomethine imines and 3-nitroindoles: an easy access to five-ring-fused tetrahydroisoquinolines

Xihong Liu, Dongxu Yang, Kezhou Wang, Jinlong Zhang, and Rui Wang*

\textit{a}School of Life Sciences, Institute of Biochemistry and Molecular Biology, Lanzhou University, Lanzhou 730000, P. R. China
\textit{b}State Key Laboratory of Chiroscience, Department of Applied Biology and Chemical Technology, The Hong Kong Polytechnic University, Kowloon, Hong Kong, P. R. China

E-mail: wangrui@lzu.edu.cn

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**A) General Information**

Unless stated otherwise, all reactions were carried out in flame dried glassware. All solvents were purified and dried according to standard methods prior to use. Reactions were monitored by thin layer chromatography (TLC), column chromatography purifications were carried out using silica gel. Proton nuclear resonance (\(^1\)H NMR) spectra were recorded on 300 MHz spectrometer in CDCl\(_3\) and carbon nuclear magnetic resonance (\(^{13}\)C NMR) spectra were recorded on 75 MHz spectrometer in CDCl\(_3\) using tetramethylsilane (TMS) as internal standard. Data for \(^1\)H NMR are recorded as follows: chemical shift (\(\delta\), ppm), multiplicity (s = singlet, d = doublet, t = triplet, m = multiplet, q = quartet or unresolved, coupling constant(s) in Hz, integration). Data for \(^{13}\)C NMR are reported in terms of chemical shift (\(\delta\), ppm).

High resolution mass spectra (HRMS) were obtained by the ESI ionization sources. Substrates C,N-cyclic azomethine imines 1\(^1\) and 3-nitroindoles 2\(^2\) were synthesized according to the previously reported procedures.

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B) General procedure for the catalyst-free 1,3-dipolar cycloaddition of C,N-cyclic azomethine imines and 3-nitroindoles

A mixture of C,N-cyclic azomethine imines \(1\) (0.12 mmol, 1.2 equiv) and 3-nitroindoles \(2\) (0.1 mmol, 1.0 equiv) in dry ethyl acetate (0.4 mL) was stirred at room temperature for appropriate time, the process of which was monitored by TLC analysis. Then the solvent was removed under vacuum. And the residue was purified by silica gel chromatography \((\text{PE} : \text{EA} = 15:1 \text{ to } 5:1 \text{ as eluent})\) to afford the desired products \(3\).

C) Characterization of products

\[\text{ethyl 13b-nitro-8-tosyl-8,8a,13b,13c-tetrahydro-5H-indolo[2',3':3,4]pyrazolo[5,1-a]isoquinoline-9(6H)-carboxylate: White solid, m.p. 153 – 154 °C; 94% yield; }^{1}H\text{ NMR (300 MHz, CDCl}_3\text{)} \delta 7.86 (d, J = 8.2 Hz, 2H), 7.78 (d, J = 7.9 Hz, 1H), 7.30 – 7.13 (m, 5H), 7.1 (s, 1H), 7.05 – 6.94 (m, 1H), 6.94 – 6.87 (m, 1H), 6.59 (t, J = 7.6 Hz, 3H), 6.28 (d, J = 7.6 Hz, 1H), 4.78 (s, 1H), 4.37 (q, J = 7.1 Hz, 2H), 2.80 – 2.58 (m, 2H), 2.33 (s, 3H), 2.31 – 2.11 (m, 2H), 1.41 (t, J = 7.1 Hz, 3H) ppm; }^{13}C\text{ NMR (75 MHz, CDCl}_3\text{)} \delta 152.1, 144.6, 142.6, 134.0, 132.1, 129.3, 129.0, 128.7, 128.3, 127.5, 127.3, 126.2, 122.8, 121.1, 115.5, 104.5, 84.9, 70.7, 62.8, 48.5, 29.1, 21.6, 14.3 ppm; }\text{HRMS (ESI): } C_{27}H_{26}NaNO_{5}S [M + Na]^+ \text{ calcd: 557.1465, found: 557.1476.} \]
methyl 13b-nitro-8-tosyl-8,8a,13b,13c-tetrahydro-5H-indolo[2',3':3,4]pyrazolo[5,1-a]isoquinoline-9(6H)-carboxylate: White solid, m.p. 141 – 142 °C; 92% yield; \(^1\)H NMR (300 MHz, CDCl\(_3\)) \(\delta\) 7.95 (d, \(J = 8.3\) Hz, 2H), 7.91 – 7.81 (m, 1H), 7.32 (d, \(J = 8.1\) Hz, 3H), 7.31 – 7.20 (m, 2H), 7.18 (s, 1H), 7.14 – 7.05 (m, 1H), 7.05 – 6.96 (m, 1H), 6.77 – 6.65 (m, 1H), 6.37 (d, \(J = 7.3\) Hz, 1H), 4.85 (s, 1H), 4.02 (s, 3H), 2.87 – 2.68 (m, 2H), 2.44 (s, 3H), 2.38 – 2.22 (m, 1H) ppm; \(^{13}\)C NMR (75 MHz, CDCl\(_3\)) \(\delta\) 152.6, 144.7, 142.6, 134.1, 132.2, 129.5, 129.1, 128.8, 128.4, 127.6, 127.5, 126.3, 123.0, 121.2, 115.5, 104.6, 85.1, 70.7, 53.2, 48.6, 29.2, 21.6 ppm; HRMS (ESI): C\(_{26}\)H\(_{24}\)N\(_4\)NaO\(_6\)S \([\text{M} + \text{Na}]^+\) calcd: 543.1309, found: 543.1316.

\[\text{3ab}\]

tert-butyl 13b-nitro-8-tosyl-8,8a,13b,13c-tetrahydro-5H-indolo[2',3':3,4]pyrazolo[5,1-a]isoquinoline-9(6H)-carboxylate: White solid, m.p. 145 – 146 °C; 81% yield; \(^1\)H NMR (300 MHz, CDCl\(_3\)) \(\delta\) 7.96 (d, \(J = 8.3\) Hz, 2H), 7.83 (d, \(J = 8.2\) Hz, 1H), 7.32 (d, \(J = 8.7\) Hz, 3H), 7.29 – 7.21 (m, 2H), 7.12 (s, 1H), 7.02 (t, \(J = 6.9\) Hz, 2H), 6.78 – 6.57 (m, 1H), 6.30 (d, \(J = 7.1\) Hz, 1H), 4.83 (s, 1H), 2.88 – 2.69 (m, 2H), 2.44 (s, 3H), 2.38 – 2.18 (m, 2H), 1.69 (s, 9H) ppm; \(^{13}\)C NMR (75 MHz, CDCl\(_3\)) \(\delta\) 151.21, 144.60, 143.23, 134.09, 132.05, 129.45, 129.07, 128.79, 128.75, 128.57, 127.59, 127.26, 126.29, 122.69, 121.27, 116.09, 104.09, 85.09, 83.93, 70.41, 48.52, 29.13, 28.31, 27.96, 21.67 ppm; HRMS (ESI): C\(_{29}\)H\(_{30}\)N\(_4\)NaO\(_6\)S \([\text{M} + \text{Na}]^+\) calcd: 585.1778, found: 585.1785.

\[\text{3ac}\]
**benzyl 13b-nitro-8-tosyl-8,8a,13b,13c-tetrahydro-5H-indolo[2',3':3,4]pyrazolo[5,1-a]isoquinoline-9(6H)-carboxylate**: White solid, m.p. 88 – 89 °C; 87% yield; $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 7.90 – 7.78 (m, 3H), 7.60 (d, $J$ = 6.4 Hz, 2H), 7.45 – 7.32 (m, 3H), 7.33 – 7.17 (m, 5H), 7.13 – 7.06 (m, 1H), 7.03 – 6.93 (m, 1H), 6.68 (t, $J$ = 7.7 Hz, 1H), 6.37 (d, $J$ = 7.8 Hz, 1H), 5.45 (s, 2H), 4.96 (s, 1H), 2.80 – 2.60 (m, 2H), 2.41 (s, 3H), 2.37 – 2.18 (m, 2H) ppm; $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 152.0, 144.5, 142.6, 135.6, 134.1, 132.1, 129.4, 129.2, 129.1, 128.8, 128.5, 127.6, 127.5, 126.3, 123.0, 121.3, 115.7, 104.6, 84.9, 70.8, 68.2, 48.5, 29.1, 21.6 ppm; HRMS (ESI): C$_{32}$H$_{28}$N$_4$NaO$_6$S $[M + Na]^+$ calcd: 619.1622, found: 619.1627.

**13b-nitro-8,9-ditosyl-6,8,8a,9,13b,13c-hexahydro-5H-indolo[2',3':3,4]pyrazolo[5,1-a]isoquinoline**: White solid, m.p. 169 – 170 °C; 75% yield; $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 8.03 (d, $J$ = 8.2 Hz, 2H), 7.80 – 7.70 (m, 3H), 7.40 – 7.29 (m, 3H), 7.30 – 7.17 (m, 4H), 7.14 – 7.03 (m, 2H), 7.03 – 6.90 (m, 1H), 6.74 (t, $J$ = 7.6 Hz, 1H), 6.33 (d, $J$ = 7.7 Hz, 1H), 4.99 (s, 1H), 2.79 – 2.55 (m, 2H), 2.44 (s, 3H), 2.39 (s, 3H), 2.32 – 2.12 (m, 2H) ppm; $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 145.2, 144.7, 142.6, 134.1, 134.1, 133.8, 132.3, 130.0, 129.5, 129.1, 128.8, 128.3, 127.7, 127.4, 127.4, 126.3, 124.2, 122.6, 116.3, 104.8, 86.3, 71.0, 48.4, 29.0, 21.7, 21.6 ppm; HRMS (ESI): C$_{33}$H$_{28}$N$_4$NaO$_6$S$_2$ $[M + Na]^+$ calcd: 639.1342, found: 639.1350.
ethyl 13-chloro-13b-nitro-8-tosyl-8,8a,13b,13c-tetrahydro-5H-indolo[2',3':3,4]pyrazolo[5,1-a]isoquinoline-9(6H)-carboxylate: White solid, m.p. 147 – 148 °C; 86% yield; \(^1H\) NMR (300 MHz, CDCl\(_3\)) \(\delta 7.93 - 7.81\) (m, 3H), \(7.49 - 7.16\) (m, 5H), \(7.10\) (t, \(J = 7.2\) Hz, 1H), \(6.91\) (d, \(J = 6.0\) Hz, 2H), \(6.75\) (d, \(J = 8.0\) Hz, 1H), \(5.42\) (s, 1H), \(4.47\) (q, \(J = 7.1\) Hz, 2H), \(2.93 - 2.83\) (m, 1H), \(2.84 - 2.73\) (m, 1H), \(2.68 - 2.53\) (m, 1H), \(2.47\) (s, 3H), \(2.23\) (dt, \(J = 16.3, 4.9\) Hz, 1H), \(1.51\) (t, \(J = 7.1\) Hz, 3H) ppm; \(^{13}C\) NMR (75 MHz, CDCl\(_3\)) \(\delta 151.9, 145.4, 144.9, 134.4, 133.4, 132.2, 131.5, 129.6, 128.9, 127.9, 127.8, 125.6, 125.1, 121.0, 113.9, 106.0, 86.3, 68.9, 63.2, 49.8, 28.8, 21.7, 14.4 ppm; HRMS (ESI): \(C_{27}H_{22}ClNaO_6S\) [M + Na]\(^+\) calcd: 591.1076, found: 591.1092.

ethyl 12-fluoro-13b-nitro-8-tosyl-8,8a,13b,13c-tetrahydro-5H-indolo[2',3':3,4]pyrazolo[5,1-a]isoquinoline-9(6H)-carboxylate: Pale yellow solid, m.p. 150 – 151 °C; 95% yield; \(^1H\) NMR (300 MHz, CDCl\(_3\)) \(\delta 7.95\) (d, \(J = 8.2\) Hz, 2H), \(7.85\) (d, \(J = 8.0\) Hz, 1H), \(7.39 - 7.24\) (m, 4H), \(7.20\) (s, 1H), \(7.09 - 6.97\) (m, 3H), \(6.06\) (dd, \(J = 8.5, 2.6\) Hz, 1H), \(4.84\) (s, 1H), \(4.46\) (q, \(J = 7.1\) Hz, 2H), \(2.89 - 2.70\) (m, 2H), \(2.44\) (s, 3H), \(2.41 - 2.21\) (m, 2H), \(1.51\) (t, \(J = 7.1\) Hz, 3H) ppm; \(^{13}C\) NMR (75 MHz, CDCl\(_3\)) \(\delta 158.0\) (\(J_{C-F} = 242.6\) Hz), \(152.2, 144.8, 138.9, 134.0, 133.9, 129.4, 129.1, 129.0, 128.0, 127.6, 127.1, 126.5, 122.4 (\(J_{C-F} = 9.2\) Hz), \(119.1\) (\(J_{C-F} = 23.4\) Hz), \(116.5\) (\(J_{C-F} = 7.9\) Hz), \(114.7\) (\(J_{C-F} = 26.2\) Hz), \(104.0, 85.4, 71.0, 63.1, 48.6, 29.1, 21.7, 14.4\) ppm; HRMS (ESI): \(C_{27}H_{22}FNaO_6S\)

**ethyl 12-chloro-13b-nitro-8-tosyl-8,8a,13b,13c-tetrahydro-5H-indolo[2',3':3,4]pyrazolo[5,1-a]isoquinoline-9(6H)-carboxylate:** White solid, m.p. 125 – 126 °C; 92% yield; 1H NMR (300 MHz, CDCl3) δ 7.94 (d, J = 8.2 Hz, 2H), 7.89 – 7.75 (m, 1H), 7.42 – 7.23 (m, 5H), 7.20 (s, 1H), 7.11 – 6.94 (m, 2H), 6.30 (d, J = 2.1 Hz, 1H), 4.83 (s, 1H), 4.47 (q, J = 7.1 Hz, 2H), 2.90 – 2.68 (m, 2H), 2.44 (s, 3H), 2.41 – 2.24 (m, 2H), 1.51 (t, J = 7.1 Hz, 3H) ppm; 13C NMR (75 MHz, CDCl3) δ 152.0, 144.8, 141.3, 133.9, 133.9, 132.1, 129.4, 129.1, 129.0, 128.0, 127.7, 127.1, 126.5, 125.7, 116.5, 104.1, 85.3, 71.0, 63.2, 48.6, 29.1, 21.7, 14.4 ppm; HRMS (ESI): C27H25ClN4NaO6S [M + Na]+ calcd: 591.1076, found: 591.1090.

**ethyl 12-bromo-13b-nitro-8-tosyl-8,8a,13b,13c-tetrahydro-5H-indolo[2',3':3,4]pyrazolo[5,1-a]isoquinoline-9(6H)-carboxylate:** White solid, m.p. 118 – 119 °C; 83% yield; 1H NMR (300 MHz, CDCl3) δ 7.94 (d, J = 8.2 Hz, 2H), 7.76 (d, J = 8.5 Hz, 1H), 7.41 (dd, J = 8.8, 2.0 Hz, 1H), 7.37 – 7.23 (m, 4H), 7.18 (s, 1H), 7.14 – 6.97 (m, 2H), 6.43 (d, J = 1.9 Hz, 1H), 4.82 (s, 1H), 4.47 (q, J = 7.1 Hz, 2H), 2.91 – 2.66 (m, 2H), 2.44 (s, 3H), 2.41 – 2.18 (m, 2H), 1.51 (t, J = 7.1 Hz, 3H) ppm; 13C NMR (75 MHz, CDCl3) δ 152.0, 144.8, 141.7, 135.0, 133.9, 133.9, 130.7, 129.5, 129.1, 128.9, 128.0, 127.1, 126.5, 122.8, 116.9, 115.2, 104.1, 85.2, 71.1, 63.2, 48.7, 29.7, 29.6, 29.1, 21.7, 14.4

$^1$H NMR (300 MHz, CDCl$_3$) δ 8.03 (d, $J = 8.3$ Hz, 2H), 7.74 (d, $J = 8.3$ Hz, 2H), 7.60 (d, $J = 8.4$ Hz, 1H), 7.33 (d, $J = 8.1$ Hz, 2H), 7.27 – 7.18 (m, 4H), 7.14 (d, $J = 8.4$ Hz, 1H), 7.12 – 7.02 (m, 2H), 7.02 – 6.91 (m, 1H), 6.04 (s, 1H), 4.99 (s, 1H), 2.81 – 2.54 (m, 2H), 2.44 (s, 3H), 2.38 (s, 3H), 2.31 – 2.13 (m, 2H), 1.94 (s, 3H) ppm; 

$^{13}$C NMR (75 MHz, CDCl$_3$) δ 145.0, 144.7, 144.3, 134.3, 134.1, 133.8, 133.0, 129.9, 129.5, 129.1, 128.6, 128.4, 128.1, 127.5, 127.4, 126.2, 122.8, 116.2, 104.8, 86.5, 70.9, 48.4, 29.0, 21.7, 21.6, 20.6 ppm; 


$^1$H NMR (300 MHz, CDCl$_3$) δ 7.95 (d, $J = 8.3$ Hz, 2H), 7.62 (d, $J = 9.4$ Hz, 1H), 7.32 (d, $J = 8.1$ Hz, 2H), 7.30 – 7.24 (m, 2H), 7.21 (s, 1H), 7.03 (dd, $J = 5.0$, 2.1 Hz, 2H), 6.49 – 6.22 (m, 2H), 4.82 (s, 1H), 4.48 (q, $J = 7.1$ Hz, 2H), 2.89 – 2.71 (m, 2H), 2.44 (s, 3H), 2.42 – 2.27 (m, 2H), 1.52 (t, $J = 7.1$ Hz, 3H) ppm; 

$^{13}$C NMR (75 MHz, CDCl$_3$) δδ 165.3 ($J_{CF} = 250.2$ Hz), 151.9, 144.8, 144.3 ($J_{CF} = 13.1$ Hz), 134.0, 133.9, 129.4, 129.1, 128.9, 128.3, 127.3, 126.4, 116.7, 110.2 ($J_{CF} = 23.3$ Hz), 104.0 ($J_{CF} = 14.6$ Hz), 103.5,
ethyl 11-chloro-13b-nitro-8-tosyl-8,8a,13b,13c-tetrahydro-5H-indolo[2′,3′:3,4]pyrazolo[5,1-a]isoquinoline-9(6H)-carboxylate: Pale yellow solid, m.p. 167 – 168 °C; 79% yield; \(^1\)H NMR (300 MHz, CDCl\(_3\)) \(\delta\) 8.02 – 7.89 (m, 3H), 7.42 – 7.21 (m, 4H), 7.20 (s, 1H), 7.10 – 7.97 (m, 2H), 6.67 (dd, \(J = 8.4, 1.7\) Hz, 1H), 6.29 (d, \(J = 8.4\) Hz, 1H), 4.84 (s, 1H), 4.48 (q, \(J = 7.1\) Hz, 2H), 2.88 – 2.69 (m, 2H), 2.43 (s, 3H), 2.41 – 2.25 (m, 2H), 1.52 (t, \(J = 7.1\) Hz, 3H) ppm; \(^{13}\)C NMR (75 MHz, CDCl\(_3\)) \(\delta\) 151.9, 144.8, 143.6, 138.5, 134.0, 133.9, 129.4, 129.1, 128.4, 128.2, 127.3, 126.4, 123.2, 119.6, 116.0, 104.2, 85.5, 70.9, 63.2, 48.6, 29.1, 21.6, 14.4 ppm; HRMS (ESI): C\(_{27}\)H\(_{25}\)ClN\(_4\)NaO\(_6\)S [M + Na]\(^+\) calcd: 591.1076, found: 591.1091.

ethyl 10-chloro-13b-nitro-8-tosyl-8,8a,13b,13c-tetrahydro-5H-indolo[2′,3′:3,4]pyrazolo[5,1-a]isoquinoline-9(6H)-carboxylate: White solid, m.p. 156 – 157 °C; 94% yield; \(^1\)H NMR (300 MHz, CDCl\(_3\)) \(\delta\) 7.99 (d, \(J = 8.2\) Hz, 2H), 7.41 – 7.31 (m, 3H), 7.30 – 7.14 (m, 2H), 7.11 – 6.99 (m, 2H), 6.89 (d, \(J = 7.5\) Hz, 1H), 6.75 (t, \(J = 7.9\) Hz, 1H), 6.08 (d, \(J = 7.3\) Hz, 1H), 4.70 (s, 1H), 4.49 – 4.27 (m, 2H), 2.99 – 2.77 (m, 2H), 2.45 (s, 3H), 2.40 – 2.28 (m, 1H), 1.89 – 1.72 (m, 1H), 1.52 – 1.38 (m, 3H) ppm; \(^{13}\)C NMR (75
MHz, CDCl$_3$) δ 152.5, 144.9, 140.7, 134.1, 133.3, 129.7, 129.0, 129.0, 128.9, 128.1, 126.8, 126.7, 126.5, 125.9, 125.7, 125.2, 102.9, 87.1, 69.1, 63.7, 49.0, 28.9, 21.7, 14.2 ppm; HRMS (ESI): C$_{27}$H$_{26}$ClN$_4$O$_6$S $[\text{M} + \text{H}]^+$ calcd: 569.1256, found: 569.1270.

**ethyl 8-benzoyl-13b-nitro-8,8a,13b,13c-tetrahydro-5H-indolo[2',3':3,4]pyrazolo[5,1-a]isoquinoline-9(6H)-carboxylate:** White solid, m.p. 139 – 140 °C; 67% yield; $^1$H NMR (300 MHz, CDCl$_3$) δ 7.94 (d, $J$ = 8.3 Hz, 1H), 7.83 (s, 1H), 7.78 – 7.65 (m, 2H), 7.56 – 7.31 (m, 5H), 7.31 – 7.17 (m, 2H), 7.07 – 6.93 (m, 1H), 6.83 – 6.67 (m, 1H), 6.56 (d, $J$ = 7.1 Hz, 1H), 5.02 (s, 1H), 4.48 – 4.24 (m, 2H), 3.39 – 3.16 (m, 1H), 2.87 – 2.62 (m, 2H), 2.54 – 2.29 (m, 1H), 1.36 (t, $J$ = 7.1 Hz, 3H) ppm; $^{13}$C NMR (75 MHz, CDCl$_3$) δ 173.2, 152.3, 143.3, 134.3, 133.9, 132.1, 131.2, 128.8, 128.2, 127.8, 127.4, 126.4, 122.8, 121.9, 115.3, 104.3, 82.2, 73.0, 62.6, 47.8, 29.0, 14.4 ppm; HRMS (ESI): C$_{27}$H$_{24}$NaN$_4$O$_5$ $[\text{M} + \text{Na}]^+$ calcd: 507.1639, found: 507.1637.

**ethyl 8-((4-(tert-butyl)phenyl)sulfonyl)-13b-nitro-8,8a,13b,13c-tetrahydro-5H-indolo[2',3':3,4]pyrazolo[5,1-a]isoquinoline-9(6H)-carboxylate:** White solid, m.p. 161 – 162 °C; 84% yield; $^1$H NMR (300 MHz, CDCl$_3$) δ 7.99 (d, $J$ = 8.6 Hz, 2H), 7.87 (d, $J$ = 7.4 Hz, 1H), 7.54 (d, $J$ = 8.6 Hz, 2H), 7.36 – 7.22 (m, 3H), 7.19 (s, 1H), 7.13 – 6.95 (m, 2H), 6.77 – 6.63 (m, 1H), 6.34 (d, $J$ = 7.3 Hz, 1H), 4.77 (s, 1H), 4.47 (q, $J$ = 7.1 Hz, 2H), 2.88 – 2.69 (m, 2H), 2.45 – 2.18 (m, 2H), 1.52 (t, $J$ = 7.1 Hz, 3H), 1.34 (s, 9H) ppm; $^{13}$C NMR
ethyl 8-((4-methoxyphenyl)sulfonyl)-13b-nitro-8,8a,13b,13c-tetrahydro-5H-indolo[2',3':3,4]pyrazolo[5,1-a]isoquinoline-9(6H)-carboxylate: White solid, m.p. 76 – 77 °C; 92% yield; $^1$H NMR (300 MHz, CDCl$_3$) δ 8.00 (d, $J = 8.9$ Hz, 1H), 7.87 (d, $J = 7.7$ Hz, 1H), 7.38 – 7.21 (m, 3H), 7.17 (s, 1H), 7.12 – 7.04 (m, 1H), 7.02 – 6.90 (m, 3H), 6.70 (t, $J = 7.6$ Hz, 1H), 6.37 (d, $J = 7.6$ Hz, 1H), 4.84 (s, 1H), 4.47 (q, $J = 7.1$ Hz, 2H), 3.87 (s, 3H), 2.92 – 2.65 (m, 2H), 2.40 – 2.23 (m, 2H), 1.51 (t, $J = 7.1$ Hz, 3H) ppm; $^{13}$C NMR (75 MHz, CDCl$_3$) δ 163.6, 152.2, 142.7, 134.0, 132.1, 131.3, 128.8, 128.4, 128.3, 127.6, 127.4, 126.3, 122.9, 121.1, 115.6, 113.9, 104.6, 85.1, 70.7, 62.9, 55.6, 48.6, 29.1, 14.4 ppm; HRMS (ESI): C$_{27}$H$_{26}$N$_4$NaO$_7$S [M + Na]$^+$ calcd: 573.1414, found: 573.1421.

ethyl 4-methyl-13b-nitro-8-tosyl-8,8a,13b,13c-tetrahydro-5H-indolo[2',3':3,4]pyrazolo[5,1-a]isoquinoline-9(6H)-carboxylate: White solid, m.p. 144 – 145 °C; 78% yield; $^1$H NMR (300 MHz, CDCl$_3$) δ 7.95 (d, $J = 8.2$ Hz, 2H), 7.86 (t, $J = 7.6$ Hz, 1H), 7.40 – 7.28 (m, 3H), 7.22 – 7.09 (m, 3H), 6.92 – 6.81 (m, 1H), 6.71 (t, $J = 7.6$ Hz, 1H), 6.43 (d, $J = 7.5$ Hz, 1H), 4.83 (s, 1H), 4.47 (q, $J = 7.1$ Hz, 2H), 2.87 – 2.77 (m, 2H), 2.61 – 2.45 (m, 1H), 2.43 (s, 3H), 2.40 – 2.21 (m, 2H), 2.10 (s, 3H), 1.51 (t, $J = 7.1$ Hz,
ethyl 2-methyl-13b-nitro-8-tosyl-8,8a,13b,13c-tetrahydro-5H-indolo[2',3':3,4]pyrazolo[5,1-a]isoquinoline-9(6H)-carboxylate: White solid, m.p. 87 – 88 °C; 82% yield; $^1$H NMR (300 MHz, CDCl$_3$) δ 7.95 (d, $J = 8.2$ Hz, 2H), 7.91 – 7.79 (m, 1H), 7.40 – 7.28 (m, 1H), 7.16 (s, 1H), 7.08 (d, $J = 7.6$ Hz, 1H), 6.98 – 6.79 (m, 2H), 6.71 (t, $J = 7.6$ Hz, 1H), 6.35 (d, $J = 7.7$ Hz, 1H), 4.80 (s, 1H), 4.47 (q, $J = 7.1$ Hz, 2H), 2.84 – 2.60 (m, 2H), 2.44 (s, 3H), 2.39 – 2.19 (m, 5H), 1.51 (t, $J = 7.1$ Hz, 3H) ppm; $^{13}$C NMR (75 MHz, CDCl$_3$) δ 152.2, 144.6, 142.7, 136.0, 134.0, 132.1, 131.0, 129.7, 129.4, 129.1, 128.6, 128.3, 127.7, 127.6, 122.9, 121.2, 115.6, 104.5, 85.1, 70.7, 62.9, 48.7, 28.7, 21.7, 21.0, 14.4 ppm; HRMS (ESI): C$_{28}$H$_{29}$N$_4$O$_6$S [M + H]$^+$ calcd: 549.1802, found: 549.1810.

ethyl 2-chloro-13b-nitro-8-tosyl-8,8a,13b,13c-tetrahydro-5H-indolo[2',3':3,4]pyrazolo[5,1-a]isoquinoline-9(6H)-carboxylate: White solid, m.p. 86 – 87 °C; 64% yield; $^1$H NMR (300 MHz, CDCl$_3$) δ 8.01 – 7.80 (m, 1H), 7.50 – 7.29 (m, 3H), 7.28 – 7.22 (m, 1H), 7.20 (s, 1H), 7.17 (d, $J = 1.8$ Hz, 1H), 6.94 (d, $J = 8.2$ Hz, 1H), 6.76 (m, 1H), 6.47 (d, $J = 7.8$ Hz, 1H), 4.79 (s, 1H), 4.47 (q, $J = 7.1$ Hz, 2H), 2.84 – 2.62
(m, 2H), 2.46 (s, 3H), 2.41 – 2.22 (m, 2H), 1.51 (t, $J = 7.1$ Hz, 3H) ppm; $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 152.2, 144.9, 142.8, 133.9, 132.7, 132.4, 132.1, 130.2, 130.2, 129.5, 129.0, 129.0, 127.4, 127.2, 123.1, 121.2, 121.1, 115.7, 104.5, 85.0, 69.8, 63.0, 48.5, 28.7, 21.7, 14.4 ppm; HRMS (ESI): C$_{27}$H$_{25}$ClN$_4$NaO$_6$S [M + Na]$^+$ calcd: 591.1076, found: 591.1081.

![3ha](image)

ethyl 3-bromo-13b-nitro-8-tosyl-8,8a,13b,13c-tetrahydro-5H-indolo[2',3':3,4]pyrazolo[5,1-a]isoquinoline-9(6H)-carboxylate: White solid, m.p. 157 – 158 °C; 55% yield; $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 7.99 – 7.81 (m, 3H), 7.45 – 7.28 (m, 4H), 7.21 (s, 1H), 7.17 (d, $J = 1.6$ Hz, 1H), 7.03 (d, $J = 8.4$ Hz, 1H), 6.76 (dd, $J = 11.1, 4.2$ Hz, 1H), 6.46 (d, $J = 7.3$ Hz, 1H), 4.78 (s, 1H), 4.48 (q, $J = 7.1$ Hz, 2H), 2.86 – 2.65 (m, 2H), 2.44 (s, 3H), 2.38 – 2.20 (m, 2H), 1.51 (t, $J = 7.1$ Hz, 3H) ppm; $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 152.2, 144.8, 142.8, 136.4, 133.9, 132.4, 131.8, 129.6, 129.5, 129.2, 129.1, 127.5, 127.3, 123.1, 122.8, 121.0, 115.7, 104.5, 84.9, 70.1, 63.0, 48.2, 29.0, 21.7, 14.4 ppm; HRMS (ESI): C$_{27}$H$_{25}$BrN$_4$NaO$_6$S [M + Na]$^+$ calcd: 635.0570, found: 635.0579.

![3ia](image)

ethyl 2-bromo-13b-nitro-8-tosyl-8,8a,13b,13c-tetrahydro-5H-indolo[2',3':3,4]pyrazolo[5,1-a]isoquinoline-9(6H)-carboxylate: White solid, m.p. 160 – 161 °C; 60% yield; $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 8.04 – 7.77 (m, 3H), 7.45 – 7.29 (m, 5H), 7.20 (s, 1H), 6.88 (d, $J = 8.2$ Hz, 1H), 6.76 (t, $J = 7.6$ Hz, 1H), 6.47 (d, $J = 7.5$ Hz, 1H),
4.79 (s, 1H), 4.47 (q, \( J = 7.1 \) Hz, 2H), 2.83 – 2.72 (m, 1H), 2.73 – 2.60 (m, 1H), 2.46 (s, 3H), 2.42 – 2.18 (m, 2H), 1.51 (t, \( J = 7.1 \) Hz, 3H) ppm; \(^{13}\)C NMR (75 MHz, CDCl\(_3\)) \( \delta \) 152.2, 144.9, 142.8, 133.9, 133.2, 132.4, 131.9, 130.7, 130.4, 130.3, 129.5, 129.0, 127.2, 123.1, 121.1, 119.9, 115.8, 104.6, 85.0, 69.7, 63.0, 48.4, 28.8, 21.7, 14.4 ppm; HRMS (ESI): C\(_{27}\)H\(_{26}\)BrN\(_4\)O\(_6\)S [M + H]\(^+\) calcd: 613.0751, found: 613.0756.

ethyl 13b-nitro-8-tosyl-8,8a,13b,13c-tetrahydro-5H-benzo[f]indolo[2',3':3,4]pyrazolo[5,1-a]isoquinoline-9(6H)-carboxylate: White solid, m.p. 83 – 84 °C; 84% yield; \(^1\)H NMR (300 MHz, CDCl\(_3\)) \( \delta \) 7.97 (d, \( J = 8.2 \) Hz, 2H), 7.92 – 7.80 (m, 2H), 7.81 – 7.70 (m, 2H), 7.60 – 7.43 (m, 2H), 7.39 – 7.18 (m, 4H), 7.11 (d, \( J = 8.6 \) Hz, 1H), 6.59 (t, \( J = 7.5 \) Hz, 1H), 6.50 (d, \( J = 7.4 \) Hz, 1H), 4.95 (s, 1H), 4.49 (q, \( J = 7.1 \) Hz, 2H), 3.09 – 2.83 (m, 3H), 2.56 – 2.29 (m, 4H), 1.53 (t, \( J = 7.1 \) Hz, 3H) ppm; \(^{13}\)C NMR (75 MHz, CDCl\(_3\)) \( \delta \) 152.2, 144.7, 142.6, 134.0, 133.0, 132.1, 131.2, 130.6, 129.4, 129.2, 128.6, 127.7, 127.2, 126.8, 126.6, 125.6, 124.5, 123.2, 123.0, 121.2, 115.6, 104.6, 85.5, 71.3, 63.0, 53.4, 48.2, 25.8, 21.6, 14.4 ppm; HRMS (ESI): C\(_{31}\)H\(_{28}\)NaN\(_4\)O\(_6\)S [M + Na]\(^+\) calcd: 607.1622, found: 607.1632.

D) Synthesis of compounds 6a and 7a

A mixture of C,N-cyclic azomethine imines 1a (0.12 mmol, 1.2 equiv) and alkylidene azlactone 4 or methyleneindolinone 5 (0.1 mmol, 1.0 equiv) in dry ethyl acetate (0.4 mL) was stirred at room temperature for appropriate time, the process of which was monitored by TLC analysis. Then the solvent was removed under vacuum. And the residue was purified by silica gel chromatography (PE : EA = 15:1 to 5:1 as eluent) to afford the desired product 6a or 7a.
2,2'-diphenyl-6',10b'-dihydro-5H,5'H-spiro[oxazole-4,1'-pyrazolo[5,1-a]isoquinolin]-5-one: Yellow solid, m.p. 147 – 148 °C; 77% yield; \(^1\)H NMR (300 MHz, CDCl\(_3\)) \(\delta\) 7.93 – 7.80 (m, 2H), 7.57 (t, \(J = 7.4\) Hz, 1H), 7.51 – 7.35 (m, 4H), 7.35 – 7.21 (m, 3H), 7.20 – 7.11 (m, 2H), 7.11 – 7.01 (m, 1H), 6.78 (d, \(J = 7.6\) Hz, 1H), 5.45 (s, 1H), 4.12 (ddd, \(J = 12.9, 4.5, 3.1\) Hz, 1H), 3.55 – 3.40 (m, 1H), 3.16 (ddd, \(J = 15.9, 11.3, 4.8\) Hz, 1H), 2.78 (dt, \(J = 15.7, 2.9\) Hz, 1H) ppm; \(^{13}\)C NMR (75 MHz, CDCl\(_3\)) \(\delta\) 177.1, 160.9, 146.3, 136.8, 133.4, 130.7, 129.9, 129.2, 128.9, 128.8, 128.8, 128.3, 127.6, 126.9, 126.3, 125.7, 125.4, 124.9, 82.8, 73.2, 49.1, 28.2 ppm; HRMS (ESI): C\(_{25}\)H\(_{20}\)N\(_3\)O\(_2\) [M + H]\(^{+}\) calcd: 394.1550, found: 394.1562.

1-tert-butyl 2'-ethyl 2-oxo-6', 10b'-dihydro-5'H-spiro[indoline-3,1'-pyrazolo[5,1-a]isoquinoline]-1,2'-dicarboxylate: Yellow solid, m.p. 53 – 54 °C; 92% yield; \(^1\)H NMR (300 MHz, CDCl\(_3\)) \(\delta\) 7.82 (d, \(J = 8.2\) Hz, 1H), 7.22 – 7.13 (m, 1H), 7.12 – 7.01 (m, 2H), 6.84 (t, \(J = 7.3\) Hz, 1H), 6.76 (t, \(J = 7.5\) Hz, 1H), 6.36 (d, \(J = 7.4\) Hz, 1H), 6.26 (d, \(J = 7.7\) Hz, 1H), 5.71 (s, 1H), 4.36 (dd, \(J = 13.1, 4.5\) Hz, 1H), 4.05 (q, \(J = 7.1\) Hz, 2H), 3.60 (td, \(J = 12.6, 3.5\) Hz, 1H), 3.29 – 3.09 (m, 1H), 2.86 (d, \(J = 14.4\) Hz, 1H), 1.70 (s, 9H), 1.08 (t, \(J = 7.1\) Hz, 3H) ppm; \(^{13}\)C NMR (75 MHz, CDCl\(_3\)) \(\delta\) 175.0, 160.3, 149.0, 139.1, 139.1, 137.7, 134.8, 130.6, 129.1, 128.9, 127.3, 126.8, 126.4, 125.4, 124.6, 124.2, 114.6, 84.7, 72.8, 64.8, 60.9, 47.7, 29.2, 28.0, 13.7 ppm; HRMS (ESI): C\(_{26}\)H\(_{27}\)N\(_3\)NaO\(_5\) [M + Na]\(^{+}\) calcd: 484.1843, found: 484.1863.
E) Large-scale preparation of 3ah

A mixture of C,N-cyclic azomethine imine 1a (2.4 mmol, 720 mg, 1.2 equiv) and 3-nitroindole 2h (2.0 mmol, 504 mg, 1.0 equiv) in dry ethyl acetate (4.0 mL) was stirred at room temperature for 48 h. After the complete consumption of 2h (the process of which was monitored by TLC analysis), the solvent was removed under vacuum. And the residue was purified by silica gel chromatography (PE : EA = 15:1 to 5:1 as eluent) to afford the desired products 3ah, which was then further purified by recrystallization. (Note: An obvious decomposition of 3ah in the purification process of silica gel chromatography was observed.)

F) Synthesis of compound 8

To a solution of cycloadduct 3aa (0.15 mmol, 80.1 mg) and TMSCl (0.6 mL) in methanol (1.5 mL) was added Zn nanopowder (3.0 mmol, 196.1 mg). The mixture was then stirred at room temperature for 30 min. After the complete consumption of the start material, the reaction mixture was filtrated and washed with CH$_2$Cl$_2$ (5 mL x 2). Then NaHCO$_3$ aq. solution (20 mL) was added to the obtained solution and the resulting mixture was extracted with CH$_2$Cl$_2$. The combined organic phases were dried over anhydrous Na$_2$SO$_4$ and concentrated under reduced pressure. The crude mixture was purified by column chromatography on silica gel (eluting with PE/EA = 1:1) to afford the corresponding product 8 in 71% yield. White solid, m.p. 147 – 148 °C; $^1$H NMR (300
MHz, CDCl$_3$) δ 8.17 (d, $J = 8.2$ Hz, 1H), 7.46 (d, $J = 7.8$ Hz, 1H), 7.38 (s, 1H), 7.36 – 7.25 (m, 1H), 7.22 – 7.10 (m, 3H), 7.11 – 7.00 (m, 1H), 6.96 (d, $J = 7.6$ Hz, 1H), 5.40 (s, 1H), 4.45 (q, $J = 7.1$ Hz, 2H), 3.32 – 3.18 (m, 1H), 3.18 – 2.95 (m, 2H), 2.95 – 2.80 (m, 1H), 2.03 (s, 1H), 1.43 (t, $J = 7.1$ Hz, 3H) ppm; $^{13}$C NMR (75 MHz, CDCl$_3$) δ 151.0, 137.0, 136.0, 135.2, 129.3, 129.1, 127.5, 126.4, 125.7, 124.6, 124.5, 122.8, 120.1, 115.3, 63.1, 53.7, 41.8, 29.6, 14.4 ppm; HRMS (ESI): C$_{20}$H$_{21}$N$_2$O$_2$ [M + H]$^+$ calcld: 321.1598, found: 321.1606.

G) X-ray structure and data of 3aa

Displacement ellipsoids are drawn at the 50% probability level.

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S16
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**Diagram:**

![Diagram of a chemical structure](image)

**Label:**

- 3ja
- COOEt
- O,N
- Ts

The diagram includes a spectrum graph with ppm values from 10 to 100.