Highly Diastereoselective Vinylogous Mukaiyama Aldol Reaction of Isatins with 2-(Trimethylsilyloxy)furans Catalyzed by Quinine

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Supporting Information

Experimental Section

General Comments.

All reactions were carried out under an inert atmosphere and in heat-dried glassware. Anhydrous THF were obtained by distillation from sodium. Flash column chromatography was performed on silica gel (particle size 10-40 μm , Ocean Chemical Factory of Qingdao, China). Nitrogen gas (99.999%) was purchased from Boc Gas Inc. ^1H NMR and ^{13}C NMR spectra were recorded on Bruker-400 (400 MHz for ^1H , 101MHz for ^{13}C) spectrometers. Chemical shifts were reported in ppm downfield from internal $\text{Si}(\text{CH}_3)_4$. The crystal structure was determined on a Bruker SMART 1000 CCD diffractometer. Mass spectra were recorded on a LCQ advantage spectrometer with ESI resource. HR-MS were recorded on APEXII and ZAB-HS spectrometer. Melting points were determined on a T-4 melting point apparatus (uncorrected).

Typical procedure for quinine catalyzed vinylogous Mukaiyama aldol reaction:

To a solution of isatin **1** (0.5 mmol) in THF (2 mL) was added quinine (0.017 g, 10 mol%). The mixture was cooled to $-78\text{ }^\circ\text{C}$ and stirred at this temperature for 15 minutes. Then the solution of 2-(trimethylsilyloxy)furan **2** (0.156 g, 1 mmol) in THF (1 mL) was added dropwise. The mixture was stirred at $-78\text{ }^\circ\text{C}$ for 15 minutes. The reaction was monitored by TLC. After the completion of the reaction it was quenched by addition of 10% aqueous HCl (2.0 mL) and the mixture was extracted with ethyl acetate (3 $\times$ 5 mL). The combined organic layer was washed with brine solution, dried over MgSO_4 , and concentrated under reduced pressure (rotary evaporator). The crude products were purified by silica gel column chromatography (AcOEt/hexane) to afford the product as a white solid.

3-(2,5-Dihydro-5-oxofuran-2-yl)-3-hydroxyindolin-2-one (3a).

Yield: 103 mg, (89%); white solid; mp 190-192 °C. ¹H NMR (400 MHz,

DMSO): δ 10.44 (s, 1H), 7.73 (d, *J* = 5.6 Hz, 1H), 7.32 (d, *J* = 7.3 Hz, 1H),

7.25 (t, *J* = 7.6 Hz, 1H), 6.99 (t, *J* = 7.5 Hz, 1H), 6.82 (d, *J* = 7.7 Hz, 1H),

6.77 (s, 1H), 6.21 (d, *J* = 4.7 Hz, 1H), 5.45 (s, 1H). ¹³C NMR (101 MHz, DMSO): δ 175.09, 172.50,

154.42, 141.92, 129.88, 128.24, 124.62, 122.08, 121.81, 109.89, 85.09, 76.65. HRMS (ESI): *m/z*

calcd for [C₁₂H₉NO₄+Na]⁺: 254.0424 [M+Na]⁺; found 254.0421.

3-(2,5-Dihydro-5-oxofuran-2-yl)-3-hydroxy-5-methylindolin-2-one (3b).

Yield: 122 mg, (89%); white solid; mp 201-204 °C. ¹H NMR (400 MHz, DMSO): δ 10.44 (s, 1H), 8.01 (d, *J* = 5.8 Hz, 1H), 7.05 (d, *J* = 7.8 Hz, 1H), 6.87 (s, 1H), 6.70-6.71 (m, 1H), 6.69 (s, 1H), 6.38 (dd, *J* = 5.7, 1.7

Hz, 1H), 5.30 (s, 1H), 2.21 (s, 3H). ¹³C NMR (101 MHz, DMSO): δ 176.33, 171.94, 154.74, 140.00, 130.19, 129.98, 126.21, 125.26, 122.62, 109.60, 84.02, 75.87, 20.62. HRMS (ESI): *m/z* calcd for [C₁₃H₁₁NO₄+Na]⁺: 268.0580 [M+Na]⁺; found 268.0585.

7-Chloro-3-(2,5-dihydro-5-oxofuran-2-yl)-3-hydroxyindolin-2-one (3c).

Yield: 125 mg, (94%); white solid; mp 173-176 °C. ^1H NMR (400 MHz, DMSO): δ 10.93 (s, 1H), 7.79 (d, $J = 5.8$ Hz, 1H), 7.31-7.36 (m, 2H), 7.04 (t, $J = 7.8$ Hz, 1H), 6.96 (s, 1H), 6.27 (dd, $J = 5.7, 1.7$ Hz, 1H), 5.50 (s, 1H). ^{13}C

NMR (101 MHz, DMSO): δ 174.97, 172.31, 154.38, 139.67, 130.44, 129.86, 124.16, 123.25, 122.14, 114.10, 84.74, 77.15. HRMS (ESI): m/z calcd for $[\text{C}_{12}\text{H}_8\text{ClNO}_4 + \text{Na}]^+$: 288.0039 $[\text{M} + \text{Na}]^+$; found 288.0043.

3-(2,5-Dihydro-5-oxofuran-2-yl)-3-hydroxy-5-methoxyindolin-2-one (3d).

Yield: 116 mg, (89%); white solid; mp 204-207 °C. ¹H NMR (400

MHz, DMSO): δ 10.40 (s, 1H), 8.04 (s, 1H), 6.84-6.98 (m, 2H), 6.67 (s,

1H), 6.41 (s, 1H), 5.35 (s, 1H), 3.70 (s, 3H), 3.38 (s, 1H). ¹³C NMR

(101 MHz, DMSO): δ 176.22, 171.89, 154.80, 135.61, 127.70, 122.75, 114.31, 112.84, 111.53,

110.21, 83.98, 76.16, 55.44. HRMS (ESI): *m/z* calcd for [C₁₃H₁₁NO₅+Na]⁺: 284.0529 [M+Na]⁺;

found 284.0532.

5-Bromo-3-(2,5-dihydro-5-oxofuran-2-yl)-3-hydroxyindolin-2-one (3e).

Yield: 130 mg, (84%); white solid; mp 196-198 °C. ¹H NMR (400 MHz, DMSO): δ 10.59 (s, 1H), 7.80 (d, *J* = 5.8 Hz, 1H), 7.51 (s, 1H), 7.45 (d, *J* = 8.2 Hz, 1H), 6.94 (s, 1H), 6.79-6.82 (m, 1H), 6.27 (dd, *J* = 9.2, 4.6 Hz, 1H), 5.52 (s, 1H). ¹³C NMR (101 MHz, DMSO): δ 174.50, 172.30, 154.61, 141.30, 132.56, 130.88, 127.52, 122.04, 113.47, 111.93, 84.66, 76.68. HRMS (ESI): *m/z* calcd for [C₁₂H₈BrNO₄+Na]⁺: 331.9529 [M+Na]⁺; found 331.9525.

3-(2,5-Dihydro-5-oxofuran-2-yl)-3-hydroxy-5,7-dimethylindolin-2-one (3f).

Yield: 112 mg, (87%); white solid; mp 190-192 °C. ^1H NMR (400 MHz, DMSO): δ 10.41 (s, 1H), 7.75 (d, $J = 5.8$ Hz, 1H), 6.98 (s, 1H), 6.90 (s, 1H), 6.69 (s, 1H), 6.24 (dd, $J = 5.8, 2.0$ Hz, 1H), 5.42 (s, 1H), 2.21 (s,

3H), 2.15 (s, 3H). ^{13}C NMR (101 MHz, DMSO): δ 175.50, 172.52, 154.66, 138.02, 131.45, 130.56, 128.19, 122.54, 121.91, 118.82, 85.12, 76.83, 20.56, 16.12. HRMS (ESI): m/z calcd for $[\text{C}_{14}\text{H}_{13}\text{NO}_4 + \text{Na}]^+$: 282.0737 $[\text{M} + \text{Na}]^+$; found 282.0742.

1-Benzyl-3-(2,5-dihydro-5-oxofuran-2-yl)-3-hydroxyindolin-2-one (3g).

Yield: 136 mg, (85%); white solid; mp 125-128 °C. ^1H NMR (300 MHz,

CDCl_3): δ 7.44 (d, $J = 7.4$ Hz, 1H), 7.29-7.37 (m, 7H), 7.08 (t, $J = 7.3$ Hz, 1H),

6.77 (d, $J = 7.8$ Hz, 1H), 6.09 (dd, $J = 5.8, 2.1$ Hz, 1H), 5.45 (t, $J = 1.7$ Hz,

1H), 5.00 (d, $J = 15.6$ Hz, 1H), 4.76 (d, $J = 15.6$ Hz, 1H), 3.27 (s, 1H). ^{13}C NMR (101 MHz, CDCl_3)

δ 174.06, 172.05, 151.43, 142.44, 134.80, 130.69, 129.00, 127.98, 127.20, 126.15, 125.54, 124.71,

123.79, 123.72, 109.97, 85.37, 44.02. HRMS (ESI): m/z calcd for $[\text{C}_{19}\text{H}_{15}\text{NO}_4 + \text{Na}]^+$: 344.0893

$[\text{M} + \text{Na}]^+$; found 344.0889.

7-Chloro-3-(2,5-dihydro-5-oxofuran-2-yl)-3-hydroxy-1-methylindolin-2-one (3h).

Yield: 116 mg, (83%); white solid; mp 145-149 °C. ^1H NMR (400 MHz, CDCl_3): δ 7.38 (d, $J = 5.7$ Hz, 1H), 7.29-7.35 (m, 1H), 7.04 (t, $J = 7.8$ Hz, 1H), 6.12 (dd, $J = 5.7, 1.4$ Hz, 1H), 5.39 (s, 1H), 3.57 (s, 2H), 3.24 (s, 1H). ^{13}C

NMR (101 MHz, CDCl_3): δ 174.15, 171.86, 150.94, 139.18, 133.17, 128.61, 124.64, 124.03, 123.25, 116.51, 89.19, 84.11, 29.99. HRMS (ESI): m/z calcd for $[\text{C}_{13}\text{H}_{10}\text{NO}_4\text{Cl}+\text{Na}]^+$: 302.0191 $[\text{M}+\text{Na}]^+$; found 302.0189.

3-(2,5-Dihydro-5-oxofuran-2-yl)-3-hydroxy-1-methylindolin-2-one (3i).

Yield: 105 mg, (86%); white solid; mp 138-140 °C. ^1H NMR (400 MHz, CDCl_3): δ 7.80 (d, $J = 5.6$ Hz, 1H), 7.38 (t, $J = 7.7$ Hz, 2H), 7.07 (t, $J = 7.6$ Hz, 1H), 6.87 (d, $J = 7.5$ Hz, 1H), 6.28 (dd, $J = 5.6, 1.5$ Hz, 1H), 5.29 (d, $J = 1.1$

Hz, 1H), 3.55 (s, 1H), 3.22 (d, $J = 7.8$ Hz, 3H). ^{13}C NMR (101 MHz, CDCl_3): δ 175.04, 171.81, 151.96, 143.82, 130.96, 125.49, 124.74, 124.19, 123.81, 123.19, 109.02, 84.20, 26.59. HRMS (ESI):

m/z calcd for $[\text{C}_{13}\text{H}_{11}\text{NO}_4 + \text{Na}]^+$: 268.0580 $[\text{M} + \text{Na}]^+$; found 268.0585.

5-Chloro-3-(2,5-dihydro-5-oxofuran-2-yl)-3-hydroxy-1-methylindolin-2-one (3j).

Yield: 118 mg, (85%); white solid; mp 156-159 °C. ^1H NMR (400 MHz,

CDCl_3) δ : 7.82 (dd, J = 5.8, 1.3 Hz, 1H), 7.35 (dd, J = 8.3, 2.0 Hz, 1H),

7.27 (d, J = 2.0 Hz, 1H), 6.80 (d, J = 8.3 Hz, 1H), 6.32 (dd, J = 5.7, 1.8

Hz, 1H), 5.27 (s, 1H), 3.97 (s, 1H), 3.21 (s, 3H). ^{13}C NMR (101 MHz, CDCl_3): δ 174.61, 171.65,

151.59, 142.34, 130.86, 128.72, 126.70, 126.05, 125.16, 124.48, 110.01, 83.94, 26.76. HRMS (ESI):

m/z calcd for $[\text{C}_{13}\text{H}_{10}\text{NO}_4\text{Cl}+\text{Na}]^+$: 302.0191 $[\text{M}+\text{Na}]^+$; found 302.0190.