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Supplementary Information

Synthesis and Antifungal Activities of Novel Spirooxindole Derivatives

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1. General Methods:

NMR spectra were recorded with tetramethylsilane as the internal standard. TLC was performed on glass-backed silica plates. Column chromatography was performed using silica gel (150-200 mesh) eluting with ethyl acetate and petroleum ether. ¹H NMR spectra were recorded at 400 MHz or 600 MHz, and ¹³C NMR spectra were recorded at 100 MHz or 150 MHz (Bruker Avance). Chemical shifts (δ) are reported in ppm downfield from CDCl₃ (δ = 7.26 ppm) for ¹H NMR and relative to the central CDCl₃ resonance (δ = 77.0 ppm) for ¹³C NMR spectroscopy. Coupling constants (*J*) are given in Hz. ESI-HRMS spectrometer was measured with a Finnigan LCQ^{DECA} ion trap mass spectrometer. Commercial grade solvents were dried and purified by standard procedures as specified in Purification of Laboratory Chemicals. Substrates were prepared according to literature procedures.

General procedure for synthesis of 1a-b

To a solution of **3-hydroxyindolin-2-one** (0.5 g, 3 mmol) and in dry DMF (1 mL), ethyl propiolate (0.37g, 3.75 mmol) and DABCO (0.07mg, 0.6 mmol) were added. The mixture was stirred at 0 °C for 6 h. Then purified by column chromatography (20% ethyl ether/ petroleum ether) to give the corresponding compounds **1a-1b**.



Ethyl 3-(3-hydroxy-1-methyl-2-oxoindolin-3-yl)acrylate (1a) ¹H NMR (400 MHz, CDCl₃) δ 7.40 – 7.34 (m, 1H), 7.34 – 7.31 (m, 1H), 7.14 – 7.09 (m, 1H), 6.87 (t, J = 3.9 Hz, 1H), 6.84 (s, 1H), 6.23 (d, J = 15.5 Hz, 1H), 4.16 (q, J = 7.1 Hz, 2H), 3.91 (s, 1H), 3.21 (s, 3H), 1.26 (t, J = 7.1 Hz, 3H). ¹³C NMR (151 MHz, CDCl₃) δ 175.7, 165.8, 144.2, 143.1, 130.4, 128.3, 124.8, 123.6, 122.3, 108.9, 76.6, 60.7, 26.5, 14.1. ESI-HRMS calcd for C₁₄H₁₅NO₄ + Na 284.0893, found 284.0898.

Ethyl 3-(1-benzyl-3-hydroxy-2-oxoindolin-3-yl)acrylate (**1b**) ¹H NMR (600 MHz, CDCl₃) δ 7.34 – 7.31 (m, 3H), 7.28 (d, *J* = 7.3 Hz, 3H), 7.24 (dd, *J* = 7.8, 1.0 Hz, 1H), 7.08 (t, *J* = 7.5 Hz, 1H), 6.92 (d, *J* = 15.6 Hz, 1H), 6.75 (d, *J* = 7.9 Hz, 1H), 6.29 (d, *J* = 15.5 Hz, 1H), 4.97 (d, *J* = 15.7 Hz, 1H), 4.84 (d, *J* = 15.7 Hz, 1H), 4.19 (q, *J* = 7.1 Hz, 2H), 3.56 (s, 1H), 1.28 (t, *J* = 7.1 Hz, 4H). ¹³C NMR (150 MHz, CDCl₃) δ 175.7, 165.8, 144.0, 142.3, 134.9, 130.4, 128.9, 128.1, 127.9, 127.2, 124.9, 123.7, 122.5, 110.0, 60.8, 53.4, 44.1, 14.2. ESI-HRMS calcd for C₂₀H₁₉NO₄ +Na 360.1206, found 360.1209.

2. Crystal data for 3ak and 4am and the relative configuration



Crystal data for 3ak: $C_{26}H_{25}CIN_2O_6$ (496.93), Monoclinic, space group P2(1)/c, a = 11.9606(11) Å, alpha = 90 deg. b = 21.1995(17) Å, beta = 109.815(5) deg.. c = 10.6937(8) Å, gamma = 90 deg. U = 2550.9(4) Å³, specimen 0.231 x 0.0187 x 0.114 mm³, Z = 11, T = 296(2) K, SIEMENS P4 diffractometer, absorption coefficient 0.192 mm⁻¹, reflections collected 40523, unique 5963 [R(int) = 0.0487], refinement by Full-matrix least-squares on F^2 , data/ restraints/ parameters 5963 / 0 / 317, goodness-of-fit on $F^2 = 1.051$, final *R* indices [I > 2sigma(I)] R1 = 0.0575, wR2 = 0.1679, *R* indices (all data) R1 = 0.1152, wR2 = 0.2007, largest diff. peak and hole 0.485 and -0.324 e. Å⁻³.

Crystal data for 4am: $C_{25}H_{21}F_{3}N_{2}O_{6}$ (502.44), Triclinic, space group P-1, a = 12.3631(10) Å, alpha = 102.619(6) deg. b = 14.6129(12) Å, beta = 90.115(5) deg. c = 15.0199(12) Å, gamma = 114.981(5) deg. U = 2386.6(3) Å³, specimen 0.254 x 0.0177 x 0.123 mm³, Z = 11, T = 296(2) K, SIEMENS P4 diffractometer, absorption coefficient 0.116 mm⁻¹, reflections collected 37184, unique 10698 [R(int) = 0.0506], refinement by Full-matrix least-squares on F^{2} , data/ restraints/ parameters 10698 / 0 / 650, goodness-of-fit on $F^{2} = 1.067$, final *R* indices [*I*>2*sigma*(*I*)] R1 = 0.0742, wR2 = 0.2142, *R* indices (all data) R1 = 0.1321, wR2 = 0.2560, largest diff. peak and hole 0.948 and -0.475 e. Å⁻³.

The relative configuration to all products 3 was established by a single crystal X-ray diffraction study of **3ak**. In fact, it was also established by a single crystal X-ray diffraction study of **4am** which was prepared from **3am**.



Due to the different spatial environments and the weak hydrogen bond, high diastereoselectivity was observed. In addition, the proton at the 5-position of the furan ring of minor stereoisomer has different chemical shift and resonate at higher field than that of major stereoisomer (e.g. 6.28 ppm for **3ak**, 6.24 ppm for **3ak'**; 6.04 ppm for **3aa**, 5.96 ppm for **3aa'**; and so on), as described below.









5.045 6.040 6.035 6.030 6.025 6.020 6.015 6.010 6.005 6.000 5.995 5.990 5.965 5.960 5.975 5.970 5.965 5.960 5.955 5.960 5.945 1 (gam)



3. ¹H NMR, ¹³C NMR Spetra





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3aa



3ab

3ac





3ad

3ae







3ag

3ah



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3aj



3ak

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3al

3am







3ao



3ba



4aa









4ad







4af



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