Supplementary Materials for Synthetic Communications

Brønsted acid catalyzed Friedel-Crafts reaction of indoles to α -ketimino esters

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1. General methods

All reactions were carried out in the dried glassware with magnetic stirring. Reagents were obtained from commercial supplier and used without further purification unless otherwise noted. NMR spectra were recorded on BrukerAvance 400 MHz (¹H NMR) and 100 MHz spectrometer (¹³C NMR). CDCl₃ was used as solvent. Spectra were referenced internally to the residual proton resonance in DMSO-d₆ (δ 2.50 ppm). Chemical shifts (δ) were reported as part per million (ppm). ¹³C NMR spectra were referenced to DMSO-d₆ (δ 39.6 ppm, the middle peak). High-resolution mass spectra (HRMS) were obtained on a Brüker APEX 47e FT-ICR mass spectrometer (ESIMS).

2. Friedel-Crafts reaction of indoles to α -ketimino esters

To a stirring mixture of indole (**5a**, 23.4mg, 0.2mmol) and phenyl α -ketimino ester (**4a**, 26.8mg, 0.1mmol) in THF was added DL-camphorsulfonic acid (3.3mg, 0.01mmol), the reaction was stirred under room temperature until **4a** was disappeared on TLC (about 12 hours), the crude product was purified by flash chromatography on silica gel (petroleum ether-EA, 5:1) to give **6a** as yellow solid (35.4mg, 92%).

3-(1H-indol-3-yl)-3-phenyl-3,4-dihydro-2H-benzo[b][1,4]oxazin-2-one (6a). ^1H NMR (400 MHz, DMSO- d_6) δ 11.21 (s, 1H), 8.84 (s, 1H), 7.95 (dd, J = 8.8, 1.8 Hz, 1H), 7.83 (d, J = 2.0 Hz, 1H), 7.45-7.41 (m, 7H), 7.15-7.11 (m, 2H), 6.99 (t, J = 7.8 Hz, 1H), 6.69 (d, J = 2.0 Hz, 1H); ^{13}C NMR (100 MHz, DMSO- d_6) δ 164.6, 141.3, 139.8, 139.5, 139.1, 137.8, 129.4, 127.9, 127.0, 125.7, 122.7, 122.6, 120.7, 120.2, 114.9, 114.7, 112.9, 112.7, 64.4. HRMS calcd for $\text{C}_{22}\text{H}_{16}\text{N}_3\text{O}_4$ $[\text{M}+\text{H}]^+$: 386.1141, found: 386.1138.

3-(4-bromophenyl)-3-(1H-indol-3-yl)-3,4-dihydro-2H-benzo[b][1,4]oxazin-2-one(6b). ^1H NMR (400 MHz, DMSO- d_6) δ 11.26 (d, J = 2.0 Hz, 1H), 8.83 (s, 1H), 7.96 (dd, J = 8.8, 2.8 Hz, 1H), 7.84 (d, J = 2.4Hz, 1H), 7.63 (d, J = 8.4 Hz, 2H), 7.41 (d, J = 8.8 Hz, 2H), 7.33 (d, J = 8.4 Hz, 2H), 7.15-7.10 (m, 2H), 6.99 (t, J = 7.8 Hz, 1H), 6.79 (d, J = 2.8 Hz, 1H); ^{13}C NMR (100 MHz, DMSO- d_6) δ 164.5, 141.2, 139.9, 139.4, 139.1, 138.0, 132.6, 130.5, 127.2, 125.6, 123.1, 122.9,

120.8, 120.5, 115.2, 114.0, 113.1, 112.9, 64.3. HRMS calcd for $C_{22}H_{15}BrN_3O_4$ $[M+H]^+$: 464.0246, found: 464.0243.

3-(4-chlorophenyl)-3-(1H-indol-3-yl)-3,4-dihydro-2H-benzo[b][1,4]oxazin-2-one (6c). 1H NMR (400 MHz, DMSO- d_6) δ 11.28 (s, 1H), 8.84 (s, 1H), 7.96 (dd, J = 8.8, 2.4 Hz, 1H), 7.86 (d, J = 2.4 Hz, 1H), 7.49-7.33 (m, 6H), 7.16-7.11 (m, 2H), 7.00 (t, J = 7.6 Hz, 1H), 6.83 (d, J = 2.8 Hz, 1H); ^{13}C NMR (100 MHz, DMSO- d_6) δ 164.3, 142.1, 141.0, 139.8, 139.4, 137.9, 134.3, 131.5, 129.7, 128.1, 127.1, 127.1, 125.7, 122.91, 122.88, 120.7, 120.5, 115.1, 113.7, 113.1, 112.9, 64.3. HRMS calcd for $C_{22}H_{15}ClN_3O_4$ $[M+H]^+$: 420.0751, found: 420.0745.

3-(1H-indol-3-yl)-3-(4-methoxyphenyl)-3,4-dihydro-2H-benzo[b][1,4]oxazin-2-one (6d). 1H NMR (400 MHz, DMSO- d_6) δ 11.19 (d, J = 1.6 Hz, 1H), 8.76 (s, 1H), 7.94 (dd, J = 8.4, 2.4 Hz, 1H), 7.82 (d, J = 2.4 Hz, 1H), 7.43-7.40 (m, 2H), 7.29 (d, J = 8.8 Hz, 2H), 7.14-7.09 (m, 2H), 7.00-6.95 (m, 3H), 6.70 (d, J = 2.8 Hz, 1H), 3.75 (s, 3H); ^{13}C NMR (100 MHz, DMSO- d_6) δ 164.9, 160.2, 141.5, 139.9, 139.2, 137.9, 131.4, 129.3, 127.1, 125.8, 122.8, 122.7, 120.8, 120.3, 115.1, 115.0, 114.9, 112.9, 112.8, 64.0, 56.1. HRMS calcd for $C_{23}H_{18}N_3O_5$ $[M+H]^+$: 416.1246, found: 416.1244.

3-(1H-indol-3-yl)-3-(p-tolyl)-3,4-dihydro-2H-benzo[b][1,4]oxazin-2-one (6e). ^1H NMR (400 MHz, DMSO- d_6) δ 11.19 (d, J = 2.0 Hz, 1H), 8.78 (s, 1H), 7.94 (dd, J = 9.0, 2.6 Hz, 1H), 7.81 (d, J = 2.4 Hz, 1H), 7.44-7.40 (m, 2H), 7.28-7.10 (m, 6H), 6.99 (t, J = 7.6 Hz, 1H), 6.66 (d, J = 2.8 Hz, 1H), 2.23 (s, 3H); ^{13}C NMR (100 MHz, DMSO- d_6) δ 164.8, 141.5, 139.9, 139.2, 139.0, 137.9, 136.6, 130.1, 127.8, 127.1, 125.8, 122.74, 122.72, 120.8, 120.3, 115.1, 115.0, 112.9, 112.8, 64.3, 21.5. HRMS calcd for $\text{C}_{23}\text{H}_{18}\text{N}_3\text{O}_4$ $[\text{M}+\text{H}]^+$: 400.1297, found: 400.1293.

3-(1H-indol-3-yl)-3-(4-nitrophenyl)-3,4-dihydro-2H-benzo[b][1,4]oxazin-2-one (6f). ^1H NMR (400 MHz, DMSO- d_6) δ 11.33 (d, J = 2.0 Hz, 1H), 8.95 (s, 1H), 8.29 (d, J = 7.2 Hz, 2H), 7.97 (dd, J = 9.0, 2.6 Hz, 1H), 7.87 (d, J = 2.4 Hz, 1H), 7.68-7.66 (m, 2H), 7.44-7.40 (m, 2H), 7.17-7.13 (m, 2H), 7.00 (t, J = 7.4 Hz, 1H), 6.86 (d, J = 2.8 Hz, 1H); ^{13}C NMR (100 MHz, DMSO- d_6) δ 164.1, 148.6, 146.7, 140.8, 139.8, 139.6, 138.0, 129.9, 127.3, 125.5, 124.8, 123.0, 122.9, 120.6, 115.3, 113.3, 113.13, 113.08, 64.5. HRMS calcd for $\text{C}_{22}\text{H}_{15}\text{N}_4\text{O}_6$ $[\text{M}+\text{H}]^+$: 431.0992, found: 431.0989.

3-(1H-indol-3-yl)-3-(thiophen-2-yl)-3,4-dihydro-2H-benzo[b][1,4]oxazin-2-one (6g). ^1H NMR (400 MHz, DMSO- d_6) δ 11.27 (s, 1H), 8.91 (s, 1H), 7.97 (dd, J = 9.2, 2.4 Hz, 1H), 7.87 (d, J =

2.4 Hz, 1H), 7.60 (dd, $J = 4.8, 1.2$ Hz, 1H), 7.46 (d, $J = 8.4$ Hz, 1H), 7.41 (d, $J = 8.0$ Hz, 1H), 7.14-6.98 (m, 6H); ^{13}C NMR (100 MHz, DMSO- d_6) δ 164.3, 144.3, 140.7, 139.8, 139.5, 137.8, 128.43, 128.40, 127.8, 126.7, 122.9, 122.8, 120.6, 120.5, 115.2, 114.3, 113.0, 112.9, 61.9. HRMS calcd for $\text{C}_{20}\text{H}_{14}\text{N}_3\text{O}_4\text{S}$ $[\text{M}+\text{H}]^+$: 392.0705, found: 392.0700.

3-(4-hydroxy-1H-indol-3-yl)-3-phenyl-3,4-dihydro-2H-benzo[*b*][1,4]oxazin-2-one (6h). ^1H NMR (400 MHz, DMSO- d_6) δ 10.90 (s, 1H), 9.60 (s, 1H), 8.67 (s, 1H), 7.91 (dd, $J = 9.2, 2.4$ Hz, 1H), 7.76 (d, $J = 2.4$ Hz, 1H), 7.60-7.53 (m, 2H), 7.48-7.39 (m, 3H), 6.98 (d, $J = 8.8$ Hz, 1H), 6.85 (d, $J = 8.0$ Hz, 1H), 6.31 (d, $J = 7.2$ Hz, 1H), 6.20 (d, $J = 2.4$ Hz, 1H); ^{13}C NMR (100 MHz, DMSO- d_6) δ 165.0, 151.9, 143.5, 140.5, 140.2, 139.9, 139.0, 137.8, 129.6, 127.7, 125.1, 124.1, 123.1, 117.7, 116.1, 113.8, 112.7, 105.4, 104.2, 64.3. HRMS calcd for $\text{C}_{22}\text{H}_{15}\text{N}_3\text{O}_5$ $[\text{M}+\text{H}]^+$: 402.1090, found: 402.1084.

3-(4-(benzyloxy)-1H-indol-3-yl)-3-phenyl-3,4-dihydro-2H-benzo[*b*][1,4]oxazin-2-one (6i). ^1H NMR (400 MHz, DMSO- d_6) δ 11.07 (s, 1H), 8.65 (s, 1H), 7.83 (dd, $J = 9.0, 2.6$ Hz, 1H), 7.49-7.36 (m, 5H), 7.22 (d, $J = 2.4$ Hz, 1H), 7.16-7.00 (m, 7H), 6.90 (d, $J = 8.8$ Hz, 1H), 6.62-6.57 (m, 1H), 6.16 (d, $J = 2.4$ Hz, 1H), 4.98-4.90 (m, 2H); ^{13}C NMR (100 MHz, DMSO- d_6) δ 164.7, 153.1, 140.2, 139.8, 139.6, 138.5, 137.7, 137.2, 129.62, 129.57, 129.0, 128.8, 128.2, 127.6, 125.9,

123.9, 122.7, 117.7, 116.5, 113.5, 112.9, 106.2, 102.2, 70.7, 64.2. HRMS calcd for C₂₉H₂₂N₃O₅

[M+H]⁺: 492.1559, found: 492.1557.

3-(5-bromo-1H-indol-3-yl)-3-phenyl-3,4-dihydro-2H-benzo[b][1,4]oxazin-2-one (6j). ¹H NMR

(400 MHz, DMSO-d₆) δ 11.44 (s, 1H), 8.84 (s, 1H), 7.95 (dd, *J* = 8.8, 2.4 Hz, 1H), 7.84 (d, *J* = 2.4 Hz, 1H), 7.56 (d, *J* = 1.2 Hz, 1H), 7.45-7.36 (m, 5H), 7.27-7.24 (m, 1H), 7.12 (d, *J* = 9.2 Hz, 1H), 6.78 (d, *J* = 2.8 Hz, 1H); ¹³C NMR (100 MHz, DMSO-d₆) δ 164.6, 141.2, 139.9, 139.4, 139.2, 136.6, 129.7, 129.6, 128.7, 127.9, 127.5, 125.3, 122.8, 115.2, 115.1, 114.3, 113.0, 112.9, 64.4. HRMS calcd for C₂₂H₁₅BrN₃O₄ [M+H]⁺: 464.0246, found: 464.0244.

3-(5-methyl-1H-indol-3-yl)-3-phenyl-3,4-dihydro-2H-benzo[b][1,4]oxazin-2-one (6k). ¹H

NMR (400 MHz, DMSO-d₆) δ 11.07 (s, 1H), 8.80 (s, 1H), 7.95 (dd, *J* = 8.8, 2.4 Hz, 1H), 7.82 (d, *J* = 2.4 Hz, 1H), 7.45-7.37 (m, 5H), 7.30 (d, *J* = 8.4 Hz, 1H), 7.23 (s, 1H), 7.12 (d, *J* = 8.8 Hz, 1H), 6.96 (d, *J* = 8.0 Hz, 1H), 6.58 (d, *J* = 2.4 Hz, 1H), 2.30 (s, 3H); ¹³C NMR (100 MHz, DMSO-d₆) δ 164.7, 141.5, 139.9, 139.6, 139.2, 136.3, 129.5, 128.8, 127.2, 126.0, 124.4, 122.8, 120.2, 115.1, 114.2, 112.8, 112.7, 64.5, 22.2. HRMS calcd for C₂₃H₁₈N₃O₄ [M+H]⁺: 400.1297, found: 400.1294.

3-(5-chloro-1H-indol-3-yl)-3-phenyl-3,4-dihydro-2H-benzo[*b*][1,4]oxazin-2-one (6l). ^1H NMR (400 MHz, DMSO- d_6) δ 11.43 (s, 1H), 8.84 (s, 1H), 7.95 (dd, J = 9.0, 2.2 Hz, 1H), 7.84 (d, J = 2.4 Hz, 1H), 7.46-7.36 (m, 7H), 7.15-7.11 (m, 3H), 6.81 (d, J = 2.4 Hz, 1H); ^{13}C NMR (100 MHz, DMSO- d_6) δ 164.7, 141.2, 139.9, 139.4, 139.3, 136.4, 129.7, 128.9, 128.0, 126.8, 125.0, 122.8, 119.9, 115.2, 114.7, 114.4, 112.9, 112.1, 109.6, 64.4. HRMS calcd for $\text{C}_{22}\text{H}_{15}\text{ClN}_3\text{O}_4$ $[\text{M}+\text{H}]^+$: 420.0751, found: 420.0749.

3-(5-methoxy-1H-indol-3-yl)-3-phenyl-3,4-dihydro-2H-benzo[*b*][1,4]oxazin-2-one (6m). ^1H NMR (400 MHz, DMSO- d_6) δ 11.09 (s, 1H), 8.82 (s, 1H), 7.94 (dd, J = 8.8, 2.4 Hz, 1H), 7.82 (d, J = 2.0 Hz, 1H), 7.41-7.39 (m, 5H), 7.31 (d, J = 8.8 Hz, 1H), 7.12 (d, J = 8.8 Hz, 1H), 6.85 (s, 1H), 6.80-6.77 (m, 1H), 6.72 (d, J = 2.4 Hz, 1H), 6.16 (s, 1H), 3.63 (s, 3H); ^{13}C NMR (100 MHz, DMSO- d_6) δ 164.7, 141.5, 139.9, 139.7, 139.2, 133.0, 129.6, 129.5, 128.2, 127.6, 126.4, 122.7, 119.2, 115.1, 113.9, 113.6, 112.8, 112.1, 109.6, 64.6, 56.4. HRMS calcd for $\text{C}_{23}\text{H}_{18}\text{N}_3\text{O}_5$ $[\text{M}+\text{H}]^+$: 416.1246, found: 416.1244.

3-(1H-indol-3-yl)-3-phenyl-3,4-dihydro-2H-benzo[*b*][1,4]oxazin-2-one (6n). ^1H NMR (400

MHz, DMSO-d₆) δ 11.09 (s, 1H), 7.58 (s, 1H), 7.50 (d, J = 8.0 Hz, 1H), 7.42-7.30 (m, 6H), 7.10 (t, J = 7.2 Hz, 1H), 7.01-6.89 (m, 4H), 6.68-6.65 (m, 1H), 6.58 (s, 1H); ¹³C NMR (100 MHz, DMSO-d₆) δ 165.5, 140.6, 139.5, 136.9, 134.0, 128.3, 128.1, 127.2, 125.9, 125.3, 124.8, 121.5, 120.3, 119.0, 118.6, 115.5, 115.2, 115.0, 111.8, 63.9. HRMS calcd for C₂₃H₁₈N₃O₅ [M+H]⁺: 341.1296, found: 341.1290.