SUPPORTING INFORMATION

A Tandem Heck-Carbocyclization/Suzuki-Coupling Approach to the Stereoselective Syntheses of Asymmetric 3,3-(Diarylmethylene)indolinones

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Experimental Section

Materials and Methods

¹H NMR data were obtained using TMS as an internal standard. HPLC (ELSD) data were obtained using a Princeton SPHER HTS C18, 5- μ m, 60- $\text{\AA}$, 3 $\times$ 50 mm column (Princeton Chromatography, Inc.). Each HPLC (ELSD) run was carried out using a linear gradient of 25-100% CH₃CN/H₂O (0.1% TFA) in 2.4 min, and the retention time (*R*_t) for the expected (major) product was recorded. Accurate mass values are reported as the averages of 20 measurements.

General Procedure (Table 3)

To a solution of **8** (0.050 g, 0.132 mmol) in 2.5 mL of anhydrous THF was added Pd(PPh₃)₄ (0.023 g, 0.0199 mmol), CuTC (0.053 g, 0.277 mmol), and the boronic acid (0.277 mmol). The mixture was stirred for 12 h at room temperature, then concentrated under reduced pressure and purified by silica gel chromatography [hexanes / EtOAc mixtures] to afford the desired product.

(*E*)-5-Chloro-3-[(6-methoxypyridin-3-yl)phenylmethylene]-1,3-dihydroindol-2-one (Table 3, entry 1)

¹H-NMR (300 MHz, CDCl₃) δ 8.77 (bs, 1H), 8.13 (d, *J* = 2.4 Hz, 1H), 7.51 (dt, *J* = 3.9, 0.15 Hz, 1H), 7.48-7.30 (m, 5H), 7.04 (dt, *J* = 9.3, 1.7 Hz, 1H), 6.83 (d, *J* = 8.7 Hz, 1H), 6.64 (br.s, 1H), 6.52 (d, *J* = 8.4, 1H). ¹³C-NMR (100 MHz, CDCl₃) δ 168.4, 165.3, 153.6, 148.8, 140.6, 139.6, 139.3, 131.0, 130.2, 129.8, 128.8, 128.3, 126.9, 125.6, 124.1, 122.8, 111.4, 111.1, 54.2. LRMS (CI) *m/z*, 404 (*M*⁺ + AcCN); HRMS Calcd for C₂₀H₁₆Cl₂N₂O (*MH*⁺) 363.0900, found 363.0887.

(*E*)-5-Chloro-3-[(1H-indol-5-yl)phenylmethylene]-1,3-dihydroindol-2-one (Table 3, entry 2)

¹H-NMR (300 MHz, DMSO-*d*₆) δ 11.40 (bs, 1H), 10.56 (bs, 1H), 7.50 (d, *J* = 8.4 Hz, 1H), 7.45 (t, *J* = 2.6, 1H), 7.40-7.23 (m, 6H), 7.09 (dd, *J* = 6.9, 2.3 Hz, 1H), 7.00 (dd, *J* = 8.6, 1.7 Hz, 1H), 6.76 (d, *J* = 8.1 Hz, 1H), 6.49 (s, 1H), 6.17 (d, *J* = 2.1 Hz, 1H). ¹³C-NMR (100 MHz, DMSO-*d*₆) δ 167.9, 158.2, 141.3, 140.9, 137.1, 132.0, 131.1, 129.6, 128.5, 128.4, 128.2, 127.5, 126.5, 124.9, 123.5, 123.2, 122.5, 122.4, 112.6, 111.2, 102.7. mp 222 °C. LRMS (CI) *m/z*, 371 (*M*⁺); HRMS Calcd for C₂₃H₁₅ClN₂O (*M*⁺) 370.0873, found 370.0856.

(*E*)- 3-[(1-Benzyl-1H-pyrazol-4-yl)phenylmethylene]-5-chloro-1,3-dihydroindol-2-one (Table 3, entry 3)

¹H-NMR (300 MHz, CDCl₃) δ 8.43 (bs, 1H), 7.58, (s, 1H), 7.46 (s, 1H), 7.43-7.25 (m, 11H), 7.05 (br. d, *J* = 8.1 Hz, 1H), 6.57 (d, *J* = 8.4 Hz, 1H), 5.35 (s, 2H). ¹³C-NMR (100 MHz, CDCl₃) δ 168.8, 148.0, 141.8, 140.0, 138.9, 135.8, 132.0, 130.9, 130.1, 129.4, 128.7, 128.3, 128.1, 128.0, 126.7, 126.0, 122.6, 122.1, 121.9, 110.8, 56.7. LRMS (CI) *m/z*, 412 (M⁺); HRMS Calcd for C₂₅H₁₉ClN₃O (MH⁺) 412.1217, found 412.1202.

(E)- 5-Chloro-3-[(2,6-dimethoxypyrimidin-4-yl)phenylmethylene]-1,3-dihydroindol-2-one (Table 3, entry 4)

¹H-NMR (300 MHz, CDCl₃) δ 8.45 (br.s, 1H), 8.10 (s, 1H), 7.38-7.33 (m, 5H), 7.08 (ddd, *J* = 8.3, 2.1, 0.9 Hz, 1H), 6.58 (d, *J* = 8.1 Hz, 1H), 6.51 (br.s, 1H), 4.08 (s, 3H), 3.84 (s, 3H). ¹³C-NMR (100 MHz, CDCl₃) δ 168.3, 167.8, 166.1, 159.6, 147.5, 139.3, 138.7, 130.0, 129.7, 129.1, 128.1, 127.1, 125.7, 125.4, 123.0, 115.8, 110.9, 55.6, 54.6. LRMS (CI) *m/z*, 435 (M⁺ + AcCN); HRMS Calcd for C₂₁H₁₇ClN₃O₃ (MH⁺) 394.0958, found 394.0957.

(E)- 5-Chloro-3-(phenylpyrimidin-4-yl-methylene)1,3-dihydroindol-2-one (Table 3, entry 5)

¹H-NMR (300 MHz, CDCl₃) δ 9.35 (s, 1H), 8.70 (s, 2H), 8.31 (bs, 1H), 7.46-7.38 (m, 3H), 7.32-7.28 (m, 2H), 7.12 (dd, *J* = 8.4, 2.1 Hz, 1H), 6.61 (d, *J* = 8.4, 1H), 6.35 (d, *J* = 2.1 Hz, 1H). ¹³C-NMR (100 MHz, CDCl₃) δ 167.4, 159.4, 157.5, 148.4, 139.7, 138.2, 135.1, 130.6, 123.0, 128.7, 127.4, 126.3, 124.4, 123.1, 111.4. LRMS (CI) *m/z*, 375 (M⁺ + AcCN); HRMS Calcd for C₁₉H₁₃ClN₃O (MH⁺) 334.0747, found 334.0744.

General procedure (Table 5)

To a solution of **8** (0.050 g, 0.132 mmol) in 3.0 mL of anhydrous mixed solvent (THF : DMF = 4 : 1) was added Pd(PPh₃)₄ (0.015 g, 0.0132 mmol), CuTC (0.050 g, 0.264 mmol), and the boronic acid (0.264 mmol). The mixture was stirred for 12 h at room temperature, then concentrated under reduced pressure and purified by silica gel chromatography [hexanes / EtOAc mixtures] to afford the desired product.

(E)- 5-Chloro-3-[(6-chloropyridin-3-yl)phenylmethylene]-1,3-dihydroindol-2-one (Table 5, entry 1)

¹H-NMR (300 MHz, CDCl₃) δ 8.37 (dd, *J* = 2.1, 0.6 Hz, 1H), 8.17 (bs, 1H), 7.58 (dd, *J* = 8.7, 2.7 Hz, 1H), 7.46 (d, *J* = 0.6 Hz, 1H), 7.44-7.36 (m, 3H), 7.30-7.26 (m, 2H), 7.11 (dd, *J* = 8.3, 2.0 Hz, 1H), 6.65 (d, *J* = 8.7 Hz, 1H), 6.46 (d, *J* = 2.1 Hz, 1H). ¹³C-NMR (100 MHz, CDCl₃) δ 167.5, 152.9, 151.0, 150.4, 140.2, 139.5, 138.7, 135.6, 130.7, 130.4, 129.6, 129.5, 128.5, 127.2, 125.4, 125.0, 124.8, 123.2, 111.1. LRMS (CI) *m/z*, 408 (M⁺ + AcCN); HRMS Calcd for C₂₀H₁₃Cl₂N₂O (MH⁺) 367.0405, found 367.0393.

(*E*)- 5-Chloro-3-(phenylquinolin-3-ylmethylene)-1,3-dihydroindol-2-one (Table 5, entry 2)

¹H-NMR (300 MHz, CDCl₃) δ 8.87 (d, *J* = 2.1 Hz, 1H), 8.20 (d, *J* = 8.2 Hz, 1H), 8.07 (d, *J* = 1.5 Hz, 1H), 7.84 (dd, *J* = 8.7, 1.8 Hz, 1H), 7.81 (dd, *J* = 8.1, 1.2 Hz, 1H), 7.65-7.60 (m, 2H), 7.45-7.40 (m, 5H), 7.10 (dd, *J* = 7.5, 2.0 Hz, 1H), 6.73 (d, *J* = 8.1 Hz, 1H), 6.42 (d, *J* = 1.8 Hz, 1H). ¹³C-NMR (100 MHz, CDCl₃) δ 168.0, 152.8, 150.8, 148.4, 139.5, 139.5, 138.0, 134.1, 131.3, 131.0, 130.3, 129.7, 129.4, 128.6, 128.4, 127.9, 127.6, 127.1, 125.2, 123.1, 111.0. LRMS (CI) *m/z*, 424 (M⁺ + AcCN); HRMS Calcd for C₂₄H₁₆ClN₂O (MH⁺) 383.0951, found 367.0958.

(*E*)- 5-Chloro-3-[(2-chloro-pyridin-4-yl)phenylmethylene]-1,3-dihydroindol-2-one (Table 5, entry 3)

¹H-NMR (300 MHz, CDCl₃) δ 8.54 (d, *J* = 4.8 Hz, 1H), 8.14 (bs, 1H), 7.45-7.37 (m, 3H), 7.32-7.26 (m, 3H), 7.22 (dd, *J* = 4.8, 1.5 Hz, 1H), 7.12 (dd, *J* = 8.7, 1.8 Hz, 1H), 6.66 (d, *J* = 8.7 Hz, 1H), 6.39 (d, *J* = 2.1 Hz, 1H). ¹³C-NMR (100 MHz, CDCl₃) δ 167.0, 152.7, 151.3, 150.7, 150.6, 139.3, 137.4, 130.1, 129.9, 129.7, 129.6, 128.6, 128.3, 127.2, 125.1, 124.0, 123.9, 123.6, 122.2, 110.8. mp 196 °C. LRMS (CI) *m/z*, 408 (M⁺ + AcCN); HRMS Calcd for C₂₀H₁₃Cl₂N₂O (MH⁺) 367.0405, found 367.0393.

3-Benzhydrylidene-6-methoxy-1,3-dihydro-indol-2-one (Table 6, 9b)

¹H-NMR (300 MHz, CDCl₃) δ 7.97 (s, 1H), 7.36-7.33 (m, 4H), 7.25-7.23 (m, 6H), 6.24-6.20 (m, 2H), 6.10 (dd, *J* = 2.4, 8.4 Hz, 1H), 3.67 (s, 3H). ¹³C-NMR (100 MHz, CDCl₃) δ 168.9, 160.6, 151.9, 142.0, 141.6, 139.9, 130.2, 129.4, 128.9, 127.7, 124.5, 124.1, 117.0, 106.5, 96.2, 55.4. LRMS (CI) *m/z*, 328 (M⁺ + H); HRMS Calcd for C₂₂H₁₈NO₂ (MH⁺) 328.1338, found 328.1344.

¹H nmr

NOE

¹H nmr

NOE

¹H nmr

(E)-13 (Table 2, entry 2)

(Z)-13 (Table 2, entry 2)

NOE

¹H nmr

Mass Chromatogram (m/z=363.50-364.50+385.50-386.50)

Analog Channel 1

Peak Information For Analog Channel 1

Peak ID	RT	Purity	BP Mass
1	1.43	0.03	n/a
2	1.82	99.97	n/a

Peak ID: 1 MS1 - RT: 1.43 mins; ESI+ 00

Peak ID: 2 MS1 - RT: 1.82 mins; ESI+ 00

Mass Chromatogram (m/z=371.50-372.50+393.50-394.50)

Analog Channel 1

Peak Information For Analog Channel 1

Peak ID	RT	Purity	BP Mass
1	0.31	0.01	n/a
2	1.40	0.26	n/a
3	1.80	99.72	n/a

Peak ID: 1 MS1 - RT: 0.31 mins; ESI+ 00

Peak ID: 2 MS1 - RT: 1.40 mins; ESI+ 00

Peak ID: 3 MS1 - RT: 1.80 mins; ESI+ 00

5078-147 in CDCl₃
COSY

Current Data Parameters
NAME 5078-147
EXPNO 2
PROCNO 1

F2 - Acquisition Parameter
Date 20041109
Time 15.12
INSTRUM spect
PROBHD 5 mm QNP 1H
PULPROG cosygs
TD 1024
SOLVENT CDCl₃
NS 2
DS 8
SWH 1034.768 Hz
FIDRES 1.010516 Hz
AQ 0.4948468 sec
RG 574.7
DW 483.200 usec
DE 6.00 usec
TE 300.0 K
d0 0.00000300 sec
D1 2.00000000 sec
d13 0.00000300 sec
D16 0.00010000 sec
IN0 0.00096640 sec

===== CHANNEL
NUC1 1H
P0 7.50 usec
P1 7.50 usec
PL1 3.60 dB
SFO1 400.1330187 MI

===== GRADIENT
P16 1000.00 usec

F1 - Acquisition parameter
ND0 1
TD 150
SFO1 400.133 MHz
FIDRES 6.898455 Hz
SW 2.586 ppm

F2 - Processing parameter
SI 1024
SF 400.1300010 MHz
WDW SINE

5078-147 in CDCl₃
NoeDiff w/irr at 7.61 ppm

Current Data Parameters
NAME 5078-147
EXPNO 3
PROCNO 2

F2 - Acquisition Parameters
Date_ 20041110
Time 7.15
INSTRUM spect
PROBHD 5 mm QNP 1H/
PULPROG zg2pr
TD 65536
SOLVENT CDCl₃
NS 504
DS 2
SWH 7621.951 Hz
FIDRES 0.116302 Hz
AQ 4.2992115 sec
RG 362
DW 65.600 usec
DE 6.00 usec
TE 300.0 K
D1 4.00000000 sec

===== CHANNEL f1
NUC1 1H
P1 7.50 usec
PL1 3.60 dB
SFO1 400.1326205 MHz

F2 - Processing parameters
SI 32768
SF 400.1300002 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

3dp

RT: 0.00 - 2.40

NL:
7.21E5
TIC MS
5078-147-
110270004
_091457

5078-147-110270004_091457 #140 RT: 1.82 AV: 1 NL: 2.78E5

T: {0,0} + c ESI sid=33.00 Full ms [133.00-972.00]

S14

Mass Chromatogram (m/z=394.50-395.50+416.50-417.50)

Analog Channel 1

Peak Information For Analog Channel 1

Peak ID	RT	Purity	BP Mass
1	1.17	0.00	n/a
2	1.66	99.63	n/a
3	2.15	0.36	n/a

Peak ID: 1 MS1 - RT: 1.17 mins; ESI+ 00

Peak ID: 2 MS1 - RT: 1.66 mins; ESI+ 00

Peak ID: 3 MS1 - RT: 2.15 mins; ESI+ 00

¹H nmr

NOE

Sampl Name:5078-152-1
Raw File:d:\Data\5078-152-110270005_091457.raw

LC-MS/ELS Report
ESI Pos. Std. 2.4 Min.Run

Target Mass:3

Mass Chromatogram (m/z=334.50-335.50+356.50-357.50)

Analog Channel 1

Peak Information For Analog Channel 1

Peak ID	RT	Purity	BP Mass
1	1.39	100.00	n/a

Peak ID: 1 MS1 - RT: 1.39 mins; ESI+ 00

¹H nmr

Table 5, entry 1

Mass Chromatogram (m/z=367.50-368.50+389.50-390.50)

Analog Channel 1

Peak Information For Analog Channel 1

Peak ID	RT	Purity	BP Mass
1	0.30	0.01	n/a
2	1.39	0.02	n/a
3	1.81	99.97	n/a

Peak ID: 1 MS1 - RT: 0.30 mins; ESI+ 00

Peak ID: 2 MS1 - RT: 1.39 mins; ESI+ 00

Peak ID: 3 MS1 - RT: 1.81 mins; ESI+ 00

S20

Mass Chromatogram (m/z=383.50-384.50+405.50-406.50)

Analog Channel 1

Peak Information For Analog Channel 1

Peak ID	RT	Purity	BP Mass
1	0.32	0.04	n/a
2	1.49	95.24	n/a
3	2.14	4.72	n/a

Peak ID: 1 MS1 - RT: 0.32 mins; ESI+ 00

Peak ID: 2 MS1 - RT: 1.49 mins; ESI+ 00

Peak ID: 3 MS1 - RT: 2.14 mins; ESI+ 00

S22

¹H nmr

Table 5, entry 2

ppm (t1)

NOE

ppm (t1)

S21

¹H nmr

Table 5, entry 3

NOE

Mass Chromatogram (m/z=367.50-368.50+389.50-390.50)

Analog Channel 1

Peak Information For Analog Channel 1

Peak ID	RT	Purity	BP Mass
1	0.35	0.03	n/a
2	0.61	0.02	n/a
3	1.44	0.02	n/a
4	1.80	98.70	n/a
5	2.14	1.23	n/a

Peak ID: 1 MS1 - RT: 0.35 mins; ESI+ 00

Peak ID: 2 MS1 - RT: 0.61 mins; ESI+ 00

Peak ID: 3 MS1 - RT: 1.44 mins; ESI+ 00

Peak ID: 4 MS1 - RT: 1.80 mins; ESI+ 00

Peak ID: 5 MS1 - RT: 2.14 mins; ESI+ 00