

Supplementary data

**Discovery of β -Carboline Oxadiazole Derivatives as
Fungicidal Agents Against Rice Sheath Blight**

Zhi-Jun Zhang, Zhi-Yan Jiang, Qi Zhu and Guo-Hua Zhong*

Key Laboratory of Natural Pesticide and Chemical Biology, Ministry of Education,
Key Laboratory of Crop Integrated Pest Management in South China, Ministry of
Agriculture, South China Agricultural University, Guangzhou, 510642, People's
Republic of China.

*Author to whom correspondence should be addressed. E-mail:
guohuazhong@scau.edu.cn

24 **1. Synthesis and Characterizations of the Target Compounds**

25 *Data for Compound 2c.* Yield: 63%. Melting point (mp): 274-276 °C. ¹H NMR
26 (600 MHz, DMSO-*d*₆): δ 14.71 (s, 1H, NH), 12.04 (s, 1H, 9-NH), 8.71 (s, 1H, 4-H),
27 8.40 (d, *J* = 7.9 Hz, 1H, 5-H), 7.66 (d, *J* = 8.2 Hz, 1H, 8-H), 7.60 (t, *J* = 7.6 Hz, 1H,
28 7-H), 7.30 (t, *J* = 7.4 Hz, 1H, 6-H), 3.05 (d, *J* = 7.3 Hz, 2H, 1'-CH₂), 2.31 (dt, *J* = 13.6,
29 6.8 Hz, 1H, 2'-CH), 0.97 (s, 6H, CH₃). ¹³C NMR (150 MHz, DMSO-*d*₆): δ 177.5,
30 161.3, 146.3, 140.8, 135.7, 130.2, 128.6, 127.4, 122.2, 121.0, 120.1, 113.0, 112.3,
31 42.1, 28.0, 22.4. HRMS: [M + H]⁺ Calcd for C₁₇H₁₆N₄OS, 325.1118; found,
32 325.1120.

33 *Data for Compound 2y.* Yield: 71%. mp: 280-282 °C. ¹H NMR (600 MHz,
34 DMSO-*d*₆): δ 11.93 (s, 1H, 9-NH), 8.81 (s, 1H, 4-H), 8.46 (d, *J* = 7.9 Hz, 1H, 5-H),
35 8.18 (d, *J* = 3.6 Hz, 1H, 3'-H), 7.83 (d, *J* = 5.0 Hz, 1H, 5'-H), 7.78 (d, *J* = 8.2 Hz, 1H,
36 8-H), 7.65 (t, *J* = 7.6 Hz, 1H, 7-H), 7.40-7.34 (m, 2H, 6-H, 4'-H). ¹³C NMR (150 MHz,
37 DMSO-*d*₆): δ 177.9, 160.8, 142.0, 141.7, 137.0, 131.8, 131.0, 130.1, 129.2, 129.1,
38 128.6, 127.0, 122.2, 120.8, 120.8, 113.5, 113.0. HRMS: [M + H]⁺ Calcd for
39 C₁₇H₁₀N₄OS₂, 351.0369; found, 351.0372.

40 *Data for Compound 2z.* Yield: 72%. mp: >300 °C. ¹H NMR (600 MHz, DMSO-*d*₆):
41 δ 11.70 (s, 1H, 9-NH), 8.70 (s, 1H, 4-H), 8.41 (d, *J* = 7.9 Hz, 1H, 5-H), 8.36 (s, 1H,
42 2'-H), 7.92 (d, *J* = 4.9 Hz, 1H, 4'-H), 7.81 (d, *J* = 4.9 Hz, 1H, 5'-H), 7.72 (d, *J* = 8.2
43 Hz, 1H, 8-H), 7.61 (t, *J* = 7.6 Hz, 1H, 7-H), 7.32 (t, *J* = 7.4 Hz, 1H, 6-H). ¹³C NMR
44 (150 MHz, DMSO-*d*₆): δ 141.5, 139.3, 137.8, 133.7, 132.5, 129.8, 128.6, 127.9, 126.5,

125.2, 121.9, 121.0, 120.1, 112.6, 111.8. HRMS: $[M + H]^+$ Calcd for $C_{17}H_{10}N_4OS_2$,
351.0369; found, 351.0372.

Data for Compound 2aa. Yield: 78%. mp: 249-252 °C. 1H NMR (600 MHz, DMSO- d_6): δ 14.82 (s, 1H, NH), 12.33 (s, 1H, 9-NH), 8.97 (s, 1H, 4-H), 8.92 (d, J = 4.0 Hz, 1H, 3'-H), 8.67 (d, J = 8.0 Hz, 1H, 6'-H), 8.50 (d, J = 7.9 Hz, 1H, 5-H), 8.11 (td, J = 7.8, 1.8 Hz, 1H, 4'-H), 7.94 (d, J = 8.2 Hz, 1H, 8-H), 7.65 (t, J = 7.1 Hz, 1H, 7-H), 7.61-7.57 (m, 1H, 5'-H), 7.36 (t, J = 7.2 Hz, 1H, 7-H). ^{13}C NMR (150 MHz, DMSO- d_6): δ 177.6, 160.9, 155.8, 148.8, 141.6, 138.2, 137.5, 134.3, 130.4, 130.1, 129.1, 124.0, 122.2, 121.2, 120.5, 120.4, 115.2, 113.3. HRMS: $[M + H]^+$ Calcd for $C_{18}H_{11}N_5OS$, 346.0757; found, 346.0759.

Data for Compound 2ab. Yield: 70%. mp: 264-266 °C. 1H NMR (600 MHz, DMSO- d_6): δ 12.19 (s, 1H, 9-NH), 9.24 (d, J = 1.8 Hz, 1H, 2'-H), 8.93 (s, 1H, 4-H), 8.80 (dd, J = 4.8, 1.6 Hz, 1H, 4'-H), 8.50 (d, J = 7.9 Hz, 1H, 5-H), 8.46-8.43 (m, 1H, 6'-H), 7.72-7.69 (m, 2H, 8-H, 5'-H), 7.66-7.62 (m, 1H, 7-H), 7.36 (dd, J = 11.0, 4.0 Hz, 1H, 6-H). ^{13}C NMR (150 MHz, DMSO- d_6): δ 177.6, 160.9, 149.7, 148.9, 141.6, 139.7, 136.5, 134.2, 133.0, 131.1, 129.8, 129.2, 124.1, 122.3, 120.8, 120.6, 114.4, 112.8. HRMS: $[M + H]^+$ Calcd for $C_{18}H_{11}N_5OS$, 346.0757; found, 346.0759.

Data for Compound 2ac. Yield: 75%. mp: >300 °C. 1H NMR (600 MHz, DMSO- d_6): δ 12.16 (s, 1H, 9-NH), 8.98 (s, 1H, 4-H), 8.89 (d, J = 4.4 Hz, 2H, 3', 5'-H), 8.51 (d, J = 7.9 Hz, 1H, 5-H), 8.10 (d, J = 4.6 Hz, 2H, 2', 6'-H), 7.72 (d, J = 8.2 Hz, 1H, 8-H), 7.66 (t, J = 7.6 Hz, 1H, 7-H), 7.37 (t, J = 7.5 Hz, 1H, 6-H). ^{13}C NMR (150 MHz, DMSO- d_6): δ 177.6, 160.6, 149.3, 145.0, 141.7, 139.2, 134.2, 131.1, 130.3,

129.3, 123.1, 122.2, 120.7, 120.6, 115.0, 112.7. HRMS: $[M + H]^+$ Calcd for $C_{18}H_{11}N_5OS$, 346.0757; found, 346.0759.

Synthesis of Compound 4c. To a solution of 1-(2-naphthyl)- β -carboline-3-carbonylhydrazine (352 mg, 1 mmol) in dioxane (10 mL) were added 1.5 mL $NaHCO_3$ (84 mg, 1mmol) solution and 81 μ L cyanogen bromide (1.1 mmol), and the mixture was stirred for 4h, and then diluted with water. After filtration, compound **4c** was obtained by recrystallization from methanol as a buff solid (yield 64%). mp: 234-236 °C. 1H NMR (600 MHz, $DMSO-d_6$): δ 11.94 (s, 1H, 9-NH), 8.81 (s, 1H, 4-H), 8.60 (s, 1H, Ar-H), 8.43 (d, $J = 7.8$ Hz, 1H, 5-H), 8.17 (s, 2H, Ar-H), 8.09 (dd, $J = 53.4, 7.4$ Hz, 2H, 8-H, Ar-H), 7.70 (d, $J = 8.2$ Hz, 1H, Ar-H), 7.63 (dd, $J = 13.9, 7.3$ Hz, 4H, 7-H, Ar-H), 7.33 (t, $J = 7.4$ Hz, 1H, 6-H), 7.28 (s, 2H, 2'-NH₂). ^{13}C NMR (150 MHz, $DMSO-d_6$): δ 164.1, 158.4, 142.0, 141.7, 134.8, 133.7, 133.4, 133.0, 132.8, 129.8, 128.8, 128.7, 128.2, 127.8, 127.6, 126.8, 126.4, 126.4, 122.1, 120.9, 120.1, 112.6, 112.1. HRMS: $[M + H]^+$ Calcd for $C_{23}H_{15}N_5O$, 378.1349; found, 378.1353.

Data for Compound 5e. Yield: 75%. mp: 197-199 °C. 1H NMR (600 MHz, $DMSO-d_6$): δ 11.93 (s, 1H, 9-NH), 8.97 (s, 1H, 4-H), 8.47 (d, $J = 7.9$ Hz, 1H, 5-H), 8.06 (d, $J = 7.0$ Hz, 2H, Ar-H), 7.70 (d, $J = 8.2$ Hz, 1H, 8-H), 7.67 (t, $J = 7.6$ Hz, 2H, Ar-H), 7.64-7.58 (m, 2H, 7-H, Ar-H), 7.34 (t, $J = 7.5$ Hz, 1H, 6-H), 2.99 (t, $J = 7.5$ Hz, 2H), 1.79 (m, 2H), 1.44 (m, 2H), 0.95 (t, $J = 7.4$ Hz, 3H, CH₃). ^{13}C NMR (150 MHz, $DMSO-d_6$): δ 167.1, 164.7, 142.8, 141.7, 137.4, 134.0, 132.4, 129.8, 129.2, 129.0, 129.7, 122.2, 121.0, 120.5, 114.0, 112.9, 28.1, 24.5, 21.7, 13.6. HRMS: $[M + H]^+$ Calcd for $C_{23}H_{20}N_4O$, 369.1710; found, 369.1712.

89 *Data for Compound 5f.* Yield: 86%. mp: 182-185 °C. ¹H NMR (600 MHz,
90 DMSO-*d*₆): δ 11.93 (s, 1H, 9-NH), 8.97 (s, 1H, 4-H), 8.46 (d, *J* = 7.7 Hz, 1H, 5-H),
91 8.05 (d, *J* = 7.2 Hz, 2H, Ar-H), 7.70 (d, *J* = 8.1 Hz, 1H, 8-H), 7.67 (t, *J* = 7.6 Hz, 2H,
92 Ar-H), 7.61 (dd, *J* = 17.2, 9.1 Hz, 2H, 7-H, Ar-H), 7.34 (t, *J* = 7.8 Hz, 1H, 6-H), 2.98
93 (t, *J* = 7.5 Hz, 2H), 1.84-1.76 (m, 2H), 1.42-1.30 (m, 4H), 0.90 (t, *J* = 7.1 Hz, 3H). ¹³C
94 NMR (150 MHz, DMSO-*d*₆): δ 167.0, 164.7, 142.7, 141.7, 137.4, 134.0, 132.3, 129.7,
95 129.2, 128.9, 128.8, 128.7, 122.2, 120.9, 120.5, 114.0, 112.9, 30.7, 25.7, 24.7, 21.7.
96 HRMS: [M + H]⁺ Calcd for C₂₄H₂₂N₄O, 383.1866; found, 383.1869.

97 *Data for Compound 5g.* Yield: 80%. mp: 109-112 °C. ¹H NMR (600 MHz,
98 DMSO-*d*₆): δ 11.93 (s, 1H, 9-NH), 8.97 (s, 1H, 4-H), 8.46 (d, *J* = 7.9 Hz, 1H, 5-H),
99 8.05 (d, *J* = 7.1 Hz, 2H, Ar-H), 7.70 (d, *J* = 8.2 Hz, 1H, 8-H), 7.67 (t, *J* = 7.6 Hz, 2H,
100 Ar-H), 7.65-7.58 (m, 2H, 7-H, Ar-H), 7.34 (t, *J* = 7.9 Hz, 1H, 6-H), 2.98 (t, *J* = 7.5 Hz,
101 2H), 1.83-1.77 (m, 2H), 1.44-1.39 (m, 2H), 1.35-1.27 (m, 4H), 0.87 (t, *J* = 6.8 Hz,
102 3H). ¹³C NMR (150 MHz, DMSO-*d*₆): δ 167.0, 164.7, 142.7, 141.7, 137.4, 133.9,
103 132.3, 129.7, 129.2, 128.9, 128.8, 128.7, 122.2, 120.9, 120.4, 114.0, 112.8, 30.8, 28.1,
104 26.0, 24.7, 22.0, 13.9. HRMS: [M + H]⁺ Calcd for C₂₅H₂₄N₄O, 397.2023; found,
105 397.2027.

106 *Data for Compound 5h.* Yield: 78%. mp: 135-137 °C. ¹H NMR (600 MHz,
107 DMSO-*d*₆): δ 11.93 (s, 1H, 9-NH), 8.97 (s, 1H, 4-H), 8.47 (d, *J* = 7.9 Hz, 1H, 5-H),
108 8.06 (d, *J* = 7.3 Hz, 2H, Ar-H), 7.71 (d, *J* = 8.2 Hz, 1H, 8-H), 7.67 (t, *J* = 7.6 Hz, 2H,
109 Ar-H), 7.62 (dd, *J* = 16.6, 8.1 Hz, 2H, 7-H, Ar-H), 7.35 (t, *J* = 7.5 Hz, 1H, 6-H), 1.48
110 (s, 9H, CH₃). ¹³C NMR (150 MHz, DMSO-*d*₆): δ 164.7, 163.9, 142.7, 141.7, 140.8,

137.3, 134.0, 132.3, 129.7, 129.2, 129.0, 128.8, 128.7, 122.3, 121.0, 120.5, 114.2,
112.9, 32.2, 28.0. HRMS: $[M + H]^+$ Calcd for $C_{23}H_{20}N_4O$, 369.1710; found, 369.1712.

Data for Compound 5j. Yield: 85%. mp: 220-222 °C. 1H NMR (600 MHz, DMSO- d_6): δ 11.93 (s, 1H, 9-NH), 8.98 (s, 1H, 4-H), 8.47 (d, $J = 7.8$ Hz, 1H, 5-H), 8.05 (d, $J = 7.2$ Hz, 2H, Ar-H), 7.70 (d, $J = 8.2$ Hz, 1H, 8-H), 7.67 (t, $J = 7.6$ Hz, 2H, Ar-H), 7.61 (dd, $J = 17.2, 8.1$ Hz, 2H, 7-H, Ar-H), 7.34 (t, $J = 7.4$ Hz, 1H, 6-H), 3.91 (dt, $J = 16.8, 8.6$ Hz, 1H), 2.48-2.43 (m, 4H), 2.15-2.09 (m, 2H). ^{13}C NMR (150 MHz, DMSO- d_6): δ 169.0, 164.7, 142.7, 141.6, 137.4, 133.9, 132.3, 129.6, 129.1, 128.9, 128.8, 128.7, 122.2, 120.9, 120.4, 114.0, 112.8, 29.8, 26.4, 18.4. HRMS: $[M + H]^+$ Calcd for $C_{23}H_{18}N_4O$, 367.1553; found, 367.1556.

Data for Compound 5k. Yield: 73%. mp: 158-160 °C. 1H NMR (600 MHz, DMSO- d_6): δ 11.92 (s, 1H, 9-NH), 8.96 (s, 1H, 4-H), 8.47 (d, $J = 7.9$ Hz, 1H, 5-H), 8.05 (d, $J = 7.1$ Hz, 2H, Ar-H), 7.70 (d, $J = 8.2$ Hz, 1H, 8-H), 7.67 (t, $J = 7.6$ Hz, 2H, Ar-H), 7.61 (dd, $J = 16.8, 8.5$ Hz, 2H, 7-H, Ar-H), 7.34 (t, $J = 7.8$ Hz, 1H, 6-H), 2.14 (dt, $J = 12.7, 7.3$ Hz, 2H), 1.96 (dt, $J = 15.1, 7.9$ Hz, 2H), 1.81-1.75 (m, 2H), 1.74-1.67 (m, 2H). ^{13}C NMR (150 MHz, DMSO- d_6): δ 170.0, 164.7, 142.7, 141.6, 137.4, 134.0, 132.3, 129.9, 129.1, 128.9, 128.8, 128.7, 122.2, 120.9, 120.4, 35.4, 30.7, 25.1. HRMS: $[M + H]^+$ Calcd for $C_{24}H_{20}N_4O$, 381.1710; found, 381.1712.

Data for Compound 5l. Yield: 68%. mp: 286-288 °C. 1H NMR (600 MHz, DMSO- d_6): δ 11.92 (s, 1H, 9-NH), 8.97 (s, 1H, 4-H), 8.47 (d, $J = 7.8$ Hz, 1H, 5-H), 8.05 (d, $J = 7.3$ Hz, 2H, Ar-H), 7.70 (d, $J = 8.2$ Hz, 1H, 8-H), 7.67 (t, $J = 7.6$ Hz, 2H, Ar-H), 7.61 (dd, $J = 16.4, 8.1$ Hz, 2H, 7-H, Ar-H), 7.34 (t, $J = 7.5$ Hz, 1H, 6-H),

3.13-3.07 (m, 1H), 2.12 (dd, $J = 13.1, 3.6$ Hz, 2H), 1.82-1.77 (m, 3H), 1.66 (dt, $J = 20.9, 12.1$ Hz, 4H), 1.44 (dd, $J = 24.6, 12.1$ Hz, 3H), 1.35-1.30 (m, 1H). ^{13}C NMR (150 MHz, DMSO- d_6): δ 169.7, 164.4, 142.7, 141.7, 137.7, 133.9, 132.4, 129.7, 129.2, 128.9, 128.9, 128.8, 128.7, 122.2, 120.9, 120.4, 114.0, 112.8, 34.6, 29.8, 25.2, 24.8. HRMS: $[\text{M} + \text{H}]^+$ Calcd for $\text{C}_{25}\text{H}_{22}\text{N}_4\text{O}$, 395.1866; found, 395.1869.

Data for Compound 5m. Yield: 80%. mp: 164-166 °C. ^1H NMR (600 MHz, DMSO- d_6): δ 11.92 (s, 1H, 9-NH), 8.97 (s, 1H, 4-H), 8.47 (d, $J = 7.9$ Hz, 1H, 5-H), 8.05 (d, $J = 7.3$ Hz, 2H, Ar-H), 7.70 (d, $J = 8.2$ Hz, 1H, 8-H), 7.67 (t, $J = 7.6$ Hz, 2H, Ar-H), 7.61 (dt, $J = 14.8, 7.5$ Hz, 2H, 7-H, Ar-H), 7.34 (t, $J = 7.5$ Hz, 1H, 6-H), 3.57 (s, 1H), 2.12 (s, 8H), 1.80 (s, 6H). ^{13}C NMR (150 MHz, DMSO- d_6): δ 172.3, 164.4, 142.8, 141.7, 137.4, 134.0, 132.4, 129.7, 129.2, 129.0, 128.8, 128.7, 122.2, 121.0, 120.5, 114.2, 112.9, 38.5, 36.0, 35.8, 34.0, 27.4, 27.3. HRMS: $[\text{M} + \text{H}]^+$ Calcd for $\text{C}_{29}\text{H}_{26}\text{N}_4\text{O}$, 447.2179; found, 447.2181.

Data for Compound 12a. Yield: 84%. ^1H NMR (600 MHz, DMSO- d_6): δ 12.15 (s, 1H, -CONH-), 12.05 (s, 1H, 9-NH), 11.55 (s, 1H, OH), 8.88 (s, 1H, -N=CH-), 8.80 (s, 1H, 4-H), 8.39 (d, $J = 7.9$ Hz, 1H, 5-H), 7.67 (d, $J = 8.2$ Hz, 1H, 8-H), 7.60 (m, 1H, 7-H), 7.49 (dd, $J = 7.6, 1.5$ Hz, 1H, Ar-H), 7.33-7.29 (m, 2H, 6-H, Ar-H), 6.97-6.93 (m, 2H, Ar-H), 2.91 (s, 3H, 1-CH₃).

Data for Compound 12b. Yield: 90%. ^1H NMR (600 MHz, DMSO- d_6): δ 12.10 (s, 1H, -CONH-), 11.95 (s, 1H, 9-NH), 11.53 (s, 1H, OH), 8.96 (s, 1H, -N=CH-), 8.89 (s, 1H, 4-H), 8.47 (d, $J = 7.9$ Hz, 1H, 5-H), 8.23 (d, $J = 7.2$ Hz, 2H, 8-H, Ar-H), 7.73-7.67 (m, 3H, Ar-H, 7-H), 7.62 (q, $J = 7.9$ Hz, 2H, Ar-H), 7.52 (dd, $J = 7.7, 1.4$

Hz, 1H, Ar-H), 7.36-7.30 (m, 2H, 6-H, Ar-H), 6.95 (dd, $J = 13.1, 7.7$ Hz, 2H, Ar-H).

Data for Compound 12c. Yield: 88%. ^1H NMR (600 MHz, DMSO- d_6): δ 12.11 (s, 1H, -CONH-), 11.99 (s, 1H, 9-NH), 11.49 (s, 1H, OH), 8.98 (s, 1H, -N=CH-), 8.89 (s, 1H, 4-H), 8.48 (d, $J = 7.9$ Hz, 1H, 5-H), 8.28-8.26 (m, 2H, Ar-H), 7.74 (d, $J = 8.5$ Hz, 2H, Ar-H), 7.71 (d, $J = 8.2$ Hz, 1H, 8-H), 7.65-7.62 (m, 1H, 7-H), 7.54 (dd, $J = 7.7, 1.5$ Hz, 1H, Ar-H), 7.37-7.30 (m, 2H, 6-H, Ar-H), 6.95 (dd, $J = 13.1, 8.2$ Hz, 2H, Ar-H).

Data for Compound 12d. Yield: 74%. ^1H NMR (600 MHz, DMSO- d_6): δ 12.10 (s, 1H, -CONH-), 11.57 (s, 1H, 9-NH), 11.48 (s, 1H, OH), 10.21 (s, 1H, OH), 8.95 (s, 1H, -N=CH-), 8.85 (s, 1H, 4-H), 8.44 (d, $J = 7.9$ Hz, 1H, 5-H), 7.74 (d, $J = 7.5$ Hz, 1H, Ar-H), 7.67 (d, $J = 8.2$ Hz, 1H, 8-H), 7.59 (t, $J = 7.6$ Hz, 1H, 7-H), 7.48 (d, $J = 7.7$ Hz, 1H, Ar-H), 7.44-7.40 (m, 1H, Ar-H), 7.32 (t, $J = 7.2$ Hz, 2H, 6-H, Ar-H), 7.12 (d, $J = 7.9$ Hz, 1H, Ar-H), 7.07 (t, $J = 7.4$ Hz, 1H, Ar-H), 6.97-6.93 (m, 2H, Ar-H).

Data for Compound 12e. Yield: 84%. ^1H NMR (600 MHz, DMSO- d_6): δ 12.02 (s, 1H, -CONH-), 11.64 (s, 1H, 9-NH), 9.54 (s, 1H, OH), 8.78 (s, 1H, -N=CH-), 8.53 (s, 1H, 4-H), 8.40 (d, $J = 7.8$ Hz, 1H, 5-H), 7.66 (d, $J = 8.2$ Hz, 1H, 8-H), 7.61-7.58 (m, 1H, 7-H), 7.35 (d, $J = 1.8$ Hz, 1H, Ar-H), 7.32-7.29 (m, 1H, 6-H), 7.11 (dd, $J = 8.2, 1.8$ Hz, 1H, Ar-H), 6.87 (d, $J = 8.0$ Hz, 1H, Ar-H), 3.86 (s, 3H, -OCH₃), 2.90 (s, 3H, 1-CH₃).

Data for Compound 12f. Yield: 92%. ^1H NMR (600 MHz, DMSO- d_6): δ 12.95 (s, 1H, -CONH-), 12.06 (s, 1H, 9-NH), 9.01 (s, 1H, -N=CH-), 8.49 (d, $J = 7.9$ Hz, 1H, 4-H), 8.20 (d, $J = 7.1$ Hz, 2H, 5, Ar-H), 7.86 (d, $J = 1.4$ Hz, 1H, Ar-H), 7.77 (t, $J = 7.7$

177 Hz, 2H, Ar-H), 7.73 (d, J = 8.2 Hz, 1H, 8-H), 7.64 (dt, J = 8.2, 4.2 Hz, 2H, 7-H, Ar-H),
178 7.58 (s, 1H, Ar-H), 7.36 (t, J = 7.5 Hz, 1H, 6-H), 7.15 (d, J = 3.5 Hz, 1H, Ar-H), 6.83
179 (dd, J = 3.5, 1.7 Hz, 1H, Ar-H).

180 *Data for Compound 12g.* Yield: 79%. ^1H NMR (600 MHz, DMSO- d_6): δ 12.86 (s,
181 1H, -CONH-), 12.08 (s, 1H, 9-NH), 9.03 (s, 1H, -N=CH-), 8.49 (d, J = 7.9 Hz, 1H,
182 4-H), 8.20 (d, J = 8.4 Hz, 2H, 5, Ar-H), 7.92 (d, J = 1.4 Hz, 1H, Ar-H), 7.85 (d, J =
183 8.4 Hz, 2H, Ar-H), 7.71 (d, J = 8.2 Hz, 1H, 8-H), 7.66–7.62 (m, 1H, 7-H), 7.58 (s, 1H,
184 Ar-H), 7.36 (t, J = 7.4 Hz, 1H, 6-H), 7.14 (d, J = 3.5 Hz, 1H, Ar-H), 6.84 (dd, J = 3.5,
185 1.8 Hz, 1H, Ar-H).

186 *Data for Compound 12h.* Yield: 87%. ^1H NMR (600 MHz, DMSO- d_6): δ 11.64 (s,
187 1H, -CONH-), 8.95 (s, 1H, -N=CH-), 8.54 (s, 1H, 4-H), 8.48 (d, J = 7.9 Hz, 1H, 5-H),
188 8.26 (d, J = 8.5 Hz, 2H, Ar-H), 7.72 (d, J = 8.5 Hz, 2H, Ar-H), 7.70 (d, J = 8.2 Hz, 1H,
189 8-H), 7.64–7.61 (m, 1H, 7-H), 7.37 (d, J = 1.7 Hz, 1H, Ar-H), 7.34 (t, J = 7.5 Hz, 1H,
190 6-H), 7.13 (dd, J = 8.2, 1.7 Hz, 1H, Ar-H), 6.87 (d, J = 8.0 Hz, 1H, Ar-H), 3.86 (s, 3H,
191 -OCH₃).

192 *Data for Compound 6b.* Yield: 74%. mp: 250-252 °C. ^1H NMR (600 MHz,
193 DMSO- d_6): δ 11.94 (s, 1H, 9-NH), 11.90 (s, 1H, OH), 8.98 (s, 1H, 2'-H), 8.69 (s, 1H,
194 4-H), 8.47 (d, J = 7.9 Hz, 1H, 5-H), 8.19 (d, J = 7.1 Hz, 2H, Ar-H), 7.90 (d, J = 6.4
195 Hz, 1H, Ar-H), 7.72 – 7.66 (m, 3H, 8-H, Ar-H), 7.61 (dd, J = 18.1, 7.7 Hz, 2H, 7-H,
196 Ar-H), 7.49 (t, J = 6.9 Hz, 1H, Ar-H), 7.39 (t, J = 7.4 Hz, 1H, Ar-H), 7.34 (t, J = 7.4
197 Hz, 1H, 6-H), 7.21 (d, J = 8.0 Hz, 1H, Ar-H), 2.46 (s, 3H, 3'-COCH₃). ^{13}C NMR (151
198 MHz, DMSO- d_6): δ 169.6, 161.5, 148.9, 143.9, 141.6, 141.1, 139.0, 137.3, 134.6,

130.8, 129.9, 128.8, 128.2, 126.8, 126.3, 123.6, 122.1, 121.2, 120.4, 114.2, 112.8,
21.0. HRMS: $[M + H]^+$ Calcd for $C_{27}H_{20}N_4O_3$, 449.1608; found, 449.1609.

Data for Compound 6c. Yield: 66%. mp: 246-248 °C. 1H NMR (600 MHz, DMSO- d_6): δ 11.97 (s, 1H, 9-NH), 11.91 (s, 1H, OH), 9.00 (s, 1H, 2'-H), 8.69 (s, 1H, 4-H), 8.48 (d, J = 7.9 Hz, 1H, 5-H), 8.24 (d, J = 8.5 Hz, 2H, Ar-H), 7.90 (dd, J = 7.8, 1.4 Hz, 1H, Ar-H), 7.73 (d, J = 8.5 Hz, 2H, Ar-H), 7.70 (d, J = 8.1 Hz, 1H, 8-H), 7.63 (t, J = 7.6 Hz, 1H, 7-H), 7.49 (td, J = 7.9, 1.6 Hz, 1H, Ar-H), 7.40 (t, J = 7.3 Hz, 1H, Ar-H), 7.35 (t, J = 7.5 Hz, 1H, 6-H), 7.22 (d, J = 7.3 Hz, 1H, Ar-H), 2.46 (s, 3H, 3'-COCH₃). ^{13}C NMR (151 MHz, DMSO- d_6): δ 169.5, 161.3, 157.0, 148.9, 143.8, 141.6, 139.7, 139.0, 136.1, 134.5, 133.8, 130.9, 130.3, 130.1, 128.8, 128.1, 126.8, 126.3, 125.9, 123.5, 122.1, 121.1, 120.4, 114.4, 112.6, 21.0. HRMS: $[M + H]^+$ Calcd for $C_{27}H_{19}ClN_4O_3$, 483.1218; found, 483.1220.

Data for Compound 6d. Yield: 76%. mp: 236-238 °C. 1H -NMR (600 MHz, DMSO- d_6): δ 11.86 (s, 1H, 9-NH), 11.55 (s, 1H, OH), 9.01 (s, 1H, 2'-H), 8.52 (s, 1H, 4-H), 8.49 (d, J = 7.9 Hz, 1H, 5-H), 7.94 (d, J = 7.5 Hz, 1H, Ar-H), 7.91 (d, J = 7.7 Hz, 1H, Ar-H), 7.69-7.65 (m, 2H, , Ar-H), 7.62 (t, J = 7.6 Hz, 1H, 8-H), 7.57 (t, J = 7.5 Hz, 1H, Ar-H), 7.52-7.46 (m, 2H, 7-H, Ar-H), 7.39 (t, J = 7.5 Hz, 1H, Ar-H), 7.35 (t, J = 7.4 Hz, 1H, 6-H), 7.22 (d, J = 8.0 Hz, 1H, Ar-H), 2.43 (s, 3H, 3'-COCH₃). ^{13}C NMR (151 MHz, DMSO- d_6): δ 169.4, 160.8, 149.0, 148.5, 143.1, 141.5, 138.0, 135.2, 131.2, 131.0, 130.2, 130.0, 129.7, 128.9, 127.8, 126.6, 126.5, 126.3, 123.8, 123.4, 122.2, 121.0, 120.3, 114.3, 112.0, 20.8. HRMS: $[M + H]^+$ Calcd for $C_{27}H_{20}N_4O_4$, 465.1557; found, 465.1559.

221 *Data for Compound 6e.* Yield: 76%. mp: 285-288 °C. ¹H-NMR (600 MHz,
222 DMSO-*d*₆): δ 12.05 (s, 1H, 9-NH), 11.87 (s, 1H, OH), 8.81 (s, 1H, 2'-H), 8.67 (s, 1H,
223 4-H), 8.40 (d, *J* = 7.8 Hz, 1H, 5-H), 7.66 (d, *J* = 8.2 Hz, 1H, 8-H), 7.60 (t, *J* = 7.6 Hz,
224 1H, 7-H), 7.49 (d, *J* = 1.3 Hz, 1H, Ar-H), 7.32-7.29 (m, 2H, 6-H, Ar-H), 7.20 (d, *J* =
225 8.0 Hz, 1H, Ar-H), 3.87 (s, 3H, OCH₃), 2.91 (s, 3H, 1-CH₃), 2.29 (s, 3H, 3'-COCH₃).
226 ¹³C NMR (151 MHz, DMSO-*d*₆): δ 168.9, 161.6, 151.7, 147.8, 141.6, 141.3, 141.2,
227 138.6, 136.6, 133.9, 128.9, 128.0, 123.8, 122.7, 121.9, 121.0, 120.6, 113.6, 112.7,
228 110.2, 56.3, 20.9, 20.8. HRMS: [M + H]⁺ Calcd for C₂₃H₂₀N₄O₄, 417.1557; found,
229 417.1558.

230 *Data for Compound 6f.* Yield: 67%. mp: 276-278 °C. ¹H-NMR (600 MHz,
231 DMSO-*d*₆): δ 11.89 (s, 1H, 9-NH), 8.98 (s, 1H, 2'-H), 8.70 (s, 1H, 4-H), 8.47 (d,
232 *J*=7.8 Hz, 1H, 5-H), 8.19 (t, *J*=8.4 Hz, 2H, Ar-H), 7.89 (q, *J*=9.0 Hz, 1H, Ar-H), 7.69
233 (m, 1H, 8-H), 7.59 (m, 2H, 7-H, Ar-H), 7.48 (m, 1H, Ar-H), 7.40 (d, *J*=7.2 Hz, 1H,
234 Ar-H), 7.34 (t, *J*=7.2 Hz, 1H, 6-H), 7.21 (q, *J*=9.0 Hz, 1H, Ar-H), 6.98 (q, *J*=5.6 Hz,
235 1H, Ar-H), 2.46 (s, 3H, 3'-COCH₃). ¹³C NMR (151 MHz, DMSO-*d*₆): δ 168.5, 163.9,
236 155.7, 149.7, 148.9, 144.8, 143.2, 142.0, 141.3, 139.2, 137.8, 134.8, 134.4, 132.8,
237 130.3, 129.5, 129.4, 129.0, 122.5, 121.7, 121.3, 120.8, 114.7, 114.0, 113.3, 111.4, 21.8.
238 HRMS: [M + H]⁺ Calcd for C₂₅H₁₈ClN₄O₃, 423.1452; found, 423.1455.

239 *Data for Compound 6g.* Yield: 70%. mp: 294-296 °C. ¹H-NMR (600 MHz,
240 DMSO-*d*₆): δ 12.04 (s, 1H, 9-NH), 8.93 (d, *J* = 5.1 Hz, 1H, 2'-H), 8.78 (s, 1H, 4-H),
241 8.46 (d, *J* = 7.2 Hz, 1H, 5-H), 8.11 (d, *J* = 8.4 Hz, 1H, Ar-H), 8.03 (d, *J* = 8.3 Hz, 1H,
242 Ar-H), 7.89 (d, *J* = 8.5 Hz, 1H, Ar-H), 7.75-7.67 (m, 3H, 8-H, Ar-H), 7.65-7.61 (m,

2H, 7-H, Ar-H), 7.38-7.32 (m, 2H, 6-H, Ar-H), 2.46 (s, 3H, 3'-COCH₃). ¹³C NMR (151 MHz, DMSO-*d*₆): δ 167.1, 155.6, 148.9, 144.9, 142.0, 141.8, 136.6, 134.4, 134.3, 132.8, 130.9, 130.0, 129.3, 122.7, 121.3, 120.9, 114.9, 113.1, 111.5, 111.4, 21.8. HRMS: [M + H]⁺ Calcd for C₂₅H₁₇ClN₄O₃, 457.1062; found, 457.1064.

Data for Compound 6h. Yield: 74%. mp: 296-298 °C. ¹H-NMR (600 MHz, DMSO-*d*₆): δ 11.98 (s, 1H, 9-NH), 11.85 (s, 1H, OH), 8.97 (s, 1H, 2'-H), 8.67 (s, 1H, 4-H), 8.49 (d, *J*=7.8 Hz, 1H, 5-H), 8.26 (d, *J*=7.8 Hz, 2H, Ar-H), 8.03 (q, *J*=9.0 Hz, 1H, Ar-H), 7.72 (d, *J*=8.4 Hz, 2H, 8-H), 7.51 (d, *J*=1.8 Hz, 1H, 7-H), 7.35 (d, *J*=7.8 Hz, 1H, Ar-H), 7.34 (d, *J*=1.8 Hz, 1H, Ar-H), 7.32 (t, *J*=7.2 Hz, 1H, 6-H), 7.20 (d, *J*=7.8 Hz, 1H, Ar-H), 3.88 (s, 3H, -OCH₃), 2.29 (s, 3H, 3'-COCH₃). ¹³C NMR (151 MHz, DMSO-*d*₆): δ 168.9, 161.6, 151.7, 148.3, 142.1, 141.3, 140.1, 139.5, 136.6, 135.0, 134.3, 133.9, 131.3, 130.9, 130.6, 129.3, 129.2, 123.8, 122.7, 121.6, 120.9, 114.8, 113.2, 110.4, 56.3, 20.9. HRMS: [M + H]⁺ Calcd for C₂₈H₂₁ClN₄O₄, 513.1324; found, 513.1326.

Synthesis of Compound 7. 1-Phenyl-β-carboline-3-carbonylhydrazine (302 mg, 1 mmol) was dissolved in formic acid (5 mL), and the reaction mixture was refluxed for 2 h and then concentrated. The residue was dissolved in 10 mL xylene, and phosphorus pentasulfide (191 mg, 1mmol) was added. After reflux for 1 h, the reaction mixture was cooled to room temperature, concentrated, and diluted with water (10 mL). The aqueous layer was extracted with chloroform (3×15 mL). The extracts were combined, dried over MgSO₄, filtered and concentrated in vacuo to give the desired compound 7 as a yellow solid (yield 58%). mp: >300 °C. ¹H NMR (600

265 MHz, DMSO-*d*₆): δ 11.92 (s, 1H, 9-NH), 9.62 (s, 1H, 2'-H), 9.11 (s, 1H, 4-H), 8.48 (d,
266 J = 7.9 Hz, 1H, 5-H), 8.09 (d, J = 7.1 Hz, 2H, Ar-H), 7.71 (d, J = 8.2 Hz, 1H, 8-H),
267 7.68 (t, J = 7.6 Hz, 2H, Ar-H), 7.61 (dt, J = 15.0, 7.7 Hz, 2H, 7-H, Ar-H), 7.35 (t, J =
268 7.4 Hz, 1H, 6-H). ¹³C NMR (150 MHz, DMSO-*d*₆): δ 170.9, 154.3, 142.3, 141.8,
269 137.6, 137.2, 133.9, 130.1, 129.1, 128.9, 128.5, 122.2, 121.1, 120.3, 112.8, 111.4.
270 HRMS: [M + H]⁺ Calcd for C₁₉H₁₂N₄S, 329.0855; found, 329.0858.

271 *Synthesis of Compound 8.* To a solution of 1-phenyl- β -carboline-3-carbonyl-
272 hydrazine (302 mg, 1 mmol) in absolute ethanol (10 mL) were added potassium
273 hydroxide (84 mg, 1.5 mmol) and carbon disulfide (0.3 mL, 5 mmol) and the mixture
274 was then stirred at room temperature overnight. The solid was filtered, washed with
275 ethanol and diethyl ether, and then was dissolved in 4 mL of conc. H₂SO₄. After
276 stirred at room temperature for 2 h, the reaction mixture was poured over crushed ice.
277 The resulting solid was kept in 2 N NaOH for 2 h and was then filtered, washed with
278 water and recrystallized for ethanol as yellow solid (yield 42%). mp: >300 °C. ¹H
279 NMR (600 MHz, DMSO-*d*₆): δ 14.69 (s, 1H, NH), 12.00 (s, 1H, 9-NH), 8.87 (s, 1H,
280 4-H), 8.48 (d, J = 7.7 Hz, 1H, 5-H), 8.06 (d, J = 8.1 Hz, 2H, Ar-H), 7.71 (d, J = 8.1
281 Hz, 1H, 8-H), 7.67 (t, J = 7.5 Hz, 2H, Ar-H), 7.61 (dd, J = 14.7, 7.3 Hz, 2H, 7-H,
282 Ar-H), 7.34 (t, J = 7.8 Hz, 1H, 6-H). ¹³C NMR (150 MHz, DMSO-*d*₆): δ 188.7, 177.6,
283 163.2, 161.1, 142.8, 141.6, 137.2, 134.0, 130.9, 129.2, 129.0, 128.9, 128.6, 122.2,
284 120.9, 120.4, 113.9, 112.8. HRMS: [M + H]⁺ Calcd for C₁₉H₁₂N₄S₂, 361.0576; found,
285 361.0578.

286 *Synthesis of Compound 9.* To a solution of 1-phenyl- β -carboline-3-carbonylhydrazine

(302 mg, 1 mmol) in a minimum amount of 1M HCl and ammonium thiocyanate (152 mg, 2 mmol) was added. The reaction mixture was heated under reflux for 8 h. After cooling, the product was filtered, washed with water and recrystallized from alcohol. Then this intermediate was dissolved in 4 mL of conc. H₂SO₄. After stirred at room temperature for 2 h, the reaction mixture was poured over crushed ice. The resulting solid was kept in 2 N NaOH for 2 h and was then filtered, washed with water and recrystallized for ethanol as yellow solid (yield 48%). mp: 230-232 °C. ¹H NMR (600 MHz, DMSO-*d*₆): δ 11.84 (s, 1H, 9-NH), 9.70 (s, 1H,), 8.79 (s, 1H, 4-H), 8.42 (d, *J* = 7.8 Hz, 1H, 5-H), 8.23-8.20 (m, 2H, NH₂), 8.08 (d, *J* = 7.1 Hz, 2H, Ar-H), 7.70-7.68 (m, 1H, 8-H), 7.64 (t, *J* = 7.6 Hz, 2H, Ar-H), 7.61-7.56 (m, 2H, 7-H, Ar-H), 7.31 (t, *J* = 7.4 Hz, 1H, 6-H). ¹³C NMR (150 MHz, DMSO-*d*₆): δ 166.9, 164.0, 141.5, 140.7, 137.5, 134.0, 129.8, 128.9, 128.8, 128.7, 128.6, 122.0, 121.2, 120.2, 112.8, 112.6. HRMS: [M + H]⁺ Calcd for C₁₉H₁₃N₅S, 344.0964; found, 344.0965.

2. Acute Oral Toxicity Test

Animals. Healthy Kunming mice were acquired from Southern Medical University, Guangdong, China. Animal experiments were approved and performed in accordance with the Animal Care and Use Committee at South China Agricultural University and guided for the Care and Use of Laboratory Animals published by the US National Institutes of Health (NIH Publication NO.85-23, revised 1996).

Acute oral toxicity test. The acute oral toxicity of compound **5i** in mice was determined according to the OECD Guide protocol 423/2001 (Acute Oral Toxicity-Acute Toxic Class Method).¹ Three animals were exposed to an initial dose and

another three animals were used to confirm the results. Individual weights of animals were determined prior to administration and weekly thereafter. Animals were observed daily after administration and euthanized by CO₂ exposure to gross necropsy on day 14, and the heart, liver, spleen, lung, kidney and stomach of each animal were macroscopically analyzed and weighted.

REFERENCES

1. OECD. Acute oral toxicity-acute toxic class method. 423. OECD Guideline for testing of chemicals. Organisation for economic cooperation and development, **2001**, 14.

Table S1. The Mortality and Organ Weight of the Control Group and Compound **5i**Treated Mice.^a

	Control	Compound 5i (mg/kg)			
		2000	300	50	5
Number of animals	6	6	6	6	6
Mortality (%)	0	0	0	0	0
Organ weight (g)					
Heart	0.15 ± 0.02	0.16 ± 0.02	0.17 ± 0.03	0.15 ± 0.02	0.15 ± 0.01
Liver	1.36 ± 0.09	1.30 ± 0.12	1.24 ± 0.15	1.32 ± 0.08	1.29 ± 0.14
Spleen	0.12 ± 0.01	0.12 ± 0.03	0.11 ± 0.02	0.11 ± 0.02	0.12 ± 0.01
Lung	0.20 ± 0.02	0.21 ± 0.03	0.20 ± 0.02	0.20 ± 0.02	0.21 ± 0.02
Kidney	0.35 ± 0.04	0.33 ± 0.02	0.32 ± 0.05	0.32 ± 0.04	0.33 ± 0.04
Stomach	0.36 ± 0.04	0.36 ± 0.06	0.34 ± 0.06	0.35 ± 0.04	0.35 ± 0.06

^a Values are the mean ± standard error.

331

332